



(51) International Patent Classification:

A61K 31/517 (2006.01) A61P 1/16 (2006.01)
C07D 239/91 (2006.01)

(21) International Application Number:

PCT/IN2021/050621

(22) International Filing Date:

25 June 2021 (25.06.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

202011027502 29 June 2020 (29.06.2020) IN

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

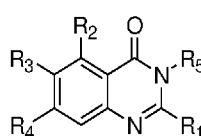
Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
- with amended claims and statement (Art. 19(1))

(54) Title: QUINAZOLINONES DERIVATIVES FOR TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE, PREPARATION AND USE THEREOF



Structure I

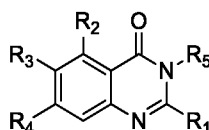
(57) Abstract: The present invention described herein relates to a compound having Structure I for treating diseases and disorders for which inhibition or modulation of the Ubiquitin Ligase COP1 enzyme produces a physiologically beneficial response, in particular for the treatment of Non-Alcoholic Fatty Liver Disease (NAFLD). These compounds having Structure I are capable of increasing the level of adipose triglyceride lipase (ATGL). Also provided is the process of preparing compounds having Structure I.



QUINAZOLINONES DERIVATIVES FOR TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE, PREPARATION AND USE THEREOF

FIELD OF THE INVENTION

- 5 The present invention relates to the preparation of new compounds having structure I in free form or in an acceptable salt form for modulation of Ubiquitin Ligase COP1 through its stabilization as a potential therapeutic target for Non-Alcoholic Fatty Liver Disease (NAFLD).



Structure I

- 10 The present invention relates to a compound having structure I, where R₁, R₂, R₃, R₄ and R₅ are as defined in the description. Some of the synthesized molecules are capable of increasing the level of adipose triglyceride lipase (ATGL) through modulation of Ubiquitin Ligase COP1 through its stabilization as a potential therapeutic target for treatment of Non-Alcoholic Fatty Liver Disease (NAFLD).

15 BACK GROUND OF THE INVENTION

- Non Alcoholic Fatty Liver Disease (NAFLD) has garnered considerable attention due to the increasing worldwide prevalence of this disease spectrum. NAFLD is an umbrella term encompassing simple steatosis progressing to steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Steatosis is mostly a reversible condition whereby fat droplets, mostly in the form of triglycerides, accumulate in the liver without pronounced hepatocyte injury. Steatohepatitis (nonalcoholic steatohepatitis, NASH) denotes the stage wherein hepatocytes are significantly injured and is histologically characterised by the presence of ballooned hepatocytes, Mallory-Denk bodies, glycogenated nuclei and other distinguishing features. NASH may, in some cases, progress to fibrosis and cirrhosis which are more critical stages whereby extracellular matrix proteins, notably collagen fibres, accumulate in the liver encircling hepatocytes and forming scar tissue resulting in irreversible damage to the normal physiology of the liver. The prevalence of NAFLD is reported to be 20%-30% in Western countries and 5%-18% in Asia. While the incidence of NAFLD is rising at an alarming rate, with it being considered now as the second most common reason for liver
- 25

transplantation, no robust therapies are available to reverse the advanced stages of this condition.

NAFLD is a complex multifactorial disorder involving the interplay of several molecules and their associated signalling pathways. A multitude of risk factors have been attributed to the development of NAFLD with type 2 diabetes and metabolic syndrome considered as the most important ones. As is evident, the most prominent feature of NAFLD is the deposition of excessive triacylglycerols (TAG) in hepatocytes and, therefore, deregulation of enzymes responsible for controlling intracellular lipid turnover and homeostasis may play an important role in NAFLD (Ong et al. *Hepatology*. 2011, 53, 116–126). A pivotal enzyme associated with the intracellular degradation of TAG is Adipose triglyceride lipase (ATGL) also known as patatin-like phospholipase domain-containing protein 2 (PNPLA2). It catalyses the initial and rate limiting step in the TAG lipolysis cascade. Indeed, studies have shown that ATGL levels are decreased in NAFLD patients and liver injury is aggravated in mice with liver specific ATGL depletion (Jha et al. *Hepatology*, 2014, 59, 858-869).

Ubiquitin-proteasome system is a pivotal pathway for regulation of protein turnover in cells. Ubiquitination of a protein requires the stepwise involvement of 3 enzymes: E1-ubiquitin-activating enzymes, E2-ubiquitin-conjugating enzymes, and E3 ubiquitin ligases. COP1 is one such evolutionary conserved ubiquitin ligase which plays a central role in a myriad of important cellular pathways like insulin secretion from pancreatic β cells, regulating the stability of p53, etc.

Our previous study has identified a novel interaction between COP1 and the VP motif of ATGL. This interaction targets ATGL for proteasomal degradation by K-48 linked polyubiquitination, predominantly at the lysine 100 residue. In NAFLD, increased degradation of ATGL by COP1 would cause more TAG to accumulate in the liver manifesting a more severe form of the disease (Ghosh et al. *Diabetes*, 2016, 65, 3561–3572). Therefore, curtailing the ubiquitin mediated degradation of ATGL by inhibiting COP1 can be a potential area for therapeutics. In the same study, it was validated that steatosis in mice liver could be ameliorated with adenovirus mediated depletion of COP1 in mice. In this context, if small molecules with the potential to target the interacting site of COP1 and ATGL can be developed to target COP1 and hinder its capability to ubiquitinate ATGL, ATGL would be able to hydrolyse the accumulated TAG in the liver and abort the progression of NAFLD. Therefore, if this increased lipolysis in liver in the context of NAFLD can be achieved, then a robust therapy is available at hand to combat the progression of steatosis to steatohepatitis

ultimately restricting NAFLD at its very onset (Niyogi et al., Biochemical and Biophysical Research Communications, 2019, 512, 806-811).

At present, treatment strategies are mainly directed towards various targets that mediate hepatocyte dysregulation, inflammation, apoptosis and oxidative stress. Extrahepatic targets whose role are implicated in NASH like microbiome, gut liver axis, organs like muscle and adipose tissue are also being considered for designing therapeutic targets. Certain drugs are in clinical trials at various phases. Notably, elafibranor (PPAR- α/δ ligand), selonsertib (ASK-1 inhibitor), obeticholic acid (FXR agonist), cenicriviroc (CCR 2/5 inhibitor) are in Phase 3 trial. All these drugs aim at a much advanced stage of fibrosis in NASH. Few drugs like Aramchol (SCD-1 inhibitor), IMM-124E (Anti-LPS), MGL-3196 (THR- β agonist), NGM282 (FGF19 analog), and PF-05221304 (ACC inhibitor), which are in Phase 2 clinical trials aim at an improvement in liver fat and therefore, target mainly the steatotic stage. Targeting the fibrotic stage in NASH may not always prove to be beneficial since mostly the stage is irreversible and much damage has already been inflicted in liver with deposition of collagen fibres and beginning of scar tissue formation. Hence, if the progression of NASH can be curbed at the reversible stage of steatosis by curtailing the deposition of fat, a much effective therapy can be established.

OBJECTIVES OF THE INVENTION

The main objective of the present invention is to provide a compound having structure I.

Another objective of the present invention is to provide a process for the preparation of compound having structure I.

Still another objective of the present invention is to evaluate the efficacy of active compounds using screening methods including fluorescence microscopy and measurement of levels of ATGL protein.

Yet another objective of the present invention is to provide a method for testing the specificity of the compounds for targeting the interaction of ATGL-COP1.

Still another objective of the present invention is to increase the level of ATGL in hepatocytes that can decrease the level of cellular lipids.

Yet another objective of the present invention is to decrease the ubiquitination and proteasomal degradation of ATGL.

Still another objective of the present invention is to identify the specific E1 and E2 enzyme in ubiquitination process.

Yet another objective of the present invention is to decrease the level of triglycerides in hepatocytes.

- 5 Still another objective of the present invention is to test the efficacy of the compounds *in vivo* in preclinical models.

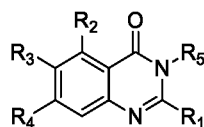
Yet another objective of the present invention is to provide a composition comprising compounds of structure I for use in a number of clinical applications, including pharmaceutical agents and methods for treating conditions like Non-Alcoholic Fatty Liver

- 10 Disease (NAFLD).

Still another objective of the present invention is to provide a composition and methods of using the compounds having general structure I without considerable cytotoxicity in hepatocytes.

15 SUMMARY OF THE INVENTION

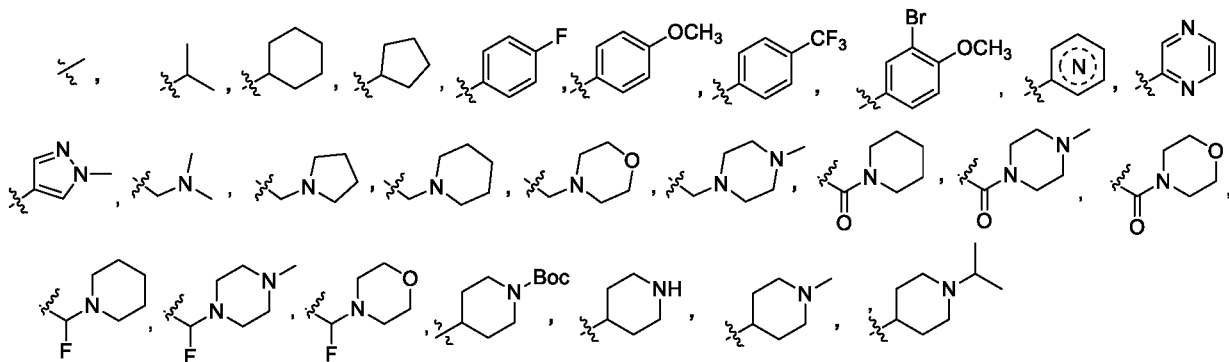
An embodiment of present invention provides compound having structure I or a pharmaceutically acceptable salt thereof:



Structure I

wherein

- 20 R₁ is independently selected from the group consisting of:



- 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (18),
1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(morpholine-4-carbonyl)phenyl)urea (19),
5 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (20),
1-(3-(benzo[d]oxazol-2-yl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (21),
N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide
10 (22),
N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)-N-methylacetamide (23),
N-benzyl-N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (24),
15 N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)acetamide (25),
N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)-N-methylacetamide (26),
1-(5-acetyl-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
20 (32),
1-(3-acetyl-5-chloro-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (33),
1-(3-acetyl-2-hydroxy-5-methylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (34),
25 1-(4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (35),
1-(3-chloro-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (36),
1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea (37),
30 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethyl)phenyl)urea (38),
1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-(trifluoromethyl)phenyl)urea (39),

- 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-methoxyphenyl)urea (40),
1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-methoxyphenyl)urea (41),
ethyl 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (42),
3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoic acid(42a),
5 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-phenyl-3,4-dihydroquinazolin-6-yl)urea
(45),
1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-
yl)urea (47),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-2-yl)-3,4-dihydroquinazolin-6-
10 yl)urea (49),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-3-yl)-3,4-dihydroquinazolin-6-
yl)urea (51),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-4-yl)-3,4-dihydroquinazolin-6-
yl)urea (53),
15 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(6-methoxypyridin-3-yl)-4-oxo-3,4-
dihydroquinazolin-6-yl)urea (55),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(2-methoxypyridin-3-yl)-4-oxo-3,4-
dihydroquinazolin-6-yl)urea (57),
tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-
20 5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (59),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(1,2,3,6-tetrahydropyridin-4-yl)-3,4-
dihydroquinazolin-6-yl)urea (60),
tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-
5-yl)piperidine-1-carboxylate (61),
25 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(piperidin-4-yl)-3,4-dihydroquinazolin-6-
yl)urea (62),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(4-methoxyphenyl)-4-oxo-3,4-
dihydroquinazolin-6-yl)urea (64),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(4-(trifluoromethyl)phenyl)-3,4-
30 dihydroquinazolin-6-yl)urea (66),
1-(3-acetylphenyl)-3-(5-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-
yl)urea (68),

- 1-(3-acetylphenyl)-3-(5-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (70),
1-(3-acetylphenyl)-3-(5-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (72),
5 1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (73),
ethyl 2-(6-(3-(3-chloro-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (83),
ethyl 2-(4-oxo-6-(3-(4-(trifluoromethoxy)phenyl)ureido)quinazolin-3(4H)-yl)acetate (84),
ethyl 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (85),
10 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetic acid(85a),
1-(3-acetylphenyl)-3-(3-(3-methoxypropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (89),
1-(3-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (93),
1-(4-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (94),
1-(3-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (98),
15 1-(4-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (99),
1-(3-acetylphenyl)-3-(3-(3-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (103),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (107),
1-(3-acetylphenyl)-3-(2-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
20 (111),
1-(3-acetylphenyl)-3-(2-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (115),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (119),
25 1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (123),
1-(3-acetylphenyl)-3-(2-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (127),
1-(3-acetylphenyl)-3-(3-(2-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (131),
30 1-(3-acetylphenyl)-3-(3-(2-morpholinoethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (135),
1-(3-acetylphenyl)-3-(3-(3-morpholinopropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (139),
1-(3-acetylphenyl)-3-(3-(2-(dimethylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (143),

- 1-(3-acetylphenyl)-3-(4-oxo-3-(2-(piperidin-1-yl)ethyl)-3,4-dihydroquinazolin-6-yl)urea (147),
- 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (151),
- 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (155),
- 5 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (159),
- 1-(3-acetylphenyl)-3-(3-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (163),
- 1-(3-acetylphenyl)-3-(3-(2-(methylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (167),
- 10 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (171),
- 1-(3-acetylphenyl)-3-(3-butyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (175),
- 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (179),
- 1-(3-acetylphenyl)-3-(3-(2-isopropoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (183),
- 15 1-(3-acetylphenyl)-3-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (187),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (192),
- 1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (193),
- 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-methoxyphenyl)urea (194),
- 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-methoxyphenyl)urea (195),
- 20 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (196),
- 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (197),
- 1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (198),
- 25 N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)ureido)phenyl)-N-methylacetamide (199),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea (203),
- 30 1-(3-acetylphenyl)-3-(2-(3-bromo-4-methoxyphenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (207),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (211),

- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (215),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (219),
- 5 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrazin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (223),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methyl-1H-pyrazol-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (227),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrrolidin-1-ylmethyl)-3,4-
- 10 dihydroquinazolin-6-yl)urea (232),
- 1-(3-acetylphenyl)-3-(2-((dimethylamino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (235),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (238),
- 15 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholinomethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (241),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (244),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-ethylacetamide (247),
- 20 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N,N-diethylacetamide (250),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (253),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-methoxyphenyl)acetamide (256),
- 25 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-bromophenyl)acetamide (259),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide (262),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-
- 30 (trifluoromethyl)phenyl)acetamide (265),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-methoxyphenyl)acetamide (268),

- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-fluorophenyl)acetamide (271),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide (274),
- 5 N-(2-(1H-imidazol-1-yl)ethyl)-2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetamide (277),
- 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (281),
- 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (285),
- 10 1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (289),
- 1-(3-acetylphenyl)-3-(2-cyclohexyl-5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (292),
- 15 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (295),
- tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (299),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (300),
- 20 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (304),
- 1-(3-acetylphenyl)-3-(2-(1-isopropylpiperidin-4-yl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (307),
- 25 1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (308),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea (309),
- 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-hydroxyurea (310),
- 30 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea (311),

- 1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (312),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-1-methylurea (313),
5 2-(6-(3-(3-acetylphenyl)-3-hydroxyureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (314),
2-(6-(3-(3-acetylphenyl)-3-methylureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (315),
1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-
10 trifluoroacetyl)phenyl)urea (316),
1-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (317),
1-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (318),
15 1-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (319),
N-(2-fluorophenyl)-2-(4-oxo-6-(3-(3-(2,2,2-trifluoroacetyl)phenyl)ureido)quinazolin-3(4H)-yl)acetamide (320),
1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
20 (321),
1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (322),
1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (323),
25 1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (324),
2-(6-(3-(3-acetyl-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (325),
1-(3-acetylphenyl)-3-(2-(fluoro(piperidin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-
30 dihydroquinazolin-6-yl)urea (330),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidine-1-carbonyl)-3,4-dihydroquinazolin-6-yl)urea (330a),

1-(3-acetylphenyl)-3-(2-(fluoro(4-methylpiperazin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333 a),

5 1-(3-acetylphenyl)-3-(2-(fluoro(morpholino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (336),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholine-4-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (336 a),

1-(3-acetylphenyl)-3-(3-morpholino-4-oxo-3,4-dihydroquinazolin-6-yl)urea (340),

10 (Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (341),

(Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (342),

15 (Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (343), and

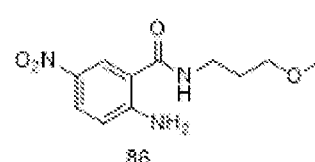
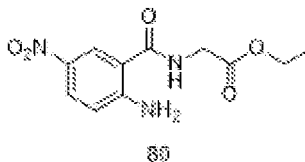
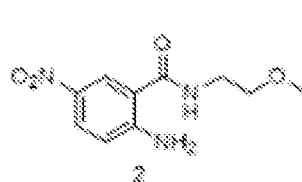
1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (345),

20 Yet another embodiment of the present invention provides a process for the preparation of compounds having structure I, wherein the steps comprising:

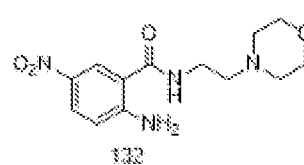
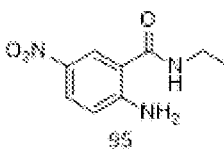
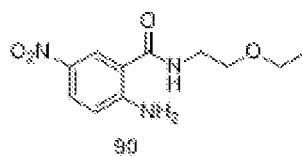
- (i) reacting 2-amino-5-nitrobenzoic acid (**compound 1**) with an aliphatic or an aromatic amine selected from the group consisting of 2-methoxyethylamine, glycine ethylester hydrochloride, 3-methoxypropylamine, 2-ethoxyethylamine, ethylamine 2M in THF, 4-(2-aminoethyl)morpholine, 3-(4-morpholinyl)propylamine, N,N-dimethylethylenediamine, 1-(2-aminoethyl)piperidine, 4-amino-1-methylpiperidine, N-methylethylenediamine, 2-amino-1-methoxybutane, 1-butylamine, 1-methoxy-2-propylamine, 2-aminoethyl isopropyl ether, cyclohexylamine, 4-aminomorpholine, m-anisidine, o-anisidine, 4-aminopyridine, 3-aminopyridine, and 2-aminopyridine in presence of HATU/DMF followed by TEA as a base at room temperature for 1-3 hours to obtain an amide compound selected from the group consisting of **2, 80, 86, 90, 95**,
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132, 136, 140, 144, 160, 164, 168, 172, 176, 180, 184, 337, 100, 128, 148, 152, and 156;

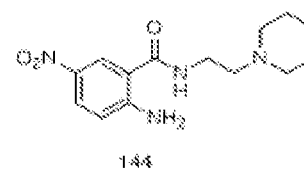
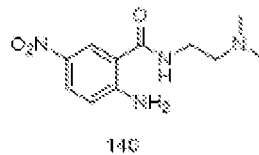
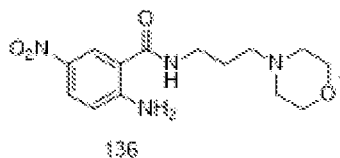
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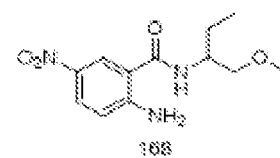
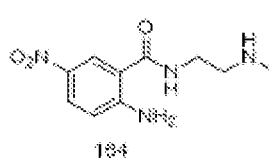
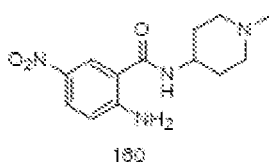
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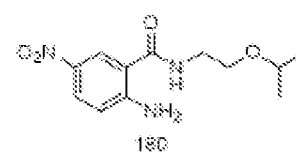
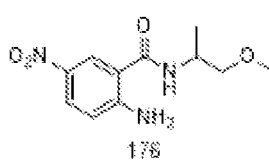
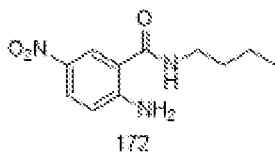
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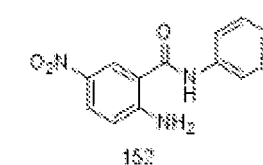
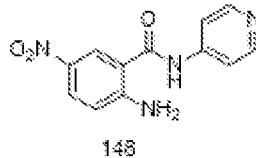
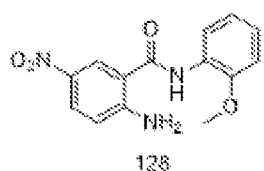
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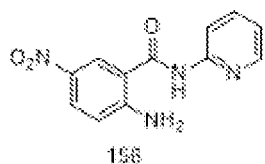


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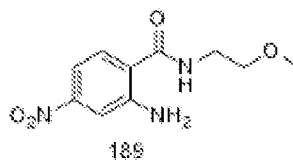
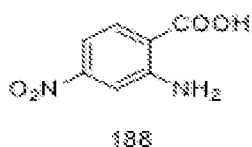
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- (ii) separately, reacting 2-amino-4-nitrobenzoic acid (**compound 188**) with 2-methoxyethylamine in presence of HATU/ DMF followed by TEA as a base at room temperature for 1 hour to obtain a compound **189**;

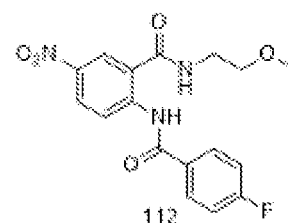
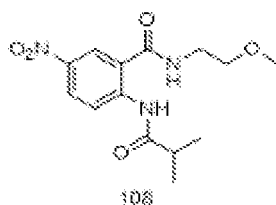
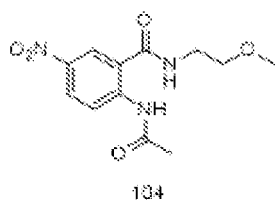
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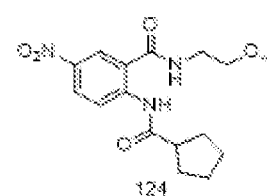
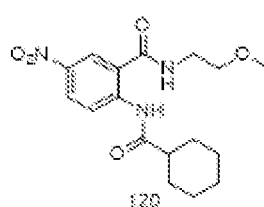
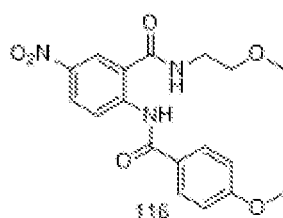
- (iii) adding an acid chloride selected from the group consisting of acetyl chloride, isopropyl chloride, 4-fluorobenzoyl chloride, 4-methoxybenzoyl chloride, cyclohexanecarbonyl chloride, cyclopentanecarbonyl chloride, 4-(trifluoromethyl)benzoyl chloride, 3-Bromo-4-methoxybenzoyl chloride, Picolinoyl chloride, Nicotinoyl chloride, Isonicotinoyl chloride, Pyrazinecarbonyl chloride, 1-methyl-1H-pyrazole-4-carbonyl chloride, and 2-chloroacetyl chloride to compound **2** obtained in step (i) in DCM at a temperature range from 0 °C to room temperature for 1-8 hours to obtain a compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, and 228**;

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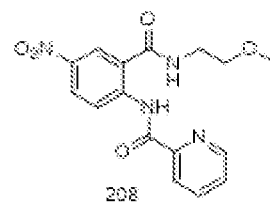
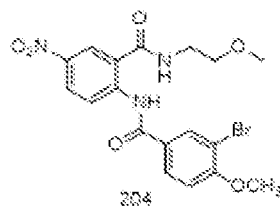
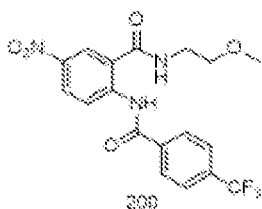


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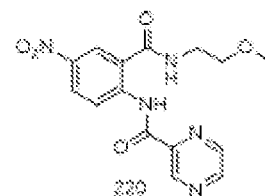
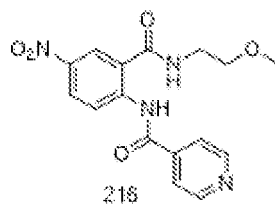
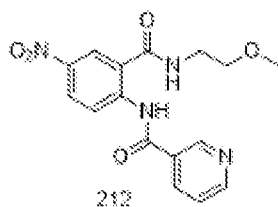


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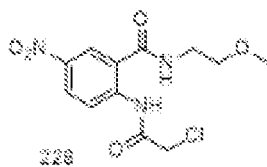
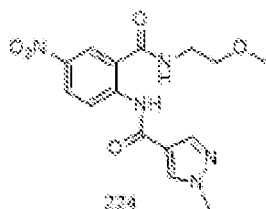
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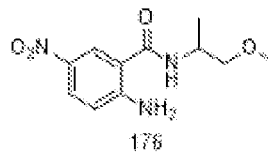
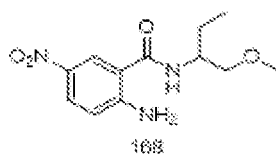


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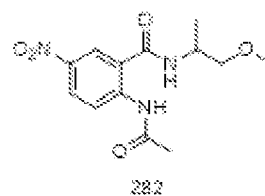
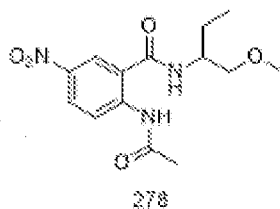


- (iv) acetylating a compound selected from the group consisting of **168**, and **176** obtained in step (i) using acetyl chloride and triethylamine (TEA) as a base in DCM at a temperature range of 0 °C to room temperature for 8 hours to obtain a compound selected from the group consisting of **278** and **282**;

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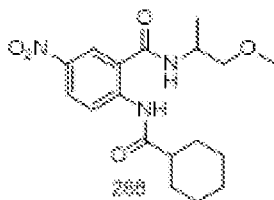


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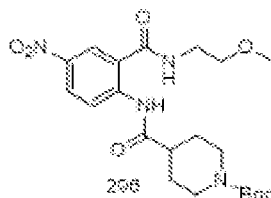
- (v) alternately, adding cyclohexanecarbonyl chloride to compound **176** obtained in step (i) to obtain a compound **286**;

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- (vi) alternately, adding tert-butyl 4-(chlorocarbonyl)piperidine-1-carboxylate to compound **2** obtained in step (i) to obtain a compound **296**;

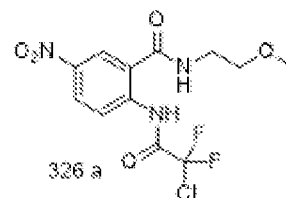
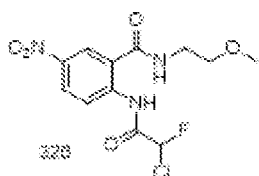
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- (vii) alternately, treating compound **2** obtained in step (i) with 2-chloro-2-fluoroacetic acid or 2-chloro-2-difluoroacetic acid along with POCl₃ in pyridine solvent to obtain a compound selected from the group consisting of **326** and **326a**;

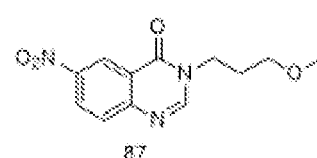
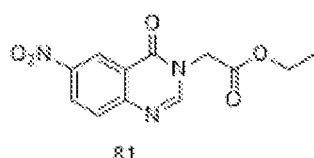
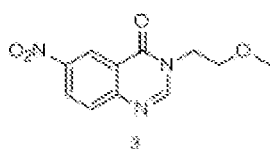
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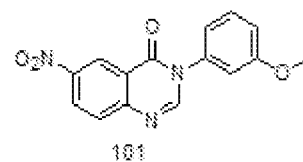
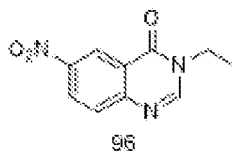
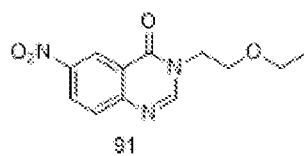


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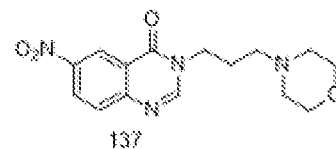
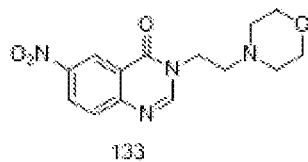
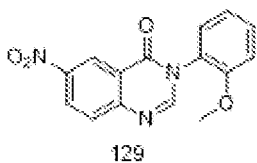
- (viii) cyclizing the compound selected from the group consisting of **2**, **80**, **86**, **90**, **95**, **100**, **128**, **132**, **136**, **140**, **144**, **148**, **152**, **156**, **160**, **164**, **168**, **172**, **176**, **180**, **184**, **189**, and **337** obtained in step (i) and (ii) using a cyclizing agent selected from trimethylorthoformate or triethylorthoformate at 100 °C for 12-16 hours to obtain a compound selected from the group consisting of **3**, **81**, **87**, **91**, **96**, **101**, **129**, **133**, **137**, **141**, **145**, **149**, **153**, **157**, **161**, **165**, **169**, **173**, **177**, **181**, **185**, **190** and **338**;

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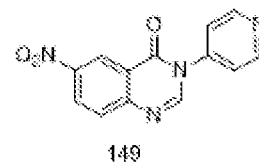
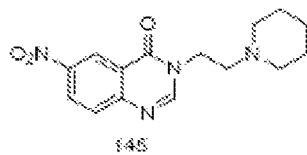
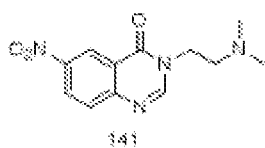




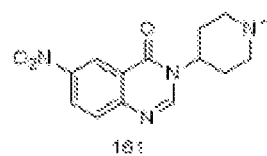
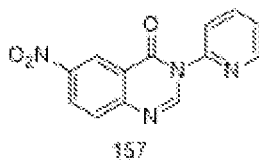
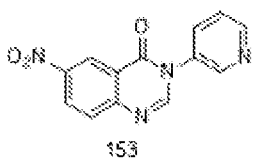
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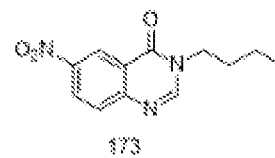
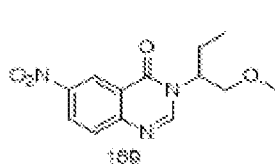
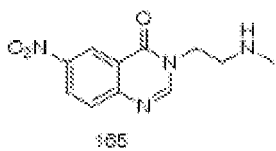
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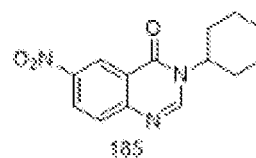
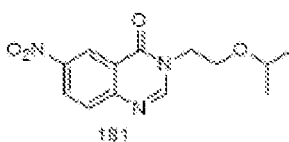
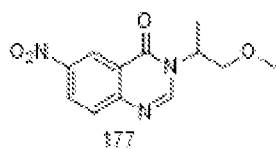
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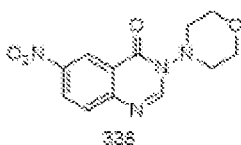
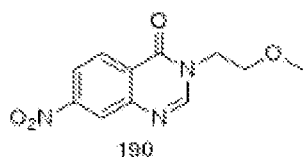
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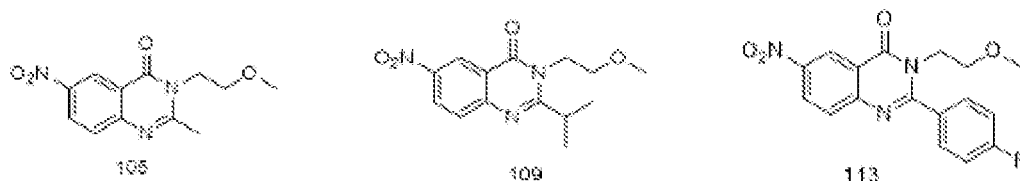
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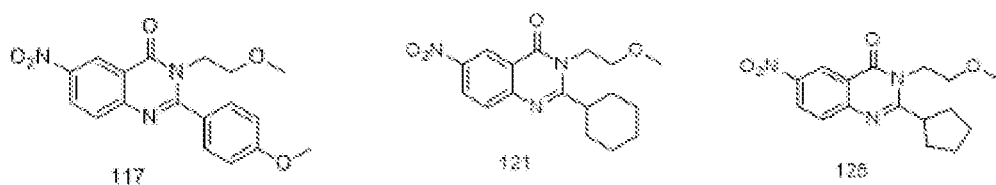
- (ix) cyclizing the compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, 228, 278, 282, 286, 296, 326,** and

326a obtained in step (iii), (iv), (v), (vi) and (vii) using a cyclizing agent $ZnCl_2$ and hexamethyldisilazane (HMDS) in DMF at 100 °C for 12 -16 hours to obtain a compound selected from the group consisting of **105**, **109**, **113**, **117**, **121**, **125**, **201**, **205**, **209**, **213**, **217**, **221**, **225**, **229**, **279**, **283**, **287**, **297**, **327** and **327a**;

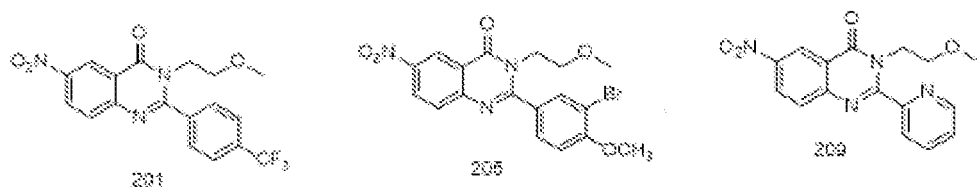
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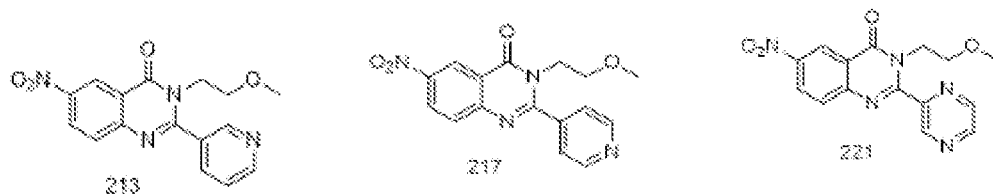
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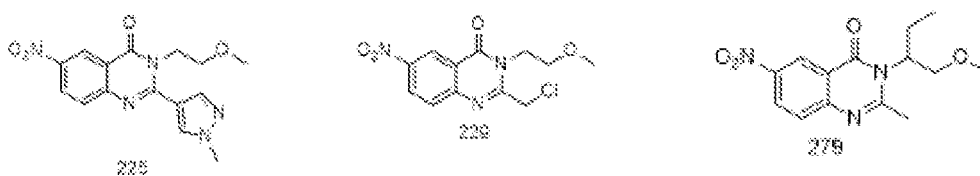
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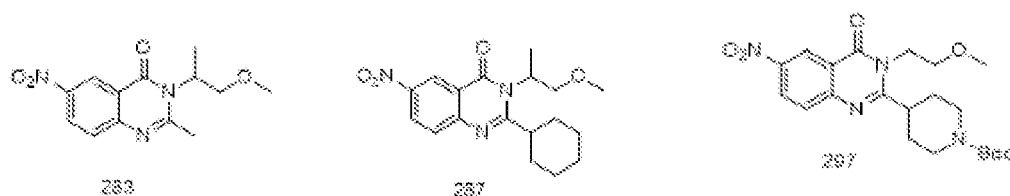
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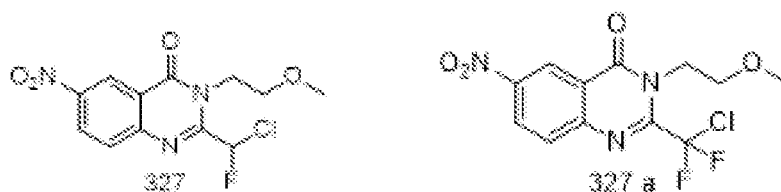


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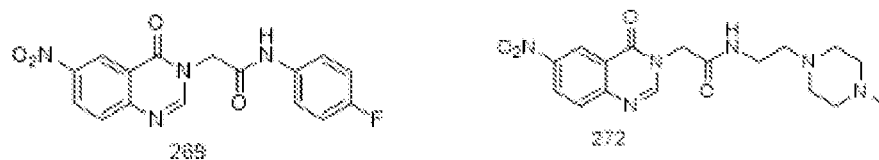
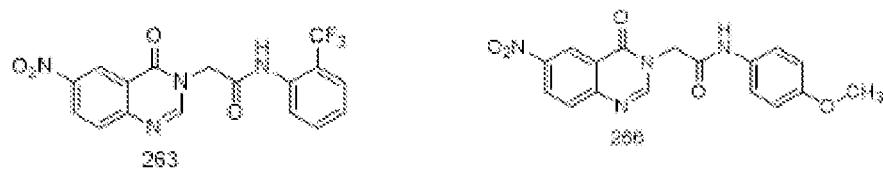
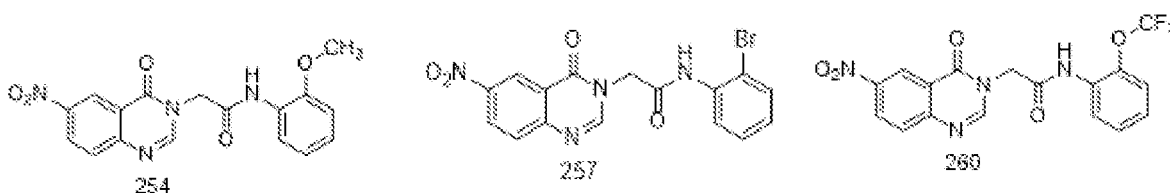
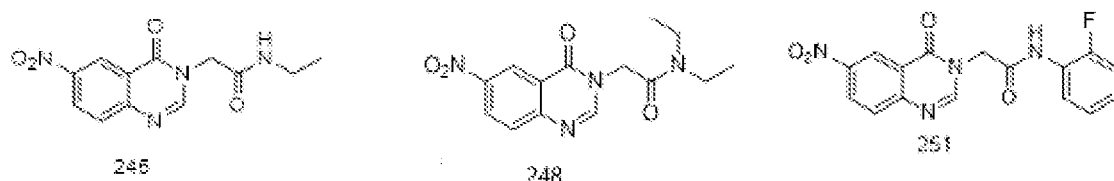


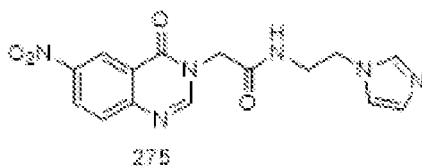
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- (x) reacting the compound **81** obtained in step (viii) with an amine selected from the group consisting of ethyl amine, diethylamine, 2-fluoroaniline, *o*-anisidine, 2-bromoaniline, 2-(trifluoromethoxy)aniline, 2-(trifluoromethyl)aniline, *p*-anisidine, 4-fluoroaniline, 1-(2-aminoethyl)-4-methylpiperazine, and 1*H*-Imidazole-1-ethanamine in presence of anhydrous AlCl₃ in toluene at a temperature range from room temperature to 110 °C to obtain a compound selected from the group consisting of **245**, **248**, **251**, **254**, **257**, **260**, **263**, **266**, **269**, **272** and **275**;
- 10
- 15

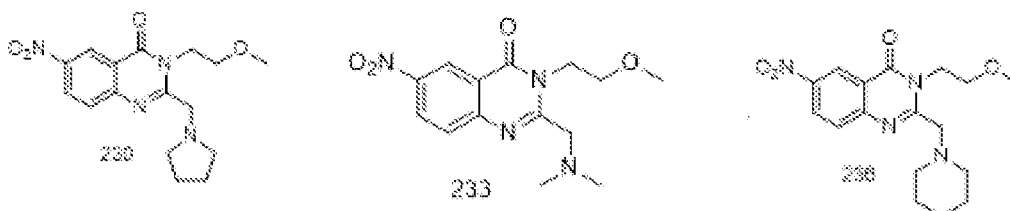




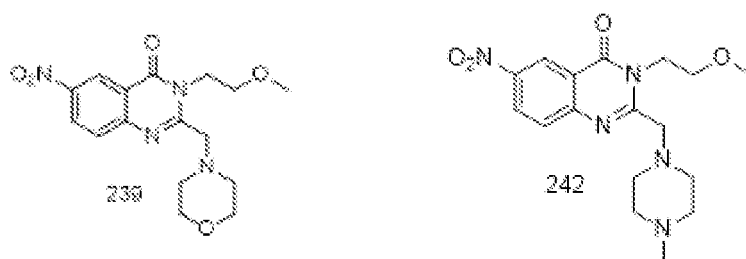
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- (xi) reacting the compound **229** obtained in step (ix) with an amine selected from the group consisting of pyrrolidine, dimethylamine, piperidine, morpholine, and 1-methylpiperazine in toluene at 100 °C for 2 hours to obtain a compound selected from the group consisting of **230**, **233**, **236**, **239**, and **242**;

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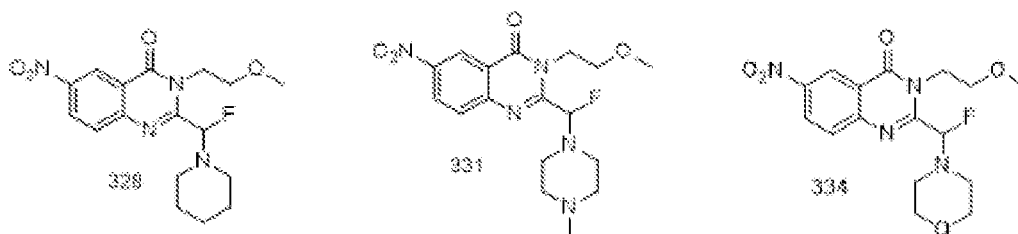
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- (xii) reacting the compound **327** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of toluene to obtain a compound selected from the group consisting of **328**, **331**, and **334**;

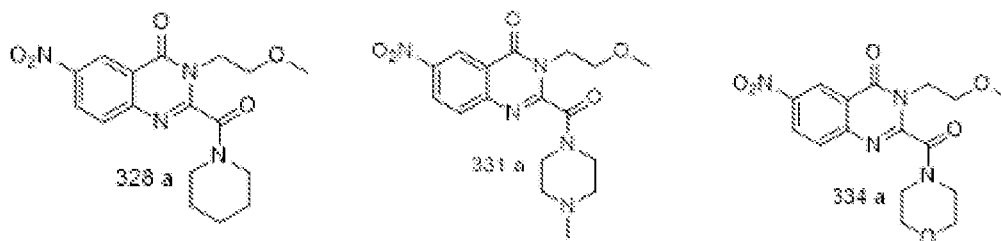
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- (xiii) reacting the compound **327a** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of a solvent selected from the group consisting of toluene, DMF, and THF in absence or presence of a base selected from K_2CO_3 , or N,N-diethylaniline to obtain a compound selected from the group consisting of **328a**, **331a**, and **334a**;

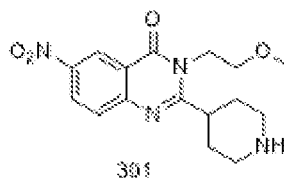
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- (xiv) separately reacting the compound **297** obtained in step (ix) with trifluoroacetic acid (TFA) in DCM at a temperature range of 0 °C to room temperature for 2 hours to obtain a compound **301**;

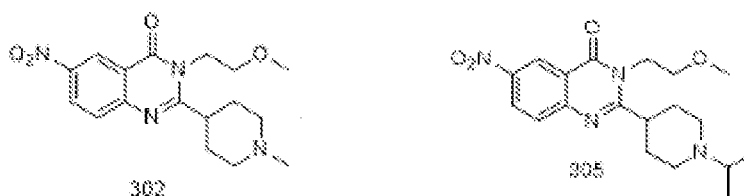
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- (xv) reacting the compound **301** obtained in step (xiv) with sodium hydride (NaH) in DMF at a temperature range of 0 °C to room temperature for 3 hours with methyl iodide and 2-chloropropane, respectively to obtain a compound selected from the group consisting of **302** and **305**;

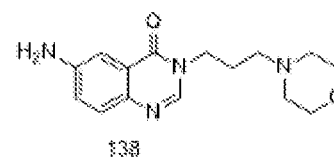
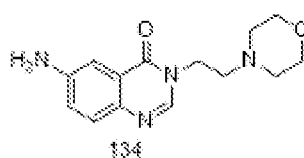
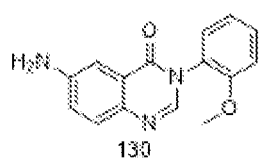
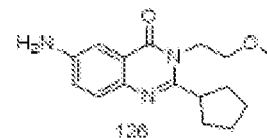
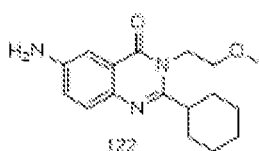
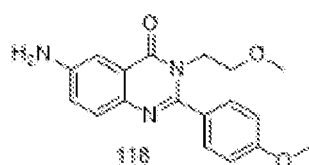
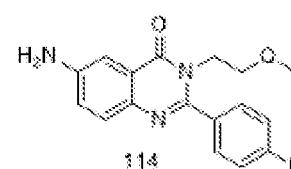
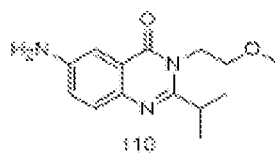
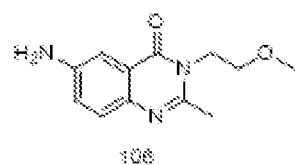
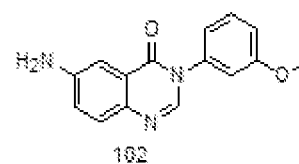
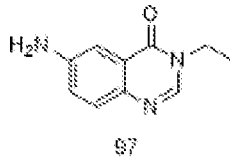
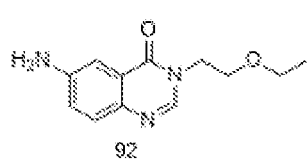
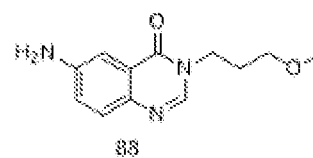
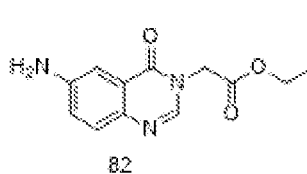
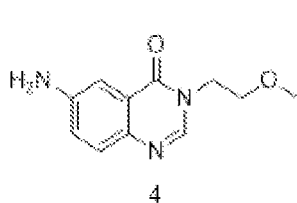
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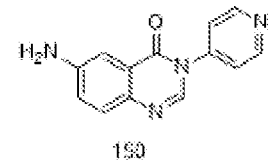
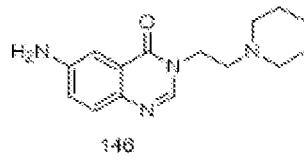
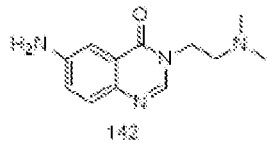


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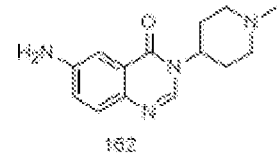
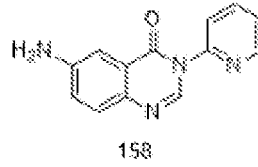
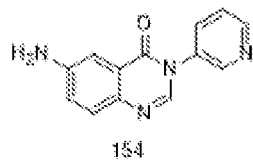
- (xvi) reducing the compound selected from the group consisting of **3**, **81**, **87**, **91**, **96**, **101**, **105**, **109**, **113**, **117**, **121**, **125**, **129**, **133**, **137**, **141**, **145**, **149**, **153**, **157**, **161**,

165, 169, 173, 177, 181, 185, 190, 201, 209, 213, 217, 221, 225, 230, 233, 236, 239, 242, 245, 248, 251, 254, 260, 263, 266, 269, 272, 275, 279, 283, 287, 297, 302, 305, 328, 328a, 331, 331a, 334, 334a and 338 obtained in steps (viii), (ix), (x), (xi), (xii), (xiii) and (xv) using Palladium-Charcoal (5% or 10 % wet) at room temperature for 3-5 hours in presence of H₂ to obtain an amine compound selected from the group consisting of 4, 82, 88, 92, 97, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 191, 202, 210, 214, 218, 222, 226, 231, 234, 237, 240, 243, 246, 249, 252, 255, 261, 264, 267, 270, 273, 276, 280, 284, 288, 298, 303, 306, 329, 329a, 332, 332a, 335, 335a, and 339;

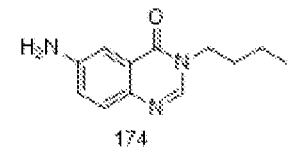
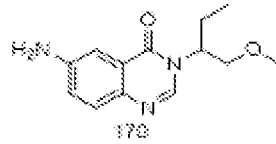
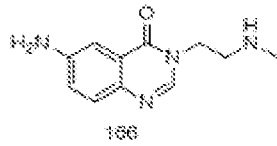




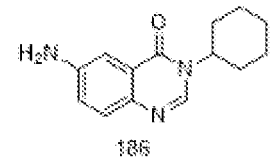
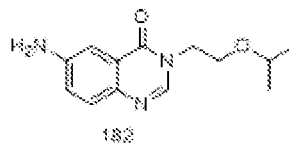
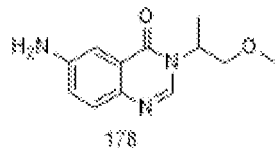
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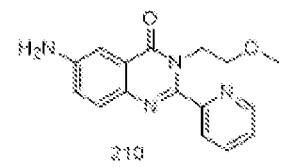
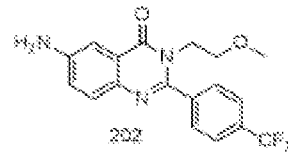
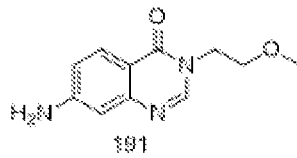
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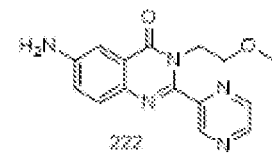
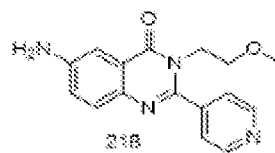
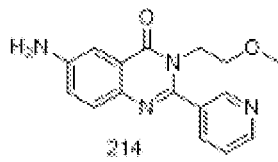
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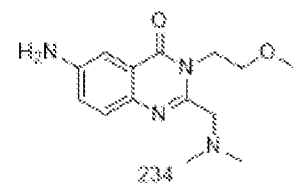
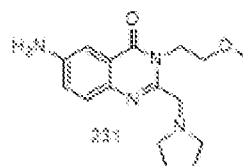
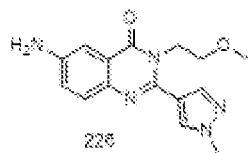
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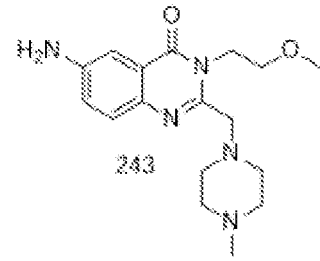
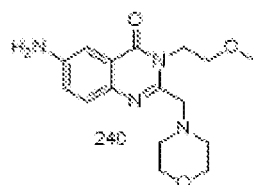
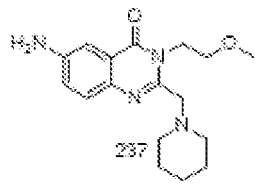
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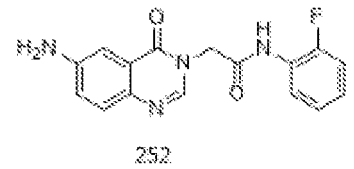
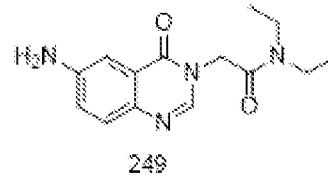
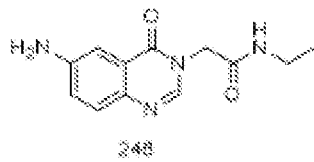
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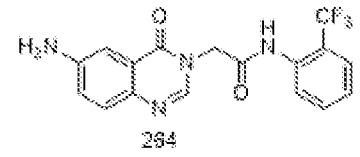
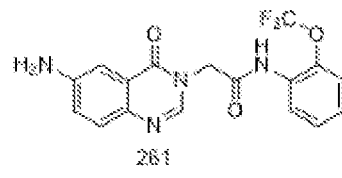
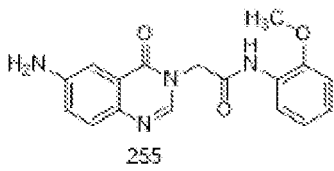
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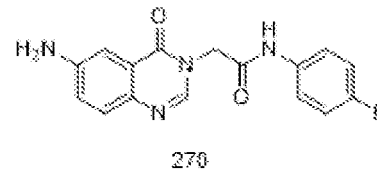
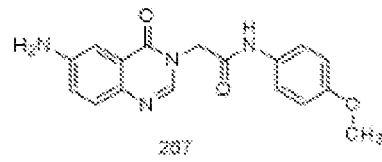
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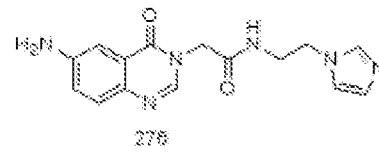
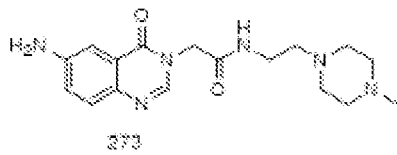
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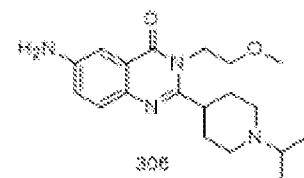
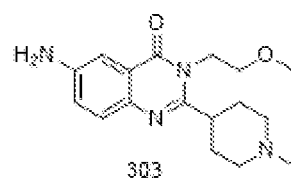
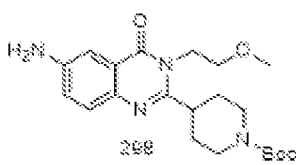
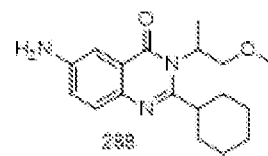
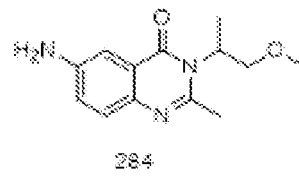
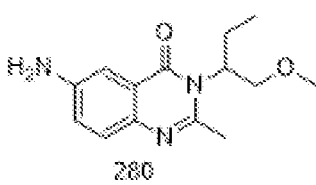
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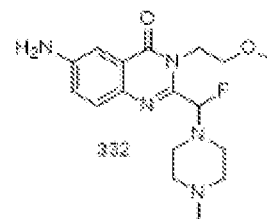
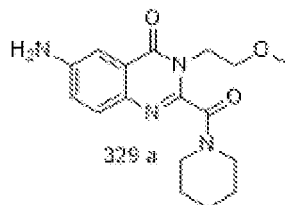
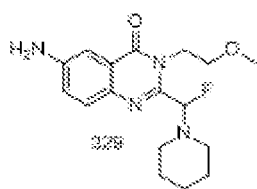
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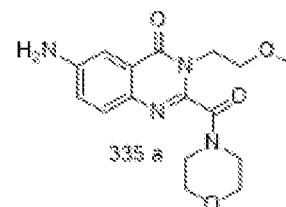
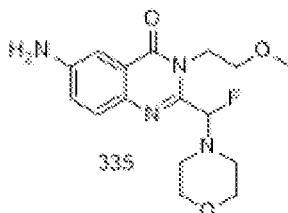
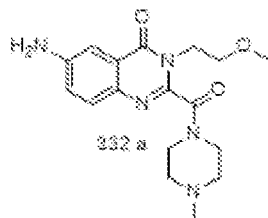
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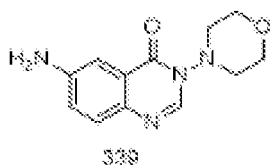
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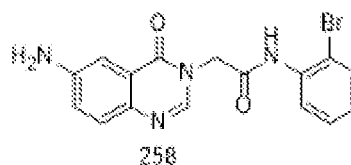
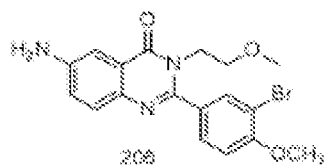


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(xvii) reducing the compound selected from **205** or, **257** obtained in step (ix) and (x) using $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ to obtain the compound selected from **206** or **258**;

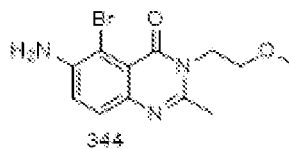
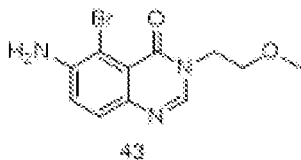
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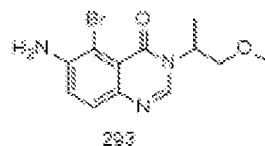
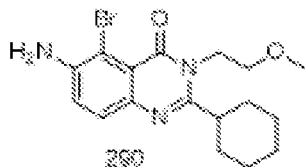
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(xviii) brominating the compound selected from the group consisting of **4**, **106**, **122**, and **178** obtained in step (xvi) diluted in dichloromethane or chloroform solution by carrying out reaction in acetic acid medium followed by drop wise addition of liquid bromine on the compound at room temperature for 3-4 hours to obtain a compound selected from the group consisting of **43**, **344**, **290**, and **293**;



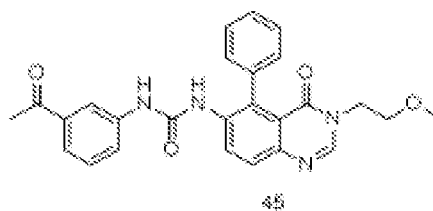
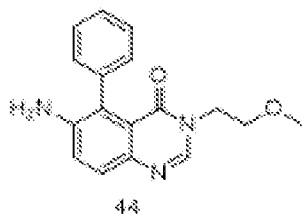
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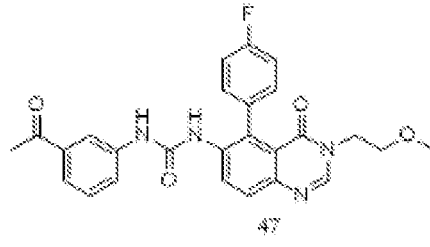
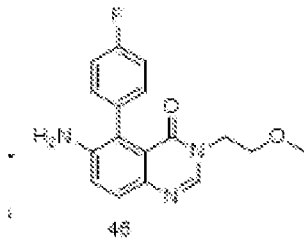
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- (xix) carrying out Suzuki reaction on a compound selected from the group consisting of **43**, **290**, and **293** obtained in step (xviii) by Pd₂(dba)₃ or Pd(PPh₃)₄ in presence of Cs₂CO₃ or 2M Na₂CO₃ solution in dioxane and X-Phos as a ligand at 100 °C over a period of 10-12 hours along with a boronic acid selected from the group consisting of benzenboronic acid, 4-fluorobenzenboronic acid, pyridine-2-boronic acid, pyridine-3-boronic acid, pyridine-4-boronic acid, 6-methoxypyridine-3-boronic acid, 2-methoxypyridine-3-boronic acid, (1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)boronic acid, 4-methoxybenzenboronic acid, 4-trifluoromethylbenzenboronic acid, cyclohexylboronic acid, cyclopentyl boronic acid, and isopropylboronic acid to obtain a compound selected from the group consisting of **44**, **46**, **48**, **50**, **52**, **54**, **56**, **58**, **63**, **65**, **67**, **69**, **71**, **291**, and **294** which is treated with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 5-8 hours to obtain the compound having structure I selected from the group consisting of **45**, **47**, **49**, **51**, **53**, **55**, **57**, **59**, **64**, **66**, **68**, **70**, **72**, **292**, and **295**;

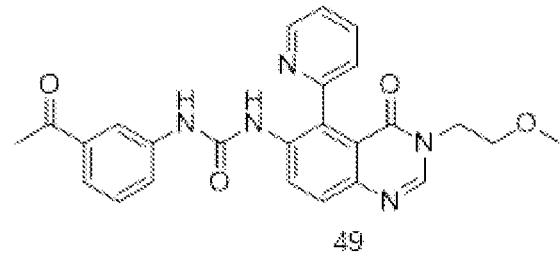
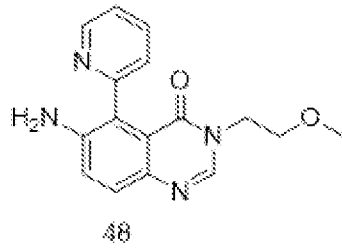
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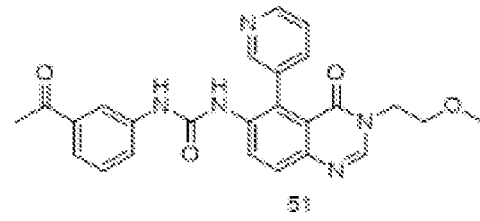
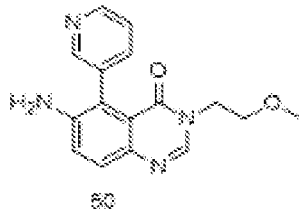
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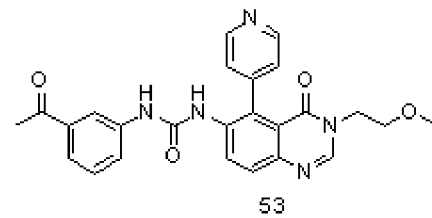
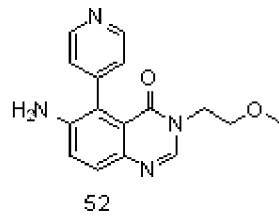
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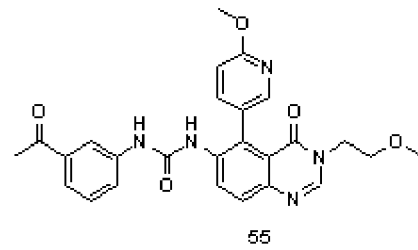
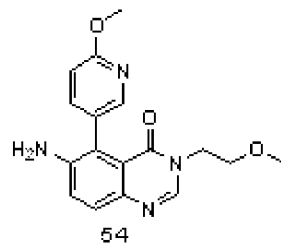
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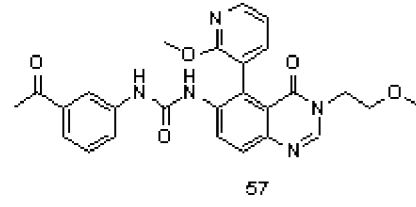
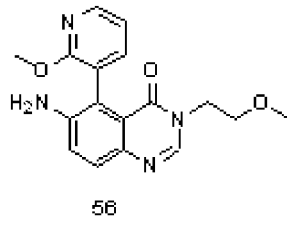


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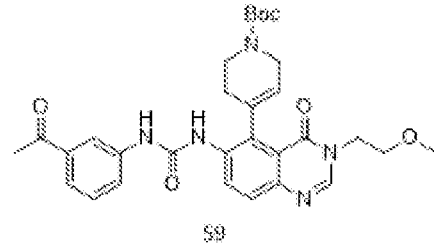
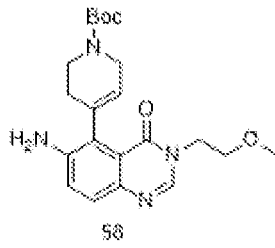


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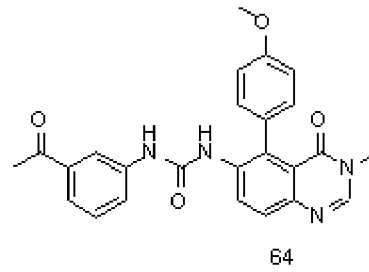
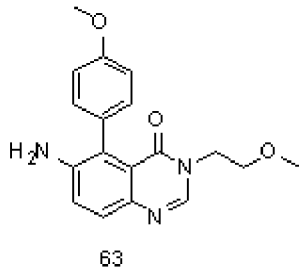
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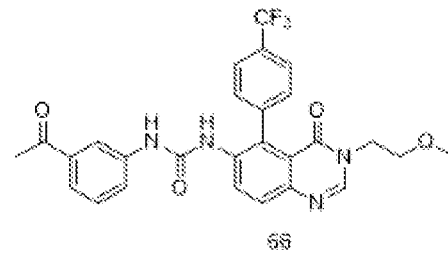
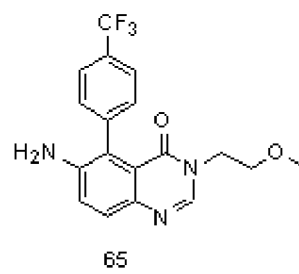
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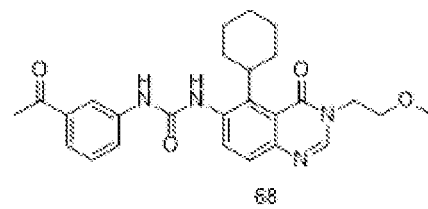
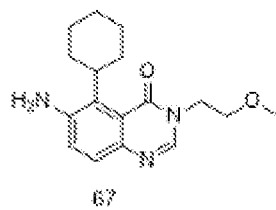


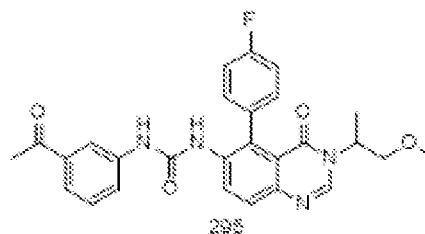
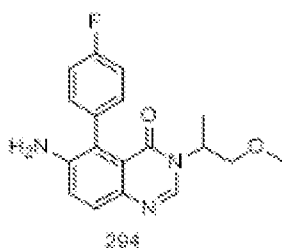
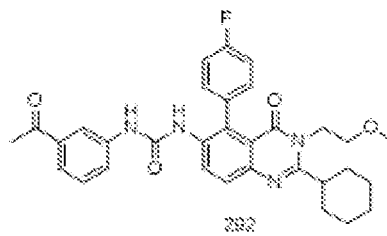
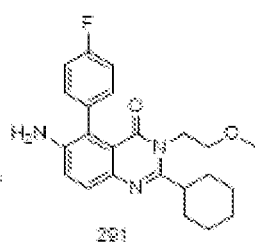
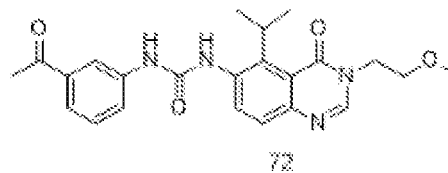
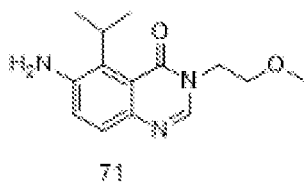
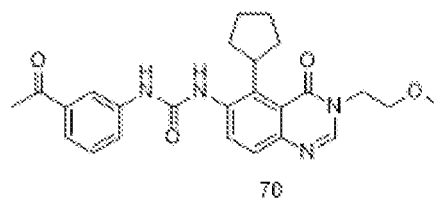
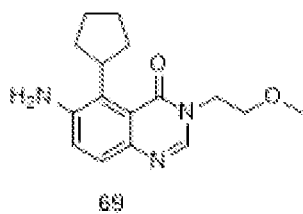
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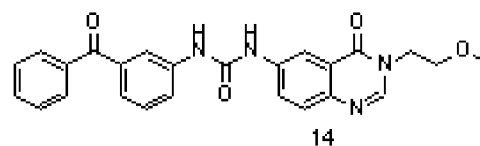
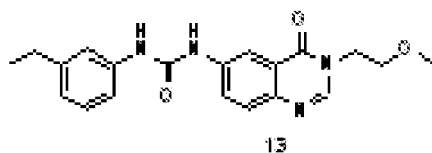
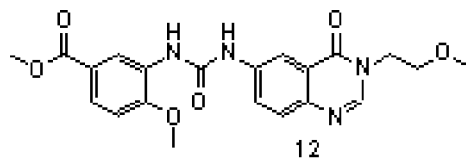
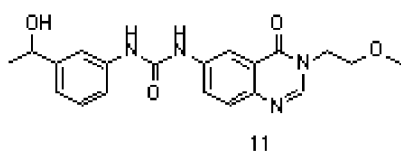
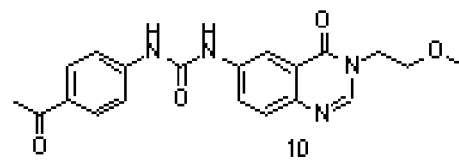
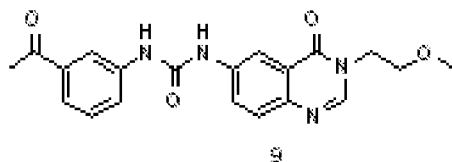
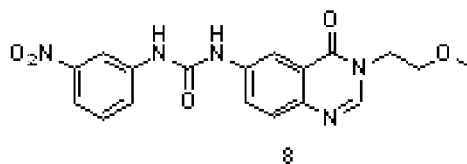
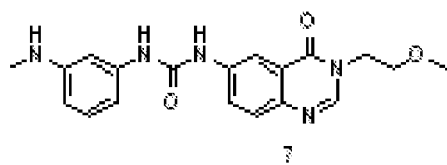
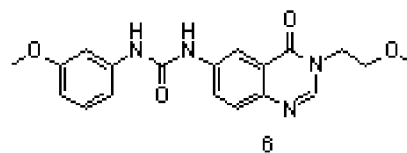
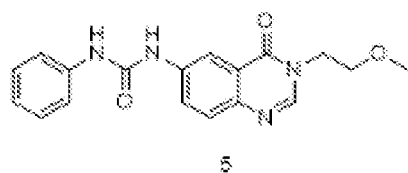


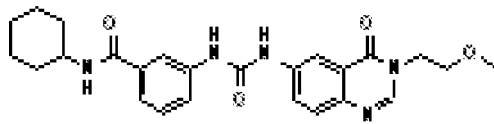
(xx) alternately, treating compound 4 obtained in step (xvi) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of aniline, m-anisidine, N1-methylbenzene-1,3-diamine, m-nitroaniline, 3-aminoacetophenone, 4-aminoacetophenone, 1-(3-aminophenyl)ethanol, methyl 3-amino-4-methoxybenzoate, 3-ethylaniline, 3'-aminobenzophenone, 3-amino-N-cyclohexylbenzamide, methyl 2-(3-aminobenzamido)-3-methylbutanoate, 3-amino-N,N-dimethylbenzamide, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 3-(benzo[d]oxazol-2-yl)aniline, N-(3-aminophenyl)acetamide, N-

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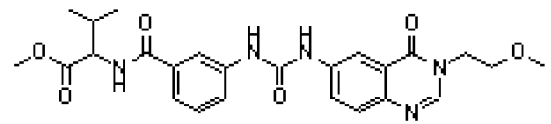
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(3-aminophenyl)-N-methylacetamide, N-(3-aminophenyl)-N-benzylacetamide, N-(3-aminobenzyl)acetamide, N-(3-aminobenzyl)-N-methylacetamide, dimethylamine, piperdine, 4-amino-1-methylpiperdine, 4-benzylpiperidine, 1-benzylpiperidin-4-amine, 1-(3-amino-4-hydroxyphenyl)ethanone, 1-(3-amino-5-chloro-2-hydroxyphenyl)ethanone, 1-(3-amino-2-hydroxy-5-methylphenyl)ethanone, 1-(3-aminophenyl)-2,2,2-trifluoroethanol in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, and 34;**



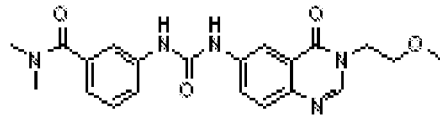


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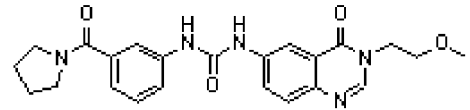


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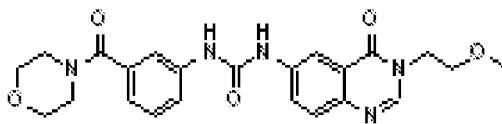


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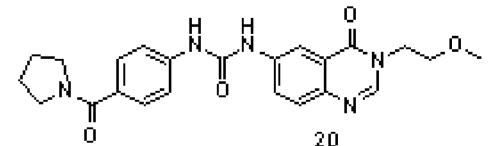


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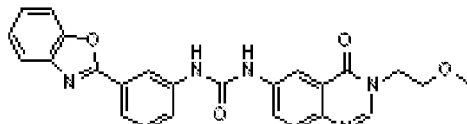


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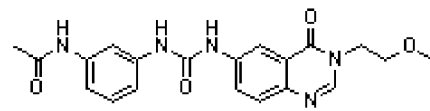


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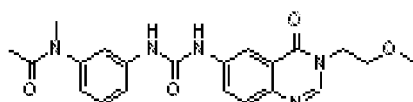


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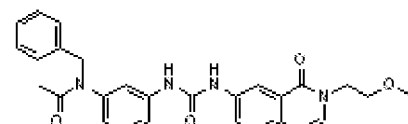


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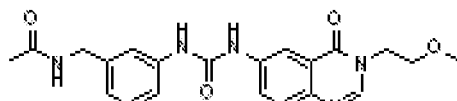


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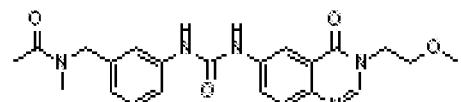


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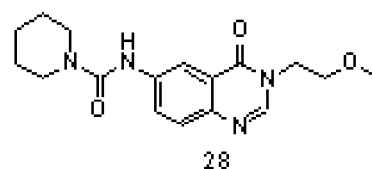
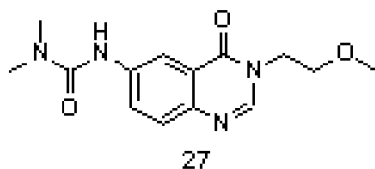
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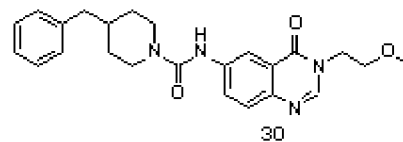
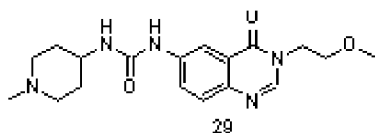
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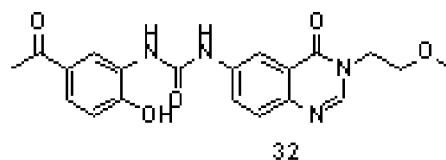
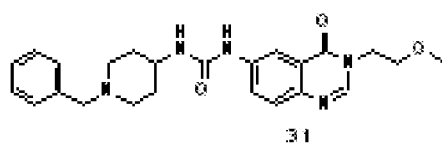
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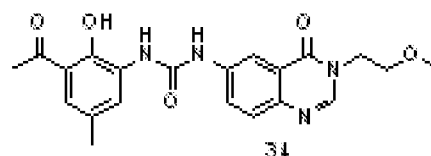
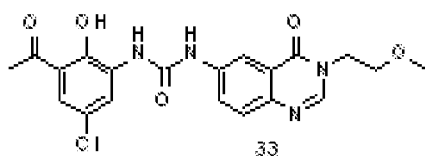
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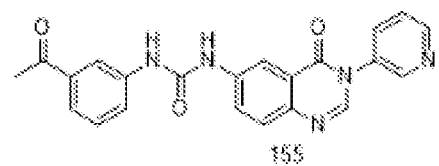
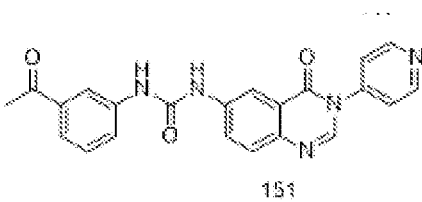
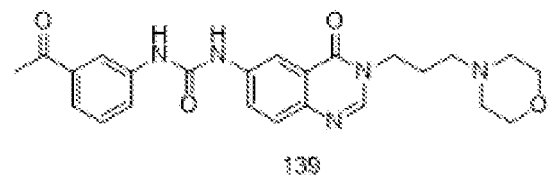
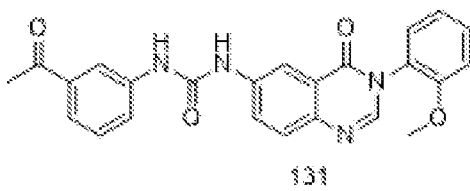
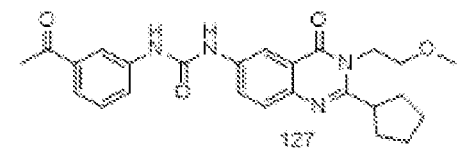
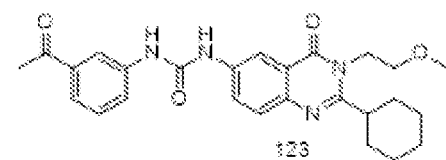
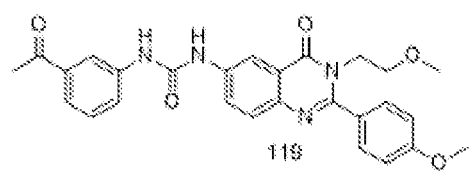
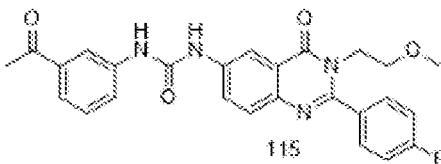
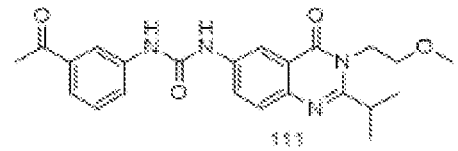
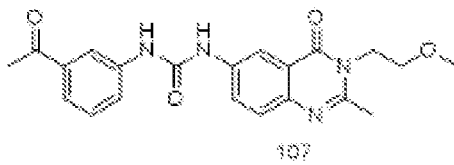
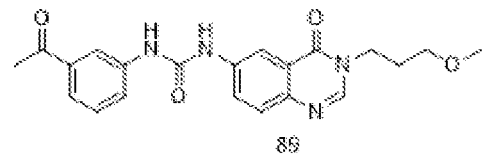
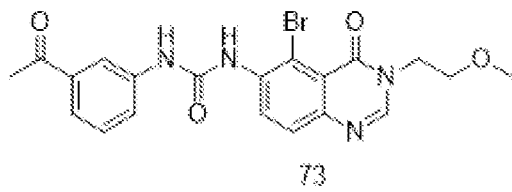


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(xxi) alternately, treating the compound selected from the group consisting of **43**, **88**,
106, **110**, **114**, **118**, **122**, **126**, **130**, **138**, **150**, **154**, **158**, **162**, **166**, **170**, **174**, **178**,
182, **186**, **191**, **202**, **206**, **210**, **214**, **218**, **222**, **226**, **231**, **234**, **237**, **240**, **243**, **246**,
249, **252**, **255**, **258**, **261**, **264**, **267**, **270**, **273**, **276**, **280**, **284**, **288**, **298**, **303**, **306**,
329, **329a**, **332**, **332a**, **335**, **335a**, **339**, and **344** obtained in step (xvi), (xvii) and
(xviii) with 4-nitrophenylchloroformate in presence of TEA as a base followed by
reaction with 3-aminoacetophenone in dry THF at room temperature for 3-8 hours
to obtain the compound having structure I selected from the group consisting of
73, **89**, **107**, **111**, **115**, **119**, **123**, **127**, **131**, **139**, **151**, **155**, **159**, **163**, **167**, **171**, **175**,
179, **183**, **187**, **192**, **193**, **194**, **195**, **196**, **197**, **198**, **199**, **203**, **207**, **211**, **215**, **219**,
223, **227**, **232**, **235**, **238**, **241**, **244**, **247**, **253**, **256**, **259**, **262**, **268**, **274**, **277**, **281**,
285, **289**, **304**, **307**, **330**, **330a**, **333**, **333a**, **336**, **336a**, **340**, and **345**;

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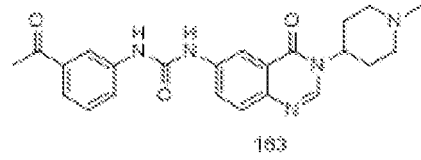
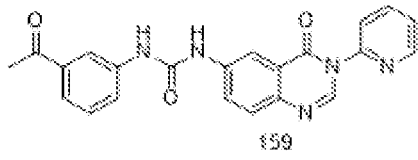
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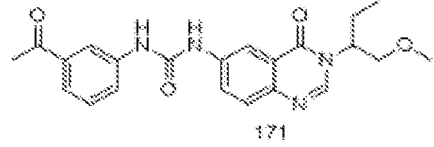
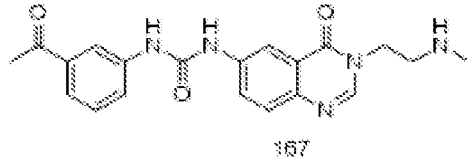
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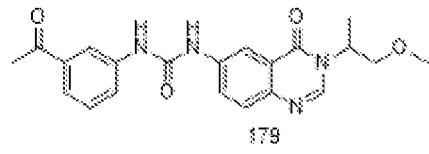
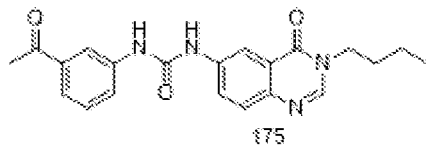
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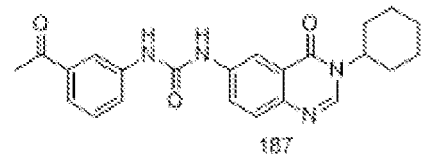
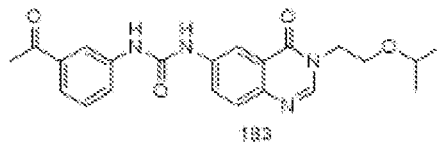
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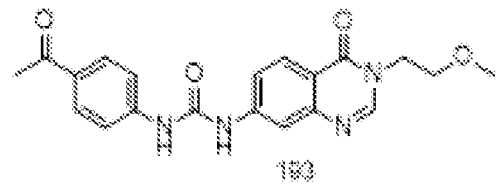
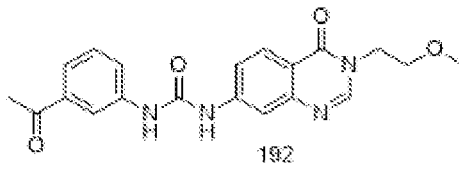
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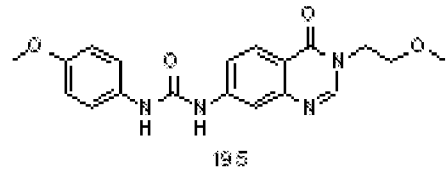
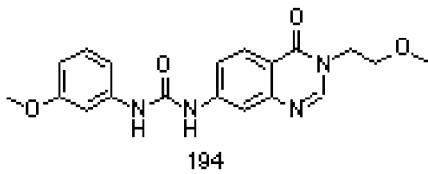
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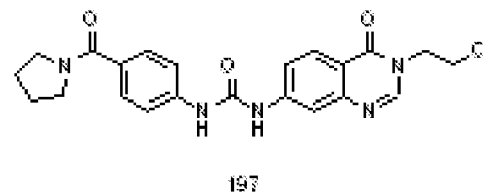
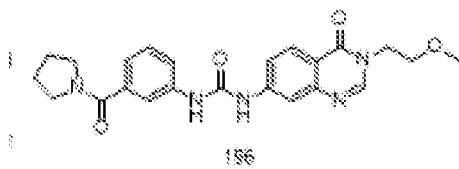
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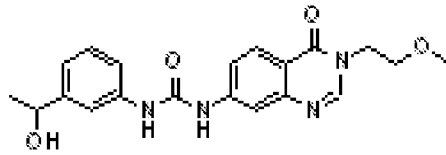
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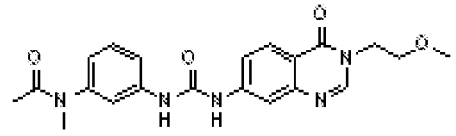
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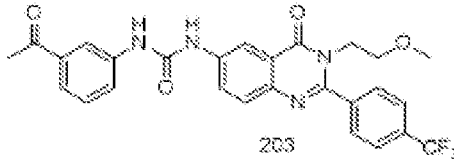


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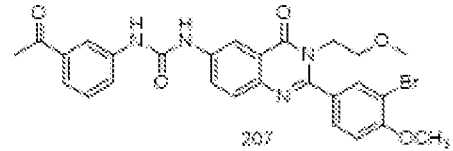


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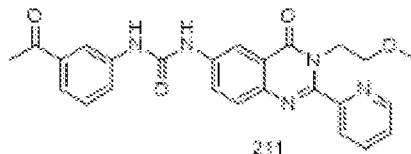


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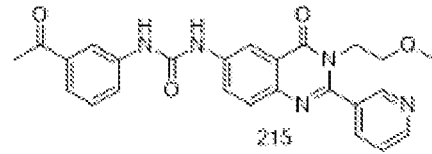


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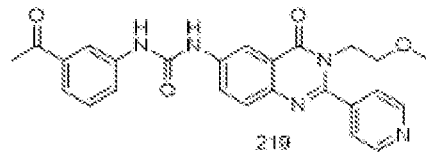


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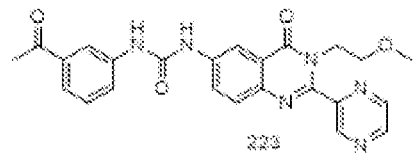


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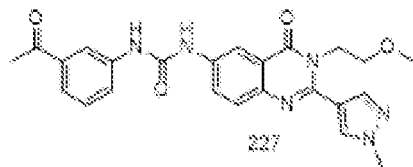


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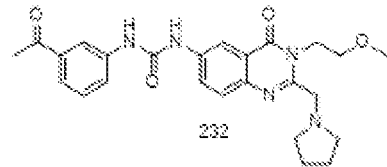


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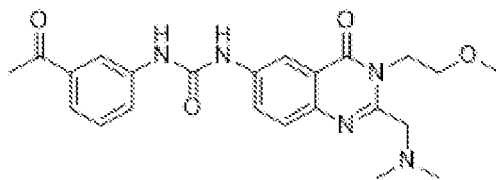


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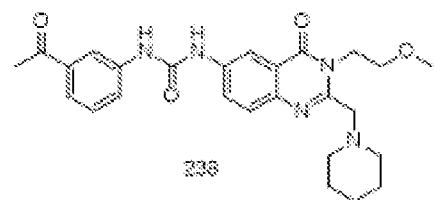


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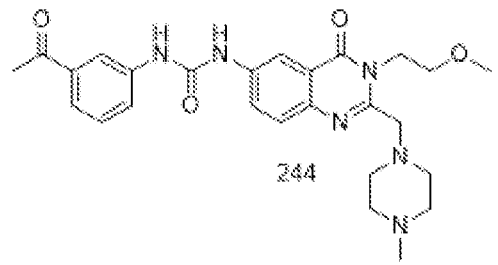
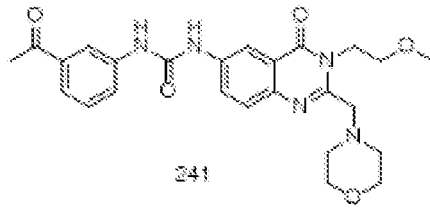


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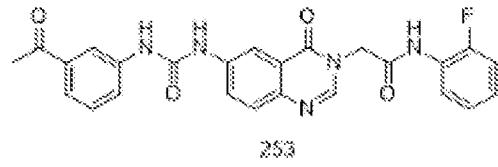
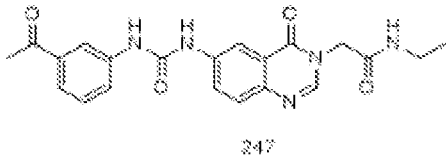


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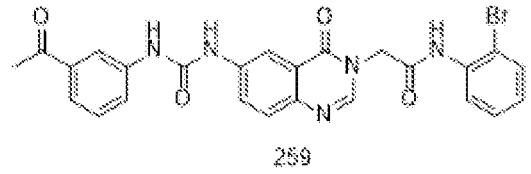
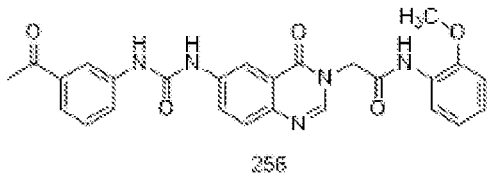
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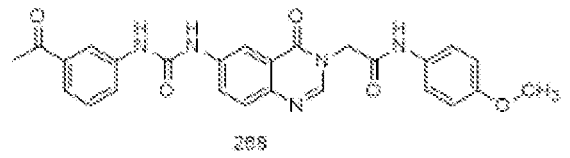
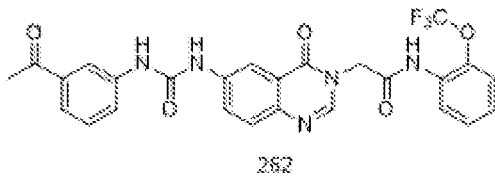
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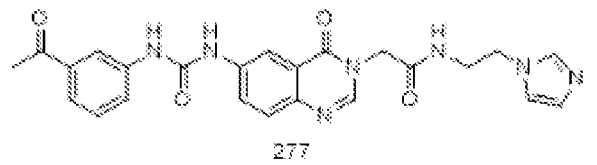
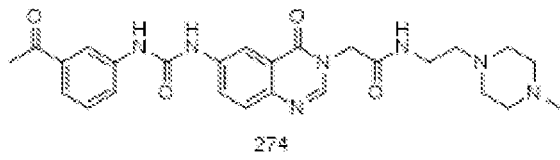
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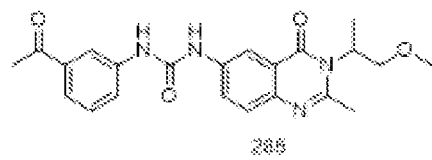
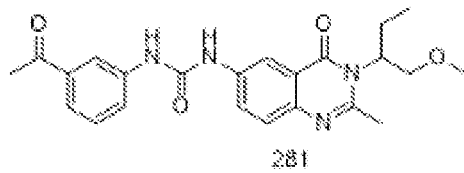
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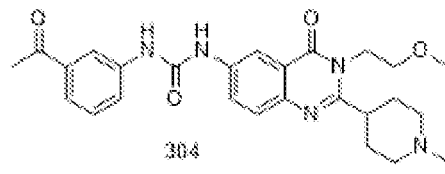
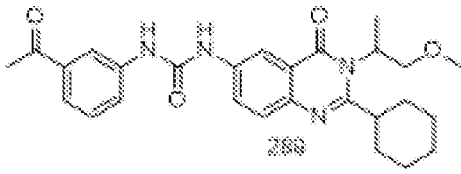


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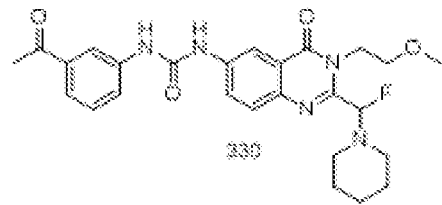
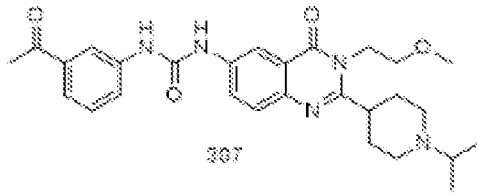


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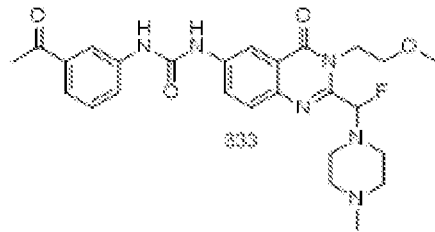
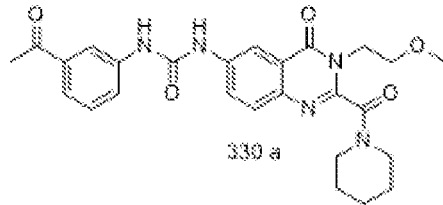




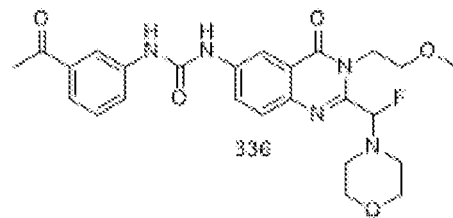
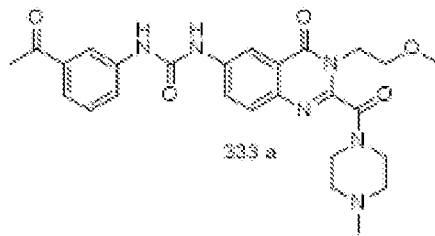
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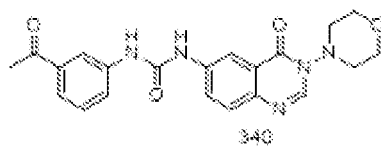
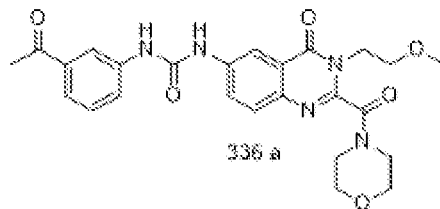
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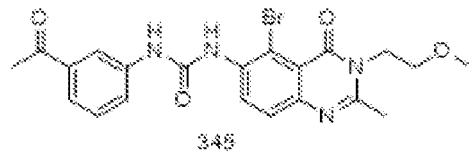
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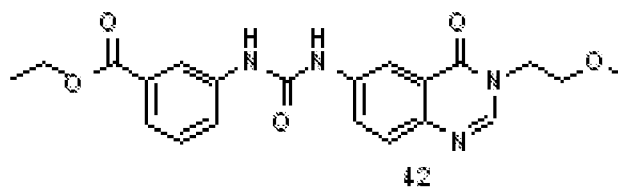
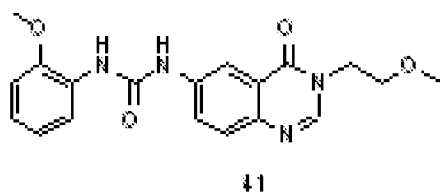
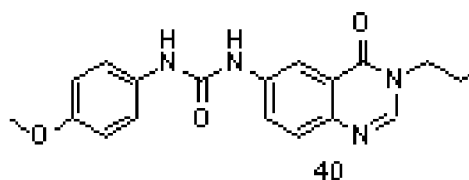
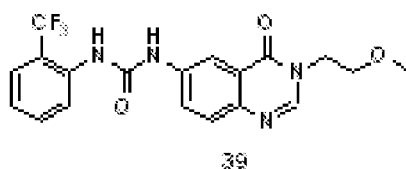
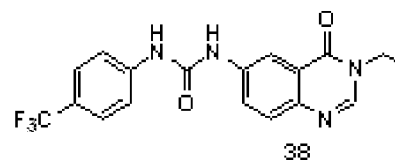
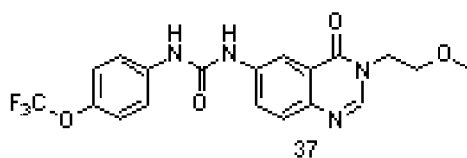
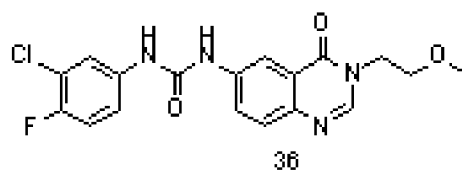
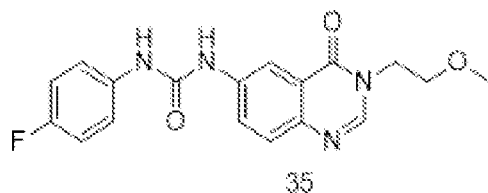


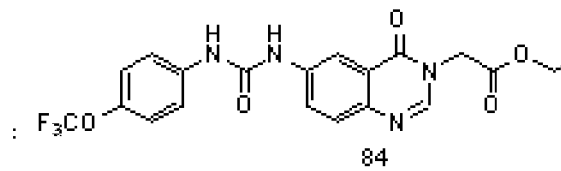
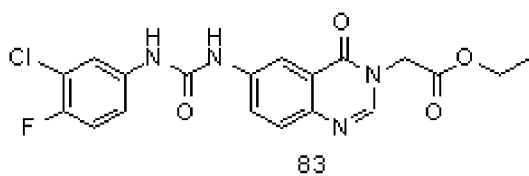
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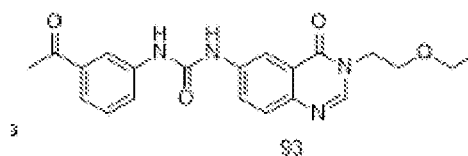
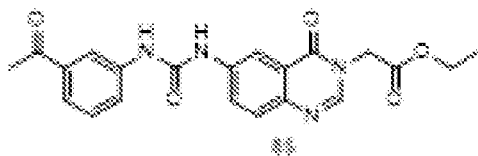
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(xxii) alternately, treating the compound selected from the group consisting of **4**, **82**, **92**, **97**, **102**, **134**, **142**, and **146** obtained in step (xvi) with a substituted aromatic isocyanate selected from the group consisting of 4-fluorophenylisocyanate, 3-chloro-4-fluorophenylisocyanate, (4-trifluoromethoxy)phenylisocyanate, (4-trifluoromethyl)phenylisocyanate, (2-trifluoromethyl)phenylisocyanate, 4-methoxyphenylisocyanate, 2-methoxyphenylisocyanate, ethyl 3-isocyanatobenzoate, 3-acetylphenylisocyanate, and 4-acetylphenylisocyanate in presence of TEA as a base in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **35**, **36**, **37**, **38**, **39**, **40**, **41**, **42**, **83**, **84**, **85**, **93**, **94**, **98**, **99**, **103**, **135**, **143**, and **147**;

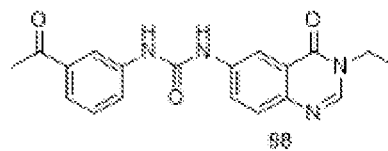
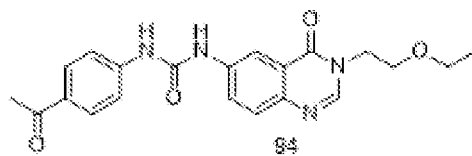




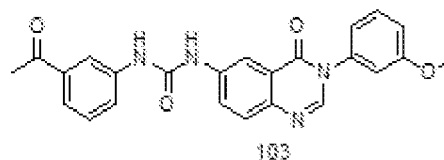
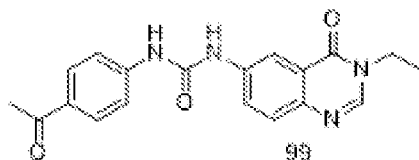
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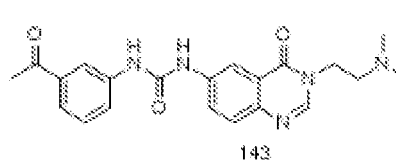
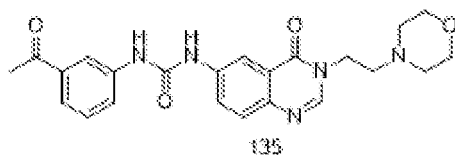
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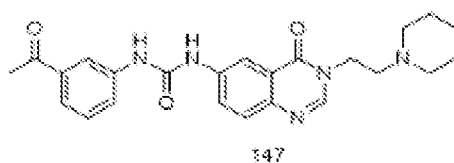
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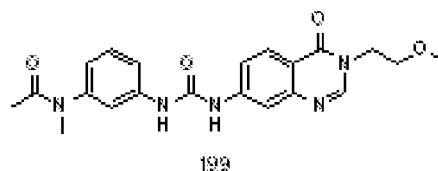
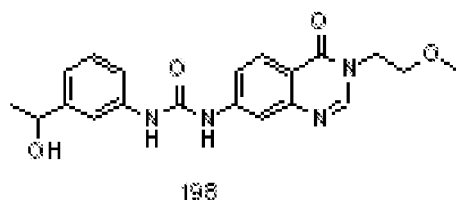
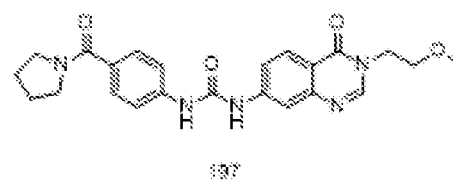
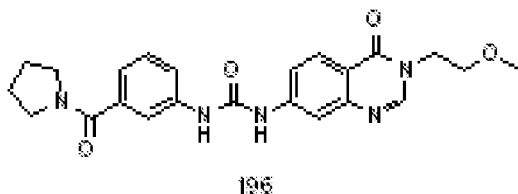
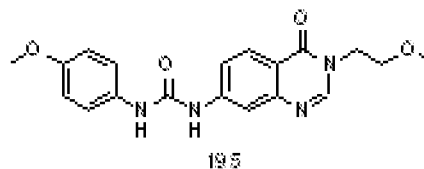
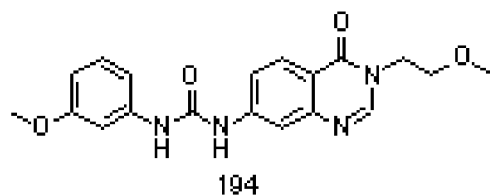


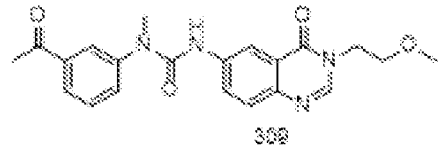
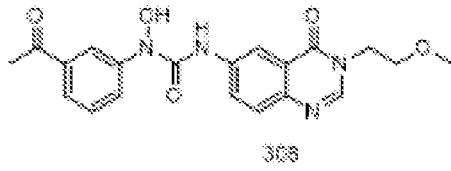
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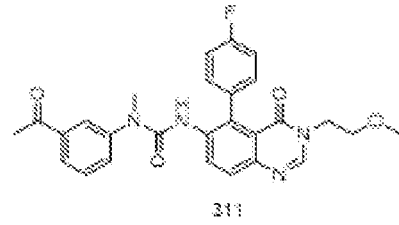
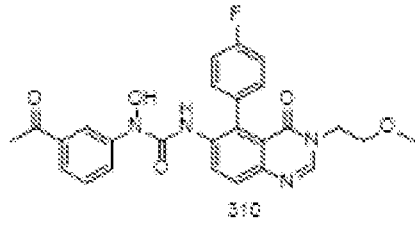
(xxiii) alternately, reacting compound **4** obtained in step (xvi) with HATU/ TEA in DMF at room temperature with 5 hours of stirring to obtain a compound **74**;

(xxvii) alternately, treating the compound selected from the group consisting of **191**, **4**, **46**, **237**, **249**, **106**, **243**, and **252** obtained in step (xvi) and (xix) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of 3-aminoacetophenone, 4-aminoacetophenone, m-anisidine, p-anisidine, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 1-(3-aminophenyl)-2,2,2-trifluoroethanol, (3-aminophenyl)-N-methylacetamide, 1-(3-(hydroxyamino)phenyl)ethanone, 1-(3-(methylamino)phenyl)ethanone, and 1-(3-aminophenyl)-2,2,2-trifluoroethanone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **194**, **195**, **196**, **197**, **198**, **199**, **308**, **309**, **310**, **311**, **312**, **313**, **314**, **315**, **316**, **317**, **318**, **319**, **320**, **321**, **322**, **323**, **324**, and **325**;

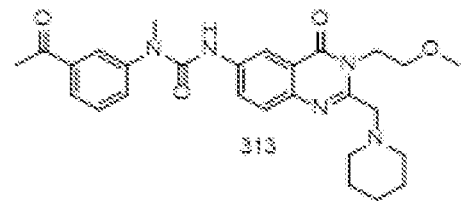
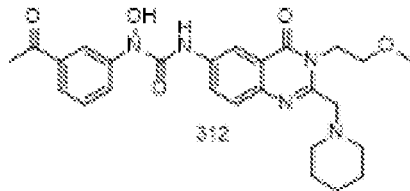




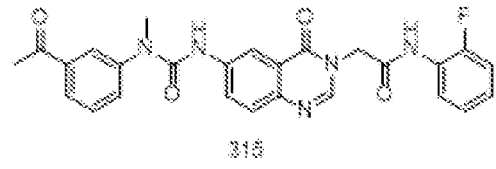
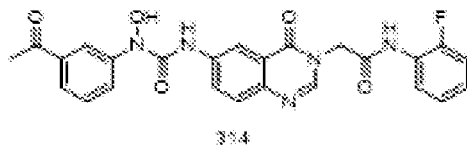
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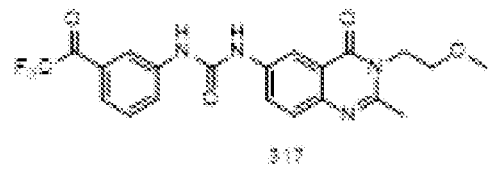
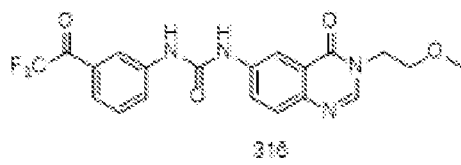
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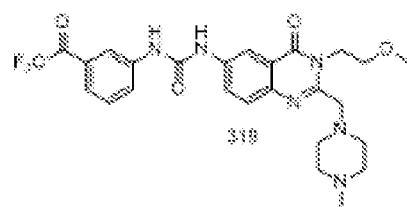
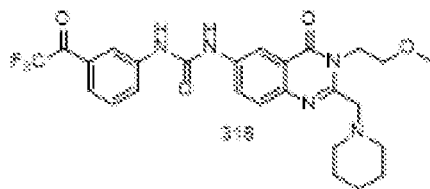
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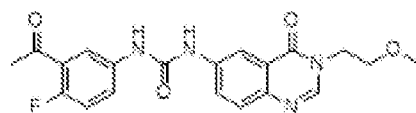


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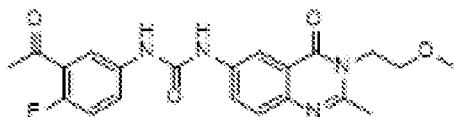


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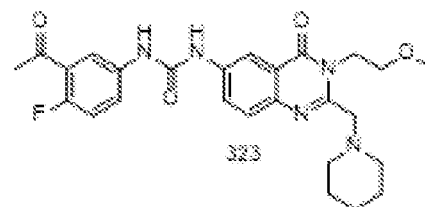


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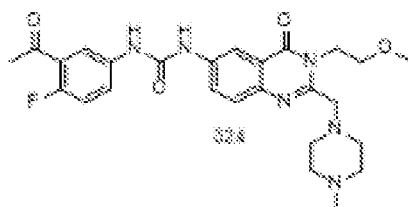


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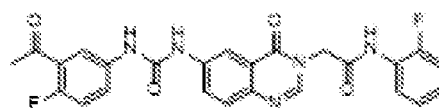


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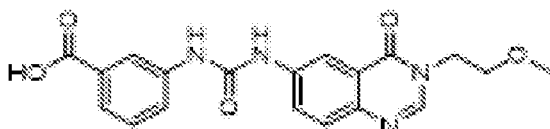


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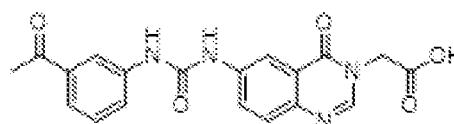
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(xxviii) subjecting the compound selected from **42** and **85** obtained in step (xxii) to ester hydrolysis by LiOH monohydrate in presence of THF: EtOH: Water (3:2:1) proportion at room temperature for 1-2 hours to obtain the compound having structure I selected from the group consisting of **42a** and **85a**;

20



42 a



85 a

25

(xxix) reacting the compound **238** obtained in step (xxi) with 1M HCl in dioxane to obtain the compound having structure I **238a**; and

Yet another aspect of the present invention provides a method of increasing the level of ATGL by compound having structure I.

BRIEF DESCRIPTION OF DRAWING

5 The objects and features of the present invention will become apparent from the following description of the invention, when taken in conjunction with the accompanying drawings.

Fig. 1(A to Y) illustrates results of Western Blot Analysis in HepG2 cells after treatment with compounds **9, 10, 107, 171, 179, 73, 232, 238, 211, 340, 11, 17, 18, 23, 24, 123, 127, 139,**
10 **223, 241, 244, 299, 333a, 215, 219 and 308.** Increase in intensity of ATGL and COP1 bands with respect to control denotes elevation in the respective protein levels upon compound treatment. Actin is used as a loading control.

Fig. 2 illustrates images of compound screening on HepG2 cells using confocal microscopy. The white foci in the cells denote lipid droplets. Increase or decrease in the number of white
15 foci therefore indicate the corresponding status of lipid droplets in the cells. Oleate induction resulted in an increase in lipid droplets whereas treatment with compounds **9** and **10** caused a decrease in the number of lipid droplets upon oleate induction.

Fig. 3(A to C) illustrates ATGL protein status in mouse primary hepatocytes and adipose explants after compound treatment. Compounds **9** and **107** could increase ATGL level in
20 primary mouse hepatocytes as evidenced by increase in intensity of the corresponding band with respect to control in Western blot analysis. While in adipose explants no such changes were observed.

Fig. 4 illustrates identification of the E2 conjugating enzyme responsible for ATGL ubiquitination by the E3 Ubiquitin Ligase, COP1. The presence of poly Ubiquitin smear only
25 in case of UbcH6 indicate that is the specific E2 enzyme in the ubiquitination reaction of ATGL by COP1.

Fig. 5 illustrates effect of compounds **9, 107, 171, 179** and **73** on ATGL ubiquitination *in vitro*. The above compounds were effective in reducing the ubiquitination of ATGL by COP1 in an *in vitro* reaction reconstituted with purified ATGL protein, COP1 overexpressing cell
30 lysate, recombinant UbcH6 identified in the experiment before and other essential components of the reaction.

Fig. 6 (A to F) illustrates results of immunoprecipitation assay to check ubiquitination status of ATGL and COP1 after treatment with compounds. Compound **9** and **107** was effective in

reducing the ATGL ubiquitination by COP1 in HepG2 cells as well as COP1 autoubiquitination as evidenced by the decrease in the intensity of the poly Ubiquitin smear. Compound **107** was effective in reducing ATGL ubiquitination by COP1 whereas compounds **215** and **219** had no such effects.

5 **Fig. 7** illustrates reversal of ATGL degradation promoted by COP1 upon treatment with compounds. COP1 overexpression reduces ATGL level in HepG2 cells by causing increased ubiquitination and degradation of ATGL. Treatment with compounds **9** and **10** could restore the reduced ATGL level in cells overexpressing COP1.

10 **Fig. 8** illustrates that compounds exert no effect on the mRNA levels of ATGL. Because ubiquitination of ATGL by COP1 is a post translational modification, the resultant decrease in ATGL protein due to ubiquitination mediated degradation must not have any impact on its corresponding mRNA status. Thus the compounds do not alter the mRNA level of ATGL in HepG2 cells.

15 **Fig. 9** illustrates results of *in vivo* study of compounds in mice measuring ATGL and COP1 levels. Compound 107 could modestly increase ATGL level, with no such effect on COP1, in mice after 8 hours and 16 hours feeding of mice via oral gavage.

20 **Fig. 10(A to D)** illustrate compilation of effect of compounds in increasing ATGL and COP1 levels in HepG2, out of which compound 238 was most potent in increasing ATGL and COP1 levels in HepG2 cells also in dose dependent manner. Compound 238 could also decrease ATGL ubiquitination by COP1 in HepG2 cells and increase ATGL and COP1 levels dose dependently in primary mouse hepatocytes.

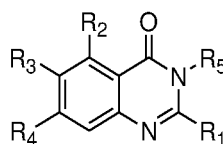
Fig. 11 illustrates crystal structure of **238a** (HCl salt) CCDC Deposition no 1988445.

25 **Fig. 12** illustrates basal oxygen consumption rate of compounds. Compounds 9, 107, 238a, 238 at 5 μ M concentration showed higher oxygen consumption rate compared to control indicative of an increase in the basal respiration rate of the cell.

DETAILED DESCRIPTION OF THE INVENTION

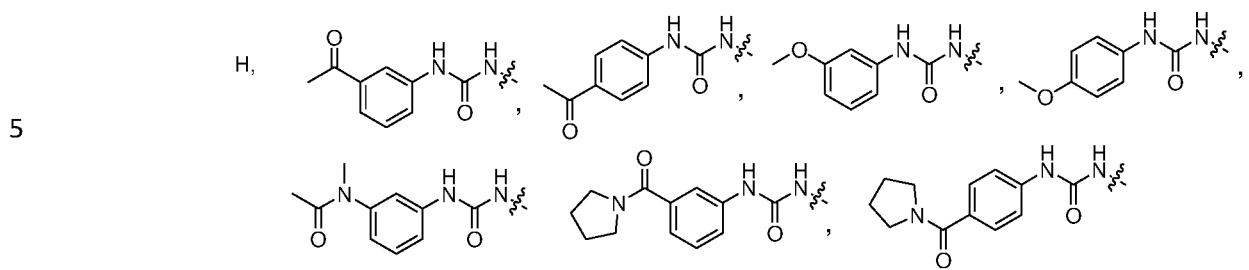
The present invention relates to a compound having structure I or salts thereof:

30

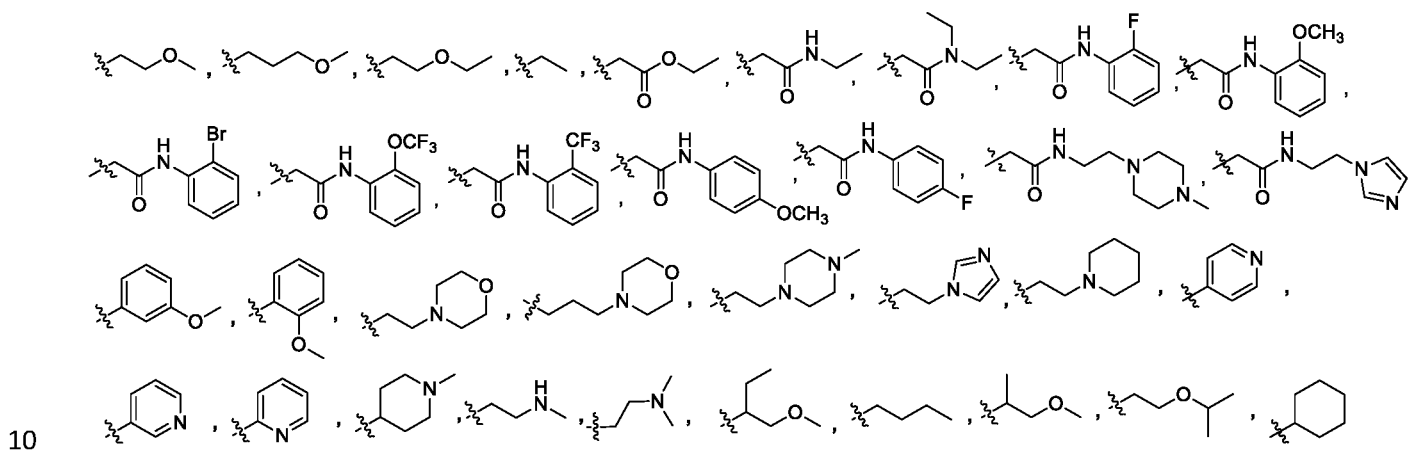


Structure I

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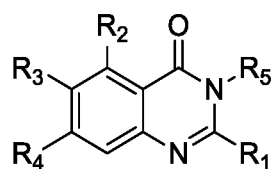


R₅ is independently selected from the group consisting of:



All the compounds disclosed in present invention having Structure I are depicted in the table

I:

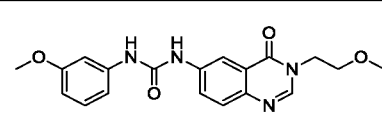
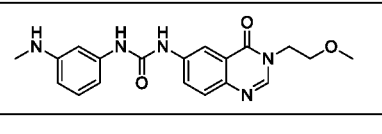
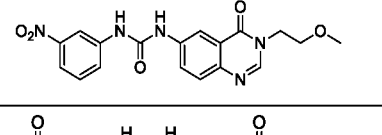
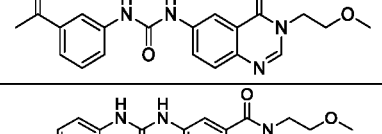
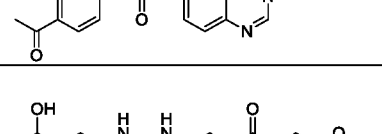
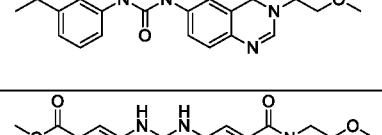
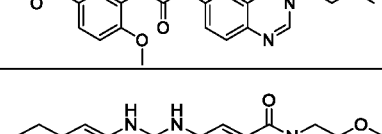
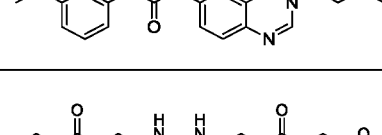
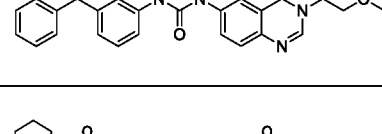
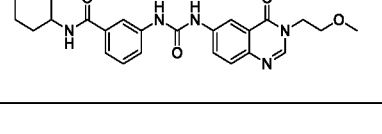
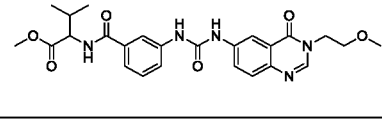
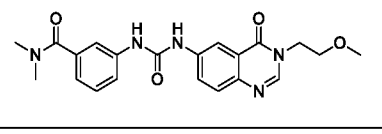
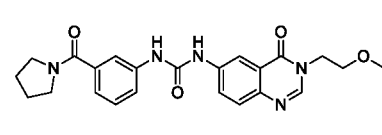


Structure I

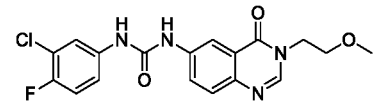
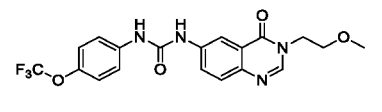
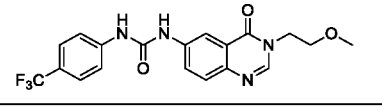
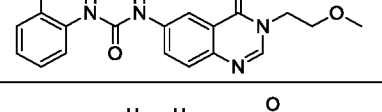
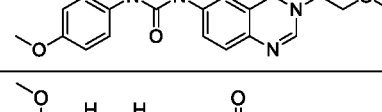
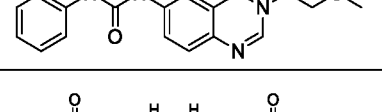
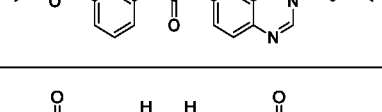
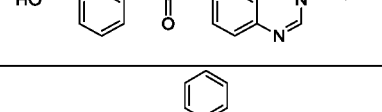
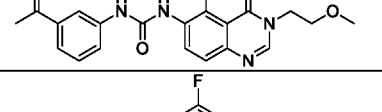
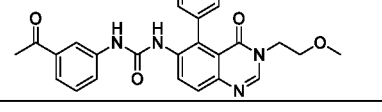
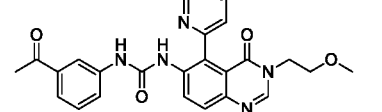
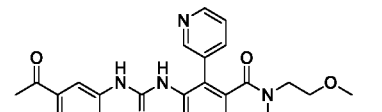
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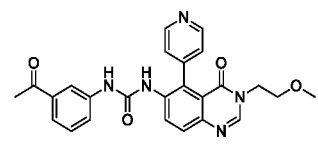
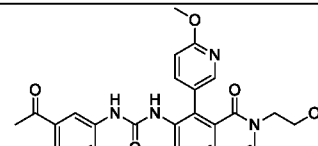
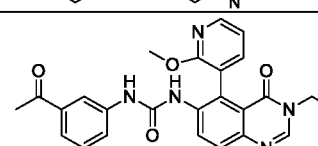
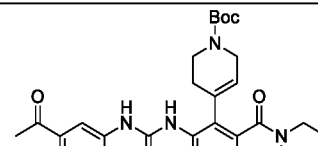
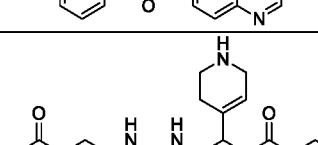
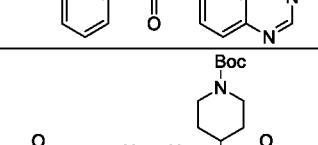
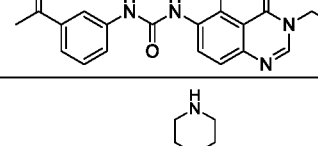
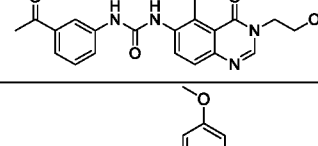
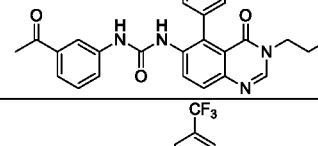
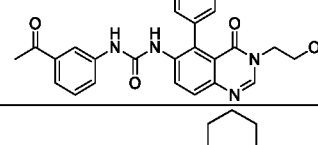
Table 1: Structure of the compounds disclosed

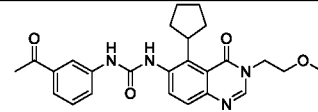
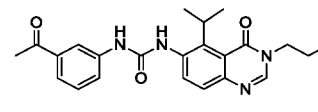
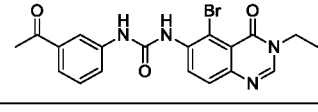
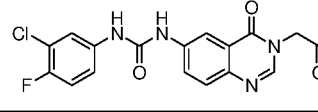
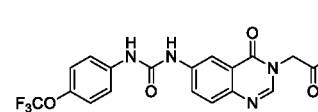
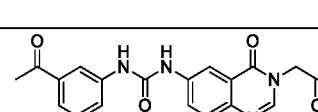
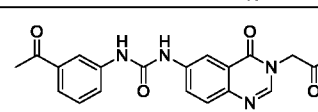
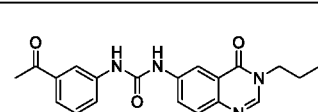
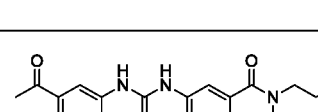
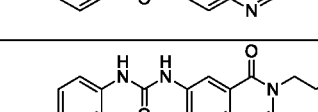
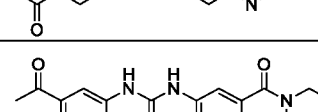
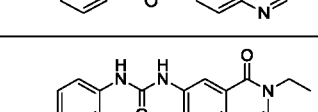
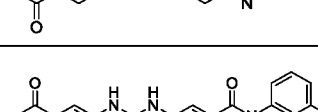
Serial No.	Compound No.	Structure	IUPAC Name
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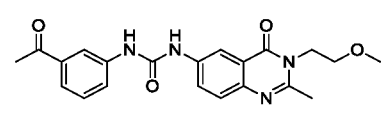
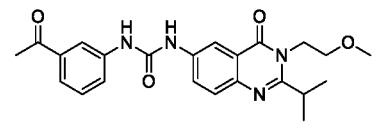
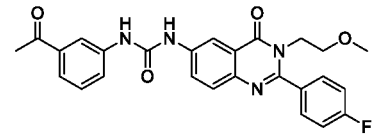
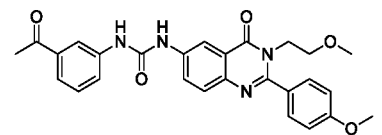
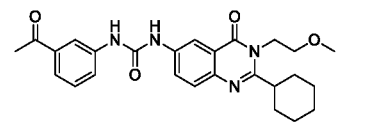
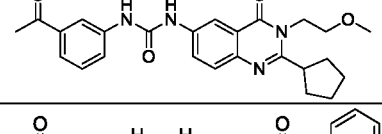
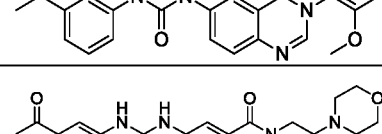
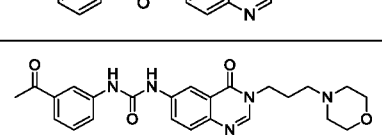
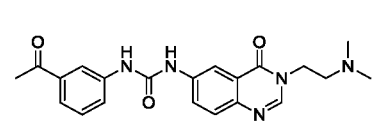
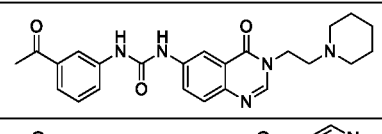
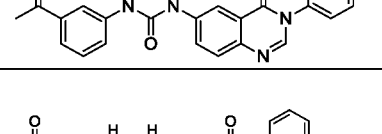
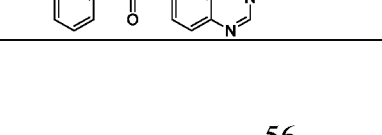
2	6		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-methoxyphenyl)urea
3	7		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(methylamino)phenyl)urea
4	8		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-nitrophenyl)urea
5	9		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
6	10		1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
7	11		1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
8	12		methyl 4-methoxy-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate
9	13		1-(3-ethylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
10	14		1-(3-benzoylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
11	15		N-cyclohexyl-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamide
12	16		methyl 2-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamido)-3-methylbutanoate
13	17		3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)-N,N-dimethylbenzamide
14	18		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea

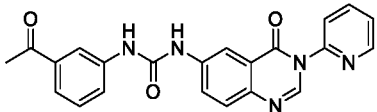
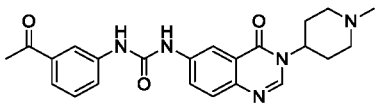
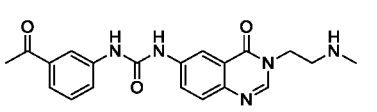
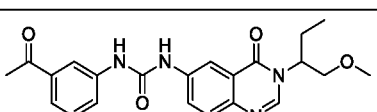
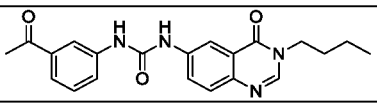
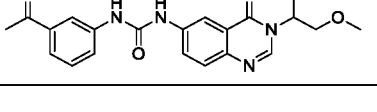
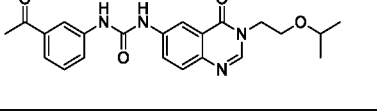
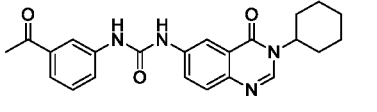
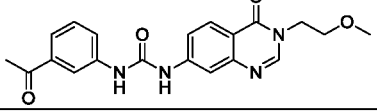
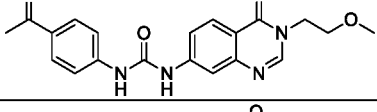
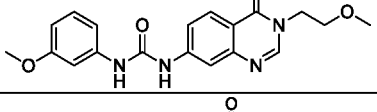
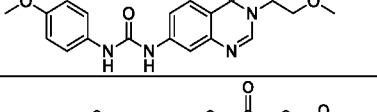
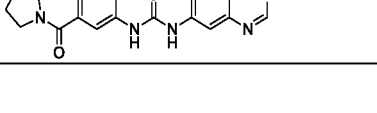
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16	20		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea
17	21		1-(3-(benzo[d]oxazol-2-yl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
18	22		N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide
19	23		N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)-N-methylacetamide
20	24		N-benzyl-N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide
21	25		N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)acetamide
22	26		N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)-N-methylacetamide
23	32		1-(5-acetyl-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
24	33		1-(3-acetyl-5-chloro-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
25	34		1-(3-acetyl-2-hydroxy-5-methylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
26	35		1-(4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea

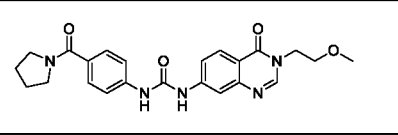
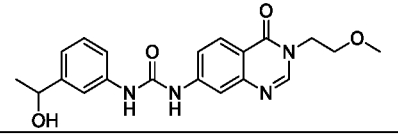
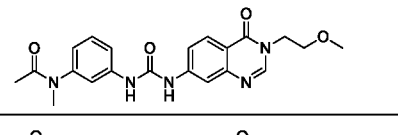
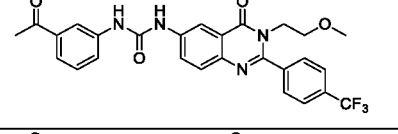
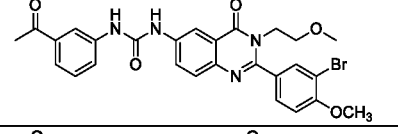
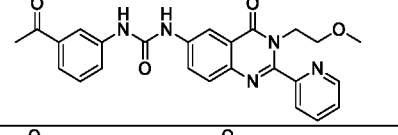
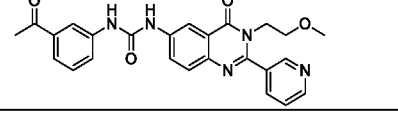
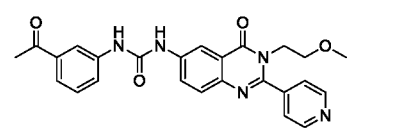
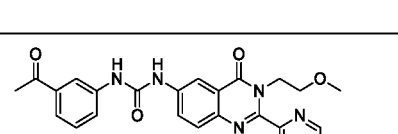
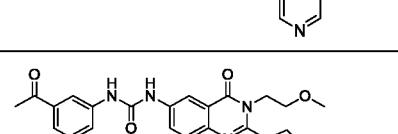
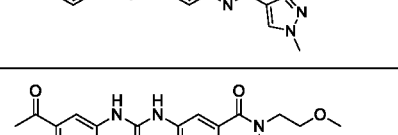
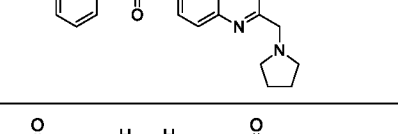
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28	37		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea
29	38		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethyl)phenyl)urea
30	39		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-(trifluoromethyl)phenyl)urea
31	40		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-methoxyphenyl)urea
32	41		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-methoxyphenyl)urea
33	42		ethyl 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate
34	42a		3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoic acid
35	45		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-phenyl-3,4-dihydroquinazolin-6-yl)urea
36	47		1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
37	49		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea
38	51		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea

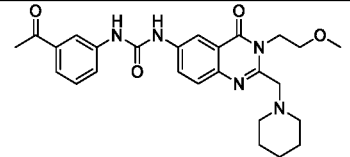
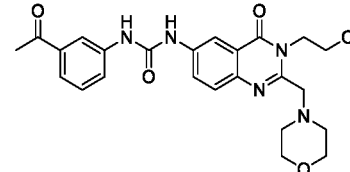
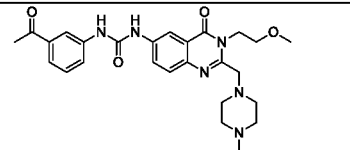
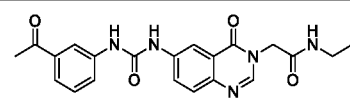
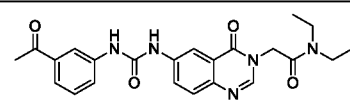
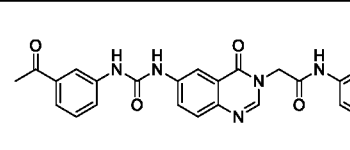
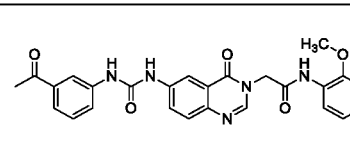
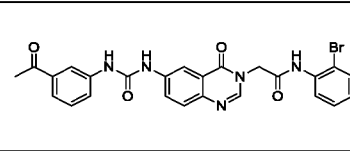
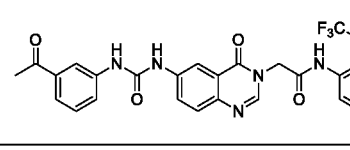
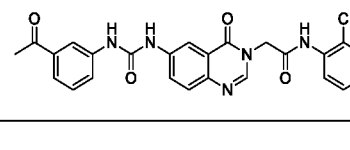
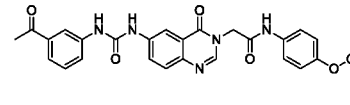
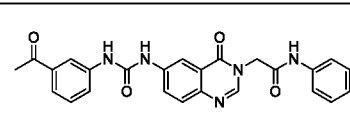
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40	55		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(6-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
41	57		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(2-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
42	59		tert-butyl 4-(6-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate
43	60		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(1,2,3,6-tetrahydropyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea
44	61		tert-butyl 4-(6-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)piperidine-1-carboxylate
45	62		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea
46	64		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
47	66		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea
48	68		1-(3-acetylphenyl)-3-(5-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea

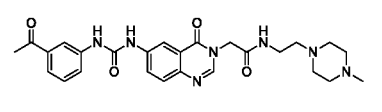
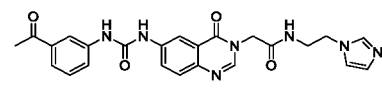
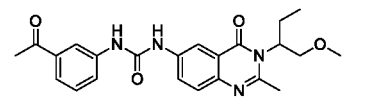
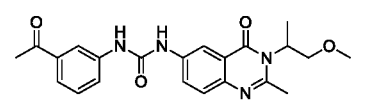
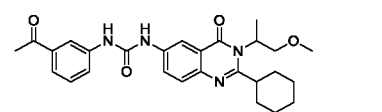
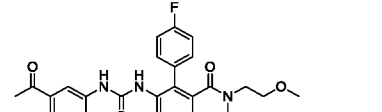
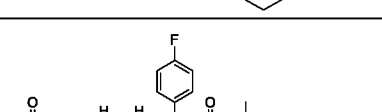
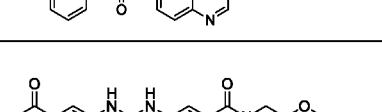
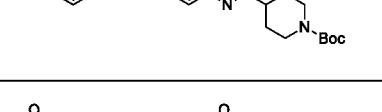
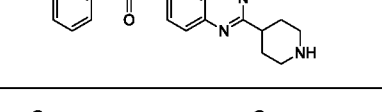
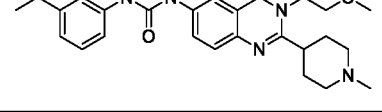
49	70		1-(3-acetylphenyl)-3-(5-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
50	72		1-(3-acetylphenyl)-3-(5-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
51	73		1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
52	83		ethyl 2-(6-(3-(3-chloro-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate
53	84		ethyl 2-(4-oxo-6-(3-(4-(trifluoromethoxy)phenyl)ureido)quinazolin-3(4H)-yl)acetate
54	85		ethyl 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate
55	85a		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetic acid
56	89		1-(3-acetylphenyl)-3-(3-(3-methoxypropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
57	93		1-(3-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
58	94		1-(4-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
59	98		1-(3-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
60	99		1-(4-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
61	103		1-(3-acetylphenyl)-3-(3-(3-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea

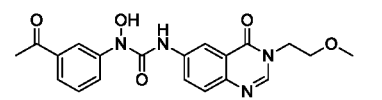
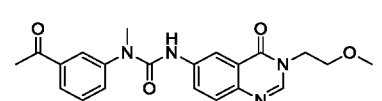
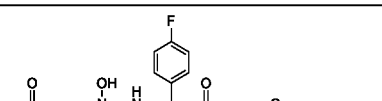
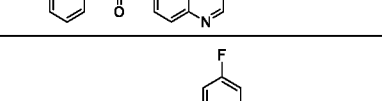
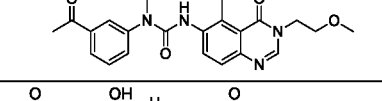
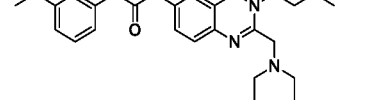
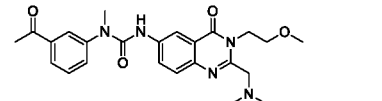
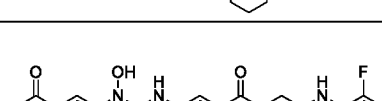
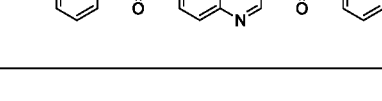
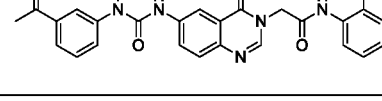
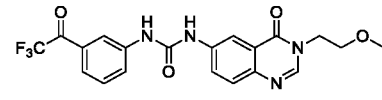
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63	111		1-(3-acetylphenyl)-3-(2-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
64	115		1-(3-acetylphenyl)-3-(2-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
65	119		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
66	123		1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
67	127		1-(3-acetylphenyl)-3-(2-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
68	131		1-(3-acetylphenyl)-3-(3-(2-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
69	135		1-(3-acetylphenyl)-3-(3-(2-morpholinoethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
70	139		1-(3-acetylphenyl)-3-(3-(3-morpholinopropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
71	143		1-(3-acetylphenyl)-3-(3-(2-(dimethylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
72	147		1-(3-acetylphenyl)-3-(4-oxo-3-(2-(piperidin-1-yl)ethyl)-3,4-dihydroquinazolin-6-yl)urea
73	151		1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea
74	155		1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea

75	159		1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea
76	163		1-(3-acetylphenyl)-3-(3-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
77	167		1-(3-acetylphenyl)-3-(3-(2-(methylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
78	171		1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
79	175		1-(3-acetylphenyl)-3-(3-butyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
80	179		1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
81	183		1-(3-acetylphenyl)-3-(3-(2-isopropoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
82	187		1-(3-acetylphenyl)-3-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
83	192		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea
84	193		1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea
85	194		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-methoxyphenyl)urea
86	195		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-methoxyphenyl)urea
87	196		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea

88	197		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea
89	198		1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea
90	199		N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)ureido)phenyl)-N-methylacetamide
91	203		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea
92	207		1-(3-acetylphenyl)-3-(2-(3-bromo-4-methoxyphenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
93	211		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea
94	215		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea
95	219		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea
96	223		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrazin-2-yl)-3,4-dihydroquinazolin-6-yl)urea
97	227		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methyl-1H-pyrazol-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
98	232		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrrolidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea
99	235		1-(3-acetylphenyl)-3-(2-((dimethylamino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea

100	238		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea
101	241		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholinomethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
102	244		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
103	247		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-ethylacetamide
104	250		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N,N-diethylacetamide
105	253		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide
106	256		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-methoxyphenyl)acetamide
107	259		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-bromophenyl)acetamide
108	262		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide
109	265		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethyl)phenyl)acetamide
110	268		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-methoxyphenyl)acetamide
111	271		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-fluorophenyl)acetamide

112	274		2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide
113	277		N-(2-(1H-imidazol-1-yl)ethyl)-2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetamide
114	281		1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
115	285		1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
116	289		1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
117	292		1-(3-acetylphenyl)-3-(2-cyclohexyl-5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
118	295		1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
119	299		tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate
120	300		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea
121	304		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
122	307		1-(3-acetylphenyl)-3-(2-(1-isopropylpiperidin-4-yl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea

123	308		1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
124	309		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea
125	310		1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-hydroxyurea
126	311		1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea
127	312		1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea
128	313		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-1-methylurea
129	314		2-(6-(3-(3-acetylphenyl)-3-hydroxyureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide
130	315		2-(6-(3-(3-acetylphenyl)-3-methylureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide
131	316		1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea
132	317		1-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea
133	318		1-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea

134	319		1-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea
135	320		N-(2-(2-fluorophenyl)-2-(4-oxo-6-(3-(3-(2,2,2-trifluoroacetyl)phenyl)ureido)quinazolin-3(4H)-yl)acetamide
136	321		1-(3-(acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
137	322		1-(3-(acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
138	323		1-(3-(acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea
139	324		1-(3-(acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
140	325		2-(6-(3-(3-(acetyl-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide
141	330		1-(3-(acetylphenyl)-3-(2-(fluoro(piperidin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
142	330a		1-(3-(acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidine-1-carbonyl)-3,4-dihydroquinazolin-6-yl)urea
143	333		1-(3-(acetylphenyl)-3-(2-(fluoro(4-methylpiperazin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
144	333a		1-(3-(acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea

145	336		1-(3-acetylphenyl)-3-(2-(fluoro(morpholino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
146	336a		1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholine-4-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
147	340		1-(3-acetylphenyl)-3-(3-morpholino-4-oxo-3,4-dihydroquinazolin-6-yl)urea
148	341		(Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea
149	342		(Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
150	343		(Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea
151	345		1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea

General process for preparation:

The process for preparation of the compound having structure I as given in table 1 comprises the following steps:

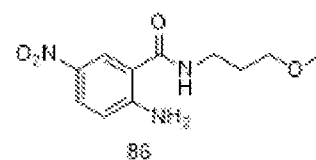
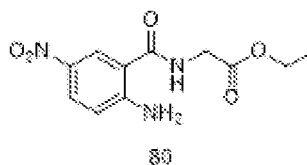
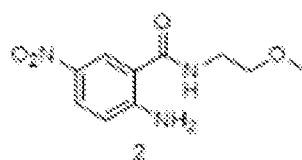
- (i) reacting 2-amino-5-nitrobenzoic acid (**compound 1**) with an aliphatic or an aromatic amine selected from the group consisting of 2-methoxyethylamine, glycine ethylester hydrochloride, 3-methoxypropylamine, 2-ethoxyethylamine, ethylamine 2M in THF, 4-(2-aminoethyl)morpholine, 3-(4-morpholinyl)propylamine, N,N-dimethylethylenediamine, 1-(2-aminoethyl)piperidine, 4-amino-1-methylpiperidine, N-methylethylenediamine, 2-

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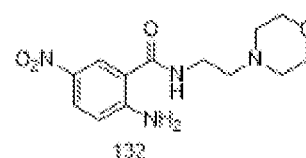
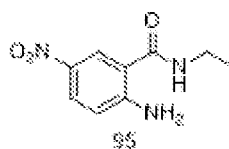
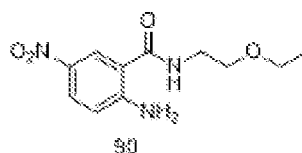
amino-1-methoxybutane, 1-butylamine, 1-methoxy-2-propylamine, 2-aminoethyl isopropyl ether, cyclohexylamine, 4-aminomorpholine, m-anisidine, o-anisidine, 4-aminopyridine, 3-aminopyridine, and 2-aminopyridine in presence of HATU/DMF followed by TEA as a base at room temperature for 1-3 hours to

5 obtain an amide compound selected from the group consisting of **2**, **80**, **86**, **90**, **95**, **132**, **136**, **140**, **144**, **160**, **164**, **168**, **172**, **176**, **180**, **184**, **337**, **100**, **128**, **148**, **152**, and **156**;

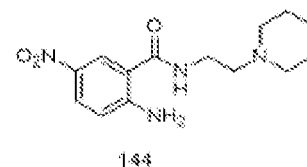
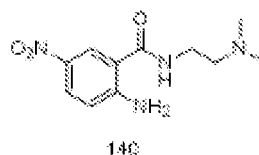
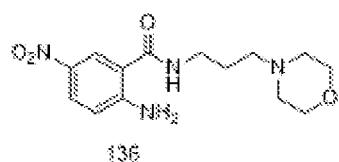
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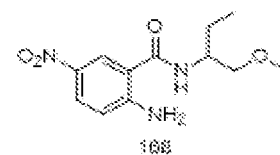
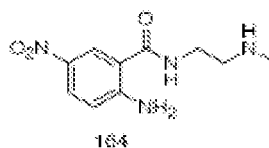
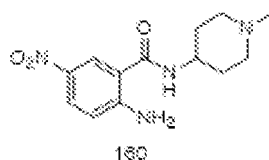
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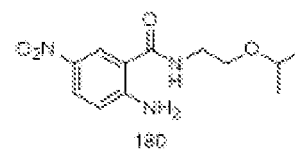
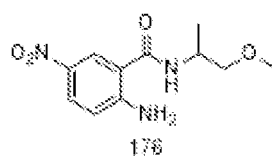
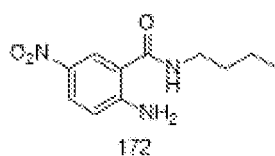
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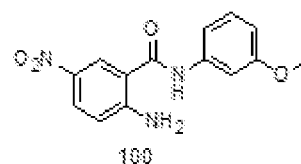
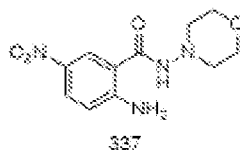
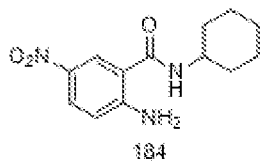


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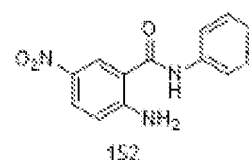
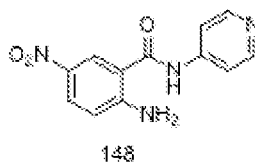
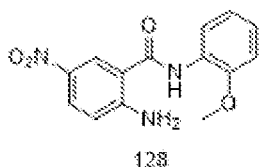


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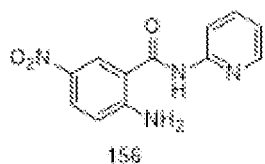




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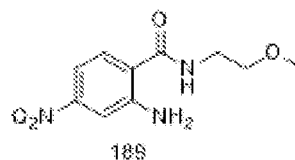
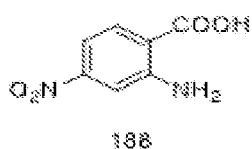


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- (ii) separately, reacting 2-amino-4-nitrobenzoic acid (**compound 188**) with 2-methoxyethylamine in presence of HATU/ DMF followed by TEA as a base at room temperature for 1 hour to obtain a compound **189**;

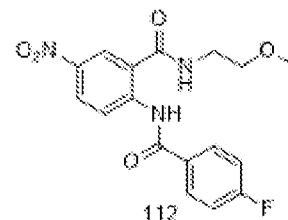
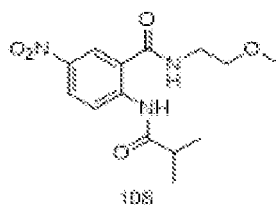
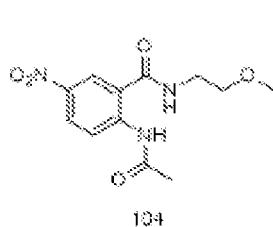
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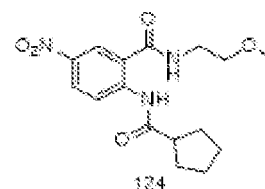
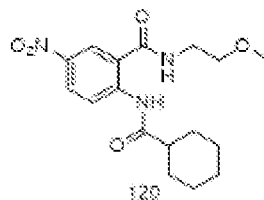
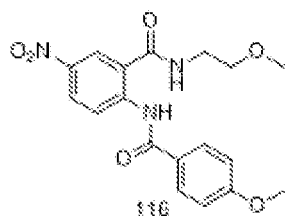
- (iii) adding an acid chloride selected from the group consisting of acetyl chloride, isopropyl chloride, 4-fluorobenzoyl chloride, 4-methoxybenzoyl chloride, cyclohexanecarbonyl chloride, cyclopentanecarbonyl chloride, 4-(trifluoromethyl)benzoyl chloride, 3-Bromo-4-methoxybenzoyl chloride, Picolinoyl chloride, Nicotinoyl chloride, Isonicotinoyl chloride, Pyrazinecarbonyl chloride, 1-methyl-1H-pyrazole-4-carbonyl chloride, and 2-chloroacetyl chloride to compound **2** obtained in step (i) in DCM at a temperature range from 0 °C to room temperature for 1-8 hours to obtain a compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, and 228**;

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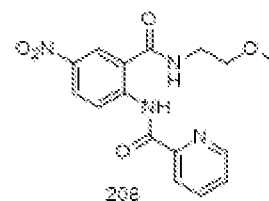
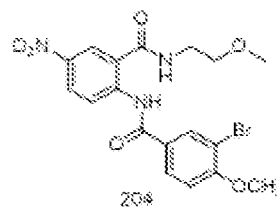
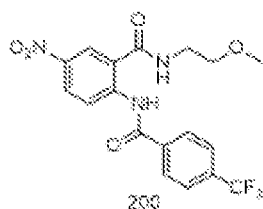
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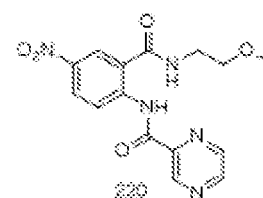
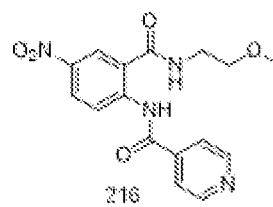
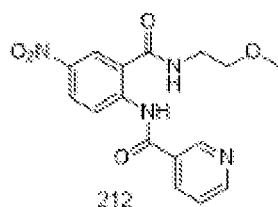
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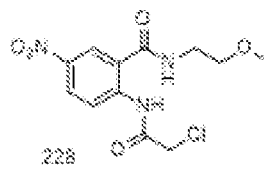
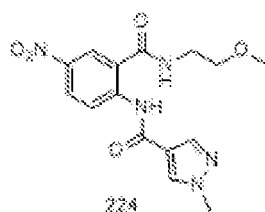
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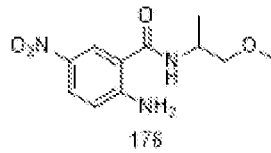
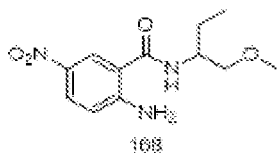


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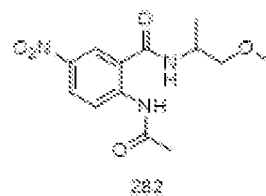
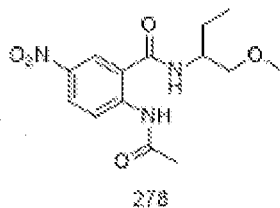


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- (iv) acetylating a compound selected from the group consisting of **168**, and **176** obtained in step (i) using acetyl chloride and triethylamine (TEA) as a base in DCM at a temperature range of 0 °C to room temperature for 8 hours to obtain a compound selected from the group consisting of **278** and **282**;

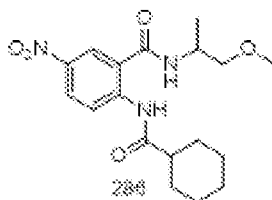


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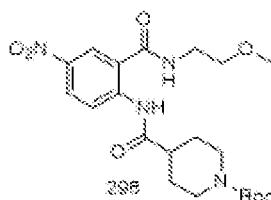
- (v) alternatly, adding cyclohexanecarbonyl chloride to compound **176** obtained in step (i) to obtain a compound **286**;



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- (vi) alternatly, adding tert-butyl 4-(chlorocarbonyl)piperidine-1-carboxylate to compound **2** obtained in setp (i) to obtain a compound **296**;

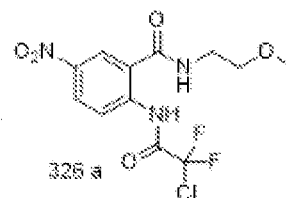
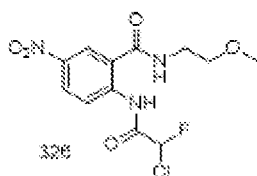
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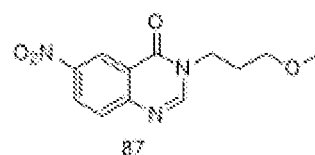
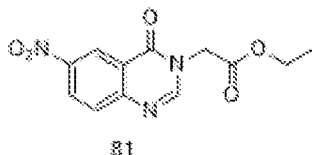
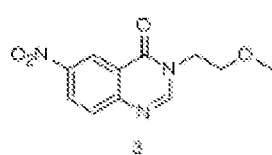
- (vii) alternately, treating compound **2** obtained in step (i) with 2-chloro-2-fluoroacetic acid or 2-chloro-2-difluoroacetic acid along with POCl₃ in pyridine solvent to obtain a compound selected from the group consisting of **326** and **326a**;

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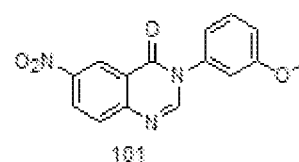
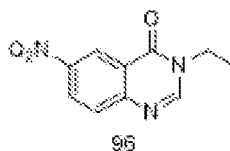
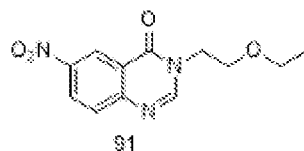


(viii) cyclizing the compound selected from the group consisting of **2**, **80**, **86**, **90**, **95**, **100**, **128**, **132**, **136**, **140**, **144**, **148**, **152**, **156**, **160**, **164**, **168**, **172**, **176**, **180**, **184**, **189**, and **337** obtained in step (i) and (ii) using a cyclizing agent selected from trimethylorthoformate or triethylorthoformate at 100 °C for 12-16 hours to obtain a compound selected from the group consisting of **3**, **81**, **87**, **91**, **96**, **101**, **129**, **133**, **137**, **141**, **145**, **149**, **153**, **157**, **161**, **165**, **169**, **173**, **177**, **181**, **185**, **190** and **338**;

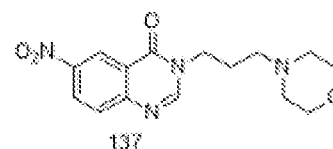
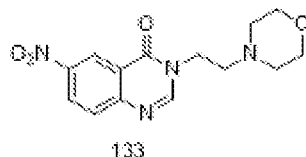
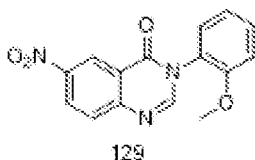
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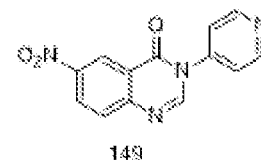
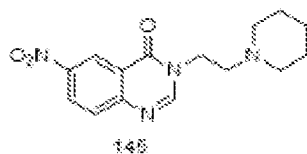
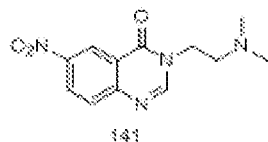
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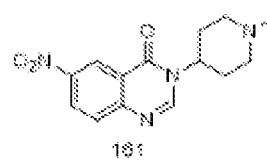
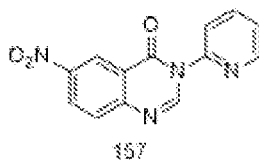
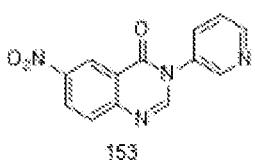
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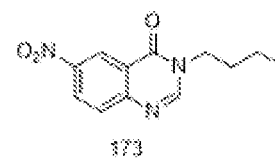
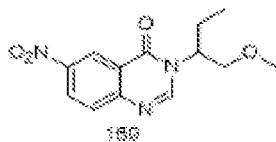
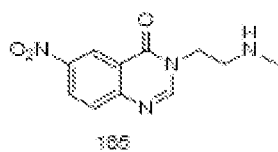


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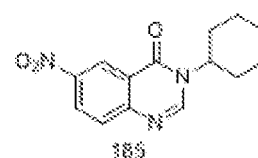
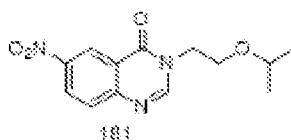
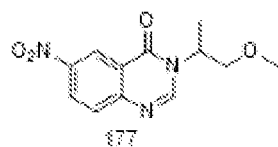


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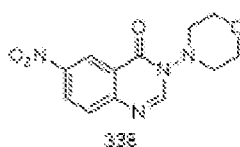
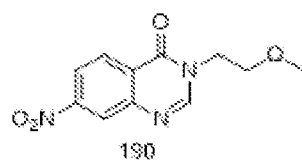




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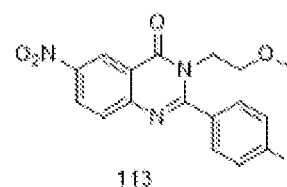
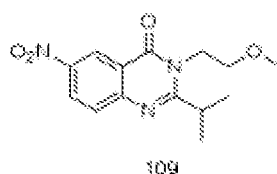
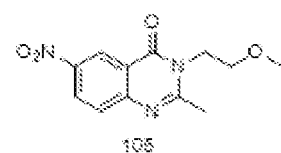
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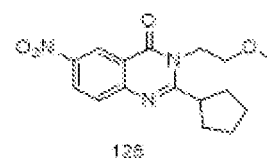
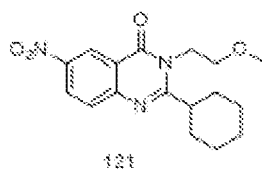
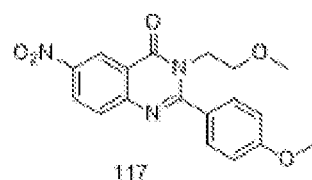
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- (ix) cyclizing the compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, 228, 278, 282, 286, 296, 326, and 326a** obtained in step (iii), (iv), (v), (vi) and (vii) using a cyclizing agent $ZnCl_2$ and hexamethyldisilazane (HMDS) in DMF at 100 °C for 12 -16 hours to obtain a compound selected from the group consisting of **105, 109, 113, 117, 121, 125, 201, 205, 209, 213, 217, 221, 225, 229, 279, 283, 287, 297, 327 and 327a**;

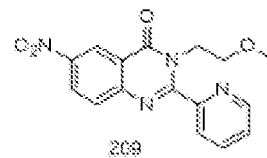
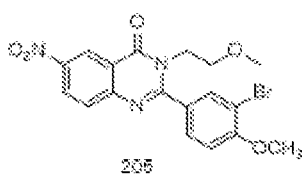
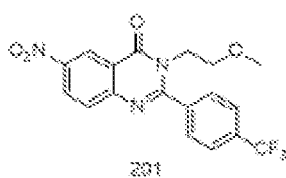
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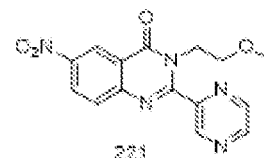
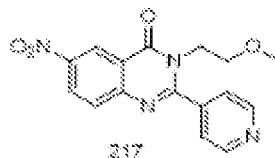
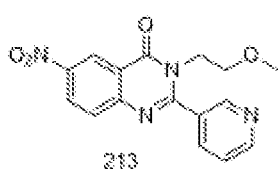
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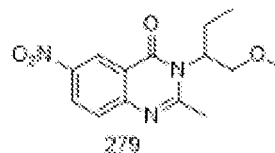
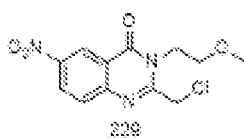
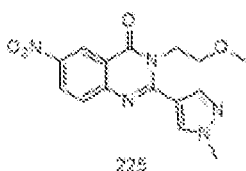
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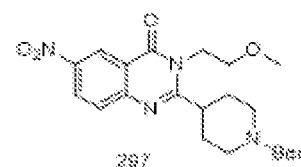
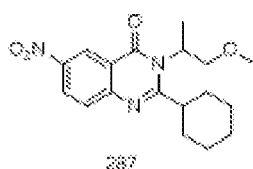
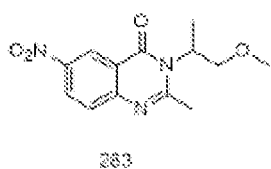
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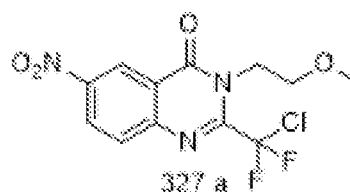
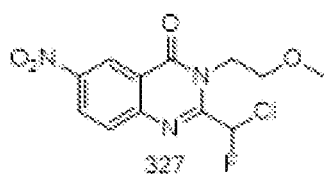
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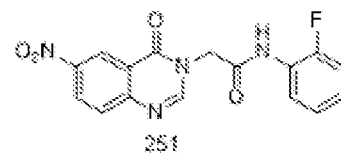
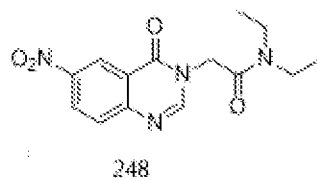
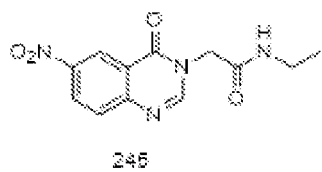
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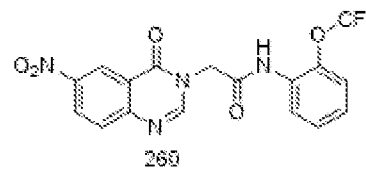
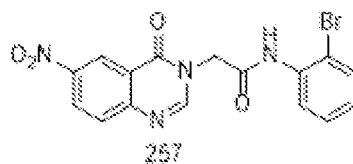
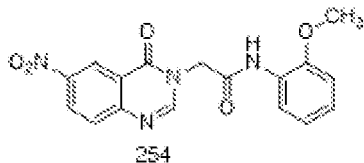
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- (x) reacting the compound **81** obtained in step (viii) with an amine selected from the group consisting of ethyl amine, diethylamine, 2-fluoroaniline, *o*-anisidine, 2-bromoaniline, 2-(trifluoromethoxy)aniline, 2-(trifluoromethyl)aniline, *p*-anisidine, 4-fluoroaniline, 1-(2-aminoethyl)-4-methylpiperazine, and 1*H*-Imidazole-1-ethanamine in presence of anhydrous AlCl₃ in toluene at a temperature range from room temperature to 110 °C to obtain a compound selected from the group consisting of **245**, **248**, **251**, **254**, **257**, **260**, **263**, **266**, **269**, **272** and **275**;

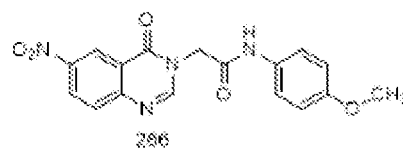
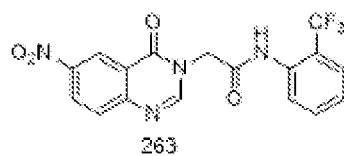
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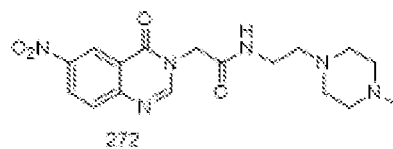
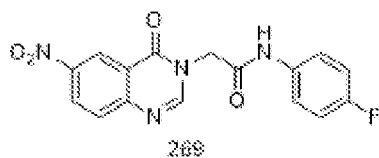
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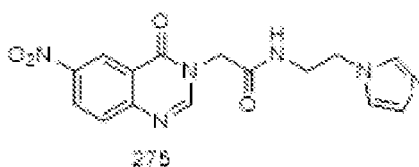
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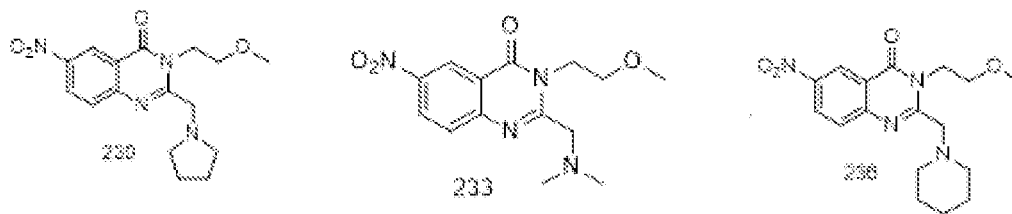
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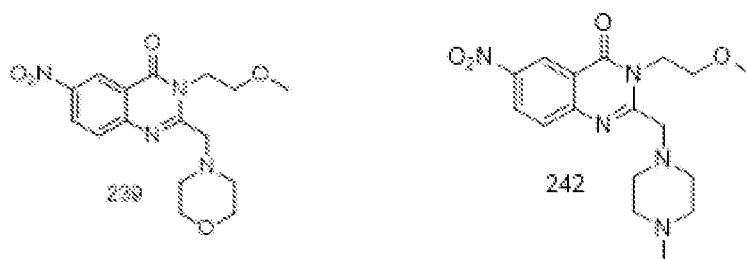
- (xi) reacting the compound **229** obtained in step (ix) with an amine selected from the group consisting of pyrrolidine, dimethylamine, piperidine, morpholine, and 1-methylpiperazine in toluene at 100 °C for 2 hours to obtain a compound selected from the group consisting of **230**, **233**, **236**, **239**, and **242**;

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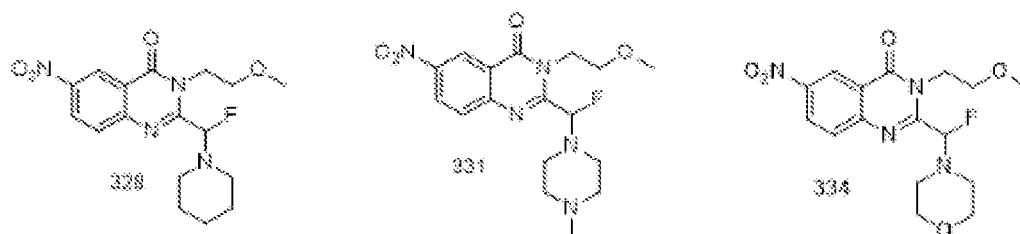
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- (xii) reacting the compound **327** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of toluene to obtain a compound selected from the group consisting of **328**, **331**, and **334**;

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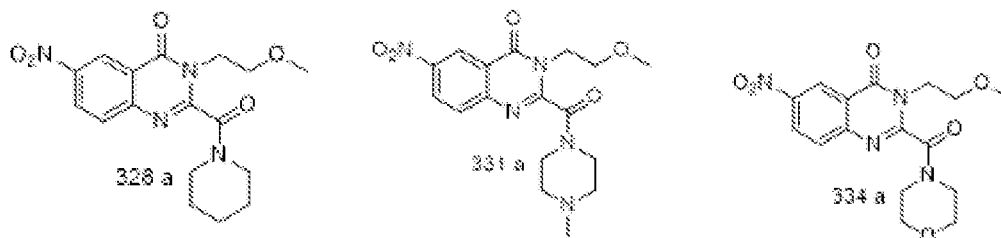


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- (xiii) reacting the compound **327a** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of a solvent selected from the group consisting of toluene, DMF, and THF in absence or presence of a base selected from K_2CO_3 , or *N,N*-diethylaniline to obtain a compound selected from the group consisting of **328a**, **331a**, and **334a**;

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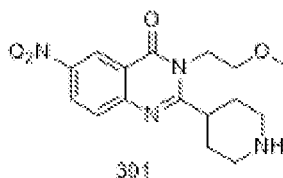
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- (xiv) separately reacting the compound **297** obtained in step (ix) with trifluoroacetic acid (TFA) in DCM at a temperature range of 0 °C to room temperature for 2 hours to obtain a compound **301**;

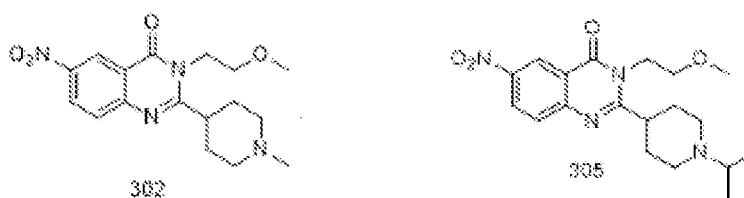
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- (xv) reacting the compound **301** obtained in step (xiv) with sodium hydride (NaH) in DMF at a temperature range of 0 °C to room temperature for 3 hours with methyl iodide and 2-chloropropane, respectively to obtain a compound selected from the group consisting of **302** and **305**;

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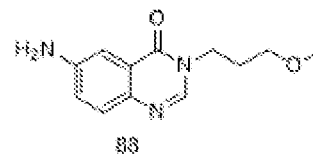
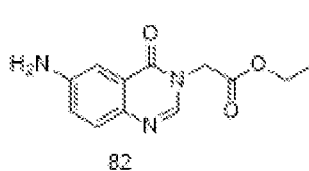
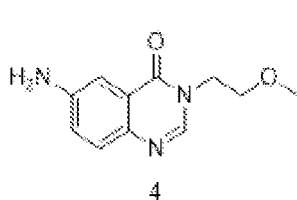


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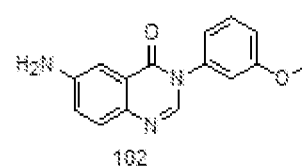
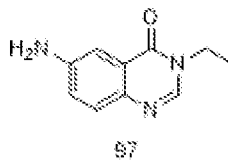
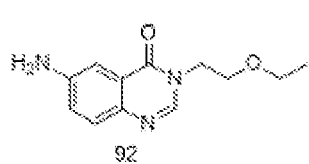
- (xvi) reducing the compound selected from the group consisting of **3**, **81**, **87**, **91**, **96**, **101**, **105**, **109**, **113**, **117**, **121**, **125**, **129**, **133**, **137**, **141**, **145**, **149**, **153**, **157**, **161**, **165**, **169**, **173**, **177**, **181**, **185**, **190**, **201**, **209**, **213**, **217**, **221**, **225**, **230**, **233**, **236**, **239**, **242**, **245**, **248**, **251**, **254**, **260**, **263**, **266**, **269**, **272**, **275**, **279**, **283**, **287**, **297**, **302**, **305**, **328**, **328a**, **331**, **331a**, **334**, **334a** and **338** obtained in steps (viii), (ix), (x), (xi), (xii), (xiii) and (xv) using Palladium-Charcoal (5% or 10 % wet) at room temperature for 3-5 hours in presence of H₂ to obtain an amine compound selected

from the group consisting of 4, 82, 88, 92, 97, 102, 106, 110, 114, 118, 122, 126,
130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 191,
202, 210, 214, 218, 222, 226, 231, 234, 237, 240, 243, 246, 249, 252, 255, 261,
264, 267, 270, 273, 276, 280, 284, 288, 298, 303, 306, 329, 329a, 332, 332a, 335,
335a, and 339;

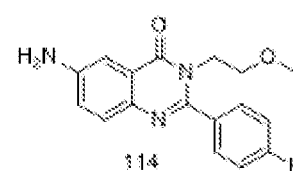
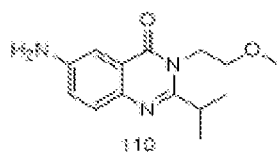
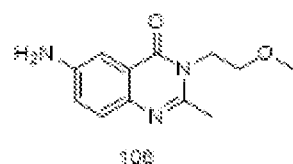
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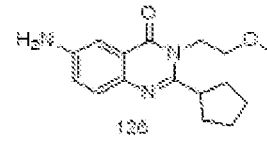
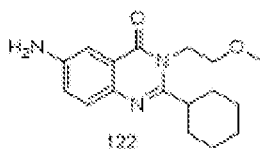
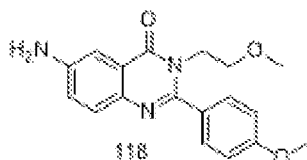
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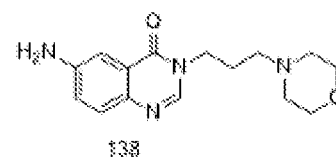
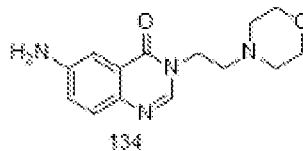
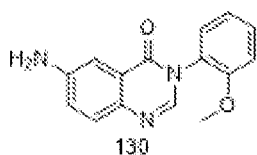
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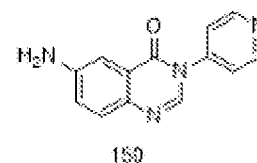
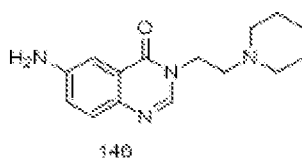
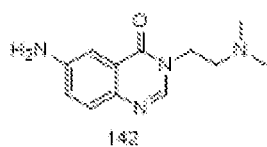
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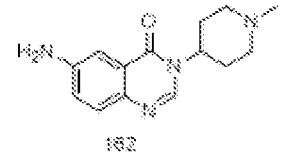
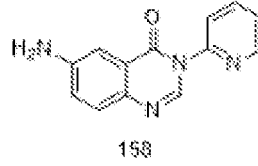
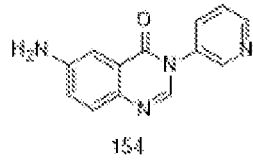
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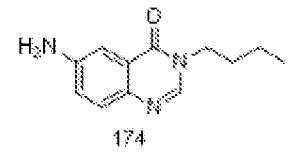
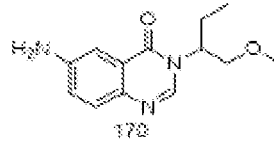
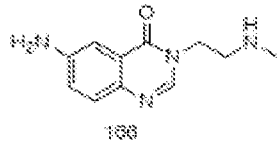
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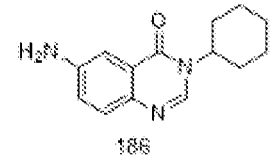
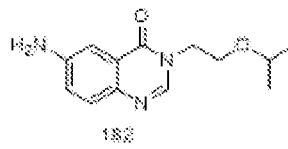
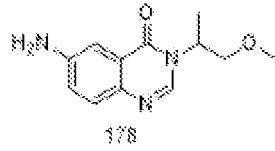
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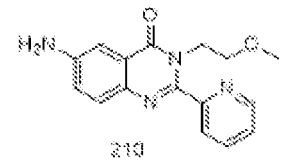
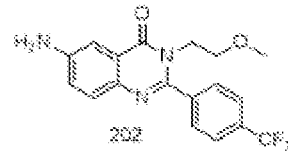
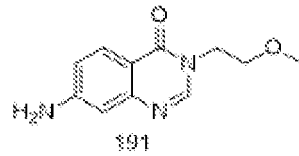
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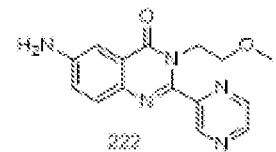
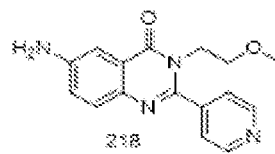
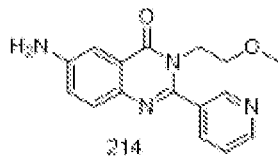
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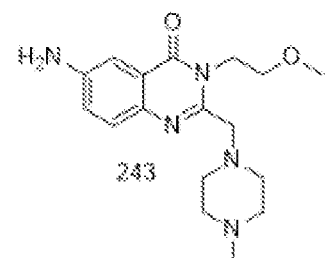
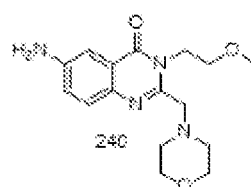
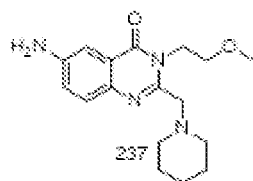
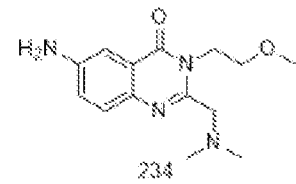
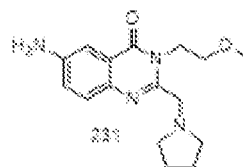
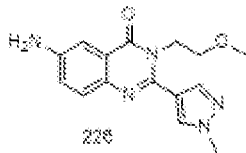
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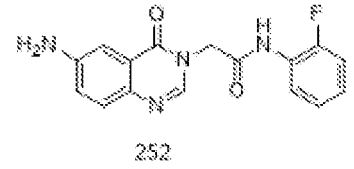
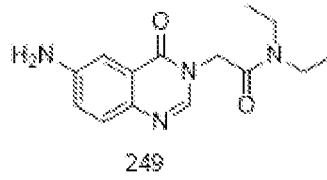
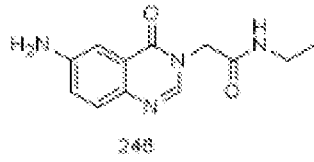
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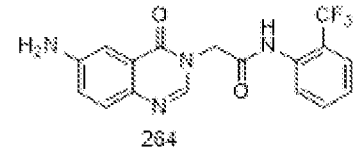
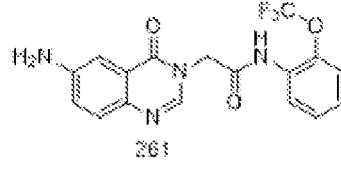
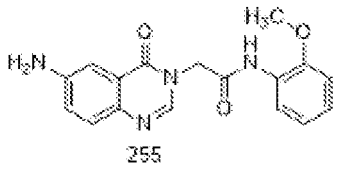
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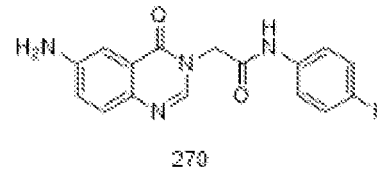
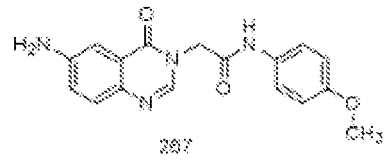
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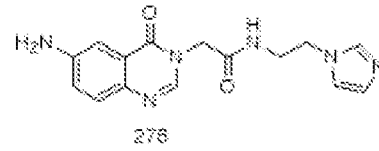
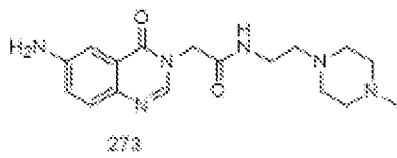
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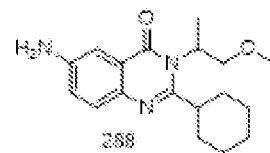
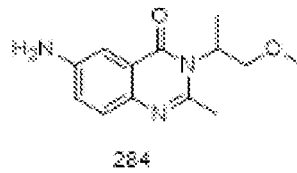
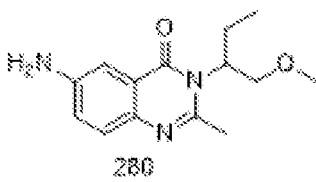
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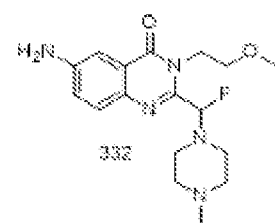
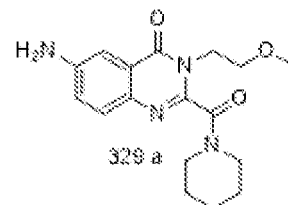
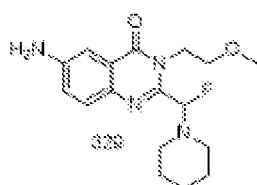
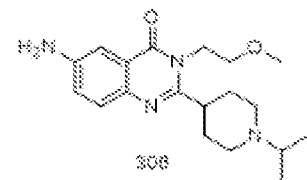
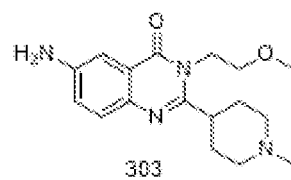
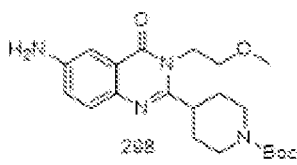
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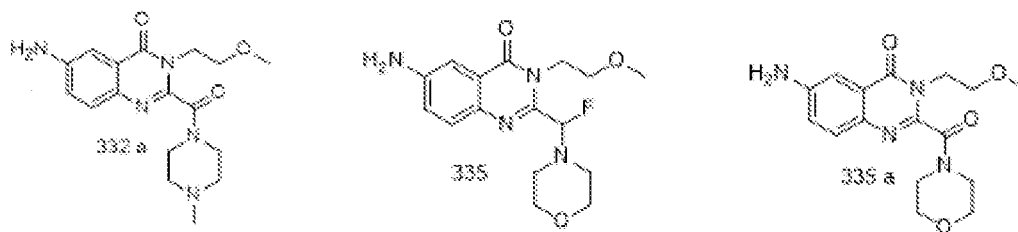


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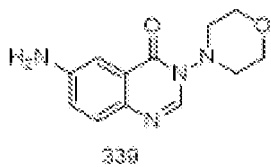


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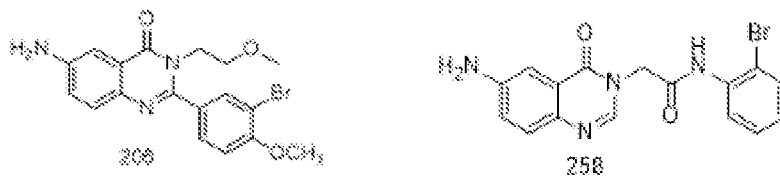
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(xvii) reducing the compound selected from **205** or, **257** obtained in step (ix) and (x) using $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ to obtain the compound selected from **206** or **258**;

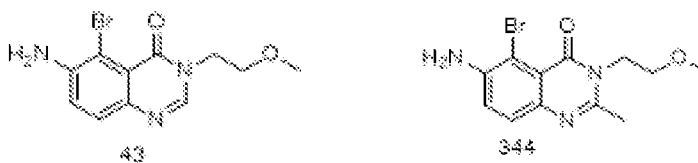
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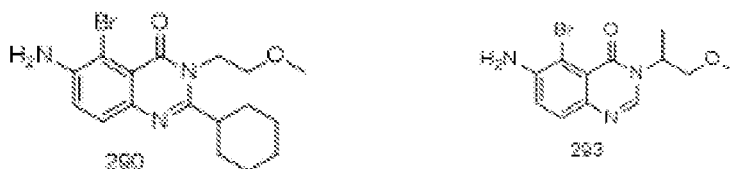
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(xviii) brominating the compound selected from the group consisting of **4**, **106**, **122**, and **178** obtained in step (xvi) diluted in dichloromethane or chloroform solution by carrying out reaction in acetic acid medium followed by drop wise addition of liquid bromine on the compound at room temperature for 3-4 hours to obtain a compound selected from the group consisting of **43**, **344**, **290**, and **293**;

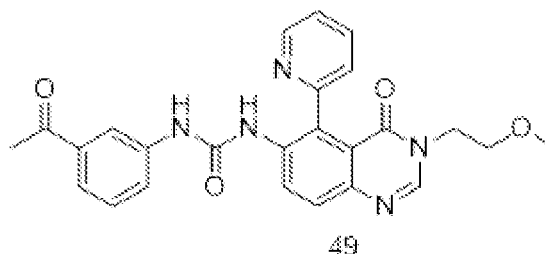
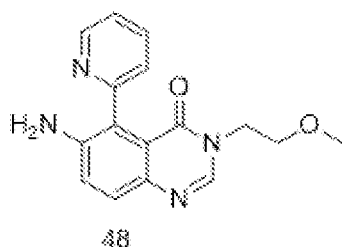
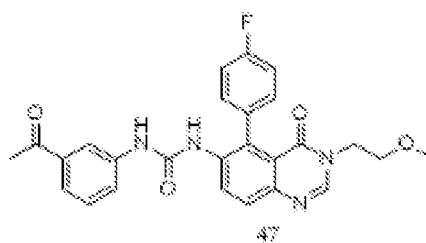
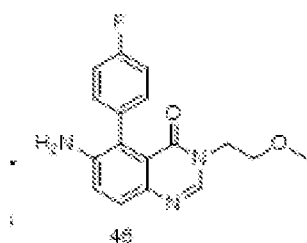
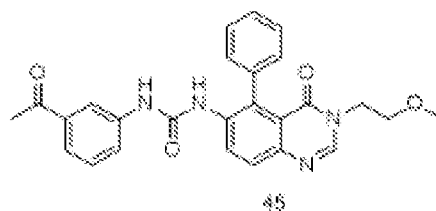
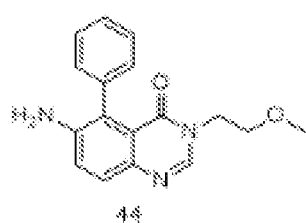
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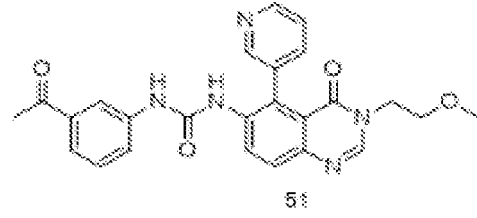
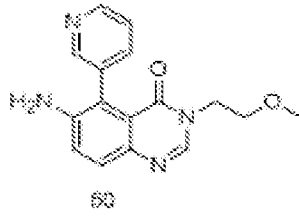
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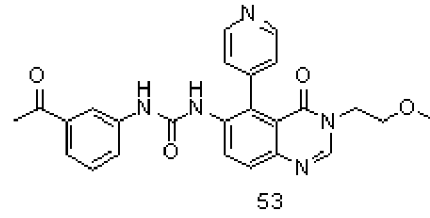
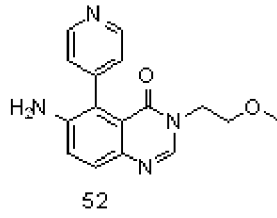
- (xix) carrying out Suzuki reaction on a compound selected from the group consisting of **43**, **290**, and **293** obtained in step (xviii) by $\text{Pd}_2(\text{dba})_3$ or $\text{Pd}(\text{PPh}_3)_4$ in presence of Cs_2CO_3 or $2\text{M Na}_2\text{CO}_3$ solution in dioxane and X-Phos as a ligand at 100°C over a period of 10-12 hours along with a boronic acid selected from the group consisting of benzenboronic acid, 4-fluorobenzenboronic acid, pyridine-2-boronic acid, pyridine-3-boronic acid, pyridine-4-boronic acid, 6-methoxypyridine-3-boronic acid, 2-methoxypyridine-3-boronic acid, (1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)boronic acid, 4-methoxybenzenboronic acid, 4-trifluoromethylbenzenboronic acid, cyclohexylboronic acid, cyclopentyl boronic acid, and isopropylboronic acid to obtain a compound selected from the group consisting of **44**, **46**, **48**, **50**, **52**, **54**, **56**, **58**, **63**, **65**, **67**, **69**, **71**, **291**, and **294** which is treated with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 5-8 hours to obtain the compound having structure I selected from the group consisting of **45**, **47**, **49**, **51**, **53**, **55**, **57**, **59**, **64**, **66**, **68**, **70**, **72**, **292**, and **295**;



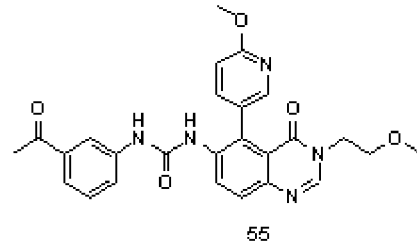
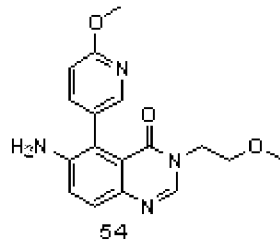
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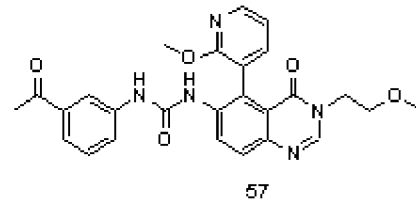
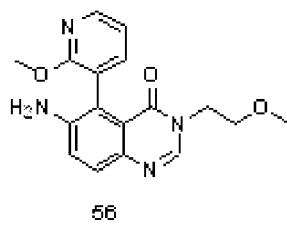
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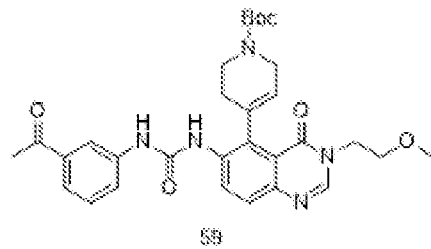
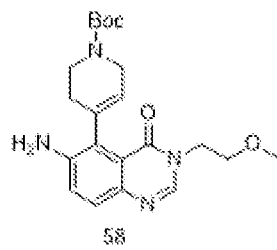
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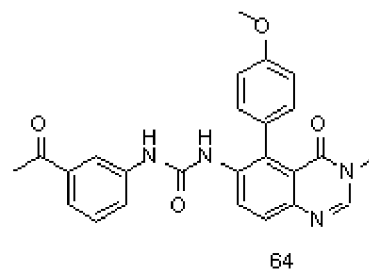
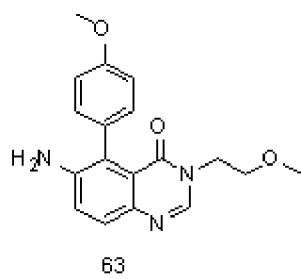
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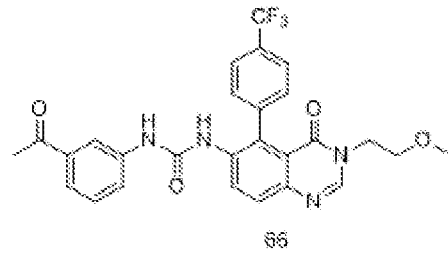
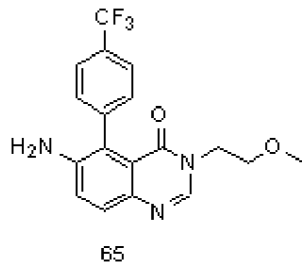
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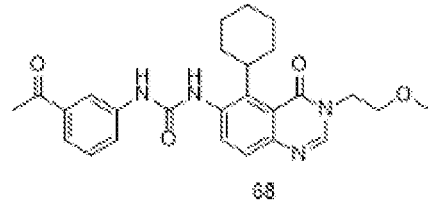
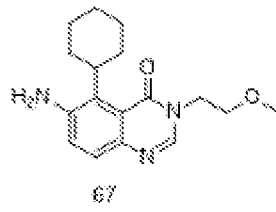
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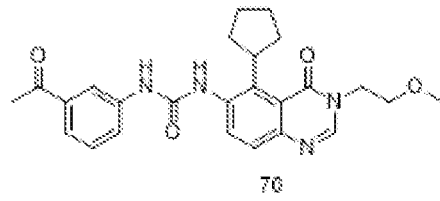
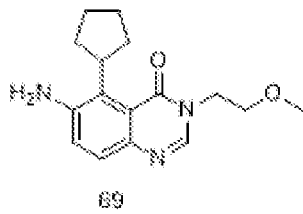
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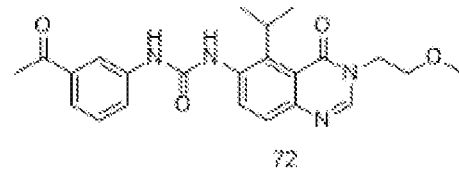
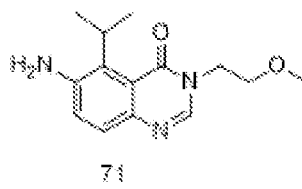
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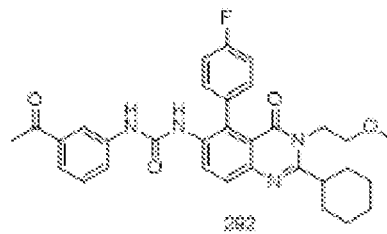
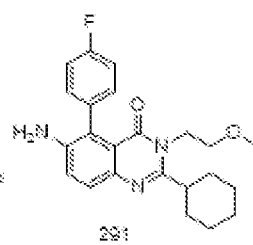
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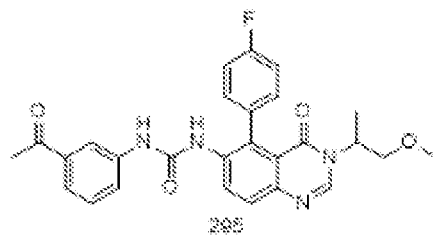
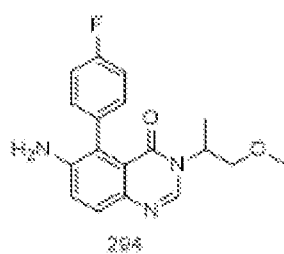
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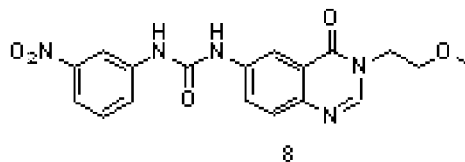
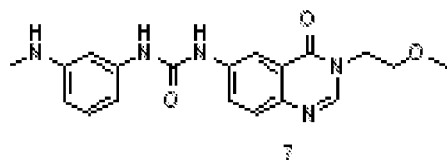
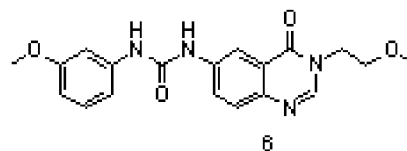
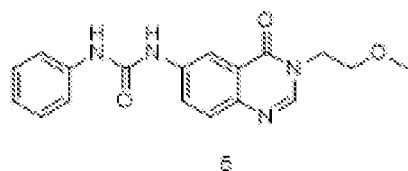
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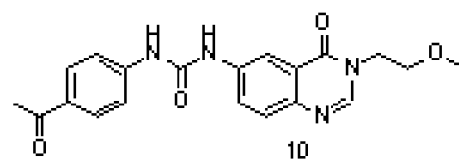
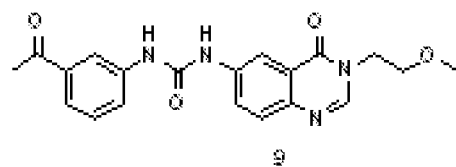


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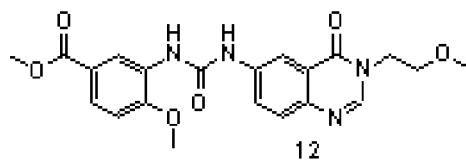
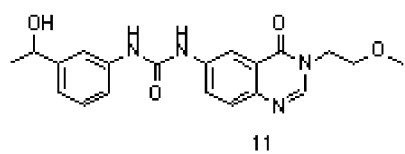


(xx) alternately, treating compound **4** obtained in step (xvi) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of aniline, m-anisidine, N1-methylbenzene-1,3-diamine, m-nitroaniline, 3-aminoacetophenone, 4-aminoacetophenone, 1-(3-aminophenyl)ethanol, methyl 3-amino-4-methoxybenzoate, 3-ethylaniline, 3'-aminobenzophenone, 3-amino-N-cyclohexylbenzamide, methyl 2-(3-aminobenzamido)-3-methylbutanoate, 3-amino-N,N-dimethylbenzamide, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 3-(benzo[d]oxazol-2-yl)aniline, N-(3-aminophenyl)acetamide, N-(3-aminophenyl)-N-methylacetamide, N-(3-aminophenyl)-N-benzylacetamide, N-(3-aminobenzyl)acetamide, N-(3-aminobenzyl)-N-methylacetamide, dimethylamine, piperdine, 4-amino-1-methylpiperdine, 4-benzylpiperidine, 1-benzylpiperidin-4-amine, 1-(3-amino-4-hydroxyphenyl)ethanone, 1-(3-amino-5-chloro-2-hydroxyphenyl)ethanone, 1-(3-amino-2-hydroxy-5-methylphenyl)ethanone, 1-(3-aminophenyl)-2,2,2-trifluoroethanol in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, and 34**;

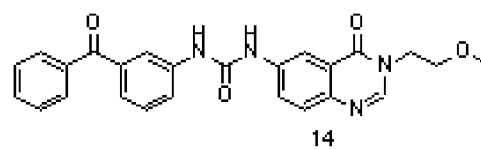
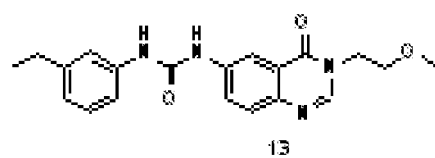




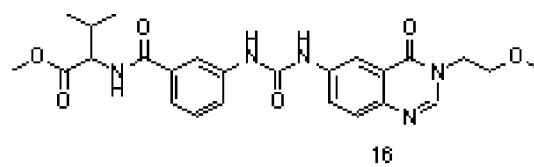
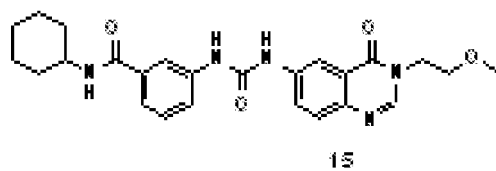
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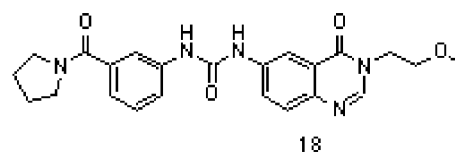
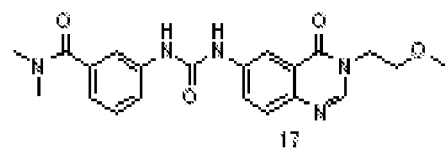
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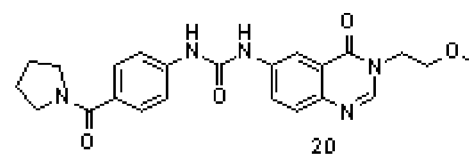
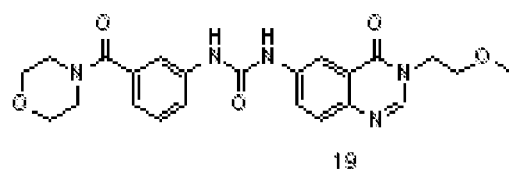
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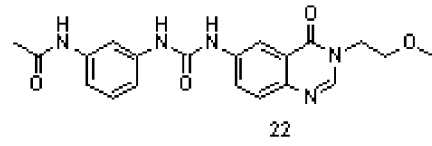
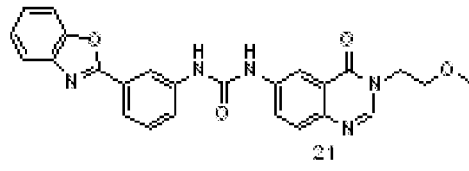


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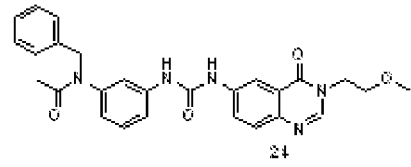
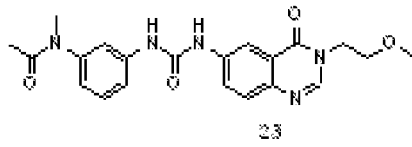


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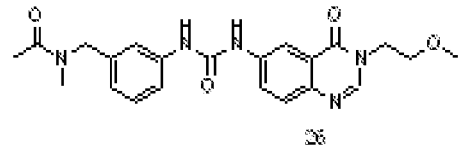
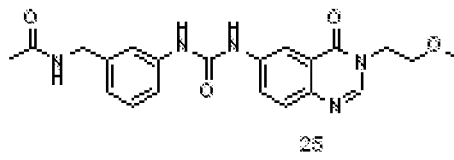




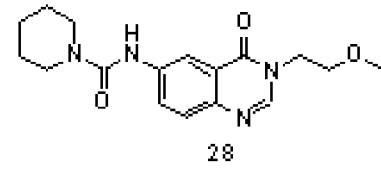
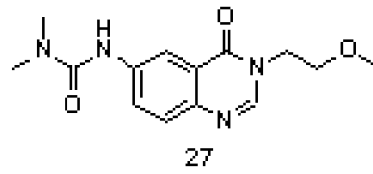
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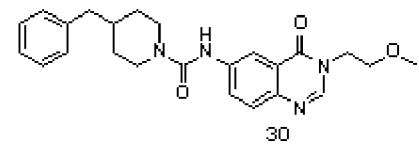
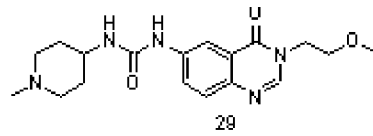
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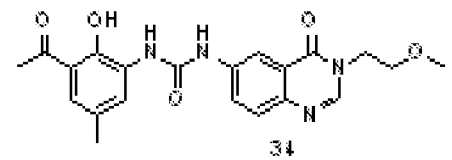
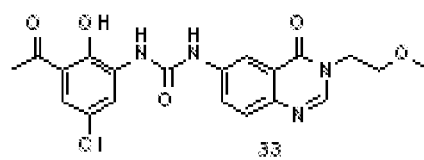
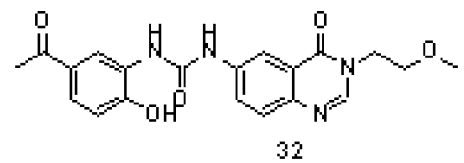
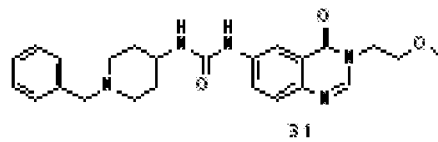
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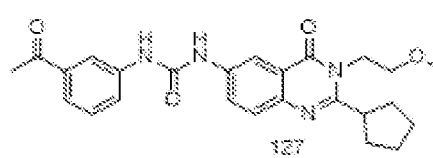
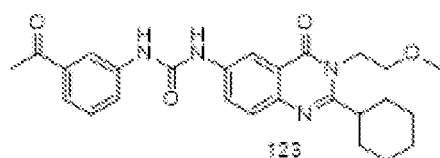
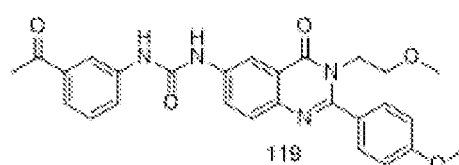
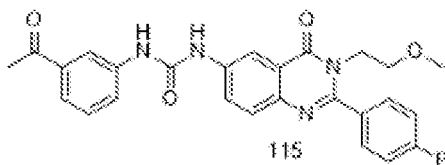
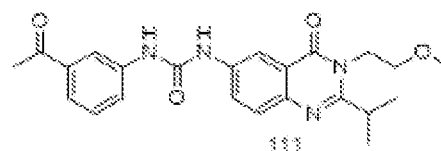
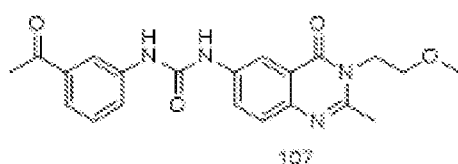
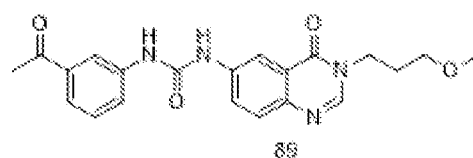
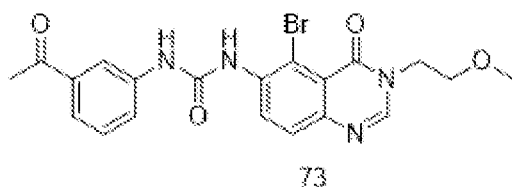
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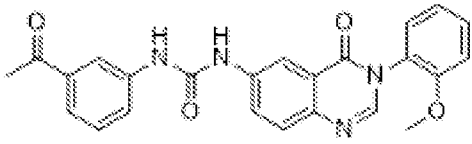
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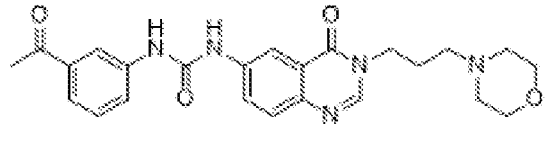
(xxi) alternately, treating the compound selected from the group consisting of **43**, **88**, **106**, **110**, **114**, **118**, **122**, **126**, **130**, **138**, **150**, **154**, **158**, **162**, **166**, **170**, **174**, **178**, **182**, **186**, **191**, **202**, **206**, **210**, **214**, **218**, **222**, **226**, **231**, **234**, **237**, **240**, **243**, **246**, **249**, **252**, **255**, **258**, **261**, **264**, **267**, **270**, **273**, **276**, **280**, **284**, **288**, **298**, **303**, **306**, **329**, **329a**, **332**, **332a**, **335**, **335a**, **339**, and **344** obtained in step (xvi), (xvii) and (xviii) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **73**, **89**, **107**, **111**, **115**, **119**, **123**, **127**, **131**, **139**, **151**, **155**, **159**, **163**, **167**, **171**, **175**, **179**, **183**, **187**, **192**, **193**, **194**, **195**, **196**, **197**, **198**, **199**, **203**, **207**, **211**, **215**, **219**, **223**, **227**, **232**, **235**, **238**, **241**, **244**, **247**, **253**, **256**, **259**, **262**, **268**, **274**, **277**, **281**, **285**, **289**, **304**, **307**, **330**, **330a**, **333**, **333a**, **336**, **336a**, **340**, and **345**;



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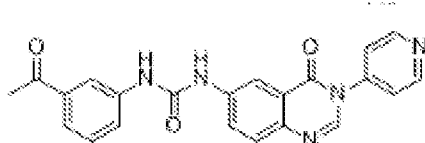


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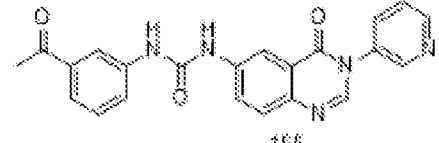


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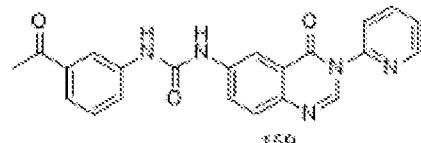


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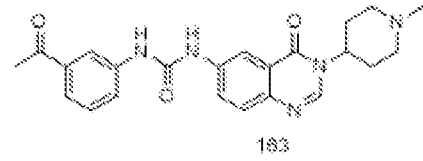


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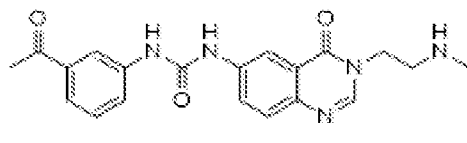


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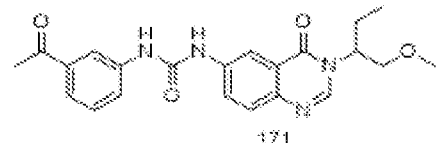


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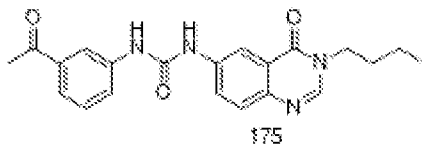


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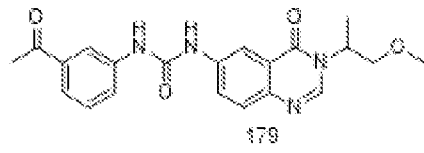


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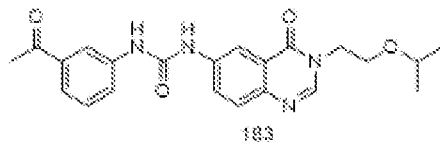


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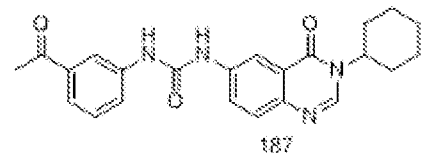


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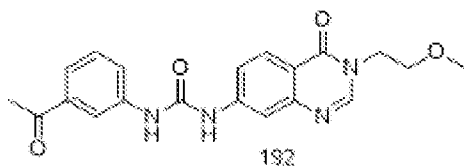
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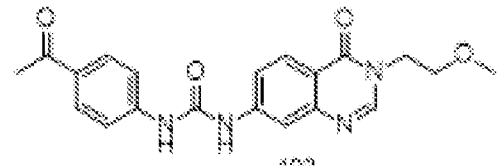
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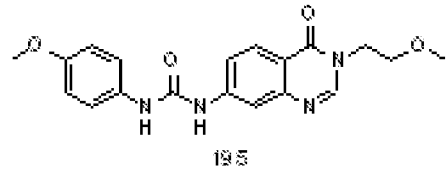
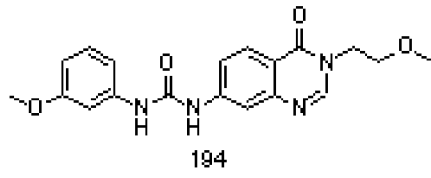
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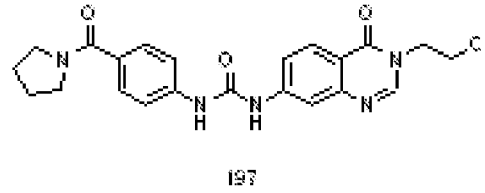
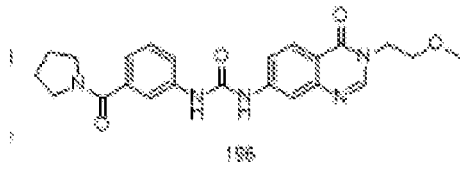
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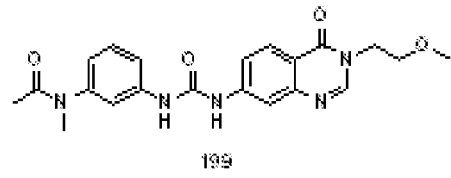
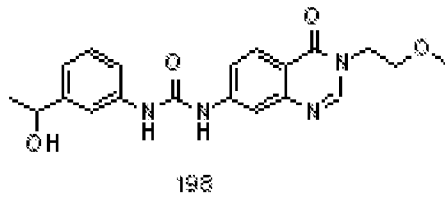
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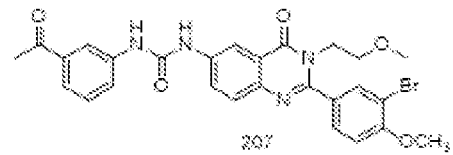
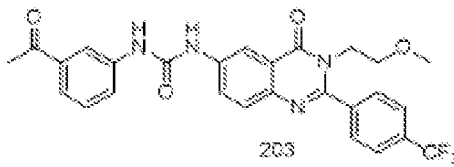
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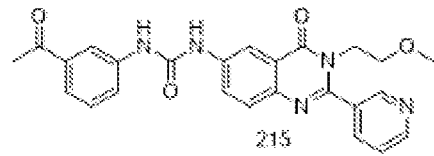
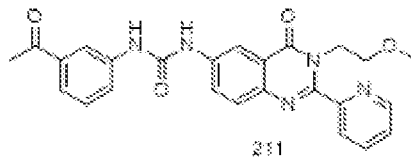
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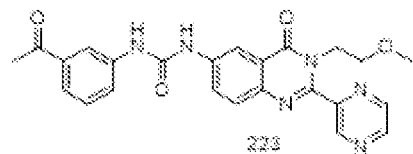
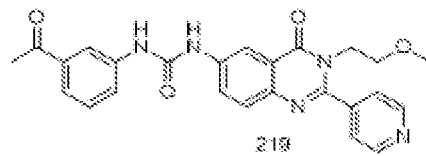
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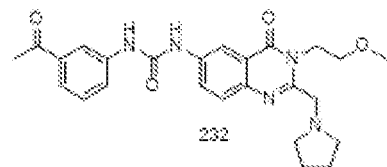
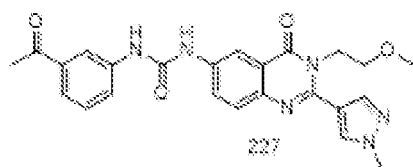
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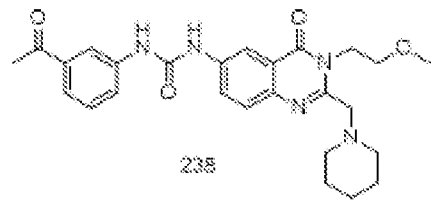
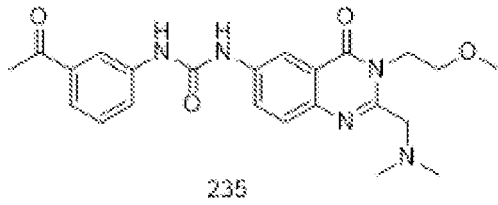
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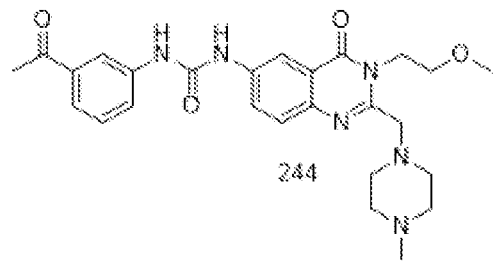
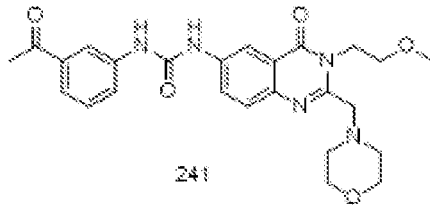
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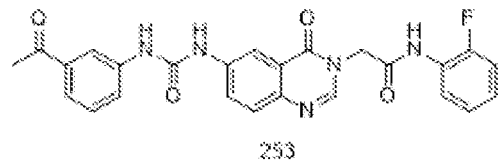
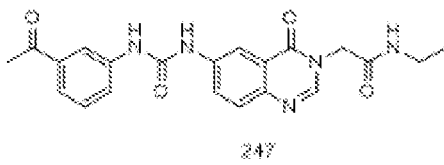
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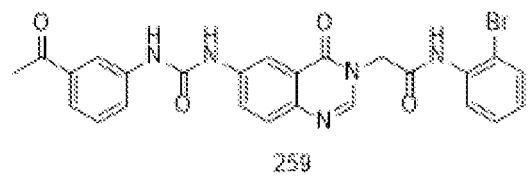
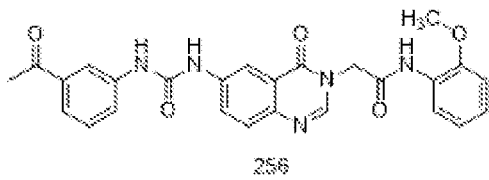
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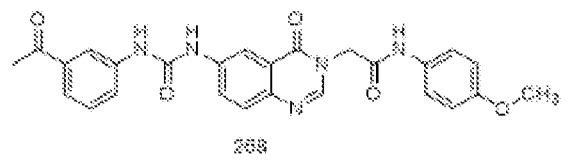
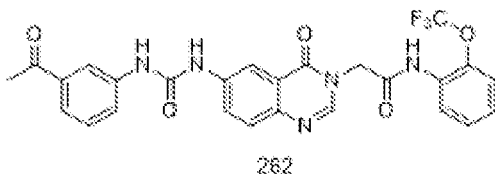
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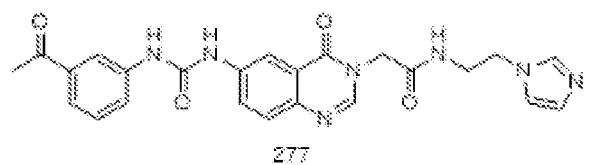
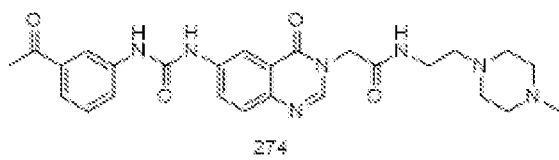
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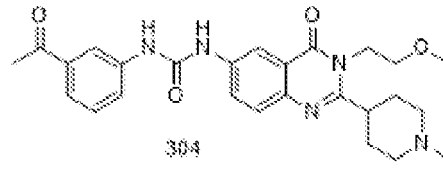
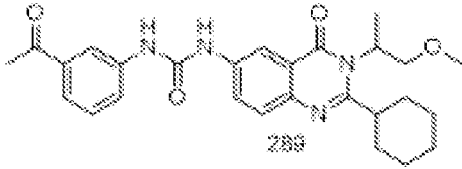
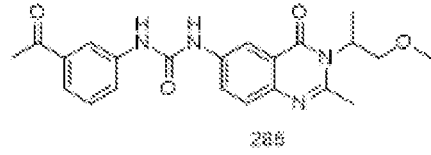
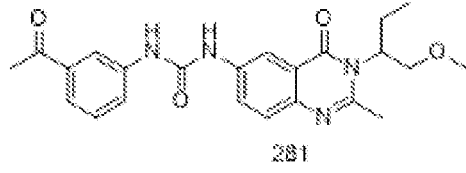
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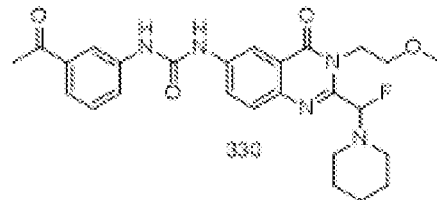
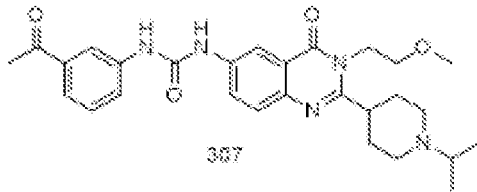
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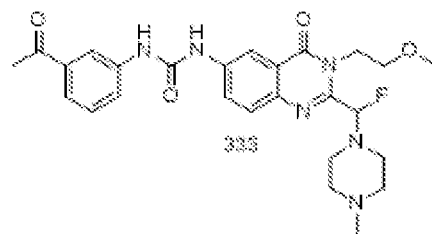
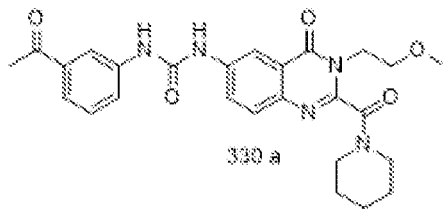
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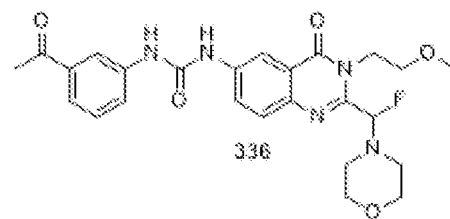
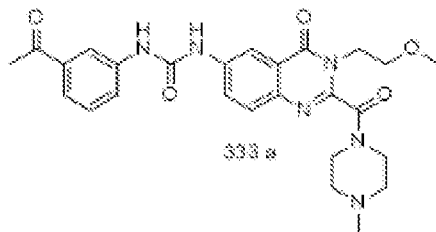
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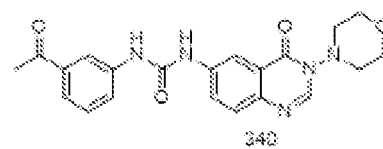
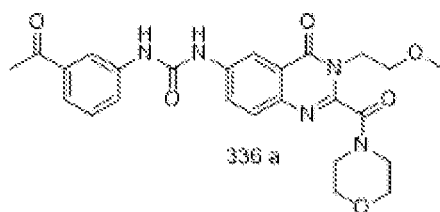
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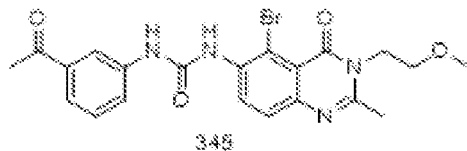


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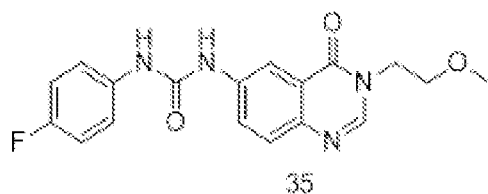




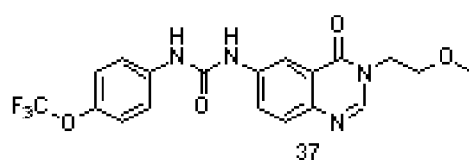
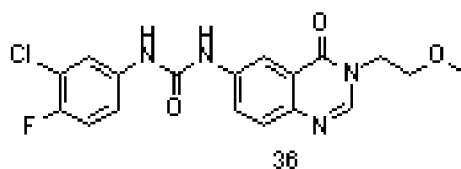
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(xxii) alternately, treating the compound selected from the group consisting of **4, 82, 92, 97, 102, 134, 142, and 146** obtained in step (xvi) with a substituted aromatic isocyanate selected from the group consisting of 4-fluorophenylisocyanate, 3-chloro-4-fluorophenylisocyanate, (4-trifluoromethoxy)phenylisocyanate, (4-trifluoromethyl)phenylisocyanate, (2-trifluoromethyl)phenylisocyanate, 4-methoxyphenylisocyanate, 2-methoxyphenylisocyanate, ethyl 3-isocyanatobenzoate, 3-acetylphenylisocyanate, and 4-acetylphenylisocyanate in presence of TEA as a base in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **35, 36, 37, 38, 39, 40, 41, 42, 83, 84, 85, 93, 94, 98, 99, 103, 135, 143, and 147**;

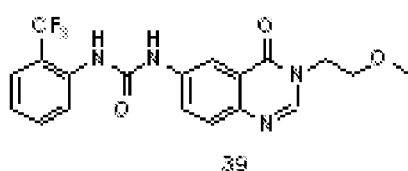
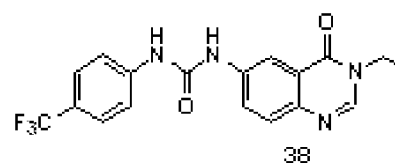
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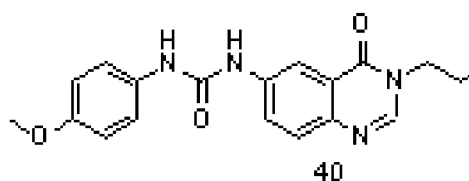
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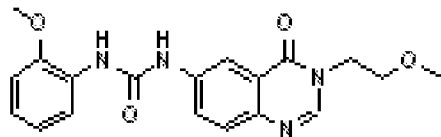


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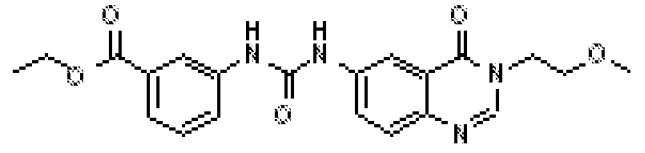


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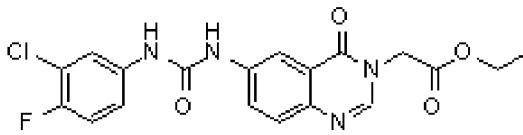




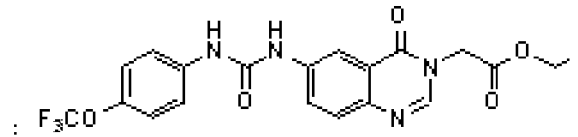
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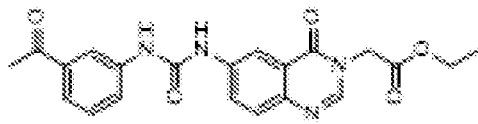


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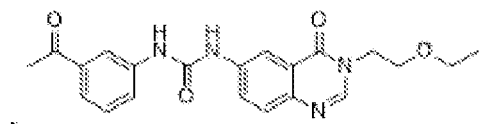


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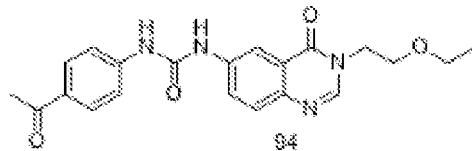


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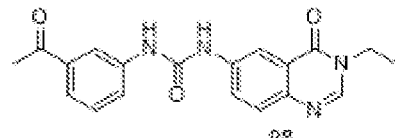


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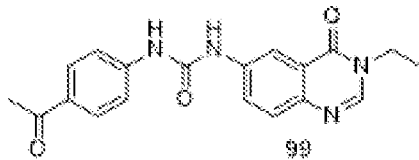


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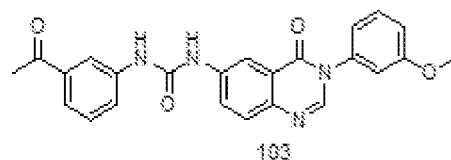


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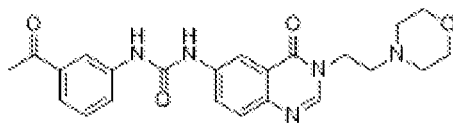


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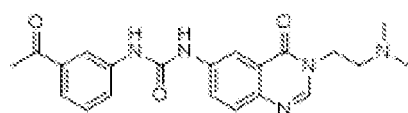


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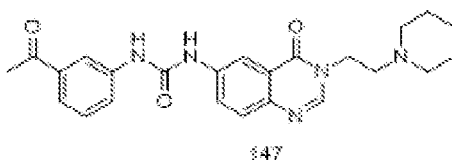
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135



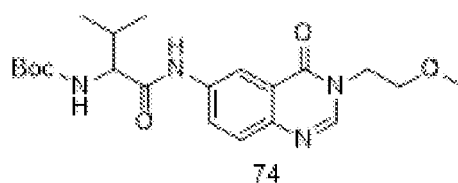
143



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(xxiii) alternately, reacting compound **4** obtained in step (xvi) with HATU/ TEA in DMF at room temperature with 5 hours of stirring to obtain a compound **74**;

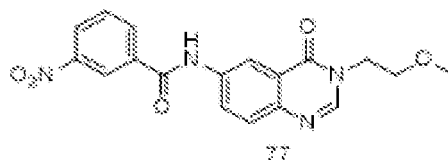
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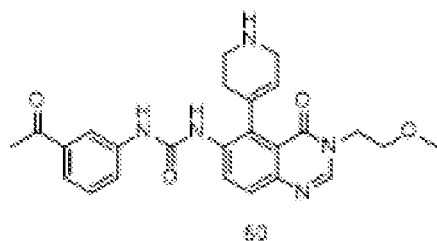
(xxiv) separately adding 3-nitrobenzoyl chloride (3-nitrobenzoic acid and Oxalyl Chloride) at 0 °C in DCM and TEA and stirring for 5 hours at room temperature to obtain a compound **77**;

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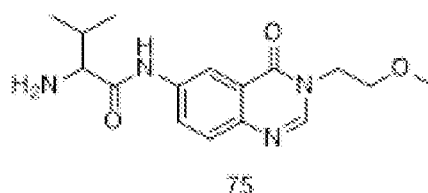


(xxv) separately Boc deprotecting the compound **59** obtained in step (xix) and the compound **74** obtained in step (xxiii) by TFA at room temperature for 2 hours to obtain a compound selected from **60** or **75**;

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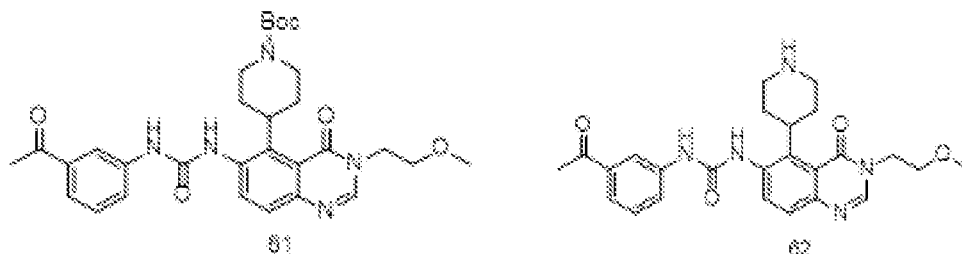


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(xxvi) treating the compound **59** obtained in step (xix) and compound **60** obtained in step (xxv) with H₂/ Pd-C (5% wet) to obtain the compound having structure I selected from the group consisting of **61** and **62**;

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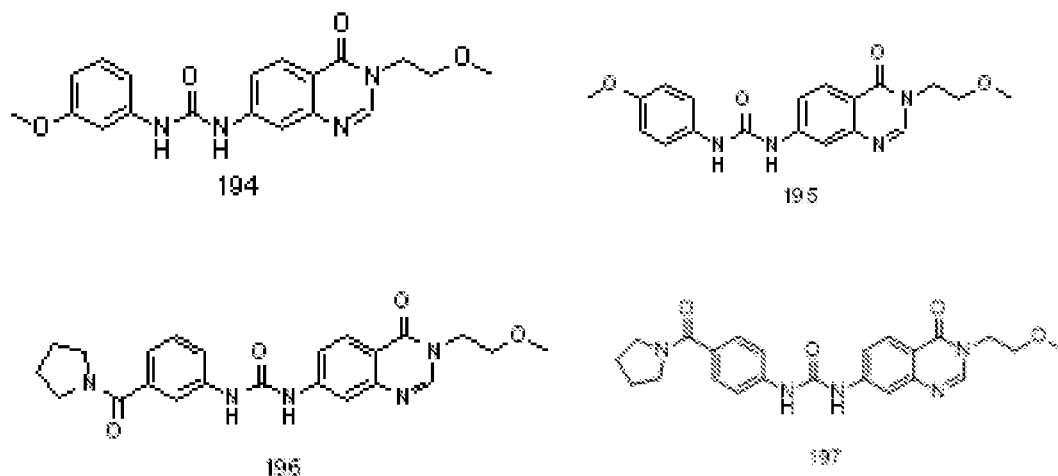
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(xxvii) alternately, treating the compound selected from the group consisting of **191**, **4**, **46**, **237**, **249**, **106**, **243**, and **252** obtained in step (xvi) and (xix) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of 3-aminoacetophenone, 4-aminoacetophenone, m-anisidine, p-anisidine, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 1-(3-aminophenyl)-2,2,2-trifluoroethanol, -(3-aminophenyl)-N-methylacetamide, 1-(3-(hydroxyamino)phenyl)ethanone, 1-(3-(methylamino)phenyl)ethanone, and 1-(3-aminophenyl)-2,2,2-trifluoroethanone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **194**, **195**, **196**, **197**, **198**, **199**, **308**, **309**, **310**, **311**, **312**, **313**, **314**, **315**, **316**, **317**, **318**, **319**, **320**, **321**, **322**, **323**, **324**, and **325**;

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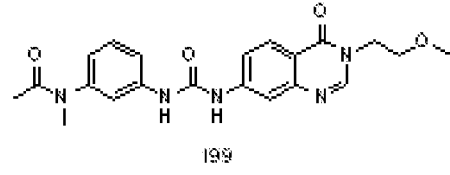
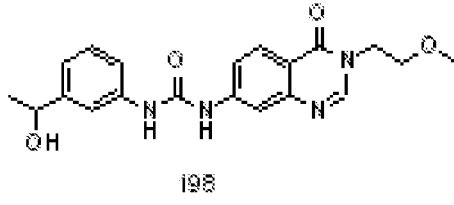
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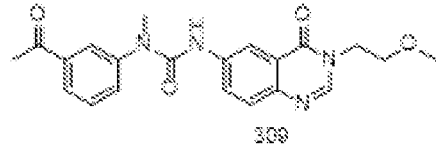
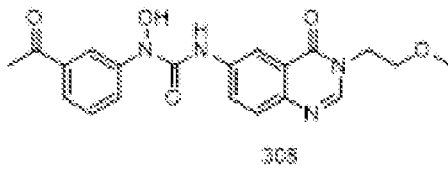


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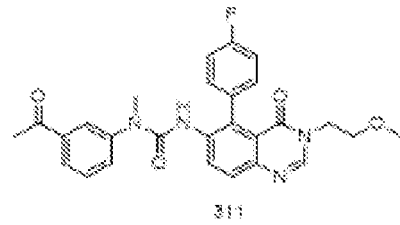
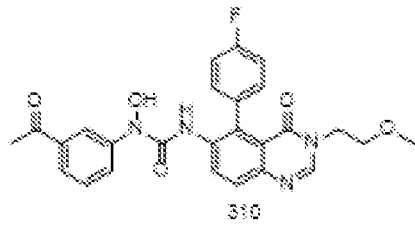
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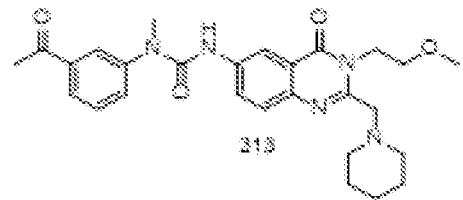
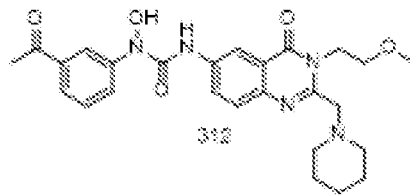
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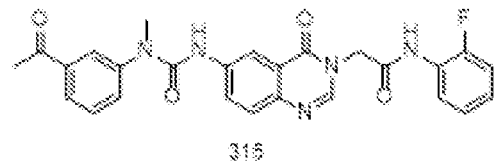
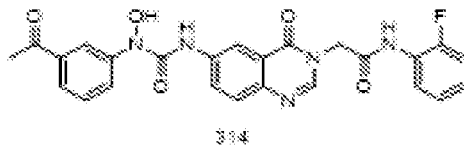
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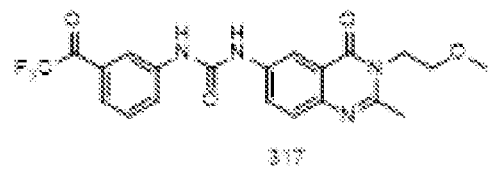
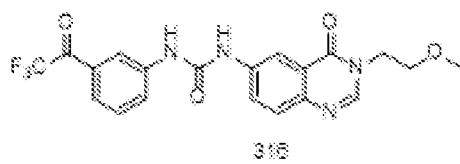
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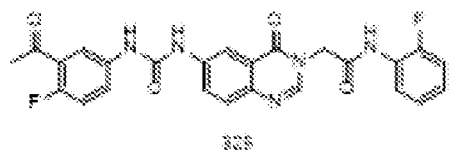
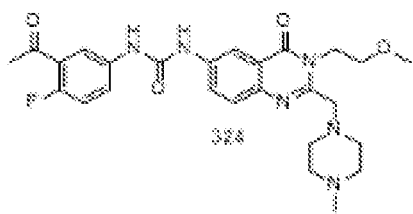
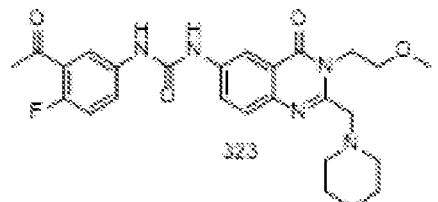
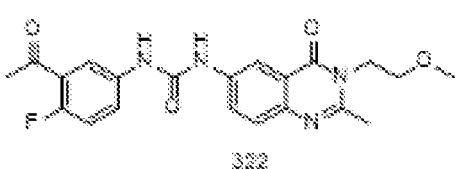
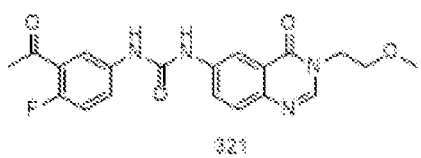
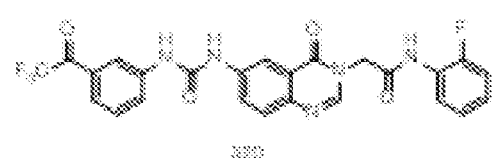
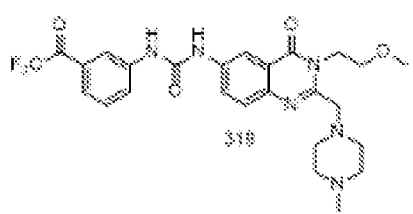
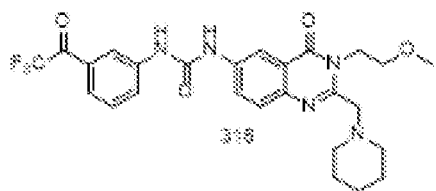
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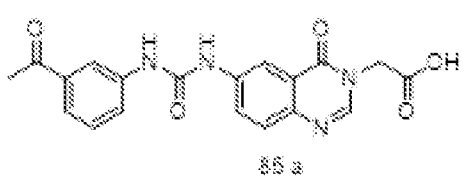
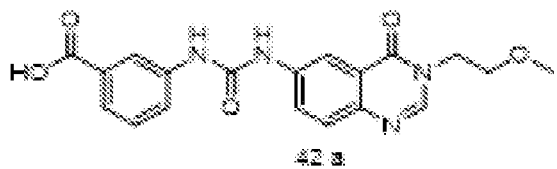


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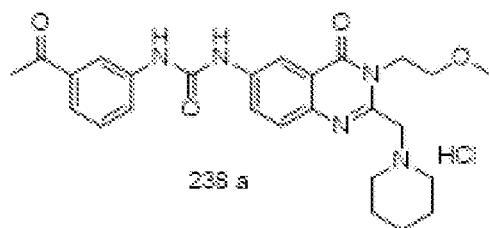
(xxviii)subjecting the compound selected from **42** and **85** obtained in step (xxii) to ester hydrolysis by LiOH monohydrate in presence of THF: EtOH: Water (3:2:1) proportion at room temperature for 1-2 hours to obtain the compound having structure I selected from the group consisting of **42a** and **85a**;

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(xxix) reacting the compound **238** obtained in step (xxi) with 1M HCl in dioxane to obtain the compound having structure I **238a**; and

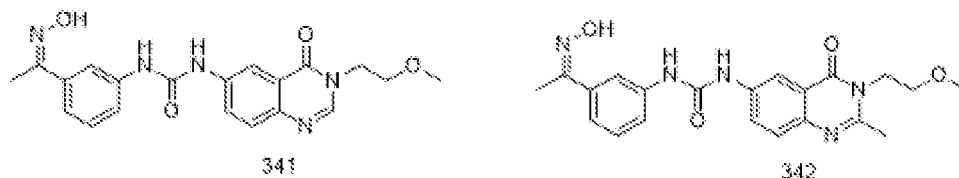
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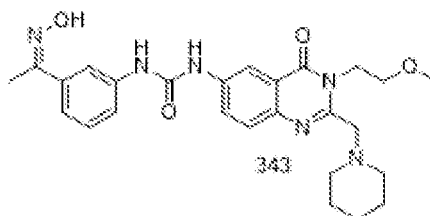
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(xxx) reacting the compound selected from the group consisting of **9**, **107**, and **238** obtained in step (xx) and (xxi) with hydroxylamine hydrochloride ($\text{NH}_2\text{OH} \cdot \text{HCl}$) in ethanol (EtOH) at 80 °C for 12- 16 hours to obtain the compound having structure I selected from the group consisting of **341**, **342** and **343**

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General procedure for urea formation via chloroformate intermediate

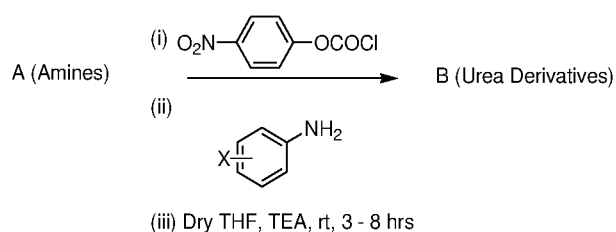
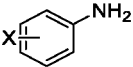
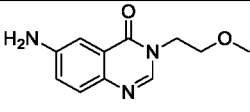
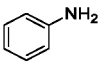
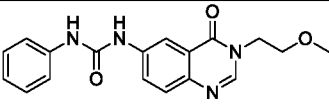
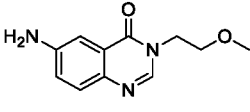
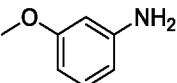
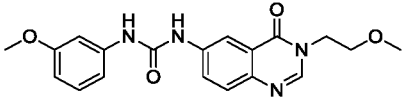
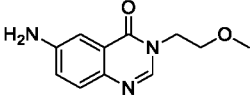
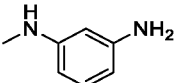
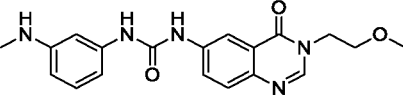
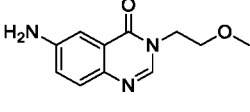
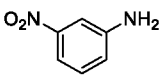
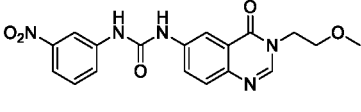
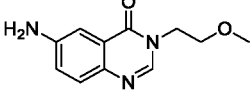
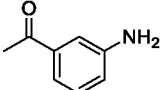
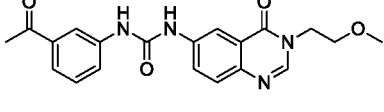
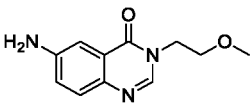
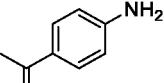
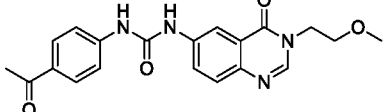
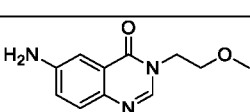
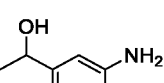
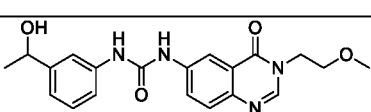
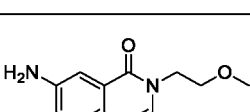
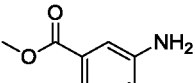
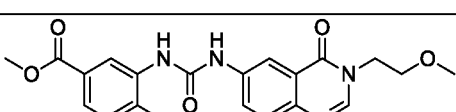
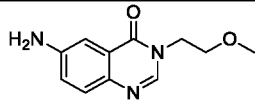
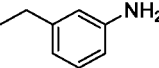
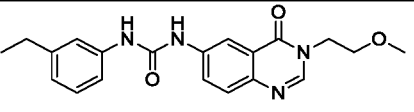
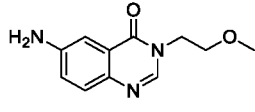
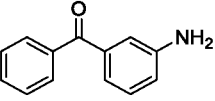
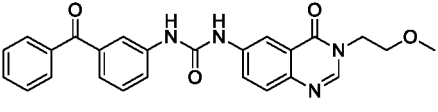
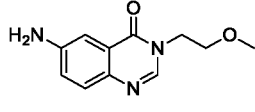
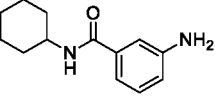
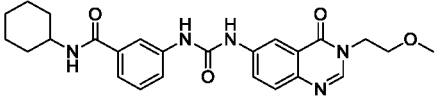
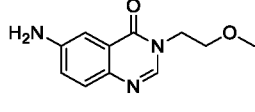
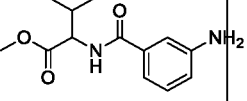
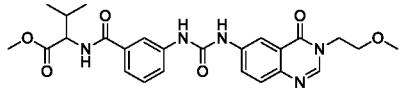
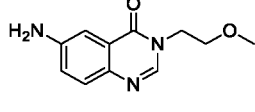
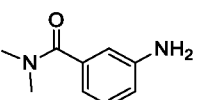
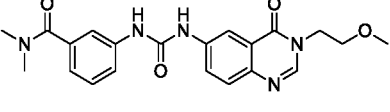
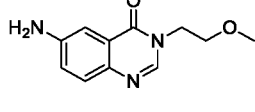
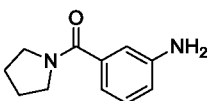
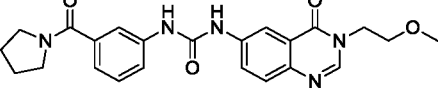
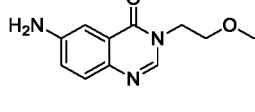
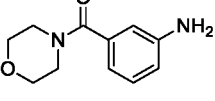
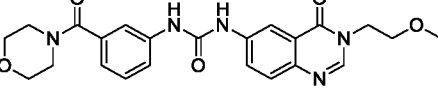
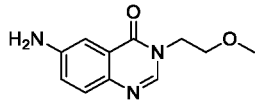
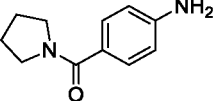
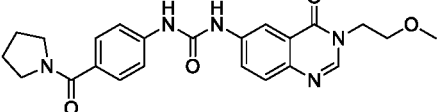
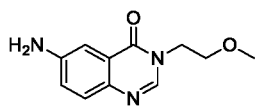
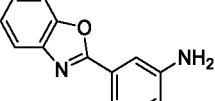
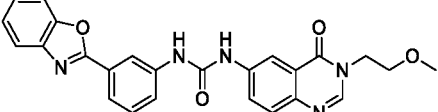


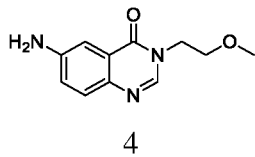
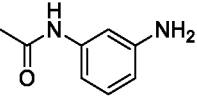
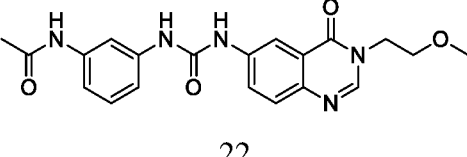
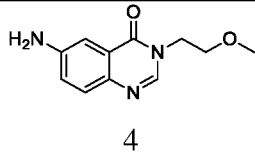
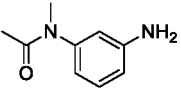
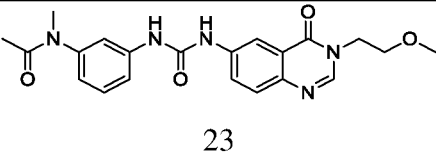
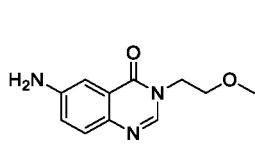
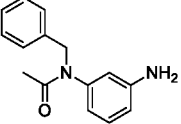
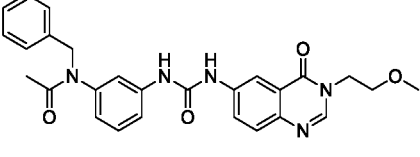
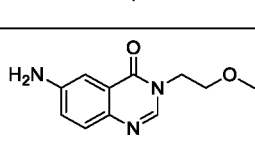
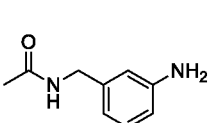
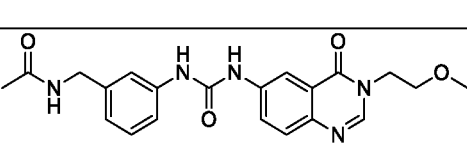
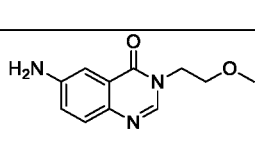
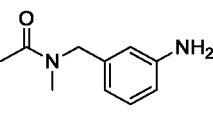
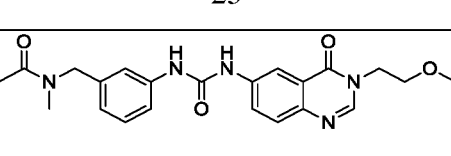
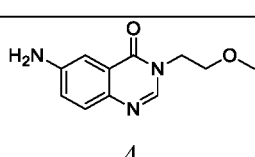
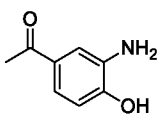
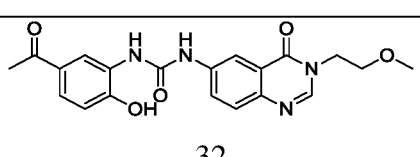
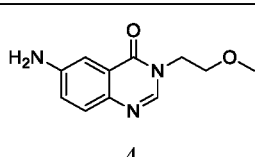
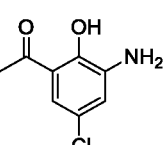
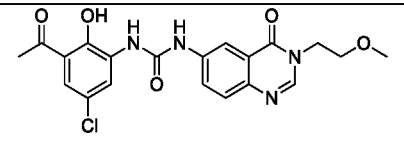
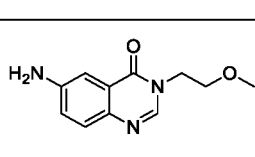
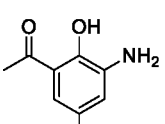
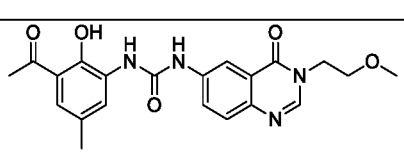
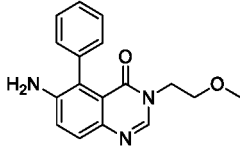
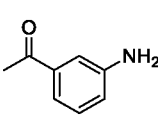
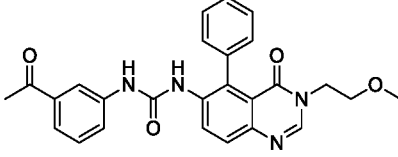
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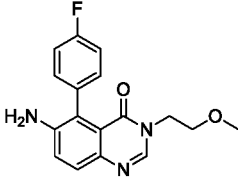
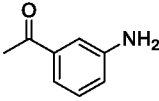
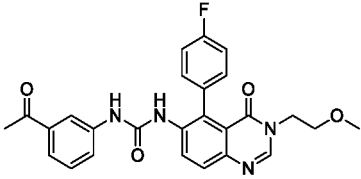
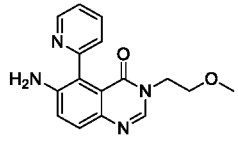
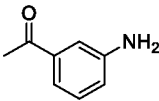
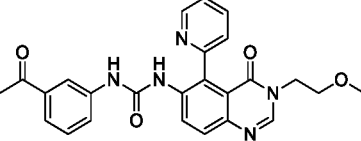
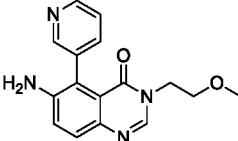
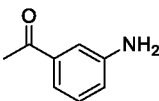
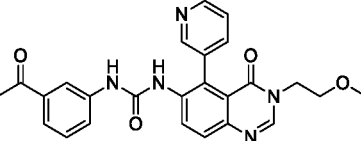
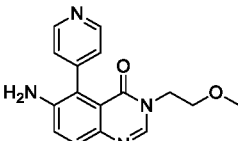
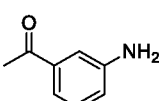
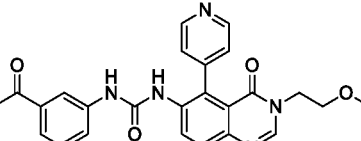
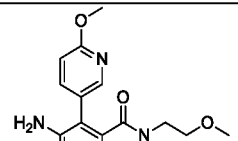
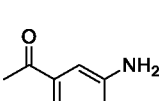
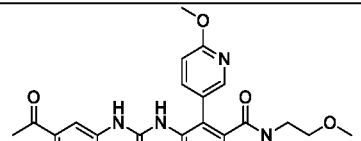
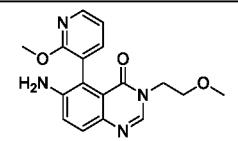
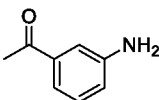
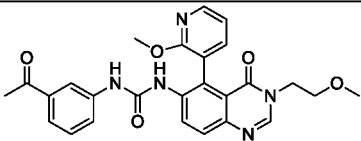
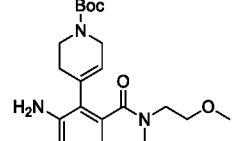
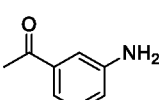
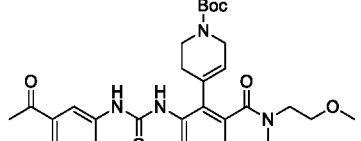
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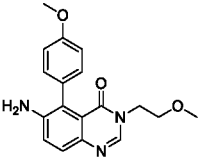
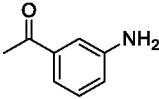
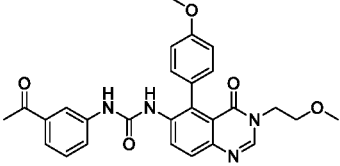
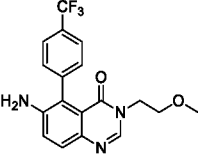
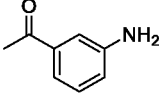
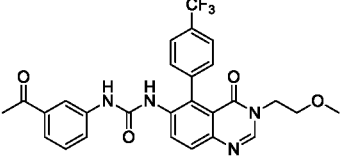
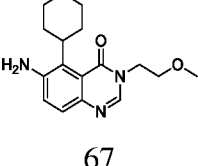
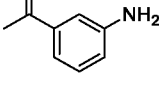
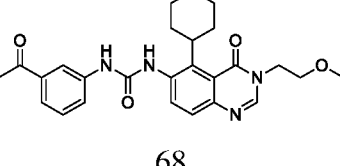
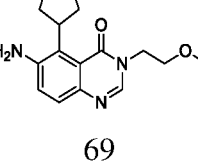
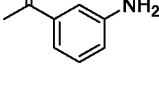
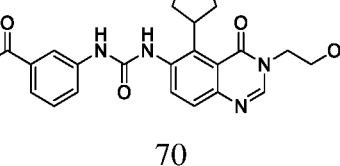
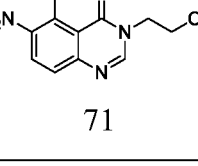
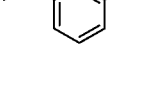
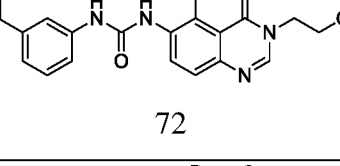
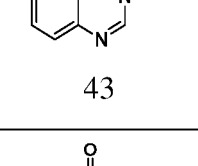
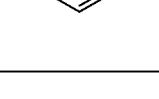
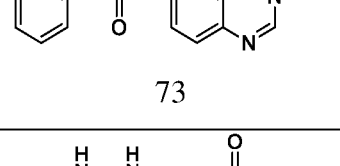
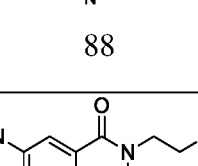
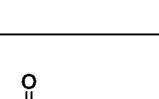
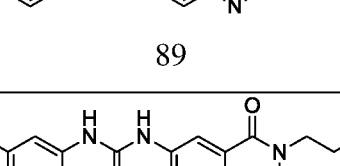
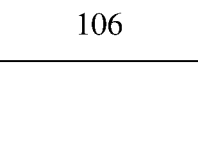

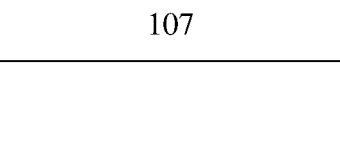
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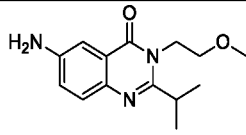
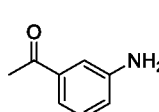
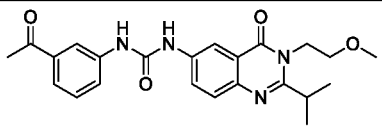
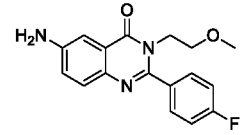
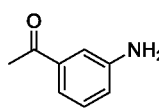
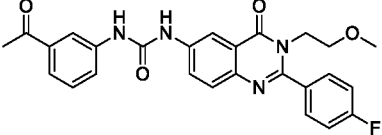
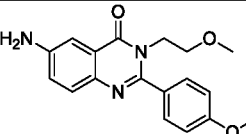
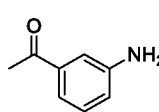
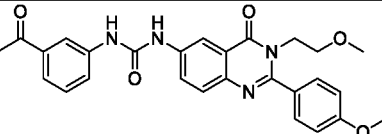
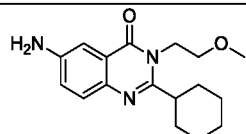
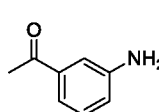
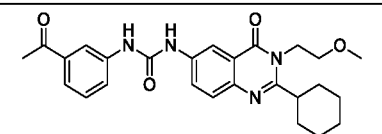
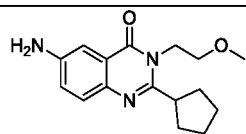
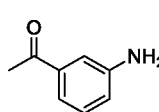
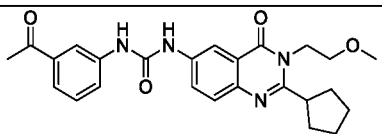
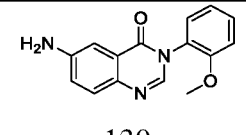
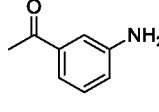
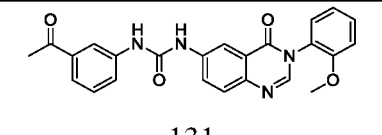
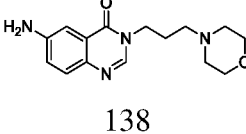
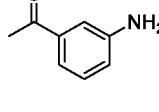
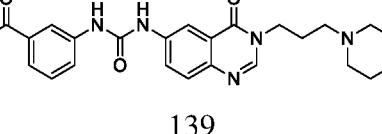
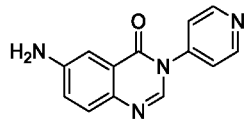
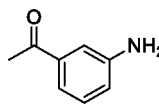
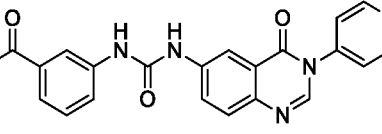
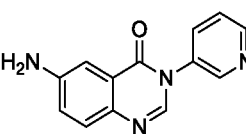
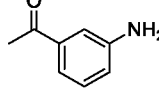
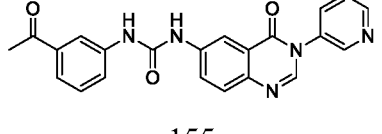
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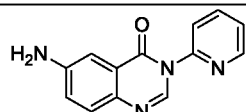
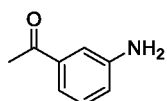
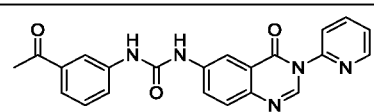
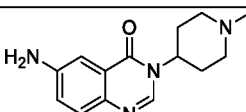
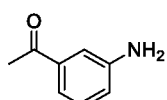
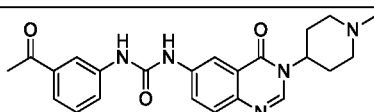
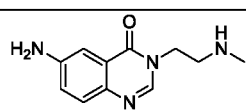
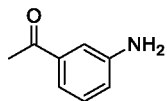
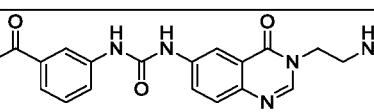
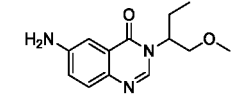
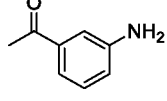
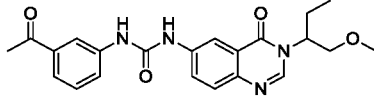
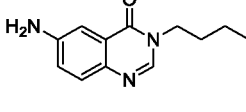
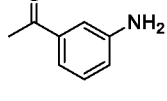
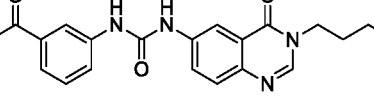
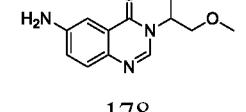
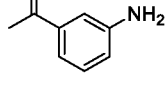
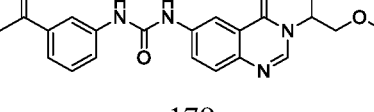
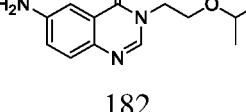
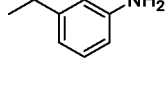
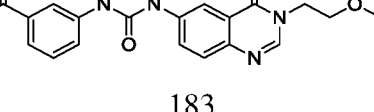
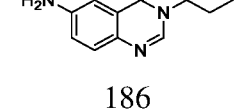
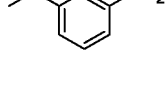
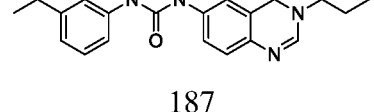
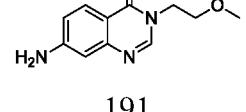
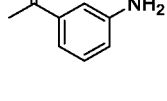
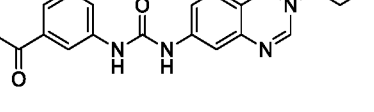
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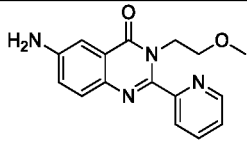
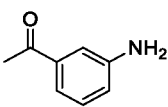
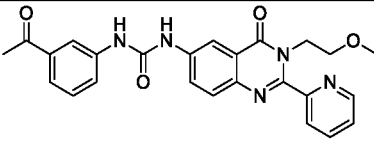
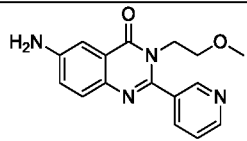
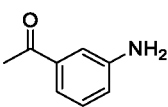
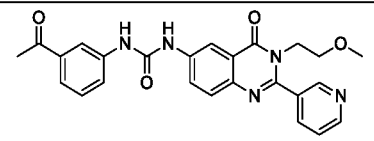
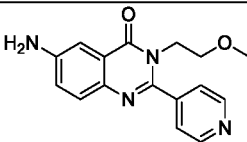
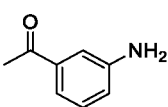
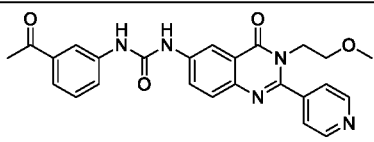
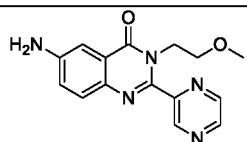
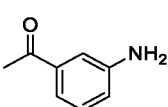
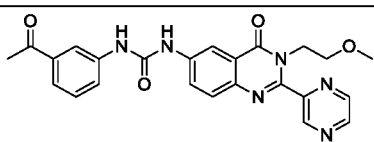
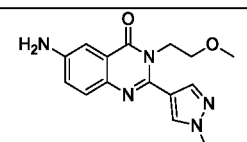
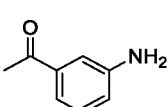
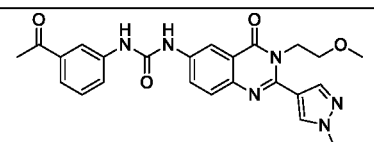
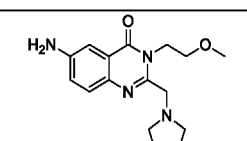
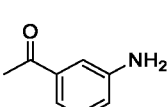
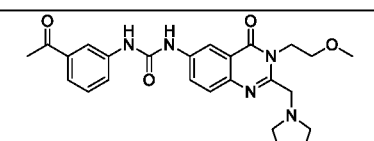
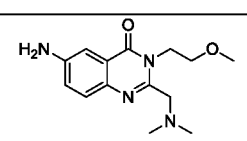
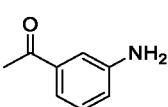
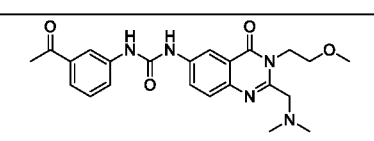
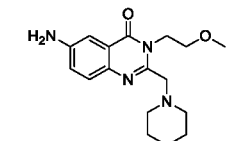
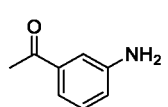
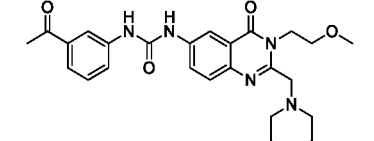
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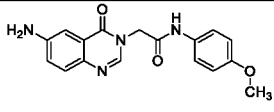
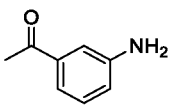
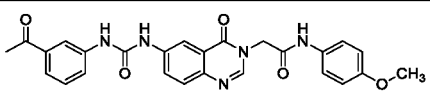
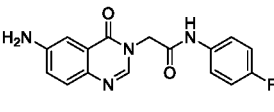
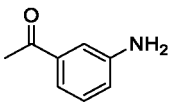
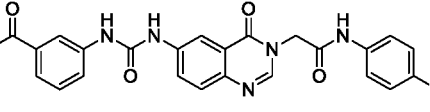
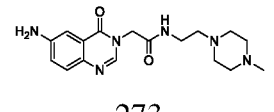
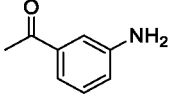
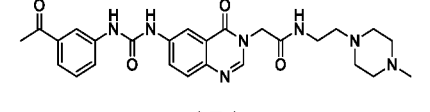
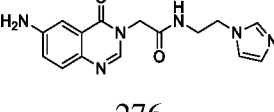
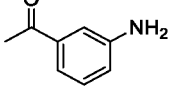
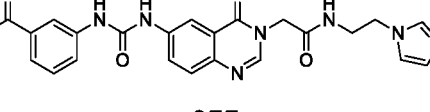
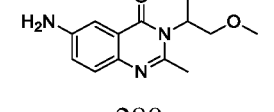
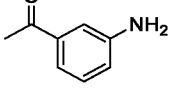
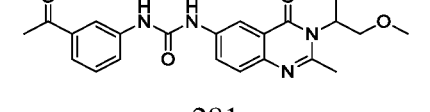
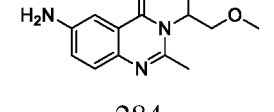
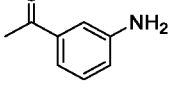
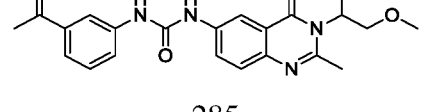
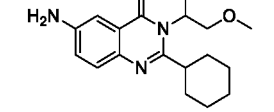
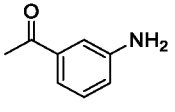
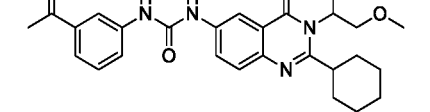
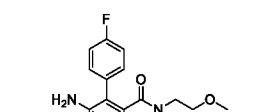
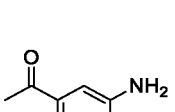
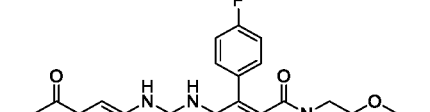
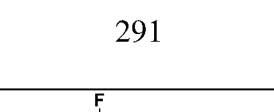
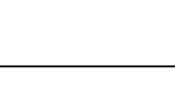
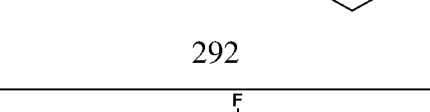
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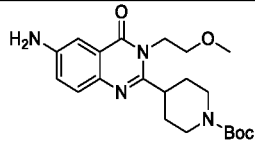
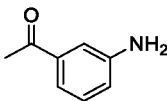
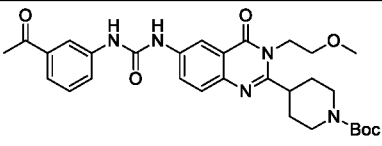
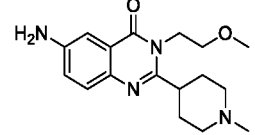
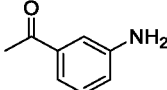
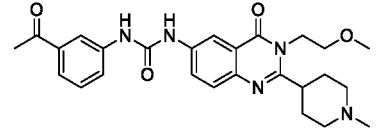
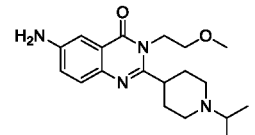
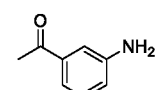
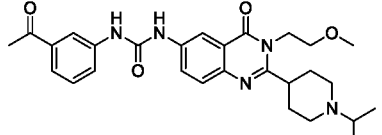
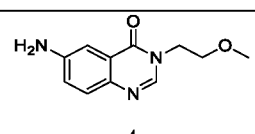
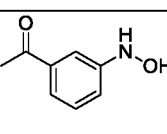
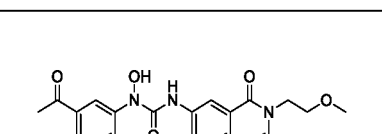
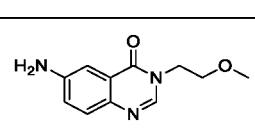
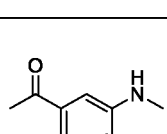
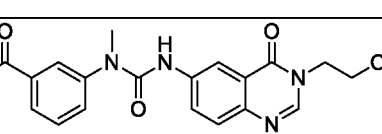
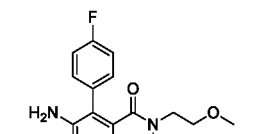
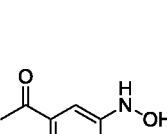
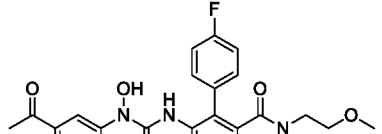
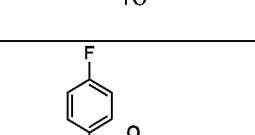
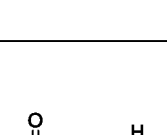
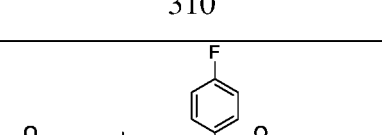
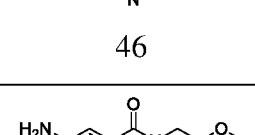
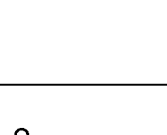
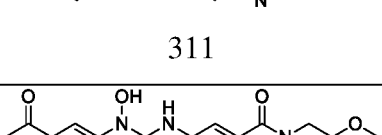
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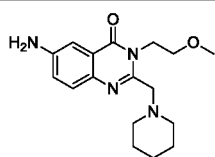
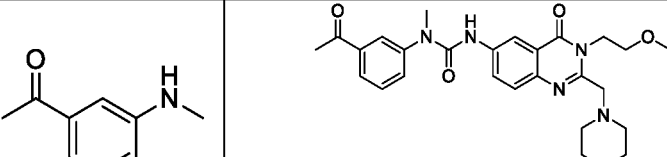
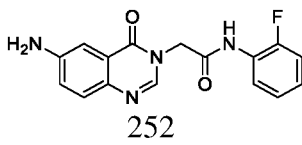
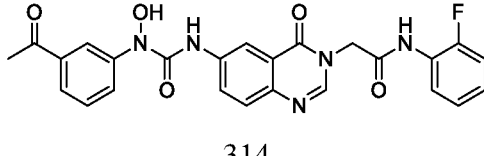
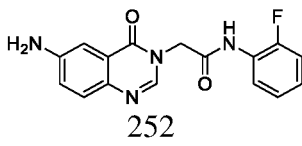
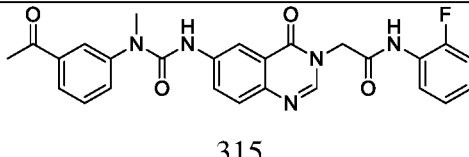
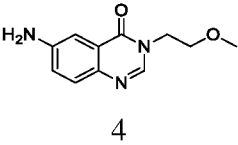
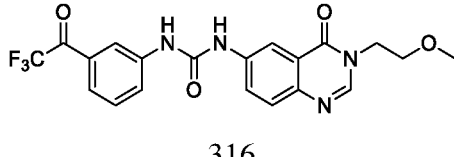
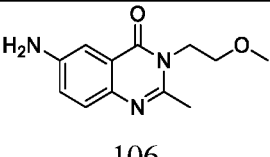
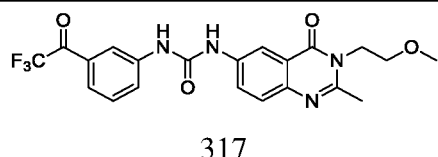
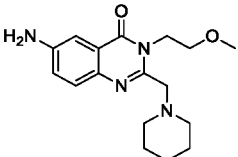
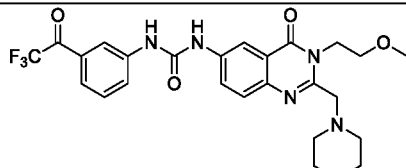
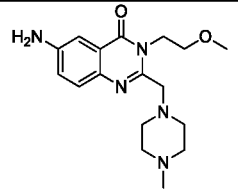
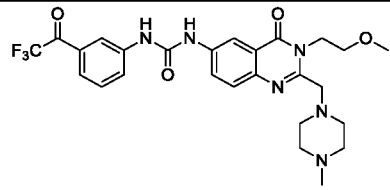
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66	 191	 NH ₂	 199
67	 202	 NH ₂	 203
68	 206	 NH ₂	 207

<p>69</p>	 <p>210</p>		 <p>211</p>
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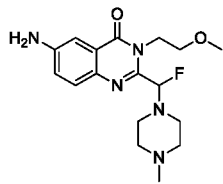
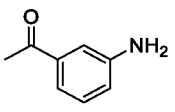
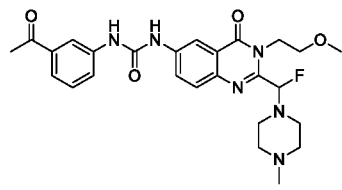
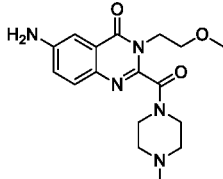
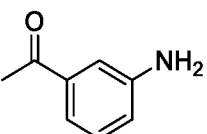
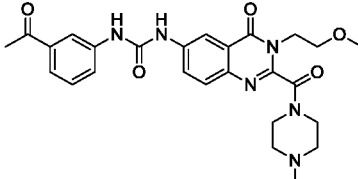
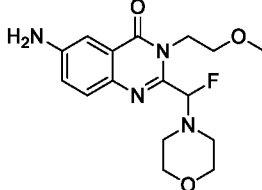
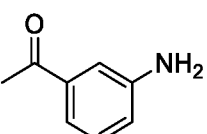
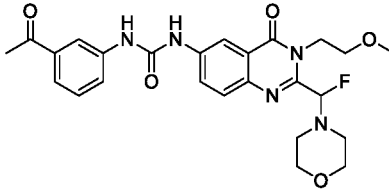
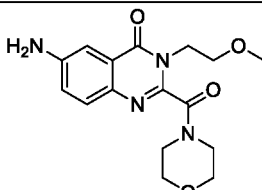
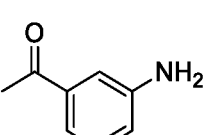
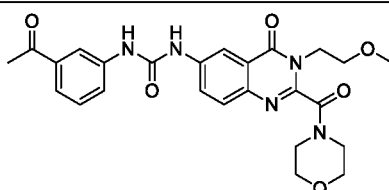
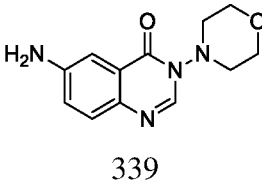
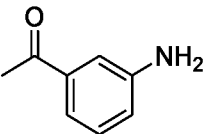
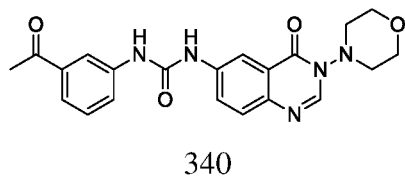
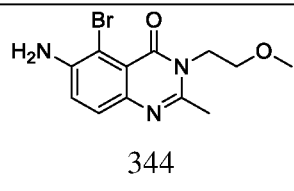
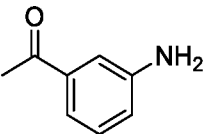
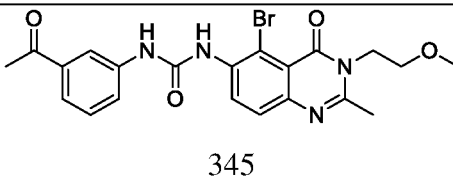
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112	 106	 F	 322
113	 237	 F	 323
114	 243	 F	 324
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116	 329	 NH_2	 330
117	 329a	 NH_2	 330a

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General procedure of urea formation from isocyanates

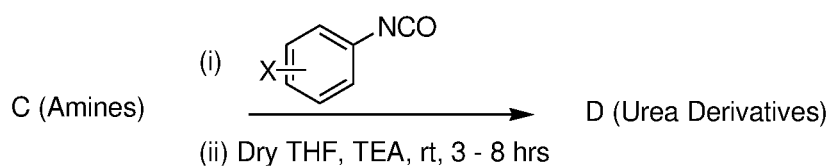
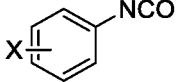
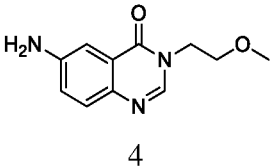
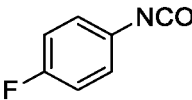
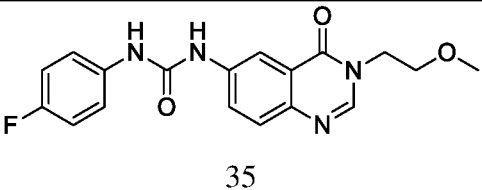
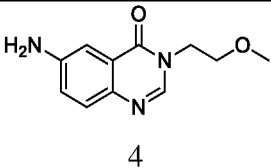
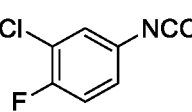
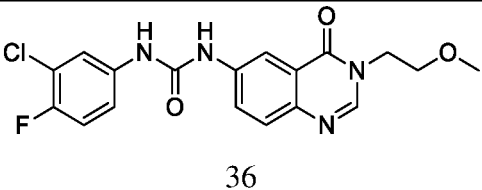
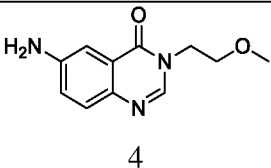
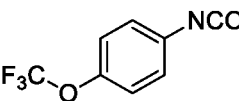
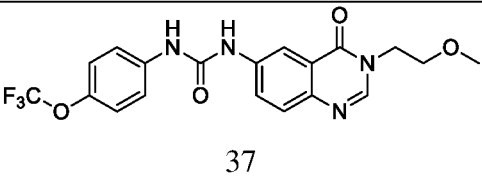
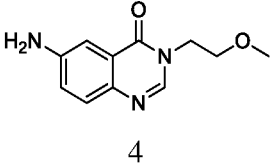
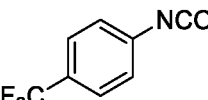
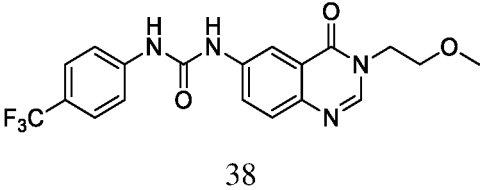
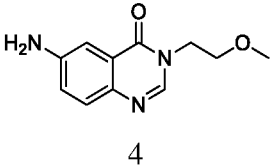
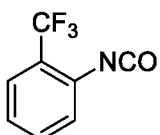
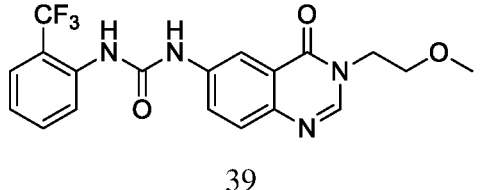
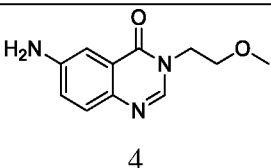
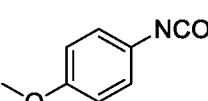
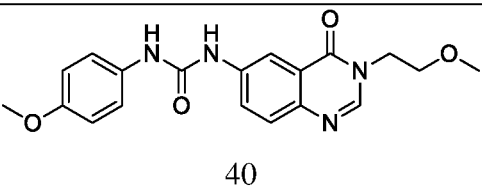
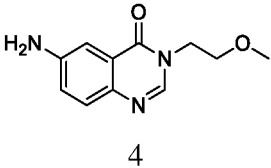
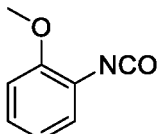
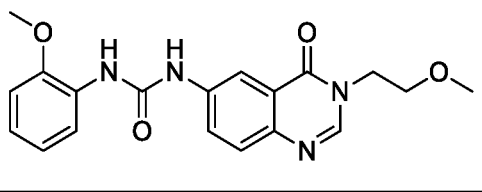
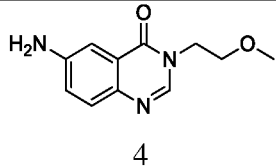
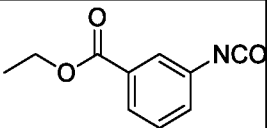
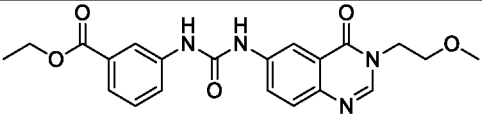
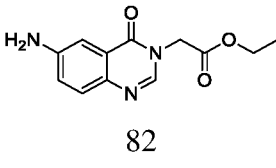
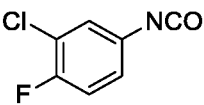
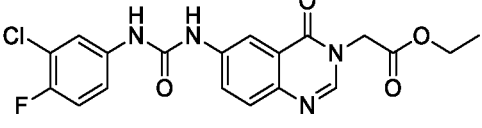
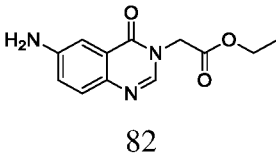
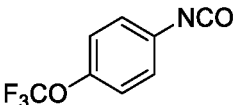
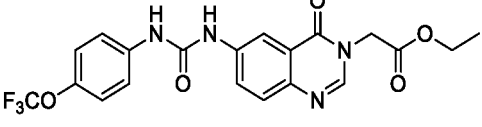
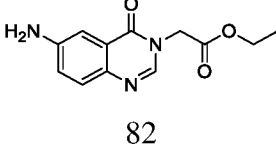
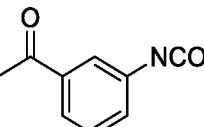
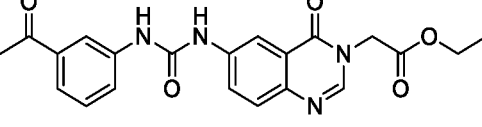
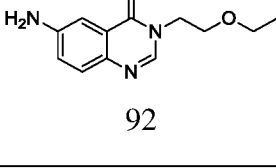
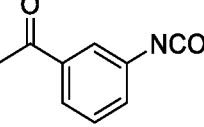
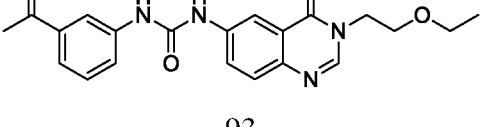
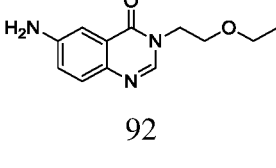
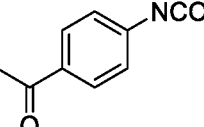
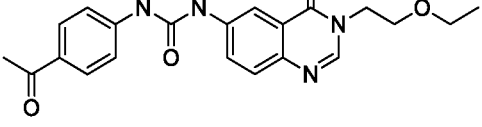
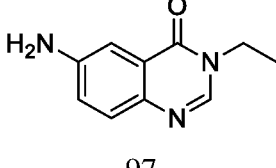
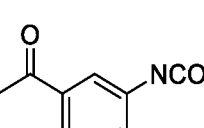
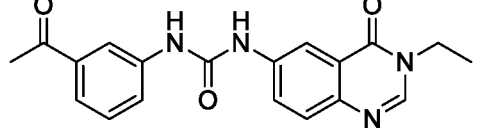
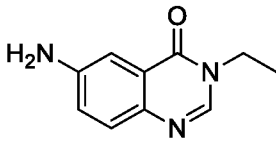
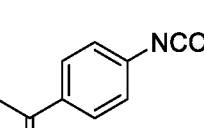
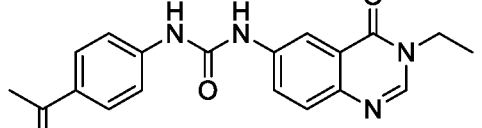


Table 3 provide the structure of reactants and products obtained with reaction with isocyanates

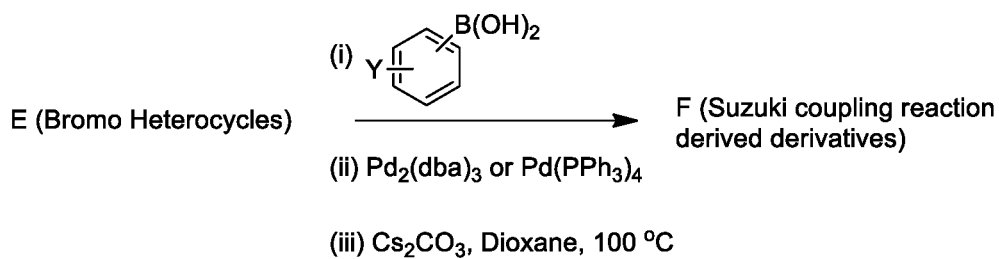
Table 3

Serial No	Amine (C)		D (Urea derivatives)
01			
02			
03			
04			
05			
06			
07			

			41
08	 4	 NCO	 42
09	 82	 Cl F NCO	 83
10	 82	 F ₃ CO NCO	 F ₃ CO 84
11	 82	 NCO	 85
12	 92	 NCO	 93
13	 92	 NCO	 94
14	 97	 NCO	 98
15	 97	 NCO	 99

16	 102	 NCO	 103
17	 134	 NCO	 135
18	 142	 NCO	 143
19	 146	 NCO	 147

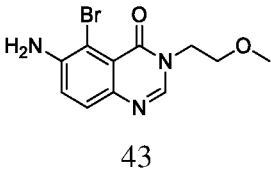
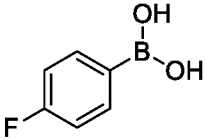
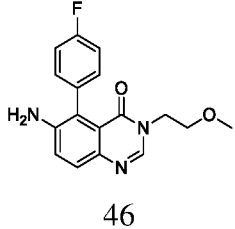
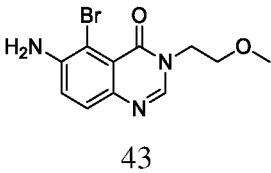
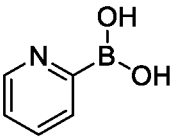
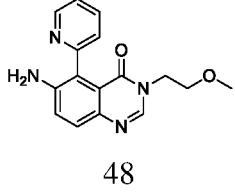
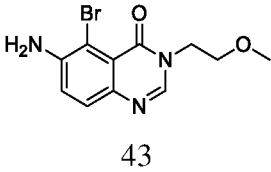
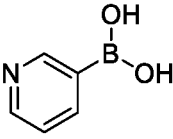
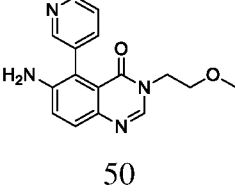
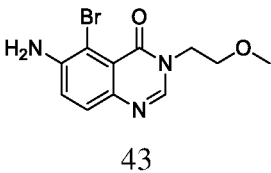
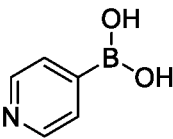
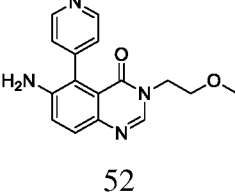
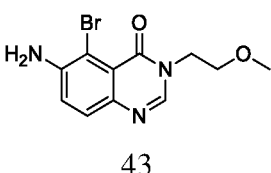
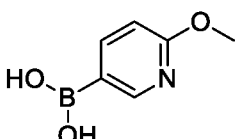
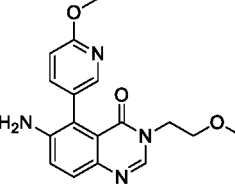
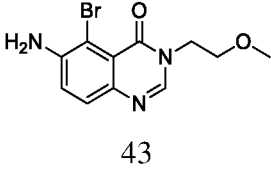
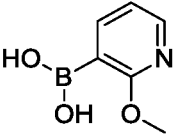
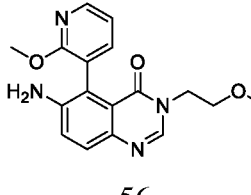
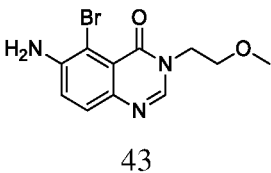
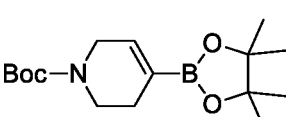
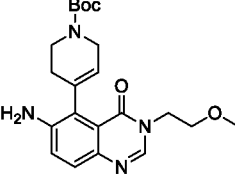
General procedure of suzuki coupling reaction

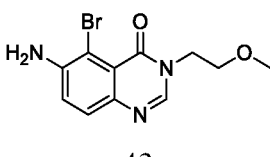
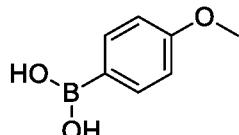
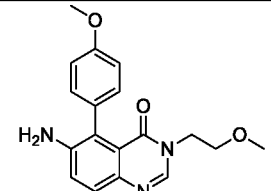
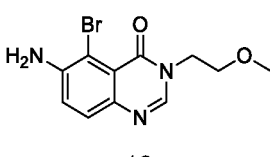
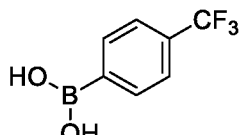
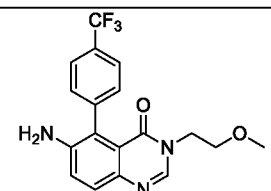
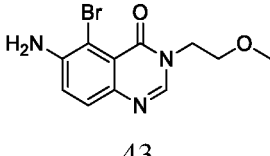
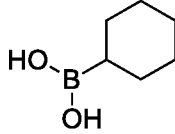
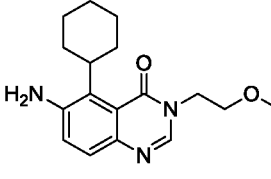
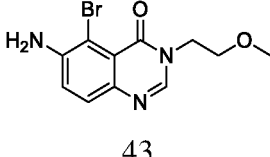
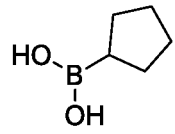
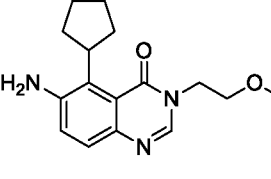
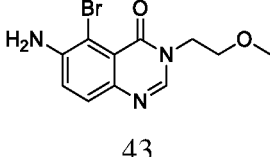
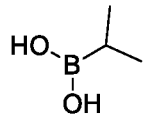
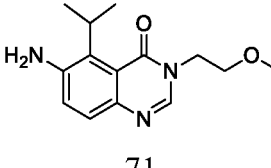
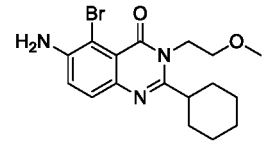
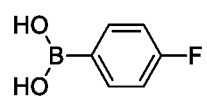
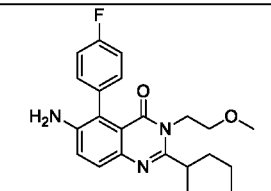
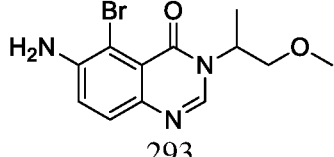
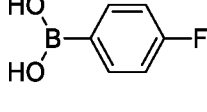
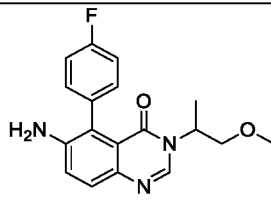


5 Table 4 provide the structure of reactants and products obtained for suzuki reaction

Table 4

Serial No	Bromo Heterocycles (E)		F (Suzuki coupled Product)
1	 43		 43

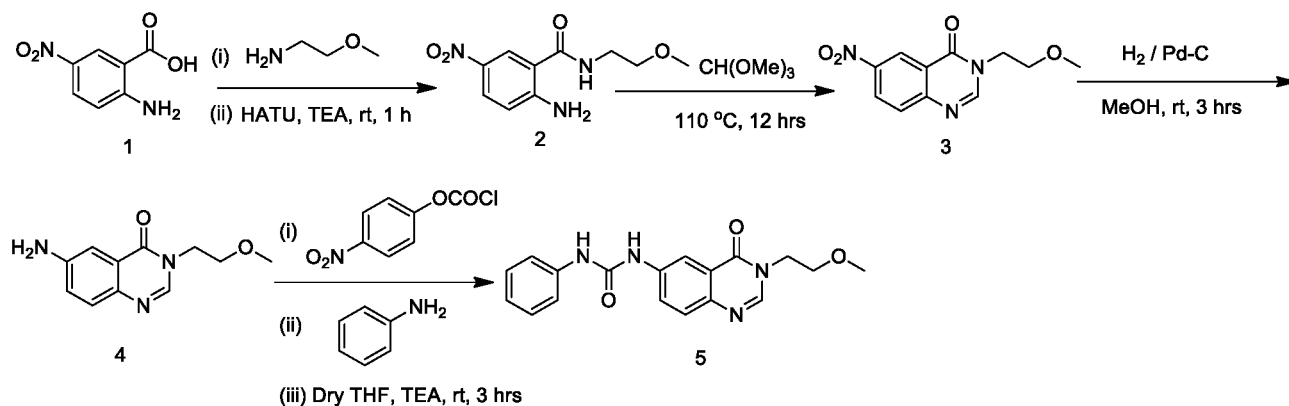
			44
2	 43		 46
3	 43		 48
4	 43		 50
5	 43		 52
6	 43		 54
7	 43		 56
8	 43		 58

9	 <p>43</p>		 <p>63</p>
10	 <p>43</p>		 <p>65</p>
11	 <p>43</p>		 <p>67</p>
12	 <p>43</p>		 <p>69</p>
13	 <p>43</p>		 <p>71</p>
14	 <p>290</p>		 <p>291</p>
15	 <p>293</p>		 <p>294</p>

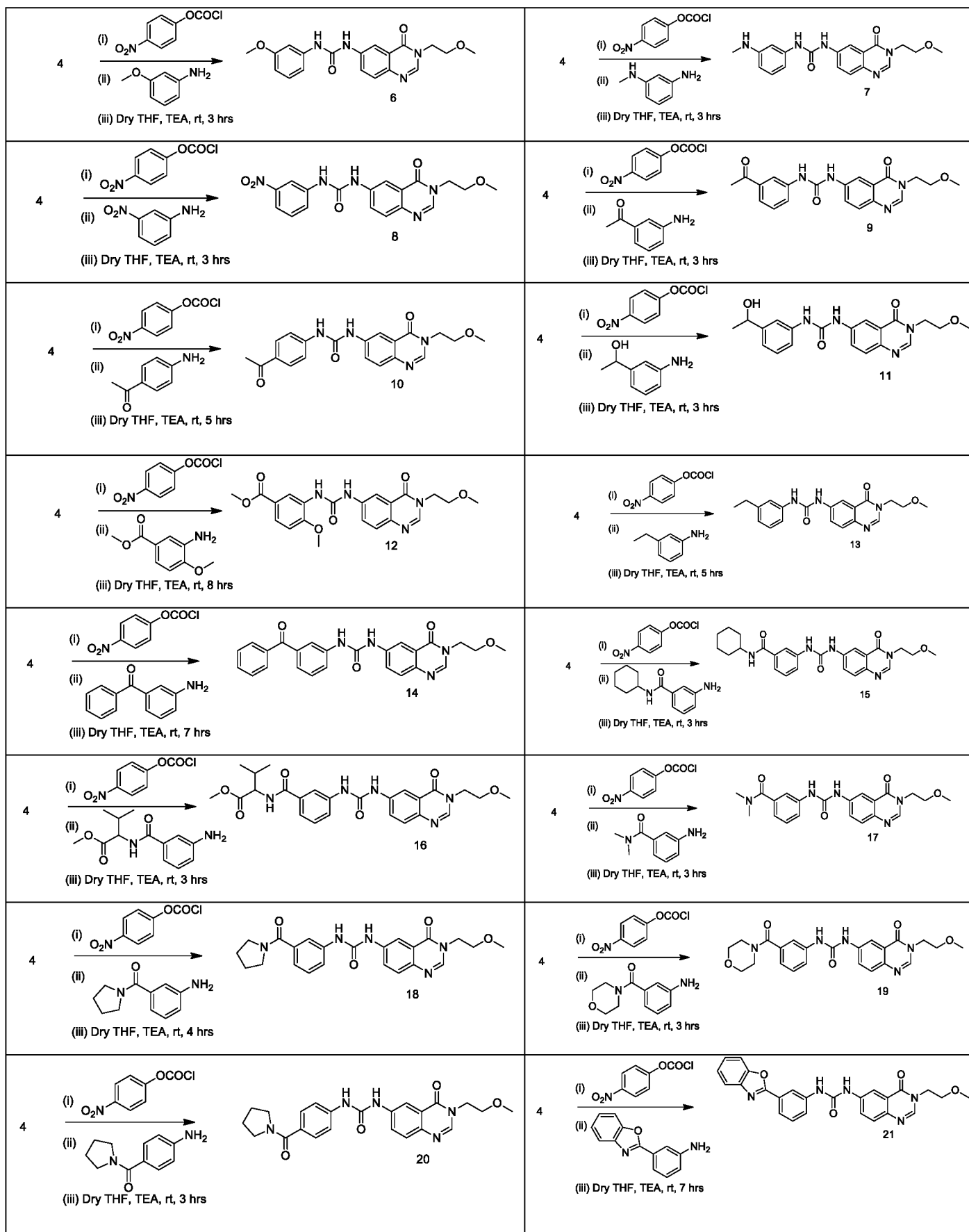
Abbreviations:

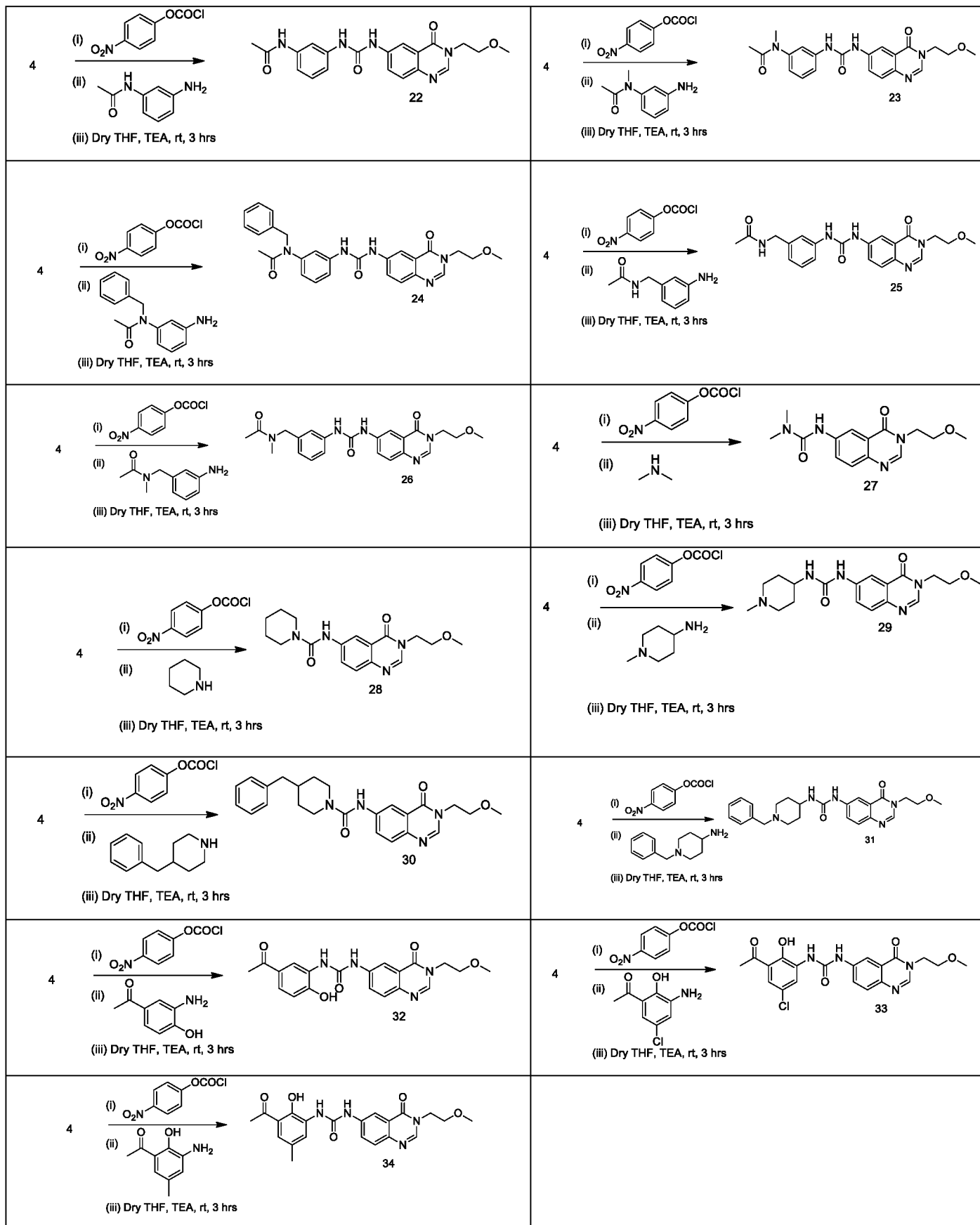
DMF	N,N-dimethylformamide
HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium oxidehexafluorophosphate
5	
TEA	Triethylamine
MeOH	Methanol
HMDS	Hexamethyldisilazane
CHCl ₃	Chloroform
10	
Br ₂	Bromine
ZnCl ₂	Zinc chloride
Cs ₂ CO ₃	Cesium carbonate
Pd ₂ (dba) ₃	Tris(dibenzylideneacetone)dipalladium(0)
CH(OMe) ₃	Trimethylorthoformate (TMOF)
15	
Pd(PPh ₃) ₄	Tetrakis(triphenylphosphine)palladium(0)
THF	Tetrahydrofuran
LiOH. H ₂ O	Lithium hydroxide monohydrate
Ar	Argon

20 Provided below are the schemes for preparing the compounds disclosed in the present application.

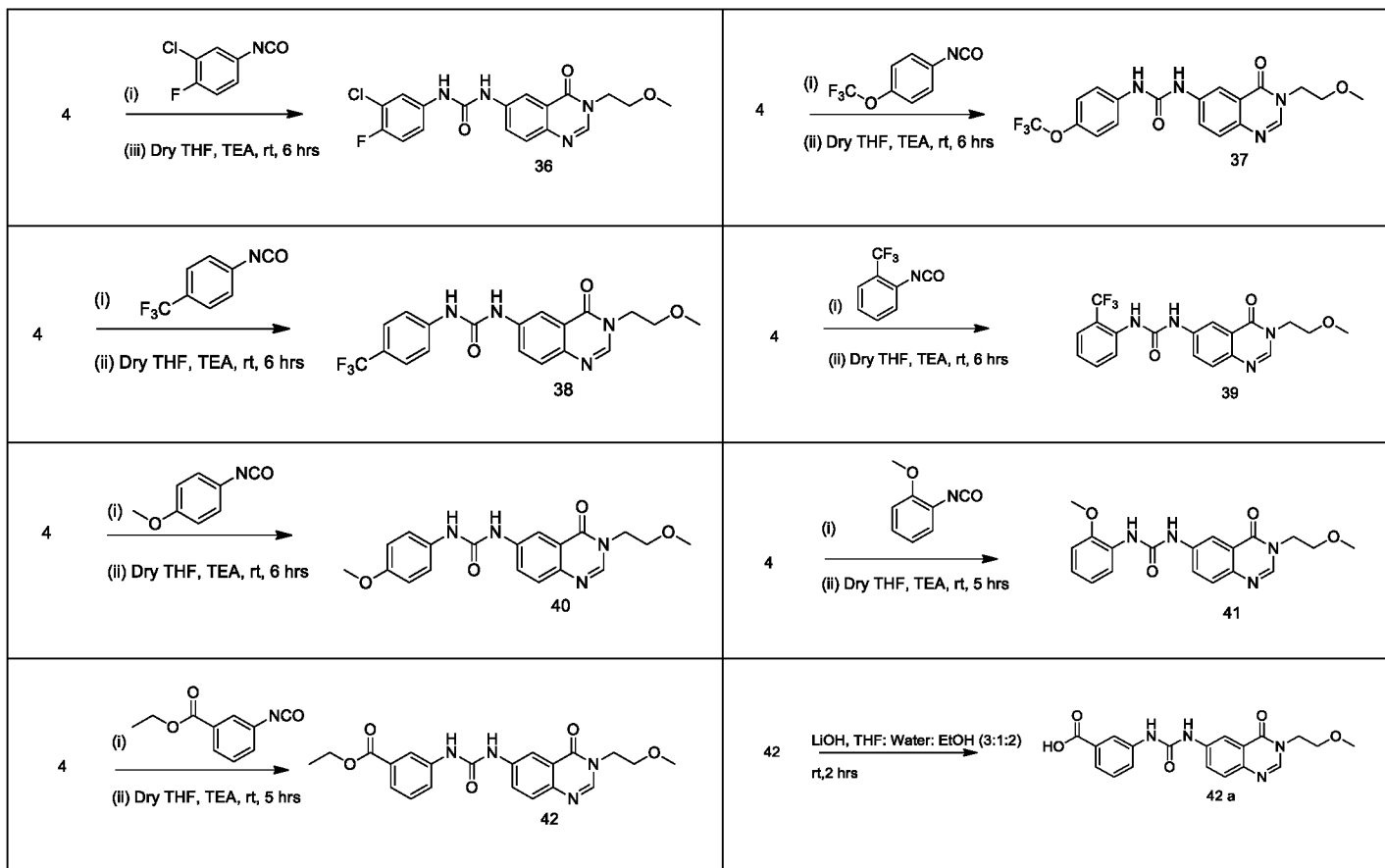
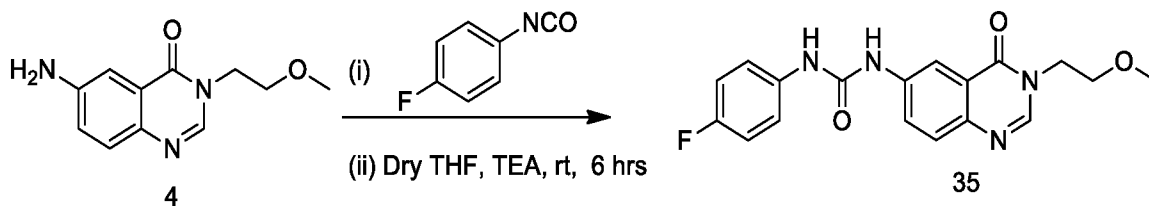
Scheme 1

25

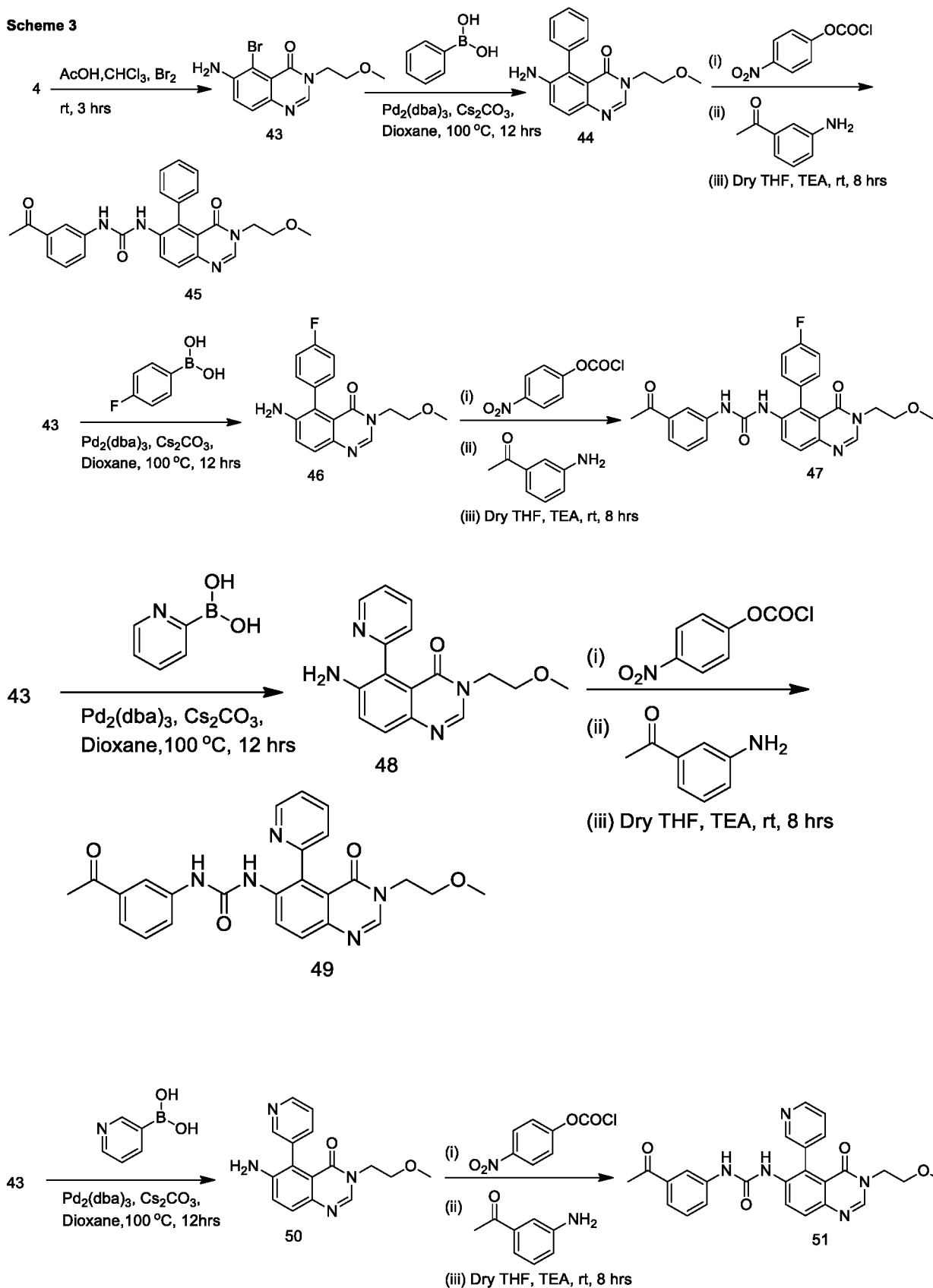




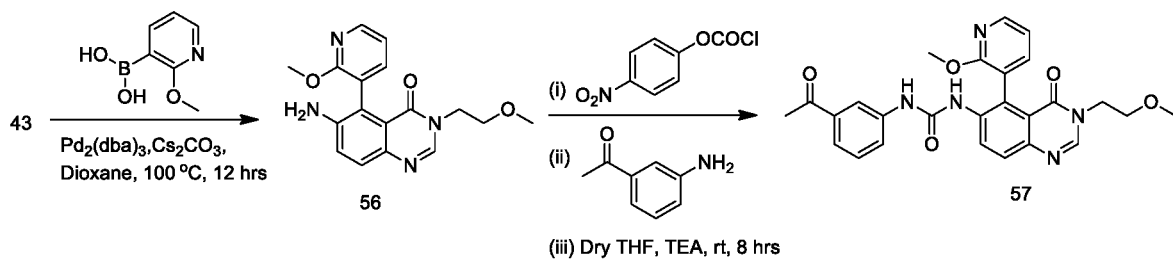
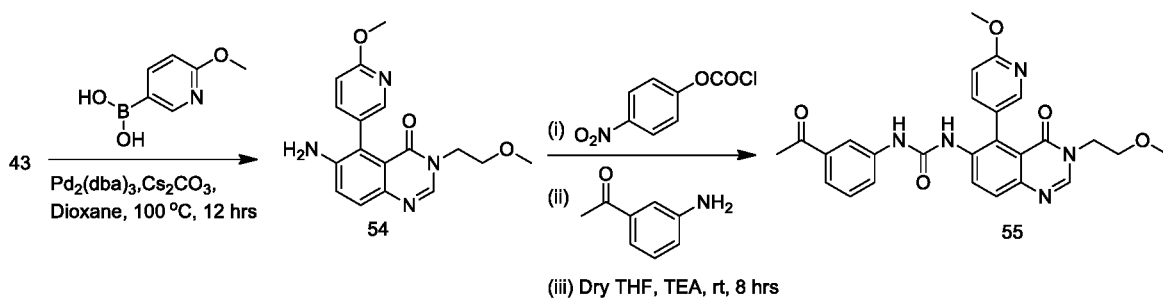
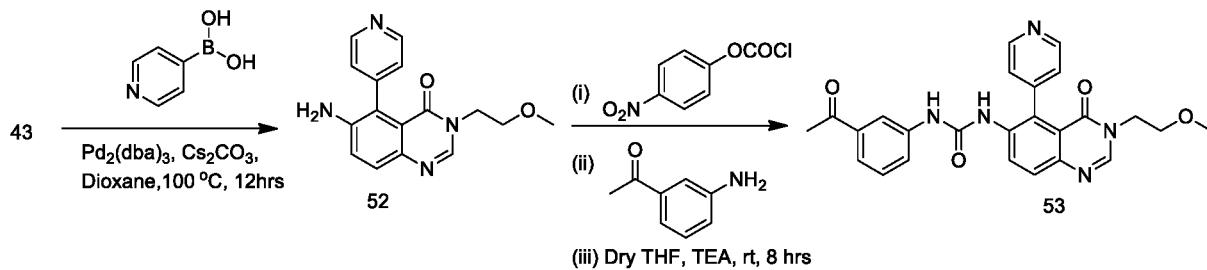
Scheme 2



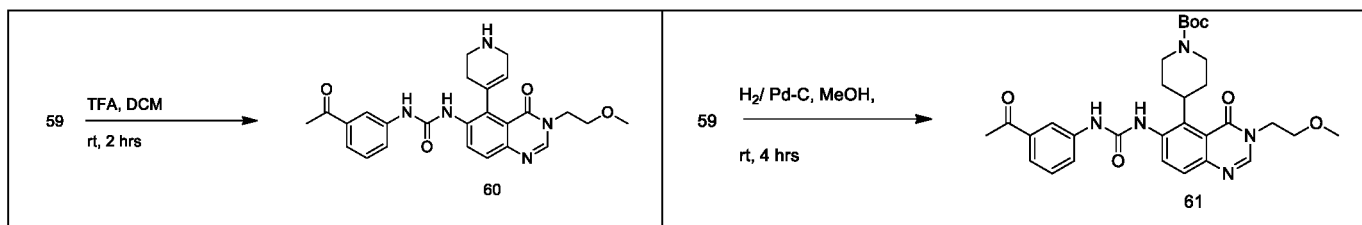
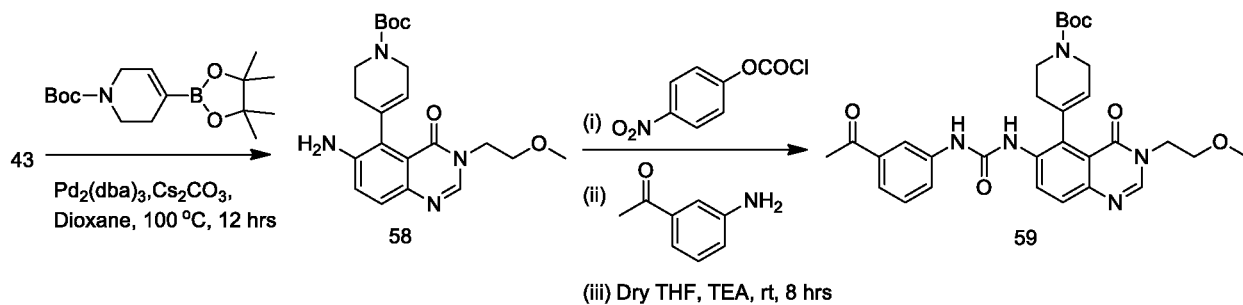
Scheme 3

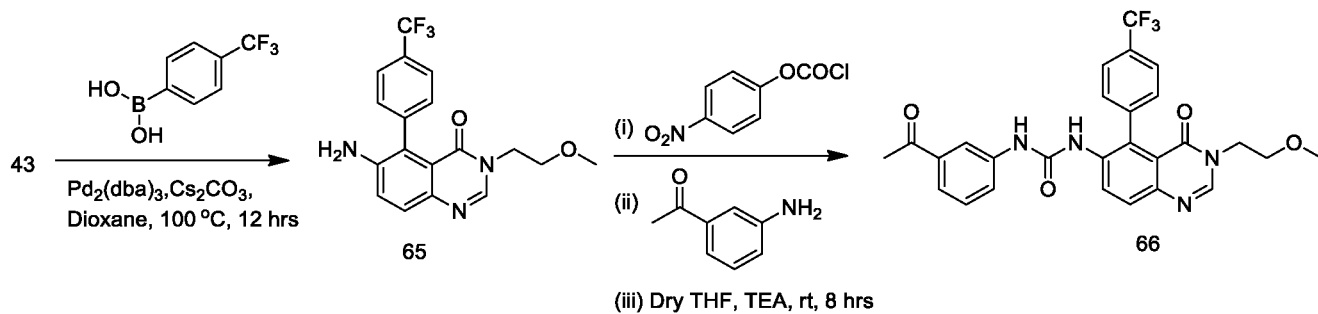
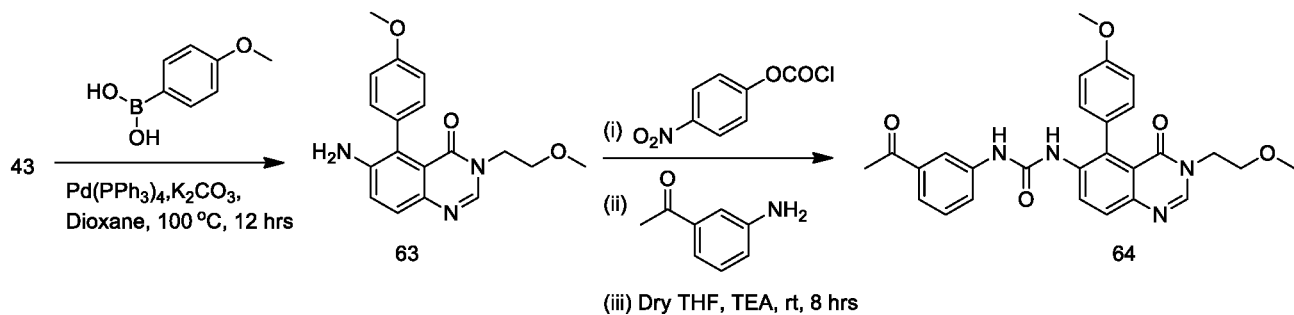
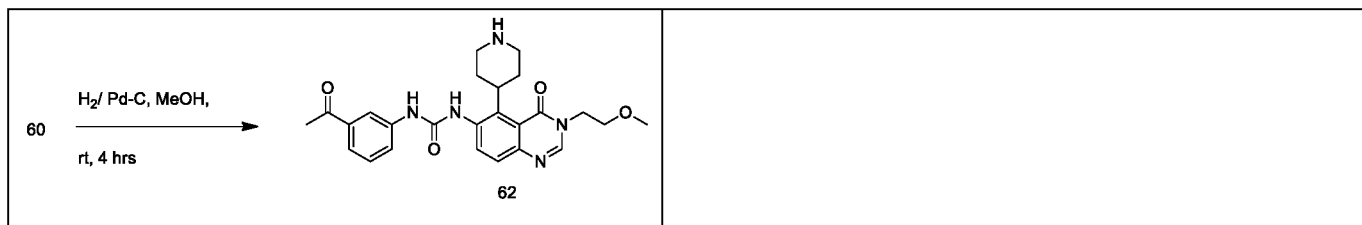


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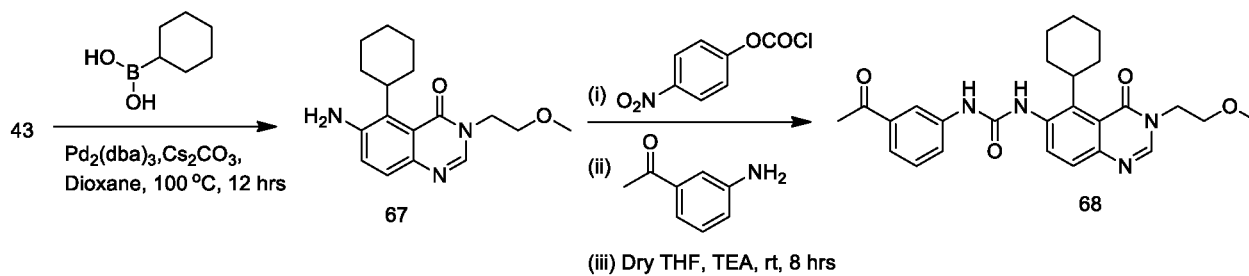


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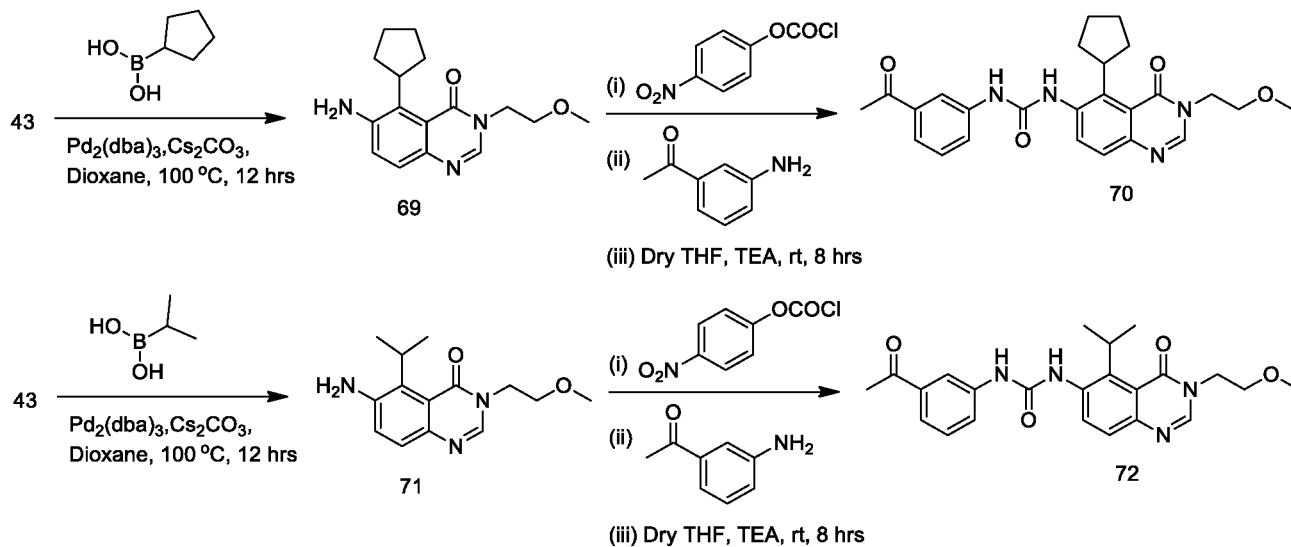




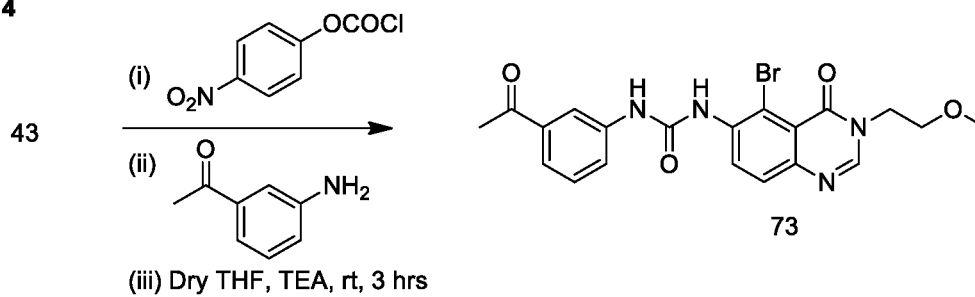
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10

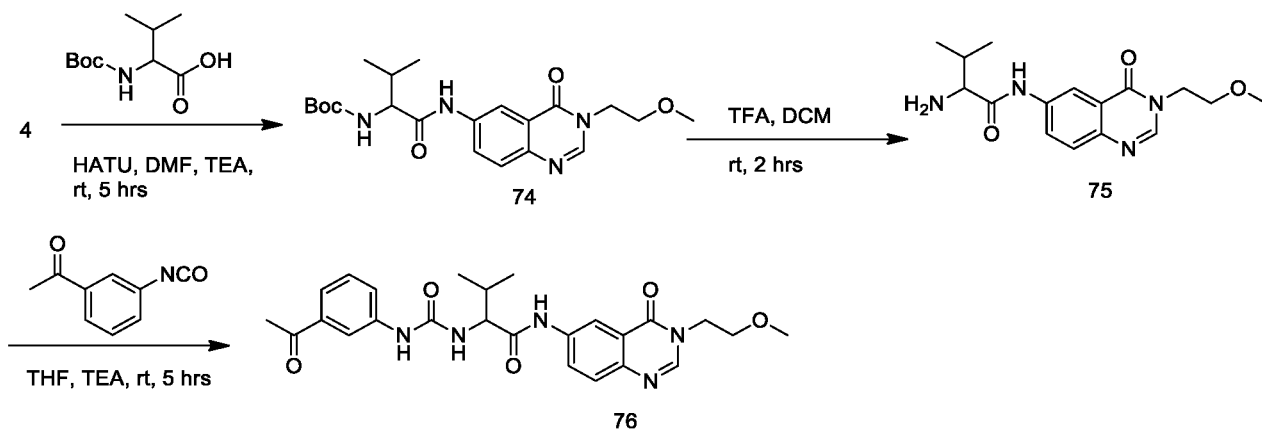


Scheme 4

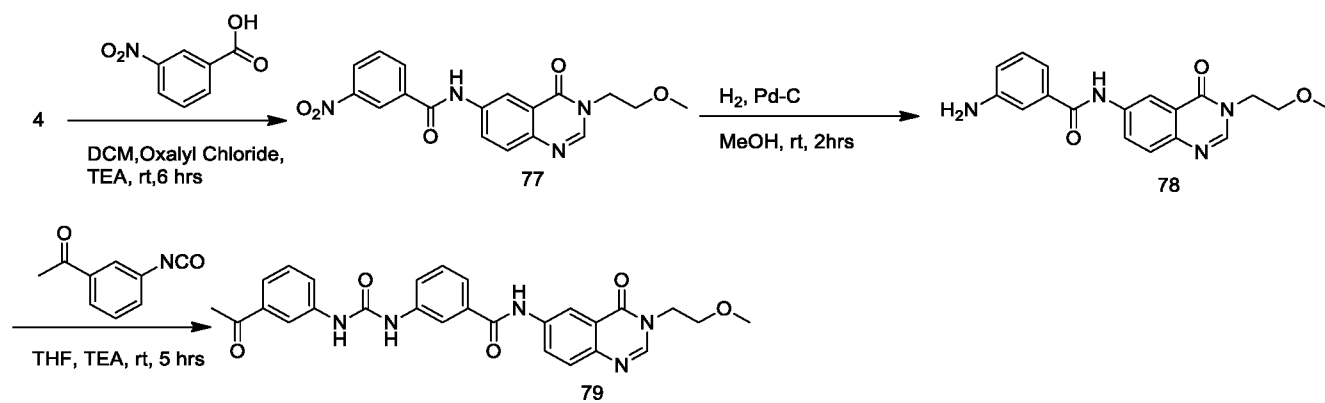


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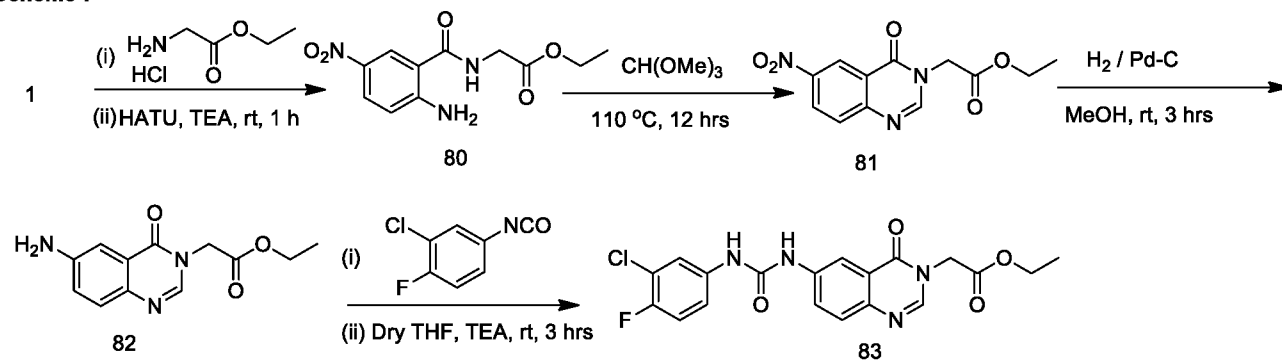
Scheme 5



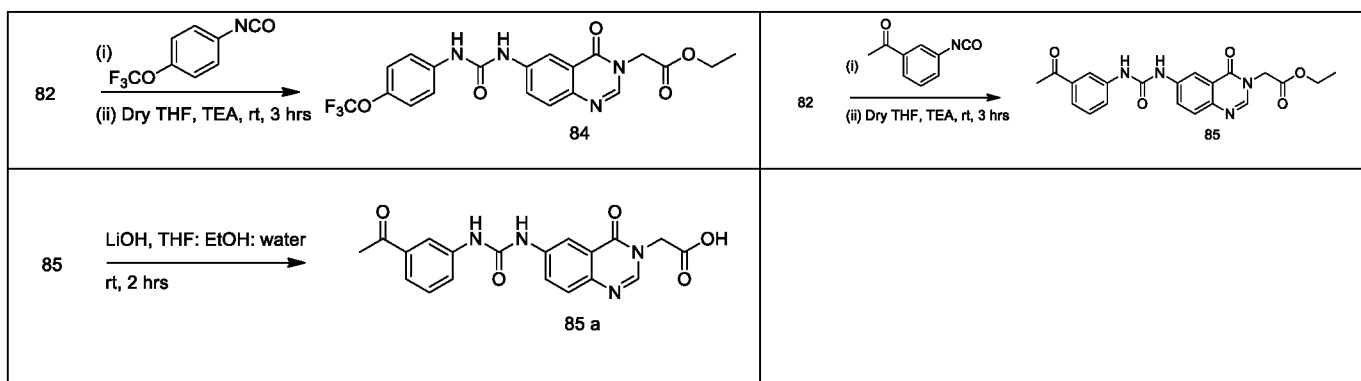
Scheme 6



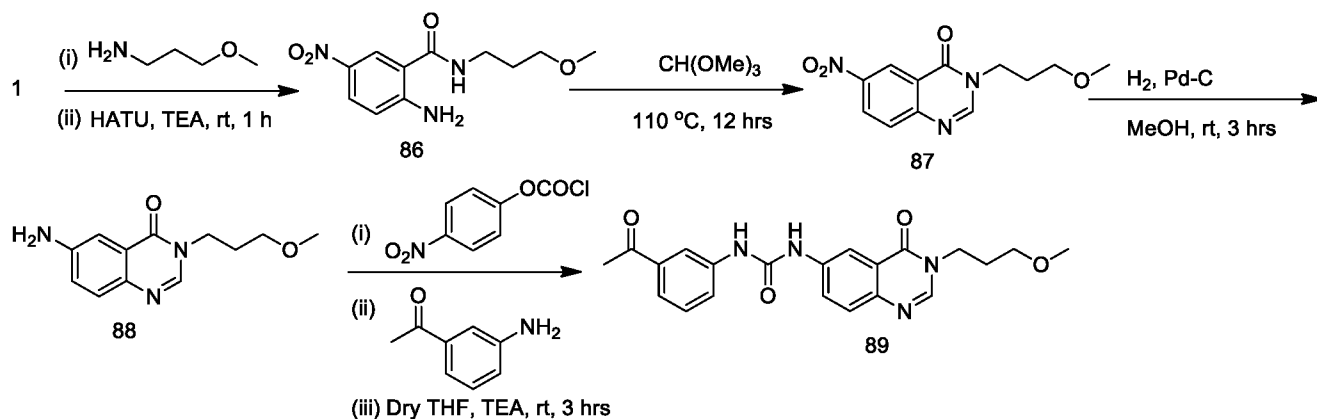
Scheme 7



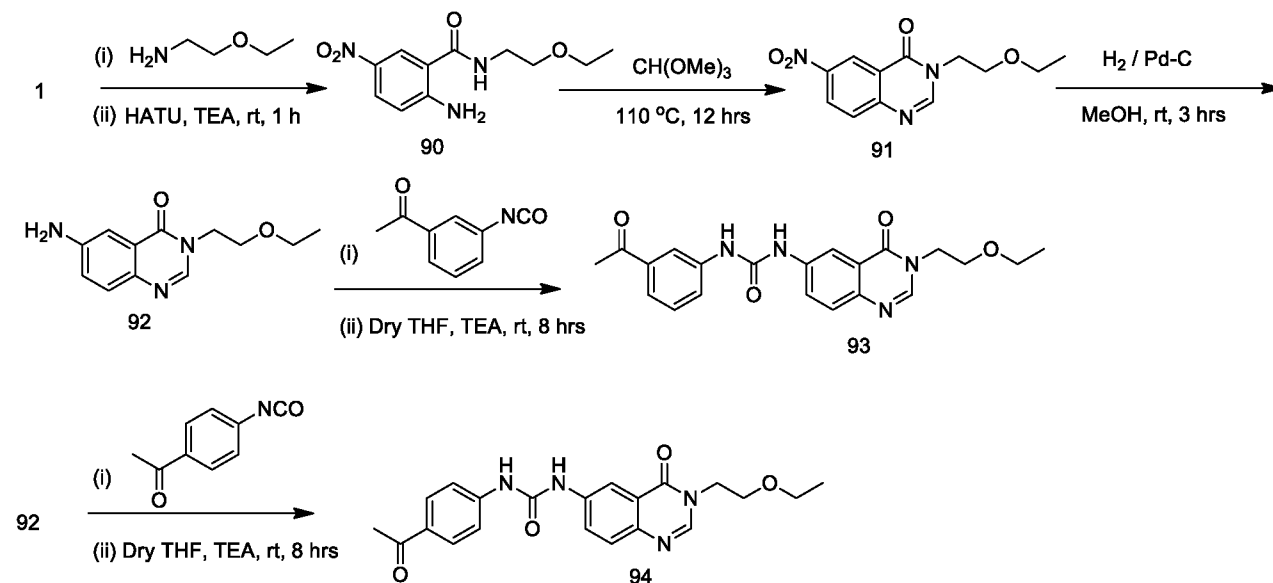
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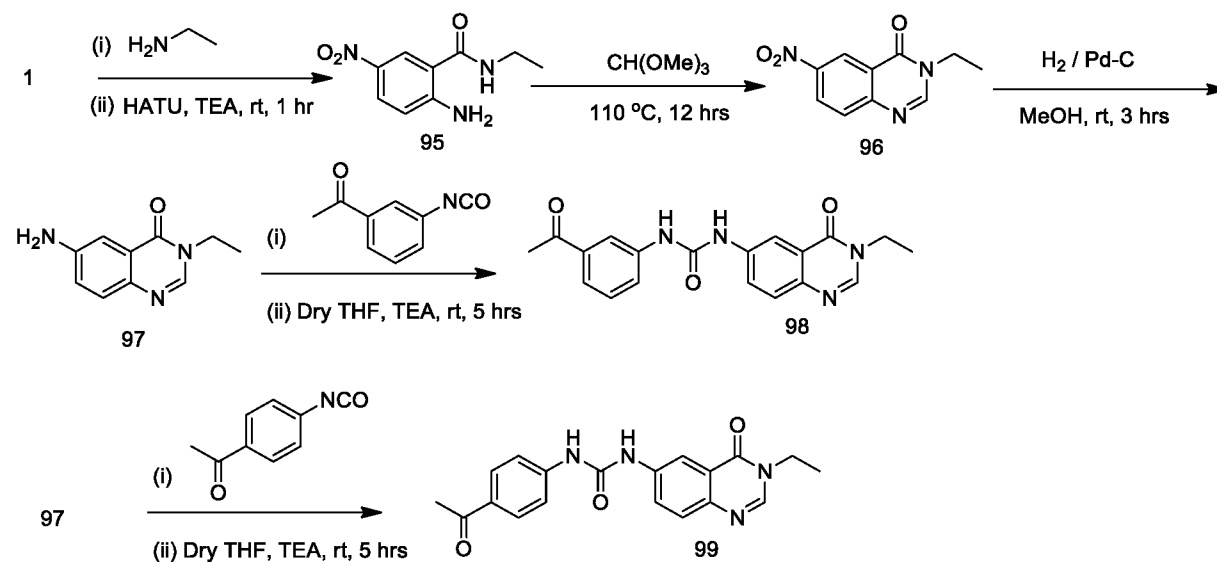
Scheme 8



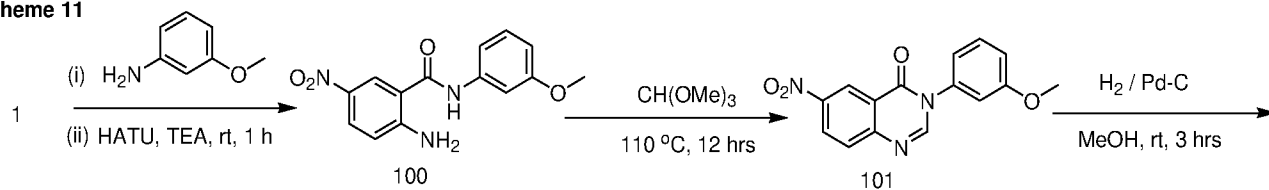
Scheme 9



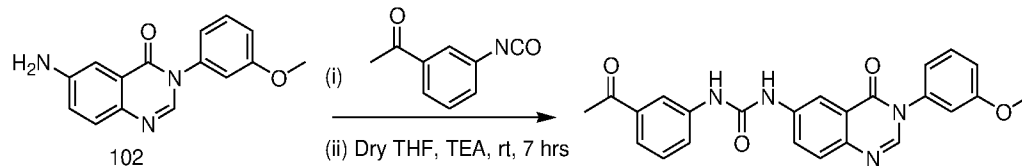
Scheme 10



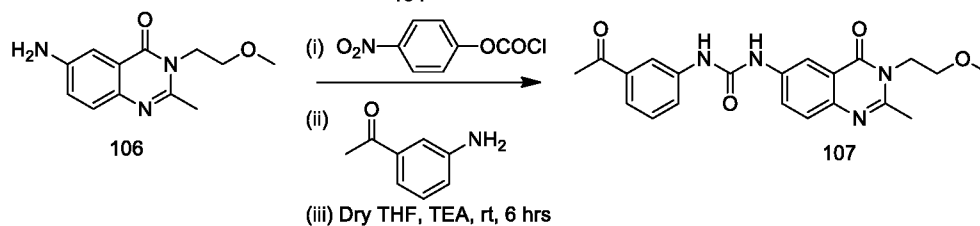
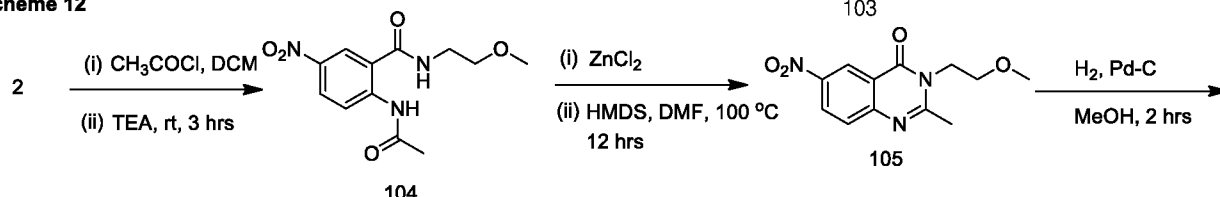
Scheme 11



5

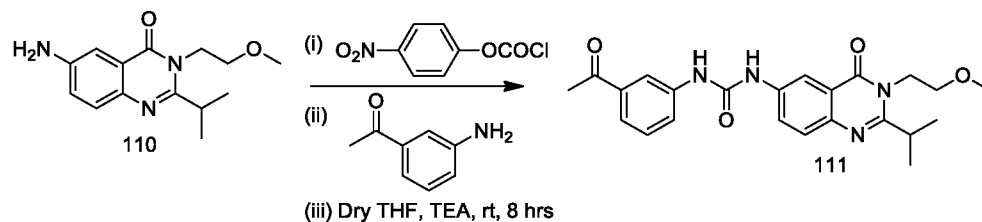
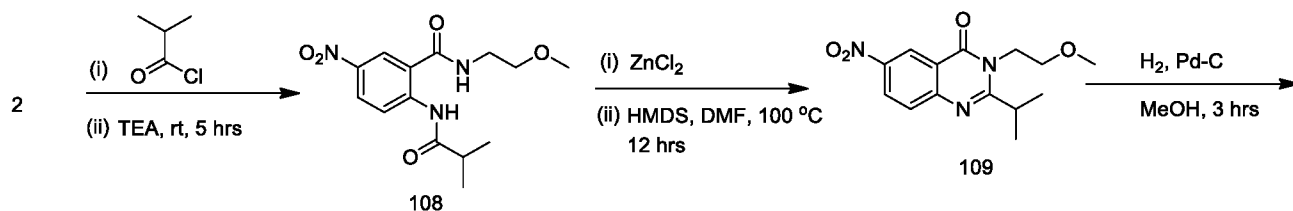


Scheme 12



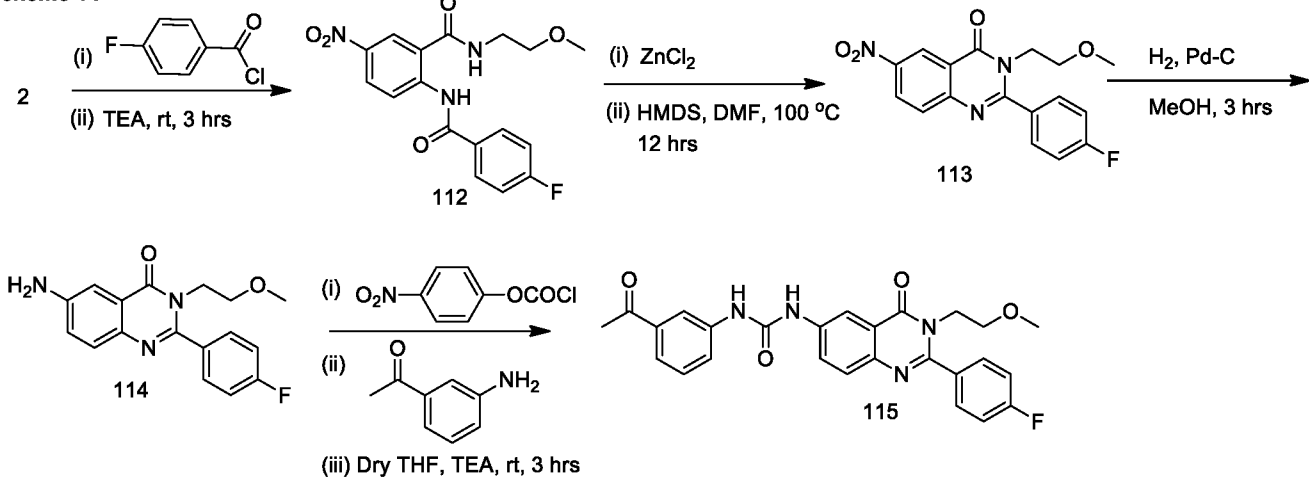
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Scheme 13

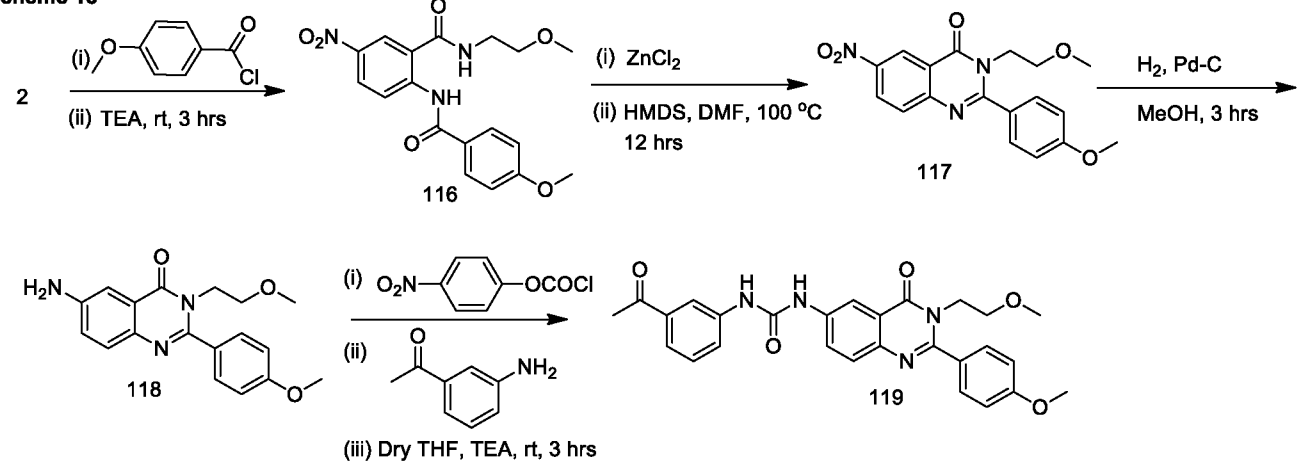


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Scheme 14

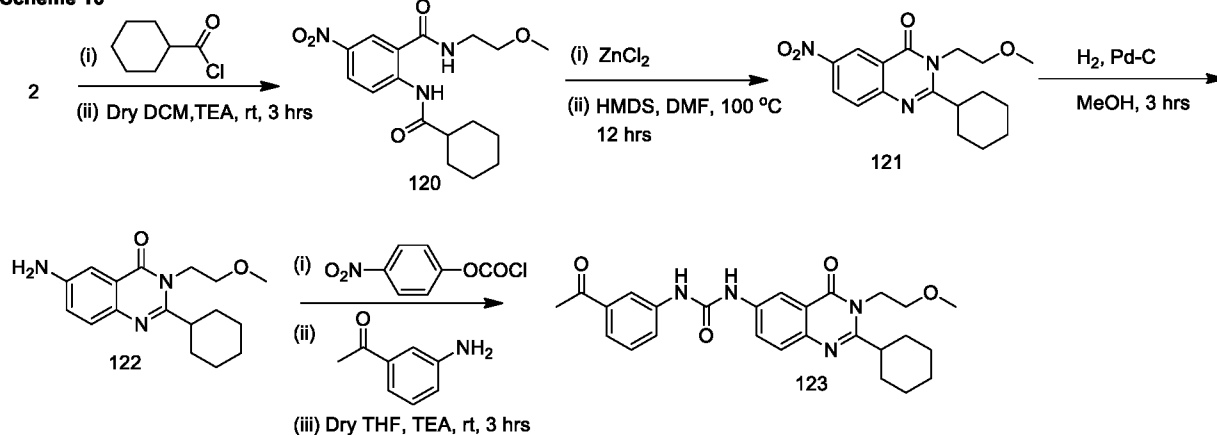


Scheme 15

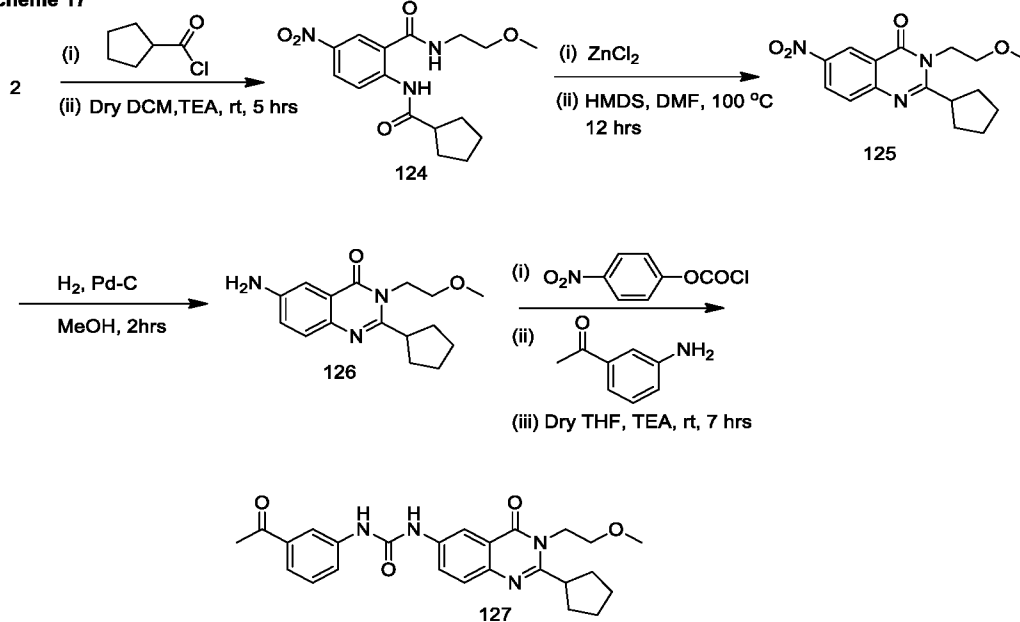


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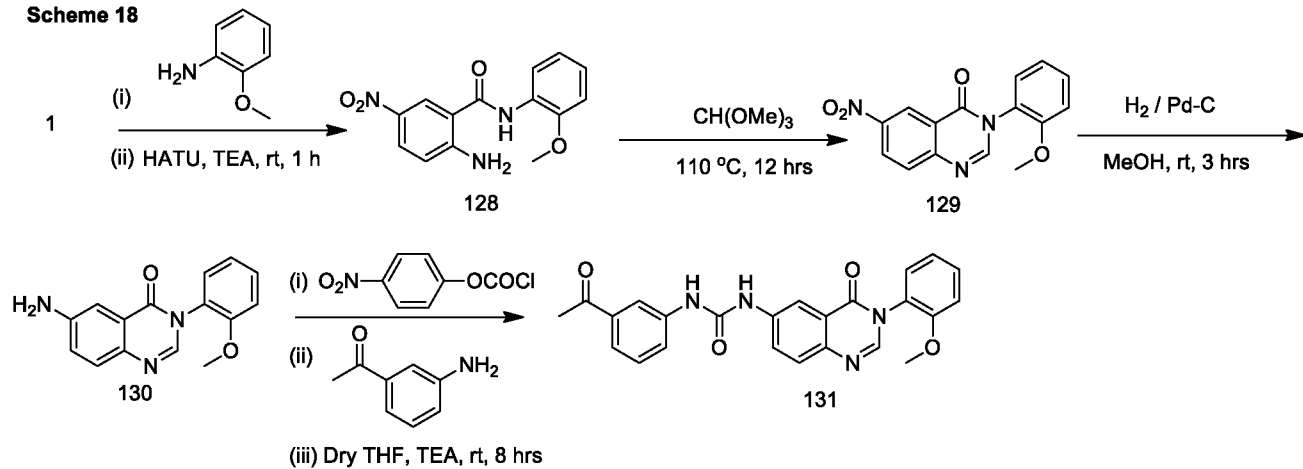
Scheme 16



Scheme 17

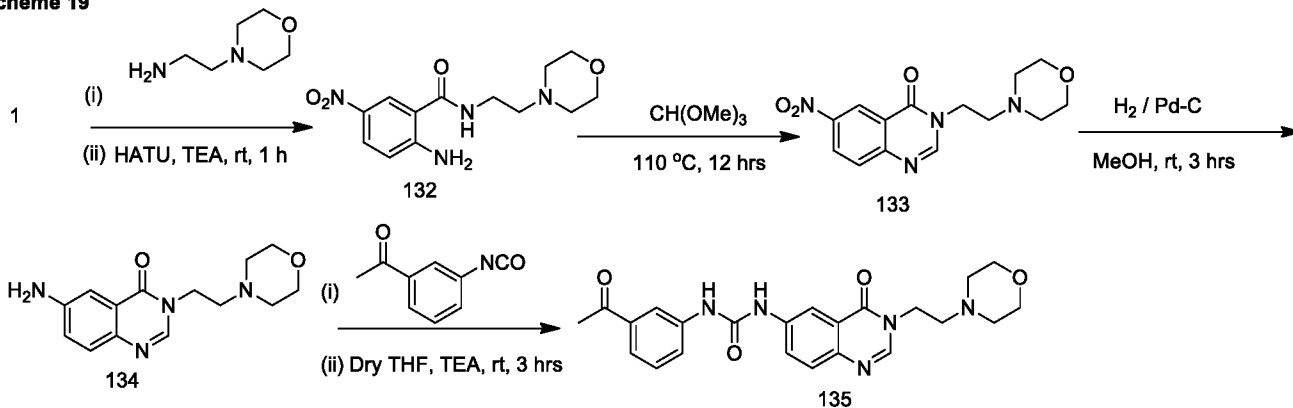


Scheme 18

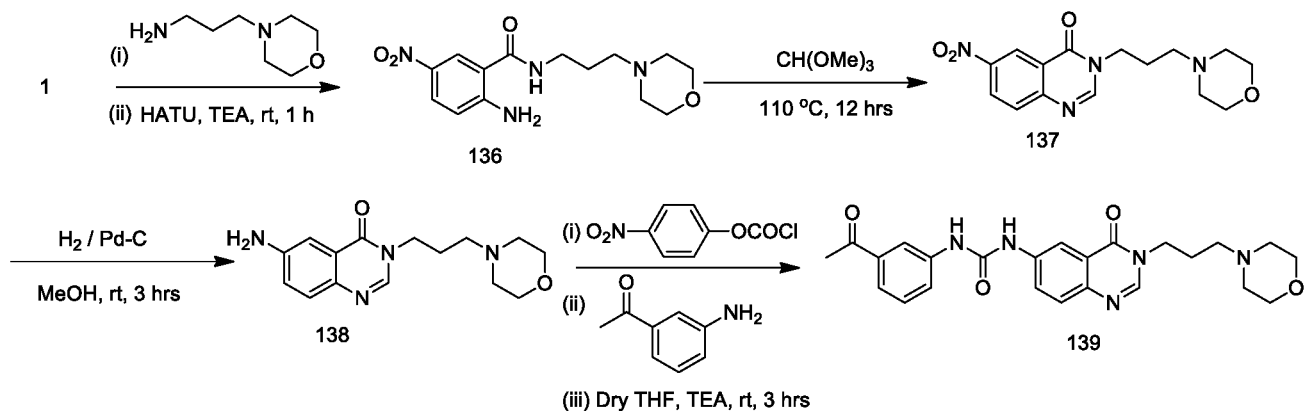


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Scheme 19

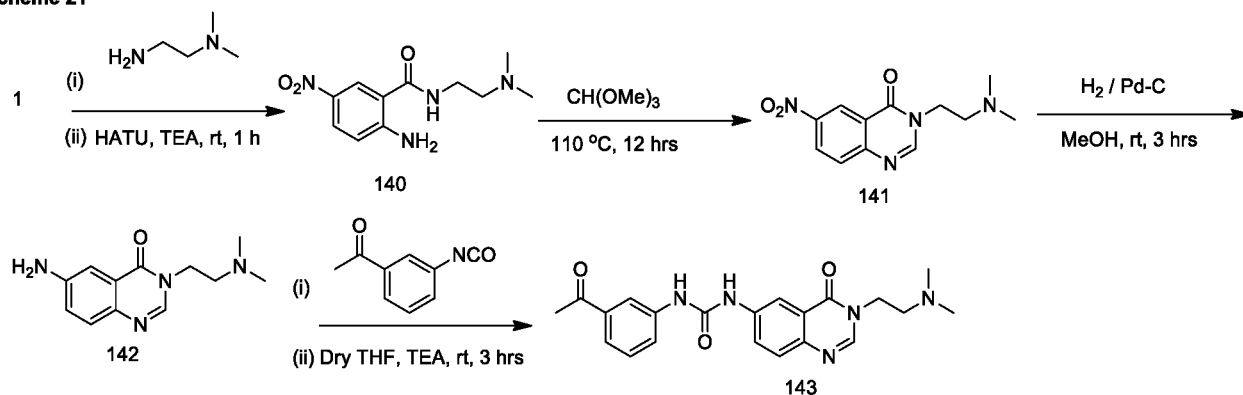


Scheme 20

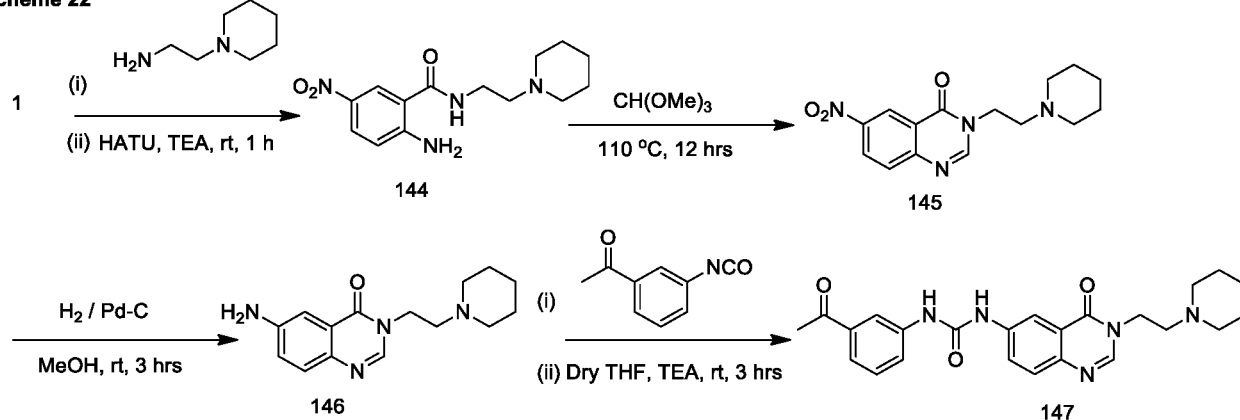


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Scheme 21

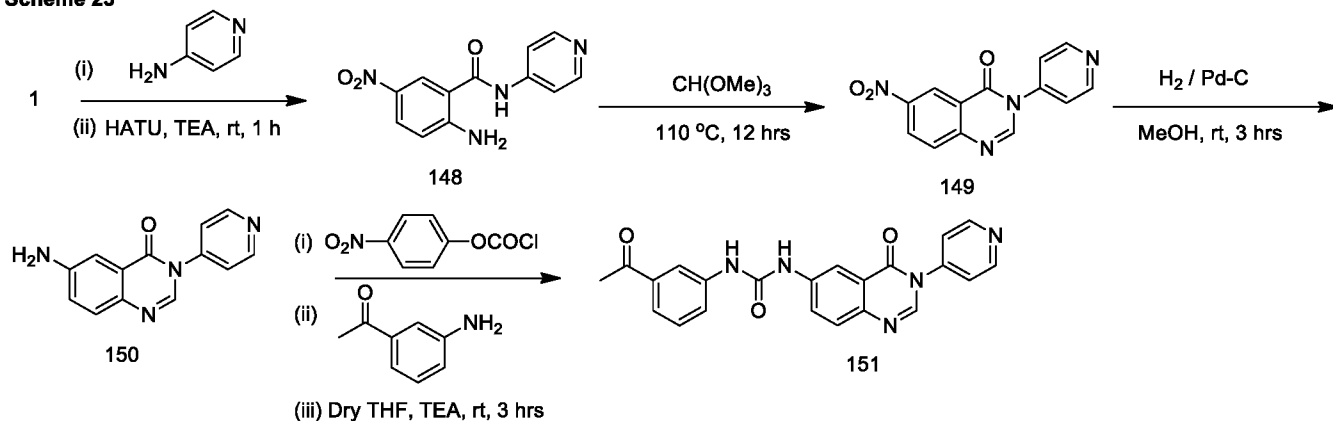


Scheme 22

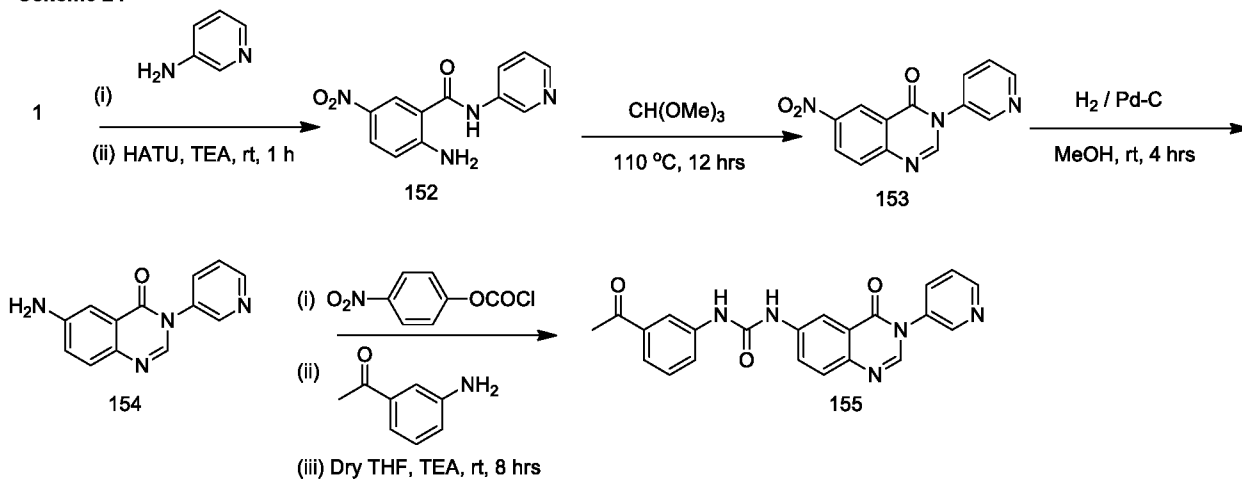


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Scheme 23

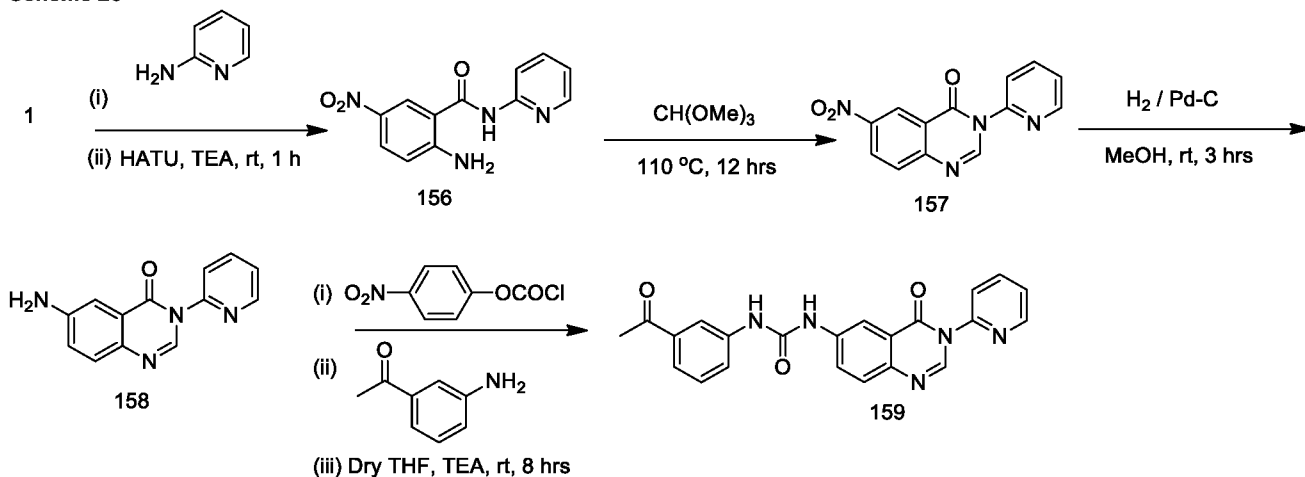


Scheme 24

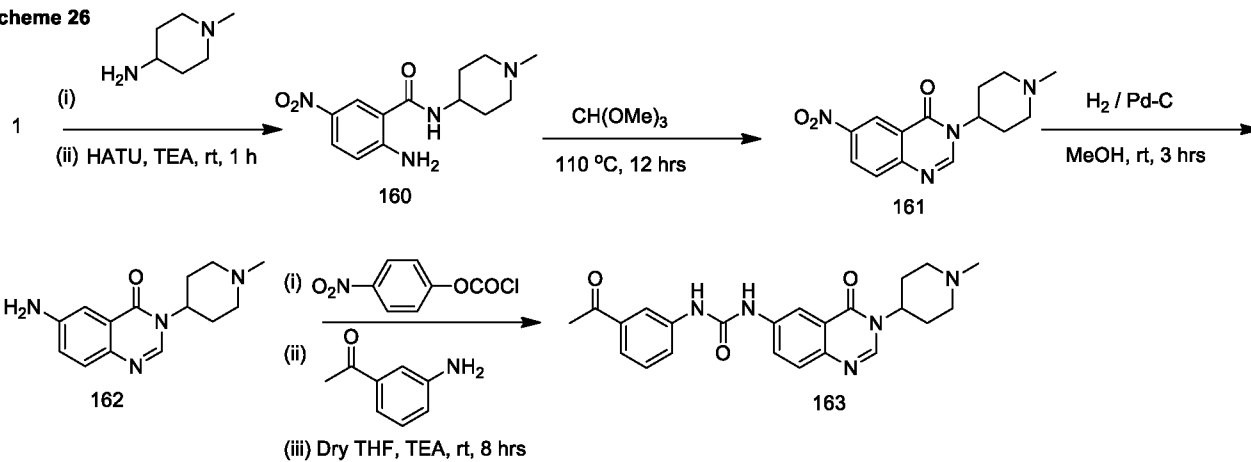


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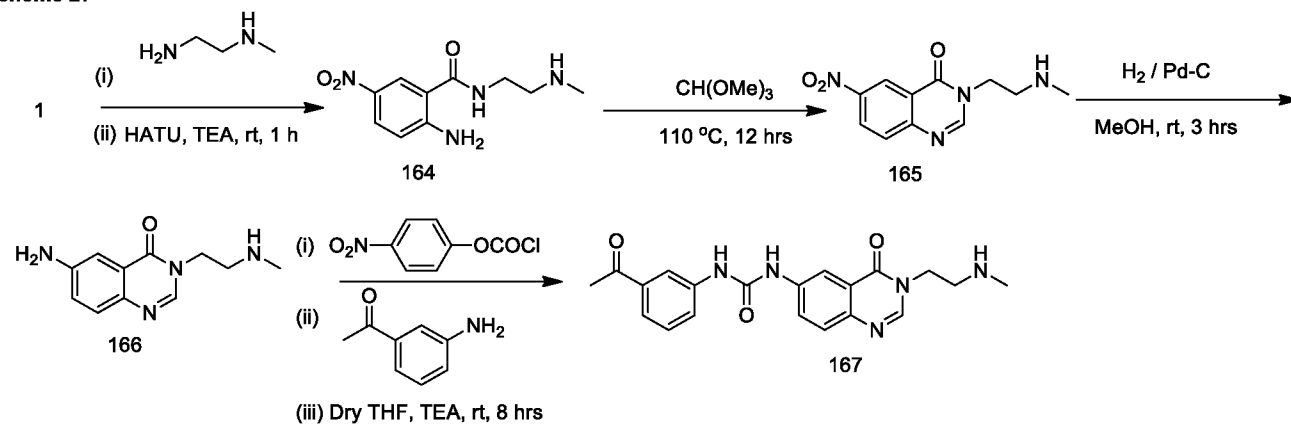
Scheme 25



Scheme 26

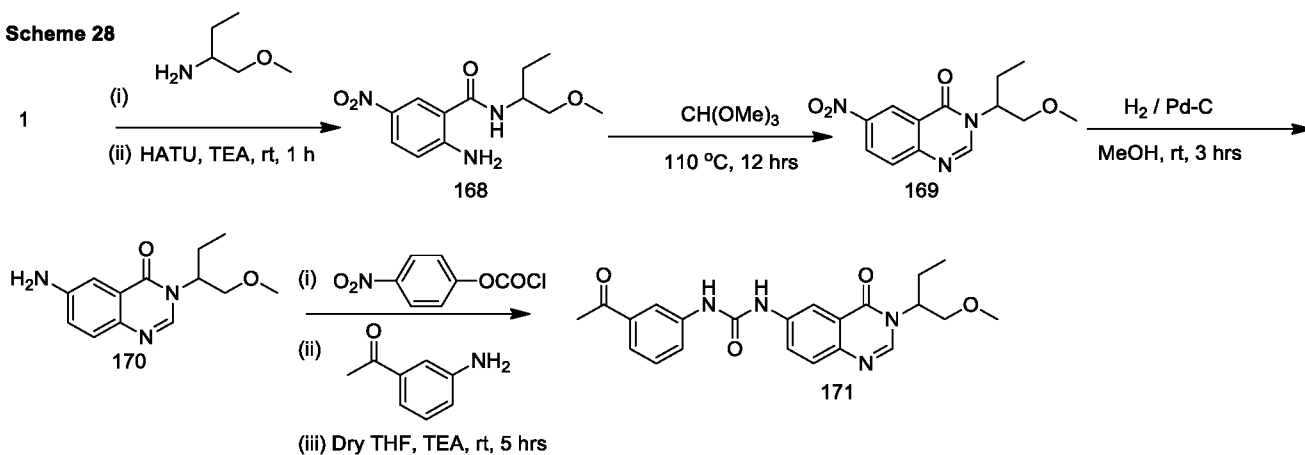


Scheme 27

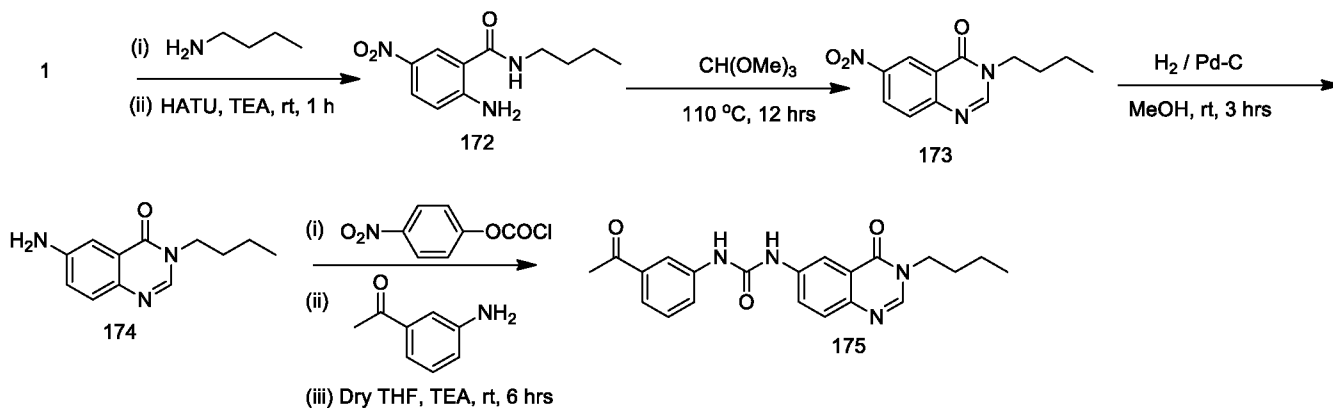


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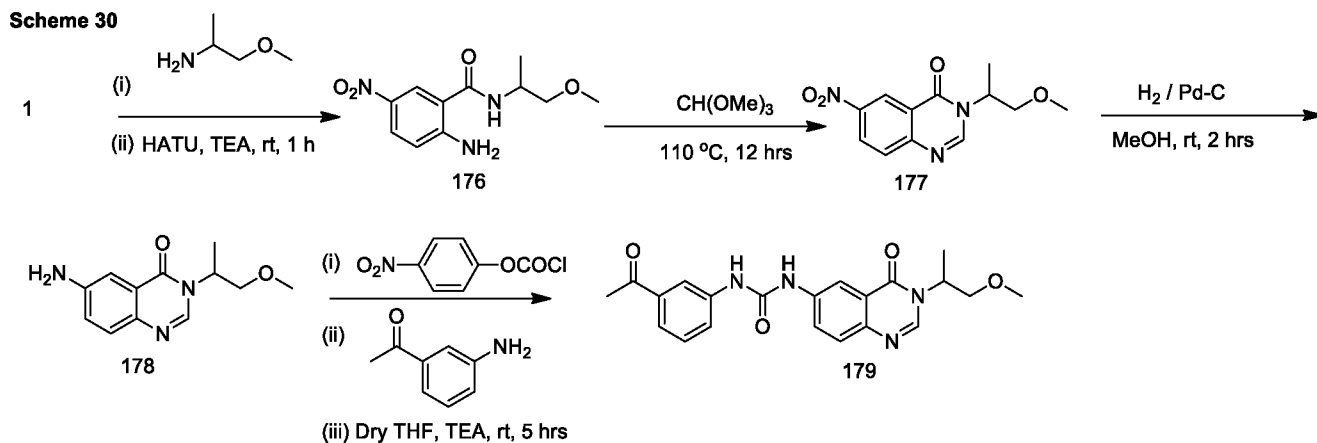
Scheme 28



Scheme 29

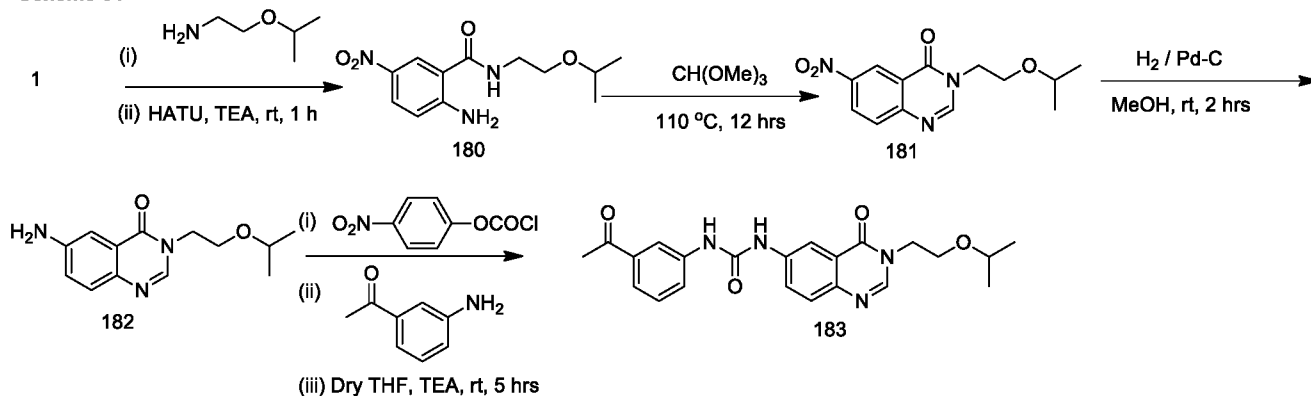


Scheme 30



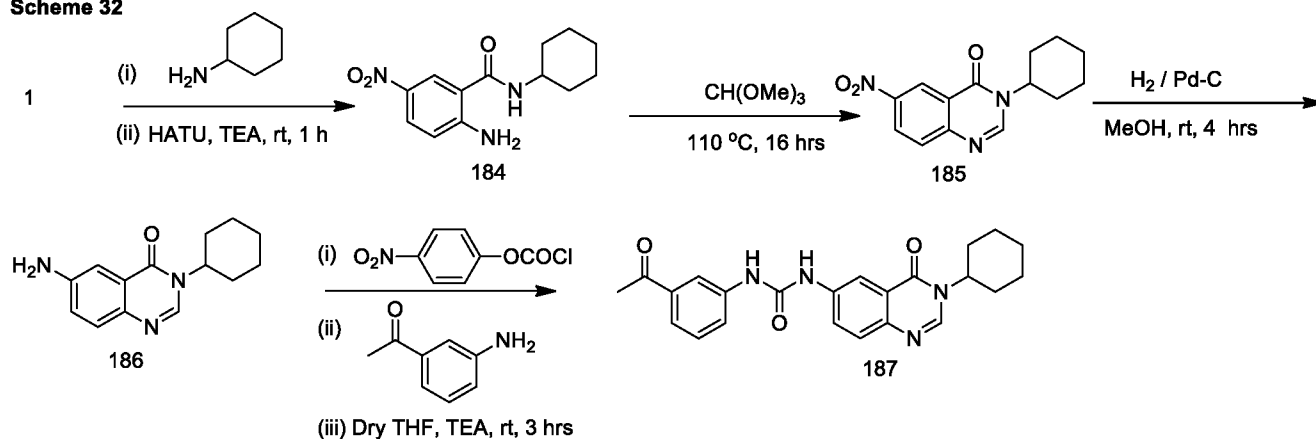
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Scheme 31

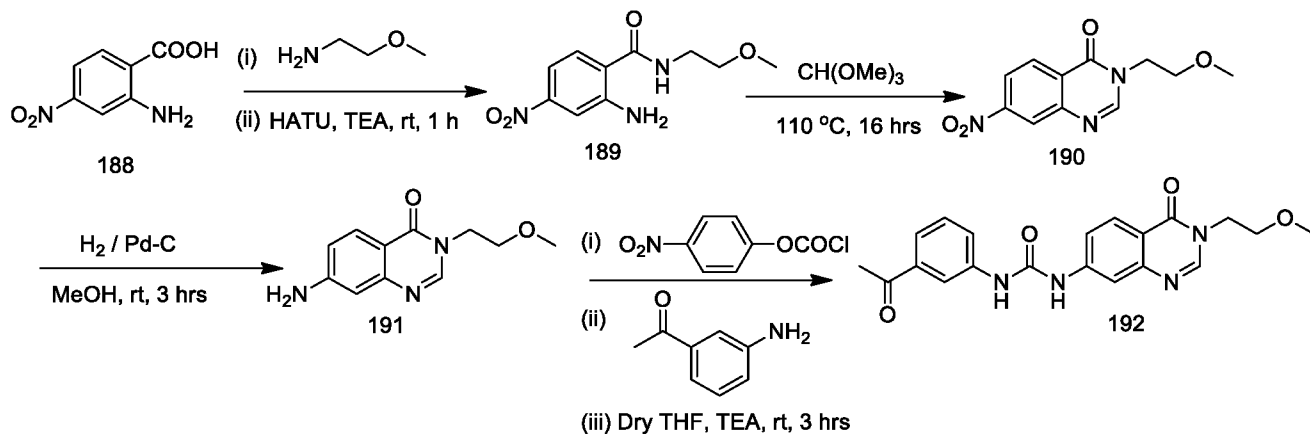


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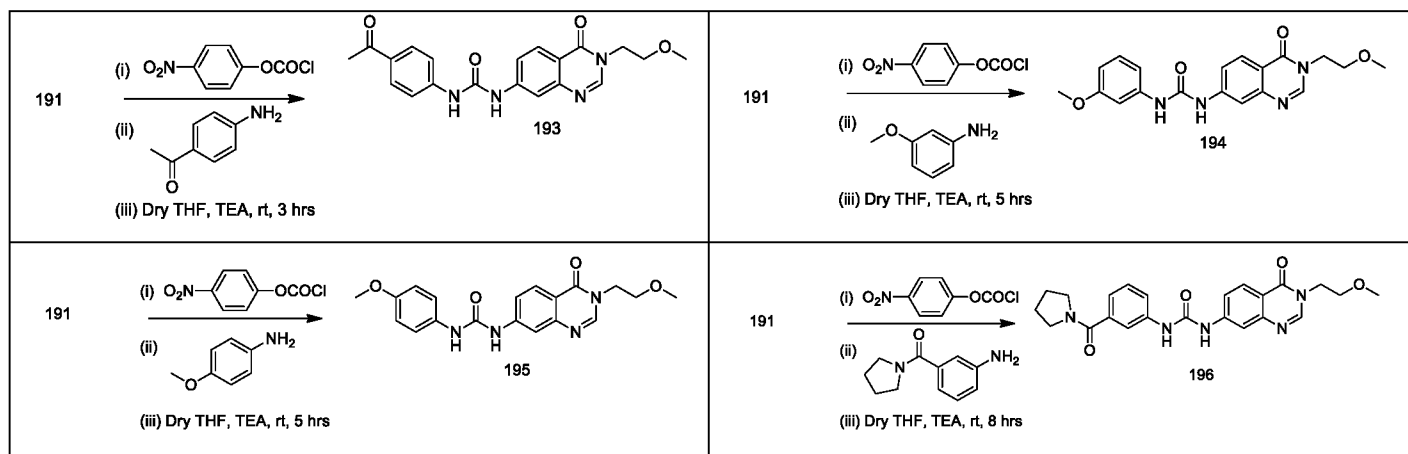
Scheme 32

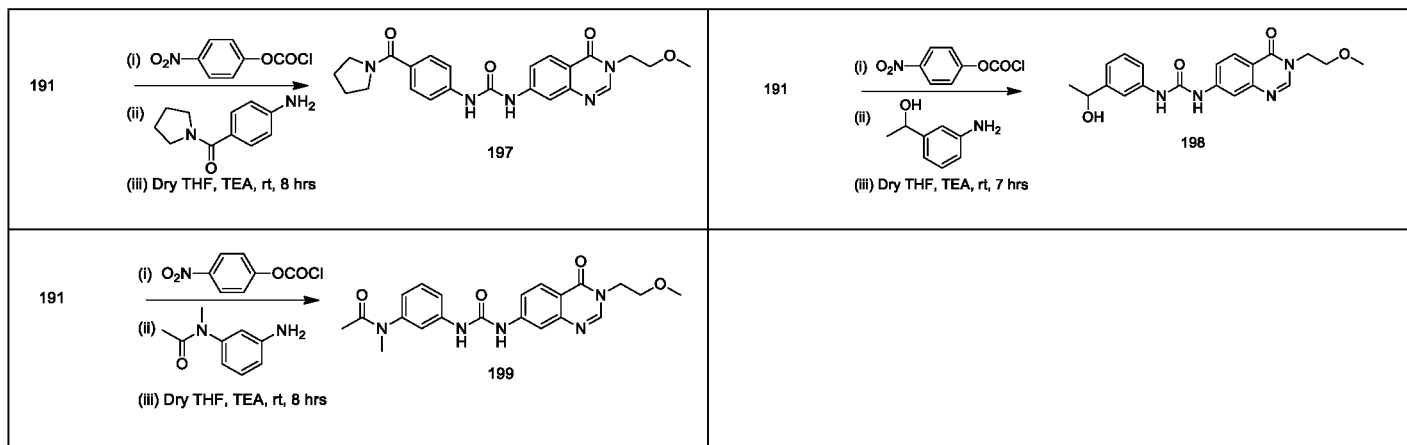


Scheme 33

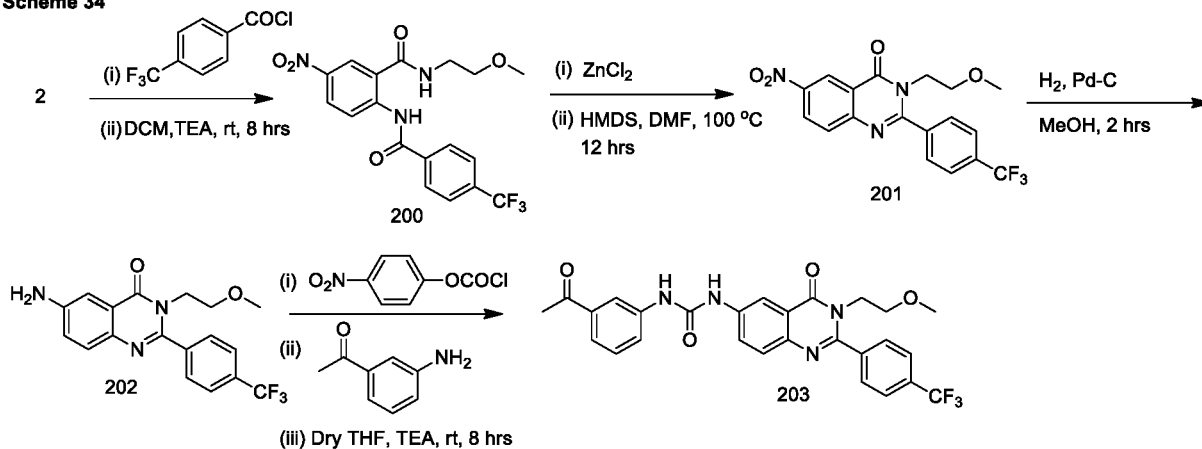


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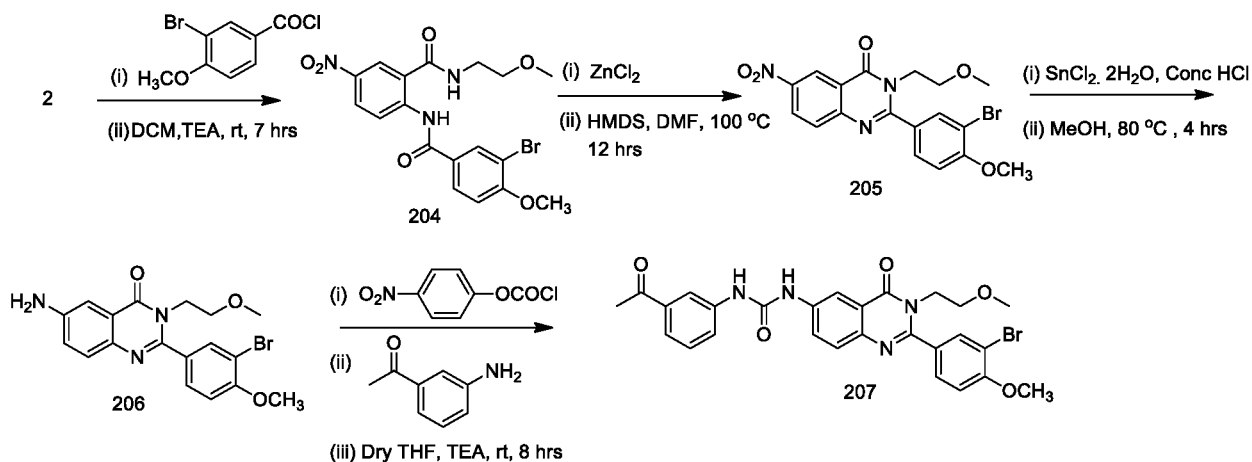




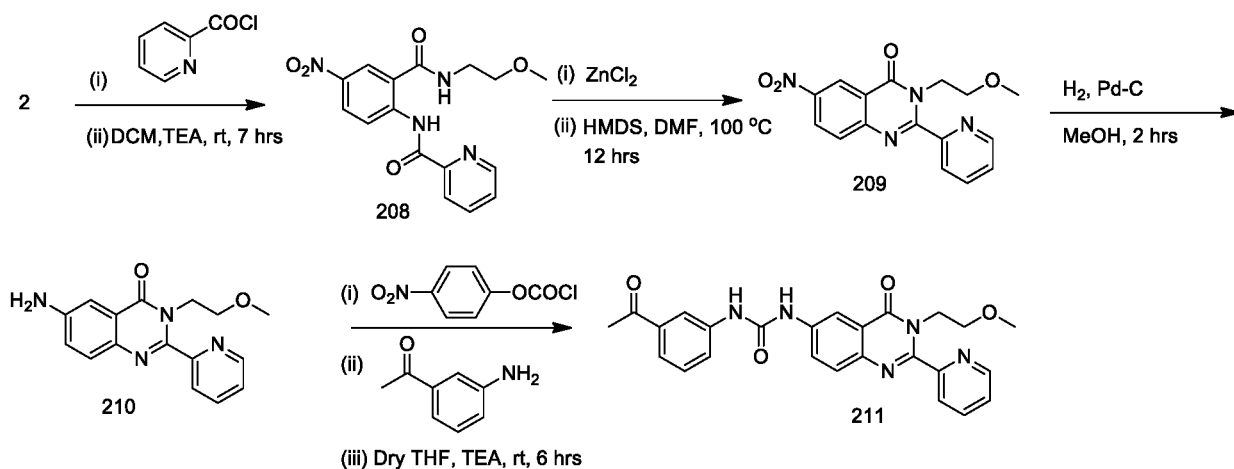
Scheme 34



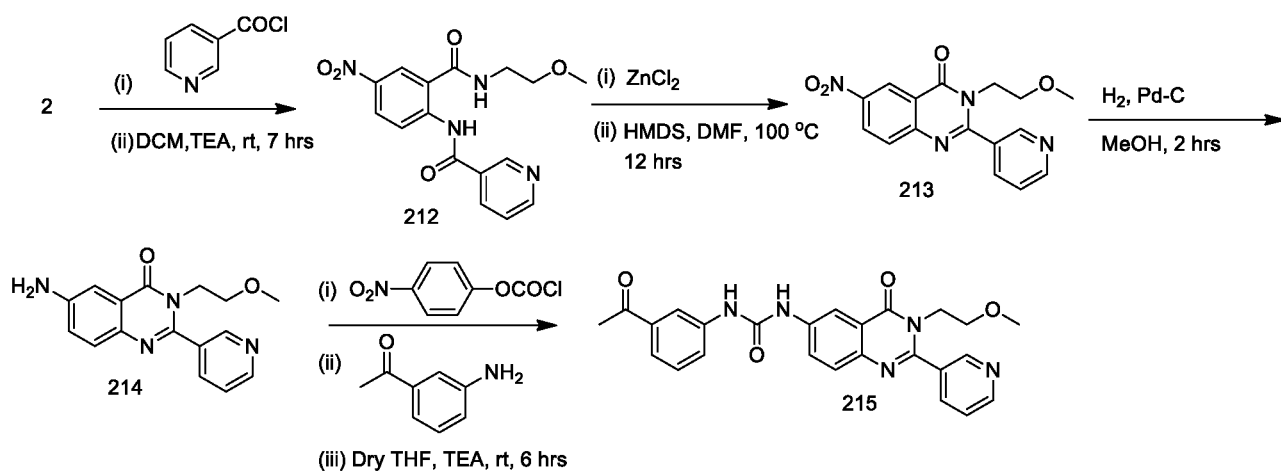
Scheme 35



Scheme 36

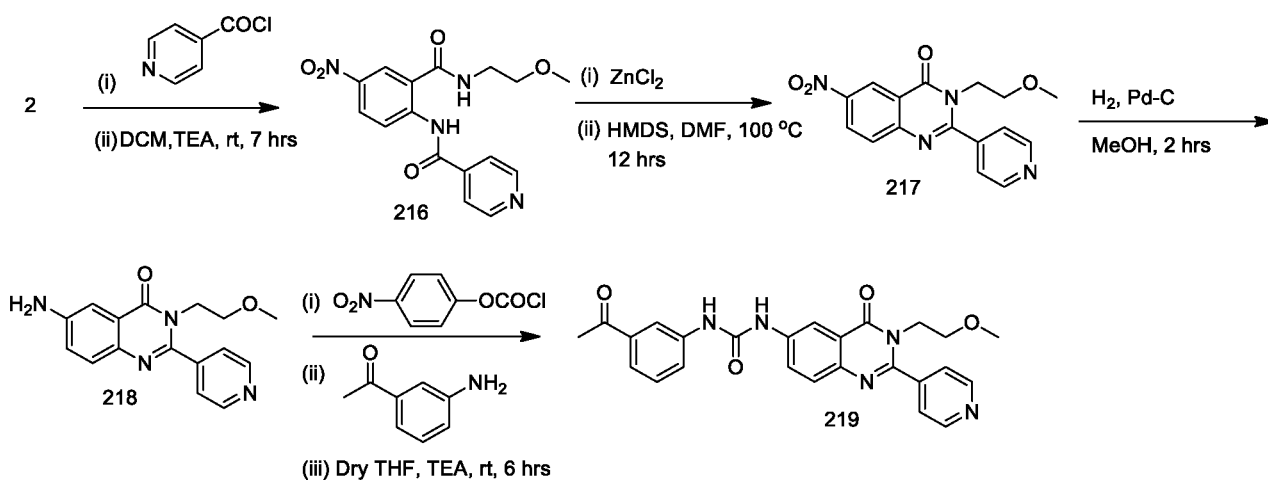


Scheme 37

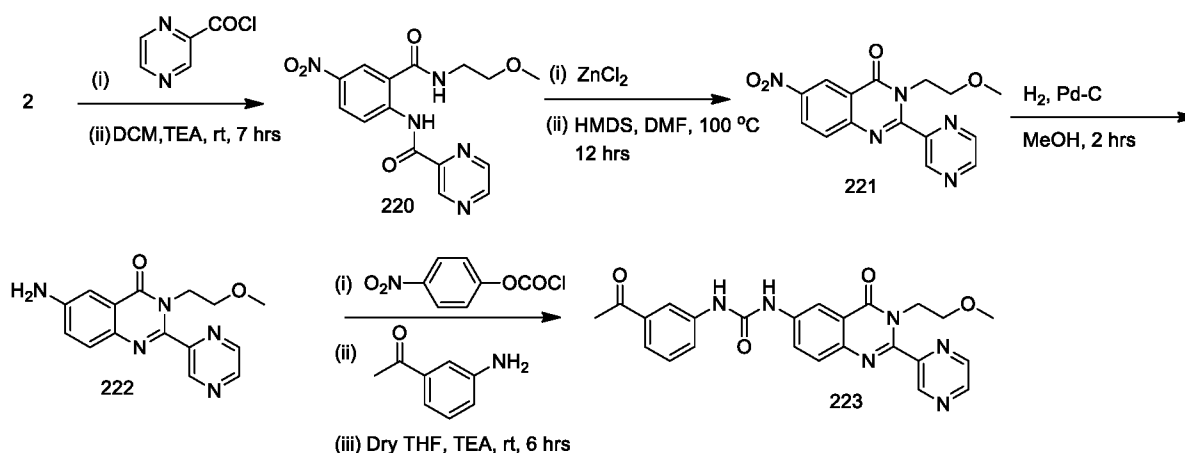


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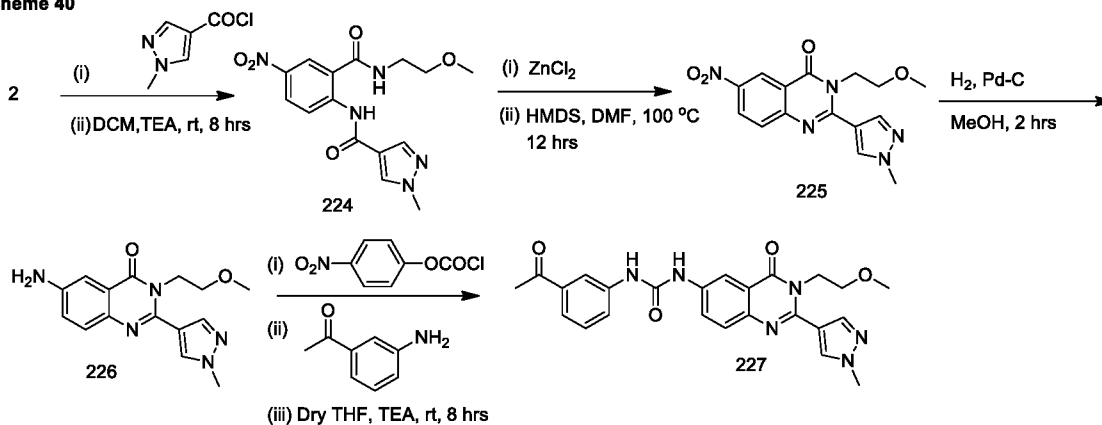
Scheme 38



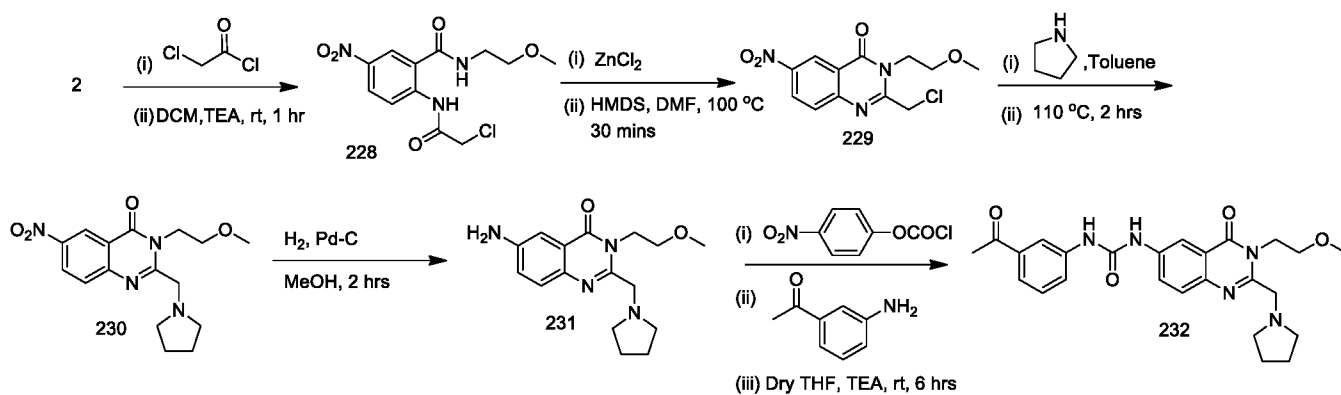
Scheme 39



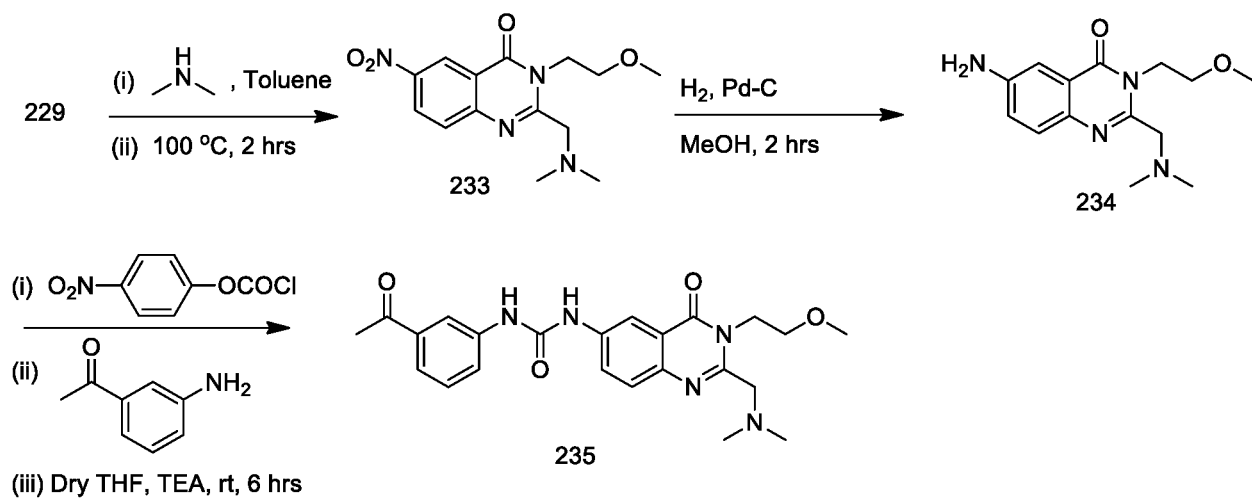
Scheme 40



Scheme 41

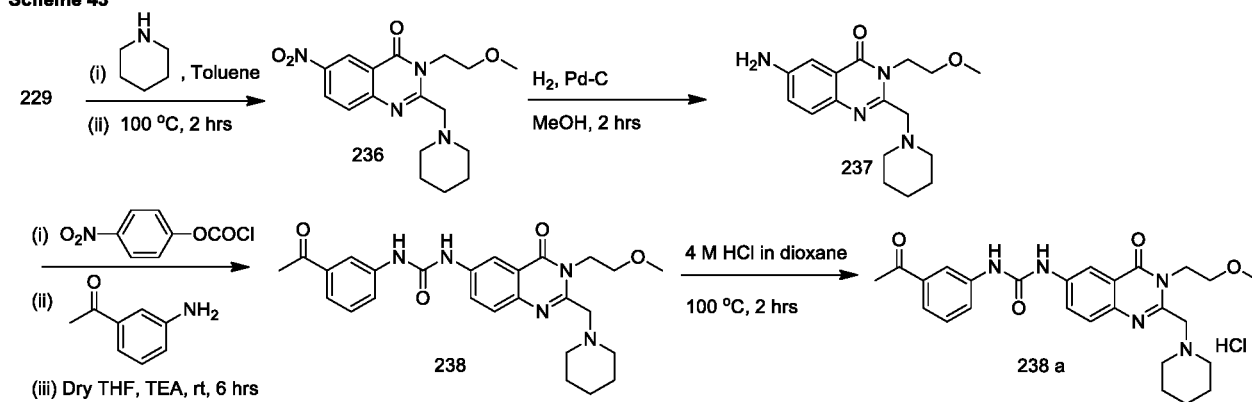


Scheme 42

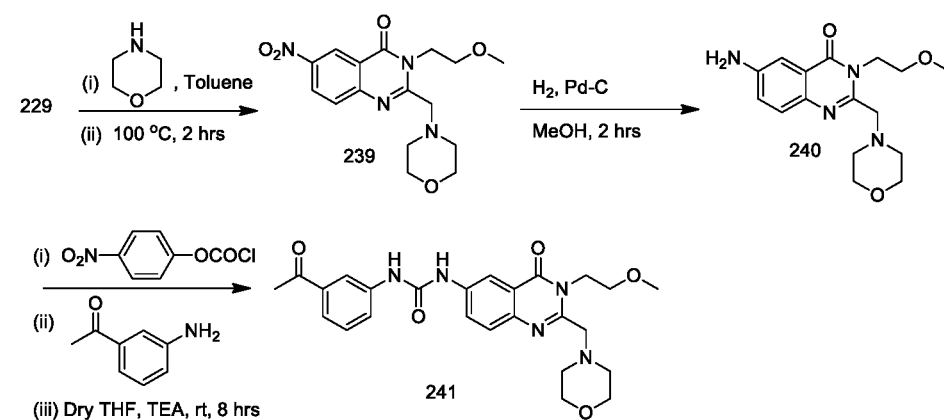


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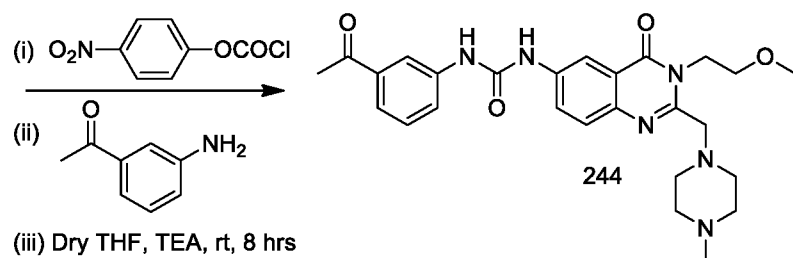
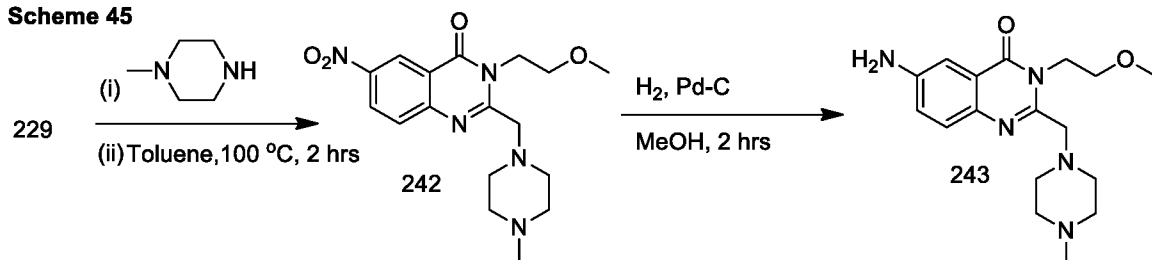
Scheme 43



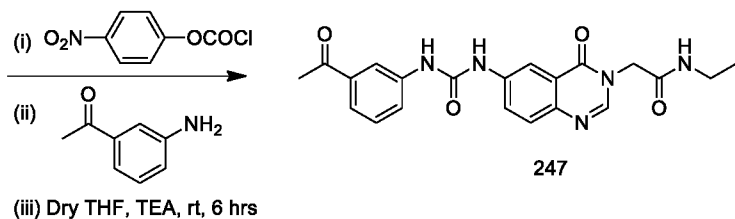
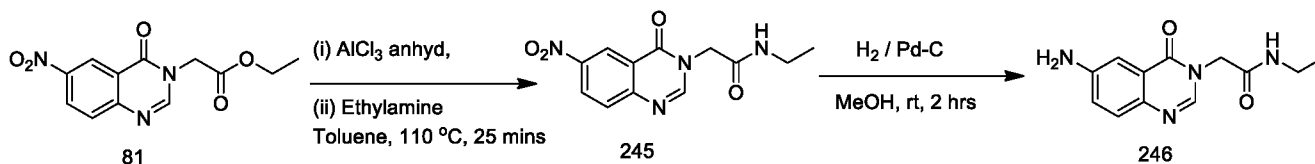
Scheme 44



Scheme 45

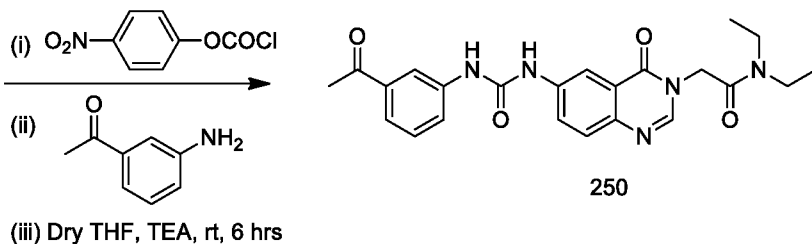
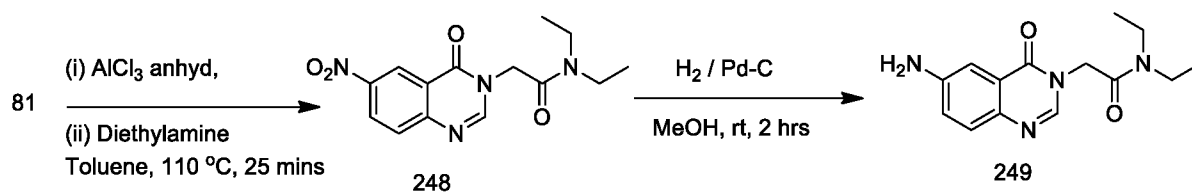


Scheme 46

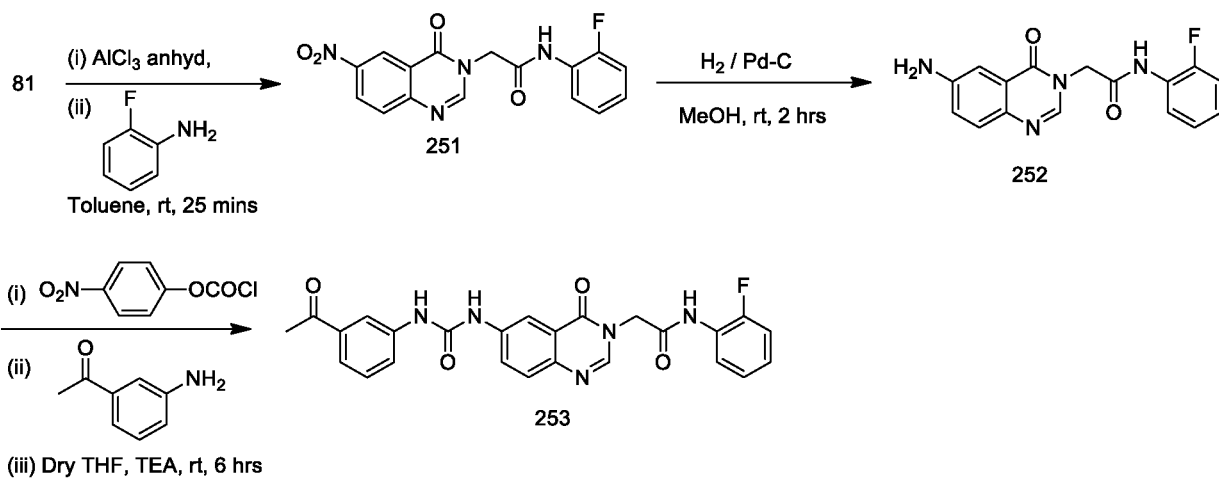


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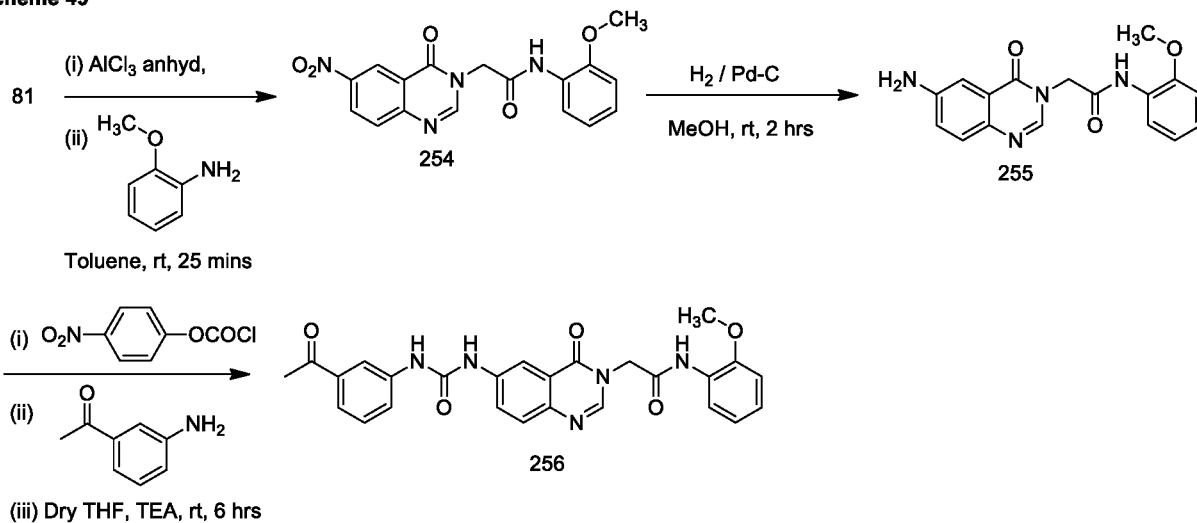
Scheme 47



Scheme 48

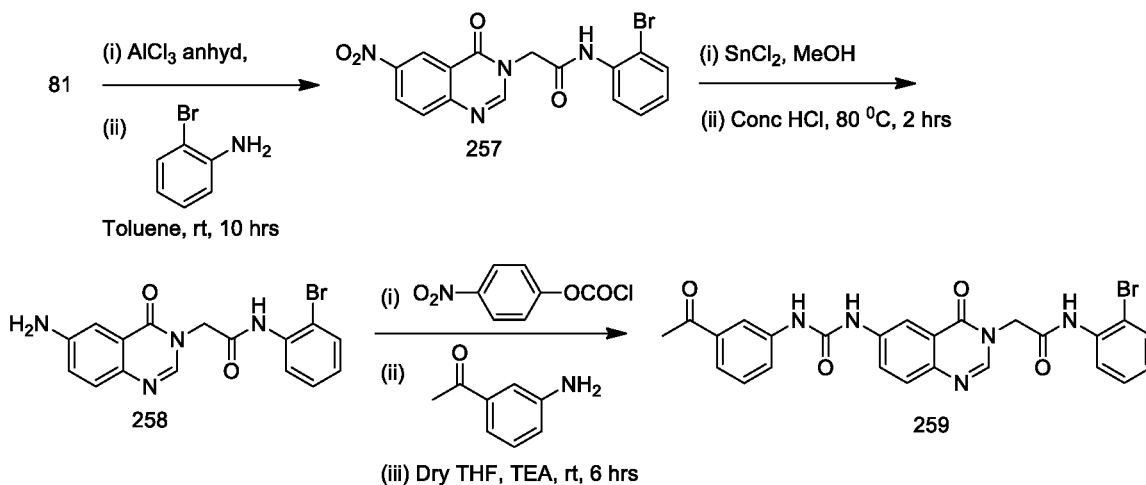


Scheme 49

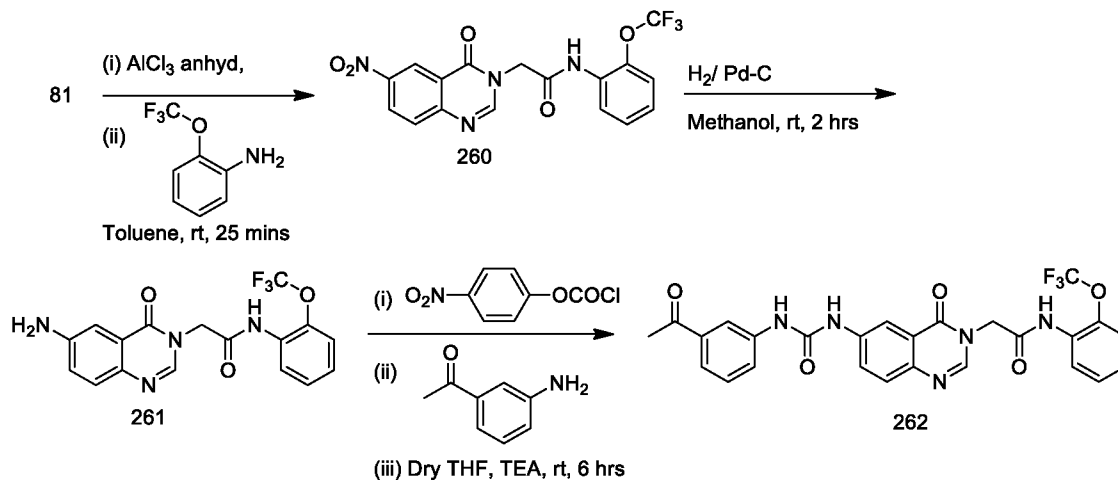


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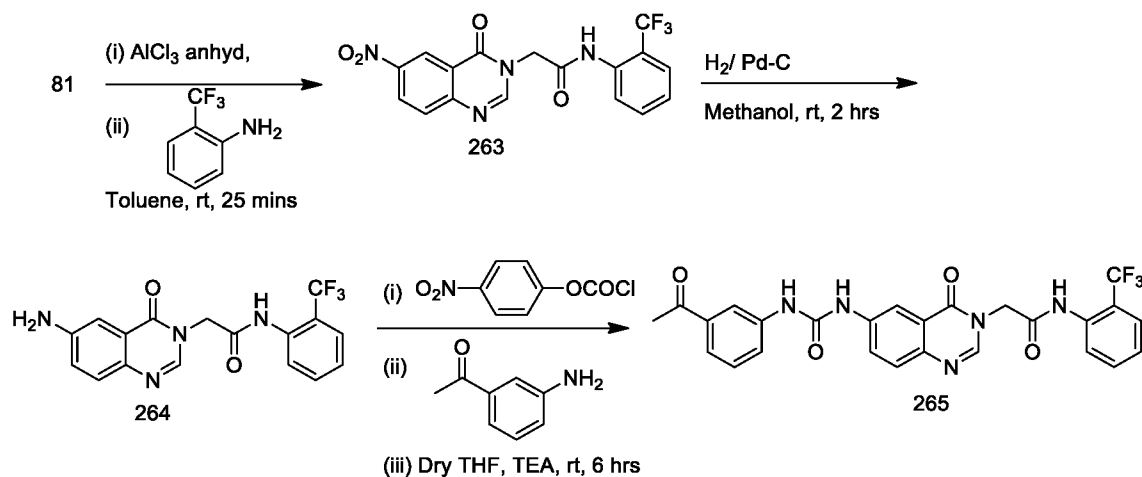
Scheme 50



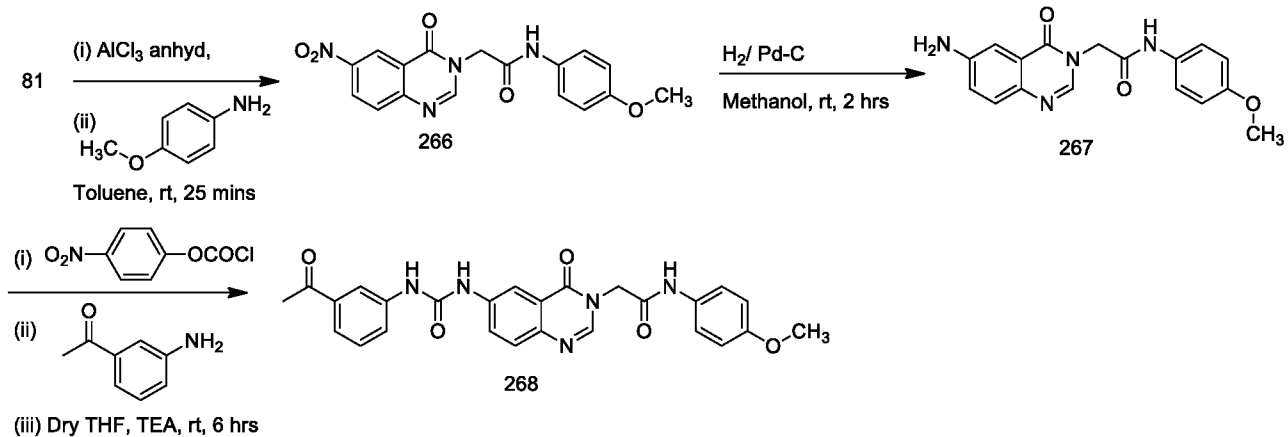
Scheme 51



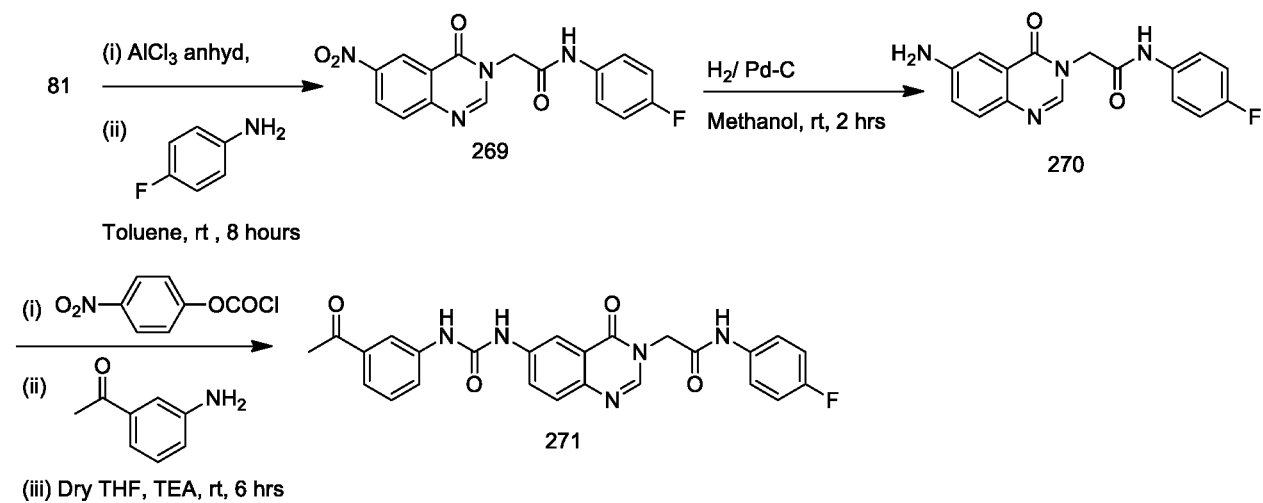
Scheme 52



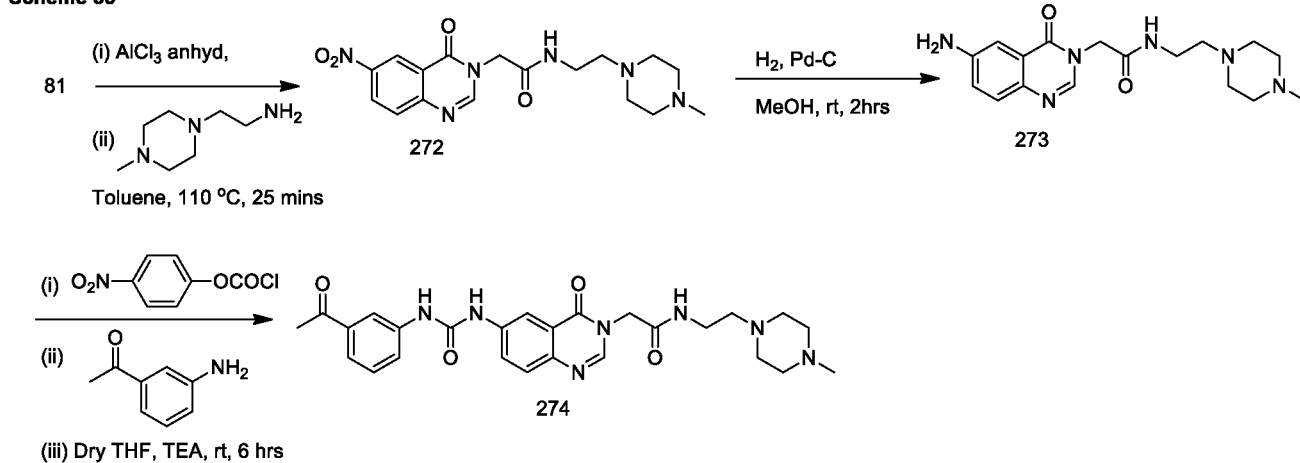
Scheme 53



Scheme 54

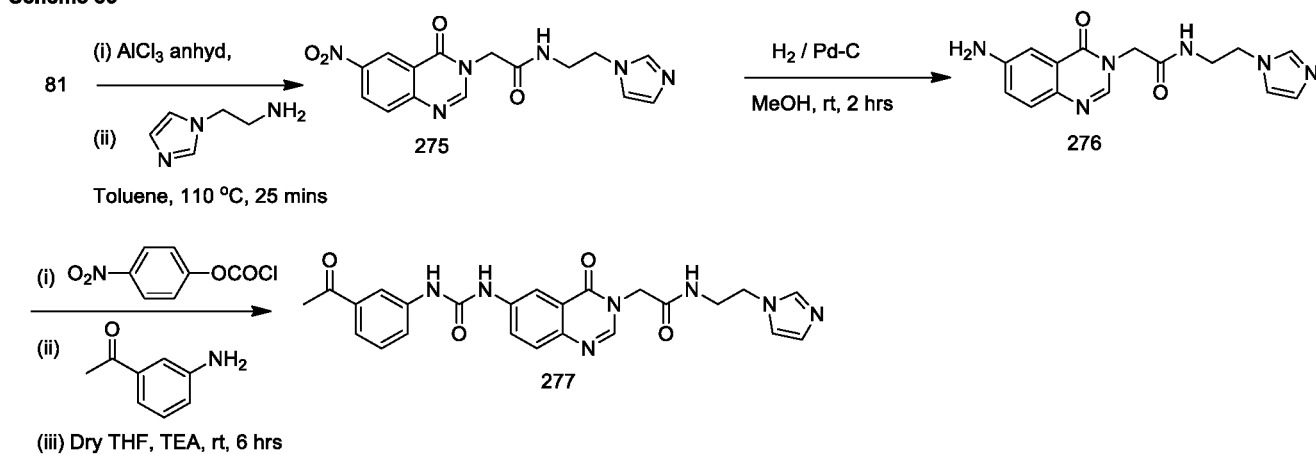


Scheme 55

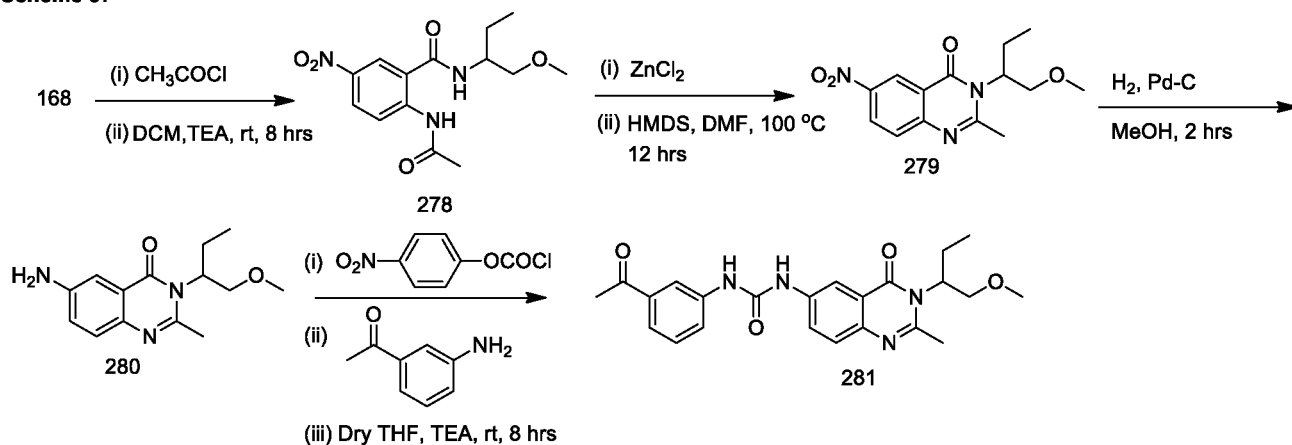


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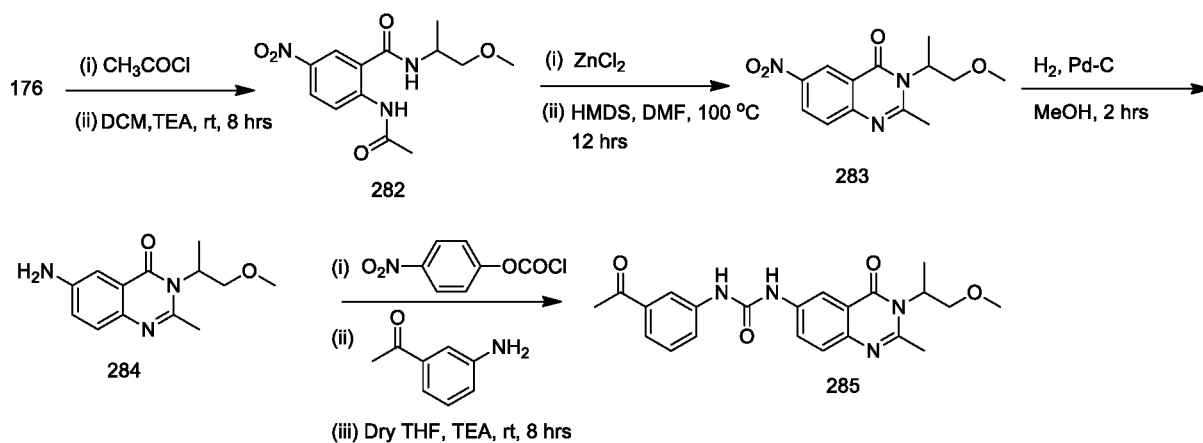
Scheme 56



Scheme 57

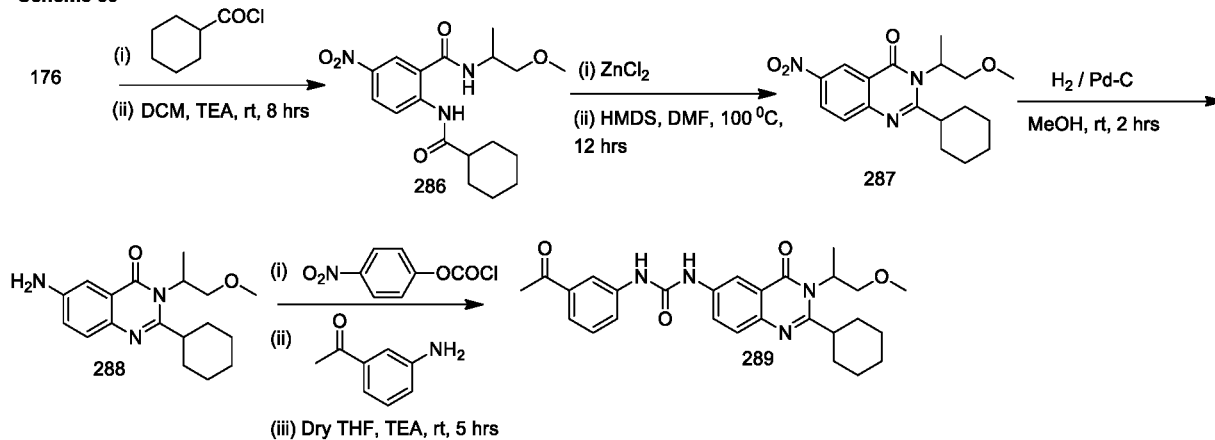


Scheme 58



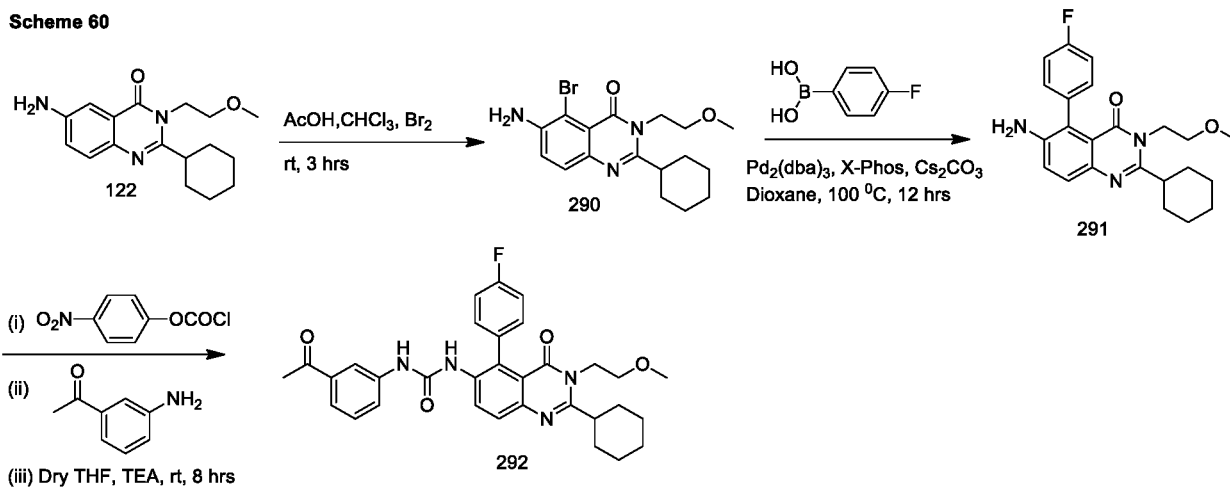
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Scheme 59

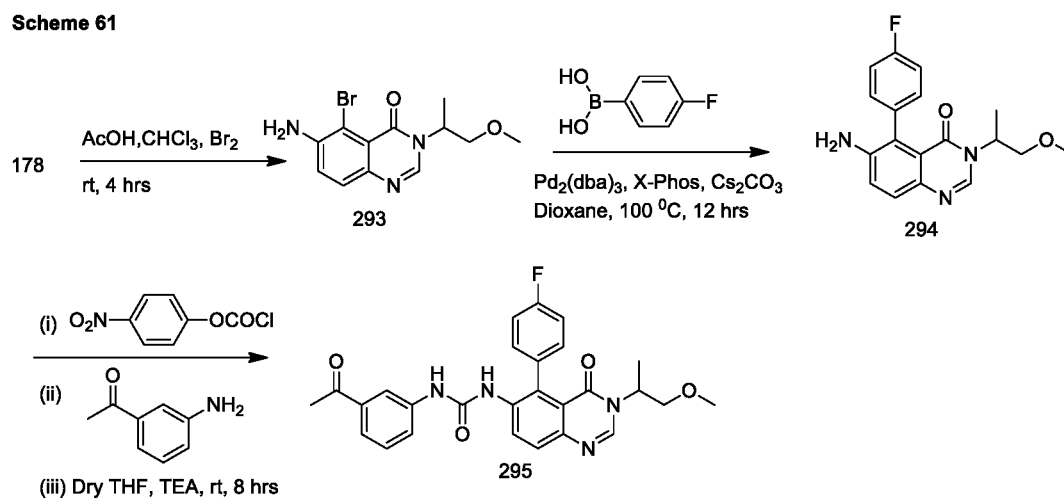


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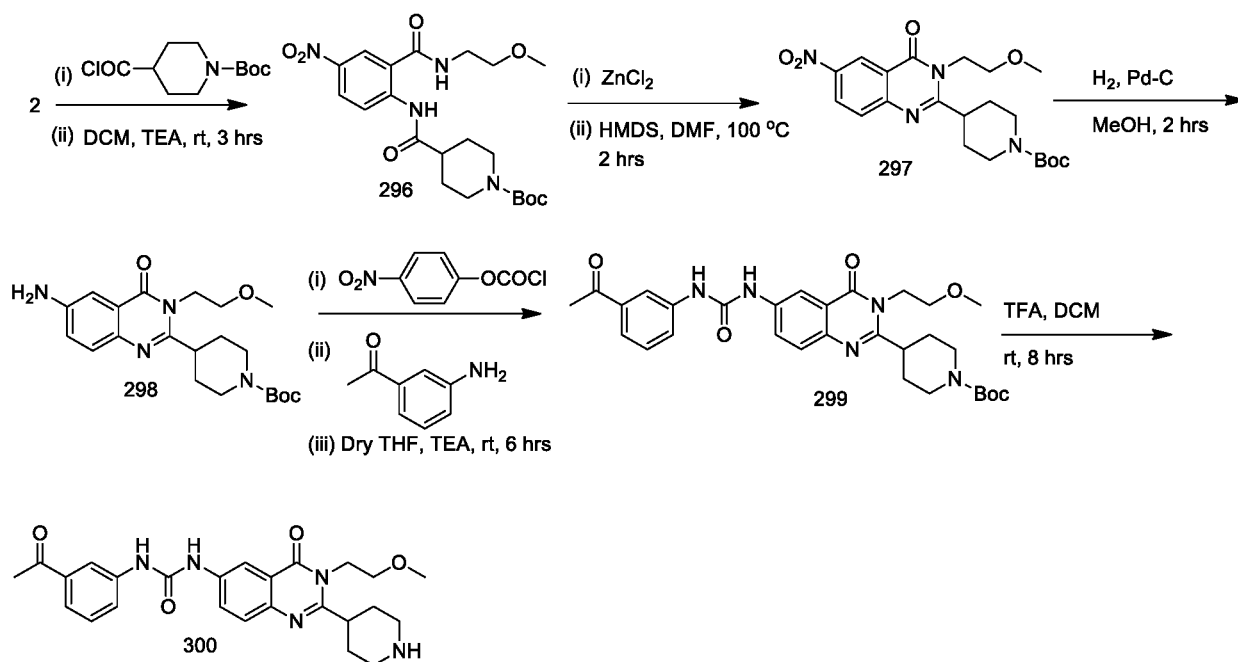
Scheme 60



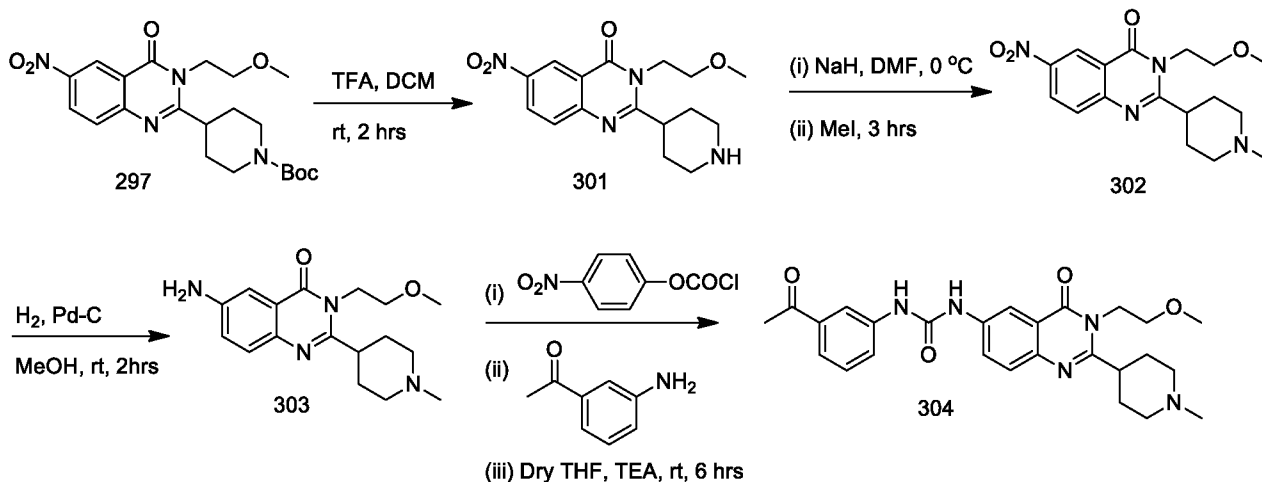
Scheme 61



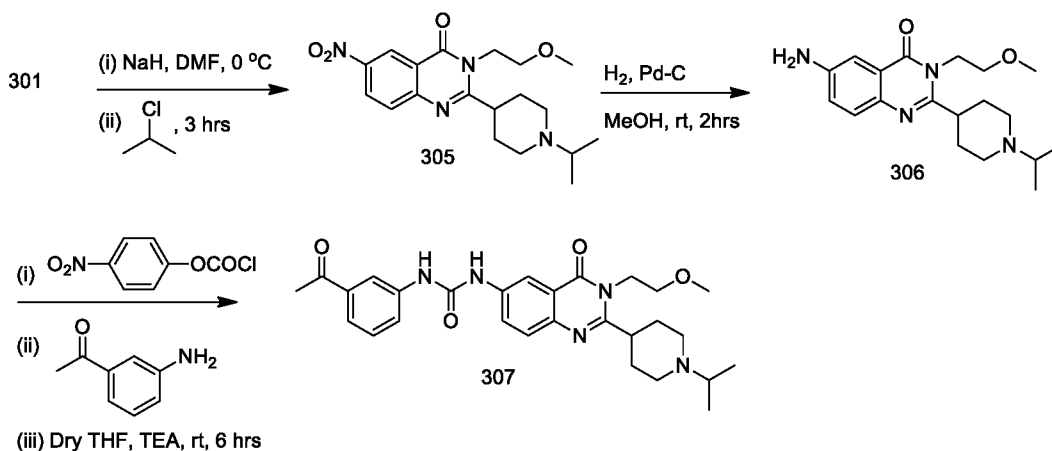
Scheme 62



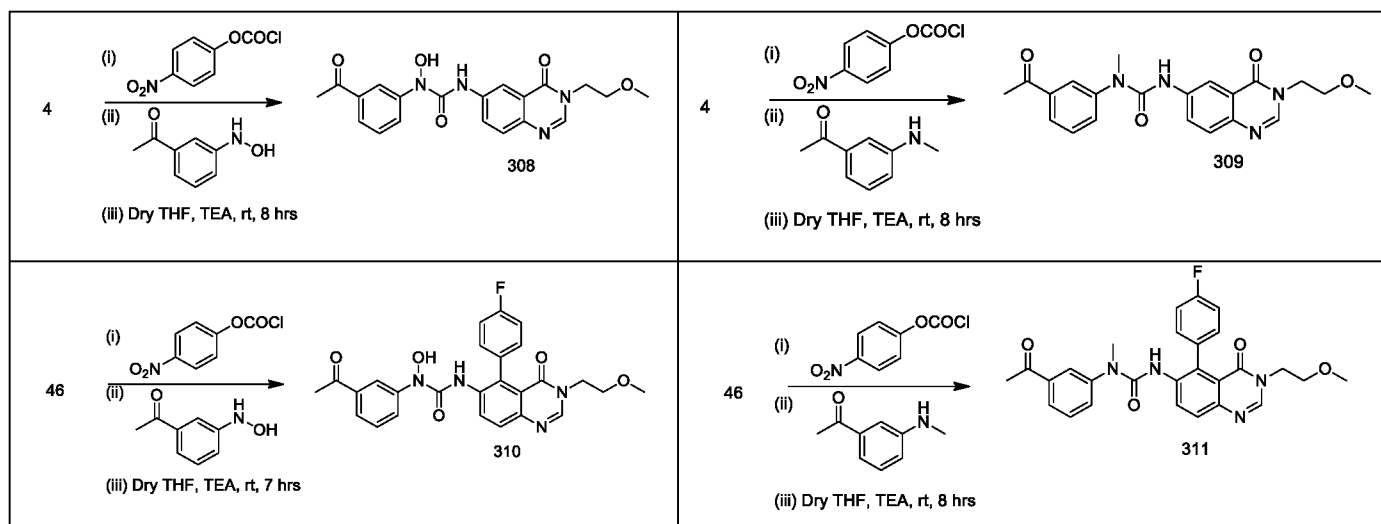
Scheme 63

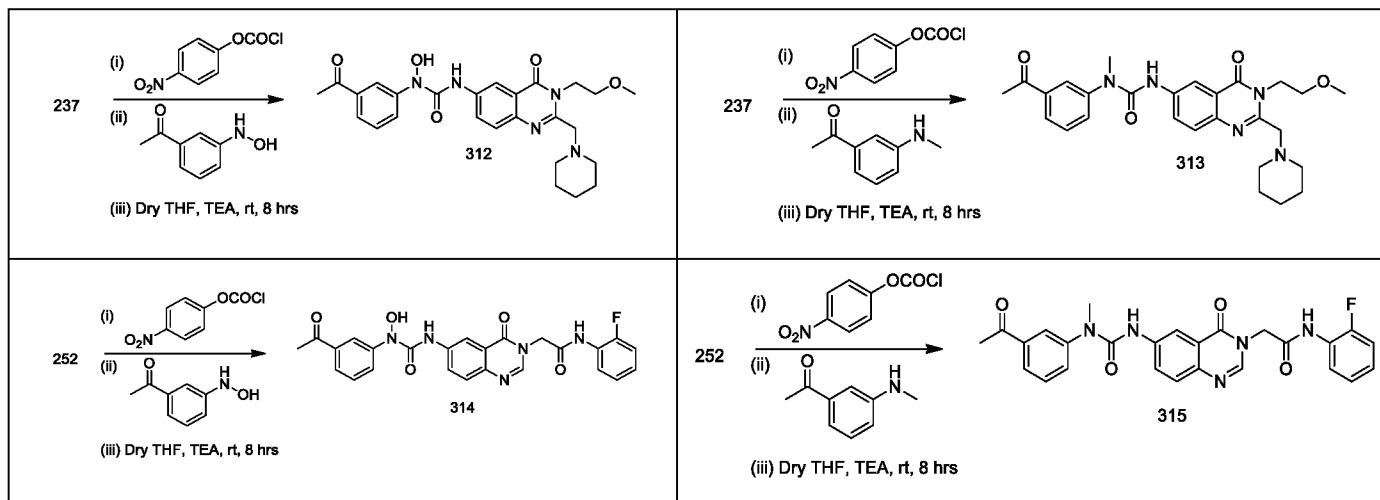


Scheme 64

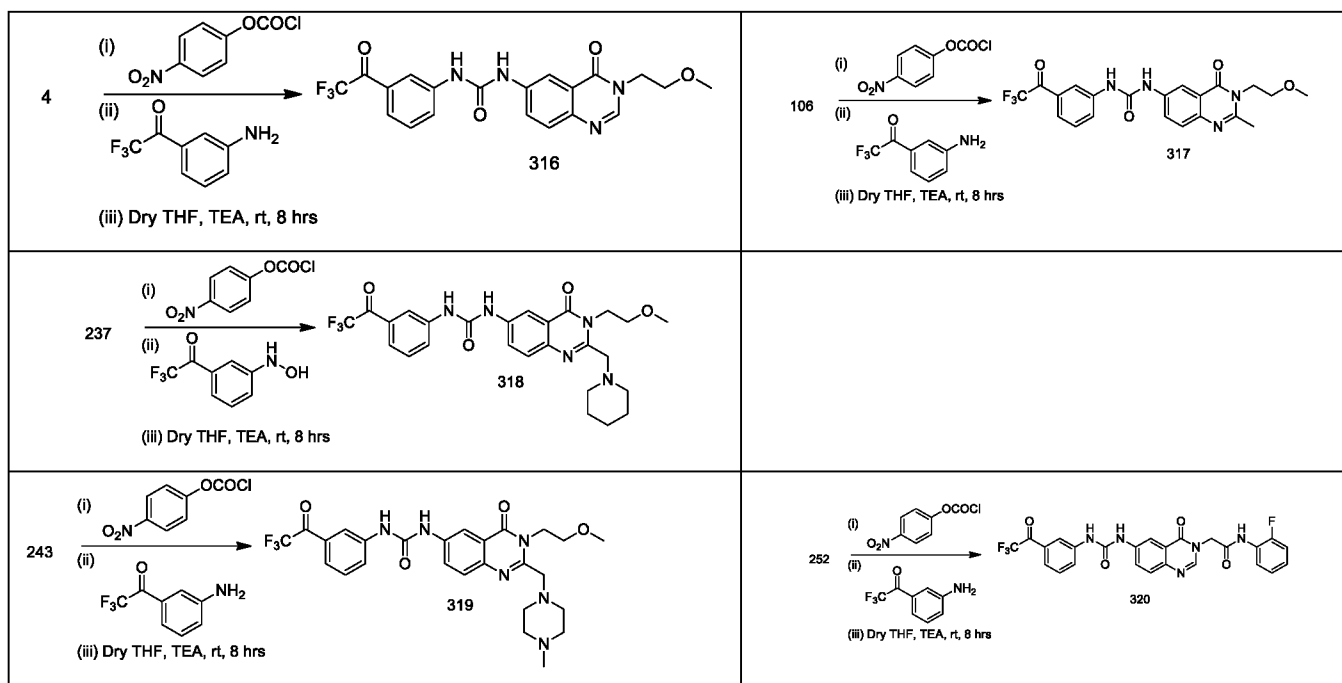


5 **Scheme 65**

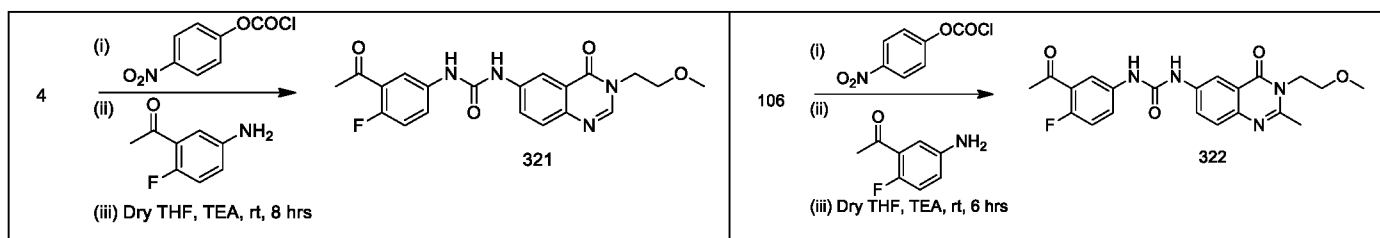


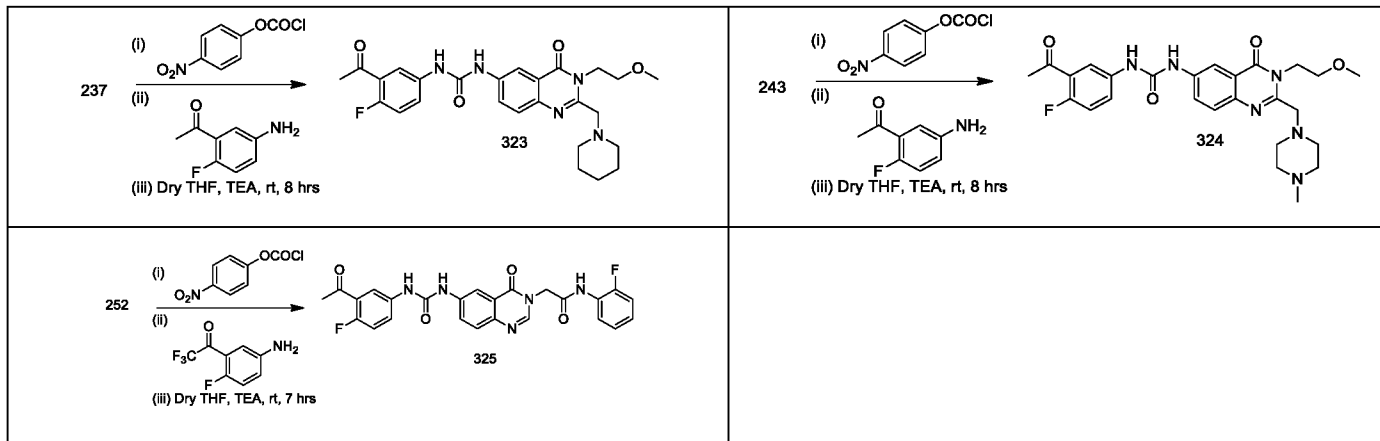


Scheme 66

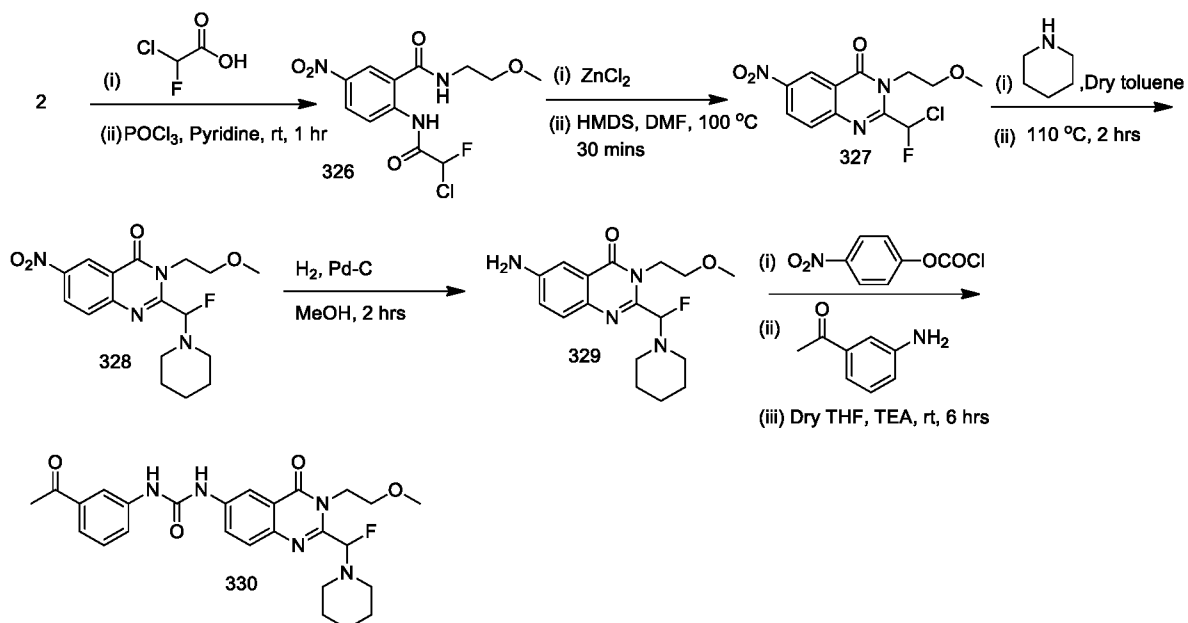


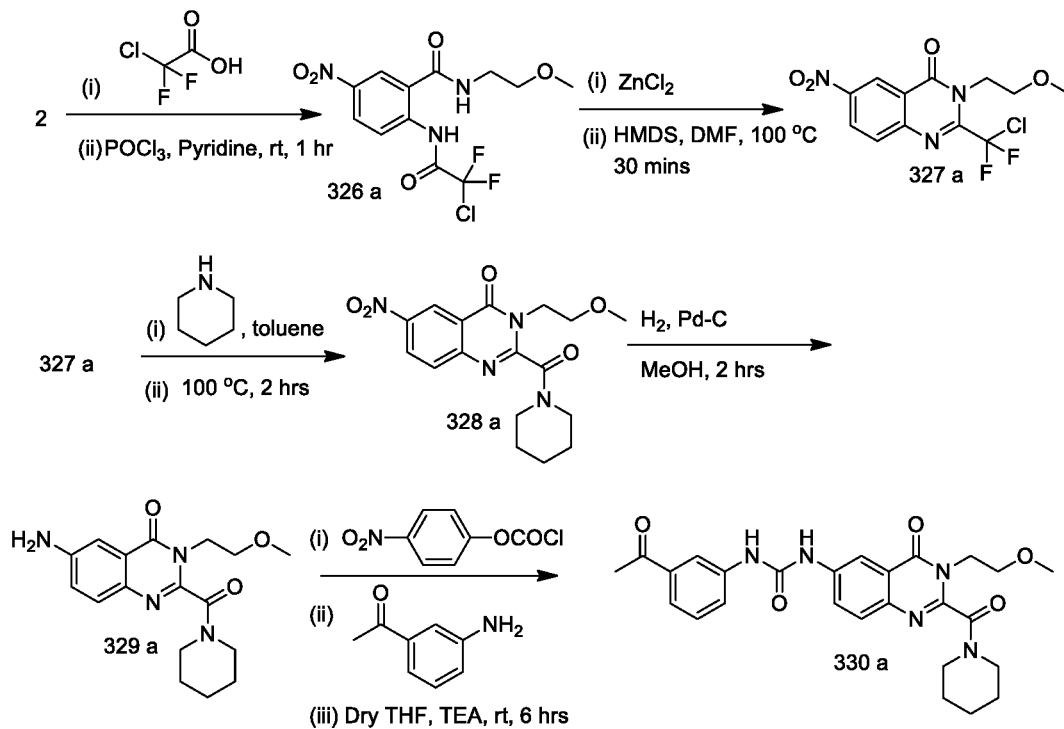
Scheme 67



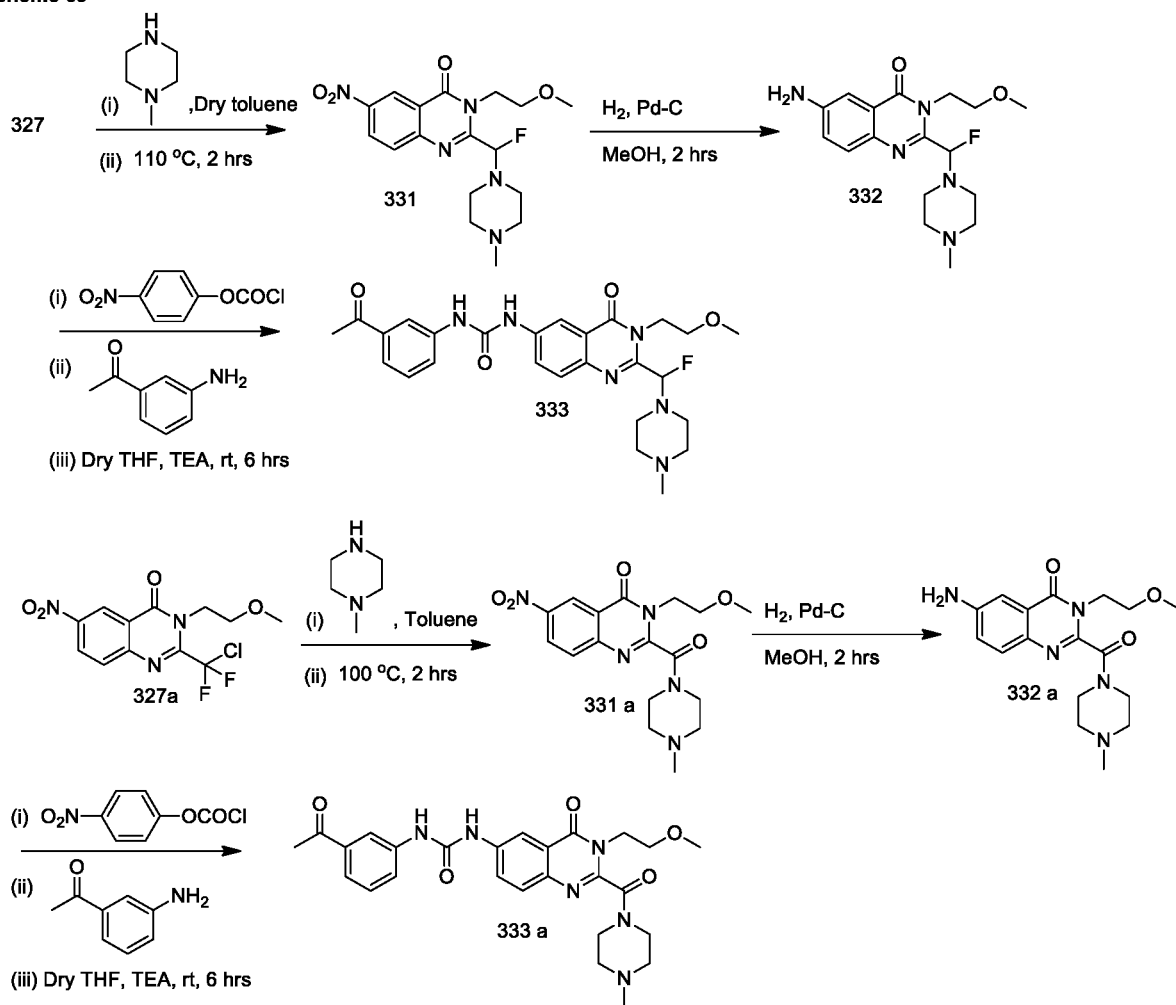


Scheme 68

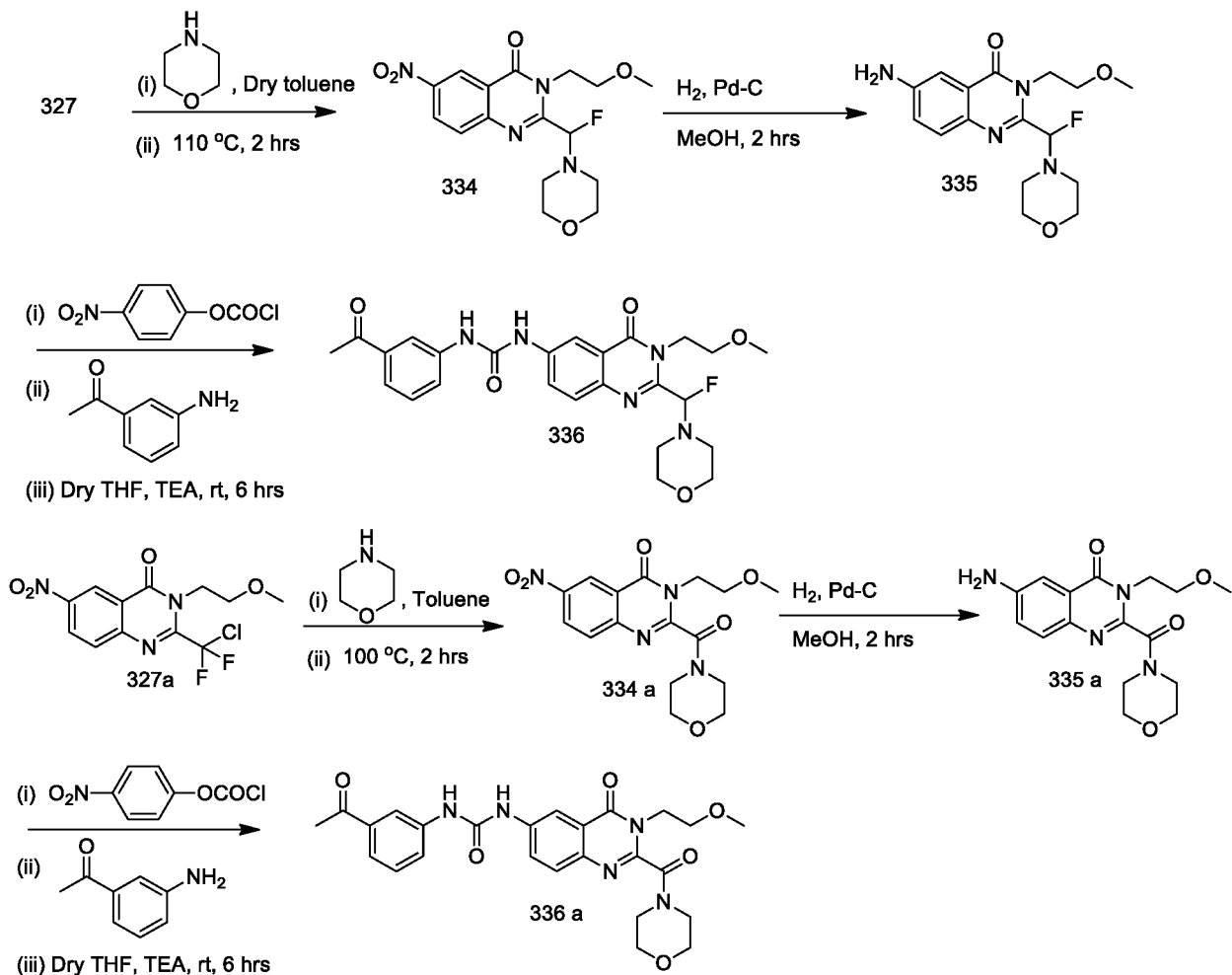




Scheme 69

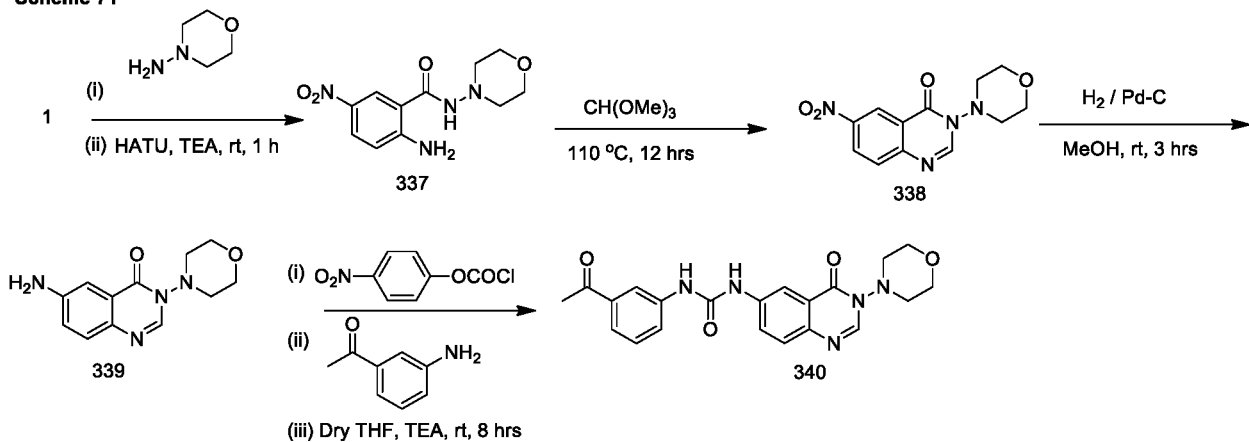


Scheme 70

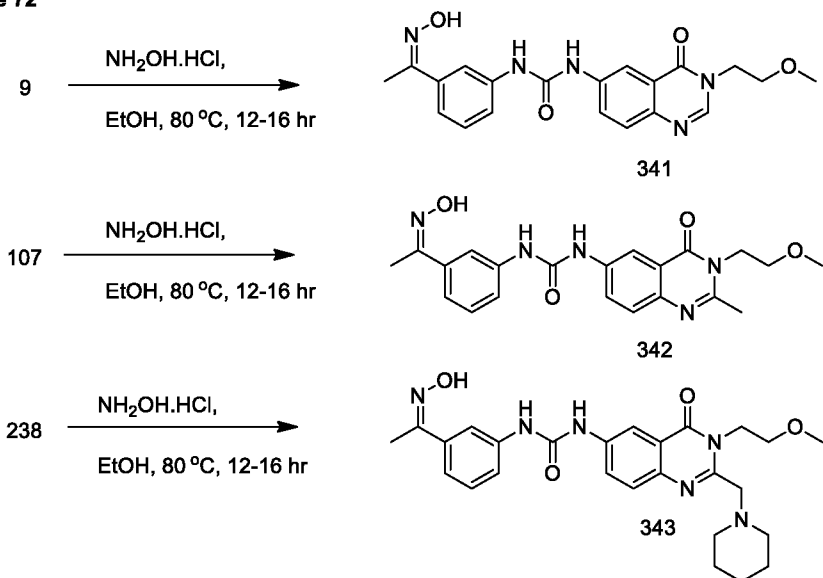


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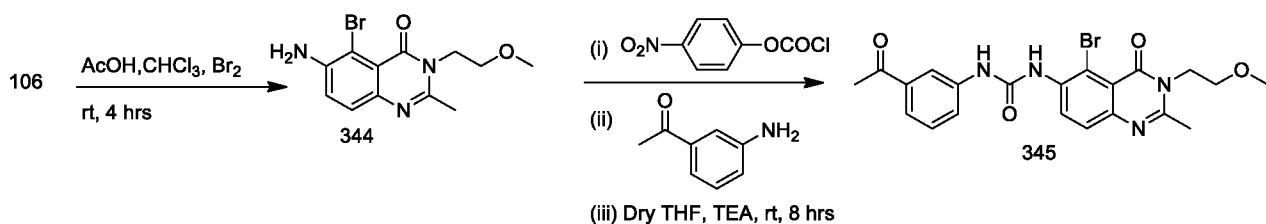
Scheme 71



Scheme 72



Scheme 73



5

In an embodiment of the present invention, there is provided a compound having structure I for use in treating diseases and disorders related to modulation of COP1 enzyme through its stabilization or modulation of ATGL.

10 In another embodiment of the present invention, there is provided a compound having structure I for use in decreasing the level of triglycerides in hepatocytes.

In yet another embodiment of the present invention, there is provided a compound having structure I for use in treatment of disease selected from Non-Alcoholic Fatty Liver Disease (NAFLD) or Non-Alcoholic Steatohepatitis (NASH).

15 In still another embodiment of the present invention, there is provided a composition comprising the compound having structure I along with pharmaceutically acceptable excipients.

Another embodiment of the present invention provides a method of modulation COP1 enzyme through its stabilization by the compound having structure I.

Yet another embodiment of the present invention provides a method of increasing the level of ATGL by the compound having structure I.

5

EXAMPLES

Following examples are given by way of illustration and therefore should not be construed to limit the scope of the present invention.

10

Temperatures are given in degree Celsius. The structures of final products, intermediates and starting materials are confirmed by standard analytical methods, spectroscopic characterization e.g., MS, NMR. Abbreviations used are those conventional in the art.

All starting materials, reagents, catalysts, building blocks, acids, bases, dehydrating agents and solvents utilized to synthesize the compounds of the present invention are either commercially available or can be produced by known organic synthesis methods in the art.

15

Example 1

General Procedure A: Amide formation reaction

20

Suitable carboxylic acid (1 mmol) was taken in DMF (1-2 mL) and HATU (1- 1.2 equivalent) was added followed by stirring for 15 min- 1 hour to obtain a reaction mixture. Suitable substituted aliphatic or aromatic amine was added drop wise (1-1.5 equivalent) to the reaction mixture followed by TEA (2.5- 3 equivalent) and the contents of the reaction mixture were stirred for another 45 min. Reaction was monitored by checking TLC. Upon completion, the reaction mixture was washed thoroughly with ice cold water to remove DMF and extracted with EtOAc. Column chromatography was performed to get the pure product.

25

Example 2

General Procedure B: Cyclization using trimethylorthoformate

30

An amide compound (1 mmol) prepared by general procedure A provided in Example 1 was taken in trimethylorthoformate (TMOF) (5- 10 equivalent) and heated at 110 °C for 12-18 hrs. Reaction was monitored by checking TLC. Upon completion, the reaction mixture was evaporated in vacuum to remove excess TMOF and washed with water followed by extraction with EtOAc. Column chromatography was performed to get the pure product.

Example 3**General Procedure C: Reduction**

A compound prepared by general procedure **B** (1 mmol) provided in example 2 was dissolved in methanol (2-5 mL) and a pinch of 10 % wet Pd-C was added. The reaction mixture was degassed by passing nitrogen and H₂ gas for 2-5 hours to get fully reduced compound. Reaction was thoroughly monitored by checking TLC. Upon completion of the reaction, Pd-C was filtered through celite bed and methanol was evaporated in vacuum to get the desired compound. Column chromatography was performed to get the pure product.

10 Example 4**General Procedure D: Urea derivative formation via chloroformate intermediate**

A compound prepared by general procedure **C** (1 mmol) provided in example 3 was dissolved in dry THF (5-10 mL). 4-nitrophenylchloroformate (1- 1.5 equivalent) was added portion wise and reaction mixture was stirred for 15 min - 3 hour till the amine got consumed. Reaction was monitored by checking TLC. Further, suitable amine (1- 1.5 equivalent) was added to the reaction mixture followed by TEA (2- 4 equivalent) and reaction mixture was stirred for another 2-8 hours. Upon completion of the reaction, reaction mass was evaporated in vacuum to remove THF and washed with satd. NaHCO₃ solution and extracted with EtOAc. Column chromatography was performed to get the pure product.

20

Example 5**General Procedure E: Urea derivative formation via isocyanate**

A compound prepared by general procedure **C** (1 mmol) provided in example 3 was taken in dry THF (5-10 mL) and suitable aromatic substituted isocyanate (1-1.5 equivalent) was added followed by TEA (2- 4 equivalent). The reaction mixture was stirred for 2-8 hours. Reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated in vacuum to remove THF and washed with satd. NaHCO₃ solution and extracted with EtOAc. Column chromatography was performed to get the pure product.

30 Example 6**General Procedure F: Suzuki coupling**

Suzuki reaction was performed with suitable halo compound (1 mmol), an aliphatic or aromatic (substituted) boronic acid (1 – 2 equivalent) in presence of Cs₂CO₃ or 2M Na₂CO₃ or

2M K₂CO₃(2-4 equivalent) solution taken in a pressure tube and dissolved in dioxane: H₂O (9:1) (8 mL). The reaction mixture was purged with Ar-gas for 15 minutes. Pd₂(dba)₃ or Pd(PPh₃)₄ (10 mol %) and ligands such as X-phos (20 mol %) were added and the reaction mixture was stirred at 100 °C -110 °C for 10-16 hours. Reaction was monitored by checking
5 TLC. After completion, reaction mass was washed with water and extracted with ethyl acetate and evaporated. Column chromatography was performed to purify the compound.

Example 7

General Procedure G: Zinc chloride mediated cyclization

10 An uncyclized diamide compound(1 mmol) was taken in DMF (8- 10 mL) and ZnCl₂ (4- 8 equivalent) was added followed by HMDS (8-10 equivalent) and the reaction mixture was heated at 100 °C -110 °C for 30 mins- 16 hours. Reaction was monitored by checking TLC. After completion; the reaction mixture was washed with ice cold water and extracted with EtOAc. Column chromatography was performed to purify the compound.

15

Example 8

General Procedure H: Side chain modification

An ester compound (1 mmol) was dissolved in toluene (5-7 mL) and anhydrous AlCl₃ (4-8 equivalent) was added under N₂ atmosphere to obtain a reaction mixture. Suitable aliphatic or
20 aromatic or substituted aromatic amine (1-2 equivalent) was added to the reaction mixture followed by TEA (0.3 mL, 2.43 mmol) and the reaction mixture was stirred for 25 mins- 10 hours at a temperature ranging from room temperature to 100 °C - 110 °C. The reaction was monitored by checking TLC. Upon completion of the reaction, the reaction mass was washed with water and 0.1 (N) NaOH solution and extracted with EtOAc. Compound was purified by
25 column chromatography.

Example 9

Synthesis of 2-amino-N-(2-methoxyethyl)-5-nitrobenzamide(2): The compound was prepared by general procedure A provided in example 1 using 2-amino-5-nitrobenzoic acid **1**
30 (4 g, 21.97 mmol), DMF (12 mL), HATU (9.1 g, 24.17 mmol), 2-methoxyethylamine (2.1 mL, 24.17 mmol) and TEA (7.6 mL, 54.93 mmol). After evaporation, the crude mass was diluted with chloroform and pet ether was added to obtain the precipitation. The precipitate was washed with pet ether to afford compound **2**(4.2 g, 80%) as yellow solid. ¹H NMR (400

MHz, d₆-DMSO) δ in ppm 8.71 (br.s, -NH), 8.46 (d, J = 2.8 Hz, 1H), 7.96 (dd, J = 9.4 Hz, 2.4 Hz, 1H), 7.71 (br.s, 2H), 6.75 (d, J = 9.2 Hz, 1H), 3.43- 3.40 (m, 2H), 3.37- 3.33 (m, 2H), 3.23 (s, 3H).ESI-HRMS m/z 240.0995 (M+H⁺). Melting Point: 168 °C.

5 Example 10

Synthesis of 3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one(3): The compound was prepared by general procedure B provided in example 2 using compound 2 (2 g, 8.63 mmol), (TMOF) (9 mL, 86.3 mmol) to obtain compound 3 (1.8 g, 87 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.78 (d, J = 2.4 Hz, 1H), 8.50 (dd, J = 9 Hz, 2.8 Hz, 1H), 8.45 (s, 1H), 7.82 (d, J = 9.2 Hz, 1H), 4.16 (t, J = 5.2 Hz, 2H), 3.59 (t, J = 4.8 Hz, 2H), 3.21 (s, 3H).ESI-HRMS m/z 250.0834 (M+H⁺). Melting Point: 152 °C.

Example 11

Synthesis of 6-amino-3-(2-methoxyethyl)quinazolin-4(3H)-one (4): The compound was prepared by general procedure C provided in example 3 using compound 3 (1g, 4.01 mmol), methanol (10 mL) to obtain compound 4 (0.8 g, 91 %) as brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 7.94 (s, 1H), 7.37 (d, J = 8.7 Hz, 1H), 7.21 (d, J = 2.4 Hz, 1H), 7.07 (dd, J = 8.5 Hz, 2.7 Hz, 1H), 5.66 (br.s, 2H), 4.09 (t, J = 5.4 Hz, 2H), 3.58 (t, J = 5.1 Hz, 2H), 3.24 (s, 3H).ESI-HRMS m/z 220.1095 (M+H⁺). Melting Point: 172 °C.

Example 12

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-phenylurea (5): The compound was prepared by general procedure D provided in example 4 using compound 4 (0.14 g, 0.63 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.16 g, 0.79 mmol), aniline (0.07 mL, 0.79 mmol), TEA (0.4 mL, 2.63 mmol) to obtain compound 5 (0.075 g, 35%) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.09 (s, 1H), 8.78 (s, 1H), 8.35 (d, J = 2.4 Hz, 1H), 8.17 (s, 1H), 7.79 (dd, J = 8.7 Hz, J = 2.4 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H), 7.48 (d, J = 7.8 Hz, 2H) 7.32- 7.27 (m, 2H), 7.01-6.96 (m, 1H), 4.15 (t, J = 5.7 Hz, 2H), 3.61 (t, J = 5.1 Hz, 2H), 3.25 (s, 3H). ESI-MS m/z 339.0 (M+H⁺). Melting Point: 218 °C.

Example 13

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-methoxyphenyl)urea (6): The compound was prepared by general procedure D provided in

example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), m-anisidine (0.076 mL, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **6** (0.066 g, 33 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.01 (s, 1H), 8.71 (s, 1H), 8.30 (d, *J* = 2.4 Hz, 1H), 8.10 (d, *J* = 1.2 Hz, 1H), 7.73 (dd, *J* = 8 Hz, *J* = 2.8 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.17-7.11 (m, 2H) 6.90 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 10.8 Hz, 1H), 4.09 (t, *J* = 4.8 Hz, 2H), 3.68 (s, 3H), 3.56 (t, *J* = 5.2 Hz, 2H), 3.19 (s, 3H). ESI-MS *m/z* 369.0 (M+H⁺). Melting Point: 150 °C.

Example 14

10 **Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(methylamino)phenyl)urea (7):** The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), *N*¹-methylbenzene-1,3-diamine (0.083 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **7** (0.05 g, 25 %) as light yellow solid.

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Example 15

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-nitrophenyl)urea (8): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), 3-nitroaniline (0.094 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **8** (0.07, 33%) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.31 (d, *J* = 16.2 Hz, 2H), 8.57 (s, 1H), 8.37 (d, *J* = 2.1 Hz, 1H), 8.18 (s, 1H), 7.86- 7.75 (m, 3H), 7.65- 7.55 (m, 2H), 4.16 (t, *J* = 5.1 Hz, 2H), 3.62 (t, *J* = 4.8 Hz, 2H), 3.25 (s, 3H). ESI-MS *m/z* 384.07 (M+H⁺). Melting Point: 208 °C.

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Example 16

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (9): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.1 g, 0.45 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 3'-aminoacetophenone (0.077 g, 0.57 mmol), TEA (0.3 mL, 1.88 mmol) to obtain compound **9** (0.08, 46 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.15 (s, 1H), 9.02 (s, 1H), 8.37 (d, *J* = 1.5 Hz, 1H), 8.17 (s, 1H), 8.10 (s, 1H), 7.82 (dd, *J* = 8.7 Hz, *J* = 1.8 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.64-7.59 (m, 2H), 7.48- 7.43 (m, 1H), 4.15 (t, *J* = 4.8

30

Hz, 2H), 3.61 (t, $J = 4.8$ Hz, 2H), 3.25 (s, 3H), 2.57 (s, 3H). ESI-MS m/z 381.03 ($M+H^+$). Melting Point: 210 °C.

Example 17

5 **Synthesis of 1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (10):** The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), 4'-aminoacetophenone (0.092 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **10** (0.08 g, 46 %) as off white solid. ^1H NMR (300 MHz, d_6 -DMSO) δ in ppm
10 9.26 (s, 1H), 9.24 (s, 1H), 8.37 (d, $J = 2.4$ Hz, 1H), 8.17 (s, 1H), 7.92 (s, 1H), 7.89 (s, 1H), 7.81 (dd, $J = 8.8$ Hz, 2.7 Hz, 1H), 7.64-7.60 (m, 3H), 4.15 (t, $J = 5.1$ Hz, 2H), 3.61 (t, $J = 5.1$ Hz, 2H), 3.24 (s, 3H), 2.51 (s, 3H). ESI-MS m/z 381.07 ($M+H^+$). Melting Point: 202 °C.

Example 18

15 **Synthesis of 1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (11):** The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), 1-(3-aminophenyl)ethanol (0.093 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **11** (0.08 g, 38%) as light yellow
20 solid. ^1H NMR (300 MHz, d_6 -DMSO) δ in ppm 9.02 (s, 1H), 8.73 (s, 1H), 8.34 (d, $J = 2.4$ Hz, 1H), 8.14 (s, 1H), 7.77 (dd, $J = 9$ Hz, 2.4 Hz, 1H), 7.59 (d, $J = 9$ Hz, 1H), 7.44 (s, 1H), 7.32 (d, $J = 7.8$ Hz, 1H), 7.23 – 7.17 (m, 1H), 6.94 (d, $J = 7.5$ Hz, 1H), 5.14 (d, $J = 3.9$ Hz, 1H), 4.70-4.62 (m, 1H), 4.13 (t, $J = 5.1$ Hz, 2H), 3.59 (t, $J = 4.8$ Hz, 2H), 3.23 (s, 3H), 1.29 (d, $J = 6.6$ Hz, 3H). ESI-MS m/z 383.02 ($M+H^+$). Melting Point: 168 °C.

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Example 19

Synthesis of methyl 4-methoxy-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (12): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.13 g, 0.593 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.15 mg, 0.74 mmol), methyl 3-amino-4-methoxybenzoate (0.134 g, 0.74 mmol), TEA (0.3 mL, 2.44 mmol) to obtain compound **12** (0.08 g, 32%) as offwhite
30 solid. ^1H NMR (300 MHz, d_6 -DMSO) δ in ppm 9.75 (s, 1H), 8.84 (s, 1H), 8.43 (s, 1H), 8.39 (d, $J = 2.1$ Hz, 1H), 8.17 (s, 1H), 7.77 (dd, $J = 8.7$ Hz, 2.1 Hz, 1H), 7.66-7.61 (m, 2H), 7.15 (d, $J =$

8.4 Hz, 1H), 4.16 (t, $J = 4.8$ Hz, 2H), 3.98 (s, 3H), 3.83 (s, 3H) 3.62 (t, $J = 4.8$ Hz, 2H), 3.25 (s, 3H). ESI-MS m/z 427.1 (M+H⁺). Melting Point: 224 °C.

Example 20

5 **Synthesis of 1-(3-ethylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (13):**The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), 3-ethylaniline (0.085 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **13** (0.07 g, 35 %) as offwhite solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm
10 9.00 (s, 1H), 8.63 (s, 1H), 8.30 (d, $J = 2.4$ Hz, 1H), 8.10 (s, 1H), 7.73 (dd, $J = 8.8$ Hz, 2.4 Hz, 1H), 7.56 (d, $J = 8.8$ Hz, 1H), 7.30-7.29 (m, 1H), 7.21 (d, $J = 8.8$ Hz, 1H), 7.15-7.12 (m, 1H), 6.78 (d, $J = 7.6$ Hz, 1H), 4.09 (t, $J = 5.2$ Hz, 2H), 3.56 (t, $J = 5.32$ Hz, 2H), 3.19 (s, 3H), 2.52 (q, $J =$ Hz, 2H), 1.12 (t, $J =$ Hz, 3H). ESI-MS m/z 367.3 (M+H⁺). Melting Point: 182 °C.

15 Example 21

Synthesis of 1-(3-benzoylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (14):The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), (3-aminophenyl)(phenyl)methanone (0.135 g, 0.68 mmol), TEA (0.3 mL, 2.25
20 mmol) to obtain compound **14** (0.065 g, 27 %) as offwhite solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.17 (s, 1H), 9.10 (s, 1H), 8.34 (d, $J = 2.4$ Hz, 1H), 8.16 (s, 1H), 7.93 (s, 1H), 7.82-7.77 (m, 4H), 7.68 (d, $J = 7.2$ Hz, 1H), 7.63- 7.55 (m, 3H), 7.52- 7.46 (m, 1H), 7.35 (d, $J = 7.8$ Hz, 1H), 4.15 (t, $J = 5.1$ Hz, 2H), 3.61 (t, $J = 5.1$ Hz, 2H), 3.24 (s, 3H). ESI-MS m/z 443.2 (M+H⁺). Melting Point: 136 °C.

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Example 22

Synthesis of N-cyclohexyl-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamide (15): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 4-
30 nitrophenylchloroformate (0.137 g, 0.68 mmol), 3-amino-*N*-cyclohexylbenzamide (0.15 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol) to obtain compound **15** (0.085 g, 33 %) as offwhite solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.12 (s, 1H), 8.94 (s, 1H), 8.37 (d, $J = 2.4$ Hz, 1H), 8.20 (s, 1H), 8.17 (s, 1H), 7.85 (s, 1H), 7.81 (dd, $J = 9$ Hz, 2.7 Hz, 1H), 7.66- 7.61 (m,

2H), 7.44 (d, $J = 7.8$ Hz, 1H), 7.38- 7.33 (m, 1H), 4.15 (t, $J = 5.1$ Hz, 2H), 3.77- 3.70 (m, 1H), 3.61 (t, $J = 5.1$ Hz, 2H), 3.25 (s, 3H), 1.83- 1.79 (m, 2H), 1.75- 1.71 (m, 2H), 1.64- 1.57 (m, 1H), 1.38- 1.23 (m, 4H), 1.17- 1.1 (m, 1H).ESI-MS m/z 464.2 (M+H⁺). Melting Point: 206 °C.

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Example 23

Synthesis of methyl 2-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamido)-3-methylbutanoate (16):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), methyl 2-(3-aminobenzamido)-3-methylbutanoate (0.17 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol)to obtain compound **16**(0.08 g, 30 %)as offwhite solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.14 (s, 1H), 8.94 (s, 1H), 8.60 (d, $J = 7.8$ Hz, 1H), 8.36 (d, $J = 2.1$ Hz, 1H), 8.17 (s, 1H), 7.86 (s, 1H), 7.81 (dd, $J = 9$ Hz, 2.1 Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.62 (d, $J = 8.7$ Hz, 1H), 7.50 (d, $J = 7.8$ Hz, 1H), 7.42- 7.37 (m, 1H), 4.29 (t, $J = 7.5$ Hz, 1H), 4.15 (t, $J = 4.8$ Hz, 2H), 3.66 (s, 3H), 3.61 (t, $J = 5.1$ Hz, 2H), 3.25 (s, 3H), 2.24- 2.13 (m ,1H), 0.965 (q, $J = 6.9$ Hz, 6H).ESI-HRMS m/z 496.2181 (M+H⁺). Melting Point: 198 °C.

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Example 24

Synthesis of 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)-*N,N*-dimethylbenzamide (17):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.06 g, 0.27 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.069 g, 0.34 mmol), 3-amino-*N,N*-dimethylbenzamide (0.056 g, 0.34 mmol), TEA (0.1 mL, 1.12 mmol) to obtain compound **17** (0.056 g, 50%) as off white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.32 (d, $J = 18.3$ Hz, 1H), 9.02 (d, $J = 18.3$ Hz, 1H), 8.36 (s, 1H), 8.17 (s, 1H), 7.86-7.79 (m, 1H), 7.65-7.57 (m, 2H),7.47-7.30 (m, 2H), 7.00-6.96 (m, 1H), 4.15 (t, $J = 4.5$ Hz, 2H), 3.61 (t, $J = 4.8$ Hz, 2H), 3.25 (s, 3H), 2.98 (s, 3H), 2.92 (s, 3H). ESI-HRMS m/z 410.1837 (M+H⁺). Melting Point: 182 °C.

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Example 25

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (18):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.12 g, 0.54 mmol), dry THF (8 mL), 4-

nitrophenylchloroformate (0.137 mg, 0.68 mmol), (3-aminophenyl)(pyrrolidin-1-yl)methanone(0.13 g, 0.68 mmol), TEA (0.3 mL, 2.25 mmol)to obtain compound **18** (0.052 g, 22 %) as light yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.19 (s, 1H), 8.95 (s, 1H), 8.36 (d, *J*= 2.1 Hz, 1H), 8.17 (s, 1H), 7.80 (dd, *J*= 9 Hz, 2.4 Hz, 1H), 7.70 (s, 1H), 7.62 (d, *J*= 8.7 Hz, 1H), 7.47- 7.41 (m, 1H), 7.37- 7.33 (m, 1H), 7.12- 7.08 (m, 1H), 4.15 (t, *J*= 4.2 Hz, 2H), 3.61 (t, *J*= 4.8 Hz, 2H), 3.46 (t, *J*= 4.8 Hz, 4H), 3.25 (s, 3H), 1.89- 1.79 (m, 4H).ESI-MS *m/z* 435.8 (M+H⁺). Melting Point: 198 °C.

Example 26

10 **Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(morpholine-4-carbonyl)phenyl)urea (19):**The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (8 mL) and 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), (3-aminophenyl)(morpholino)methanone (0.12 g, 0.54 mmol), TEA (0.3 mL, 1.88 mmol) to obtain compound **19**(0.05 g, 24 %) as light
15 yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.09 (s, 1H), 8.86 (s, 1H), 8.30 (s, 1H), 8.10 (s, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.55- 7.51 (m, 2H), 7.43- 7.37 (m, 1H), 7.32- 7.29 (m, 1H), 6.96-6.92 (m, 1H), 4.09 (t, *J*= 4.4 Hz, 2H), 3.58- 3.53 (m, 8H), 3.34-3.31 (m, 2H), 3.19 (s, 3H).ESI-MS *m/z*452.3 (M+H⁺). Melting Point: 102 °C.

20 Example 27

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (20):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.12 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol), (4-aminophenyl)(pyrrolidin-1-yl)methanone(0.13 g, 0.68 mmol) ,TEA (0.3 mL, 2.25 mmol)to obtain compound **20** (0.075 g,
25 31 %) as light yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.21 (d, *J*= 14.4 Hz, 1H), 8.99 (d, *J*= 12.9 Hz, 1H), 8.37 (d, *J*= 2.4 Hz, 1H), 8.17 (s, 1H), 7.80 (dd, *J* = 9 Hz, 2.7 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.55-7.47 (m, 4H), 4.15 (t, *J*= 4.5 Hz, 2H), 3.61 (t, *J*= 4.8 Hz, 2H), 3.47-3.42 (m, 4H) 3.25 (s, 3H), 1.88- 1.79 (m, 4H). ESI-HRMS *m/z* 436.1987
30 (M+H⁺). Melting Point: 202 °C.

Example 28

Synthesis of 1-(3-(benzo[d]oxazol-2-yl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (21): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.08 g, 0.36 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.092 g, 0.45 mmol), 3-(benzo[d]oxazol-2-yl)aniline (0.096 g, 0.45 mmol), TEA (0.2 mL, 1.50 mmol) to obtain compound **21** (0.042 g, 25 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.06 (s, 1H), 8.81 (s, 1H), 8.33 (s, 1H), 8.16 (s, 1H), 7.76 (dd, *J* = 8.8 Hz, 2.7 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.33-7.29 (m, 4H), 7.26-7.20 (m, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.25 (s, 3H). Melting Point: 176 °C.

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Example 29

Synthesis of N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (22): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.13 g, 0.59 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.149 g, 0.74 mmol), *N*-(3-aminophenyl)acetamide (0.111 g, 0.74 mmol), TEA (0.4 mL, 2.44 mmol) to obtain compound **22** (0.05 g, 21 %) as light yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.93 (s, 1H), 9.09 (s, 1H), 8.89 (s, 1H), 8.38 (d, *J* = 2.4 Hz, 1H), 8.16 (s, 1H), 7.80-7.75 (m, 2H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.24-7.16 (m, 3H), 4.15 (t, *J* = 5.1 Hz, 2H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.25 (s, 3H), 2.04 (s, 3H). ESI-HRMS *m/z* 396.1689 (M+H⁺). Melting Point: 162 °C.

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Example 30

Synthesis of N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)-*N*-methylacetamide (23): The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.130 g, 0.59 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.149 g, 0.74 mmol), *N*-(3-aminophenyl)-*N*-methylacetamide (0.12 g, 0.74 mmol), TEA (0.4 mL, 2.44 mmol) to obtain compound **23** (0.052 g, 21 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.25 (s, 1H), 8.96 (s, 1H), 8.36 (s, 1H), 8.17 (s, 1H), 7.80 (d, *J* = 9.3 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.51 (s, 1H), 7.37-7.32 (m, 2H), 6.94 (s, 1H), 4.15 (t, *J* = 4.5 Hz, 2H), 3.61 (t, *J* = 4.8 Hz, 2H), 3.25 (s, 3H), 3.15 (s, 3H), 1.80 (s, 3H). ESI-MS *m/z* 410.4 (M+H⁺). Melting Point: 98 °C.

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Example 31

Synthesis of *N*-benzyl-*N*-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (24):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.15 g, 0.68 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.172 g, 0.85 mmol),*N*-(3-aminophenyl)-*N*-benzylacetamide(0.20 g, 0.85 mmol), TEA (0.4 mL, 2.82 mmol)to obtain compound **24** (0.08 g, 24%) as light yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.13 (s, 1H), 8.86 (s, 1H),8.34 (s, 1H),8.16 (s, 1H),7.77 (dd, *J* = 8.7 Hz, 1.5 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.38-7.35 (m, 2H), 7.31-7.27 (m, 3H),7.24-7.19 (m, 3H), 6.80 (d, *J* = 7.5 Hz, 1H), 4.85 (s, 2H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.61 (t, *J* = 4.8 Hz, 2H), 3.24 (s, 3H), 1.88 (s, 3H).ESI-MS *m/z* 486.2 (M+H⁺). Melting Point: 184 °C.

Example 32

Synthesis of *N*-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)acetamide (25):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.137 g, 0.68 mmol) , *N*-(3-aminobenzyl)acetamide(0.089 g, 0.54 mmol), TEA (0.3 mL, 1.88 mmol)to obtain compound **25** (0.08 g, 43 %) as off white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.08 (s, 1H), 8.81 (s, 1H), 8.37 (s, 1H), 8.36 (s, 1H), 8.16 (s, 1H), 7.78 (dd, *J* = 8.7 Hz, *J* = 1.2 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.39-7.31 (m, 2H), 7.26- 7.21 (m, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 4.17 (t, *J* = 4.8 Hz, 2H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.61 (t, *J* = 4.8 Hz, 2H), 3.25 (s, 3H), 1.88 (s, 3H). ESI-HRMS *m/z*410.1827 (M+H⁺). Melting Point: 202 °C.

Example 33

Synthesis of *N*-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)-*N*-methylacetamide (26):The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (6 mL) and 4-nitrophenylchloroformate (0.114 g, 0.68 mmol),*N*-(3-aminobenzyl)-*N*-methylacetamide (0.097 g, 0.54 mmol),TEA (0.3 mL, 1.88 mmol) to obtain compound **26** (0.075 g, 39 %) as off white solid.

Example 34

Synthesis of 3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1,1-dimethylurea (27) : The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), dimethylamine 2M in THF solution(1.1 mL, 0.57 mmol), TEA (0.3 mL, 1.88 mmol)to
5 obtain compound **27** (0.047 g, 35 %) as off white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.86 (s, 1H), 8.29 (d, *J* = 2.1 Hz, 1H), 8.13 (s, 1H), 7.97 (dd, *J* = 8.8 Hz, 2.1 Hz, 1H), 7.55 (d, *J* = 9 Hz, 1H), 4.13 (t, *J* = 5.1 Hz, 2H), 3.60 (t, *J* = 5.1 Hz, 2H), 3.24 (s, 3H), 2.95 (s, 6H).ESI-MS *m/z*291.2 (M+H⁺). Melting Point: 182 °C.

10 Example 35

Synthesis of N-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)piperidine-1-carboxamide (28) : The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.08 g, 0.36 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.092 g, 0.45 mmol), piperidine(0.04 mL, 0.45 mmol), TEA (0.2
15 mL, 1.50 mmol) to obtain compound **28** (0.052 g, 43 %) as off white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.84 (s, 1H), 8.27 (d, *J* = 2.1 Hz, 1H), 8.13 (s, 1H), 7.95 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.55 (d, *J* = 9 Hz, 1H), 4.13 (t, *J* = 5.1 Hz, 2H), 3.60 (t, *J* = 5.1 Hz, 2H), 3.44 (t, *J* = 4.2 Hz, 4H), 3.24 (s, 3H), 1.61- 1.56 (m, 2H), 1.51- 1.48 (m, 4H).ESI-HRMS *m/z* 331.1769 (M+H⁺). Melting Point: 162 °C.

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Example 36

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(1-methylpiperidin-4-yl)urea (29) :The compound was prepared by general procedure **D** provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 4-amino-1-methylpiperidine(0.07 mL, 0.57
25 mmol), TEA (0.3 mL, 1.88 mmol)to obtain compound **29** (0.072, 44 %) as light yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.94 (s, 1H), 8.26 (d, *J* = 2.1 Hz, 1H), 8.11 (s, 1H), 7.73 (dd, *J* = 8.7 Hz, 2.1 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 1H), 4.14- 4.07 (m, 3H), 3.60 (t, *J* = 5.1 Hz, 2H), 3.24 (s, 3H), 2.66- 2.63 (m, 2H), 2.15 (s, 3H),
30 2.02- 1.96 (m, 2H), 1.80- 1.76 (m, 2H), 1.46- 1.35 (m, 2H).ESI-HRMS *m/z* 360.2032 (M+H⁺). Melting Point: 142 °C.

Example 37

Synthesis of 4-benzyl-N-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)piperidine-1-carboxamide (30):The compound was prepared by general procedure D provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 4-benzylpiperidine(0.1 mL, 0.57 mmol),
5 TEA (0.3 mL, 1.88 mmol)to obtaincompound **30** (0.066 g, 35%) as light yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.85 (s, 1H), 8.27 (d, *J* = 1.2 Hz, 1H), 8.13 (s, 1H), 7.94 (dd, *J* = 8.7 Hz, 1.5 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.31-7.26 (m, 2H), 7.19-7.17 (m, 3H), 4.15- 4.10 (m, 4H), 3.60 (t, *J* = 4.5 Hz, 2H), 3.24 (s, 3H), 2.78- 2.70 (m, 2H), 2.54- 2.52 (m, 2H), 1.76- 1.70 (m, 1H), 1.61- 1.57 (m, 2H), 1.19- 1.06 (m, 2H).ESI-HRMS *m/z* 421.2242
10 (M+H⁺). Melting Point: 146 °C.

Example 38

Synthesis of 1-(1-benzylpiperidin-4-yl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (31):The compound was prepared by general procedure D
15 provided in example 4 using compound **4**(0.10 g, 0.45 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 4-amino-1-benzylpiperidine (0.1 mL, 0.57 mmol), TEA (0.3 mL, 1.88 mmol) to obtaincompound **31**(0.059 g, 30 %) as light brown solid.ESI-HRMS *m/z* 436.2340 (M+H⁺).

20 Example 39

Synthesis of 1-(5-acetyl-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (32):The compound was prepared by general procedure D provided in example 4 using compound **4**(0.1 g, 0.45 mmol), THF (6 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 1-(3-amino-4-hydroxyphenyl)ethanone
25 (0.103 g, 0.68 mmol), TEA (0.3 mL, 1.88 mmol)to obtain compound **32** (0.0, 38 %) as off white solid.

Example 40

Synthesis of 1-(3-acetyl-5-chloro-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (33): The compound was prepared by general procedure D
30 provided in example 4 using compound **4** (0.1 g, 0.45 mmol), dry THF (6 mL) ,4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 1-(3-amino-5-chloro-2-

hydroxyphenyl)ethanone (0.126 g, 0.68 mmol), TEA (0.3 mL, 1.88 mmol) to obtain compound **33** (0.065, 33 %) as white solid.

Example 41

5 **Synthesis of 1-(3-acetyl-2-hydroxy-5-methylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (34):** The compound was prepared by general procedure **D** provided in example 4 using compound **4** (0.1 g, 0.45 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.114 g, 0.57 mmol), 1-(3-amino-2-hydroxy-5-methylphenyl)ethanone (0.113 g, 0.68 mmol), TEA (0.3 mL, 1.88 mmol) to obtain compound
10 **34** (0.07, 37 %) as yellow solid.

Example 42

Synthesis of 1-(4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (35): The compound was prepared by general procedure **E** provided in example 5
15 using compound **4** (0.085 g, 0.38 mmol), dry THF (5 mL), 4-fluorophenyl isocyanate (0.05 mL, 0.48 mmol), TEA (0.1 mL, 0.81 mmol) to obtain compound **35** (0.056 g, 43 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.04 (s, 1H), 8.75 (s, 1H), 8.29 (d, *J* = 2.4 Hz, 1H), 8.11 (s, 1H), 7.75 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.46- 7.42 (m, 2H), 7.11- 7.06 (m, 2H), 4.10 (t, *J* = 5.2 Hz, 2H), 3.56 (t, *J* = 5.2 Hz, 2H), 3.20 (s, 3H). ESI-
20 MS *m/z* 357.03 (M+H⁺). Melting Point: 206 °C.

Example 43

Synthesis of 1-(3-chloro-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (36):

25 The compound was prepared by general procedure **E** provided in example 5 using compound **4** (0.10 g, 0.45 mmol), dry THF (5 mL), 3-chloro-4-fluorophenyl isocyanate (0.085 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound **36** (0.052 g, 29 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.19 (s, 1H), 8.98 (s, 1H), 8.34 (d, *J* = 2.4 Hz, 1H), 8.17 (s, 1H), 7.82-7.78 (m, 2H), 7.62 (d, *J* = 9 Hz, 1H), 7.36- 7.33 (m, 2H), 4.15 (t, *J* = 5.1
30 Hz, 2H), 3.61 (t, *J* = 4.8 Hz, 2H), 3.24 (s, 3H). ESI-MS *m/z* 390.99 (M+H⁺). Melting Point: 202 °C.

Example 44

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea (37): The compound was prepared by general procedure E provided in example 5 using compound 4 (0.10 g, 0.45 mmol), dry THF (6 mL), 4-(trifluoromethoxy)phenyl isocyanate (0.1 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound 37 (0.06 g, 31 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.31 (s, 1H), 9.15 (s, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.17 (s, 1H), 7.81 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.63 -7.57 (m, 3H), 7.31 (s, 1H), 7.29 (s, 1H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.61 (t, *J* = 4.8 Hz, 2H), 3.24 (s, 3H). ESI-MS *m/z* 423.0 (M+H⁺). Melting Point: 182 °C.

10 **Example 45**

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethyl)phenyl)urea (38): The compound was prepared by general procedure E provided in example 5 using compound 4 (0.10 g, 0.45 mmol), dry THF (5 mL), 4-(trifluoromethyl)phenyl isocyanate (0.1 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound 38 (0.07 g, 38 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.25 (d, *J* = 6.3 Hz, 2H), 8.37 (d, *J* = 2.4 Hz, 1H), 8.18 (s, 1H), 7.82 (dd, *J* = 9 Hz, 2.4 Hz, 1H), 7.71- 7.62 (m, 5H), 4.15 (t, *J* = 5.1 Hz, 2H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.25 (s, 3H). ESI-MS *m/z* 407.2 (M+H⁺). Melting Point: 196 °C.

20 **Example 46**

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-(trifluoromethyl)phenyl)urea (39): The compound was prepared by general procedure E provided in example 5 using compound 4 (0.10 g, 0.45 mmol), dry THF (5 mL), 2-(Trifluoromethyl)phenyl isocyanate (0.1 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound 39 (0.066 g, 37 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.79 (s, 1H), 8.38 (d, *J* = 2.4 Hz, 1H), 8.19 (s, 1H), 8.17 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.78 (dd, *J* = 9 Hz, *J* = 2.7 Hz, 1H), 7.71-7.62 (m, 3H), 7.33- 7.28 (m, 1H), 4.15 (t, *J* = 5.1 Hz, 2H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.25 (s, 3H). ESI-MS *m/z* 407.2 (M+H⁺). Melting Point: 220 °C.

30 **Example 47**

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-methoxyphenyl)urea (40): The compound was prepared by general procedure E provided in example 5 using compound 4 (0.10 g, 0.45 mmol), dry THF (5 mL), 4-

methoxyphenylisocyanate (0.083 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound **40** (0.072 g, 43%) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.02 (s, 1H), 8.58 (s, 1H), 8.33 (s, 1H), 8.15 (s, 1H), 7.79 (dd, *J* = 8.7 Hz, *J* = 1.2 Hz, 1H), 7.60 (d, *J* = 9 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.14 (t, *J* = 5.1 Hz, 2H), 3.72 (s, 3H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.24 (s, 3H). ESI-HRMS *m/z* 369.1 (M+H⁺). Melting Point: 206 °C.

Example 48

Synthesis of 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-methoxyphenyl)urea (41): The compound was prepared by general procedure E provided in example 5 using compound **4** (0.10 g, 0.45 mmol), dry THF (5 mL), 2-methoxyphenylisocyanate (0.083 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound **41** (0.070 g, 41%) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.71 (s, 1H), 8.37 (d, *J* = 2.4 Hz, 1H), 8.29 (s, 1H), 8.17 (s, 1H), 8.14 (d, *J* = 1.8 Hz, 1H), 7.76 (dd, *J* = 8.8 Hz, 2.7 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.05-6.88 (m, 3H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.89 (s, 3H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.25 (s, 3H). ESI-MS *m/z* 369.3 (M+H⁺). Melting Point: 192 °C.

Example 49

Synthesis of ethyl 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (42): The compound was prepared by general procedure E provided in example 5 using compound **4** (0.12 g, 0.54 mmol), dry THF (8 mL), 3-(Ethoxycarbonyl)phenyl isocyanate (0.1 mL, 0.65 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound **41** (0.080 g, 36%) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.14 (s, 1H), 9.07 (s, 1H), 8.36 (s, 1H), 8.17 (s, 2H), 7.81 (d, *J* = 7.2 Hz, 1H), 7.69-7.57 (m, 3H), 7.46-7.41 (m, 1H), 4.32 (q, *J* = 4.5 Hz, 2H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.61 (t, *J* = 5.1 Hz, 2H), 3.25 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H). ESI-MS *m/z* 411.2 (M+H⁺). Melting Point: 170 °C.

Example 50

Synthesis of 6-amino-5-bromo-3-(2-methoxyethyl) quinazolin-4(3H)-one (43): Compound **4** (2 g, 6.73 mmol) was dissolved in acetic acid (15 mL). Liq. bromine (0.56 mL, 1.2 equiv.) was added in DCM (4 mL) and then the resultant solution was added drop wise at

0°C to the reaction mixture over a period for 15 minutes. Then, the reaction mixture was allowed to stir at room temperature for 3 hrs. After completion of reaction, it was worked up with ethyl acetate and aqueous NaHCO₃ soln. Then, it was purified by column chromatography (Silica gel, mesh size 100-200) eluting (70 % EtOAc/ Pet ether) to obtain compound **43** as light brown solid at 66% yield. ¹H NMR (400 MHz, CDCl₃) δ in ppm 7.90 (s, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 1H), 4.56 (s, 2H), 4.11 (t, *J* = 4.4 Hz, 2H), 3.65 (t, *J* = 4.4 Hz, 2H), 3.30 (s, 3H). ESI-HRMS *m/z* 298.0184 (M+H⁺). Melting Point: 132 °C.

Example 51

Synthesis of 6-amino-3-(2-methoxyethyl)-5-phenylquinazolin-4(3H)-one (44): The compound was prepared by general procedure **F** provided in example 6 using compound **43** (0.20 g, 0.67 mmol), benzene boronic acid (0.099 g, 0.80 mmol), cesium carbonate (0.44 g, 1.34 mmol), solution of dioxane, H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.061 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **44** (0.125 g, 63 %) as light yellow solid. ¹H NMR (400 MHz, CDCl₃) δ in ppm 7.88 (s, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.48- 7.45 (m, 2H), 7.40- 7.36 (m, 1H), 7.24- 7.22 (m, 2H), 7.15 (d, *J* = 8.4 Hz, 1H), 3.97 (t, *J* = 4.4 Hz, 2H), 3.68 (br.s., 2H), 3.49 (t, *J* = 4.4 Hz, 2H), 3.26 (s, 3H). ESI-HRMS *m/z* 296.1410 (M+H⁺).

Example 52

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-phenyl-3,4-dihydroquinazolin-6-yl)urea (45):

The compound was prepared by general procedure **D** provided in example 4 using compound **44** (0.10 g, 0.33 mmol), dry THF (5 mL), 4-nitrophenylchloroformate (0.096 g, 0.47 mmol), 3'-aminoacetophenone (0.051 g, 0.37 mmol), TEA (0.19 mL, 1.35 mmol) to obtain compound **45** (0.07 g, 45 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.35 (s, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 8.13 (s, 1H), 7.88 (s, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.42-7.32 (m, 5H), 7.12 (s, 1H), 7.11 (s, 1H), 3.90 (t, *J* = 5.2 Hz, 2H), 3.39 (t, *J* = 5.2 Hz, 2H), 3.16 (s, 3H), 2.48 (s, 3H). ESI-HRMS *m/z* 457.1876 (M+H⁺).

Example 53

Synthesis of 6-amino-5-(4-fluorophenyl)-3-(2-methoxyethyl)quinazolin-4(3H)-one (46):

The compound was prepared by general procedure **F** provided in example 6 using

compound **43** (0.20 g, 0.67 mmol), 4-fluorophenylboronic acid (0.112 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **46** (0.094 g, 45 %) as yellow solid. ¹H NMR (600 MHz, d₆-DMSO) δ in ppm 7.93 (s, 1H), 7.42 (d, *J*= 9 Hz, 1H), 7.23 (d, *J*= 9 Hz, 1H), 7.19- 7.16 (m, 2H), 7.12- 7.09 (m, 2H), 4.77 (s, 2H), 3.89 (t, *J*= 4.8 Hz, 2H), 3.41 (t, *J*= 2.7 Hz, 2H), 3.19 (s, 3H).ESI- MS *m/z* 314.1 (M+H⁺).

Example 54

Synthesis of 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (47): The compound was prepared by general procedure **D** provided in example 4 using compound **46** (0.08 g, 0.25 mmol), dry THF (4 mL), 4-nitrophenylchloroformate (0.072 g, 0.35 mmol), 3'-aminoacetophenone (0.037 g, 0.28 mmol), TEA (0.17 mL, 1.22 mmol) to obtain compound **47** (0.049 g, 41 %) as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ in ppm 8.66 (d, *J*= 9 Hz, 1H), 8.02 (s, 1H), 7.77 (d, *J*= 9 Hz, 1H), 7.71- 7.67 (m, 2H), 7.46- 7.43 (m, 1H), 7.37- 7.32 (m, 1H), 7.13- 7.09 (m, 2H), 7.05- 6.99 (m, 2H), 6.86 (s, 1H), 6.43 (s, 1H), 3.99 (t, *J*= 4.5 Hz, 2H), 3.50 (t, *J*= 4.8 Hz, 2H), 3.28 (s, 3H), 2.58 (s, 3H).ESI- MS *m/z* 475.1 (M+H⁺).

Example 55

Synthesis of 6-amino-3-(2-methoxyethyl)-5-(pyridin-2-yl)quinazolin-4(3H)-one (48): The compound was prepared by general procedure **F** provided in example 6 using compound **43**(0.20 g, 0.67 mmol), 2-pyridineboronic acid (0.98 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol) dioxane/ H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **48** (0.103 g, 52 %) as yellow solid.

Example 56

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (49):The compound was prepared by general procedure **D** provided in example 4 using compound **48** (0.08 g, 0.25 mmol),dry THF, 4-nitrophenylchloroformate (0.072 g, 0.35 mmol). 3'-aminoacetophenone (0.037 g, 0.28 mmol), TEA (0.17 mL, 1.22 mmol) to obtain compound **49** (0.046 g, 38 %) as yellow solid.

Example 57

Synthesis of 6-amino-3-(2-methoxyethyl)-5-(pyridin-3-yl)quinazolin-4(3H)-one (50): The compound was prepared by general procedure **F** provided in example 6 using compound **43** (0.20 g, 0.67 mmol), 3-pyridineboronic acid (0.98 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), (0.064 g, 0.13 mmol) to obtain compound **50** (0.115 g, 58 %) as yellow solid.¹H NMR (600 MHz, d₆-DMSO) δ in ppm 8.49 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 8.27 (d, J = 1.8 Hz, 1H), 7.95 (s, 1H), 7.54- 7.52 (m, 1H), 7.46 (d, J = 9 Hz, 1H), 7.40- 7.38 (m, 1H), 7.26 (d, J = 9 Hz, 1H), 4.91 (s, 2H), 3.90 (t, J = 4.8 Hz, 2H), 3.42 (t, J = 5.4 Hz, 2H), 3.18 (s, 3H). ESI-MS m/z 297.2 (M+H⁺).

10 Example 58

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (51): The compound was prepared by general procedure **D** provided in example 4 using compound **50** (0.08 g, 0.25 mmol), dry THF (4 mL) and 4-nitrophenylchloroformate (0.072 g, 0.35 mmol), 3'-aminoacetophenone (0.037 g, 0.28 mmol), TEA (0.17 mL, 1.22 mmol) to obtain compound **51** (0.046 g, 38 %) as yellow solid. ESI- MS m/z 458.3 (M+H⁺).

Example 59

Synthesis of 6-amino-3-(2-methoxyethyl)-5-(pyridin-4-yl)quinazolin-4(3H)-one (52): The compound was prepared by general procedure **F** provided in example 6 using compound **43** (0.20 g, 0.67 mmol), 4-pyridineboronic acid (0.98 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **52** (0.103 g, 52 %) as yellow solid.¹H NMR (600 MHz, CDCl₃) δ in ppm 8.73 (d, J = 3.6 Hz, 2H), 7.92 (s, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.23 (d, J = 6 Hz, 2H), 7.18 (d, J = 8.4 Hz, 1H), 4.00 (t, J = 4.8 Hz, 2H), 3.68 (s, 2H), 3.53 (t, J = 4.8 Hz, 2H), 3.29 (s, 3H). ESI- MS m/z 297.2 (M+H⁺).

Example 60

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (53): The compound was prepared by general procedure **D** provided in example 4 using compound **52** (0.08 g, 0.25 mmol), dry THF (4 mL), 4-nitrophenylchloroformate (0.072 g, 0.35 mmol), 3'-aminoacetophenone (0.037 g, 0.28 mmol), TEA (0.17 mL, 1.22 mmol) to obtain compound **53** (0.039 g, 32 %) as yellow solid.

Example 61**Synthesis of 6-amino-3-(2-methoxyethyl)-5-(6-methoxypyridin-3-yl)quinazolin-4(3H)-****one (54):** The compound was prepared by general procedure **F** provided in example 6 using

5 compound **43** (0.20 g, 0.67 mmol), 2-methoxypyridine-5-boronic acid pinacol ester (0.19 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **54** (0.1 g, 46 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 7.95 (s, 1H), 7.86 (d, *J* = 2.1 Hz, 1H), 7.46- 7.42 (m, 2H), 7.25 (d, *J* = 8.7 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.95 (s, 2H), 3.92 (t, *J* = 5.1 Hz, 2H), 3.89 (s, 3H), 3.44 (t, *J* = 5.1 Hz, 2H), 3.20 (s, 3H). ESI- HRMS *m/z* 327.1470 (M+H⁺).

Example 62**Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(6-methoxypyridin-3-yl)-4-oxo-****3,4-dihydroquinazolin-6-yl)urea (55):** The compound was prepared by general procedure **D**

15 provided in example 4 using compound **54** (0.10 g, 0.30 mmol), dry THF (4 mL), 4-nitrophenylchloroformate (0.087 g, 0.42 mmol), 3'-aminoacetophenone (0.046 g, 0.33 mmol), TEA (0.17 mL, 1.22 mmol) to obtain compound **55** (0.075 g, 46 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.30 (s, 1H), 8.41 (d, *J* = 8.8 Hz, 1H), 8.13 (s, 1H), 7.90- 7.88 (m, 2H), 7.64 (d, *J* = 9.2 Hz, 1H), 7.58 (d, *J* = 6.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.46 (dd, *J* = 8.4 Hz, 1H), 7.39-7.36 (m, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 3.92 (t, *J* = 5.2 Hz, 2H), 3.88 (s, 3H), 3.40 (t, *J* = 5.2 Hz, 2H), 3.16 (s, 3H), 2.49 (s, 3H). ESI- MS *m/z* 488.1 (M+H⁺).

Example 63**Synthesis of 6-amino-3-(2-methoxyethyl)-5-(2-methoxypyridin-3-yl)quinazolin-4(3H)-****one (56):** The compound was prepared by general procedure **F** provided in example 6 using

30 compound **43** (0.20 g, 0.67 mmol), 2-methoxy-3-pyridinylboronic acid (0.123 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **56** (0.12 g, 58 %) as yellow solid.

Example 64

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(2-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (57): The compound was prepared by general procedure **D** provided in example 4 using compound **56** (0.10 g, 0.30 mmol), dry THF (4 mL), 4-nitrophenylchloroformate (0.087 g, 0.42 mmol), 3'-aminoacetophenone (0.046 g, 0.33 mmol),
5 TEA (0.17 mL, 1.22 mmol) to obtain compound **57** (0.075 g, 46 %) as yellow solid.

Example 65

Synthesis of tert-butyl 4-(6-amino-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate(58): The compound was prepared by general
10 procedure **F** provided in example 6 using compound **43**(0.2 g, 0.67 mmol), tert-butyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate(0.25 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane, H₂O (9:1) (10 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **58**(0.12 g, 47%) as
15 light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 7.93 (s, 1H), 7.32 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 5.36 (s, 1H), 5.18 (s, 1H), 4.12- 4.09 (m, 2H), 4.03 (t, *J* = 4.8 Hz, 2H), 3.80- 3.73 (m, 2H), 3.53 (t, *J* = 5.1 Hz, 2H), 3.23 (s, 3H), 2.82- 2.31 (m, 1H), 2.09- 2.03 (m, 1H), 1.45 (s, 9H). ESI- MS *m/z* 401.2185 (M+H⁺).

Example 66

Synthesis of tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (59): The compound
20 was prepared by general procedure **D** provided in example 4 using compound **58**(0.1 g, 0.25 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.071 g, 0.35 mmol), 3'-aminoacetophenone(0.037 g, 0.27 mmol), TEA (0.07 mL, 0.50 mmol) to obtain compound **59**
25 (0.07 g, 53 %) as off white solid. ¹H NMR (400 MHz, CDCl₃), δ in ppm 8.55 (d, *J* = 9.2 Hz, 1H), 8.36 (brs, 1H), 8.07 (s, 1H), 8.00 (s, 1H), δ 7.71 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 9.2 Hz, 1H), 7.62 (d, *J* = 6.4 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 5.55 (brs, 1H), 4.38 (d, *J* = 11.4 Hz, 1H), 4.10 (t, *J* = 4.8 Hz, 2H), 4.38 (d, *J* = 15.4 Hz, 1H), 3.61 (t, *J* = 5.2 Hz, 2H), 3.50- 3.43 (m, 1H), 3.31 (s, 3H), 2.58 (s, 3H), 2.27 (brs, 3H), 1.45 (s, 9H). ESI- HRMS *m/z*
30 562.2667 (M+H⁺).

Example 67

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(1,2,3,6-tetrahydropyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (60): Compound **59** (0.10 g, 0.17 mmol) was dissolved in dry DCM (2 mL) and TFA (0.5 mL) was added drop wise at 0°C and reaction mixture was stirred at room temperature for 2 hours. After completion of reaction, it was washed with ethyl acetate and aq. NaHCO₃ solution and purified by column chromatography (Silica gel, mesh size 100-200, Merck) eluting (5 % MeOH-CHCl₃) to obtain compound **60** (0.05 g, 61 %) as off white solid. ¹H NMR (300 MHz, CDCl₃), δ in ppm 8.71 (d, *J* = 9.0 Hz, 1H), 8.10 (s, 1H), 7.94 (s, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 9.0 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 5.52 (s, 1H), 4.02 (t, *J* = 4.5 Hz, 2H), 3.68-3.62 (m, 2H), 3.54 (t, *J* = 4.5 Hz, 2H), 3.37-3.30 (m, 2H), 3.24 (s, 3H), 2.73-2.66 (m, 1H), 2.52 (s, 3H), 2.38-2.33 (m, 1H).ESI- HRMS *m/z* 462.2142 (M+H⁺).

Example 68

Synthesis of tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)piperidine-1-carboxylate (61): The compound was prepared by general procedure C provided in example 3 using compound **59** (0.10 g, 0.17 mmol), MeOH (5 mL), a pinch of Pd/C under hydrogen atmosphere to obtain compound **61** (0.032 g, 32 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO), δ in ppm 9.41 (s, 1H), 8.38-8.32 (m, 1H), 8.17 (s, 1H), 7.77 (s, 1H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 5.47 (s, 1H), 5.14 (s, 1H), 4.69-4.67 (m, 1H), 4.17 (d, *J* = 18.0 Hz, 1H), 4.08 (t, *J* = 4.8 Hz, 2H), 3.86-3.80 (m, 2H), 3.56 (t, *J* = 4.8 Hz, 2H), 3.25 (s, 3H), 2.24-2.15(m, 3H), 1.45 (s, 9H), 1.30 (d, *J* = 6.3 Hz, 3H).ESI- HRMS *m/z* 564.2819 (M+H⁺).

Example 69

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (62): The compound was prepared by general procedure C provided in example 3 using compound **60** (0.10 g, 0.21 mmol), MeOH (8 mL), pinch of Pd/C was added under nitrogen hydrogen atmosphere to obtain compound **62** (0.023 g, 23%) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.74 (d, *J* = 9.3 Hz, 1H), 7.96 (br.s, 2H), 7.62 (d, *J* = 9.3 Hz, 1H), 7.44 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.16- 7.10 (m, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 5.55 (s, 1H), 4.05 (t, *J* = 4.5 HZ, 2H), 3.91- 3.86 (m, 1H), 3.72-3.66 (m, 1H),

3.57 (t, $J = 4.5$ Hz, $J = 4.5$ Hz, 2H), 3.43- 3.40 (m, 2H), 3.28 (s, 3H), 3.08 (s, 3H), 3.01- 2.95 (m, 3H), 2.60- 2.43 (m, 3H).ESI-MS m/z 464.2 (M+H⁺).

Example 70

5 **Synthesis of 6-amino-3-(2-methoxyethyl)-5-(4-methoxyphenyl)quinazolin-4(3H)-one (63):**The compound was prepared by general procedure F provided in example 6 using compound **43**(0.150 g, 0.50 mmol), 4-methoxyphenylboronic acid (0.1 g, 0.60 mmol), dioxane/ H₂O (9:1) (5 mL) and K₂CO₃ (0.2 mL, 2 M) solution, Pd(PPh₃)₄ (0.058 g, 0.05 mmol) to obtain compound **63**(0.1 g, 61 %) as brown solid.¹H NMR (600 MHz, d₆-DMSO) δ
10 in ppm 7.92 (s, 1H), 7.40 (d, $J = 9$ Hz, 1H), 7.22 (d, $J = 9$ Hz, 1H), 7.00 (d, $J = 9$ Hz, 2H), 6.94 (d, $J = 9$ Hz, 2H), 4.70 (t, $J = 5.4$ Hz, 2H), 3.89 (t, $J = 5.4$ Hz, 2H), 3.78 (s, 3H), 3.42 (t, $J = 5.4$ Hz, 2H), 3.19 (s, 3H).ESI-MS m/z 326.1 (M+H⁺).

Example 71

15 **Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (64):** The compound was prepared by general procedure D provided in example 4 using compound **63** (0.1 g, 0.30 mmol), dry THF (3 mL),4-nitrophenylchloroformate (0.093 g, 0.46 mmol), 3'-Aminoacetophenone(0.06 g, 0.46 mmol), TEA (0.1 mL, 0.75 mmol) to obtain compound **64** (0.06 g, 40 %) as off white solid. ¹H NMR
20 (300 MHz, CDCl₃) δ in ppm 8.68 (d, $J = 9$ Hz, 1H), 7.99 (s, 1H), 7.74 (d, $J = 9$ Hz, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.49 (d, $J = 7.8$ Hz, 1H), 7.33- 7.30 (m, 1H), 7.05 (d, $J = 8.1$ Hz, 3H), 6.85 (d, $J = 8.4$ Hz, 2H), 6.58 (s, 1H), 3.97 (t, $J = 4.8$ Hz, 2H), 3.76 (s, 3H), 3.49 (t, $J = 4.8$ Hz, 2H), 3.26 (s, 3H), 2.56 (s, 3H). ESI-MS m/z 487.2003 (M+H⁺).

25 Example 72

Synthesis of 6-amino-3-(2-methoxyethyl)-5-(4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one (65): The compound was prepared by general procedure F provided in example 6 using compound **43** (0.20 g, 0.67 mmol), 4-(trifluoromethyl)phenylboronic acid (0.153 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (8 mL), Pd₂(dba)₃ (0.062
30 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **65** (0.146 g, 60 %) as yellow solid.ESI-HRMS m/z 364.1281 (M+H⁺).

Example 73

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea (66): The compound was prepared by general procedure **D** provided in example 4 using compound **65** (0.1 g, 0.27 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.081 g, 0.40 mmol), 3'-Aminoacetophenone (0.054 g, 0.40 mmol), TEA (0.1 mL, 0.65 mmol) to obtain compound **66** (0.054 g, 38 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.29 (s, 1H), 8.37 (d, *J* = 9 Hz, 1H), 8.21 (s, 1H), 7.94 (brs, 1H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 9 Hz, 1H), 7.62-7.55 (m, 3H), 7.43 (d, *J* = 2.7 Hz, 1H), 7.41 (d, *J* = 3 Hz, 1H), 7.27 (s, 1H), 3.96 (t, *J* = 4.5 Hz, 2H), 3.44 (t, *J* = 4.8 Hz, 2H), 3.21 (s, 3H), 2.54 (s, 3H). ESI-HRMS *m/z* 525.1769 (M+H⁺).

Example 74

Synthesis of 6-amino-5-cyclohexyl-3-(2-methoxyethyl)quinazolin-4(3H)-one (67): The compound was prepared by general procedure **F** provided in example 6 using compound **43** (0.20 g, 0.67 mmol), cyclohexylboronic acid (0.102 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (8 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **67** (0.121 g, 60 %) as yellow solid.

Example 75

Synthesis of 1-(3-acetylphenyl)-3-(5-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (68): The compound was prepared by general procedure **D** provided in example 4 using compound **67** (0.1 g, 0.33 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.100 g, 0.49 mmol), 3'-Aminoacetophenone (0.066 g, 0.49 mmol), TEA (0.11 mL, 0.82 mmol) to obtain compound **68** (0.053 g, 35 %) as off white solid.

Example 76

Synthesis of 6-amino-5-cyclopentyl-3-(2-methoxyethyl)quinazolin-4(3H)-one (69): The compound was prepared by general procedure **F** provided in example 6 using compound **43** (0.20 g, 0.67 mmol), cyclopentylboronic acid (0.091 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (8 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **69** (0.116 g, 60 %) as yellow solid.

Example 77

Synthesis of 1-(3-acetylphenyl)-3-(5-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (70): The compound was prepared by general procedure **D** provided in example 4 using compound **69** (0.1 g, 0.34 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.102 g, 0.51 mmol), 3'-Aminoacetophenone (0.068 g, 0.51 mmol), TEA (0.10 mL, 0.85 mmol) to obtain compound **70** (0.065 g, 42 %) as off white solid.

Example 78

Synthesis of 6-amino-5-isopropyl-3-(2-methoxyethyl)quinazolin-4(3H)-one (71): The compound was prepared by general procedure **F** provided in example 6 using compound **43** (0.20 g, 0.67 mmol), isopropylboronic acid (0.070 g, 0.80 mmol), cesium carbonate (0.437 g, 1.34 mmol), dioxane/ H₂O (9:1) (8 mL), Pd₂(dba)₃ (0.062 g, 0.06 mmol), X-phos (0.064 g, 0.13 mmol) to obtain compound **71** (0.126 g, 72 %) as yellow solid.

Example 79

Synthesis of 1-(3-acetylphenyl)-3-(5-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (72): The compound was prepared by general procedure **D** provided in example 4 using compound **71** (0.1 g, 0.38 mmol), dry THF (3 mL) and 4-Nitrophenylchloroformate (0.114 g, 0.57 mmol), 3'-Aminoacetophenone (0.07 g, 0.57 mmol), TEA (0.13 mL, 0.85 mmol) to obtain compound **72** (0.072 g, 45 %) as off white solid.

Example 80

Synthesis of 1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (73):

The compound was prepared by general procedure **D** provided in example 4 using compound **43** (0.1 g, 0.33 mmol), dry THF (6 mL) and 4-nitrophenylchloroformate (0.101 g, 0.50 mmol), 3'-aminoacetophenone (0.054 g, 0.40 mmol), TEA (0.2 mL, 1.38 mmol) to obtain compound **73** (0.071 g, 46 %) as off white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.80 (s, 1H), 8.46 (s, 1H), 8.41 (d, *J* = 9.2 Hz, 1H), 8.20 (s, 1H), 8.04-8.03 (m, 1H), 7.67-7.64 (m, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.43-7.39 (m, 1H), 4.07 (t, *J* = 5.2 Hz, 2H), 3.55 (t, *J* = 5.2 Hz, 2H), 3.20 (s, 3H), 2.52 (s, 3H). ESI- MS *m/z* 459.2 (M+H⁺). Melting Point: 204 °C.

Example 81

Synthesis of tert-butyl (1-((3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (74): N-Boc Valine (1 g, 4.60 mmol) was taken in DMF (8 mL) and HATU (2 g, 5.06 mmol) was added followed by TEA (1.5 mL, 11.41 mmol) and compound **4** (1 g, 5.06 mmol) and reaction mixture was stirred at room temperature for 5 hours. After completion of reaction, reaction mixture was washed thoroughly with cold water and extracted with EtOAc to afford reddish coloured crude mass which was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (50 % EtOAc/ Pet ether) to obtain compound **74** (0.8 g, 42%) as brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 10.36 (s, 1H), 8.52 (d, *J* = 1.8 Hz, 1H), 8.19 (s, 1H), 7.95 (br.s, -NH), 7.64 (d, *J* = 9 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 4.15 (t, *J* = 5.1 Hz, 2H), 3.93 (t, *J* = 7.8 Hz, 1H), 3.60 (t, *J* = 5.1 Hz, 2H), 3.24 (s, 3H), 2.04- 1.96 (m, 1H), 1.38 (s, 9H), 0.90 (d, *J* = 6.6 Hz, 6H). ESI- HRMS *m/z* 419.2296 (M+H⁺). Melting Point: 120 °C.

Example 82

Synthesis of 2-amino-N-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-methylbutanamide (75):

Compound **74** (0.2 g, 0.47 mmol) was taken in DCM (3 mL) and TFA (0.8 mL) was added drop wise under cooling condition. After 2 hours, the reaction was completed and reaction mixture was neutralized by NaHCO₃ solution and extracted with DCM; evaporated to obtain compound **75** (0.11 g, 72 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.85 (s, 1H), 8.26 (d, *J* = 7.2 Hz, 1H), 8.20 (d, *J* = 2 Hz, 1H), 7.98 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 4.14 (t, *J* = 4.4 Hz, 2H), 3.64 (t, *J* = 4.4 Hz, 2H), 3.44- 3.41 (m, 1H), 3.28 (s, 3H), 2.46- 2.40 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H). ESI- HRMS *m/z* 319.1772 (M+H⁺). Melting Point: 118 °C.

Example 83

Synthesis of 2-(3-(3-acetylphenyl)ureido)-N-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-methylbutanamide (76): The compound was prepared by general procedure **E** provided in example 5 using compound **75** (0.087 g, 0.27 mmol), dry THF (2 mL), 3-acetylphenyl isocyanate (0.05 mL, 0.32 mmol), TEA (0.1 mL, 0.60 mmol) to obtain compound **76** (0.062, 47%) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 10.55 (s, 1H), 8.95 (s, 1H), 8.53 (s, 1H), 8.20 (s, 1H), 8.00-7.95 (m, 2H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 6.6 Hz, 1H), 7.41- 7.36 (m, 1H), 6.57 (d, *J* = 8.7 Hz,

1H), 4.32 (t, $J = 6.3$ Hz, 1H), 4.14 (t, $J = 4.8$ Hz, 2H), 3.60 (t, $J = 4.8$ Hz, 2H), 3.24 (s, 3H), 2.53 (s, 3H), 2.13- 2.02 (m, 1H), 0.95 (q, $J = 5.4$ Hz, 6H). ESI-HRMS m/z 480.2266 (M+H⁺).
Melting Point: 202 °C.

5 Example 84

Synthesis of *N*-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-nitrobenzamide (77): 3-Nitrobenzoic acid (0.365 g, 2.19 mmol) was taken in dry DCM and oxalyl chloride (0.3 mL, 3.27 mmol) was added drop wise under cooling conditions and reaction mixture was stirred at room temperature for 1 hour. Excess oxalyl chloride was evaporated in rotavapor and diluted with DCM (5 mL). To it, compound **4** (0.4 g, 1.82 mmol) diluted with (5 mL) was added dropwise over a period of 5 minutes and the reaction mixture was kept for another 5 hours. After completion of reaction, reaction mixture was evaporated to obtain a yellow coloured crude mass which was purified by column chromatography (Silica gel, mesh size 100-200) eluting (50 % EtOAc/ Pet ether) to obtain compound **77** as yellow solid (0.35 g, 83 % yield).¹H NMR (400 MHz, d₆-DMSO) δ in ppm 10.85 (s, 1H), 8.80 (brs, -NH), 8.62 (d, $J = 2.4$ Hz, 1H), 8.42- 8.39 (m, 2H), 8.20- 8.17 (m, 2H), 7.83- 7.79 (m, 1H), 7.66 (d, $J = 9.2$ Hz, 1H), 4.13 (t, $J = 5.2$ Hz, 2H), 3.58 (t, $J = 5.2$ Hz, 2H), 3.21 (s, 3H). ESI-HRMS m/z 369.1214 (M+H⁺). Melting Point: 212 °C.

20 Example 85

Synthesis of 3-amino-*N*-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)benzamide (78):

The compound was prepared by general procedure **C** provided in example 3 using compound **77** (0.25 g, 0.67 mmol), MeOH (8 mL) pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **78** as yellow solid (0.2 g, 87 % yield).¹H NMR (400 MHz, d₆-DMSO) δ in ppm 10.37 (s, 1H), 8.62 (d, $J = 2.4$ Hz, 1H), 8.16 (s, 1H), 8.13 (dd, $J = 8.8$ Hz, 2.4 Hz, 1H), 7.61 (d, $J = 9.2$ Hz, 1H), 7.14- 7.05 (m, 3H), 6.72 (d, $J = 9.6$ Hz, 1H), 5.29 (brs, 2H), 4.12 (t, $J = 5.2$ Hz, 2H), 3.58 (t, $J = 5.2$ Hz, 2H), 3.21 (s, 3H). ESI-HRMS m/z 339.1214 (M+H⁺).
Melting Point: 132 °C.

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Example 86

Synthesis of 3-(3-(3-acetylphenyl)ureido)-*N*-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)benzamide (79): The compound was prepared by general procedure

E provided in example 5 using compound **78** (0.11 g, 0.32 mmol), dry THF (8 mL), 3-acetylphenyl isocyanate (0.05 mL, 0.38 mmol), TEA (0.1 mL, 0.81 mmol) to obtain compound **79** (0.08 g, 49 %) as light yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 10.62 (s, 1H), 8.99 (s, 1H), 8.98 (s, 1H), 8.69 (d, *J* = 2.4 Hz, 1H), 8.23-8.18 (m, 2H), 8.10-8.09 (m, 1H), 8.05-8.03 (m, 1H), 7.73-7.68 (m, 3H), 7.64-7.59 (m, 2H), 7.50-7.42 (m, 2H), 4.17 (t, *J* = 5.1 Hz, 2H), 3.62 (t, *J* = 5.1 Hz, 2H), 3.26 (s, 3H), 2.57 (s, 3H). ESI-HRMS *m/z* 500.1945 (M+H⁺). Melting Point: 140 °C.

Example 87

10 **Synthesis of ethyl 2-(2-amino-5-nitrobenzamido)acetate (80):** The compound was prepared by general procedure **A** provided in example 1 using compound **1** (2 g, 10.98 mmol), DMF (12 mL), HATU (4.5 g, 12.08 mmol), Glycine ethyl ester hydrochloride (1.7 g, 12.08 mmol), TEA (4.5 mL, 32.96 mmol) to obtain compound **80** (2.5 g, 85%) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.11 (br.s, -NH), 8.52 (d, *J* = 2.8 Hz, 1H), 7.99 (dd, *J* = 9.2 Hz, 2.8 Hz, 1H), 7.73 (br.s, 2H), 6.77 (d, *J* = 9.2 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.92 (d, *J* = 5.6 Hz, 2H), 1.16 (t, *J* = 6.8 Hz, 3H). ESI-HRMS *m/z* 268.0941 (M+H⁺). Melting Point: 178 °C.

Example 88

20 **Synthesis of ethyl 2-(6-nitro-4-oxoquinazolin-3(4H)-yl)acetate (81):** The compound was prepared by general procedure **B** provided in example 2 using compound **80** (2.5 g, 9.36 mmol), trimethylorthoformate (TMOF) (10 mL, 93.63 mmol) to obtain compound **81** (2.3 g, 89 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.82 (d, *J* = 2.8 Hz, 1H), 8.60- 8.57 (m, 2H), 7.92 (d, *J* = 8.8 Hz, 1H), 4.87 (s, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). ESI-HRMS *m/z* 278.0785 (M+H⁺). Melting Point: 166 °C.

Example 89

30 **Synthesis of ethyl 2-(6-amino-4-oxoquinazolin-3(4H)-yl)acetate (82):** The compound was prepared by general procedure **C** provided in example 3 using compound **81** (1 g, 3.60 mmol), methanol (10 mL) pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **82** (0.8 g, 90 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.02 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 2.4 Hz, 1H), 7.09 (dd, *J* = 8.7 Hz, 2.7 Hz, 1H), 5.71

(s, 2H), 4.75 (s, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 1.21 (t, $J = 7.2$ Hz, 3H).ESI-HRMS m/z 248.1041 (M+H⁺). Melting Point: 138 °C.

Example 90

5 **Synthesis of ethyl 2-(6-(3-(3-chloro-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (83):**The compound was prepared by general procedure E provided in example 5 using compound **82** (0.1 g, 0.40 mmol), dry THF (6 mL), 3-chloro-4-fluorophenyl isocyanate (0.08 mL, 0.68 mmol), TEA (0.2 mL, 1.36 mmol) to obtain compound **83** (0.059 g, 35 %) as yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.23 (s, 1H), 9.00 (s, 1H), 8.33 (d, $J =$
10 2.4 Hz, 1H), 8.25 (s, 1H), 7.86-7.80 (m, 2H), 7.66 (d, $J = 9$ Hz, 1H), 7.35 (d, $J = 7.5$ Hz, 2H), 4.81 (s, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 1.22 (t, $J = 6.9$ Hz, 3 H).ESI-MS m/z 419.1 (M+H⁺). Melting Point: 220 °C.

Example 91

15 **Synthesis of ethyl 2-(4-oxo-6-(3-(4-(trifluoromethoxy)phenyl)ureido)quinazolin-3(4H)-yl)acetate (84):**The compound was prepared by general procedure E provided in example 5 using compound **82** (0.1 g, 0.40 mmol), dry THF (5 mL), 4-(trifluoromethoxy)phenyl isocyanate (0.07 mL, 0.50 mmol), TEA (0.2 mL, 1.66 mmol) to obtain compound **84** (70 mg, 43 %) as white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.18 (s, 1H), 9.00 (s, 1H), 8.34
20 (d, $J = 2.1$ Hz, 1H), 8.25 (s, 1H), 7.83 (dd, $J = 8$ Hz, 2.1 Hz, 1H), 7.67- 7.56 (m, 3H), 7.30 (d, $J = 8.4$ Hz, 2H), 4.81 (s, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 1.22 (t, $J = 6.9$ Hz, 3H).ESI-MS m/z 451.13 (M+H⁺). Melting Point: 230°C.

Example 92

25 **Synthesis of ethyl 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (85):**The compound was prepared by general procedure E provided in example 5 using compound **82** (60 mg, 0.24 mmol), dry THF (5 mL) , 3-acetylphenyl isocyanate (0.04 mL, 0.34 mmol) , TEA (0.1 mL, 0.68 mmol) to obtain compound **85**(80 mg, 49%) as white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.21 (s, 1H), 9.05 (s, 1H), 8.36 (d, $J = 2.4$ Hz,
30 1H), 8.25 (s, 1H), 8.10 (s, 1H), 7.85 (dd, $J = 8.8$ Hz, 2.7 Hz, 1H),7.72-7.59 (m, 3H), 7.48-7.43 (m, 1H), 4.82 (s, 2H), 4.18 (q, $J = 7.2$ Hz, 2H), 2.57 (s, 3H), 1.22 (t, $J = 6.9$ Hz, 3H).ESI-MS m/z 409.4 (M+H⁺). Melting Point: 196 °C.

Example 93

Synthesis of 2-amino-N-(3-methoxypropyl)-5-nitrobenzamide (86): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (0.8 g, 4.93 mmol), DMF (6 mL), HATU (1.8 g, 4.83 mmol), 3-methoxypropylamine (0.5 mL, 4.83 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound **86** (0.9 g, 90 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.70 (br.s., -NH), 8.49 (d, *J* = 2.4 Hz, 1H), 8.01 (dd, *J* = 9.1 Hz, 2.4 Hz, 1H), 7.76 (br.s, 2H), 6.79 (d, *J* = 9 Hz, 1H), 3.37 (t, *J* = 6.3 Hz, 2H), 3.28 (t, *J* = 6 Hz, 2H), 3.24 (s, 3H), 1.80- 1.71 (m, 2H). ESI-HRMS *m/z* 254.1133 (M+H⁺). Melting Point: 102 °C.

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Example 94

Synthesis of 3-(3-methoxypropyl)-6-nitroquinazolin-4(3H)-one (87): The compound was prepared by general procedure **B** provided in example 2 using compound **86** (0.6 g, 2.36 mmol), trimethylorthoformate (TMOF) (5 mL, 47.43 mmol) to obtain compound **87** (0.59 g, 95 %) as pale yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.84 (d, *J* = 2.4 Hz, 1H), 8.58- 8.54 (m, 2H), 7.88 (d, *J* = 9 Hz, 1H), 4.05 (t, *J* = 7.2 Hz, 2H), 3.93 (t, *J* = 6 Hz, 2H), 3.20 (s, 3H), 1.99- 1.91 (m, 2H). ESI-MS *m/z* 264.2 (M+H⁺). Melting Point: 110 °C.

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Example 95

Synthesis of 6-amino-3-(3-methoxypropyl)quinazolin-4(3H)-one (88): The compound was prepared by general procedure **C** provided in example 3 using compound **87** (0.3 g, 1.13 mmol), methanol (6 mL), pinch of 10 % wet Pd-C under hydrogen atmosphere was added to obtain compound **88** (0.25 g, 94 %) as brown solid. ESI-HRMS *m/z* 234.1253 (M+H⁺). Melting Point: 98 °C.

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Example 96

Synthesis of 1-(3-acetylphenyl)-3-(3-(3-methoxypropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (89): The compound was prepared by general procedure **D** provided in example 4 using compound **88** (0.12 g, 0.51 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.124 g, 0.61 mmol), 3'-aminoacetophenone (0.084, 0.61 mmol), TEA (0.2 mL, 1.54 mmol) to obtain compound **89** (0.075 g, 37 %) as off white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.08 (s, 1H), 8.95 (s, 1H), 8.30 (d, *J* = 2.8 Hz, 1H), 8.16 (d, *J* = 2 Hz, 1H), 8.05- 8.04 (m, 1H), 7.77 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.67- 7.64 (m, 1H), 7.58- 7.54 (m, 2H), 7.42- 7.38 (m,

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1H), 3.97 (t, $J = 6.8$ Hz, 2H), 3.31-3.30 (m, 2H) 3.17 (s, 3H), 2.52 (s, 3H), 1.91- 1.85 (m, 2H).ESI-MS m/z 395.3 (M+H⁺). Melting Point: 162 °C.

Example 97

5 **Synthesis of 2-amino-N-(2-ethoxyethyl)-5-nitrobenzamide (90):**The compound was prepared by general procedure A provided in example 1 using compound 1 (0.8 g, 4.93 mmol), DMF (6 mL), HATU (1.8 g, 4.83 mmol), 2-ethoxyethylamine (0.5 mL, 4.83 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound 90 (1 g, 90 %) as yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.71 (br.s, -NH), 8.46 (d, $J = 2.8$ Hz, 1H), 7.96 (dd, $J = 6.4$ Hz, 2.8 Hz, 1H), 7.73 (s, 2H), 6.75 (d, $J = 9.2$ Hz, 1H), 3.46- 3.39 (m, 4H), 3.33 (q, $J = 6$ Hz, 2H), 1.07 (t, $J = 6.8$ Hz, 3H).ESI-HRMS m/z 254.1135 (M+H⁺). Melting Point: 104 °C.

Example 98

15 **Synthesis of 3-(2-ethoxyethyl)-6-nitroquinazolin-4(3H)-one (91):**The compound was prepared by general procedure B provided in example 2 using compound 90 (0.85 g, 3.37 mmol), trimethylorthoformate (TMOF) (7 mL, 67.19 mmol) to obtain compound 91(0.8 g, 96 %) as pale yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.80 (d, $J = 2.4$ Hz, 1H), 8.51 (dd, $J = 6.4$ Hz, 2.4 Hz, 1H), 8.45 (s, 1H), 7.83 (d, $J = 8.4$ Hz, 1H), 4.15 (t, $J = 5.2$ Hz, 2H), 3.62 (t, $J = 5.2$ Hz, 2H), 3.40 (q, $J = 7.2$ Hz, 2H), 1.00 (t, $J = 6.8$ Hz, 3H).ESI-HRMS m/z 264.0975 (M+H⁺). Melting Point: 138 °C.

Example 99

25 **Synthesis of 6-amino-3-(2-ethoxyethyl)quinazolin-4(3H)-one (92):**The compound was prepared by general procedure C provided in example 3 using compound 91 (0.55 g, 2.09 mmol), methanol (6 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound 92 (0.45 g, 92 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.94 (s, 1H), 7.37 (d, $J = 8.4$ Hz, 1H), 7.21 (d, $J = 2.4$ Hz, 1H), 7.07 (dd, $J = 8.7$ Hz, 2.7 Hz, 1H), 5.66 (s, 2H), 4.08 (t, $J = 5.4$ Hz, 2H), 3.61 (t, $J = 5.4$ Hz, 2H), 3.42 (q, $J = 6.9$ Hz, 2H), 1.04 (t, $J = 7.2$ Hz, 3H).ESI-HRMS m/z 234.1229 (M+H⁺). Melting Point: 102 °C.

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Example 100

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (93):The compound was prepared by general procedure E provided in example 5

using compound **92** (0.12 g, 0.51 mmol), THF (6 mL), 3-acetylphenyl isocyanate (0.09 mL, 0.61 mmol), TEA (0.2 mL, 1.28 mmol) to obtain compound **93** (0.06 g, 30 %) as light yellow solid. ¹H NMR (600 MHz, d₆-DMSO) δ in ppm 9.12 (s, 1H), 8.99 (s, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.16 (s, 1H), 8.08 (s, 1H), 7.80 (dd, *J* = 9 Hz, 2.4 Hz, 1H), 7.70- 7.68 (m, 1H), 7.62- 7.58 (m, 2H), 7.45- 7.42 (m, 1H), 4.12 (t, *J* = 5.4 Hz, 2H), 3.63 (t, *J* = 5.4 Hz, 2H), 3.42 (q, *J* = 7.2 Hz, 2H), 2.56 (s, 3H), 1.03 (t, *J* = 6.6 Hz, 3H). ESI-HRMS *m/z* 395.1728 (M+H⁺). Melting Point: 192 °C.

Example 101

10 **Synthesis of 1-(4-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (94):** The compound was prepared by general procedure **E** provided in example 5 using compound **92** (0.12 g, 0.51 mmol), dry THF (6 mL), 4-acetylphenyl isocyanate, (0.09 mL, 0.61 mmol), TEA (0.2 mL, 1.28 mmol) to obtain compound **94** (0.07 g, 34 %) as light yellow solid. ¹H NMR (600 MHz, d₆-DMSO) δ in ppm 9.21 (s, 1H), 9.18 (s, 1H), 8.36 (d, *J* = 2.4 Hz, 1H), 8.16 (s, 1H), 7.90 (d, *J* = 9 Hz, 2H), 7.79 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 7.62- 7.59 (m, 3H), 4.12 (t, *J* = 4.8 Hz, 2H), 3.63 (t, *J* = 5.4 Hz, 2H), 3.42 (q, *J* = 6.6 Hz, 2H), 2.50 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H). ESI-HRMS *m/z* 395.1727 (M+H⁺). Melting Point: 102 °C.

Example 102

20 **Synthesis of 2-amino-N-ethyl-5-nitrobenzamide (95):** The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (6 mL), HATU (2.2 g, 6.04 mmol), ethylamine 2 M in THF (2.5 mL), TEA (1.9 mL, 13.73 mmol) to obtain compound **95** (1.1 g, 96 %) as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ in ppm 8.33 (d, *J* = 2.7 Hz, 1H), 8.07 (dd, *J* = 9 Hz, 2.4 Hz, 1H), 6.65 (d, *J* = 9 Hz, 1H), 6.28 (br.s, -NH), 5.05 (br.s, 2H), 3.52- 3.43 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). ESI-HRMS *m/z* 210.0881 (M+H⁺). Melting Point: 136 °C.

Example 103

30 **Synthesis of 3-ethyl-6-nitroquinazolin-4(3H)-one (96):** The compound was prepared by general procedure **B** provided in example 2 using compound **95** (0.80 g, 3.82 mmol), trimethylorthoformate (TMOF) (8 mL, 76.55 mmol) to obtain compound **96** (0.8 g, 95 %) as pale yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.82 (d, *J* = 2.7 Hz, 1H), 8.61 (s,

1H), 8.53 (dd, $J= 9$ Hz, 2.7 Hz, 1H), 7.86 (d, $J= 8.7$ Hz, 1H), 4.03 (q, $J= 7.2$ Hz, 2H), 1.29 (t, $J= 7.2$ Hz, 3H).ESI-MS m/z 220.0728 (M+H⁺). Melting Point: 146°C.

Example 104

5 **Synthesis of 6-amino-3-ethylquinazolin-4(3H)-one (97):**The compound was prepared by general procedure C provided in example 3 using compound 96 (0.50 g, 2.28 mmol) , methanol (6 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound 97 (0.39 g, 90 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.06 (s, 1H), 7.37 (d, $J= 8.7$ Hz, 1H), 7.21 (d, $J= 2.7$ Hz, 1H), 7.06 (dd, $J = 8.7$ Hz, 2.7 Hz,
10 1H), 5.64 (s, 2H), 3.95 (q, $J= 7.2$ Hz, 2H), 1.25 (t, $J= 7.2$ Hz, 3H).ESI-MS m/z 190.1 (M+H⁺). Melting Point: 164 °C.

Example 105

Synthesis of 1-(3-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
15 **(98):**The compound was prepared by general procedure E provided in example 5 using compound 97 (0.12 g, 0.63 mmol), dry THF (6 mL), 3-acetylphenyl isocyanate (0.10 mL, 0.76 mmol), TEA (0.2 mL, 1.58 mmol) to obtain compound 98 (0.08 g, 36%) as white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.07 (s, 1H), 8.93 (s, 1H), 8.30 (d, $J = 2.4$ Hz, 1H), 8.23 (s, 1H), 8.05-8.04 (m, 1H), 7.76 (dd, $J = 9$ Hz, 2.4 Hz, 1H), 7.66- 7.63 (m, 1H), 7.57 –
20 7.53 (m, 2H), 7.41 -7.37 (m, 1H), 3.95 (q, $J = 7.2$ Hz, 2H), 2.52 (s, 3H), 1.23 (t, $J = 7.2$ Hz, 3H).ESI-HRMS m/z 351.1465 (M+H⁺). Melting Point: 202 °C.

Example 106

Synthesis of 1-(4-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea
25 **(99):**The compound was prepared by general procedure E provided in example 5 using compound 97 (0.12 g, 0.63 mmol), dry THF (6 mL), 4-acetylphenyl isocyanate (0.10 mL, 0.76 mmol), TEA (0.2 mL, 1.58 mmol) to obtain compound 99 (0.08 g, 36%) as white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.13 (d, $J= 8.8$ Hz, 2H), 8.31 (d, $J= 2.4$ Hz, 1H), 8.24 (s, 1H), 7.86 (d, $J= 8.8$ Hz, 2H), 7.75 (dd, $J= 6.4$ Hz, 2.4 Hz, 1H), 7.58- 7.55 (m,
30 3H), 3.95 (q, $J = 6.8$ Hz, 2H), 2.96 (s, 3H), 1.23 (t, $J= 7.2$ Hz, 3H).ESI-HRMS m/z 351.1464 (M+H⁺). Melting Point: 212°C.

Example 107

Synthesis of 2-amino-N-(3-methoxyphenyl)-5-nitrobenzamide (100):The compound was prepared by general procedure **A** provided in example 1 using compound **1** (0.8 g, 4.93 mmol), DMF (6 mL), HATU (1.8 g, 4.83 mmol), m-anisidine (0.55 mL, 4.83 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound **100** (1.1 g, 90 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 10.34 (s, 1H), 8.55 (d, *J* = 2.4 Hz, 1H), 8.03 (dd, *J* = 6.4 Hz, 2.8 Hz, 1H), 7.59 (s, 2H), 7.34- 7.33 (m, 1H), 7.27- 7.19 (m, 2H), 6.81 (d, *J* = 9.2 Hz, 1H), 6.67- 6.64 (m, 1H), 3.71 (s, 3H). ESI-HRMS *m/z* 288.0990 (M+H⁺). Melting Point: 178 °C.

Example 108

Synthesis of 3-(3-methoxyphenyl)-6-nitroquinazolin-4(3H)-one (101):The compound was prepared by general procedure **B** provided in example 2 using compound **100** (0.80 g, 2.78 mmol), trimethylorthoformate (TMOF) (6 mL, 55.74 mmol) to obtain compound **101** (0.79 g, 96 %) as light yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.83 (d, *J* = 2.8 Hz, 1H), 8.57 (dd, *J* = 6 Hz, 2.8 Hz, 1H), 8.51 (s, 1H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.47- 7.43 (m, 1H), 7.16- 7.15 (m, 1H), 7.10-7.06 (m, 2H), 3.76 (s, 3H). ESI-MS *m/z* 298.0 (M+H⁺). Melting Point: 204 °C.

Example 109

Synthesis of 6-amino-3-(3-methoxyphenyl)quinazolin-4(3H)-one (102):The compound was prepared by general procedure **C** provided in example 3 using compound **101** (0.7 g, 2.35 mmol), methanol (6 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **102** (0.59 g, 94 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) 8.01 (s, 1H), 7.47- 7.42 (m, 2H), 7.29 (d, *J* = 2.7 Hz, 1H), 7.15- 7.09 (m, 2H), 7.08- 7.04 (m, 2H), 3.80 (s, 3H). ESI-MS *m/z* 268.1 (M+H⁺). Melting Point: 188 °C.

Example 110

Synthesis of 1-(3-acetylphenyl)-3-(3-(3-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (103):The compound was prepared by general procedure **E** provided in example 5 using compound **102** (0.12 g, 0.45 mmol), dry THF (7 mL), 3-acetylphenyl isocyanate (0.08 mL, 0.53 mmol), TEA (0.2 mL, 1.12 mmol) to obtain compound **103** (0.072 g, 37 %) as light yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.13 (s, 1H), 8.95 (s, 1H), 8.34 (d, *J* = 2.4 Hz, 1H), 8.16 (s, 1H), 8.04- 8.03 (m, 1H), 7.84 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.67- 7.63

(m, 2H), 7.55 (d, $J = 7.6$ Hz, 1H), 7.43-7.38 (m, 2H), 7.10-7.09 (m, 1H), 7.05-7.01 (m, 2H), 3.75 (s, 3H), 2.52 (s, 3H).ESI-MS m/z 429.1 ($M+H^+$). Melting Point: 194 °C.

Example 111

5 **Synthesis of 2-acetamido-*N*-(2-methoxyethyl)-5-nitrobenzamide (104):**Compound **2** (0.6 g, 2.50 mmol) was taken in dry DCM (10 mL) and TEA (0.77 mL, 5.52 mmol) was added. Acetyl chloride (0.21 mL, 3.01 mmol) was added dropwise at 0 °C and reaction mixture was allowed to stir at room temperature for 3 hours. Reaction was monitored by checking TLC. After completion of reaction, reaction mixture was washed with satd. NaHCO₃ solution and
10 extracted with DCM, evaporated to afford yellow coloured mass which was further diluted with chloroform and pet ether was added to get precipitation. The precipitate was filtered and washed with 20% (EtOAc/Pet ether) solution to obtain compound **104**(0.5 g, 71 %) as light yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 11.57 (s, 1H), 9.18 (br.s, -NH), 8.60 (d, $J = 7.6$ Hz, 1H), 8.58 (d, $J = 1.2$ Hz, 1H), 8.32 (dd, $J = 10.8$ Hz, 2 Hz, 1H), 3.46- 3.39 (m,
15 4H), 3.24 (s, 3H), 2.12 (s, 3H).ESI-HRMS m/z 282.1089 ($M+H^+$). Melting Point: 160 °C.

Example 112

Synthesis of 3-(2-methoxyethyl)-2-methyl-6-nitroquinazolin-4(3H)-one (105):The compound was prepared by general procedure **G** provided in example **7** using compound **104**
20 (0.4 g, 1.42 mmol), DMF (6 mL), Hexamethyldisilazane (3 mL, 14.22 mmol), ZnCl₂ (0.96 g, 7.11 mmol) to obtain compound **105** (0.32 g, 86 %) as white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.75 (d, $J = 2.4$ Hz, 1H), 8.48 (dd, $J = 6$ Hz, 2.8 Hz, 1H), 7.72 (d, $J = 9.2$ Hz, 1H), 4.23 (t, $J = 5.2$ Hz, 2H), 3.60 (t, $J = 5.6$ Hz, 2H), 3.20 (s, 3H), 2.65 (s, 3H).ESI-MS m/z 264.1 ($M+H^+$). Melting Point: 154 °C.

25

Example 113

Synthesis of 6-amino-3-(2-methoxyethyl)-2-methylquinazolin-4(3H)-one (106):The compound was prepared by general procedure **C** provided in example **3** using compound **105** (0.22 g, 0.83 mmol) , methanol (6 mL) and pinch of 10 % wet Pd-C under hydrogen
30 atmosphere to obtain compound **106** (0.18 g, 93 %) as light brown solid.¹H NMR (600 MHz, d₆-DMSO) δ in ppm 7.26 (d, $J = 9$ Hz, 1H), 7.13 (d, $J = 2.4$ Hz, 1H), 7.02 (dd, $J = 8.4$ Hz, 2.4 Hz, 1H), 5.52 (br.s, 2H), 4.16 (t, $J = 5.4$ Hz, 2H), 3.56 (t, $J = 5.4$ Hz, 2H), 3.21 (s, 3H), 2.51 (s, 3H).ESI-MS m/z 234.2 ($M+H^+$). Melting Point: 196°C.

Example 114**Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (107):**

The compound was prepared by general procedure D provided in example 4 using compound **106** (0.14 g, 0.61 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.15 g, 0.76 mmol), 3'-aminoacetophenone (0.10 g, 0.76 mmol), TEA (0.4 mL, 2.53 mmol) to obtain compound **107** (0.08 g, 33 %) as light yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.06 (s, 1H), 8.99 (s, 1H), 8.30 (d, *J* = 2.4 Hz, 1H), 8.09 (s, 1H), 7.77 (dd, *J* = 8.7 Hz, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 9 Hz, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 9 Hz, 1H), 7.48- 7.42 (m, 1H), 4.23 (t, *J* = 5.4 Hz, 2H), 3.62 (t, *J* = 5.4 Hz, 2H), 3.24 (s, 3H), 2.60 (s, 3H), 2.57 (s, 3H). ESI-MS *m/z* 395.3 (M+H⁺). Melting Point: 218 °C.

Example 115**Synthesis of 2-isobutyramido-N-(2-methoxyethyl)-5-nitrobenzamide (108):**

Compound **2** (0.6 g, 2.50 mmol) was taken in dry DCM (10 mL) and TEA (0.8 mL, 5.52 mmol) was added to it. Under cooling condition, isobutyryl chloride (0.3 mL, 3.01 mmol) was added dropwise at 0 °C and reaction was monitored by checking TLC. After 5 hours, reaction was completed and reaction mixture was diluted with DCM and washed thoroughly with NaHCO₃ solution and extracted to give light brown crude mass which was purified by column chromatography (Silica gel, mesh size 100-200) eluting (50% EtOAc/ Pet ether) to obtain compound **108** (0.69 g, 89 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 11.79 (s, 1H), 9.21 (br.s, 1H), 8.64 (dd, *J* = 9.2 Hz, 2.8 Hz, 1H), 8.61- 8.60 (m, 1H), 8.31 (d, *J* = 9.2 Hz, 1H), 3.45- 3.42 (m, 4H), 3.23 (s, 3H), 2.59- 2.52 (m, 1H), 1.11 (d, *J* = 6.8 Hz, 6H). ESI- HRMS *m/z* 310.1390 (M+H⁺). Melting Point: 140 °C.

Example 116**Synthesis of 2-isopropyl-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one (109):**

The compound was prepared by general procedure G provided in example 7 using compound **108** (0.5 g, 1.61 mmol), DMF (8 mL), ZnCl₂ (0.88 g, 6.46 mmol), HMDS (2.71 mL, 12.93 mmol) to obtain compound **109** (0.39 g, 83%) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.70 (d, *J* = 6 Hz, 1H), 8.44- 8.40 (m, 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 4.27 (t, *J* = 5.2 Hz,

2H), 3.54 (t, $J = 5.2$ Hz, 2H), 3.44- 3.36 (m, 1H), 3.17 (s, 3H), 1.21 (d, $J = 6.4$ Hz, 6H).ESI-HRMS m/z 292.1291 (M+H⁺). Melting Point: 136 °C.

Example 117

5 **Synthesis of 6-amino-2-isopropyl-3-(2-methoxyethyl)quinazolin-4(3H)-one (110):**The compound was prepared by general procedure C provided in example 3 using compound 109 (0.22 g, 0.75 mmol), methanol (6 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound 110 (0.17 g, 86 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.26 (d, $J = 7.6$ Hz, 1H), 7.12 (d, $J = 2.8$ Hz, 1H), 7.01 (dd, $J = 6$ Hz, 2.8 Hz, 1H), 5.49 (s, 2H), 4.20 (t, $J = 5.6$ Hz, 2H), 3.51 (t, $J = 5.6$ Hz, 2H), 3.28- 3.23 (m, 1H), 3.17 (s, 3H), 1.17 (d, $J = 6.8$ Hz, 6H).ESI-HRMS m/z 262.1541 (M+H⁺). Melting Point: 170 °C.

Example 118

15 **Synthesis of 1-(3-acetylphenyl)-3-(2-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (111):**The compound was prepared by general procedure D provided in example 4 using compound 110 (0.12 g, 0.45 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (111 mg, 0.55 mmol), 3'-aminoacetophenone (0.075g, 0.55 mmol), TEA (0.2 mL, 1.54 mmol) to obtain compound 111 (0.08 g, 41 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.09 (s, 1H), 8.99 (s, 1H), 8.31 (d, $J = 2.4$ Hz, 1H), 8.10 (s, 1H), 7.79 (dd, $J = 8.7$ Hz, $J = 2.4$ Hz, 1H), 7.70 (d, $J = 7.8$ Hz, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.56 (d, $J = 8.7$ Hz, 1H), 7.48- 7.42 (m, 1H), 4.30 (t, $J = 5.4$ Hz, 2H), 3.59 (t, $J = 5.4$ Hz, 2H), 3.42- 3.38 (m, 1H), 3.23 (s, 3H), 2.57 (s, 3H), 1.26 (d, $J = 6.6$ Hz, 6H) ESI-MS m/z 423.3 (M+H⁺). Melting Point: 206 °C.

25

Example 119

Synthesis of 2-(4-fluorobenzamido)-N-(2-methoxyethyl)-5-nitrobenzamide (112): Compound 2(0.8 g, 3.34 mmol) was taken in dry DCM (10 mL) and TEA (1.1 mL, 8.36 mmol) was added to it. Under cooling conditions, 4-fluorobenzoyl chloride (0.5 mL, 4.01 mmol) was added dropwise at 0 °C and reaction was monitored by checking TLC. After 3 hours, reaction was completed and reaction mixture was diluted with DCM and washed thoroughly with NaHCO₃ solution and extracted to give light brown crude mass which was purified by column chromatography (Silica gel, mesh size 100-200) eluting (50%EtOAc/ Pet

ether) to obtain compound **112** (1.1 g, 91 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 13.03 (s, 1H), 9.44 (s, 1H), 8.86 (d, *J* = 9.3 Hz, 1H), 8.78 (s, 1H), 8.45 (d, *J* = 9.3 Hz, 1H), 8.04- 7.99 (m, 2H), 7.50- 7.44 (m, 2H), 3.51 (br.s, 4H), 3.28 (s, 3H). Melting Point: 256 °C.

5

Example 120

Synthesis of 2-(4-fluorophenyl)-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one (**113**):

The compound was prepared by general procedure **G** provided in example 7 using compound **112** (0.7 g, 1.93 mmol), DMF (8 mL), ZnCl₂ (1.3 g, 9.69 mmol), HMDS (4 mL, 19.38 mmol) to obtain compound **113** (0.59 g, 89 %) as white solid. ¹H NMR (600 MHz, CDCl₃) δ in ppm 9.18 (d, *J* = 3 Hz, 1H), 8.54 (dd, *J* = 9 Hz, 2.4 Hz, 1H), 7.83 (d, *J* = 9 Hz, 1H), 7.63- 7.61 (m, 2H), 7.24- 7.21 (m, 2H), 4.28 (t, *J* = 4.8 Hz, 2H), 3.62 (t, *J* = 5.4 Hz, 2H), 3.18 (s, 3H). ESI-HRMS *m/z* 344.1038 (M+H⁺). Melting Point: 156 °C.

15 Example 121

Synthesis of 6-amino-2-(4-fluorophenyl)-3-(2-methoxyethyl)quinazolin-4(3H)-one (**114**):

The compound was prepared by general procedure **C** provided in example 3 using compound **113** (0.25 g, 0.72 mmol), methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **114** (0.19 g, 83 %) as brown solid. ¹H NMR (400 MHz, CDCl₃) δ in ppm 7.55- 7.51 (m, 3H), 7.46 (d, *J* = 2.8 Hz, 1H), 7.17- 7.13 (m, 2H), 7.09 (dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 4.17 (t, *J* = 5.6 Hz, 2H), 3.56 (t, *J* = 5.6 Hz, 2H), 3.15 (s, 3H). ESI-HRMS *m/z* 314.1304 (M+H⁺). Melting Point: 160 °C.

Example 122

25 Synthesis of 1-(3-acetylphenyl)-3-(2-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-

dihydroquinazolin-6-yl)urea (115**):** The compound was obtained by general procedure **D** provided in example 4 using compound **110** (0.12 g, 0.38 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (91 mg, 0.45 mmol), TEA (0.159 mL, 1.14 mmol) to obtain compound **115** (0.08 g, 44 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.18 (s, 1H), 9.04 (s, 1H), 8.43 (d, *J* = 2.4 Hz, 1H), 8.12-8.11 (m, 1H), 7.83 (dd, *J* = 8.7 Hz, 2.4 Hz, 1H), 7.73 -7.67 (m, 3H), 7.64-7.60 (m, 2H), 7.49- 7.44 (m, 1H), 7.40- 7.34 (m, 2H), 4.10 (t, *J* = 5.7 Hz, 2H), 3.45 (t, *J* = 5.7 Hz, 2H), 3.04 (s, 3H), 2.58 (s, 3H). ESI-MS *m/z* 475.1 (M+H⁺). Melting Point: 220 °C.

Example 123**Synthesis of 2-(4-methoxybenzamido)-N-(2-methoxyethyl)-5-nitrobenzamide (116):**

Compound **2** (0.6 g, 2.50 mmol) was taken in dry DCM (10 mL) and TEA (0.77 mL, 5.52
5 mmol) was added to it. Under cooling conditions, 4-methoxybenzoyl chloride (0.4 mL, 3.01
mmol) was added dropwise at 0 °C and reaction was monitored by checking TLC. After 3
hours, reaction was completed and reaction mixture was diluted with DCM and washed
thoroughly with NaHCO₃ solution and extracted to give light brown crude mass which was
purified by column chromatography (Silica gel, mesh size 100-200) eluting (60%EtOAc/ Pet
10 ether) to obtain compound **116** (0.8 g, 85 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO)
δ in ppm 12.89 (s, 1H), 9.36 (br.s, 1H), 8.84 (d, *J*= 8.8 Hz, 1H), 8.71 (d, *J*= 2.4 Hz, 1H), 8.36
(q, *J*= 6.8 Hz, 2.8 Hz, 1H), 7.87 (d, *J*= 8.8 Hz, 2H), 7.09 (d, *J*= 8.8 Hz, 2H), 3.80 (s, 3H),
3.49- 3.45 (m, 4H), 3.24 (s, 3H).ESI-HRMS *m/z* 374.1329 (M+H⁺). Melting Point: 184 °C.

15 Example 124**Synthesis of 3-(2-methoxyethyl)-2-(4-methoxyphenyl)-6-nitroquinazolin-4(3H)-one**

(**117**): The compound was prepared by general procedure **G** provided in example **7** using
compound **116** (0.6 g, 1.60 mmol), DMF (8 mL), ZnCl₂ (1.0 g, 8.04 mmol), HMDS (3.3 mL,
16.08 mmol) to obtain compound **117** (0.59 g, 87 %) as white solid. ¹H NMR (400 MHz,
20 CDCl₃) δ in ppm 9.15 (d, *J*= 2.4 Hz, 1H), 8.50 (dd, *J*= 9 Hz, 2.4 Hz, 1H), 7.80 (d, *J*= 9.2 Hz,
1H), 7.54 (d, *J*= 8.8 Hz, 2H), 7.02 (d, *J*= 8.8 Hz, 2H), 4.32 (t, *J*= 5.6 Hz, 2H), 3.87 (s, 3H),
3.59 (t, *J*= 5.6 Hz, 2H), 3.16 (s, 3H).ESI-HRMS *m/z* 356.1225 (M+H⁺). Melting Point: 162
°C.

25 Example 125**Synthesis of 6-amino-3-(2-methoxyethyl)-2-(4-methoxyphenyl)quinazolin-4(3H)-one**

(**118**):The compound was prepared by general procedure **C** provided in example **3** using
compound **117** (0.25 g, 0.70 mmol), methanol (5 mL), pinch of 10 % wet Pd-C under
hydrogen atmosphere to obtain compound **118** (0.18 g, 89 %) as brown solid. ¹H NMR (400
30 MHz, d₆-DMSO) δ in ppm 7.46 (d, *J*= 7.2 Hz, 2H), 7.31 (d, *J*= 8.4 Hz, 1H), 7.18 (d, *J*= 2.8
Hz, 1H), 7.05 (dd, *J*= 6 Hz, 2.4 Hz, 1H), 6.99 (d, *J*= 8.8 Hz, 2H), 5.62 (s, 2H), 4.05 (t, *J*= 6
Hz, 2H), 3.78 (s, 3H), 3.36 (t, *J*= 6 Hz, 2H), 2.99 (s, 3H).ESI-HRMS *m/z* 326.1478 (M+H⁺).
Melting Point: 172 °C.

Example 126

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (119):The compound was prepared by general procedure **D**

5 provided in example 4 using compound **118** (0.12 g, 0.36 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (89 mg, 0.44 mmol), 3'-aminoacetophenone (0.061 g, 0.44 mmol), TEA (0.15 mL, 1.10 mmol) to obtain compound **119** (0.075 g, 42 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.16 (s, 1H), 9.03 (s, 1H), 8.40 (s, 1H), 8.11 (s, 1H), 7.81 (d, *J* = 8.7 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.62-7.55 (m, 4H), 7.49-7.43 (m, 1H), 7.07 (d, *J* = 8.1 Hz, 2H), 4.15 (t, *J* = 5.7 Hz, 2H), 3.83 (s, 3H), 3.46-3.42 (m, 2H) 3.04 (s, 3H), 2.58 (s, 3H). ESI-MS *m/z* 487.1 (M+H⁺). Melting Point: 220 °C.

Example 127

Synthesis of 2-(cyclohexanecarboxamido)-N-(2-methoxyethyl)-5-nitrobenzamide (120):Compound **2** (0.6 g, 2.50 mmol) was taken in dry DCM (10 mL) and TEA (0.9 mL,

15 6.27 mmol) was added to it. Cyclohexanecarbonyl chloride (0.6 mL, 5.01 mmol) was added dropwise at 0 °C and reaction was monitored by checking TLC. After 3 hours, reaction was completed and reaction mixture was diluted with DCM and washed thoroughly with NaHCO₃ solution and extracted to give light brown crude mass which was purified by column chromatography (Silica gel, mesh size 100-200) eluting (50%EtOAc/ Pet ether) to obtain compound **120** (0.75 g, 86 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 11.83 (s, 1H), 9.30- 9.26 (m, 1H), 8.72 (d, *J* = 9 Hz, 1H), 8.66 (d, *J* = 2.7 Hz, 1H), 8.37 (dd, *J* = 6.9 Hz, 2.4 Hz, 1H), 3.50- 3.40 (m, 4H), 3.29 (s, 3H), 2.39 – 2.32 (m, 1H), 1.92- 1.88 (m, 2H), 1.77 -1.66 (m, 3H), 1.47- 1.30 (m, 4H), 1.29- 1.16 (m, 1H). ESI-HRMS *m/z* 350.1698 (M+H⁺). Melting Point: 130 °C.

Example 128

Synthesis of 2-cyclohexyl-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one (121):The compound was prepared by general procedure **G** provided in example 7 using compound **120**

30 (0.55 g, 1.57 mmol), DMF (8 mL), ZnCl₂ (1.07 g, 7.87 mmol), HMDS (3.3 mL, 15.75 mmol) to obtain compound **121** (0.45 g, 86 %) as white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.80 (d, *J* = 2.7 Hz, 1H), 8.51 (dd, *J* = 6.3 Hz, 2.7 Hz, 1H), 7.79 (d, *J* = 9 Hz, 1H), 4.34 (t, *J* = 5.4 Hz, 2H), 3.62 (t, *J* = 5.4 Hz, 2H), 3.24 (s, 3H), 3.15- 3.08 (m, 1H), 1.92- 1.88 (m, 3H),

1.82- 1.78 (m, 3H), 1.74 – 1.66 (m, 2H), 1.46- 1.33 (m, 2H).ESI-HRMS m/z 332.1614 (M+H⁺). Melting Point: 148 °C.

Example 129

5 **Synthesis of 6-amino-2-cyclohexyl-3-(2-methoxyethyl)quinazolin-4(3H)-one (122):**The compound was prepared by general procedure C provided in example 3 using compound **121** (0.3 g, 0.90 mmol), methanol (5 mL) and pinch of 10 % wet Pd-C to obtain compound **122** (0.25 g, 92 %) as brown solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 7.30 (d, J = 8.7 Hz, 1H), 7.15 (d, J = 2.4 Hz, 1H), 7.04 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 5.53 (s, 2H), 4.23 (t, J = 5.4
10 Hz, 2H), 3.56 (t, J = 5.4 Hz, 2H), 3.23 (s, 3H), 2.99-2.89 (m, 1H), 1.85- 1.72 (m, 5H), 1.62- 1.51 (m, 2H), 1.42- 1.25 (m, 3H).ESI-HRMS m/z 302.1852 (M+H⁺). Melting Point: 146 °C.

Example 130

15 **Synthesis of 1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (123):** The compound was prepared by general procedure D provided in example 4 using compound **122**(0.12 g, 0.39 mmol), dry THF (7 mL), 4-nitrophenylchloroformate (0.12 g, 0.59 mmol), 3'-aminoacetophenone (0.06 g, 0.47 mmol), TEA (0.2 mL, 1.64 mmol) to obtain compound **123** (0.075 g, 41 %) as white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.01 (s, 1H), 8.92 (s, 1H), 8.24 (d, J = 2.8 Hz, 1H), 8.04-8.03
20 (m, 1H), 7.73 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.66-7.63 (m, 1H), 7.56- 7.53 (m, 1H), 7.49 (d, J = 8.8 Hz, 1H), 7.41- 7.37 (m, 1H), 4.23 (t, J = 5.6 Hz, 2H), 3.54 (t, J = 5.6 Hz, 2H), 3.19 (s, 3H), 3.00- 2.93 (m, 1H), 2.52 (s, 3H), 1.83- 1.72 (m, 4H), 1.67- 1.50 (m, 3H), 1.38-1.16 (m, 3H).ESI-MS m/z 463.3 (M+H⁺). Melting Point: 202°C.

25 Example 131

Synthesis of 2-(cyclopentanecarboxamido)-N-(2-methoxyethyl)-5-nitrobenzamide (124): Compound **2** (0.6 g, 2.50 mmol) was taken in dry DCM (10 mL) and TEA (1.0 mL, 7.52 mmol) was added to it. Cyclopentanecarbonyl chloride (1 mL, 10.03 mmol) was added dropwise at 0 °C and reaction was monitored by checking TLC. After 5 hours, reaction was
30 completed and reaction mixture was diluted with DCM and washed thoroughly with NaHCO₃ solution and extracted to give light brown crude mass which was purified by column chromatography (Silica gel, mesh size 100-200) eluting (50%EtOAc/ Pet ether) to obtain compound **124** (0.75 g, 89 %) as white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 11.82

(s, 1H), 9.28- 9.25 (m, 1H), 8.70 (d, $J=9.3$ Hz, 1H), 8.66 (d, $J=2.7$ Hz, 1H), 8.37 (dd, $J=8.4$ Hz, 2.4 Hz, 1H), 3.53- 3.46 (m, 4H), 3.32 (s, 3H), 2.87- 2.79 (m, 1H), 1.94- 1.87 (m, 2H), 1.79- 1.56 (m, 6H).ESI-HRMS m/z 336.1560 (M+H⁺). Melting Point: 126 °C.

5 Example 132

Synthesis of 2-cyclopentyl-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one (125): The compound was prepared by general procedure **G** provided in example 7 using compound **124** (0.6 g, 1.79 mmol), DMF (8 mL), ZnCl₂ (0.97 g, 7.16 mmol), HMDS (3 mL, 14.32 mmol) to obtain compound **125** (0.48 g, 84 %) as white solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.79 (d, $J=2.4$ Hz, 1H), 6.51 (dd, $J=9$ Hz, 2.7 Hz, 1H), 7.77 (d, $J=9$ Hz, 1H), 4.35 (t, $J=5.4$ Hz, 2H), 3.62 (q, $J=5.4$ Hz, 2H), 3.57- 3.52 (m, 1H), 3.24 (s, 3H), 2.06- 1.94 (m, 4H), 1.82- 1.64 (m, 4H).ESI-HRMS m/z 318.1449 (M+H⁺). Melting Point: 130°C.

Example 133

15 **Synthesis of 6-amino-2-cyclopentyl-3-(2-methoxyethyl)quinazolin-4(3H)-one (126):** The compound was prepared by general procedure **C** provided in example 3 using compound **125** (0.3 g, 0.94 mmol), methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **126** (0.22 g, 81 %) as brown solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.35 (d, $J=8.4$ Hz, 1H), 7.26 (d, $J=7.2$ Hz, 1H), 7.13 (dd, $J=9$ Hz, 2.4 Hz, 1H), 4.26 (t, $J=5.7$ Hz, 2H), 3.57 (t, $J=5.7$ Hz, 2H), 3.46- 3.41 (m, 1H), 3.23 (s, 3H), 2.01- 1.87 (m, 4H), 1.84- 1.75 (m 2H), 1.70- 1.58 (m, 2H).ESI-HRMS m/z 288.1704 (M+H⁺). Melting Point: 142 °C.

Example 134

25 **Synthesis of 1-(3-acetylphenyl)-3-(2-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (127):** The compound was prepared by general procedure **D** provided in example 4 using compound **126** (0.12 g, 0.41 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.12 g, 0.62 mmol), 3'-aminoacetophenone (0.07 g, 0.52 mmol), TEA (0.2 mL, 1.72 mmol) to obtain compound **127** (0.079 g, 42 %) as brown solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.08 (s, 1H), 9.00 (s, 1H), 8.30 (d, $J=2.4$ Hz, 1H), 8.10 (s, 1H), 7.78 (dd, $J=8.8$ Hz, 2.7 Hz, 1H), 7.70 (d, $J=9$ Hz, 1H), 7.60 (d, $J=7.5$ Hz, 1H), 7.54 (d, $J=8.7$ Hz, 1H), 7.48 7.42 (m, 1H), 4.31 (t, $J=5.4$ Hz, 2H), 3.60 (t, $J=5.4$ Hz, 2H), 3.54

– 3.44 (m, 1H), 3.24 (s, 3H), 2.57 (s, 3H), 2.04- 1.86 (m, 4H), 1.82- 1.73 (m, 2H), 1.69- 1.61 (m, 2H). ESI-MS m/z 449.2 (M+H⁺). Melting Point: 204 °C.

Example 135

5 **Synthesis of 2-amino-N-(2-methoxyphenyl)-5-nitrobenzamide (128):** The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), o-anisidine (0.7 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **128** (1.2 g, 76 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.83(s, 1H), 8.64(d, $J= 2.4$ Hz, 1H), 8.07(dd, $J= 8.7$ Hz, $J = 2.4$ Hz, 1H),
10 7.68(s, 2H), 7.54(dd, $J= 7.8$ Hz, $J =1.8$ Hz, 1H), 7.24-7.19(m, 1H), 7.11-7.08(m, 1H), 6.99-6.93(m, 1H), 6.85(d, $J= 9.3$ Hz, 1H), 3.82(s, 3H). ESI-HRMS m/z 288.0998 (M+H⁺). Melting Point: 178 °C.

Example 136

15 **Synthesis of 3-(2-methoxyphenyl)-6-nitroquinazolin-4(3H)-one (129):** The compound was prepared by general procedure **B** provided in example 2 using compound **128** (1 g, 2.78 mmol), trimethylorthoformate (TMOF) (6 mL, 55.73 mmol) to obtain compound **129** (0.69 g, 83 %) as pale yellow solid. ¹H NMR (400 MHz, CDCl₃) δ in ppm 9.18 (d, $J= 2.4$ Hz, 1H), 8.55 (dd, $J= 9.2$ Hz, $J = 2.8$ Hz, 1H), 8.08 (s, 1H), 7.87 (d, $J= 9.2$ Hz, 1H), 7.51-7.47 (m, 2H),
20 7.33- 7.31(m, 1H), 7.13-7.09 (m, 1H), 3.81(s, 3H). ESI-HRMS m/z 298.0836 (M+H⁺). Melting Point: 164 °C.

Example 137

25 **Synthesis of 6-amino-3-(2-methoxyphenyl)quinazolin-4(3H)-one (130):**The compound was prepared by general procedure **C** provided in example 3 using compound **129** (0.8 g, 2.69 mmol), methanol (10 mL), pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **130** (0.65 g, 90 %) as light brown solid. ¹H NMR (300 MHz, d₆- DMSO) δ in ppm 7.83 (s, 1H), 7.52- 7.39 (m, 3H), 7.25- 7.22 (m, 2H), 7.14- 7.07 (m, 2H), 5.72 (brs, 2H), 3.76 (s, 3H). ESI-HRMS m/z 268.1096 (M+H⁺). Melting Point: 169 °C.

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Example 138

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (131):The compound was prepared by general procedure **D** provided in example 4

using compound **130** (0.12 g, 0.44 mmol), dry THF (6 mL) and 4-nitrophenylchloroformate (0.13 g, 0.67 mmol), 3'-aminoacetophenone (0.075 g, 0.56 mmol), TEA (0.3 mL, 1.85 mmol) to obtain compound **131** (0.05 g, 27 %) as light yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.18 (s, 1H), 9.01 (s, 1H), 8.37 (d, *J* = 2.8 Hz, 1H), 8.10- 8.09 (m, 1H), 8.07 (s, 1H),
5 7.89 (dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 7.77- 7.72 (m, 2H), 7.61- 7.59 (m, 1H), 7.54- 7.49 (m, 1H), 7.47- 7.43 (m, 2H), 7.26 (dd, *J* = 8.4 Hz, 1.2 Hz, 1H), 7.14- 7.10 (m, 1H), 3.77 (s, 3H), 2.57 (s, 3H).

Example 139

10 **Synthesis of 2-amino-N-(2-morpholinoethyl)-5-nitrobenzamide (132):**The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 4-(2-aminoethyl)morpholine (0.8 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **132** (0.9 g, 56 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.64 (t, *J* = 5.7 Hz, 1H), 8.46 (d, *J* = 2.7 Hz, 1H), 8.02 (dd, *J* = 9.3 Hz, *J* = 2.4 Hz, 1H), 7.73 (s, 2H), 6.78 (d, *J* = 9.3 Hz, 1H), 3.57 (t, *J* = 4.5 Hz, 4H),
15 3.39- 3.36 (m, 2H), 2.51- 2.48 (m, 2H), 2.43- 2.39 (m, 4H). ESI-HRMS *m/z* 295.1411 (M+H⁺). Melting Point: 152°C.

Example 140

20 **Synthesis of 3-(2-morpholinoethyl)-6-nitroquinazolin-4(3H)-one (133):**The compound was prepared by general procedure **B** provided in example 2 using compound **132** (0.6 g, 2.03 mmol), trimethylorthoformate (TMOF) (4 mL, 40.79 mmol) to obtain compound **133** (0.42 g, 68 %) as pale yellow solid. ESI-HRMS *m/z* 305.1247 (M+H⁺). Melting Point: 142°C.

Example 141

25 **Synthesis of 6-amino-3-(2-morpholinoethyl)quinazolin-4(3H)-one (134):**The compound was prepared by general procedure **C** provided in example 3 using compound **133** (0.25 g, 0.82 mmol), methanol (6 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **134** (0.15 g, 67 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ
30 in ppm 8.72 (s, 1H), 8.63 (d, *J* = 1.5 Hz, 1H), 8.11 (s, 1H), 7.53-7.48 (m, 2H), 7.25 (dd, *J* = 8.7 Hz, 2.4 Hz, 1H), 4.06 (t, *J* = 6 Hz, 2H), 3.52-3.51 (m, 4H), 2.59 (t, *J* = 3.9 Hz, 2H), 2.43 (m, 4H). ESI-HRMS *m/z* 275.1513 (M+H⁺). Melting Point: 186 °C.

Example 142**Synthesis of 1-(3-acetylphenyl)-3-(3-(2-morpholinoethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (135):**

The compound was prepared by general procedure **E** provided in example 5 using compound **134** (0.12 g, 0.43 mmol), dry THF (6 mL), 3-acetylphenylisocyanate (0.071 mL, 0.51 mmol), TEA (0.3 mL, 1.80 mmol) to obtain compound **135** (0.04 g, 21 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 11.00(s, 1H), 9.74(s, 1H), 8.33(d, *J*= 2.4Hz, 2H), 8.27(s, 1H), 8.16(dd, *J*= 9Hz,4Hz, 1H), 7.96(d, *J*=8.1Hz, 1H), 7.69-7.63(m, 2H), 7.48-7.43 (m, 1H), 4.10(t, *J*= 6Hz, 2H), 3.54-3.51 (m, 4H), 2.61 (t, *J*= 6Hz, 2H), 2.57(s, 3H), 2.45-2.42 (m, 4H). ESI-HRMS *m/z* 436.1987 (M+H⁺). Melting Point: 140 °C.

Example 143

Synthesis of 2-amino-N-(3-morpholinopropyl)-5-nitrobenzamide (136): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 3-morpholinopropylamine (0.9 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **136** (1 g, 59 %) as yellow solid. ESI-HRMS *m/z* 309.1568 (M+H⁺). Melting Point: 126 °C.

Example 144

Synthesis of 3-(3-morpholinopropyl)-6-nitroquinazolin-4(3H)-one (137): The compound was prepared by general procedure **B** provided in example 2 using compound **136** (0.6 g, 1.94 mmol), trimethylorthoformate (TMOF) (4 mL, 38.94 mmol) to obtain compound **137** (0.48 g, 88 %) as pale yellow solid. ESI-HRMS *m/z* 319.1398 (M+H⁺). Melting Point: 118 °C.

Example 145

Synthesis of 6-amino-3-(3-morpholinopropyl)quinazolin-4(3H)-one (138): The compound was prepared by general procedure **C** provided in example 3 using compound **137** (0.3 g, 0.94 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **138** (0.18 g, 66 %) as light brown solid. ESI-HRMS *m/z* 289.1664 (M+H⁺). Melting Point: 148 °C.

Example 146

Synthesis of 1-(3-acetylphenyl)-3-(3-(3-morpholinopropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (139):

The compound was prepared by general procedure **D** provided in example 4 using compound **138** (0.12 g, 0.41 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.13 g, 0.62 mmol), 3'-aminoacetophenone (0.07 g, 0.52 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **139** (0.04 g, 22 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.13 (s, 1H), 8.99 (s, 1H), 8.30 (s, 1H), 8.21 (s, 1H), 8.04 (s, 1H), 7.77- 7.74 (m, 1H), 7.65- 7.62 (m, 1H), 7.58- 7.53 (m, 2H), 7.55 (dd, *J* = 11.1 Hz, 6.9 Hz, 2H), 7.42- 7.38 (m, 1H), 3.96 (t, *J* = 3 Hz, 2H), 3.48- 3.41 (m, 4H), 2.52 (s, 3H), 2.37- 2.19 (m, 6H), 1.86- 1.79 (m, 2H). ESI-HRMS *m/z* 450.2160 (M+H⁺). Melting Point: 178 °C.

Example 147

Synthesis of 2-amino-N-(2-(dimethylamino)ethyl)-5-nitrobenzamide (140): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), *N,N*-dimethylethylenediamine (0.7 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **140** (0.8 g, 56 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.83(d, *J* = 2.7Hz, 1H), 8.55(dd, *J* = 9Hz, *j* = 2.7Hz, 1H), 8.52(s, 1H), 7.86(d, *J* = 9Hz, 1H), 4.11(t, *J* = 6Hz, 2H), 2.57(t, *J* = 6Hz, 2H), 2.19(s, 6H). ESI-HRMS *m/z* 253.1304 (M+H⁺). Melting Point: 116 °C.

Example 148

Synthesis of 3-(2-(dimethylamino)ethyl)-6-nitroquinazolin-4(3H)-one (141): The compound was prepared by general procedure **B** provided in example 2 using compound **140** (0.6 g, 2.37 mmol), trimethylorthoformate (TMOF) (4 mL, 38.94 mmol) to obtain compound **141** (0.49 g, 86 %) as pale yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.83(d, *J* = 2.7Hz, 1H), 8.55(dd, *J* = 9Hz, *J* = 2.7Hz, 1H), 8.52(s, 1H), 7.86(d, *J* = 9Hz, 1H), 4.11(t, *J* = 6Hz, 2H), 2.58(t, *J* = 6Hz, 2H), 2.20(s, 6H). ESI-HRMS *m/z* 263.1154 (M+H⁺). Melting Point: 115 °C.

Example 149

Synthesis of 6-amino-3-(2-(dimethylamino)ethyl)quinazolin-4(3H)-one (142): The compound was prepared by general procedure **C** provided in example 3 using compound **141** (0.3 g, 1.14 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen

atmosphere to obtain compound **142**(0.19 g, 72 %) as light brown solid. Melting Point: 178 °C.

Example 150

5 Synthesis of **1-(3-acetylphenyl)-3-(3-(2-(dimethylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (143)**:

The compound was prepared by general procedure **E** provided in example 5 using compound **142**(0.12 g, 0.51 mmol), dry THF (8 mL), 3-acetylphenylisocyanate (0.065 mL, 0.61 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **143** (0.109 g, 54 %) as yellow solid.¹H NMR
10 (300 MHz, d₆-DMSO) δ in ppm 9.17(s, 1H), 9.04(s, 1H), 8.34(d, *J*= 2.4Hz, 1H), 8.19(s, 1H), 8.09(brs, 1H), 7.79(d, *J*= 8.7Hz, *J*= 2.4Hz, 1H), 7.69(d, *J*= 8.1Hz, 1H), 7.62-7.57(m, 2H), 7.46-7.41(m, 1H), 4.06(t, *J*= 6Hz, 2H), 2.60-2.56(m, 5H), 2.20(s, 6H).ESI-HRMS *m/z* 394.1879 (M+H⁺).

15 Example 151

Synthesis of 2-amino-5-nitro-N-(2-(piperidin-1-yl)ethyl)benzamide (144): The compound was prepared by general procedure **E** provided in example 5 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 1-(2-aminoethyl)piperidine(0.83 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **144** (0.7 g, 62 %) as yellow solid.¹H
20 NMR (300 MHz, d₆-DMSO) δ in ppm 8.58 (t, *J* = 5.7Hz, 1H), 8.41 (d, *J*= 2.7Hz, 1H), 7.99(dd, *J* = 9.0Hz, *J* = 2.4 Hz, 1H), 7.70 (s, 2H), 6.76 (d, *J*= 9.3Hz, 1H), 2.42-2.33(m, 6H), 1.50-1.33 (m, 2H). ESI-HRMS *m/z* 293.1614 (M+H⁺). Melting Point: 148 °C.

Example 152

25 **Synthesis of 6-nitro-3-(2-(piperidin-1-yl)ethyl)quinazolin-4(3H)-one (145)**: The compound was prepared by general procedure **B** provided in example 2 using compound **144** (0.6 g, 2.05 mmol), trimethylorthoformate (TMOF) (4 mL, 39.56 mmol) to obtain compound **145**(0.52 g, 88 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.79(d, *J*= 2.8Hz, 1H), 8.50(dd, *J*=9.2Hz, *J*= 2.8Hz, 1H), 8.43 (s,1H), 7.82(d, *J*= 9.2Hz, 1H), 4.05(t, *J*=
30 6Hz, 2H), 2.51(t, *J*= 6Hz, 2H), 2.33 (m, 4H), 1.39-1.35 (m,4H), 1.32-1.30 (m, 2H). ESI-HRMS *m/z* 303.1453 (M+H⁺). Melting Point: 120 °C.

Example 153

Synthesis of 6-amino-3-(2-(piperidin-1-yl)ethyl)quinazolin-4(3H)-one (146): The compound was prepared by general procedure **C** provided in example 3 using compound **145** (0.3 g, 0.99 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **146** (0.189 g, 70 %) as light brown solid.

5

Example 154

Synthesis of 1-(3-acetylphenyl)-3-(4-oxo-3-(2-(piperidin-1-yl)ethyl)-3,4-dihydroquinazolin-6-yl)urea (147):

The compound was prepared by general procedure **E** provided in example 5 using compound **146** (0.130g, 0.47 mmol), dry THF (8 mL), 3-acetylphenylisocyanate (0.065 mL, 0.61 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **147** (0.095 g, 46 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.53 (s, 1H), 8.35 (s, 1H), 8.20 (dd, *J* = 8.8 Hz, 2 Hz, 1H), 8.00 (d, *J* = 2.8 Hz, 1H), 7.96 (s, 1H), 7.90- 7.87 (m, 2H), 7.61- 7.56 (m, 2H), 7.38- 7.34 (m, 1H), 4.07 (t, *J* = 5.6 Hz, 2H), 2.69 (t, *J* = 4.8 Hz, 2H), 2.59 (s, 3H), 2.45 (brs, 4H), 1.54- 1.50 (m, 4H), 1.41- 1.38 (m, 2H). ESI-HRMS *m/z* 434.2193 (M+H⁺).

15

Example 155

Synthesis of 2-amino-5-nitro-N-(pyridin-4-yl)benzamide (148): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 4-aminopyridine(0.62 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **148** (1.02 g, 72 %) as yellow solid. ESI-HRMS *m/z* 259.0833 (M+H⁺). Melting Point: 246 °C.

20

Example 156

Synthesis of 6-nitro-3-(pyridin-4-yl)quinazolin-4(3H)-one (149): The compound was prepared by general procedure **B** provided in example 2 using compound **148** (0.6 g, 2.32 mmol), trimethylorthoformate (TMOF) (4 mL, 39.56 mmol) to obtain compound **149**(0.56 g, 90 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.83 (d, *J*= 2.4 Hz, 1H), 8.77 (dd, *J*= 4.8 Hz, 1.2 Hz, 2H), 8.60- 8.57 (m, 2H), 7.92 (d, *J*= 8.8 Hz, 1H), 7.64 (dd, *J*= 4.4 Hz, 1.6 Hz, 2H) Melting Point: 202 °C.

30

Example 157

Synthesis of 6-amino-3-(pyridin-4-yl)quinazolin-4(3H)-one (150): The compound was prepared by general procedure **C** provided in example 3 using compound **149** (0.3 g, 1.11 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **150** (0.191 g, 72 %) as light brown solid.

5

Example 158

Synthesis of 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (151): The compound was prepared by general procedure **D** provided in example 4 using compound **150** (0.130 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.131 g, 0.65 mmol), 3'-aminoacetophenone (0.081 g, 0.60 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **151** (0.115 g, 53 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.29 (s, 1H), 9.09 (s, 1H), 8.79 (d, *J* = 6 Hz, 2H), 8.43 (d, *J* = 2.4 Hz, 1H), 8.30 (s, 1H), 8.10 (brs, 1H), 7.91 (dd, *J* = 9 Hz, *J* = 2.7 Hz, 1H), 7.73 (s, 1H), 7.70- 7.67 (m, 4H), 7.48- 7.43 (m, 1H), 2.58 (s, 3H). ESI-HRMS *m/z* 400.1411 (M+H⁺).

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Example 159

Synthesis of 2-amino-5-nitro-N-(pyridin-3-yl)benzamide (152): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 3-aminopyridine (0.62 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **152** (1.02 g, 72 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.19 (d, *J* = 2.8 Hz, 1H), 8.78 (dd, *J* = 4.8 Hz, *J* = 1.6 Hz, 1H), 8.70 (d, *J* = 2.8 Hz, 1H), 8.59 (dd, *J* = 9.2 Hz, *J* = 2.8 Hz, 1H), 8.22 (s, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.86- 7.83 (m, 1H), 7.56- 7.52 (m, 1H). ESI-HRMS *m/z* 259.0844 (M+H⁺). Melting Point: 266 °C.

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Example 160

Synthesis of 6-nitro-3-(pyridin-3-yl)quinazolin-4(3H)-one (153): The compound was prepared by general procedure **B** provided in example 2 using compound **152** (0.6 g, 2.32 mmol), trimethylorthoformate (TMOF) (4 mL, 39.56 mmol) to obtain compound **153** (0.56 g, 90 %) as pale yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.88 (d, *J* = 2.4 Hz, 1H), 8.80 (d, *J* = 2.1 Hz, 1H), 8.74 (dd, *J* = 4.8 Hz, *J* = 1.2 Hz, 1H), 8.65 (s, 1H), 8.63 (d, *J* = 2.7 Hz, 1H), 8.10- 8.06 (m, 1H), 7.98 (d, *J* = 9 Hz, 1H). Melting Point: 263 °C.

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Example 161

Synthesis of 6-amino-3-(pyridin-3-yl)quinazolin-4(3H)-one (154): The compound was prepared by general procedure C provided in example 3 using compound **153** (0.3 g, 1.11 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain
5 compound **154** (0.191 g, 72 %) as light brown solid.

Example 162

Synthesis of 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (155): The compound was prepared by general procedure D provided in example 4
10 using compound **154** (0.130 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.131 g, 0.65 mmol), 3'-aminoacetophenone(0.081 g, 0.60 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **155** (0.093 g, 48 %) as yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.81(d, *J* = 2.1Hz, 1H), 8.71(dd, *J* = 4.8Hz, *J* = 1.5Hz, 1H), 8.48(s, 1H), 8.34(d, *J* = 2.4Hz, 1H), 8.21-8.19(m, 1H), 8.15-8.06(m, 3H), 7.96(d, *J* = 8.7Hz, 1H), 7.88(d, *J* = 8.1Hz, 1H),
15 7.79-7.74(m, 1H), 7.67-7.63(m, 1H), 2.63(s, 3H). ESI-HRMS *m/z* 400.1412 (M+H⁺).

Example 163

Synthesis of 2-amino-5-nitro-N-(pyridin-2-yl)benzamide (156): The compound was prepared by general procedure A provided in example 1 using compound **1** (1 g, 5.49 mmol),
20 DMF (10 mL), HATU (2.2 g, 6.04 mmol), 2-aminopyridine(0.62 mL, 6.04 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **156** (0.98 g, 69 %) as yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 10.99 (s, 1H), 8.60 (d, *J* = 2.4 Hz, 1H), 8.36- 8.34 (m, 1H), 8.04- 8.00 (m, 2H), 7.81- 7.77 (m, 1H), 7.59 (brs, 2H), 7.14- 7.11 (m, 1H), 6.80 (d, *J* = 9.2 Hz, 1H). ESI-HRMS *m/z* 281.0650 (M+Na⁺). Melting Point: 180 °C.

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Example 164

Synthesis of 6-nitro-3-(pyridin-2-yl)quinazolin-4(3H)-one (157): The compound was prepared by general procedure B provided in example 2 using compound **156** (0.6 g, 2.32 mmol), trimethylorthoformate (TMOF) (4 mL, 39.56 mmol) to obtain compound **157** (0.52 g,
30 89 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.20 (d, *J* = 2.8 Hz, 1H), 8.77 (s, 1H), 8.63- 8.61 (m, 1H), 8.56 (dd, *J* = 9 Hz, 2.8 Hz, 1H), 7.94- 7.88 (m, 3H), 7.44- 7.41 (m, 1H). ESI-HRMS *m/z* 269.0677 (M+H⁺). Melting Point: 220 °C.

Example 165

Synthesis of 6-amino-3-(pyridin-2-yl)quinazolin-4(3H)-one (158): The compound was prepared by general procedure **C** provided in example 3 using compound **157** (0.3 g, 1.11 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain
5 compound **158** (0.183 g, 71 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.64 (d, *J* = 4.2 Hz, 1H), 8.23 (s, 1H), 8.07- 8.01 (m, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.56- 7.51 (m, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 2.4 Hz, 1H), 7.13 (dd, *J* = 8.7 Hz, 2.7 Hz, 1H), 5.79 (brs, 2H).

10 Example 166

Synthesis of 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (159): The compound was prepared by general procedure **D** provided in example 4 using compound **158** (0.130 g, 0.54 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.131 g, 0.65 mmol), 3'-aminoacetophenone (0.081 g, 0.60 mmol), TEA (0.3 mL, 1.71 mmol)
15 to obtain compound **159** (0.095 g, 44 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.21 (s, 1H), 9.02 (s, 1H), 8.66 (dd, *J* = 4.8 Hz, 1.2 Hz, 1H), 8.46 (s, 1H), 8.45 (s, 1H), 8.10- 8.05 (m, 2H), 7.91- 7.83 (m, 2H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.61- 7.55 (m, 2H), 7.47- 7.43 (m, 1H), 2.57 (s, 3H). ESI-HRMS *m/z* 400.1407 (M+H⁺).

20 Example 167

Synthesis of 2-amino-N-(1-methylpiperidin-4-yl)-5-nitrobenzamide (160): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 1-methylpiperidin-4-amine (0.75 mL, 6.58 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **160** (1.007 g, 66 %) as yellow
25 solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.53 (d, *J* = 7.5 Hz, 1H), 8.48 (d, *J* = 2.7 Hz, 1H), 8.01 (dd, *J* = 9.3 Hz, 2.7 Hz, 1H), 7.72 (s, 2H), 6.78 (d, *J* = 9.3 Hz, 1H), 3.75- 3.65 (m, 1H), 2.80- 2.76 (m, 2H), 2.16 (s, 3H), 1.98- 1.89 (m, 2H), 1.77- 1.72 (m, 2H), 1.64- 1.51 (m, 2H). ESI-HRMS *m/z* 279.1470 (M+H⁺).

30 Example 168

Synthesis of 3-(1-methylpiperidin-4-yl)-6-nitroquinazolin-4(3H)-one (161): The compound was prepared by general procedure **B** provided in example 2 using compound **160** (0.6 g, 2.32 mmol), trimethylorthoformate (TMOF) (4 mL, 38.23 mmol) to obtain compound

161 (0.52 g, 89 %) as pale yellow solid. ¹H NMR (300 MHz, CDCl₃) δ in ppm 9.13 (d, *J*= 2.4 Hz, 1H), 8.50 (dd, *J*= 8.8 Hz, 2.8 Hz, 1H), 8.26 (s, 1H), 7.80 (d, *J*= 9.2 Hz 1H), 3.04-3.01 (m, 2H), 2.34 (s, 3H) 2.24- 2.18 (m, 2H), 2.02- 1.97 (m, 4H).

5 **Example 169**

Synthesis of 6-amino-3-(1-methylpiperidin-4-yl)quinazolin-4(3H)-one (162): The compound was prepared by general procedure **C** provided in example 3 using compound **161** (0.3 g, 1.11 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **162** (0.166 g, 62 %) as light brown solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.10 (s, 1H), 7.37 (d, *J*= 8.4 Hz, 1H), 7.22 (d, *J*= 2.4 Hz, 1H), 7.07 (dd, *J*= 8.7 Hz, 2.7 Hz, 1H), 5.66 (brs, 2H), 4.64- 4.54 (m, 1H), 2.94- 2.91 (m, 2H), 2.23 (s, 3H), 2.13- 2.03(m, 4H), 1.75- 1.70 (m, 2H).

Example 170

15 **Synthesis of 1-(3-acetylphenyl)-3-(3-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (163):**

The compound was prepared by general procedure **D** provided in example 4 using compound **162**(0.120 g, 0.46 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.110 g, 0.55 mmol), 3'-aminoacetophenone(0.075 g, 0.55 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound
20 **163**(0.062 g, 32 %) as yellow solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.42 (s, 1H), 9.26 (s, 1H), 8.37- 8.34 (m, 2H), 8.11 (s, 1H), 7.83 (dd, *J*= 8.5 Hz, 1.5 Hz, 1H), 7.71 (d, *J*= 8.1 Hz, 1H), 7.63- 7.58 (m, 2H), 7.47- 7.42 (m, 1H), 4.62- 4.55 (m, 1H), 2.92- 2.89 (m, 2H), 2.57 (s, 3H), 2.21 (s, 3H), 2.07- 2.04 (m, 4H), 1.79- 1.76 (m, 2H). ESI-HRMS *m/z* 420.2036 (M+H⁺).

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Example 171

Synthesis of 2-amino-N-(2-(methylamino)ethyl)-5-nitrobenzamide (164): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), *N*-Methylethylenediamine(0.48 mL, 6.58
30 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **164** (0.810 g, 62 %) as yellow solid.ESI-HRMS *m/z* 239.1146 (M+H⁺).

Example 172

Synthesis of 3-(2-(methylamino)ethyl)-6-nitroquinazolin-4(3H)-one (165): The compound was prepared by general procedure **B** provided in example 2 using compound **164** (0.6 g, 2.51 mmol), trimethylorthoformate (TMOF) (4 mL, 38.23 mmol) to obtain compound **165** (0.48 g, 78 %) as pale yellow solid.

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Example 173

Synthesis of 6-amino-3-(2-(methylamino)ethyl)quinazolin-4(3H)-one (166): The compound was prepared by general procedure **C** provided in example 3 using compound **165** (0.3 g, 1.37 mmol), methanol (10 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **166** (0.147 g, 56 %) as light brown solid.

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Example 174

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-(methylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (167):

15 The compound was prepared by general procedure **D** provided in example 4 using compound **166** (0.120 g, 0.55 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.133 g, 0.66 mmol), 3'-aminoacetophenone (0.074 g, 0.54 mmol) was added followed by TEA (0.3 mL, 1.71 mmol) to obtain compound **167** (0.048 g, 23 %) as yellow solid.

20 Example 175

Synthesis of 2-amino-N-(1-methoxybutan-2-yl)-5-nitrobenzamide (168): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (0.8 g, 4.39 mmol), DMF (8 mL), HATU (1.8 g, 4.83 mmol), 2-amino-1-methoxybutane (0.6 mL, 5.27 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound **168** (0.8 g, 68 %) as yellow solid.¹H

25 NMR (300 MHz, d₆-DMSO) δ in ppm 8.51 (d, $J=2.4$ Hz, 1H), 8.43 (d, $J=8.4$ Hz, 1H), 8.02 (dd, $J=9.1$ Hz, 2.7 Hz, 1H), 7.73 (s, 2H), 6.79 (d, $J=9.3$ Hz, 1H), 4.07-4.00 (m, 1H), 3.44-3.40 (m, 1H), 3.38-3.30 (m, 1H), 3.26 (s, 3H), 1.65-1.41 (m, 2H), 0.88 (t, $J=4.5$ Hz, 3H). ESI-HRMS m/z 268.1289 (M+H⁺). Melting Point: 122 °C.

30 Example 176

Synthesis of 3-(1-methoxybutan-2-yl)-6-nitroquinazolin-4(3H)-one (169): The compound was prepared by general procedure **B** provided in example 2 using compound **168** (0.8 g, 2.99 mmol), trimethylorthoformate (TMOF) (6.5 mL, 59.89 mmol) to obtain compound **169** (0.70

g, 84 %) as pale yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.84 (d, *J*= 2.7 Hz, 1H), 8.61 (s, 1H), 8.57 (dd, *J*= 9 Hz, 2.7 Hz, 1H), 7.89 (d, *J*= 8.7 Hz, 1H), 4.92- 4.83 (m, 1H), 3.87- 3.81 (m, 1H), 3.65- 3.60 (m, 1H), 3.23 (s, 3H), 1.92- 1.82 (m, 2H), 0.84 (t, *J*= 7.5 Hz, 3H).ESI-HRMS *m/z* 278.1138 (M+H⁺). Melting Point: 104 °C.

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Example 177

Synthesis of 6-amino-3-(1-methoxybutan-2-yl)quinazolin-4(3H)-one (170): The compound was prepared by general procedure C provided in example 3 using compound **169**(0.3 g, 1.08 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **170** (0.23 g, 86 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.02 (s, 1H), 7.37 (d, *J*= 8.7 Hz, 1H), 7.20 (d, *J*= 2.7 Hz, 1H), 7.07 (dd, *J*= 9.1 Hz, 2.4 Hz, 1H), 5.65 (s, 2H), 4.91- 4.76 (m, 1H), 3.81- 3.75 (m, 1H), 3.56 (q, *J*= 6.3 Hz, 1H), 3.21 (s, 3H), 1.85- 1.75 (m, 2H), 0.78 (t, *J*= 7.2 Hz, 3H).ESI-HRMS *m/z* 248.1384 (M+H⁺). Melting Point: 140 °C.

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Example 178

Synthesis of 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (171):

The compound was prepared by general procedure D provided in example 4 using compound **170**(0.10 g, 0.40 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.12 g, 0.60 mmol), 3'-aminoacetophenone(0.065 g, 0.48 mmol), TEA (0.2 mL, 1.66 mmol) to obtain compound **171** (0.07 g, 42 %) as off white solid. ¹H NMR (300 MHz, CDCl₃) δ in ppm 9.09 (s, 1H), 8.96 (s, 1H), 8.30 (d, *J*= 2.4 Hz, 1H), 8.21 (s, 1H), 8.06- 8.05 (m, 1H), 7.79 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.67- 7.65 (m, 1H), 7.59- 7.54 (m, 2H), 7.43-7.39 (m, 1H), 4.86- 4.80 (m, 1H), 3.80- 3.75 (m, 1H), 3.57- 3.53 (m, 1H), 3.19 (s, 3H), 2.53 (s, 3H), 1.83- 1.76 (m, 2H), 0.77 (t, *J* = 7.2 Hz, 3H).ESI-MS *m/z* 409.2 (M+H⁺). Melting Point: 182 °C.

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Example 179

Synthesis of 2-amino-N-butyl-5-nitrobenzamide (172): The compound was prepared by general procedure A provided in example 1 using compound **1** (0.8 g, 4.39 mmol), DMF (8 mL), HATU (1.8 g, 4.83 mmol), 1-butylamine(0.5 mL, 5.27 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound **172** (0.82g, 79 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.62 (br.s, -NH), 8.43 (d, *J*= 2.4 Hz, 1H), 7.96 (dd, *J*= 9.2 Hz, 2.8 Hz, 1H),

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7.70 (br.s, 2H), 6.74 (d, $J= 9.6$ Hz, 1H), 3.18 (q, $J= 5.6$ Hz, 2H), 1.50- 1.42 (m, 2H), 1.33- 1.25 (m, 2H), 0.86 (t, $J= 7.6$ Hz, 3H).ESI-HRMS m/z 238.1173 (M+H⁺). Melting Point: 128 °C.

5 Example 180

Synthesis of 3-butyl-6-nitroquinazolin-4(3H)-one (173): The compound was prepared by general procedure **B** provided in example 2 using compound **172** (0.6 g, 2.53 mmol), trimethylorthoformate (TMOF) (5.5 mL, 50.60 mmol) to obtain compound **173** (0.55 g, 88 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.76 (d, $J= 2.4$ Hz, 1H), 8.55 (s, 1H), 8.48 (dd, $J= 9$ Hz, 2.4 Hz, 1H), 7.81 (d, $J= 9.6$ Hz, 1H), 3.95 (t, $J= 7.2$ Hz, 2H), 1.67- 1.60 (m, 2H), 1.31- 1.22 (m, 2H), 0.86 (t, $J= 7.2$ Hz, 3H).ESI-HRMS m/z 248.1042 (M+H⁺). Melting Point: 104 °C.

Example 181

15 **Synthesis of 6-amino-3-butylquinazolin-4(3H)-one (174):** The compound was prepared by general procedure **C** provided in example 3 using compound **173** (0.25 g, 1.01 mmol) was dissolved in methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **174** (0.20 g, 91 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.03 (s, 1H), 7.37 (d, $J= 8.7$ Hz, 1H), 7.20 (d, $J= 2.7$ Hz, 1H), 7.06 (dd, $J= 8.7$ Hz, 2.7 Hz, 1H), 5.64 (s, 2H), 3.91 (t, $J= 7.2$ Hz, 2H), 1.68- 1.58 (m, 2H), 1.33- 1.23 (m, 2H), 0.90 (t, $J= 7.5$ Hz, 3H).ESI-HRMS m/z 218.1293 (M+H⁺). Melting Point: 98 °C.

Example 182

Synthesis of 1-(3-acetylphenyl)-3-(3-butyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (175):
25 The compound was prepared by general procedure **D** provided in example 4 using compound **174**(0.12 g, 0.55 mmol), dry THF (6 mL), 4-nitrophneylchloroformate (0.133 g, 0.66 mmol), 3'-aminoacetophenone (0.090 g, 0.66 mmol), TEA (0.2 mL, 1.38 mmol) to obtain compound **175** (0.07 g, 33 %) as off white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.09 (s, 1H), 8.96 (s, 1H), 8.29 (d, $J= 2.8$ Hz, 1H), 8.22 (s, 1H), 8.05- 8.04 (m, 1H), 7.77 (dd, $J= 6.8$ Hz, 2.8 Hz, 1H), 7.66- 7.64 (m, 1H), 7.58- 7.53 (m, 2H), 7.41- 7.37 (m, 1H), 3.91 (t, $J= 7.6$ Hz, 2H), 2.52 (s, 3H), 1.65- 1.58 (m, 2H), 1.30 -1.21 (m, 2H), 0.86 (t, $J= 7.6$ Hz, 3H). ESI-MS m/z 379.2 (M+H⁺). Melting Point: 196 °C.

Example 183

Synthesis of 2-amino-N-(1-methoxypropan-2-yl)-5-nitrobenzamide (176): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (0.8 g, 4.39 mmol), DMF (8 mL), HATU (1.8 g, 4.83 mmol), 1-methoxy-2-propylamine (0.5 mL, 5.27 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound **176** (0.83 g, 75 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.46 (br.s, -NH), 8.44 (d, *J*= 2.8 Hz, 1H), 7.96 (dd, *J*= 9.2 Hz, 2.8 Hz, 1H), 7.68 (br.s, 2H), 6.74 (d, *J*= 9.6 Hz, 1H), 4.17- 4.10 (m, 1H), 3.38- 3.34 (m, 1H), 3.26- 3.23 (m, 1H), 3.22 (s, 3H), 1.08 (d, *J*= 6.8 Hz, 3H). ESI-HRMS *m/z* 254.1130 (M+H⁺). Melting Point: 118 °C.

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Example 184

Synthesis of 3-(1-methoxypropan-2-yl)-6-nitroquinazolin-4(3H)-one (177): The compound was prepared by general procedure **B** provided in example 2 using compound **176** (0.6 g, 2.37 mmol), trimethylorthoformate (TMOF) (5.1 mL, 47.41 mmol) to obtain compound **177** (0.57 g, 91 %) as pale yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.84 (s, 1H), 8.62 (s, 1H), 8.57 (d, *J*= 9 Hz, 1H), 7.88 (d, *J*= 9.3 Hz, 1H), 5.11- 5.00 (m, 1H), 3.83 – 3.77 (m, 1H), 3.62- 3.57 (m, 1H) 3.24 (s, 3H), 1.43 (d, *J*= 6.9 Hz, 3H). ESI-HRMS *m/z* 264.0977 (M+H⁺). Melting Point: 100 °C.

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20 **Example 185**

Synthesis of 6-amino-3-(1-methoxypropan-2-yl)quinazolin-4(3H)-one (178): The compound was prepared by general procedure **C** provided in example 3 using compound **177** (0.6 g, 2.28 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **178** (0.48 g, 90 %) as light brown solid. ESI-HRMS *m/z* 234.1229 (M+H⁺). Melting Point: 130 °C.

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Example 186

Synthesis of 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (179):

30 The compound was prepared by general procedure **D** provided in example 4 using compound **178** (0.12 g, 0.51 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.15 g, 0.60 mmol), 3'-aminoacetophenone (0.087 g, 0.64 mmol), TEA (0.3 mL, 2.12 mmol) to obtain compound **179** (0.07 g, 41 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 9.16 (s, 1H),

9.03 (s, 1H), 8.35 (s, 1H), 8.29 (s, 1H), 8.10 (s, 1H), 7.83 (d, $J = 8.7$ Hz, 1H), 7.71 (d, $J = 7.5$ Hz, 1H), 7.64- 7.60 (m, 2H), 7.48- 7.43 (m, 1H), 5.11-5.01 (m, 1H), 3.79 (t, $J = 8.4$ Hz, 1H), 3.60- 3.55 (m, 1H), 3.24 (s, 3H), 2.58 (s, 3H), 1.40 (d, $J = 6.9$ Hz, 3H). ESI-HRMS m/z 395.1728 ($M+H^+$). Melting Point: 146 °C.

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Example 187

Synthesis of 2-amino-*N*-(2-isopropoxyethyl)-5-nitrobenzamide (180): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (0.8 g, 4.39 mmol), DMF (8 mL), HATU (1.8 g, 4.83 mmol), 2-aminoethyl isopropyl ether (0.6 mL, 4.83 mmol), TEA (1.5 mL, 10.98 mmol) to obtain compound **180** (0.83 g, 68 %) as yellow solid. ^1H NMR (300 MHz, d_6 -DMSO) 8.74 (br.s, 1H), 8.49 (d, $J = 2.7$ Hz, 1H), 8.01 (dd, $J = 9.3$ Hz, 1H), 7.74 (br.s, 2H), 6.79 (d, $J = 9.3$ Hz, 1H), 3.62- 3.53 (m, 1H), 3.48 (t, $J = 6$ Hz, 2H), 3.38- 3.33 (m, 2H), 1.05 (d, $J = 6.3$ Hz, 6H). (ESI-HRMS m/z 268.1304 ($M+H^+$). Melting Point: 88 °C.

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Example 188

Synthesis of 3-(2-isopropoxyethyl)-6-nitroquinazolin-4(3H)-one (181): The compound was prepared by general procedure **B** provided in example 2 using compound **180** (0.80 g, 2.99 mmol), trimethylorthoformate (TMOF) (6.5 mL, 59.89 mmol) to obtain compound **181** (0.70 g, 84 %) as pale yellow solid. ^1H NMR (300 MHz, d_6 -DMSO) 8.85 (d, $J = 2.7$ Hz, 1H), 8.56 (dd, $J = 9$ Hz, 2.7 Hz, 1H), 8.49 (s, 1H), 7.89 (d, $J = 9$ Hz, 1H), 4.16 (t, $J = 5.4$ Hz, 2H), 3.66 (t, $J = 5.4$ Hz, 2H), 3.57- 3.49 (m, 1H), 1.01 (d, $J = 6.3$ Hz, 6H). ESI-HRMS m/z 278.1139 ($M+H^+$). Melting Point: 82 °C.

Example 189

Synthesis of 6-amino-3-(2-isopropoxyethyl)quinazolin-4(3H)-one (182): The compound was prepared by general procedure **C** provided in example 3 using compound **181** (0.6 g, 2.16 mmol), methanol (8 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **182** (0.40 g, 78 %) as light brown solid. ^1H NMR (300 MHz, d_6 -DMSO) 7.93 (s, 1H), 7.37 (d, $J = 8.4$ Hz, 1), 7.21 (d, $J = 2.7$ Hz, 1H), 7.06 (dd, $J = 8.7$ Hz, 2.4 Hz, 1H), 5.64 (s, 2H), 4.04 (t, $J = 5.4$ Hz, 2H), 3.61 (t, $J = 5.4$ Hz, 2H), 3.55- 3.47 (m, 1H), 1.00 (d, $J = 6.3$ Hz, ESI-HRMS m/z 248.1406 ($M+H^+$). Melting Point: 80 °C.

30

Example 190**Synthesis of 1-(3-acetylphenyl)-3-(3-(2-isopropoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-**

yl)urea (183): The compound was prepared by general procedure **D** provided in example 4 using compound **182** (0.12 g, 0.48 mmol), dry THF (6 mL), 4-nitrophenylchloroformate (0.15 g, 0.72 mmol), 3'-aminoacetophenone (0.082 g, 0.60 mmol), TEA (0.3 mL, 2 mmol) to obtain compound **183** (0.075 g, 37 %) as off white solid. ¹H NMR (300 MHz, d₆-DMSO) 9.14 (s, 1H), 9.01 (s, 1H), 8.37 (d, *J* = 2.4 Hz, 1H), 8.16 (s, 1H), 8.10 (brs, 1H), 7.81 (dd, *J* = 8.8 Hz, 2.7 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.64- 7.59 (m, 2H), 7.48- 7.43 (m, 1H), 4.11 (t, *J* = 5.1 Hz, 2H), 3.64 (t, *J* = 5.1 Hz, 2H), 3.56- 3.48 (m, 1H), 2.57 (s, 3H), 1.01 (d, *J* = 6 Hz, 6H). ESI-
10 HRMS *m/z* 409.1890 (M+H⁺). Melting Point: 142 °C.

Example 191

Synthesis of 2-amino-N-cyclohexyl-5-nitrobenzamide (184): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), cyclohexylamine (0.65 mL, 6.58 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **184** (0.982 g, 68 %) as yellow solid. ESI-HRMS *m/z* 264.1346 (M+H⁺). Melting Point: 102 °C.

Example 192

Synthesis of 3-cyclohexyl-6-nitroquinazolin-4(3H)-one (185): The compound was prepared by general procedure **B** provided in example 2 using compound **184** (0.6 g, 2.28 mmol), trimethylorthoformate (TMOF) (4 mL, 38.23 mmol) to obtain compound **185** (0.49 g, 80 %) as pale yellow solid. ESI-HRMS *m/z* 274.1200 (M+H⁺).

Example 193

Synthesis of 6-amino-3-cyclohexylquinazolin-4(3H)-one (186): The compound was prepared by general procedure **C** provided in example 3 using compound **185** (0.3 g, 1.09 mmol), methanol (10 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **186** (0.160 g, 60 %) as light brown solid. ESI-HRMS *m/z* 244.1454 (M+H⁺).

Example 194

Synthesis of 1-(3-acetylphenyl)-3-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (187): The compound was prepared by general procedure **D** provided in example 4 using

compound **186** (0.120 g, 0.49 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.119 g, 0.59 mmol), 3'-aminoacetophenone (0.086 g, 0.63 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **187** (0.091 g, 46 %) as yellow solid.

5 **Example 195**

Synthesis of 2-amino-N-(2-methoxyethyl)-4-nitrobenzamide (189): The compound was prepared by general procedure **A** provided in example 1 using 2-amino-4-nitrobenzoic acid (compound **188**) (1 g, 5.49 mmol), DMF (10 mL), HATU (2.2 g, 6.04 mmol), 2-methoxyethylamine (0.50 mL, 6.58 mmol), TEA (1.9 mL, 13.73 mmol) to obtain compound **189** (0.945 g, 72 %) as yellow solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.59 (s, -NH), 7.66 (d, *J* = 8.7 Hz, 1H), 7.57 (d, *J* = 2.4 Hz, 1H), 7.28 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 6.84 (br.s, 2H), 3.45- 3.38 (m, 4H), 3.26 (s, 3H). ESI-HRMS *m/z* 240.0996 (M+H⁺).

15 **Example 196**

Synthesis of 3-(2-methoxyethyl)-7-nitroquinazolin-4(3H)-one (190): The compound was prepared by general procedure **B** provided in example 2 using compound **189** (0.6 g, 2.28 mmol), trimethylorthoformate (TMOF) (4 mL, 38.23 mmol) to obtain compound **190** (0.49 g, 80%) as pale yellow solid. ESI-HRMS *m/z* 250.0834 (M+H⁺).

20 **Example 197**

Synthesis of 7-amino-3-(2-methoxyethyl)quinazolin-4(3H)-one (191): The compound was prepared by general procedure **C** provided in example 3 using compound **190** (0.3 g, 1.20 mmol), methanol (10 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **191** (0.158 g, 60 %) as light brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 8.01 (s, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 6.73 (dd, *J* = 8.7 Hz, 2.1 Hz, 1H), 6.60 (d, *J* = 2.1 Hz, 1H), 6.11 (br.s, 2H), 4.04 (t, *J* = 5.1 Hz, 2H), 3.55 (t, *J* = 5.1 Hz, 2H), 3.23 (s, 3H). ESI-HRMS *m/z* 220.1094 (M+H⁺). Melting Point: 132 °C.

30 **Example 198**

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (192): The compound was prepared by general procedure **D** provided in example 4 using compound **191** (0.120 g, 0.49 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.119 g, 0.59 mmol), 3'-aminoacetophenone (0.086 g, 0.63 mmol), TEA (0.3 mL, 1.71

mmol) to obtain compound **192** (0.091 g, 46 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.23 (s, 1H), 9.05 (s, 1H), 8.18 (s, 1H), 8.06 (m, 1H), 8.02 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 2 Hz, 1H), 7.68- 7.65 (m, 1H), 7.59- 7.57 (m, 1H), 7.49 (dd, *J* = 8.8 Hz, 2 Hz, 1H), 7.44- 7.40 (m, 1H), 4.08 (t, *J* = 5.2 Hz, 2H), 3.56 (t, *J* = 4.8 Hz, 2H), 3.21 (s, 3H), 2.54 (s, 3H). ESI-MS *m/z* 381.3 (M+H⁺).

Example 199

Synthesis of 1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (193): The compound was prepared by general procedure **E** provided in example 5 using compound **191** (0.120 g, 0.49 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.119 g, 0.59 mmol), 4'-aminoacetophenone (0.086 g, 0.63 mmol), TEA (0.3 mL, 1.71 mmol) to obtain compound **193** (0.079 g, 38 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.30 (s, 1H), 9.24 (s, 1H), 8.17 (s, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.88- 7.82 (m, 3H), 7.56 (d, *J* = 8 Hz, 2 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 1H), 4.06 (t, *J* = 4.8 Hz, 2H), 3.53 (t, *J* = 4.4 Hz, 2H), 3.20 (s, 3H), 2.47 (s, 3H). ESI-MS *m/z* 381.2 (M+H⁺).

Example 200

Synthesis of N-(2-((2-methoxyethyl)carbamoyl)-4-nitrophenyl)picolinamide (208): Picolinic acid (0.64 g, 5.20 mmol) was dissolved in dry DCM (10 mL) followed by addition of one drop of DMF. Oxalyl Chloride (0.66 mL, 7.80 mmol) was added to the reaction mixture under ice cold condition and nitrogen atmosphere. The reaction was stirred for 15 mins for the formation of acid chloride. Then the reaction mass was evaporated to dryness to remove excess oxalyl chloride and DCM. The crude is kept under inert atmosphere and dissolved in DCM (20 mL). In another flask, compound **2** (0.5 g, 2.09 mmol) was dissolved in DCM (10 mL) followed by addition of TEA (0.7 mL, 5.64 mmol). In this reaction medium, the previously prepared acid chloride was added dropwise and under ice cold condition. The reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated to dryness and washed with water and extracted with EtOAc to get the crude. The product was purified by flash chromatography (Silica gel, mesh size 100-200) eluting (50% EtOAc/ Pet ether) to obtain compound **208** (0.26 g, 29 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 13.24 (s, 1H), 9.20 (d, *J* = 5.2 Hz, 1H), 8.94 (d, *J* = 9.2, 1H), 8.76- 8.74 (m, 1H), 8.64 (d, *J* = 2.8 Hz, 1H), 8.42 (dd, *J* = 9.2 Hz, 2.8

Hz, 1H), 8.19- 8.16 (m, 1H), 8.08- 8.04 (m, 1H), 7.69- 7.06 (m, 1H), 3.51- 3.44 (m, 4H), 3.25 (s, 3H). ESI-HRMS m/z 345.1201 (M+H⁺).Melting point 224 °C.

Example 201

5 **Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(pyridin-2-yl)quinazolin-4(3H)-one (209):** The compound was prepared by general procedure **G** provided in example 7 using compound **208**(0.25 g, 0.72 mmol), DMF (5 mL), zinc chloride (0.40 g, 2.91 mmol), HMDS (1.21 mL, 5.80 mmol) to obtain compound **209** (0.165 g, 70 %) as yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.84 (d, J = 2.8 Hz, 1H), 8.96-8.67 (m, 1H), 8.57-8.54 (m, 1H), 8.07-8.02 (m, 10 1H), 7.89-7.85 (m, 2H), 7.61-7.57 (m, 1H), 4.37 (t, J = 6 Hz, 2H), 3.43 (t, J = 6 Hz, 2H), 3.31 (s, 3H). ESI-HRMS m/z 327.1096 (M+H⁺).Melting point 144 °C.

Example 202

Synthesis of 6-amino-3-(2-methoxyethyl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (210):
15 The compound was prepared by general procedure **C** provided in example 3 using compound **209** (0.155 g, 0.47 mmol), methanol (10 mL), pinch of Pd/C under hydrogen atmosphere to obtain compound **210** (0.075 g, 54 %) as brown solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.63- 8.61 (m, 1H), 7.99- 7.94 (m, 1H), 7.77- 7.74 (m, 1H), 7.51- 7.48 (m, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.26 (d, J = 2 Hz, 1H), 7.11 (dd, J = 8 Hz, 2.4 Hz, 1H), 4.32 (t, J = 6.4 Hz, 20 2H), 3.38 (t, J = 6 Hz, 2H), 2.94 (s, 3H). ESI-HRMS m/z 297.1352 (M+H⁺).Melting point 138 °C.

Example 203

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-2-yl)-3,4-
25 **dihydroquinazolin-6-yl)urea (211):**The compound was prepared by general procedure **D** provided in example 4 using compound **210** (0.065 g, 0.21 mmol), dry THF (5 mL), 4-nitrophenyl chloroformate (0.06 g, 0.32 mmol), 3-aminoacetophenone (0.039 g, 0.26 mmol), TEA (0.073 mL, 0.52 mmol) to obtain **211** as off white solid (0.021 g, 21 %).¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.17 (s, 1H), 9.01 (s, 1H), 8.66-8.64 (m, 1H), 8.39 (d, J = 2.4 Hz, 1H), 8.07 (t, J = 1.6 Hz, 1H), 8.02-7.98 (m, 1H), 7.83-7.79 (m, 2H), 7.69-7.66 (m, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.58-7.52 (m, 2H), 7.42 (t, J = 8.0 Hz, 1H), 4.34 (t, J = 6 Hz, 2H), 3.41 (t, J = 6 Hz, 2H), 2.93 (s, 3H), 2.50 (s, 3H). ESI-HRMS m/z 458.1841 (M+H⁺).Melting point 230 °C.

Example 204**Synthesis of N-(2-((2-methoxyethyl)carbamoyl)-4-nitrophenyl)nicotinamide (212):**

Commercially available Nicotinic acid (0.64 g, 5.20 mmol) was dissolved in dry DCM (10 mL) followed by addition of one drop of DMF. Oxalyl chloride (0.66 mL, 7.80 mmol) was added to the reaction mixture under ice cold condition and nitrogen atmosphere. The reaction was stirred for 15 mins for the formation of acid chloride. Then the reaction mass was evaporated to dryness to remove excess oxalyl chloride and DCM. The crude is kept under inert atmosphere and dissolved in DCM (20 mL). In another flask, compound **2** (0.5 g, 2.09 mmol) was dissolved in DCM (10 mL) followed by addition of TEA (0.7 mL, 5.64 mmol). In this reaction medium, the previously prepared acid chloride was added dropwise and under ice cold condition. The reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated to dryness and washed with water and extracted with EtOAc to get the crude. The product was purified by flash chromatography (Silica gel, mesh size 100-200) eluting (50 % EtOAc/ Pet ether) to obtain compound **212** (0.213 g, 24 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 13.03 (s, 1H), 9.37 (s, 1H), 9.07 (s, 1H), 8.80-8.73 (m, 3H), 8.41 (d, J = 8Hz, 1H), 7.63-7.59 (m, 1H), 3.49-3.45 (m, 4H), 3.24 (s, 3H). ESI-HRMS *m/z* 345.1201 (M+H⁺). Melting point 180 °C.

Example 205

Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(pyridin-3-yl)quinazolin-4(3H)-one (213): The compound was prepared by general procedure **G** provided in example 7 using compound **212** (0.20 g, 0.58 mmol), DMF (5 mL), zinc chloride (0.40 g, 2.91 mmol), HMDS (1 mL, 4.65 mmol) to obtain compound **213** (0.163g, 86 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.85 (d, J = 2.4Hz, 1H), 8.81 (dd, J = 2.4Hz, J = 0.8 Hz, 1H), 8.72 (dd, J = 5 Hz, J = 1.6Hz, 1H), 8.57-8.54 (m, 1H), 8.09-8.06 (m, 1H), 7.80 (d, J = 8.8Hz, 1H), 7.58-7.55 (m, 1H), 4.09 (t, J = 5.6Hz, 2H), 3.44 (t, J = 5.6Hz, 2H), 3.01 (s, 3H). ESI-HRMS *m/z* 327.1097 (M+H⁺). Melting point 170 °C.

Example 206**Synthesis of 6-amino-3-(2-methoxyethyl)-2-(pyridin-3-yl)quinazolin-4(3H)-one (214):**

The compound was prepared by general procedure **C** provided in example 3 using compound **213** (0.150 g, 0.45 mmol), methanol (10 mL) to obtain compound **214** (0.06 g, 33 %) as

brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.72 (dd, *J* = 2.2 Hz, *J* = 0.8 Hz, 1H), 8.64 (dd, *J* = 4.8 Hz, *J* = 1.6 Hz, 1H), 8.00-7.97 (m, 1H), 7.51-7.47 (m, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.20 (d, *J* = 2.4 Hz, 1H), 7.06 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 5.69 (brs, 2H), 4.00 (t, *J* = 6 Hz, 2H), 3.391 (t, *J* = 6 Hz, 2H), 2.98 (s, 3H). Melting point 152 °C.

5

Example 207

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (215): The compound was prepared by general procedure D provided in example 4 using compound **214** (0.05 g, 0.16 mmol), dry THF (5 mL), 4-nitrophenyl chloroformate (0.06 g, 0.26 mmol), 3'-aminoacetophenone (0.030 g, 0.26 mmol), (0.059 mL, 0.42 mmol) to obtain compound **215** (0.037 g, 48 %) as off white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.15 (s, 1H), 8.99 (s, 1H), 8.77 (d, *J* = 1.6 Hz, 1H), 8.68 (dd, *J* = 4.8 Hz, *J* = 1.6 Hz, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 8.07 – 8.02 (m, 2H), 7.79 (dd, *J* = 8.8 Hz, *J* = 2.8 Hz, 1H), 7.69 – 7.66 (m, 1H), 7.62 – 7.55 (m, 2H), 7.54 – 7.55 (m, 1H), 7.44 – 7.40 (m, 1H), 4.05 (t, *J* = 5.6 Hz, 2H), 3.42 (t, *J* = 5.6 Hz, 2H), 3.00 (s, 3H), 2.53 (s, 3H). ESI-
15 HRMS *m/z* 458.184 (M+H⁺). Melting point 218 °C.

Example 208

Synthesis of N-(2-((2-methoxyethyl)carbamoyl)-4-nitrophenyl)isonicotinamide (216):

20 Commercially available Isonicotinic acid (0.64 g, 5.20 mmol) was dissolved in dry DCM (10 mL) followed by addition of one drop of DMF. Oxalyl Chloride (0.66 mL, 7.80 mmol) was added to the reaction mixture under ice cold condition and nitrogen atmosphere. The reaction was stirred for 15 mins for the formation of acid chloride. Then the reaction mass was evaporated to dryness to remove excess oxalyl chloride and DCM. The crude is kept under
25 inert atmosphere and dissolved in DCM (20 mL). In another flask, compound **2** (0.5 g, 2.09 mmol) was dissolved in DCM (10 mL) followed by addition of TEA (0.7 mL, 5.64 mmol). In this reaction medium, the previously prepared acid chloride was added dropwise under ice cold condition. The reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated to dryness and washed with water and extracted with
30 EtOAc to get the crude. The product was purified by flash chromatography (Silica gel, mesh size 100-200) eluting (50 % EtOAc/ Pet ether) to obtain compound **216** (0.313 g, 33 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 13.10 (s, 1H), 9.40 (d, *J* = 4.8 Hz, 1H),

8.84-8.79 (m,3H), 8.75 (d, $J=2.4$ Hz, 1H) 8.43 (dd, $J = 5.4$ Hz, $J=2.4$ Hz,1H), 7.79 (dd, $J = 4.4$ Hz, $J= 1.6$ Hz,2H), 3.49-3.46 (m, 4H), 3.24 (s,3H). Melting point 206 °C.

Example 209

5 **Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(pyridin-4-yl)quinazolin-4(3H)-one (217):** The compound was prepared by general procedure **G** provided in example 7 using compound **216** (0.30 g, 0.87 mmol), DMF (5 mL), zinc chloride (0.48 g, 3.48 mmol), HMDS (1.5 mL, 6.96mmol) to obtain compound **217** (0.210 g, 73 %) as yellow solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.85-8.85 (m, 1H), 8.75 (dd, $J = 4.4$ Hz, $J = 1.6$ Hz, 2H), 8.56 (dd, $J = 10$ Hz, $J = 2.8$ Hz, 1H), 7.86 (dd, $J = 9.0$ Hz, $J = 0.4$ Hz, 1H), 7.63 (dd, $J = 4.4$ Hz, $J = 1.6$ Hz, 2H), 4.05 (t, $J = 5.6$ Hz, 2H), 3.43 (t, $J = 5.6$ Hz, 2H), 3.01 (s, 3H). Melting point 200°C.

Example 210

15 **Synthesis of 6-amino-3-(2-methoxyethyl)-2-(pyridin-4-yl)quinazolin-4(3H)-one (218):** The compound was prepared by general procedure **C** provided in example 3 using compound **217** (0.200 g, 0.61 mmol), methanol (10 mL), pinch of 10 % Pd/C under hydrogen atmosphere to obtain compound **218** (0.065 g, 34 %) as brown solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.69-8.67 (m, 2H), 7.56-7.55 (m, 2H), 7.35 (d, $J = 8.8$ Hz, 1H), 7.20 (d, $J = 2.4$ Hz, 1H), 7.06 (dd, $J=8.8$ Hz, $J = 2.4$ Hz, 1H), 5.71 (brs, 2H), 4.00 (t, $J = 6$ Hz, 2H), 3.83 (t, $J = 5.6$ Hz, 2H), 2.98 (s, 3H). Melting point 42 °C.

Example 211

25 **Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (219):** The compound was prepared by general procedure **D** provided in example 4 using compound **218** (0.059 g, 0.19 mmol), dry THF (5 mL), 4-nitrophenyl chloroformate (0.06 g, 0.29 mmol), 3'-aminoacetophenone (0.032 g, 0.26 mmol), TEA (0.07 mL, 0.49 mmol) to obtain compound **219** (0.018 g, 20 %) as off white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.16 (s, 1H), 8.99 (s,1H), 8.71 (dd, $J = 4.4$ Hz, $J = 1.6$ Hz, 2H), 8.40 (d, $J = 2.4$ Hz, 1H), 8.06 (t, $J = 2$ Hz, 1H), 7.79 (dd, $J = 8.8$ Hz, $J = 2.8$ Hz, 1H), 7.68-7.66 (m, 1H), 7.61-7.59 (m, 3H), 7.58-7.56 (m, 1H), 7.44-7.40 (m, 1H), 4.04 (t, $J = 5.6$ Hz, 2H), 3.41 (t, $J = 5.6$ Hz, 2H), 3.00 (s, 3H), 2.53 (s, 3H). ESI-HRMS m/z 458.1828 (M+H⁺).Melting point 240 °C.

Example 212**Synthesis of N-(2-((2-methoxyethyl)carbamoyl)-4-nitrophenyl)pyrazine-2-carboxamide**

(**220**): Commercially available pyrazine-2-carboxylic acid (0.649 g, 5.22 mmol) was dissolved in dry DCM (10 mL) followed by addition of one drop of DMF. Oxalyl Chloride (0.66 mL, 7.80 mmol) was added to the reaction mixture under ice cold condition and nitrogen atmosphere. The reaction was stirred for 15 mins for the formation of acid chloride. Then the reaction mass was evaporated to dryness to remove excess oxalyl chloride and DCM. The crude is kept under inert atmosphere and dissolved in DCM (20 mL). In another flask, compound **2** (0.5 g, 2.09 mmol) was dissolved in DCM (10 mL) followed by addition of TEA (0.7 mL, 5.64 mmol) and allowed to stir at room temperature for 7 hours. In this reaction medium, the previously prepared acid chloride was added dropwise under ice cold condition. The reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated to dryness and washed with water and extracted with EtOAc to get the crude. The product was purified by flash chromatography (Silica gel, mesh size 100-200) eluting (50% EtOAc/ Pet ether) to obtain compound **220** (0.175 g, 49 %) as white solid.

Example 213**Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(pyrazin-2-yl)quinazolin-4(3H)-one (**221**)**

: The compound was prepared by general procedure **G** provided in example 7 using compound **220** (0.165 g, 0.47 mmol), DMF (5 mL), zinc chloride (0.26 g, 1.91 mmol), HMDS (0.83 mL, 3.89 mmol) to obtain compound **221** (0.125 g, 49 %) as white solid.

Example 214**Synthesis of 6-amino-3-(2-methoxyethyl)-2-(pyrazin-2-yl)quinazolin-4(3H)-one (**222**)**

: The compound was prepared by general procedure **C** provided in example 3 using compound **221** (0.118 g, 0.39 mmol), methanol (10 mL), a pinch of 10 % Pd/C under hydrogen atmosphere to obtain compound **222** (0.08 mg, 78 %) as dark green solid.

Example 215**Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrazin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (**223**)**

: The compound was prepared by general procedure **D** provided in example 4 using compound **222** (0.70 g, 0.23 mmol), dry THF (5 mL), 4-nitrophenyl chloroformate (0.072 g, 0.35 mmol), 3'-aminoacetophenone (0.039 g, 0.28

mmol), TEA (0.082 mL, 0.58 mmol) to obtain compound **223** as off white solid (0.04 g, 39 %).

Example 216

5 **Synthesis of 2-(2-chloroacetamido)-N-(2-methoxyethyl)-5-nitrobenzamide (228):** Compound **2** (1 gm, 4.18 mmol) was dissolved in dry DCM and TEA (1.16 mL, 8.36 mmol) was added followed by chloroacetyl chloride (0.39 mL, 5.01 mmole) dropwise at cooling and the reaction mixture was allowed to stir at room temperature for 1 hour. After completion of the reaction, it was worked up with ethyl acetate and water and purified by column
10 chromatography (Silica gel, mesh size 100-200) eluting (50% EtOAc/ Pet Ether) to obtain compound **228** (0.800 g, 60 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 12.26 (s, 1H), 9.26-9.24 (m, 1H), 8.64-8.62 (m, 2H), 8.36 (dd, *J* = 9.2 Hz, 2.8 Hz, 1H), 4.44 (s, 2H), 3.48-3.40 (m, 4H), 3.24 (s, 3H). ESI-HRMS *m/z* 316.0703 (M+H⁺).

15 Example 217

Synthesis of 2-(chloromethyl)-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one (229): The compound was prepared by general procedure **G** provided in example 7 using compound **228** (0.8 g, 2.53 mmol), DMF (10 mL), ZnCl₂ (1.4 g, 10.12 mmol), HMDS (4.24 mL, 20.24 mmol) to obtain compound **229** (0.60 g, 79 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO)
20 δ in ppm 8.78-8.75 (m, 1H), 8.55-8.50 (m, 1H), 7.86-7.82 (m, 1H), 4.92 (s, 2H), 4.31 (t, *J* = 5.2 Hz, 2H), 3.61 (t, *J* = 5.2 Hz, 2H), 3.20 (s, 3H). ESI-HRMS *m/z* 298.0595 (M+H⁺).

Example 218

Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(pyrrolidin-1-ylmethyl)quinazolin-4(3H)-one (230): Compound **229** (0.2 g, 0.74 mmol) and pyrrolidine (0.125 mL, 1.48 mmol) were
25 dissolved in toluene and reaction mixture was refluxed for 2 hours. After completion of the reaction, it was washed with water and extracted with ethyl acetate to obtain light yellow crude mass which was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (80% EtOAc/ Pet Ether) to obtain compound **230** (0.159 g, 64 %) as white
30 solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.76 (d, *J* = 2.8 Hz, 1H), 8.48 (dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 7.80 (d, *J* = 9.2 Hz, 1H), 4.45 (t, *J* = 6 Hz, 2H), 3.83 (s, 2H), 3.59 (t, *J* = 5.6 Hz, 2H), 3.20 (s, 3H), 2.54-2.49 (m, 4H), 1.69-1.65 (m, 4H). ESI-HRMS *m/z* 333.1572 (M+H⁺).

Example 219**Synthesis of 6-amino-3-(2-methoxyethyl)-2-(pyrrolidin-1-ylmethyl)quinazolin-4(3H)-one**

(**231**): The compound was prepared by general procedure C provided in example 3 using compound **230** (0.150 g, 0.42 mmol), methanol (10 mL), pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **231** (0.158 g, 60 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.30 (d, *J* = 8.8Hz, 1H), 7.12 (d, *J* = 2.8 Hz, 1H), 7.01 (dd, *J* = 8.4Hz, 2.4Hz, 1H), 5.57 (s, 2H), 4.36 (t, *J* = 6Hz, 2H), 3.68 (s, 2H), 3.54 (t, *J* = 5.6Hz, 2H), 3.18 (s, 3H), 2.45-2.42 (m, 4H), 1.67-1.62 (m, 4H). ESI-HRMS *m/z*303.1826 (M+H⁺).

10 Example 220**Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrrolidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea**

(**232**): The compound was prepared by general procedure D provided in example 4 using compound **231** (0.120 g, 0.39 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.094 g, 0.46 mmol), 3'-aminoacetophenone (0.062 g, 0.46 mmol), TEA (0.14 mL, 0.78 mmol) to obtain compound **232** (0.077 g, 42 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.09 (s, 1H), 8.97 (s, 1H), 8.29 (d, *J* = 2.8Hz, 1H), 8.06-8.05 (m, 1H), 7.75 (dd, *J* = 8.8Hz, 2.4Hz, 1H), 7.67-7.65 (m, 1H), 7.56 (d, *J* = 8.8Hz, 2H), 7.43-7.39 (m, 1H), 4.42 (t, *J* = 5.6Hz, 2H), 3.76 (s, 2H), 3.58 (t, *J* = 5.6Hz, 2H), 3.20 (s, 3H), 2.53 (s, 3H), 2.51-2.49 (m, 4H), 1.69-1.64 (m, 4H). ESI-HRMS *m/z*464.2317 (M+H⁺).

20

Example 221**Synthesis of 2-((dimethylamino)methyl)-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one**

(**233**): Compound **229** (0.2 g, 0.74 mmol) and dimethylamine (0.1 mL, 1.48 mmol) were dissolved in toluene and reaction mixture was refluxed for 2 hours. After completion of the reaction, it was washed with water and extracted with ethyl acetate to get yellow crude mass which was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (5% CHCl₃-MeOH) to obtain compound **233** (0.154 g, 75 %) as yellow gummy product. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.77 (d, *J* = 2.4Hz, 1H), 8.49 (dd, *J* = 9.2Hz, 2.8Hz, 1H), 7.82 (d, *J* = 8.8Hz, 1H), 4.47 (t, *J* = 5.6Hz, 2H), 3.63 (s, 2H), 3.59 (t, *J* = 5.6Hz, 2H), 3.20 (s, 3H), 2.20 (s, 6H). ESI-HRMS *m/z*307.1405 (M+H⁺).

30

Example 222

Synthesis of 6-amino-2-((dimethylamino)methyl)-3-(2-methoxyethyl)quinazolin-4(3H)-one (234): The compound was prepared by general procedure C provided in example 3 using compound **233** (0.120 g, 0.39 mmol), methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **234** (0.086 g, 80 %) as light brown gummy product.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.31(d, *J*= 8.4Hz, 1H), 7.13(d, *J*= 2.8Hz, 1H), 7.01(dd, *J*= 8.4Hz, 2.4 Hz, 1H), 5.59(s, 2H), 4.37(t, *J*= 5.6Hz, 2H), 3.54(t, *J*= 5.6Hz, 2H), 3.49(s, 2H), 3.18(s, 3H), 2.15(s, 6H).ESI-HRMS *m/z*277.1667 (M+H⁺).

Example 223

Synthesis of 1-(3-acetylphenyl)-3-(2-((dimethylamino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (235): The compound was prepared by general procedure D provided in example 4 using compound **234** (0.060 g, 0.21 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.053 g, 0.26 mmol), 3'-aminoacetophenone (0.035 g, 0.26 mmol), TEA (0.14 mL, 0.52 mmol) to obtain compound **235** (0.062 g, 54 %) as offwhite solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.10(s, 1H), 8.98(s, 1H), 8.29(d, *J*= 2.4Hz, 1H), 8.06-8.05(m, 1H), 7.76(dd, *J*= 8.8Hz, 2.4Hz, 1H), 7.67-7.65(m, 1H), 7.57-7.54(m, 2H), 7.42-7.39(m, 1H), 4.43(t, *J*= 5.6Hz, 2H), 3.59-3.56(m, 4H), 3.20(s, 3H), 2.53(s, 3H), 2.18(s, 6H).ESI-HRMS *m/z*438.2140 (M+H⁺).

Example 224

Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(piperidin-1-ylmethyl)quinazolin-4(3H)-one (236): Compound **229** (0.2 g, 0.74 mmol) and piperidine (0.15 mL, 1.48 mmol) were dissolved in toluene and reaction mixture was refluxed for 2hours. After completion of the reaction,it was washed with water and extracted with ethyl acetate to get light brown crude mass which was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (50% EtOAc/ Pet Ether) to obtain compound **233** (0.220 g, 85 %) as white solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.76(d, *J*=2.8Hz, 1H), 8.48(dd, *J*=9.2Hz, 2.8Hz, 1H), 7.80(d, *J*= 8.8Hz,1H), 4.45(t, *J*=6.0Hz, 2H), 3.66(s, 2H), 3.61(t, *J* = 6.0Hz, 2H), 3.21(s, 3H), 2.42-2.37 (m, 4H), 1.48-1.42(m, 4H), 1.37-1.309m, 2H). ESI-HRMS *m/z*347.1716 (M+H⁺).

Example 225

Synthesis of 6-amino-3-(2-methoxyethyl)-2-(piperidin-1-ylmethyl)quinazolin-4(3H)-one (237): The compound was prepared by general procedure C provided in example 3 using

compound **236** (0.150 g, 0.47 mmol), methanol (10 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **237** (0.089 g, 65 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.30(d, *J*= 8.8Hz, 1H), 7.12(d, *J*= 2.8Hz, 1H), 7.01(dd, *J*= 8.4Hz, 2.4Hz, 1H), 5.57(s, 2H), 4.36(t, *J*=6Hz, 2H), 3.68(s, 2H), 3.54(t, *J*=5.6Hz, 2H),
5 3.18(s, 3H), 2.45-2.42(m, 4H), 1.67-1.62(m, 4H).ESI-HRMS *m/z*317.1976 (M+H⁺).

Example 226

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (238): The compound was prepared by general procedure
10 **D** provided in example 4 using compound **237** (0.080 g, 0.25 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.060 g, 0.30 mmol), 3'-aminoacetophenone (0.040 g, 0.30 mmol), TEA (0.07 mL, 0.50 mmol) to obtain compound **238**(0.077 g, 42 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.08(s, 1H), 8.96(s,1H), 8.29(d, *J*= 2.4Hz, 1H), 8.06-8.05(m, 1H), 7.75(dd, *J*= 9.2Hz, 2.8Hz, 1H), 7.67-7.64(m, 1H), 7.55(d, *J*= 8.4Hz, 2H), 7.42-7.38(m,
15 1H), 4.41(t *J*= 6.0Hz, 2H), 3.61-3.58(m, 4H), 3.21(s, 3H), 2.53(s, 3H), 2.39-2.34(m, 4H), 1.47-1.41(m, 4H), 1.37-1.30(m, 2H).ESI-HRMS *m/z*478.2463 (M+H⁺).

Example 227

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea hydrochloride (238a): Compound **238** (0.05 g, 0.104 mmol) was taken in dioxane (1 mL) and 4 M HCl in dioxane (0.8 mL) was added under ice cold condition and reaction was heated at 100 °C for 2 hour. During heating, at first compound dissolved to obtain a clear solution and then slowly solidified after 2 hours of constant heating. Reaction mass was cooled and evaporated in rotary evaporator to obtain
25 compound **238 a**(53 mg, 98 %)as pale yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 10.04 (s, 1H), 9.77 (s, 1H), 9.56 (s, 1H), 8.35 (d, *J*= 2.4 Hz, 1H), 8.07-8.07 (m, 1H), 7.86 (dd, *J*= 8.8 Hz, 2.4 Hz, 1H), 7.66 (d, *J*= 8.8 Hz, 2H), 7.56 (d, *J*= 7.6 Hz, 1H), 7.43-7.39 (m, 1H), 4.64 (d, *J*= 3.6 Hz, 2H), 4.16 (t, *J*= 4.8 Hz, 2H), 3.62-3.56 (m, 4H), 3.21 (s, 3H), 3.15-3.05 (m, 2H), 2.53 (s, 3H), 1.85-1.79 (m, 4H), 1.70-1.63 (m, 1H), 1.51-1.40 (m, 1H). The crystal
30 structure of compound 238a is provided in figure 11. CCDC Deposition no 1988445.

Example 228

Synthesis of 3-(2-methoxyethyl)-2-(morpholinomethyl)-6-nitroquinazolin-4(3H)-one (239): Compound **229** (0.2 g, 0.74 mmol) and morpholine (0.13 mL, 1.48 mmol) were dissolved in toluene and reaction mixture was refluxed for 2 hours. After completion of the reaction, it was washed with water and extracted with ethyl acetate to obtain light yellow crude mass which was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (50% EtOAc/ Pet Ether) to obtain compound **239** (0.195 g, 75 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.76(d, *J*= 2.4Hz, 1H), 8.49(dd, *J*= 9.2Hz, 2.8Hz, 1H), 7.81(d, *J*= 8.4Hz, 1H), 4.46(t, *J*= 5.6Hz, 2H) 3.72(s, 2H), 3.62(t, *J*= 5.6Hz, 2H), 3.54-3.52(m, 4H), 3.28-3.27(m, 4H), 3.21(s, 3H). ESI-HRMS *m/z* 349.1513 (M+H⁺).

10

Example 229

Synthesis of 6-amino-3-(2-methoxyethyl)-2-(morpholinomethyl)quinazolin-4(3H)-one (240): The compound was prepared by general procedure C provided in example 3 using compound **239** (0.150 g, 0.43 mmol), methanol (10 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **240** (0.089 g, 65 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.30(d, *J*= 8.8Hz, 1H), 7.13(d, *J*= 2.8Hz, 1H), 7.01(dd, *J*= 8.8Hz, 2.8Hz, 1H), 5.59(s, 2H), 4.36(t, 5.6Hz, 2H), 3.58-3.55(m, 4H), 3.52-3.50(m, 4H), 3.20(s, 3H), 2.39-2.35(m, 4H). ESI-HRMS *m/z* 319.1773 (M+H⁺).

15

Example 230

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholinomethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (241): The compound was prepared by general procedure D provided in example 4 using compound **240** (0.070 g, 0.22 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.053 g, 0.26 mmol), 3'-aminoacetophenone (0.035 g, 0.26 mmol), TEA (0.14 mL, 0.52 mmol) to obtain compound **241** (0.055 g, 53 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.08(s, 1H), 8.95(s, 1H), 8.28(d, *J*=2.4Hz, 1H), 8.05-8.04(m, 1H), 7.75(dd, *J*=8.8Hz, 2.4Hz, 1H), 7.67-7.64(m, 1H), 7.56(d, *J*=8.8Hz, 2H), 7.43-7.39(m, 1H), 4.42(t, *J*=5.6Hz, 2H), 3.64(s, 2H), 3.60(t, *J*= 5.6Hz, 2H), 3.54-3.52(m, 4H), 3.21(s, 3H), 2.53(s, 3H), 2.43-2.39(m, 4H). ESI-HRMS *m/z* 480.2246 (M+H⁺).

25

30

Example 231

Synthesis of 3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-6-nitroquinazolin-4(3H)-one (242): Compound **229** (0.2 g, 0.74 mmol) and 1-methylpiperazine (0.142 mL, 1.48

mmol) were dissolved in toluene and reaction mixture was refluxed for 2 hours. After completion of the reaction, it was washed with water and extracted with ethyl acetate to obtain light yellow crude mass which was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (5% CHCl₃-MeOH) to obtain compound **242** (0.202 g, 75 %) as white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 8.76(s, 1H), 8.48(d, *J* = 8.8 Hz, 1H), 7.80(d, *J* = 8.8 Hz, 1H), 4.43(d, *J* = 5.6 Hz, 2H), 3.70(s, 2H), 3.61(t, *J* = 5.6 Hz, 2H), 3.27-3.21(m, 3H), 2.36-2.18(m, 4H), 2.10(s, 3H). ESI-HRMS *m/z* 362.1821 (M+H⁺).

Example 232

10 **Synthesis of 6-amino-3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)quinazolin-4(3H)-one (243):** The compound was prepared by general procedure C provided in example 3 using compound **242** (0.150 g, 0.41 mmol), methanol (10 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **243** (0.110 g, 80 %) as light brown solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 7.31(d, *J* = 8.8 Hz, 1H), 7.12(d, *J* = 2.8 Hz, 1H), 7.01(dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 5.59(s, 2H), 4.34(t, *J* = 6 Hz, 2H), 3.55(t, *J* = 6 Hz, 4H), 3.20(s, 3H), 2.42-2.34(m, 4H), 2.31-2.16(m, 4H), 2.09(s, 3H). ESI-HRMS *m/z* 332.2090 (M+H⁺).

Example 233

20 **Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (244):** The compound was prepared by general procedure D provided in example 4 using compound **243** (0.070 g, 0.21 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.053 g, 0.26 mmol), 3'-aminoacetophenone (0.035 g, 0.26 mmol), TEA (0.14 mL, 0.52 mmol) to obtain compound **244** (0.062 g, 54 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.17(s, 1H), 9.04(s, 1H), 8.28(d, *J* = 2.4 Hz, 1H), 8.06-8.04(m, 1H), 7.75(dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 7.56(d, *J* = 8.6 Hz, 1H), 7.43-7.39(m, 1H), 4.39(t, *J* = 6 Hz, 2H), 3.63(s, 2H), 3.59(t, *J* = 6 Hz, 2H), 3.21(s, 3H), 2.53(s, 3H), 2.44-2.40(m, 4H), 2.34-2.26(m, 4H), 2.11(s, 3H). ESI-HRMS *m/z* 493.2566 (M+H⁺).

Example 234

30 **Synthesis of N-(2-fluorophenyl)-2-(6-nitro-4-oxoquinazolin-3(4H)-yl)acetamide (251):** The compound was prepared by general procedure H provided in example 8 using compound **81** (0.25 g, 0.90 mmol), toluene (5 mL), anhydrous AlCl₃ (0.481 g, 3.6 mmol), 2-

fluoroaniline (0.120 g, 1.08 mmol), triethylamine (0.3 mL, 2.43 mmol) to obtain compound **251** (0.184g, 49 %) as bright white crystal. ESI-HRMS m/z 343.0844(M+H⁺).

Example 235

5 **Synthesis of 2-(6-amino-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (252):** The compound was prepared by general procedure C provided in example 3 using compound **251** (0.34 g, 0.99 mmol), methanol (10 mL), pinch of Pd/C under hydrogen atmosphere to obtain compound **252** (0.182 g, 43 %) as light brown solid. ESI-HRMS m/z 313.1101(M+H⁺).

10

Example 236

Synthesis of 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (253):

15 The compound was prepared by general procedure D provided in example 4 using compound **252** (0.140 g, 0.44 mmol), dry THF (5 mL), 4-nitrophenyl chloroformate (0.14 g, 0.67 mmol), 3'-aminoacetophenone (0.073 g, 0.53 mmol), TEA (0.16 mL, 1.12 mmol) to obtain compound **253** as white amorphous solid (0.064 g, 30 %). ESI-HRMS m/z 474.1580(M+H⁺).

Example 237

20 **Synthesis of N-(2-methoxyphenyl)-2-(6-nitro-4-oxoquinazolin-3(4H)-yl)acetamide (254):** The compound was prepared by general procedure H provided in example 8 using compound **81** (0.25 g, 0.90 mmol), toluene (5 mL), anhydrous AlCl₃ (0.481 g, 3.61 mmol), *o*-anisidine (0.134 g, 1.08 mmol), TEA (0.3 mL, 2.43 mmol) to obtain compound **254** (0.140g, 44 %) as white crystal. ESI-HRMS m/z 355.1045(M+H⁺).

25

Example 238

Synthesis of 2-(6-amino-4-oxoquinazolin-3(4H)-yl)-N-(2-methoxyphenyl)acetamide (255): The compound was prepared by general procedure C provided in example 3 using compound **254** (0.12 g, 0.34 mmol), methanol (10 mL), pinch of Pd/C under hydrogen atmosphere to obtain compound **255** (0.1 g, 78%) as light brown solid. ESI-HRMS m/z 325.1304 (M+H⁺).

30

Example 239

Synthesis of 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-methoxyphenyl)acetamide (256): The compound was prepared by general procedure **D** provided in example 4 using compound **255** (0.085 g, 0.26 mmol), dry THF (4 mL), 4-nitrophenyl chloroformate (0.08 g, 0.39 mmol), 3'-aminoacetophenone (0.05 g, 0.31 mmol),
5 TEA (0.1 mL, 0.65 mmol) to obtain compound **256** (0.054 g, 39 %) as off white solid.

Example 240

Synthesis of N-(2-bromophenyl)-2-(6-nitro-4-oxoquinazolin-3(4H)-yl)acetamide (257): The compound was prepared by general procedure **H** provided in example 8 using
10 compound **81** (0.25 g, 0.90 mmol), toluene (5 mL), anhydrous AlCl₃ (0.481 g, 3.6 mmol), 2-bromoaniline (0.186 g, 1.08 mmol), TEA (0.3 mL, 2.43 mmol) to obtain compound **257** (0.180g, 49 %) as white solid. ESI-HRMS *m/z* 403.0037 (M+H⁺).

Example 241

Synthesis of 2-(6-amino-4-oxoquinazolin-3(4H)-yl)-N-(2-bromophenyl)acetamide (258): Compound **257** (0.160 g, 0.39 mmol) was dissolved in methanol and SnCl₂.2H₂O (0.716 g, 3.17 mmol) was added. Two drops of concentrated HCl was added and reaction mixture was heated at 80 °C for 2 hours. The reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated to dryness and washed with
20 saturated NaHCO₃ solution, and extracted with EtOAc to afford the yellow coloured crude mass. The compound was dissolved in DCM (5 mL) and pet ether was added dropwise to get precipitation which was filtered under vacuum to obtain compound **258** (0.075 g, 50 %) as light yellow solid.

Example 242

Synthesis of 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-bromophenyl)acetamide (259):

The compound was prepared by general procedure **D** provided in example 4 using compound **258** (0.040 g, 0.11 mmol), dry THF (4 mL), 4-nitrophenyl chloroformate (0.04 g, 0.17 mmol),
30 3'-aminoacetophenone (0.018 g, 0.13 mmol), TEA (0.037 mL, 0.27 mmol) to obtain compound **259** (0.015 g, 26 %) as off white solid. ESI-HRMS *m/z* 534.0797 (M+H⁺).

Example 243

Synthesis of 2-(6-nitro-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide (260):The compound was prepared by general procedure **H** provided in example 8 using compound **81** (0.1g, 0.36 mmol), toluene (5mL), anhydrous AlCl₃ (0.192 g, 1.44 mmol), 2-(trifluoromethoxy)aniline (0.077 g, 0.43 mmol), TEA (0.13 mL, 0.97 mmol) to obtain compound **260** (0.072g, 49 %) as white solid.ESI-HRMS *m/z* 409.0755 (M+H⁺).

Example 244

Synthesis of 2-(6-amino-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide (261):The compound was prepared by general procedure **C** provided in example 3 using compound **260** (0.12 g, 0.29 mmol), methanol (10 mL), pinch of Pd/C under hydrogen atmosphere to obtain compound **261** (0.059 g, 50 %).

Example 245

Synthesis of 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide (262):The compound was prepared by general procedure **D** provided in example 4 using compound **261** (0.05 g, 0.15 mmol), dry THF (5 mL), 4-nitrophenyl chloroformate (0.04 g, 0.19 mmol), 3'-aminoacetophenone (0.022 g, 0.15 mmol), TEA (0.05 mL, 0.33 mmol) to obtain **262** (0.06 g, 84 %) as white solid. ESI-HRMS *m/z* 540.1500 (M+H⁺).

Example 246

Synthesis of 2-(6-nitro-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethyl)phenyl)acetamide (263): The compound was prepared by general procedure **H** provided in example 8 using compound **81** (0.25 g, 0.9 mmol), toluene (5 mL), anhydrous AlCl₃ (0.481 g, 3.6 mmol), 2-(trifluoromethyl)aniline (0.174 g, 1.08 mmol) to obtain compound **263** (0.160 g, 45 %) as white solid.

Example 247

Synthesis of 2-(6-amino-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethyl)phenyl)acetamide (264):The compound was prepared by general procedure **C** provided in example 3 using compound **263** (0.08 g, 0.20 mmol), methanol (10

mL), one pinch of Pd/C under hydrogen atmosphere to obtain compound **264** (0.50 g, 68 %) as light yellow solid.

Example 248

5 **Synthesis of 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethyl)phenyl)acetamide (265):**The compound was prepared by general procedure **D** provided in example 4 using compound **264** (0.04 g, 0.11 mmol), dry THF (4 mL), 4-nitrophenyl chloroformate (0.04 g, 0.16 mmol), 3'-aminoacetophenone (0.02 g, 0.13 mmol), TEA (0.04 mL, 0.27 mmol) to obtain compound **265** as off white solid (0.015g, 26
10 %).

Example 249

Synthesis of N-(4-methoxyphenyl)-2-(6-nitro-4-oxoquinazolin-3(4H)-yl)acetamide (266):The compound was prepared by general procedure **H** provided in example 8 using
15 compound **81** (0.25 g, 0.90 mmol), toluene (5 mL), anhydrous AlCl₃ (0.481 g, 3.61 mmol), *p*-anisidine (0.134 g, 1.08 mmol), TEA (0.3 mL, 2.43 mmol) to obtain compound **266** (0.142 g, 45 %) as white crystal.ESI-HRMS *m/z* 355.1045 (M+H⁺).

Example 250

20 **Synthesis of 2-(6-amino-4-oxoquinazolin-3(4H)-yl)-N-(4-methoxyphenyl)acetamide (267):**The compound was prepared by general procedure **C** provided in example 3 using compound **266** (0.21 g, 0.59 mmol), methanol (10 mL), pinch of Pd/C under hydrogen atmosphere to obtain compound **267** (0.15 g, 78 %) as light brown solid.ESI-HRMS *m/z* 325.1304 (M+H⁺).

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Example 251

Synthesis of 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-methoxyphenyl)acetamide (268):The compound was prepared by general procedure **D** provided in example 4 using compound **267** (0.085 g, 0.26 mmol), dry THF (4 mL), 4-nitrophenyl chloroformate (0.08 g, 0.39 mmol), 3'-aminoacetophenone (0.05 g, 0.31 mmol),
30 TEA (0.1 mL, 0.65 mmol) to obtain compound **268** (0.054 g, 39 %) as off white solid.

Example 252

Synthesis of 2-acetamido-N-(1-methoxybutan-2-yl)-5-nitrobenzamide (278):Compound **168** (0.5 g, 1.87 mmol) was dissolved in DCM (10 mL). Then TEA (0.522 mL, 3.74 mmol) was added. Then acetyl chloride (0.267 mL, 3.74 mmol) was added dropwise under cooling conditions and the reaction mass was stirred for 8 hours. After completion of the reaction, DCM was evaporated out and washed with water and extracted with ethyl acetate and purified by column chromatography (Silica gel, mesh size 100-200) eluting (30% Ethyl acetate-Pet ether) to obtain compound **278** (0.462 g, 80 %) as offwhite solid. ESI-HRMS m/z 310.1402 ($M+H^+$).

10 Example 253

Synthesis of 3-(1-methoxybutan-2-yl)-2-methyl-6-nitroquinazolin-4(3H)-one (279):The compound was prepared by general procedure **G** provided in example 7 using compound **278** (0.4 g, 1.29 mmol), DMF (4 mL), $ZnCl_2$ (0.703 g, 5.16 mmol), HMDS (2.16 mL, 10.32 mmol) to obtain compound **279** (0.278 g, 74 %) as offwhite solid. 1H NMR (400 MHz, d_6 -DMSO) δ in ppm 8.73(d, $J = 2.4$ Hz, 1H), 8.47(dd, $J = 9.2$ Hz, 2.8 Hz, 1H), 7.72(d, $J = 8.8$ Hz, 1H), 4.49-4.41(m, 1H), 4.07-4.02(m, 1H), 3.62-3.58(m, 1H), 3.17(s, 3H), 2.62(s, 3H), 2.21-2.11(m, 1H), 1.87-1.76(m, 1H), 0.79(t, $J = 7.6$ Hz, 3H). ESI-HRMS m/z 292.1292 ($M+H^+$).

Example 254

Synthesis of 6-amino-3-(1-methoxybutan-2-yl)-2-methylquinazolin-4(3H)-one (280): The compound was prepared by general procedure **C** provided in example 3 using compound **279** (0.150 g, 0.51 mmol), methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **280** (0.102 g, 76 %) as light brown solid. 1H NMR (400 MHz, d_6 -DMSO) δ in ppm 7.22(d, $J = 8.4$ Hz, 1H), 7.06(d, $J = 2.8$ Hz, 1H), 6.99(dd, $J = 8.4$ Hz, 2.4 Hz, 1H), 5.49(brs, 2H), 4.31-4.23(m, 1H), 3.57-3.54(m, 1H), 3.16(s, 3H), 2.45(s, 3H), 2.23-2.11(m, 1H), 1.80-1.68(m, 1H), 0.74(t, $J = 7.2$ Hz, 3H). ESI-HRMS m/z 262.1559 ($M+H^+$).

Example 255

Synthesis of 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)ureae (281): The compound was prepared by general procedure **D** provided in example 4 using compound **280** (0.080 g, 0.30 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.073 g, 0.36 mmol), 3'-aminoacetophenone (0.048 g, 0.36 mmol),

TEA (0.083 mL, 0.60 mmol) to obtain compound **281** (0.069 g, 54 %) as offwhite solid.¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.03(s, 1H), 8.97(s, 1H), 8.21(d, *J* = 2.4Hz, 1H), 8.06-8.05(m, 1H), 7.73(dd, *J* = 8.8Hz, 2.4Hz, 1H), 7.66-7.63(m, 1H), 7.56-7.54(m, 1H), 7.47(d, *J* = 8.8Hz, 1H), 7.42-7.38(m, 1H), 4.39-4.31(m, 1H), 4.08(t, *J* = 9.6Hz, 1H), 3.60-3.56(m, 1H),
5 3.17(s, 3H), 2.53(s, 6H), 2.24-2.15(m, 1H), 1.82-1.73(m, 1H), 0.77(t, *J* = 7.6 Hz, 3H).ESI-HRMS *m/z*423.2030 (M+H⁺).

Example 256

Synthesis of 2-acetamido-N-(1-methoxypropan-2-yl)-5-nitrobenzamide (282): Compound
10 **176** (0.5 g, 1.97 mmol) was dissolved in DCM (10 mL). Then TEA (0.551 mL, 3.95 mmol) was added. Then Acetyl chloride (0.281 mL, 3.95 mmol) was added dropwise under cooling conditions and the reaction mass was stirred for 8 hours. After completion of the reaction, DCM was evaporated out and worked up with ethyl acetate and water and purified by column chromatography (Silica gel, mesh size 100-200) eluting (30% Ethyl acetate-Pet ether) to
15 obtain compound **282** (0.437 g, 75 %) as offwhite solid.¹H NMR (300 MHz, d₆-DMSO) δ in ppm 11.55(s, 1H), 8.97(d, 7.85Hz, 1H), 8.64-8.59(m, 2H), 8.36(dd, *J* = 9.3Hz, 2.7Hz, 1H), 3.47-3.42(m, 2H), 3.29(s, 3H), 2.17(s, 3H), 1.17(d, *J* = 6.6Hz, 3H).ESI-HRMS *m/z*318.1074 (M+H⁺).

20 Example 257

Synthesis of 3-(1-methoxypropan-2-yl)-2-methyl-6-nitroquinazolin-4(3H)-one (283): The compound was prepared by general procedure **G** provided in example 7 using compound **282** (0.4 g, 1.35 mmol), DMF (4 mL), ZnCl₂ (0.738 g, 5.42 mmol), HMDS (2.26 mL, 10.84 mmol) to obtain compound **283** (0.255 g, 68 %) as offwhite solid.¹H NMR (300 MHz, d₆-
25 DMSO) δ in ppm 8.72(d, *J* = 2.7Hz, 1H), 8.45(dd, *J* = 9Hz, 2.7Hz, 1H), 7.72(d, 9Hz, 1H), 4.72-4.59(m, 1H), 4.10-4.04(m, 1H), 3.62-3.57(m, 1H), 3.20(s, 3H), 2.65(s, 3H), 1.50(d, *J* = 3.9Hz, 3H). ESI-HRMS *m/z*278.1151 (M+H⁺).

Example 258

Synthesis of 6-amino-3-(1-methoxypropan-2-yl)-2-methylquinazolin-4(3H)-one (284):
30 The compound was prepared by general procedure **C** provided in example 3 using compound **283** (0.150 g, 0.54 mmol), methanol (5 mL), pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **284** (0.086 g, 76 %) as light brown solid.¹H NMR (300

MHz, d_6 -DMSO) δ in ppm 7.26(d, $J = 8.7$ Hz, 1H), 7.10(d, $J = 2.4$ Hz, 1H), 7.02(dd, $J = 8.7$ Hz, 2.7Hz, 1H), 5.52(s, 2H), 4.60-4.42(m, 1H), 4.10-4.04(m, 1H), 3.63-3.57(m, 1H), 3.21(s, 3H), 2.50(s, 3H), 1.47(d, $J = 6.6$ Hz, 3H). ESI-HRMS m/z 248.1400 ($M+H^+$).

5 Example 259

Synthesis of 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (285): The compound was prepared by general procedure D provided in example 4 using compound **284** (0.070 g, 0.28 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.068 g, 0.34 mmol), 3'-aminoacetophenone (0.046 g, 0.34 mmol),
10 TEA (0.083 mL, 0.56 mmol) to obtain compound **285** (0.069 g, 54 %) as offwhite solid. 1H NMR (300 MHz, d_6 -DMSO) δ in ppm 9.06(s, 1H), 6.99(s, 1H), 8.25(d, $J = 2.4$ Hz, 1H), 8.10(brs, 1H), 7.76(dd, $J = 8.7$ Hz, 2.4Hz, 1H), 7.70(dd, $J = 8.1$ Hz, 0.9Hz, 1H), 7.60(d, $J = 7.8$ Hz, 1H), 7.50(d, $J = 9$ Hz, 1H), 7.48-7.42(m, 1H), 4.57(s, 1H), 4.12(t, $J = 9.3$ Hz, 1H), 3.63-3.59(m, 1H), 3.22(s, 3H), 2.57(s, 6H), 1.50(d, $J = 6.9$ Hz, 3H). ESI-HRMS m/z 409.1877
15 ($M+H^+$).

Example 260

Synthesis of 2-(cyclohexanecarboxamido)-N-(1-methoxypropan-2-yl)-5-nitrobenzamide (286):Compound **176** (0.5 g, 1.97 mmol) was dissolved in DCM (10 mL). Then TEA (0.6 mL, 3.95 mmol) was added. Then cyclohexanecarbonyl chloride (0.57 g, 3.95 mmol) was added dropwise under cooling conditions and the reaction mass was stirred for 8 hours. After completion of the reaction, DCM was evaporated out and worked up with ethyl acetate and water and purified by column chromatography (Silica gel, mesh size 100-200) eluting (30% Ethyl acetate-Pet ether) to obtain compound **286** (0.446 g, 75 %) as offwhite solid.

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Example 261

Synthesis of 2-cyclohexyl-3-(1-methoxypropan-2-yl)-6-nitroquinazolin-4(3H)-one (287): The compound was prepared by general procedure G provided in example 7 using compound **286** (0.4 g, 1.35 mmol), DMF (4 mL), $ZnCl_2$ (0.73 g, 5.42 mmol), HMDS (2.26 mL, 10.84 mmol) to obtain compound **287** (0.285 g, 75 %) as offwhite solid. 1H NMR (400 MHz, d_6 -DMSO) δ in ppm 8.72(d, $J = 2.8$ Hz, 1H), 8.44(dd, $J = 8.8$ Hz, 2.8Hz, 1H), 7.70(d, $J = 9.2$ Hz, 1H), 4.68(s, 1H), 4.10-4.01(m, 1H), 3.64-3.60(m, 1H), 3.17(s, 3H), 3.00-2.93(m, 1H), 1.93-

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1.80(m, 2H), 1.78-1.72(m, 2H), 1.70-1.55(m, 3H), 1.49(d, $J = 6.8\text{Hz}$, 3H), 1.44-1.33(m, 2H), 1.33-1.28(m, 1H).ESI-HRMS m/z 346.1772 ($M+H^+$).

Example 262

5 **Synthesis of 6-amino-2-cyclohexyl-3-(1-methoxypropan-2-yl)quinazolin-4(3H)-one (288):**
The compound was prepared by general procedure C provided in example 3 using compound **287** (0.200 g, 0.58 mmol), methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **288** (0.127 g, 70 %) as light brown solid.¹H NMR (400 MHz, d_6 -DMSO) δ in ppm 7.22d, $J = 8.4\text{Hz}$, 1H), 7.07(d, $J = 2.8\text{Hz}$, 1H), 6.98(dd, $J = 8.8\text{Hz}$, 2.8Hz, 1H), 5.46(s, 2H), 4.48(brs, 1H), 4.06-3.99(m, 1H), 3.65-3.61(m, 1H), 3.16(s, 3H), 10 2.83-2.75(m, 1H), 1.87-1.84(m,1H), 1.79-1.71(m, 3H), 1.66-1.63(m, 1H), 1.58-1.52(m, 2H), 1.45(d, $J = 6.8\text{Hz}$, 3H), 1.38-1.30(m, 2H), 1.24-1.16(m 1H).ESI-HRMS m/z 316.2027 ($M+H^+$).

15 Example 263

Synthesis of 1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (289): The compound was prepared by general procedure D provided in example 4 using compound **288** (0.080 g, 0.25 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.061 g, 0.30 mmol), 3'-aminoacetophenone (0.040 g, 0.30 mmol), 20 TEA (0.069 mL, 0.50 mmol) to obtain compound **289** (0.062 g, 52 %) as offwhite solid.ESI-HRMS m/z 477.2504 ($M+H^+$).

Example 264

Synthesis of tert-butyl 4-((2-((2-methoxyethyl)carbamoyl)-4-nitrophenyl)carbamoyl)piperidine-1-carboxylate (296):Commercially available *N*-Boc piperidine-4-carboxylic acid (1.2 g, 5.22 mmol) was dissolved in dry DCM (10 mL) followed by addition of one drop of DMF. Oxalyl chloride (0.66 mL, 7.80 mmol) was added to the reaction mixture at ice cold condition and under nitrogen atmosphere. The reaction is stirred for 15 mins for the formation of corresponding acid chloride. Then, the reaction mass was 25 evaporated to dryness to remove excess oxalyl chloride and DCM. The crude was kept at nitrogen atmosphere and dissolved in measured amount of DCM (20 mL). In another vessel, compound **2** (0.50 g, 2.09 mmol) was dissolved in DCM (10 mL) followed by addition of TEA (0.7mL, 5.64 mmol) and dropwise addition of prepared acid chloride. The reaction was 30

stirred for another 3 hours. The reaction was monitored by checking TLC. Upon completion of the reaction, reaction mass was evaporated to dryness and washed with saturated NaHCO₃ and extracted with EtOAc to get the crude. The product was purified by flash chromatography (Silica gel, mesh size 100-200) eluting (60 % EtOAc/ Pet ether) to obtain compound **296** (0.31 g, 48.88%) as a white solid. ESI-HRMS *m/z* 451.219 (M+H⁺). Melting point 102 °C.

Example 265

Synthesis of tert-butyl 4-(3-(2-methoxyethyl)-6-nitro-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (297): The compound was prepared by general procedure **G** provided in example 7 using compound **296** (0.30 g, 0.66 mmol), DMF (5 mL), zinc chloride (0.63 g, 4.66 mmol), HMDS (0.83 mL, 3.99 mmol) to obtain compound **297** (0.17 g, 49 %) as yellow solid. ESI-HRMS *m/z* 433.2090 (M+H⁺). Melting point 170 °C.

Example 266

Synthesis of tert-butyl 4-(6-amino-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (298): The compound was prepared by general procedure **C** provided in example 3 using compound **297** (0.16 g, 0.38 mmol), methanol (10 mL), a pinch of Pd-C under hydrogen atmosphere to obtain compound **298** (0.15 g, 78%) as light brown solid. ESI-HRMS *m/z* 403.2349 (M+H⁺). Melting point 174 °C.

Example 267

Synthesis of tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (299): The compound was prepared by general procedure **D** provided in example 4 using compound **298** (0.14 g, 0.34 mmol), dry THF (5 mL), 4-nitrophenylchloroformate (0.10 g, 0.52 mmol), 3'-aminoacetophenone (0.043 g, 0.31 mmol), TEA (0.06 mL, 0.41 mmol) to obtain compound **299** (0.09 g, 39 %) as offwhite solid. ESI-HRMS *m/z* 564.2821 (M+H⁺). Melting point 196 °C.

Example 268

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (300): Compound **299** (0.068 g, 0.12 mmol) was dissolved in DCM (3 mL) and TFA (0.05 mL, 0.60 mmol) was added dropwise under ice cold condition at inert atmosphere. The reaction was stirred for 8 hrs. The reaction was neutralised by saturated

NaHCO₃ solution and extracted with EtOAc. The product was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (70 % EtOAc/ Pet ether) to obtain compound **300**(0.009 g, 39.2 %) as off white amorphous solid. ESI-HRMS *m/z* 464.2296 (M+H⁺).

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Example 269

Synthesis of 2-(2-chloro-2,2-difluoroacetamido)-N-(2-methoxyethyl)-5-nitrobenzamide

(326a): Compound **2** (0.6g, 2.50mmol) was dissolved in dry pyridine (6mL), Chlorodifluoroacetic acid (0.360g, 2.75mmol) was added and then POCl₃ (0.281mL, 2.75mmol) was added dropwise under cooling conditions and the reaction mixture was allowed to stir at room temperature for 1hour. After completion of the reaction, workup was done with EtOAc and 1(N) HCl soln. The product was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (30% EtOAc/ Pet ether) to obtain compound **326a** as off white amorphous solid (0.634g, 72%). ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 13.56(s, 1H), 9.48(s, 1H), 8.81(d, *J*= 2.4Hz, 1H), 8.54(d, *J*=8.8Hz, 1H), 8.46(dd, *J*= 9.2Hz, 2.4Hz, 1H), 3.48-3.43(m, 4H), 3.24(s, 3H).

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Example 270

Synthesis of 2-(chlorodifluoromethyl)-3-(2-methoxyethyl)-6-nitroquinazolin-4(3H)-one

(327a): The compound was prepared by general procedure **G** provided in example 7 using compound **326a** (0.4g, 1.14mmol), DMF (5mL), zinc chloride (0.621g, 4.56mmol), HMDS (1.9mL, 9.12mmol) to obtain compound **327a** as off white amorphous solid (0.303g, 80%). ¹H NMR (400 MHz, DMSO-d₆) δ in ppm 8.80(d, *J*= 2.4Hz, 1H), 8.60(dd, *J*= 8.8Hz, 3.2Hz, 1H), 8.00(d, *J*=8.8Hz, 1H), 4.29(t, *J*= 6.8Hz, 2H), 3.60(t, *J*= 6.8Hz, 2H), 3.24(s, 3H).

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Example 271

Synthesis of 3-(2-methoxyethyl)-6-nitro-2-(piperidine-1-carbonyl)quinazolin-4(3H)-one

(328a): Compound **327a** (0.25g, 0.75mmol) and piperidine (0.15mL, 1.50mmol) were dissolved in dry toluene and refluxed for 2hrs. After completion of the reaction, workup was done with EtOAc and water. The product was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (40% EtOAc/ Pet ether) to obtain compound **328a** as off white amorphous solid (0.232g, 86%). ¹H NMR (400 MHz, CDCl₃) δ in ppm 9.12(d, *J*=

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2.8Hz, 1H), 8.51(dd, J = 8.8Hz, 2.8Hz, 1H), 7.77(d, J = 8.8Hz, 1H), 4.34(t, J = 5.2Hz, 2H), 3.78-3.66(m, 2H), 3.26(s, 3H), 1.75-1.66(m, 6H).

Example 272

5 **Synthesis of 6-amino-3-(2-methoxyethyl)-2-(piperidine-1-carbonyl)quinazolin-4(3H)-one (329a):** The compound was prepared by general procedure C provided in example 3 using compound **328a** (0.200 g, 0.55 mmol), methanol (10 mL), a pinch of Pd-C under hydrogen atmosphere to obtain compound **329a** (0.113 g, 62%) as light brown solid. ¹H NMR (400 MHz, CDCl₃) δ in ppm 7.48(d, J = 8.8Hz, 1H), 7.43(d, J = 2.8Hz, 1H), 7.06(dd, J = 8.8Hz,
10 1H), 4.29(t, J = 5.6Hz, 2H), 4.02(brs, 2H), 3.72-3.68(m, 2H), 3.26(s, 3H), 1.71-1.63(m, 6H).

Example 273

Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidine-1-carbonyl)-3,4-dihydroquinazolin-6-yl)urea (330a): The compound was prepared by general procedure
15 **D** provided in example 4 using compound **329a** (0.07 g, 0.14 mmol), dry THF (5 mL), 4-nitrophenylchloroformate (0.048 g, 0.16 mmol), 3'-aminoacetophenone (0.032 g, 0.16 mmol), TEA (0.06 mL, 0.28 mmol) to obtain compound **330a** (0.04 g, 39 %) as offwhite solid. ¹H NMR (400 MHz, CDCl₃) δ in ppm 8.31(s, 1H), 8.22(s, 1H), 8.04(dd, J = 8.8Hz, 2.4Hz, 1H), 7.94-7.93(m, 1H), 7.83(dd, J = 8.4Hz, 2.4Hz, 1H), 7.70(d, J = 2.4Hz, 1H), 7.59-7.55(m, 1H),
20 7.43(d, J =8.8Hz, 1H), 7.37-7.33(m, 1H), 4.27(t, J = 4.8Hz, 2H), 3.81-3.73(m, 2H), 3.67(t, J = 4.8Hz, 2H), 3.42-3.35(m, 2H), 3.25(s, 3H), 2.59(s, 3H), 1.88-1.65(m, 6H).

Example 274

Synthesis of 3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)-6-nitroquinazolin-4(3H)-one (331a):Compound **327a** (0.25g, 0.75mmol) and 1-methylpiperazine (0.16mL, 1.50mmol) were dissolved in dry toluene (5mL) and refluxed for 2hrs. After completion of the reaction, workup was done with EtOAc and water. The product was then purified by column chromatography (Silica gel, mesh size 100-200) eluting (40% EtOAc/ Pet ether) to obtain compound **331a** as off white amorphous solid (0.232g, 82%).

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Example 275

Synthesis of 6-amino-3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)quinazolin-4(3H)-one (332a):The compound was prepared by general procedure C provided in example

3 using compound **331a** (0.200 g, 0.55 mmol), methanol (10 mL), a pinch of Pd-C under hydrogen atmosphere to obtain compound **332a** (0.120 g, 58%) as light brown solid.

Example 276

5 **Synthesis of 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333a):** The compound was prepared by general procedure **D** provided in example 4 using compound **332a** (0.07 g, 0.14 mmol), dry THF (5 mL), 4-nitrophenylchloroformate (0.049 g, 0.16 mmol), 3'-aminoacetophenone (0.033 g, 0.16 mmol), TEA (0.06 mL, 0.28 mmol) to obtain compound **333a** (0.043 g, 42 %) as offwhite solid. ¹H NMR (400 MHz, DMSO-d₆) δ in ppm 9.19(s, 1H), 9.01(s, 1H), 8.35(d, *J*= 2.8Hz, 1H), 8.07-8.05(m, 1H), 7.81(dd, *J*= 8.8Hz, 2.4Hz, 1H), 7.68-7.65(m, 1H), 7.59(d, *J*= 8.8Hz, 1H), 4.10(t, *J*= 6.0Hz, 2H), 3.64-3.58(m, 2H), 3.53(t, *J*= 6.0Hz, 2H), 3.40-3.35(m, 2H), 3.18(s, 3H), 2.53(s, 3H), 2.40-2.37(m, 2H), 2.35-2.30(m, 2H), 2.20(s, 3H).

15 Example 277

Synthesis of 2-amino-N-morpholino-5-nitrobenzamide (337): The compound was prepared by general procedure **A** provided in example 1 using compound **1** (0.3 g, 1.64 mmol), DMF (6 mL), HATU (0.7 g, 1.81 mmol), 4-aminomorpholine (0.18 mL, 1.81 mmol), TEA (0.57 mL, 4.12 mmol) to obtain compound **337** (0.38 g, 86 %) as yellow solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.69 (s, 1H), 8.38 (d, *J* = 2 Hz, 1H), 8.02 (dd, *J* = 9.4 Hz, 2.8 Hz, 1H), 7.58 (brs, 2H), 6.79 (d, *J* = 9.6 Hz, 1H), 3.67- 3.65 (m, 4H), 2.88- 2.85 (m, 4H).

Example 278

25 **Synthesis of 3-morpholino-6-nitroquinazolin-4(3H)-one (338):** The compound was prepared by general procedure **B** provided in example 2 using compound **337** (0.35 g, 1.31 mmol), trimethylorthoformate (TMOF) (1.5 mL, 13.15 mmol) to obtain compound **338** (0.3 g, 83 %) as pale yellow solid. ¹H NMR (400 MHz, d₆-CDCl₃) δ in ppm 9.13 (d, *J* = 2.4 Hz, 1H), 8.50 (dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 8.26 (s, 1H), 7.80 (d, *J* = 9.2 Hz, 1H), 3.04- 3.01 (m, 2H), 2.24- 2.18 (m, 2H), 2.02- 1.97 (m, 4H).

30

Example 279

Synthesis of 6-amino-3-morpholinoquinazolin-4(3H)-one (339): The compound was prepared by general procedure **C** provided in example 3 using compound **338** (0.250 g, 0.90

mmol), methanol (5 mL) and pinch of 10 % wet Pd-C under hydrogen atmosphere to obtain compound **339** (0.19 g, 86 %) as brown solid. ¹H NMR (300 MHz, d₆-DMSO) δ in ppm 7.91 (s, 1H), 7.38 (d, *J* = 8.7 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.06 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 5.72 (brs, 2H), 3.75 -3.67 (m, 6H), 3.18- 3.15 (m, 2H).

5

Example 280

Synthesis of 1-(3-acetylphenyl)-3-(3-morpholino-4-oxo-3,4-dihydroquinazolin-6-yl)urea (340):The compound was prepared by general procedure **D** provided in example 4 using compound **339** (0.14 g, 0.56 mmol), dry THF (8 mL), 4-nitrophenylchloroformate (0.18 g, 0.85 mmol), 3'-aminoacetophenone (0.093 mg, 0.68 mmol), TEA (0.2 mL, 1.42 mmol) to obtain compound **340** (0.09 g, 39 %) as off white solid. ¹H NMR (400 MHz, d₆-DMSO) δ in ppm 9.11 (s, 1H), 8.95 (s, 1H), 8.31 (d, *J* = 2.8 Hz, 1H), 8.09 (s, 1H), 8.06-8.05 (m, 1H), 7.80 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.66 (dd, *J* = 8.2 Hz, 2 Hz, 1H), 7.59- 7.55 (m, 2H), 7.42- 7.39 (m, 1H), 3.73- 3.65 (m, 8H), 2.53 (s, 3H).

15

Example 281

Synthesis of 6-amino-5-bromo-3-(2-methoxyethyl)-2-methylquinazolin-4(3H)-one (344):Compound **106** (0.300 g, 1.28 mmol) was dissolved in AcOH (4 mL). Solution of bromine(0.079 mL, 1.53 mmol) in chloroform(2 mL) was added dropwise in the reaction mixture at 0 °C and reaction mass was allowed to stir at room temperature for 4 hrs. After completion of the reaction, reaction mass was washed with aq. NaSCN soln and extracted with ethyl acetate and purified by column chromatography (Silica gel, mesh size 100-200) eluting (70% EA-PE) to obtain compound **344** (0.280g, 70%) as offwhite solid. ESI-HRMS *m/z*312.0351 (M+H⁺).

25

Example 282

Synthesis of 1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (345):The compound was prepared by general procedure **D** provided in example 4 using compound **344** (0.080 g, 0.25 mmol), dry THF (3 mL), 4-nitrophenylchloroformate (0.062 g, 0.30 mmol), 3'-aminoacetophenone (0.040 g, 0.30 mmol), TEA (0.094 mL, 0.68 mmol) to obtain compound **345** (0.048 g, 40 %) as light brown solid.ESI-HRMS *m/z*473.0829 (M+H⁺).

30

BIOLOGICAL ASSAY

To select the compounds capable of inhibiting the ubiquitination of ATGL by COP1 by targeting the VP motif, confocal microscopy was performed with the provided molecules. If the compound was effective in inhibiting the interaction, there would be a reduction in the number of fat droplets in the cells after treatment. This is because the increased ATGL levels would hydrolyse the accumulated TAG in oleate induced HepG2 cells and bring about the aforementioned reduction. With this rationale in mind, HepG2 cells were induced to accumulate lipid droplets after treatment with 250 μ M of oleate and 10 μ M of the specific compounds were added. The potential of the compounds to bring about a reduction in the number of fat droplets was then checked by comparison with oleate induced cells by counting number of droplets of approximately 20 cells from each treatment and calculating the average number of lipid droplets of each cell. The selected compounds were then subjected to dose dependent treatments and the ones which could maintain its potency to reduce fat droplets at lower doses were then selected for western blot analysis. The compound which could reduce the number of fat droplets in the cells are expected to raise the levels of ATGL since they are likely to deter COP1 from ubiquitinating ATGL. This increase will be visible only in the protein level and gene expression is likely to remain unchanged since ubiquitination is a post transcriptional modification. Thus, western blot was performed to check ATGL levels in the cells with the selected molecules.

Example 283

Western Blotting

HepG2 cells were treated with the compounds 9, 10, 11, 17, 18, 23, 24, 115, 123, 127, 139, 107, 171, 179, 73, 187, 211, 215, 219, 223, 232, 238, 241, 244, 258, 299, 308, and 333a, (10 μ M for initial screening and 50nM, 100nM, 200nM, 500nM, 1 μ M and 5 μ M for dose dependent assays) for 24 hours. After removing media from the cells, the wells were washed with 1X PBS twice to remove any remnant media. Cells were then lysed in lysis buffer containing 50 mM Tris-HCl (pH 7.4), 100 mM NaCl, 1 mM EDTA, 1 mM EGTA, 1% Triton X-100 and protease inhibitor cocktail (Millipore, Billierica, MA, USA). Following centrifugation at 20,000g for 20 minutes, the protein solution was extracted from the cells. Protein was estimated using Bradford assay. Bradford's reagent (BioRad) was diluted in 1:4 ratio in double distilled water. 2 μ l of protein sample was added to 100 μ l of the reagent and

absorbance was measured at 595nm. 30µg of protein was diluted in lysis buffer. 1X loading buffer diluted from 5X stock containing 250mM Tris-HCl (pH 6.8), 10% SDS, 50% glycerol, 0.1% bromophenol Blue and 10% β-mercaptoethanol was added. The protein samples were then heated at 95°C for 10 minutes, cooled and centrifuged at 12,000g for 2 minutes prior to loading.

For western blotting, the proteins were resolved in 10% SDS PAGE (discontinuous buffer system). 1X running buffer containing SDS, Tris Base and Glycine was used to run the gel at 80V for approximately 2 hours. Transfer was done using PVDF membrane (Millipore) having pore size of 0.45µm. 1X transfer buffer containing Tris-Base, Glycine and 20% methanol was used for wet transfer. Transfer was done at 90V for 3 hours. Following transfer, the PVDF membrane containing the proteins were washed in 1X PBST comprising of 1X PBS and 1% Tween 20 (Sigma Aldrich). The membrane was then incubated for 1 hour at room temperature in 5% skim milk powder to block the non-specific sites. Following multiple washes with 1X PBST to wash away any remaining blocking buffer, the required primary antibody (COP1 [Bethyl Laboratories], ATGL [Cell Signalling Technology] or Actin[Cell Signalling Technology]) prepared with 1X PBST, 1% Bovine Serum Albumin and 0.04% Sodium Azide was added to the membrane and incubated overnight at 4°C. The next day, the membrane was again washed multiple times with 1X PBST to remove any unbound primary antibody. The membrane was then incubated with goat anti-rabbit secondary antibody (Genex) for 1 hour at room temperature and washed again for multiple times with 1X PBST. The membrane was then developed using Clarity™ ECL Western Blotting Substrate(BioRad) and viewed in ChemiDoc (BioRad). The EC₅₀ values of compounds 127, 139, 211, 215, 219, 223, 232, 238 and 299 are described in Table 6.

Figure 1(A to Y) illustrates results of Western Blot Analysis in HepG2 cells after treatment with compounds 9, 10, 107, 171, 179, 73, 232, 238, 211 and 340. The figure also describes the dose dependant Western Blot analysis of following compounds 9, 11, 17, 18, 23, 24, 123, 127, 139, 211, 223, 232, 241, 244, 299, 333a, 215, 219, 238 and 308. These compounds showed increased ATGL level irrespective of the treated doses.

Example 284

Confocal Microscopy

HepG2 cells were plated in confocal dishes (SPL, Genetix Biotech Asia Pvt. Ltd.). The cells were allowed to adhere and divide for 16 hours. 10µM for initial screening and 10nM, 20 nM,

50nM, 100nM, 200nM, 500nM, 1µM and 5µM for dose dependent assays of the compounds 9 and 107 were dissolved in DMSO and added to the cells. 250µM of oleate was used for induction. BSA (Sigma Aldrich) was used as a negative control. Post 24 hours of treatment, media was decanted from the cells and washed with 1X PBS solution to remove any remnant. 200µl of staining solution containing 200ng/ml BODIPY (Invitrogen) and 25µg/ml HOECKST342 (Invitrogen) were added to the cells and incubated at 37°C for 30 minutes under dark conditions. Cells were washed 3 times with 1X PBS to remove excess stain. FLUOVIEW FV10i (Olympus) was used to visualise the cells.

Figure 2 illustrates images of compound 9 and 107 screening on HepG2 cells using confocal microscopy.

Example 285

The effect of the compounds in primary mouse hepatocytes and adipose explant cultures

To further strengthen the efficiency of the compounds 9 and 107, primary hepatocytes were isolated from mice and these compounds were treated in a dose dependent manner for 24 hours. Primary hepatocytes and adipose tissue explants were isolated from mice and subjected to compound treatment for 24 hours at the doses of 100nM, 500nM and 1µM. Post cell harvesting, western blot was carried out with the lysate to check the ATGL level. ATGL and COP1 antibodies were used. Actin served the purpose of a loading control.

Culture of primary mouse Hepatocytes and Adipocytes

1. Hepatocytes - 2-4 months old chow-fed black male mouse (C57bl/6) was sacrificed using chloroform (SRL) and was cleaned with 70% ethanol. Under aseptic conditions, the ventral side of the mouse was cut open, until the liver, portal vein (PV) and inferior vena cava (IVC) were sufficiently exposed. Blood was drawn from the heart in order to prevent backflow into liver while perfusion. The butterfly cannula was inserted into the PV and 20ml of HBSS (Hank's Balanced Salt Solution; 5mM KCl, 0.4mM KH₂PO₄, 4mM NaHCO₃, 140mM NaCl, 0.3mM Na₂HPO₄, 6mM Glucose, HEPES, 0.5mM MgCl₂.6H₂O, 0.4mM MgSO₄.7H₂O, 0.5mM EDTA; not containing 1mM CaCl₂) was allowed to pass through the liver (Perfusion) at a constant flow rate of 3ml/min, maintained by Masterflex digital peristaltic pump (Cole-Parmer). The IVC was cut as soon as the passage of the buffer through the liver began, so that blood and perfusate from liver is drained through the IVC. The liver blanched and became pale in color upon this treatment.

After the passage of HBSS, 25ml of Collagenase (Roche) solution (1mg/ml) in HBSS (containing 1mM CaCl₂) was allowed to pass through the liver at a constant flow rate of 2 ml/min. After this digestion, the flow was stopped, the cannula removed and the pale and soggy lobes of the liver were gently excised from the body. The gall bladder was removed from the isolated liver. The pieces of digested liver tissue were then minced on a 10cm culture plate in HBSS (containing 1mM CaCl₂). The resulting suspension was then passed through a 100µ cell strainer (SPL) to allow hepatocytes to pass through to the filtrate and retain cellular clumps and undigested tissue. The filtrate was centrifuged at 50g for 2 minutes at 4°C. The supernatant was discarded and the cellular pellet was carefully resuspended in DMEM. The resulting suspension was centrifuged at 50g for 2 minutes at 4°C. The supernatant was discarded and the cellular pellet was carefully resuspended in required volume of DMEM for plating. The hepatocytes were plated according to experimental requirements and were maintained in an incubator at 37°C with 5% CO₂. Cells were washed once with HBSS and DMEM 6-7 hours after plating and the adhered hepatocytes were maintained and subjected to requisite treatments.

2. Adipocytes - 2-4 months old chow-fed black male mouse (C57bl/6) was sacrificed using chloroform (SRL) and was cleaned with 70% ethanol. Under aseptic conditions, the ventral side of the mouse was cut open, and gonadal (epididymal) white adipose tissue were excised using scissors and suspended in 1X PBS supplemented with 0.1% BSA in a 10cm culture plate. The attached blood vessels were removed and the adipose tissue was minced as much as possible. The suspension was centrifuged at 50g for 2 minutes at 4°C. After centrifugation, the adipose tissue pieces suspended at the uppermost layer of the supernatant as emulsion were carefully extracted and plated in DMEM in 35mm culture dishes. The explant tissue thus obtained was treated with different concentrations of compounds after 6-7 hours.

Figure 3(A to C) illustrates ATGL protein status in mouse primary hepatocytes and adipose explants after compound treatment. The level of ATGL was found to be increased in a dose-dependent manner. This provides a more profound and direct evidence of the effectiveness of the compounds. As is evident, in primary hepatocytes, compounds 9 and 107 had a subtle inclination towards increasing ATGL level whereas this effect was absent in adipose tissue explants.

The major source of ATGL is the adipose tissue and, therefore, it is fitting to check if the compounds had any effect on the ATGL protein level in adipose tissue. Both 9 and 107 did not show any significant changes in ATGL protein in cultured mouse adipose explants after 24 hours of compound treatment. This partly hints at a lack of a striking regulation of ATGL turnover by COP1.

Example 286

In vitro ubiquitination

Purification of ATGL protein and obtaining COP1 overexpressing cell lysate: Myc-ATGL plasmid and Myc-DDK-COP1 plasmid (2 μ g each) were transfected separately in cultured HEK293A cells with the help of Lipofectamine2000 (Invitrogen). Cells were harvested in Lysis Buffer and protein solution was extracted as described previously. The Lysis Buffer used to harvest COP1 overexpressing cells had 0.1% SDS supplemented in it. The concentration of protein was estimated using Bradford assay. For source of E3 ligase, the total cell lysate from COP1 overexpressing HEK293A cells were used.

For purification of Myc-ATGL: 1ml of Ni²⁺-NTA resin (Roche) was taken in a 15ml centrifuge tube and centrifuged at 2000 RPM for 5 minutes. The upper ethanol layer was discarded and the pellet was washed in 1X PBS twice to remove any remaining traces of ethanol. The pellet was finally washed once with Lysis Buffer for equilibration. 15 mg of protein was used for affinity purification reaction in a reaction volume of 10ml with Lysis Buffer (containing protease inhibitor cocktail). The tube was incubated overnight at 4°C in a rotary shaker.

The next day, the solution was centrifuged at 2000 RPM for 10 minutes and the supernatant collected. Lysis Buffer (containing protease inhibitor cocktail twice the previous concentration) was used for washing the beads twice to remove non-specific and unattached reactants in a stringent condition. The beads were finally washed once with 1X PBS containing the same amount of protease inhibitor for equilibration. 300 μ l of 500mM Imidazole (Sigma Aldrich) solution in 1X PBS was added to the resin for elution of ATGL and centrifuged at 2000 RPM for 30 minutes and the eluted protein was collected. To the separated resin, 300 μ l of 1M Imidazole solution was added and centrifuged at 2000 RPM for 30 minutes and the second elute was collected. 20 μ l of eluted protein from each elution was

boiled with 5 μ l of Laemmli's buffer at 95°C for 10 minutes and run in 10% SDS-PAGE gel. The supernatant collected before elution of ATGL and the proteins still attached to the Ni²⁺-NTA resin were also run in the SDS-PAGE. The resolved proteins were subsequently transferred on PVDF membranes and probed with anti-myc primary antibody to check the presence of purified ATGL in the elute. Also to check the yield of the purified protein, 40 μ l of the elute was run in 10% SDS page and stained with Coomassie Brilliant Blue solution followed by destaining with methanol, glacial acetic acid and water in a 50:40:10 ratio.

For identifying the E2 ubiquitin-conjugating enzyme responsible for ATGL ubiquitination by COP1, an *in vitro* ubiquitylation kit (Enzo Life Sciences) was used. The assay was reconstituted as per manufacturer's protocol with the panel of E2 conjugating enzymes provided and other required components at the mentioned concentrations. The reaction was carried out for 6 hours following which it was quenched as per directions with the provided 2X non-reducing gel buffer and then analysed by western blotting.

Figure 4 illustrates identification of the E2 conjugating enzyme responsible for ATGL ubiquitination by the E3 Ubiquitin Ligase, COP1. As seen in the figure 4, only UbcH6 (UBE2E1) was able to mediate the ubiquitination of ATGL by COP1. Therefore, UbcH6 was used as the E2 enzyme to check the effect of ATGL ubiquitination by COP1 upon treatment with the small molecule inhibitors.

Having identified the E2 ubiquitin conjugating enzyme as UbcH6, ubiquitination assay was set up *in vitro* as described previously with 5 μ M of the compound 9, 107, 171, 179 and 73 followed by quenching and analysis by western blotting.

Ubiquitination of a target protein is carried out in a three step process involving three different enzymes: E1 ubiquitin activating enzyme, E2 ubiquitin conjugating enzyme and E3 ubiquitin ligase. In humans, there is only one E1 ubiquitin activating enzyme and multiple E2 and E3 enzymes. COP1 is an E3 ubiquitin ligase and the E2 enzyme responsible for ATGL ubiquitination is not known. In order to assert the specificity of the compounds of the present invention to inhibit COP1 and decrease ubiquitination of ATGL, the *in vitro* ubiquitylation reaction was reconstituted with purified ATGL protein, total cell lysate of COP1 overexpressing HEK293A cells as source of E3 ubiquitin ligase, UbcH6 as E2 enzyme, 5 μ M of the compounds 9, 107, 171, 179 and 73 and other components required to carry out the ubiquitylation reaction as per the manufacturer's instructions.

Figure 5 illustrates effect of compounds 9, 107, 171, 179 and 73 on ATGL ubiquitination *in vitro*. As seen in the figure, compounds 9, 107 and 179 showed significant efficacy in curbing ATGL ubiquitination by COP1. This experiment also points, to the specificity of the compounds in inhibiting COP1 since the source of E3 ubiquitin ligase is majorly COP1 and purified ATGL protein has been used as its substrate.

Example 287

Status of ATGL ubiquitination and COP1 autoubiquitination upon compound treatment assessed by immunoprecipitation assay

COP1 is an E3 ubiquitin ligase and ATGL is one of its targets which gets ubiquitinated and ultimately degraded via proteasomal mediated pathway. Thus, the molecules inhibiting COP1 by targeting the VP motif of ATGL are actually expected to bring about a reduction in the ubiquitination levels of ATGL. The compounds of the present invention have shown a reduction in the lipid droplet count with a corresponding increase in ATGL protein levels while gene expression remained unaltered. However, it is of utmost importance to check the changes taking place at the ubiquitination level of ATGL upon treatment with the compounds.

To this end, an immunoprecipitation assay was performed wherein HepG2 cells overexpressing myc-ATGL were transfected with HA-Ubiquitin and treated with 5 μ M of the compounds 9, 10, 107, 215, 219 and 238. MG-132, a proteasomal inhibitor, was added 4 hours before harvesting the cells. Immune complexes were pulled down with anti-myc antibody and immunoblot was done using anti-HA antibody. The resultant smears on the blot reflect the ubiquitination status of ATGL.

Figure 6 (A to G) illustrate results of immunoprecipitation assay to check ubiquitination status of ATGL and COP1 after treatment with compounds 9, 10, 107, 215, 219 and 238. For compound 9, a subtle reduction in the ubiquitination smear upon treatment was observed as compared with control. This reduction, however, could not be seen in cells treated with compound 10 which indicates that compound 9 might be more potent in inhibiting COP1 by blocking the ubiquitination of ATGL to some extent compared to compound 10. Compound 107, also seemed to exhibit the capability of subtly reducing ubiquitination of ATGL (Figure 6A, 6C and 6D). For compounds 215 and 219, no subtle reduction in the ubiquitination smear upon treatment was observed as compared with control (Figure 6F).

COP1 is capable of auto ubiquitinating its own self and getting degraded via the proteasomal pathway. To probe into this, HepG2 cells were co-transfected with HA tagged Ubiquitin and myc-flag tagged COP1. The transfected cells were treated with 5 μ M of compounds 9, 10, 107 and 238 for 24 hours. MG-132, a proteasomal inhibitor, was added 4 hours before harvesting
5 the cells. Immune complexes were pulled down with anti-myc antibody and immunoblot was done using anti-HA antibody. Interestingly, the compounds being COP1 inhibitors could markedly reduce COP1's auto ubiquitination property as shown in Figure 6B and 6E compared to control. This shows that indeed the compounds are able to block the ubiquitination of COP1 as well as of its target, ATGL. Thus, the compounds of the present
10 invention could be potent therapeutic targets by being able to block the proteasomal degradation of ATGL which would then be able to carry out its lipolytic action and reverse the symptoms of steatosis.

Example 288

15 **Compounds 9 and 10 could reverse the decrease in ATGL level brought about by overexpression of COP1 in HepG2 cells**

COP1 is an E3 ubiquitin ligase with ATGL as one of its targets for ubiquitination and subsequent proteasomal degradation by 26S proteasome. Therefore, it is only legit for ATGL levels to decrease upon COP1 overexpression. To this end, HepG2 cells were transfected with
20 500ng of myc-DDK-COP1 plasmid using Lipofectamine 2000 and treated with 5 μ M of the compounds 9 and 10 for 24 hours. 48 hours post transfection, cells were harvested and western blot was carried out. Indeed, myc DDK-COP1 construct were transfected in HepG2 cells, ATGL level was dampened significantly. On treatment of the compounds of the present invention in COP1 overexpressing cells for 24 hours, ATGL level was sufficiently restored.

25 Figure 7 illustrates reversal of ATGL degradation promoted by COP1 upon treatment with compounds. Both compounds 9 and 10 could restore ATGL to its normal level upon COP1 overexpression. Thus, indeed the compounds could counteract the decrease of ATGL by COP1 and ultimately regulate the turnover of ATGL.

30

Example 289

Compounds exert no effect on the mRNA levels of ATGL

Ubiquitination of ATGL by COP1 is a post translational event, therefore, it is expected that the mRNA level of ATGL will not change compared to control upon treatment with the compound of the present invention which inhibit COP1. To establish this, HepG2 cells were treated with 5 μ M and 10 μ M of the compounds 9, 107, 171, 179 and 73 for 24 hours. RNA was isolated using TRIzol reagent followed by chloroform treatment and precipitation with isopropanol. cDNA was obtained from the isolated RNA and qPCR was carried out using SyBr green reagent. COP1 and ATGL gene expression levels were checked. 18s was used as control. Figure 8 illustrates that compounds exert no effect on the mRNA levels of ATGL. As is evident, there was no significant changes at the mRNA levels of both COP1 and ATGL upon treatment with the compound.

Example 290

***In vivo* study of compound to check the expression level of ATGL and COP1 in liver**

6-8 weeks old healthy female C57BL/6 mice (average weight: 25 grams) were taken for the study. These were then divided into three groups comprising of three mice per group (Control, compound 107 fed for 8 hours and compound 107 fed for 16 hours). Mice were fed with 30mg/kg of compound 107 orally. The compound was dissolved in 25% DMSO and 75% PBS. The control group was fed only with the solvent in which the compound was dissolved. Post 8 hours and 16 hours of feeding, mice were sacrificed and a portion of the excised liver tissue was homogenized in lysis buffer containing protease inhibitor cocktail. The homogenate was centrifuged at 20,000g for 30 minutes following which the supernatant containing the protein lysate was collected. The lysate was then diluted accordingly and protein estimation was carried out by Bradford Assay. This was followed by Western Blotting wherein the levels of ATGL and COP1 were checked. Actin was used as the loading control. Figure 9 illustrates results of *in vivo* study of compounds in mice measuring ATGL and COP1 levels. The western blotting from liver lysates revealed that the compound 107 was effective in increasing ATGL and COP1 levels after 16 hours of feeding. 8 hours of feeding had no significant impact on either ATGL or COP1.

Example 291

***In vivo* ubiquitination**

For checking the change in the ubiquitination status of ATGL on compound treatment, Myc-ATGL expressing HepG2 cells (ATGL overexpressing cell line) was transfected with 2 μ g of

a plasmid harboring the HA tagged ubiquitin gene using Lipofectamine 2000 reagent (Invitrogen) in OptiMEM media (HiMedia). Fresh DMEM complete media was added after 8-10 hours of transfection. After roughly 24 hours of transfection, 5 μ M of the compounds 9, 10 and 107 was added and cells were harvested post 24 hours of treatment. 4 hours prior to cell
5 harvesting, 10 μ M of proteasomal inhibitor MG132 (Calbiochem, Merck Millipore) was added to the cells. Proteins were isolated from the cells and protein concentration was estimated as described previously. 30 μ l of PureProteome Protein A/G Mix Magnetic Beads (Merck Millipore) was taken in a 1.5ml microcentrifuge tube, placed in a Magna Rack (Merck Millipore) and allowed to adhere to the side of the tube. 200 μ g of protein was used for
10 immunoprecipitation reaction in a reaction volume of 1ml. 2 μ l of anti-Myc primary antibody (Cell Signaling Technology) was added and the tube was incubated overnight at 4 $^{\circ}$ C in a rotary shaker. The next day, the tube was placed back in the Magna Rack and the beads were allowed to attach to the tube. To remove non-specific and unattached reactants, 1X PBS and 0.1% Triton-X was used for washing. 2X loading dye and Lysis Buffer was added and heated
15 at 95 $^{\circ}$ C for 10 minutes to allow the immune complex to dislodge from the magnetic beads. Western Blot was performed subsequently as described before with anti-HA primary antibody for immunoblotting (Cell Signaling Technology). The activity trends of the synthesized compounds are disclosed in Table-5.

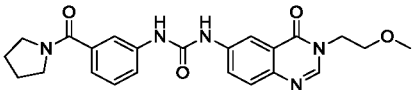
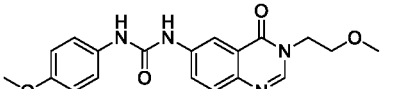
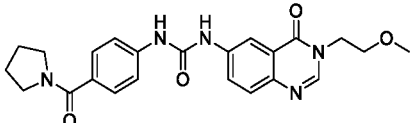
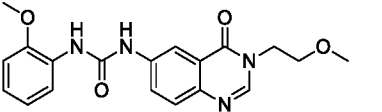
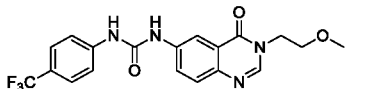
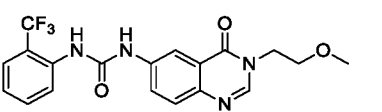
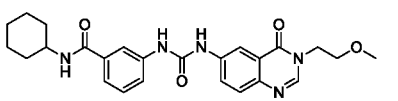
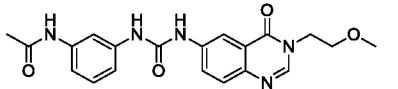
Figure 10 (A to D) illustrates compilation of effect of compounds in increasing ATGL and
20 COP1 levels in HepG2 cells in a dose dependent manner, ATGL ubiquitination assay and effect of ATGL and COP1 levels in primary mouse hepatocytes.

In Figure 10, A and B, the compound 238 showed increase in ATGL and COP1 levels in HepG2 cells in dose dependent manner. In figure 10C, the ATGL ubiquitination level was found to be decreased upon treatment with compound 238 in *in vivo* ubiquitination assay
25 carried out according to described protocol. Figure 10D describes treatment of compound 238 in primary mouse hepatocytes, for 24 hours could enhance ATGL levels at 1 μ M and 5 μ M doses. COP1 levels increased only with 5 μ M concentration.

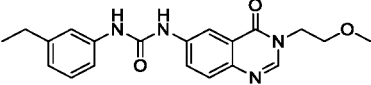
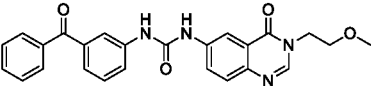
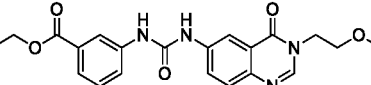
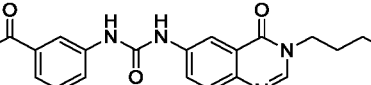
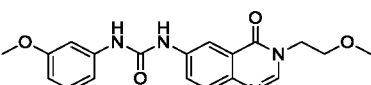
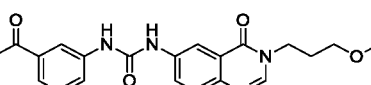
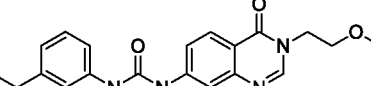
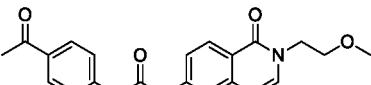
For checking the autoubiquitination status of COP1, HepG2 cells were cotransfected with 2
30 μ g each of Myc-DDK-COP1 and HA-Ub plasmids using Lipofectamine 2000 reagent (Invitrogen) in OptiMEM media (HiMedia). The rest of the procedure is similar to that done for Myc-ATGL.

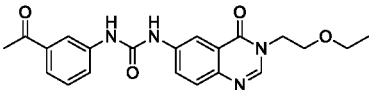
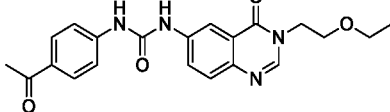
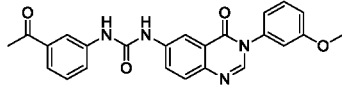
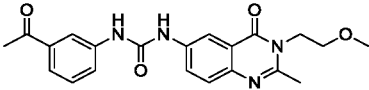
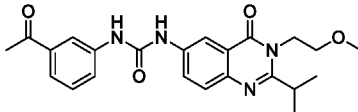
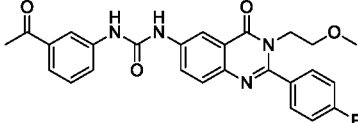
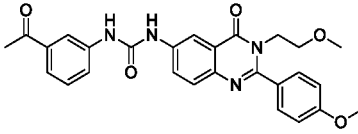
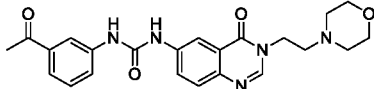
Table 5

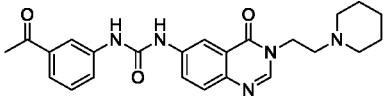
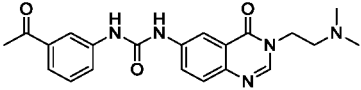
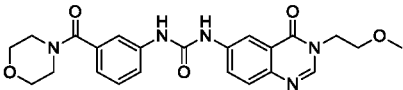
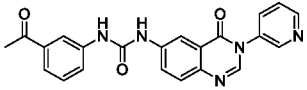
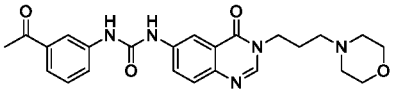
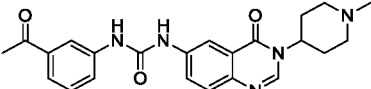
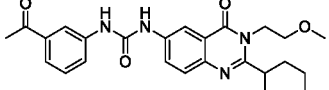
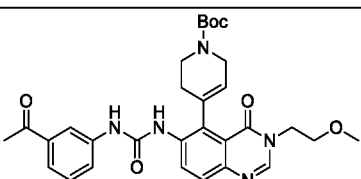
Sl No.	Compound Number	Structure	Reduction in Lipid Droplets	Increase in ATGL level
1	35		+	+
2	36		+	+++
3	83		+	+
4	9		++++	+++++
5	84		+++	++
6	37		+	+
7	8		++	+
8	10		++++	++++
9	11		+	+

10	18		+	++++
11	40		++	++++
12	20		++	++
13	41		++	++++
14	38		NT	++
15	39		NT	++
16	15		+	++++
17	22		+	+

18	16		+++	++++
19	12		++	+++
20	85		+	+
21	17		+++	+++
22	21		+	+
23	23		++	++++
24	24		+	++++
25	5		++	++

26	13		+	+
27	14		+	+
28	42		+	+
29	175		+	+
30	6		++++	++++
31	89		+++	+
32	192		++	+++
33	193		+	+

34	93		+++	++++
35	94		++	+
36	103		+	+
37	107		++++	++++
38	111		++	+++
39	115		+	+
40	119		+	+
41	135		++	+++

42	147		++	+++
43	143		+++	++++
44	19		++	+
45	155		+++	++
46	139		+++	+++
47	163		++	+
48	123		+++	++++
49	59		NT	+

50	60		NT	+
51	25		NT	+
52	61		NT	+
53	171		NT	+++
54	62		NT	+++
55	179		NT	+++++
56	64		NT	+
57	47		NT	+++

58	285		NT	+
59	345		NT	+
60	183		NT	+++
61	253		++	+
62	66		NT	++
63	281		NT	++
64	232		NT	+++
65	238		NT	+++++

66	187		NT	+++
67	259		NT	+++
68	159		NT	+
69	131		NT	+
70	340		NT	+

The ability of the compounds in reduction in lipid droplets and the increase in ATGL level were scored with + = slight or insignificant; ++ = Moderate; +++ and ++++ = active; +++++ = very active. NT = Not tested.

5

Table 6

Sl No	Compound No	Structure	EC ₅₀ (<i>in-vitro</i>) in nM
1	127		10.81
2	139		1.19

3	211		199.06
4	215		30.19
5	219		29.51
6	223		70.30
7	232		433.50
8	238		1.02
9	299		289.73

Intensity of ATGL and thus its level compared to control will increase up to 1.6 fold with COP1 knockout using siCOP1. Accordingly, EC₅₀ was calculated for COP1 modulator. The fold increase of ATGL was measured with densitometry analysis in *ImageJ* software for different doses (10 nM, 20 nM, 50 nM, 100 nM, 200 nM, 500 nM, 1000 nM, 5000 nM) of following compounds: 127, 139, 211, 215, 219, 223, 232, 238 and 299. These value obtained were divided with the ATGL level that will go up to maximum 1.6 fold with siCOP1. Thus,

the values obtained was expressed in percentage and was plotted against log[conc] of the respective compounds to obtain the EC₅₀ value in *graphpad* software.

Initial validation of the compounds has been done through (i) reduction of lipid droplets in or
5 without presence of compounds, (ii) increase in ATGL level in or without presence of
compounds through W-B (western blot) analysis. The compounds with desired properties
from the above mentioned screening procedure were further assayed for their ability to
ubiquitination of ATGL via immunoprecipitation assay (IP) in or without presence of
10 compounds. Compound **6** was the initial hit as fulfilled the first two criteria (reduction of
lipid droplet and increase in ATGL level). As compound 6 comprises terminal –OMe group
in *meta* position in urea linked phenyl moiety, the inventors started investigating and
derivatizing compounds keeping oxygen atom in that *meta* position assuming that hetroatom
plays a role in ligand-protein interaction for showing potency. The investigation showed
15 ketone function in compounds **9** and **10** is significant. Compound without the ketone function
failed to increase ATGL level. Compound with amide group such as compounds **17**, **18**, **19**,
and **20** showed ability to increase ATGL level. Quinazolinone ring N-3 position was also
substituted with substituted alkyl and aromatic moiety. Some compounds such as **89**, **93**, **135**,
139, **143**, **147**, **163**, **103**, **155**, and **159**, showed some sort of increase in ATGL level and
20 reduction in lipid droplets. Compound **175** was made, where no heteroatom is present in N-3
linker. Compound 175 did not increase ATGL level and reduced lipid droplets. Some
aliphatic substituents at C-2 position of the quinazolinone ring such as isopropyl, cyclohexyl,
cyclopentyl, piperidinyl, pyridinyl, pyrazinyl were also incorporated, which led to increase in
the ATGL level.

25 **Example 292**

Lipophilicity Assay

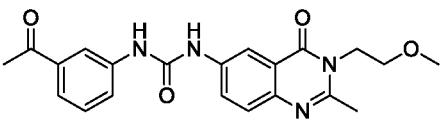
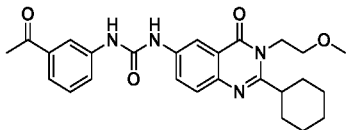
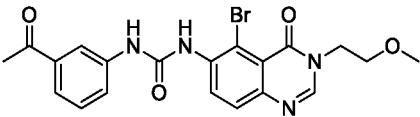
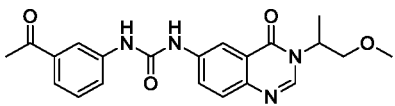
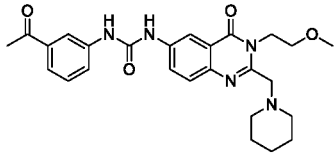
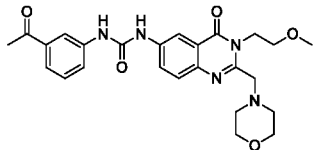
1.56 g NaH₂PO₄·2H₂O was dissolved in 0.5 L water in a 1 L beaker. After adjusting pH to 7.4
using NaOH solution, the volume was made up to 1 L. Equal volumes of sodium phosphate
buffer (10 mM, pH 7.4) and n-octanol were added to a separation funnel and mixed
30 thoroughly by shaking and inverting the funnel several times. The two layers were allowed to
separate for overnight and then dispensed in two separate glass bottles. 10 mM stock solution

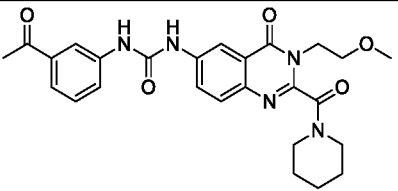
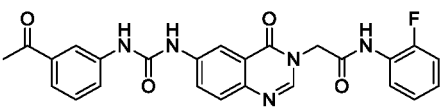
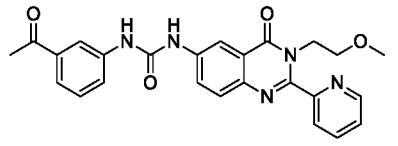
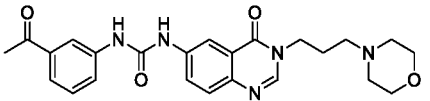
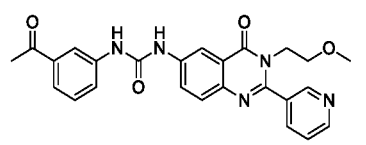
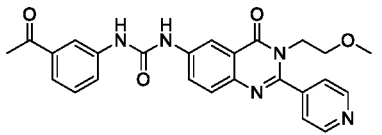
was prepared in 100% DMSO and stored at 4 °C. 495 µL of organic phase (1-octanol) was added to each well of a 2 mL deep well plate, followed by 495 µL of buffer and 10 µL of test compound was added. The plate was incubated for 3 hr at room temperature on a plate shaker at 500 rpm. After incubation, the samples were allowed to equilibrate for 20 min and then

5 centrifuged at 4000 rpm for 30 min for complete phase separation and analysed by LC-UV. The results obtained for the tested compounds is provided in table 7.

Log D = Log (area of octanol/area of buffer)

Table 7

Sl No	Compound No	Structure	LogD @ pH 7.4
1	160		2.67
2	123		0.84
3	73		1.95
4	179		1.69
5	238		1.60
6	241		2.51

7	330a		1.79
8	253		3.01
9	211		2.48
10	139		-0.50
11	215		0.42
12	219		0.19
13	Quercetin (Control)		2.81
14	Metroprolol (Control)		-0.09
15	Propranolol (Control)		1.39

Log D Criteria: <1: Hydrophilic; 1 - 4.2: Ideal Lipophilic; >4.3: High Lipophilic

Lipophilicity assay revealed that compounds 123, 139, 215 and 219 are hydrophilic in nature whereas, rest of the compounds 73, 179, 238, 330a 160, 241, 253 and 211 have ideal lipophilicity with respect to the control compounds Quercetin, Metoprolol and Propranolol.

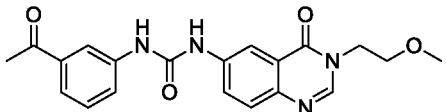
- 5 The LogD value of the compound provides insight into possible oral bioavailability of the compounds with compounds showing ideal lipophilicity may be suitable candidate for oral dosage.

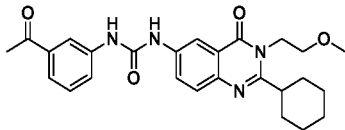
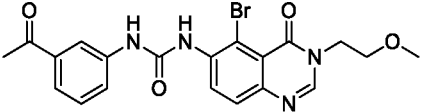
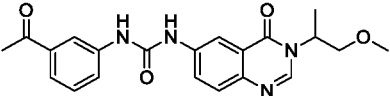
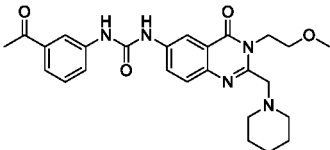
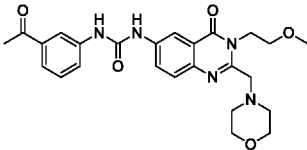
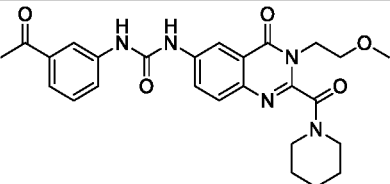
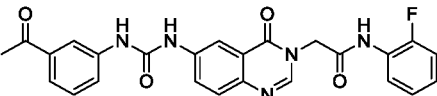
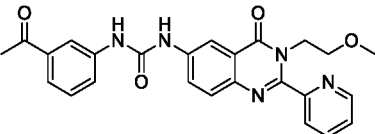
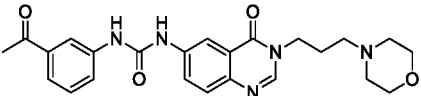
Example 293

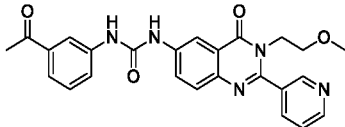
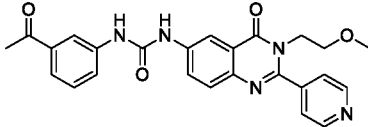
10 Plasma Stability Assay

1 mM Stock of test compound was prepared from 10 mM initial stock solution of compounds by diluting 10 μ L of 10mM stock with 90 μ L of DMSO. Then 10 μ L of 1mM stock was diluted with 90 μ L of DMSO to give 100 μ M concentration. The frozen plasma was thawed at room temperature and centrifuged at 1400 rpm at 4 °C, for 15 minutes. Approximately 90% of the clear supernatant fraction was transferred to a separate tube and was used for the assay. Final working stock of 1 μ M was prepared by diluting 3 μ L of 100 μ M with 297 μ L of plasma. Plasma containing the test compound was incubated for 120 min at 37 °C in shaker with 500 rpm. 50 μ L of aliquot of sample at 0,15,30,60 and 120 minutes were precipitated with 150 μ L of acetonitrile containing internal standard and centrifuged at 4000 rpm at 4 °C for 20 minutes. 120 μ L of supernatant was diluted with 120 μ L of water and analyzed by LC-MS/MS. The results obtained for various compounds is provided in Table 8.

Table 8

SI No	Compound No	Structure	Mean % remaining at 2 hrs in human Plasma
1	9		16.9

2	123		48.5
3	73		10.3
4	179		20.6
5	238		98.1
6	241		112.8
7	330a		45.8
8	253		67.2
9	211		110.3
10	139		55.50

11	215		80.70
12	219		73.9
13	Proprantheline (Control)		1.7

Plasma stability assay of synthesized compounds after 2 hours revealed that compounds 9, 73 and 179 have lower plasma stability whereas, compounds 123, 238, 241, 330a, 253, 211, 139, 215 and 219 have good plasma stability with respect to the control compound Proprantheline.

- 5 Plasma stability assay provides insight into the compound stability in plasma and the percentage concentration of the compounds remaining after certain time interval. The assay provides information regarding compound degradation in plasma.

Example 294

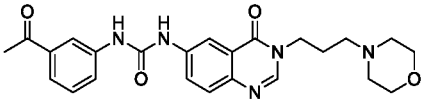
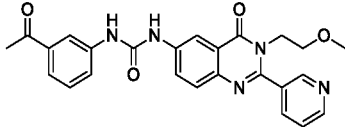
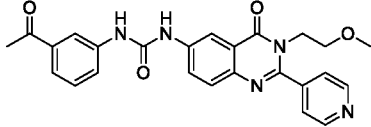
10 *In-Vitro* Evaluation of Metabolic Stability using Human Liver Microsomes (Human Liver Microsomal Stability-HLM)

- 1mM stock solution of test compound was prepared in DMSO and diluted with Acetonitrile: Water (1:1) to get a 100 μ M working concentration. 100 mL of Milli Q water was added to K₂HPO₄ (1.398 g) and KH₂PO₄ (0.27g) to get final pH 7.4 solution of potassium phosphate buffer. 3.333mg/mL microsomal suspension was prepared by diluting 499.95 μ L of 20mg/mL microsomal stock to 2500.05 μ L with buffer. 532.5 μ L of 16mM NADPH stock was added to 2467.5 μ L of potassium phosphate buffer to get 2.84mM working stock. 75 μ L of 3.333mg/mL working stock of liver microsomes and 85 μ L of buffer was added to 2.5 μ L of test compounds (100 μ M). The above mixture was pre incubated for 15 minutes at 37 °C. After pre incubation, 32.5 μ L of the mixture was added to 17.5 μ L of buffer, this was incubated for 60 minutes at 37 °C [60 min Without Cofactor (NADPH)]. 16.25 μ L of the pre incubated mixture and 8.75 μ L of cofactor was added to 150 μ L of acetonitrile containing internal

standard [0 min Sample]. 62 μ L of cofactor was added to remaining pre incubation mixture [Incubation mixture]. 25 μ L of incubation mixture at 0 ,5, 15, 30, 60 min and 60 min without cofactor were precipitated with 150 μ L of acetonitrile containing internal standard, vortexed and centrifuged at 4000 rpm at4 $^{\circ}$ C for 20 minutes. 120 μ L of supernatant was diluted with
 5 120 μ L of water and analyzed by LC-MS/MS [sample preparation]. The results obtained for the compounds is provided in Table 9.

Table 9

Sl No	Compound No	Structure	% QH (Well stirred model)
1	9		21.26
2	238		83.5
3	241		80.6
4	330a		26.0
5	253		29.8
6	211		38.8

7	139		35.3
8	215		15.5
9	219		24.5
10	Verapamil HCl (Control)		81.6

Classifications criteria: %QH; <30: Low Clearance 30-70: Medium Clearance >70: High Clearance

In-Vitro evaluation of metabolic stability using Human Liver Microsomes (HLM) study revealed that compounds 9, 330a, 253, 215, and 219 have lower clearance. Compounds 211, and 139 have medium clearance and compounds 238, and 241 have higher clearance with respect to the control compound verapamil HCl. The liver microsomal stability assay primarily provides insight into the Phase I metabolism or biotransformation of the compounds.

Figure 11 describes compound 238a (HCl salt of compound 238) co-crystallized with acetone as solvent. CCDC deposition no 1988445.

Example 295

Basal oxygen consumption rate (OCR) determination by Seahorse.

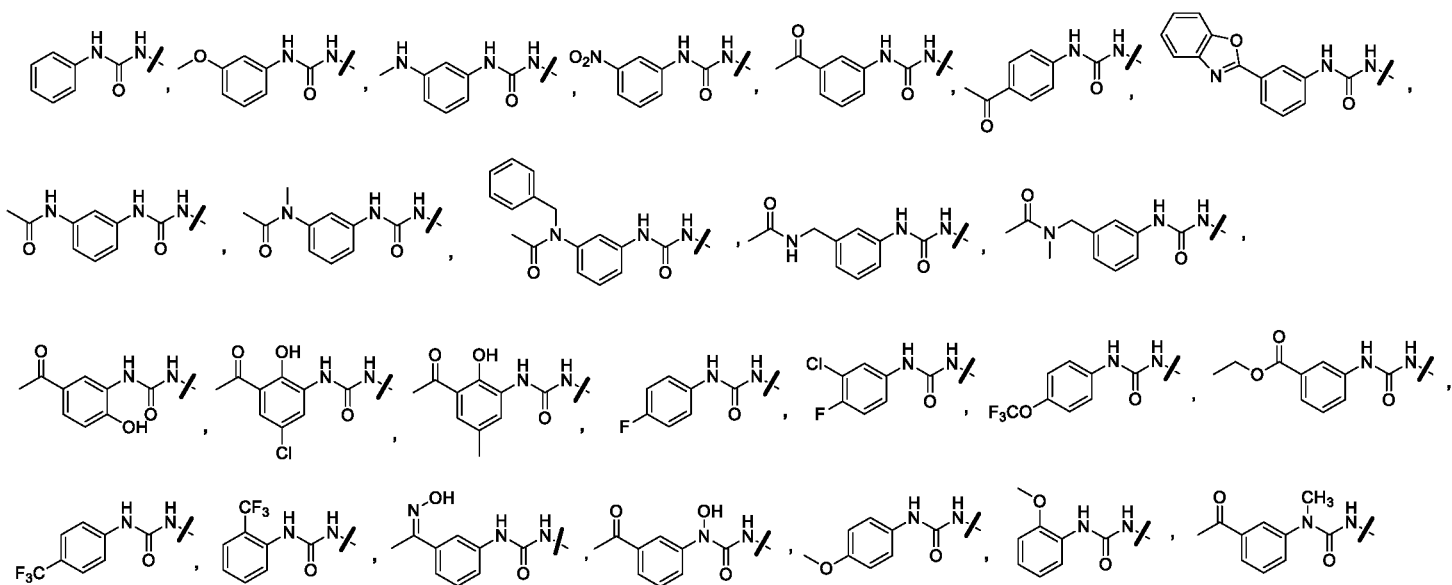
HepG2 cells were plated in Seahorse cell culture microplates (24 well). Cells were treated with 5 μ M of compounds 9, 107, 238 and 238a for 24 hours. The calibrator plate was dipped in the calibrator solution and incubated overnight at 37°C in a non-CO₂ incubator. The next day, cells were washed with Agilent Seahorse XF Base Medium, Minimal DMEM twice, making sure to leave at least 50 μ l of media in the wells and incubated for 1 hour at 37°C in a

non-CO₂ incubator. Following this, oxygen consumption rate was measured in the Seahorse instrument. Figure 12 illustrates basal oxygen consumption rate of compounds 9, 107, 238a, and 238. The results showed an increase in the basal OCR values in compound treatments with respect to control which signifies an increase in the basal respiration rate of the cells.

ADVANTAGES OF THE INVENTION

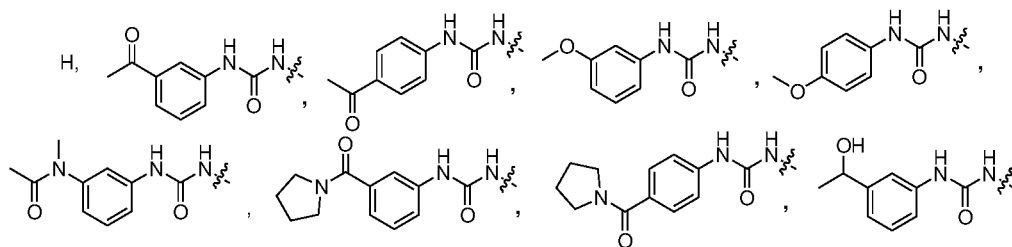
The compounds of the present invention having structure I have several advantages including:

1. The compounds having structure I are capable of modulating COP1 Ubiquitin Ligase enzyme through stabilization in hepatocytes.
2. The compounds having structure I can reduce the level of triglycerides in hepatocytes.
3. The compounds having structure I can be used in a clinical application for treating conditions involving Non-Alcoholic Fatty Liver Disease (NAFLD).

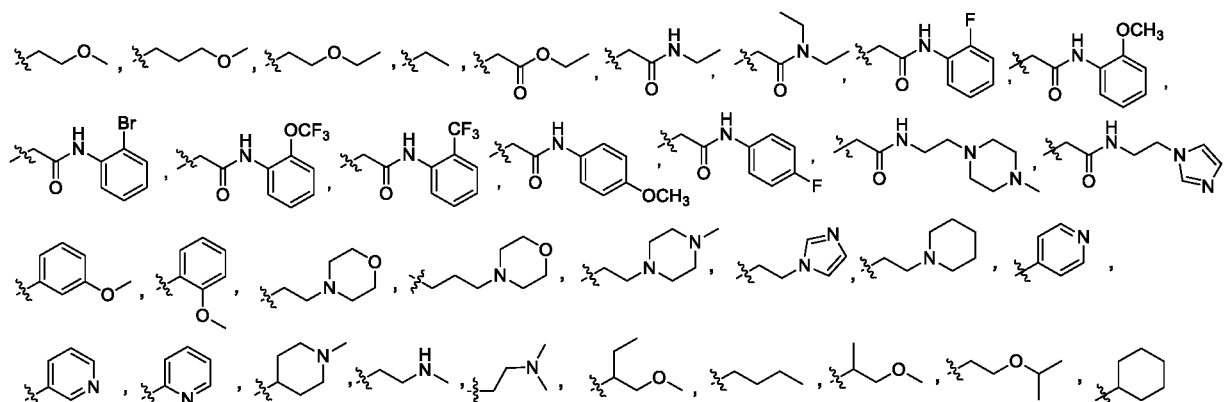


5

R₄ is independently selected from the group consisting of:



R₅ is independently selected from the group consisting of:



10

2. The compound having structure I as claimed in claim 1 selected from the group consisting of:

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-phenylurea (5),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-methoxyphenyl)urea (6),

5 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(methylamino)phenyl)urea (7),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-nitrophenyl)urea (8),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (9),

1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (10),

10 1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (11),

methyl 4-methoxy-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (12),

1-(3-ethylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (13),

15 1-(3-benzoylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (14),

N-cyclohexyl-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamide (15),

methyl 2-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamido)-3-methylbutanoate (16),

20 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)-N,N-dimethylbenzamide (17),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (18),

25 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(morpholine-4-carbonyl)phenyl)urea (19),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (20),

1-(3-(benzo[d]oxazol-2-yl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (21),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (22),

5 N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)-N-methylacetamide (23),

N-benzyl-N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (24),

10 N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)acetamide (25),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)-N-methylacetamide (26),

1-(5-acetyl-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (32),

15 1-(3-acetyl-5-chloro-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (33),

1-(3-acetyl-2-hydroxy-5-methylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (34),

1-(4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (35),

20 1-(3-chloro-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (36),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea (37),

25 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethyl)phenyl)urea (38),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-(trifluoromethyl)phenyl)urea (39),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-methoxyphenyl)urea (40),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-methoxyphenyl)urea (41),

- ethyl 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (42),
3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoic acid (42a),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-phenyl-3,4-dihydroquinazolin-6-yl)urea (45),
- 5 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (47),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (49),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (51),
- 10 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (53),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(6-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (55),
- 15 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(2-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (57),
tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (59),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(1,2,3,6-tetrahydropyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (60),
- 20 tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)piperidine-1-carboxylate (61),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (62),
- 25 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (64),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea (66),

- 1-(3-acetylphenyl)-3-(5-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (68),
- 1-(3-acetylphenyl)-3-(5-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (70),
- 5 1-(3-acetylphenyl)-3-(5-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (72),
- 1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (73),
- ethyl 2-(6-(3-(3-chloro-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (83),
- 10 ethyl 2-(4-oxo-6-(3-(4-(trifluoromethoxy)phenyl)ureido)quinazolin-3(4H)-yl)acetate (84),
- ethyl 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (85),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetic acid (85a),
- 1-(3-acetylphenyl)-3-(3-(3-methoxypropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (89),
- 1-(3-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (93),
- 15 1-(4-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (94),
- 1-(3-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (98),
- 1-(4-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (99),
- 1-(3-acetylphenyl)-3-(3-(3-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (103),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (107),
- 20 1-(3-acetylphenyl)-3-(2-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (111),
- 1-(3-acetylphenyl)-3-(2-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (115),
- 25 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (119),
- 1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (123),

- 1-(3-acetylphenyl)-3-(2-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (127),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (131),
- 1-(3-acetylphenyl)-3-(3-(2-morpholinoethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (135),
- 1-(3-acetylphenyl)-3-(3-(3-morpholinopropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (139),
- 1-(3-acetylphenyl)-3-(3-(2-(dimethylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (143),
- 1-(3-acetylphenyl)-3-(4-oxo-3-(2-(piperidin-1-yl)ethyl)-3,4-dihydroquinazolin-6-yl)urea (147),
- 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (151),
- 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (155),
- 1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (159),
- 1-(3-acetylphenyl)-3-(3-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (163),
- 1-(3-acetylphenyl)-3-(3-(2-(methylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (167),
- 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (171),
- 1-(3-acetylphenyl)-3-(3-butyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (175),
- 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (179),
- 1-(3-acetylphenyl)-3-(3-(2-isopropoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (183),
- 1-(3-acetylphenyl)-3-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (187),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (192),
- 1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (193),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-methoxyphenyl)urea (194),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-methoxyphenyl)urea (195),

5 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (196),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (197),

10 1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (198),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)ureido)phenyl)-N-methylacetamide (199),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea (203),

15 1-(3-acetylphenyl)-3-(2-(3-bromo-4-methoxyphenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (207),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (211),

20 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (215),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (219),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrazin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (223),

25 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methyl-1H-pyrazol-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (227),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrrolidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (232),

- 1-(3-acetylphenyl)-3-(2-((dimethylamino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (235),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (238),
- 5 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholinomethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (241),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (244),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-ethylacetamide (247),
- 10 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N,N-diethylacetamide (250),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (253),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-methoxyphenyl)acetamide (256),
- 15 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-bromophenyl)acetamide (259),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide (262),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-
- 20 (trifluoromethyl)phenyl)acetamide (265),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-methoxyphenyl)acetamide (268),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-fluorophenyl)acetamide (271),
- 25 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide (274),
- N-(2-(1H-imidazol-1-yl)ethyl)-2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetamide (277),

- 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (281),
- 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (285),
- 5 1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (289),
- 1-(3-acetylphenyl)-3-(2-cyclohexyl-5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (292),
- 10 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (295),
- tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (299),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (300),
- 15 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (304),
- 1-(3-acetylphenyl)-3-(2-(1-isopropylpiperidin-4-yl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (307),
- 20 1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (308),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea (309),
- 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-hydroxyurea (310),
- 25 1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea (311),
- 1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (312),

- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-1-methylurea (313),
- 2-(6-(3-(3-acetylphenyl)-3-hydroxyureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (314),
- 5 2-(6-(3-(3-acetylphenyl)-3-methylureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (315),
- 1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (316),
- 1-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (317),
- 10 1-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (318),
- 1-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (319),
- 15 N-(2-fluorophenyl)-2-(4-oxo-6-(3-(3-(2,2,2-trifluoroacetyl)phenyl)ureido)quinazolin-3(4H)-yl)acetamide (320),
- 1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (321),
- 1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (322),
- 20 1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (323),
- 1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (324),
- 25 2-(6-(3-(3-acetyl-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (325),
- 1-(3-acetylphenyl)-3-(2-(fluoro(piperidin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (330),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidine-1-carbonyl)-3,4-dihydroquinazolin-6-yl)urea (330a),

1-(3-acetylphenyl)-3-(2-(fluoro(4-methylpiperazin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333),

5 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333 a),

1-(3-acetylphenyl)-3-(2-(fluoro(morpholino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (336),

10 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholine-4-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (336 a),

1-(3-acetylphenyl)-3-(3-morpholino-4-oxo-3,4-dihydroquinazolin-6-yl)urea (340),

(Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (341),

15 (Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (342),

(Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (343), and

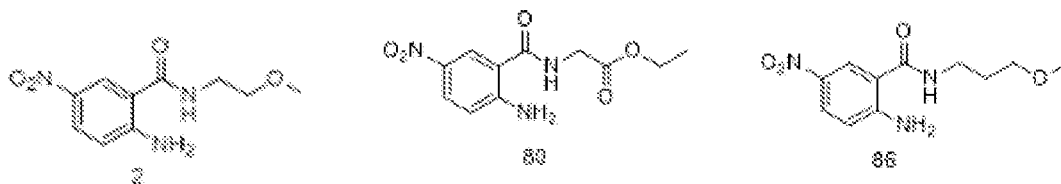
1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (345).

20 3. A process for preparation of the compound having structure I as claimed in claim 1, the process steps comprising:

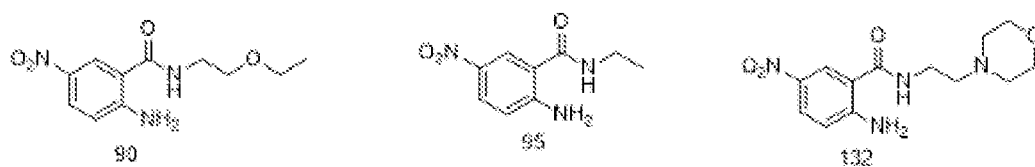
(i) reacting 2-amino-5-nitrobenzoic acid (**compound 1**) with an aliphatic or an aromatic amine selected from the group consisting of 2-methoxyethylamine, glycineethyl ester hydrochloride, 3-methoxypropylamine, 2-ethoxyethylamine, 25 ethylamine 2M in THF, 4-(2-aminoethyl)morpholine, 3-(4-morpholinyl)propylamine, N,N-dimethylethylenediamine, 1-(2-aminoethyl)piperidine, 4-amino-1-methylpiperidine, N-methylethylenediamine, 2-amino-1-methoxybutane, 1-butylamine, 1-methoxy-2-propylamine, 2-aminoethyl isopropyl ether, cyclohexylamine, 4-aminomorpholine, m-anisidine, o-anisidine, 30 4-aminopyridine, 3-aminopyridine, and 2-aminopyridine in presence of

HATU/DMF followed by TEA as a base at room temperature for 1-3 hours to obtain an amide compound selected from the group consisting of **2**, **80**, **86**, **90**, **95**, **132**, **136**, **140**, **144**, **160**, **164**, **168**, **172**, **176**, **180**, **184**, **337**, **100**, **128**, **148**, **152**, and **156**;

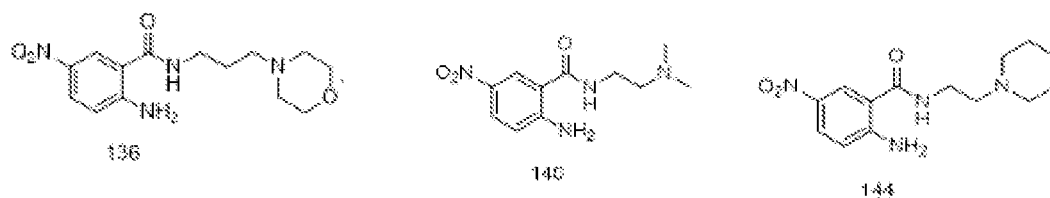
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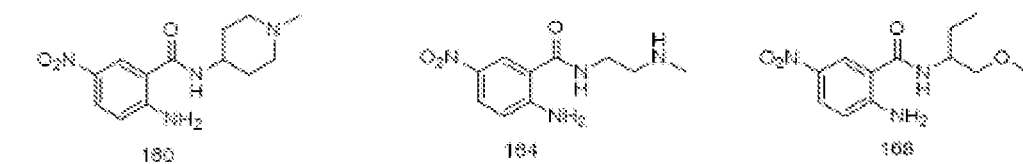
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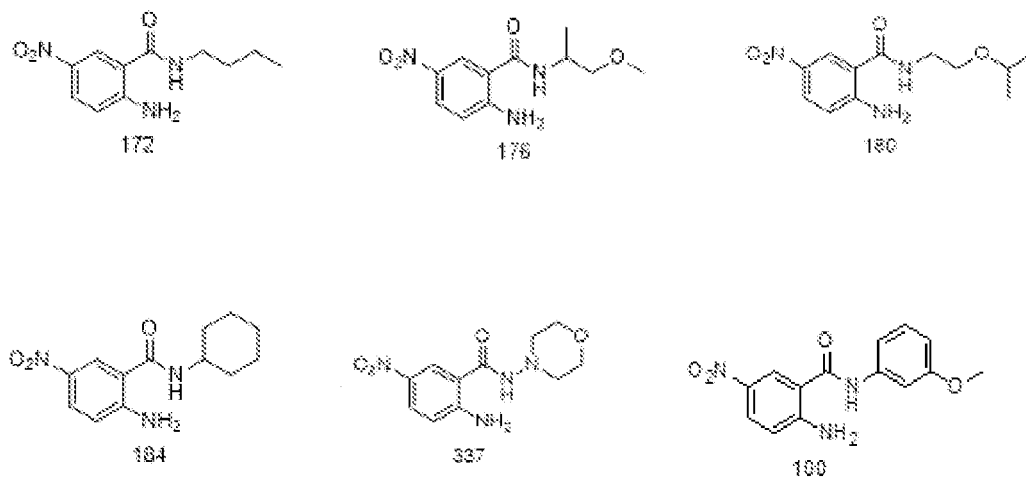
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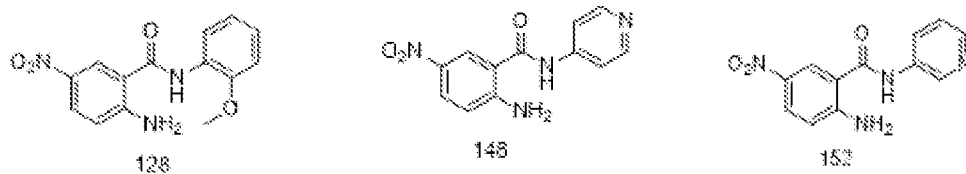


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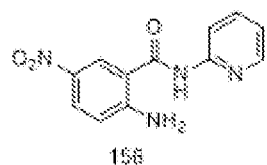


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- (ii) separately, reacting 2-amino-4-nitrobenzoic acid (**compound 188**) with 2-methoxyethylamine in presence of HATU/ DMF followed by TEA as a base at room temperature for 1 hour to obtain a compound **189**;

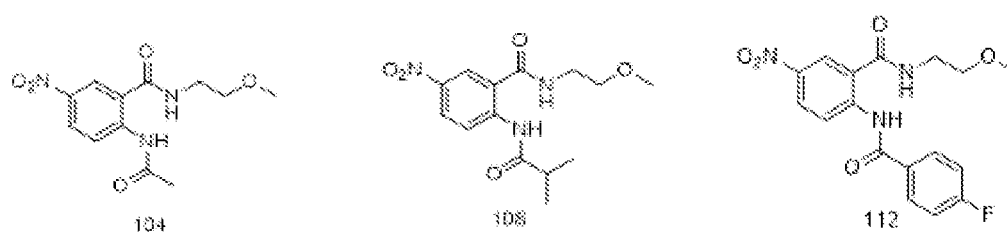
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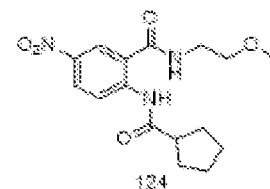
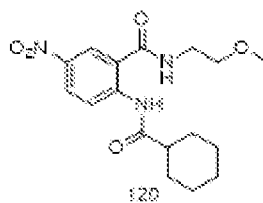
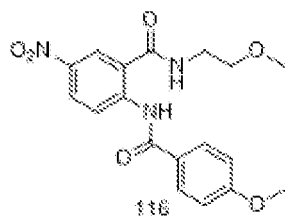
- (iii) adding an acid chloride selected from the group consisting of acetyl chloride, isopropyl chloride, 4-fluorobenzoyl chloride, 4-methoxybenzoyl chloride, cyclohexanecarbonyl chloride, cyclopentanecarbonyl chloride, 4-(trifluoromethyl)benzoyl chloride, 3-Bromo-4-methoxybenzoyl chloride, Picolinoyl chloride, Nicotinoyl chloride, Isonicotinoyl chloride, Pyrazinecarbonyl chloride, 1-methyl-1H-pyrazole-4-carbonyl chloride, and 2-chloroacetyl chloride to compound **2** obtained in step (i) in DCM at a temperature range from 0 °C to room temperature for 1-8 hours to obtain a compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, and 228**;

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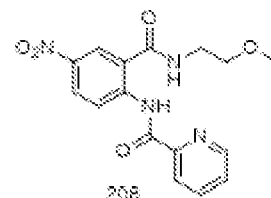
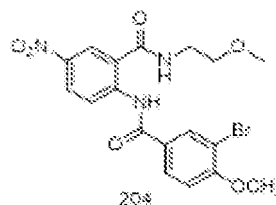
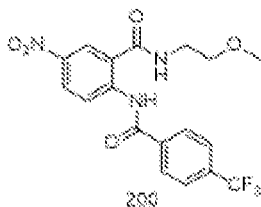
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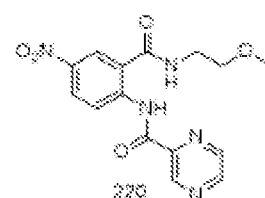
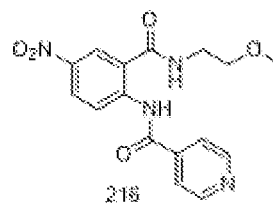
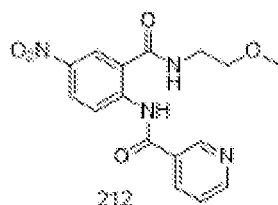
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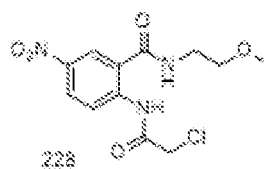
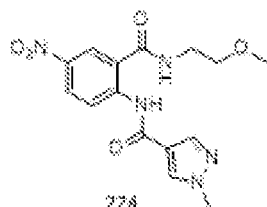
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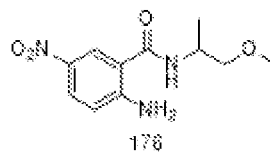
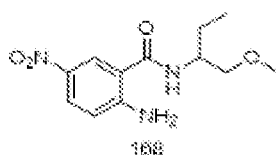
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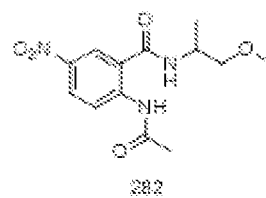
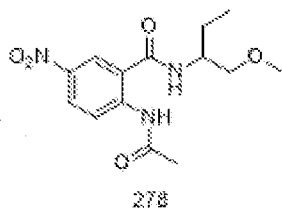


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- (iv) acetylating a compound selected from the group consisting of **168**, and **176** obtained in step (i) using acetyl chloride and triethylamine (TEA) as a base in DCM at a temperature range of 0 °C to room temperature for 8 hours to obtain a compound selected from the group consisting of **278** and **282**;

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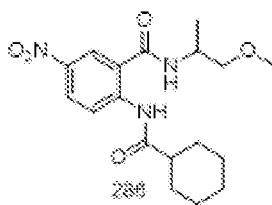




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- (v) alternately, adding cyclohexanecarbonyl chloride to compound **176** obtained in step (i) to obtain a compound **286**;

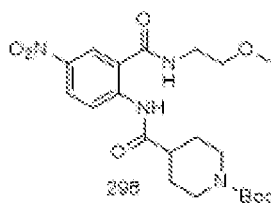
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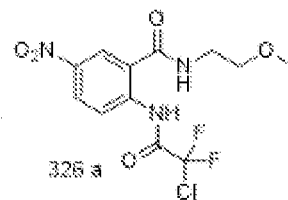
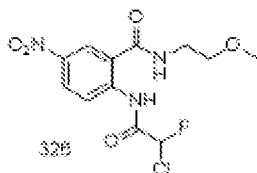
- (vi) alternately, adding tert-butyl 4-(chlorocarbonyl)piperidine-1-carboxylate to compound **2** obtained in step (i) to obtain a compound **296**;

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- (vii) alternately, treating compound **2** obtained in step (i) with 2-chloro-2-fluoroacetic acid or 2-chloro-2-difluoroacetic acid along with POCl₃ in pyridine solvent to obtain a compound selected from the group consisting of **326** and **326a**;

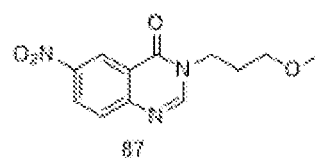
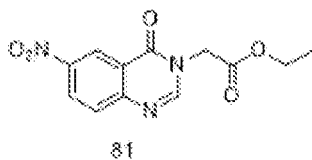
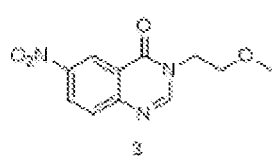


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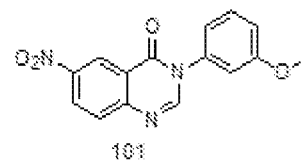
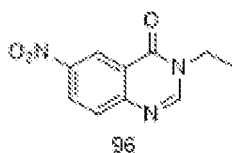
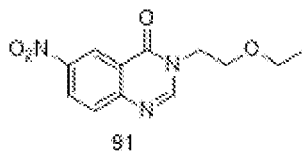
- (viii) cyclizing the compound selected from the group consisting of **2**, **80**, **86**, **90**, **95**, **100**, **128**, **132**, **136**, **140**, **144**, **148**, **152**, **156**, **160**, **164**, **168**, **172**, **176**, **180**, **184**, **189**, and **337** obtained in step (i) and (ii) using a cyclizing agent selected from trimethylorthoformate or triethylorthoformate at 100 °C for 12-16 hours to obtain

a compound selected from the group consisting of **3**, **81**, **87**, **91**, **96**, **101**, **129**, **133**, **137**, **141**, **145**, **149**, **153**, **157**, **161**, **165**, **169**, **173**, **177**, **181**, **185**, **190** and **338**;

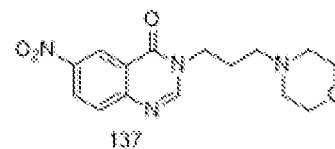
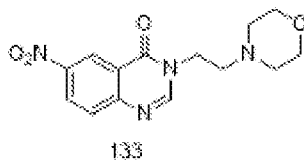
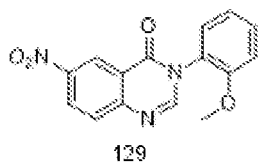
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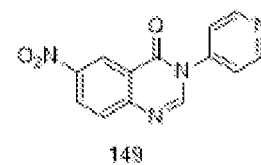
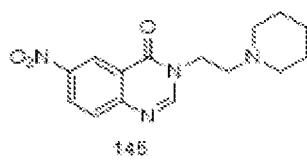
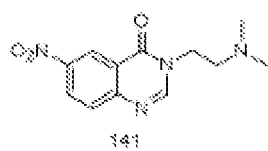
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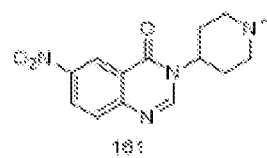
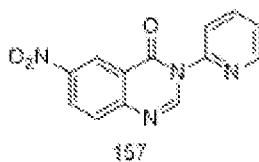
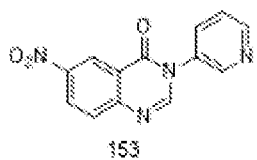
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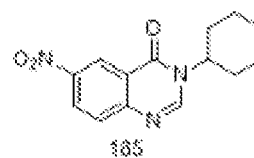
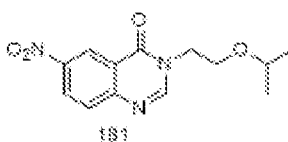
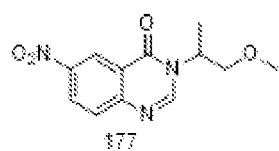
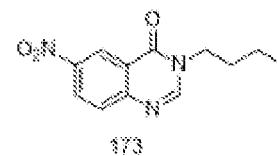
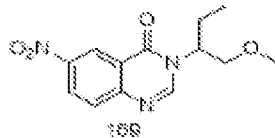
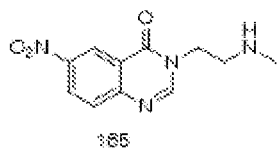
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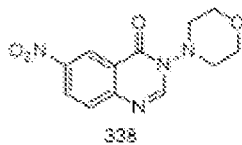
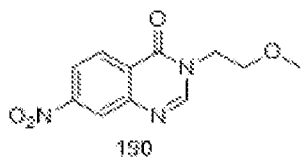


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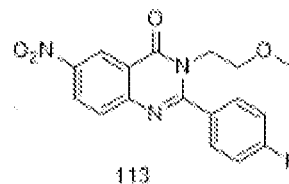
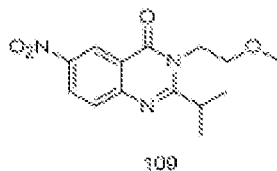
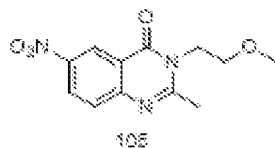




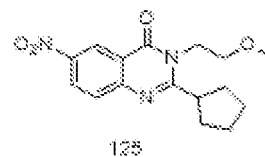
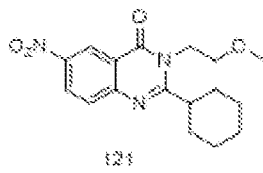
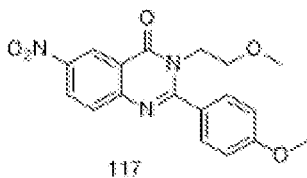
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- (ix) cyclizing the compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, 228, 278, 282, 286, 296, 326,** and **326a** obtained in step (iii), (iv), (v), (vi) and (vii) using a cyclizing agent $ZnCl_2$ and hexamethyldisilazane (HMDS) in DMF at 100 °C for 12 -16 hours to obtain a compound selected from the group consisting of **105, 109, 113, 117, 121, 125, 201, 205, 209, 213, 217, 221, 225, 229, 279, 283, 287, 297, 327** and **327a**;

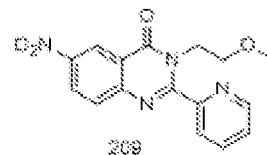
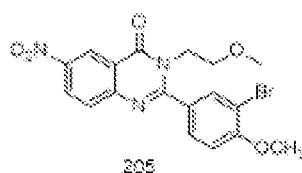
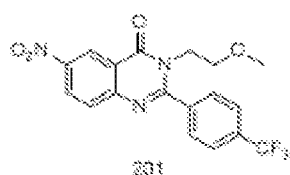
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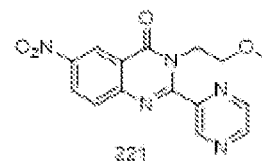
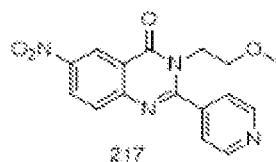
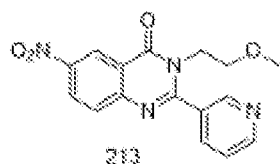
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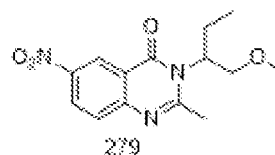
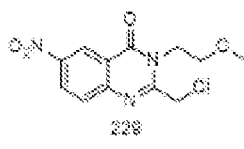
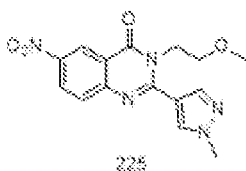
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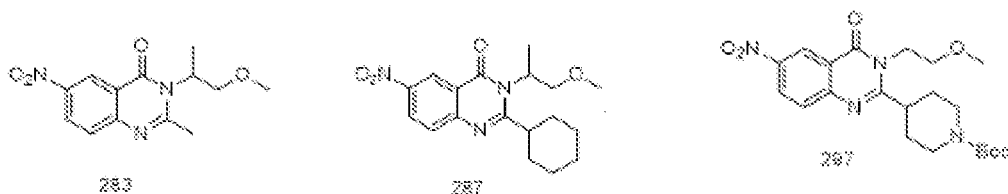
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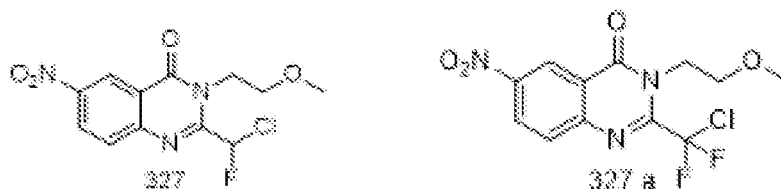
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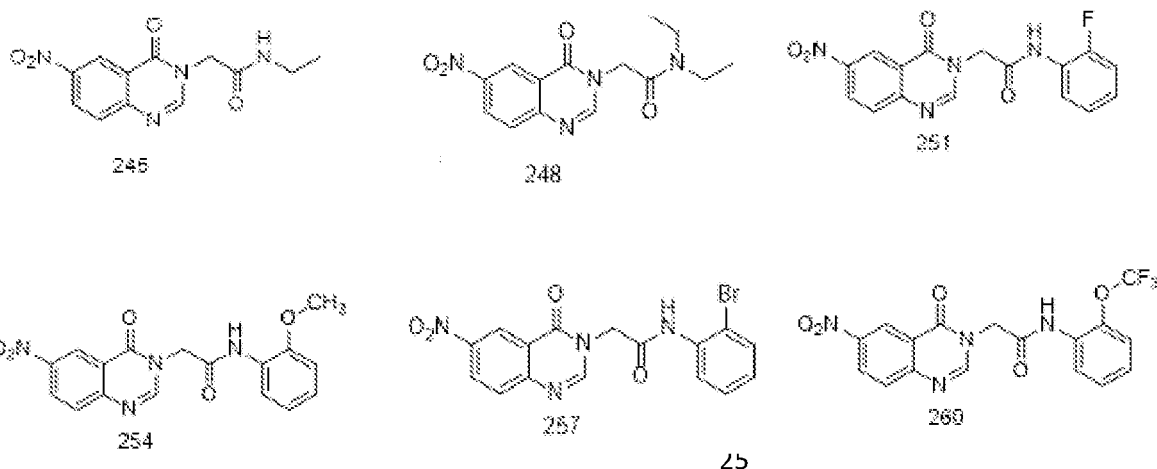
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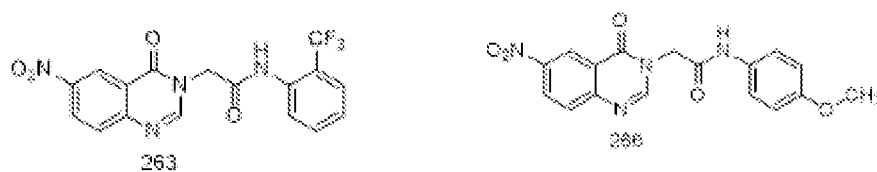
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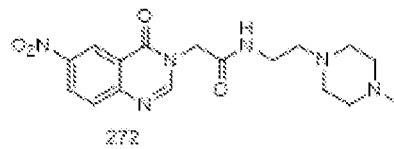
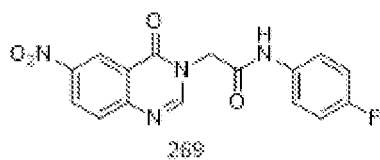
- (x) reacting the compound **81** obtained in step (viii) with an amine selected from the group consisting of ethyl amine, diethylamine, 2-fluoroaniline, *o*-anisidine, 2-bromoaniline, 2-(trifluoromethoxy)aniline, 2-(trifluoromethyl)aniline, *p*-anisidine, 4-fluoroaniline, 1-(2-aminoethyl)-4-methylpiperazine, and 1*H*-Imidazole-1-ethanamine in presence of anhydrous AlCl₃ in toluene at a temperature range from room temperature to 110 °C to obtain a compound selected from the group consisting of **245**, **248**, **251**, **254**, **257**, **260**, **263**, **266**, **269**, **272** and **275**;

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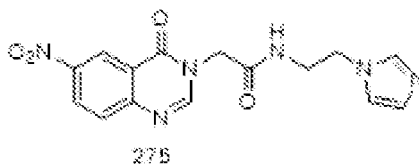


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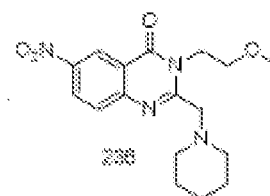
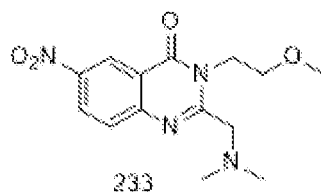
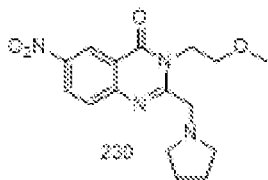
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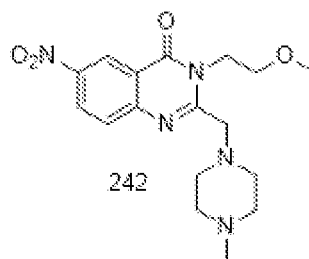
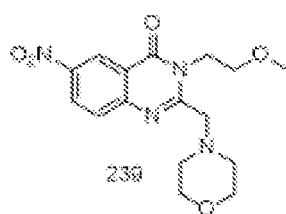
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- (xi) reacting the compound **229** obtained in step (ix) with an amine selected from the group consisting of pyrrolidine, dimethylamine, piperidine, morpholine, and 1-methylpiperazine in toluene at 100 °C for 2 hours to obtain a compound selected from the group consisting of **230**, **233**, **236**, **239**, and **242**;

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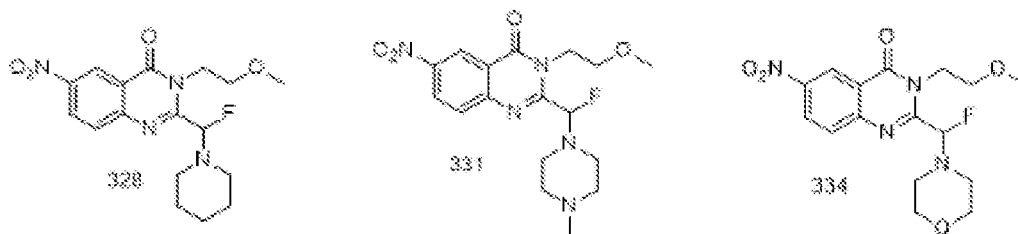
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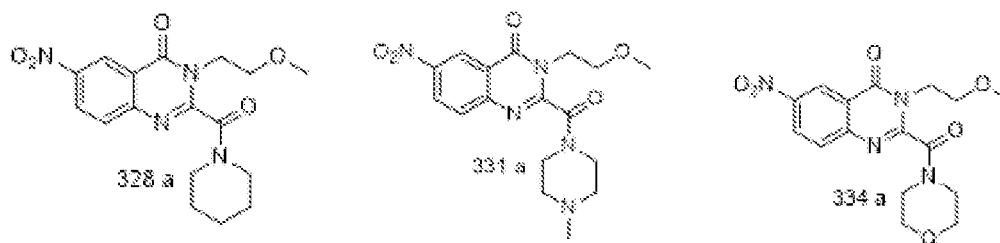
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- (xii) reacting the compound **327** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of toluene to obtain a compound selected from the group consisting of **328**, **331**, and **334**;

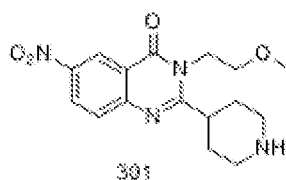
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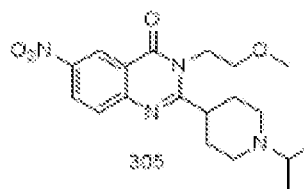
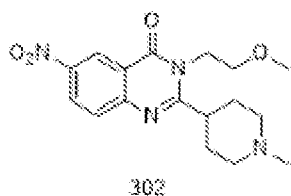
- (xiii) reacting the compound **327a** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of a solvent selected from the group consisting of toluene, DMF, and THF in absence or presence of a base selected from K_2CO_3 , or N,N-diethylaniline to obtain a compound selected from the group consisting of **328a**, **331a**, and **334a**;
- 10



- (xiv) separately reacting the compound **297** obtained in step (ix) with trifluoroacetic acid (TFA) in DCM at a temperature range of 0 °C to room temperature for 2 hours to obtain a compound **301**;
- 20



- (xv) reacting the compound **301** obtained in step (xiv) with sodium hydride (NaH) in DMF at a temperature range of 0 °C to room temperature for 3 hours with methyl iodide and 2-chloropropane, respectively to obtain a compound selected from the group consisting of **302** and **305**;
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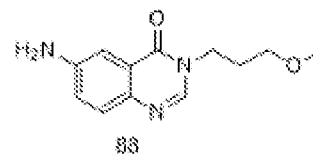
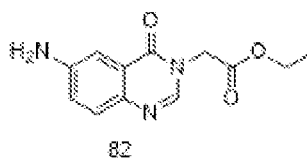
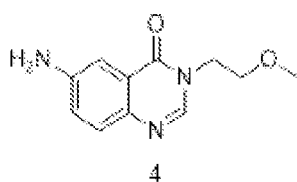
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(xvi) reducing the compound selected from the group consisting of **3, 81, 87, 91, 96, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 177, 181, 185, 190, 201, 209, 213, 217, 221, 225, 230, 233, 236, 239, 242, 245, 248, 251, 254, 260, 263, 266, 269, 272, 275, 279, 283, 287, 297, 302, 305, 328, 328a, 331, 331a, 334, 334a** and **338** obtained in steps (viii), (ix), (x), (xi), (xii), (xiii) and (xv) using Palladium-Charcoal (5% or 10 % wet) at room temperature for 3-5 hours in presence of H₂ to obtain an amine compound selected from the group consisting of **4, 82, 88, 92, 97, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 191, 202, 210, 214, 218, 222, 226, 231, 234, 237, 240, 243, 246, 249, 252, 255, 261, 264, 267, 270, 273, 276, 280, 284, 288, 298, 303, 306, 329, 329a, 332, 332a, 335, 335a, and 339**;

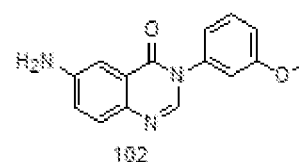
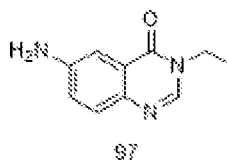
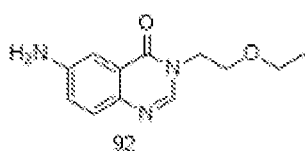
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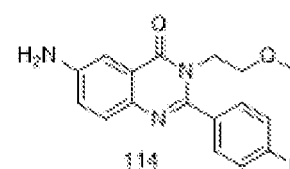
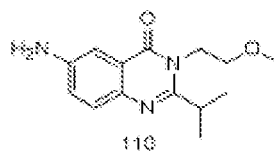
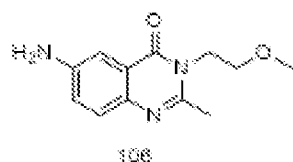
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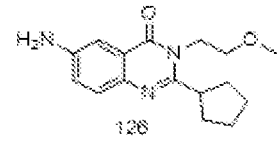
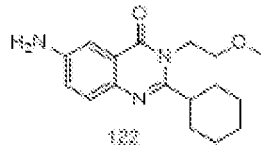
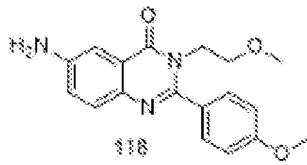


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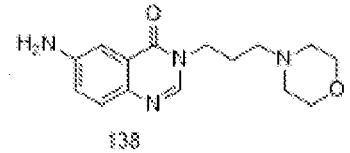
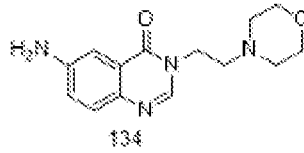
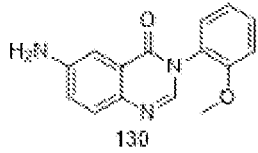


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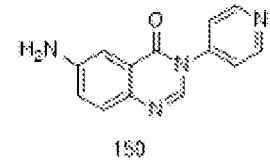
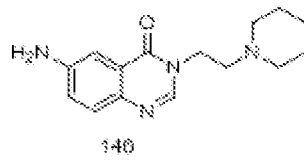
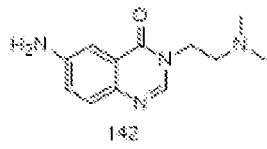




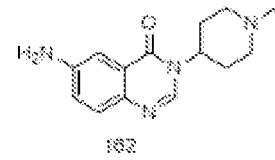
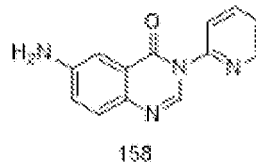
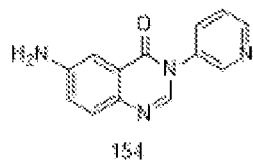
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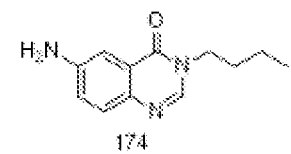
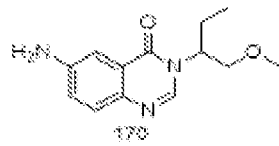
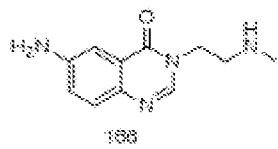
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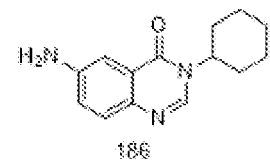
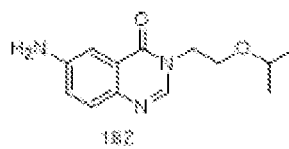
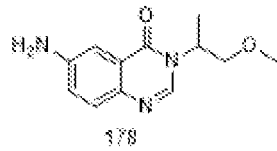
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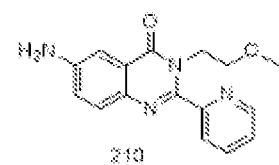
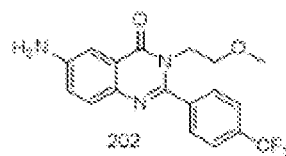
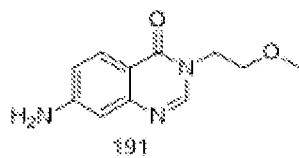
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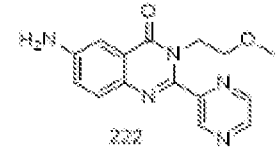
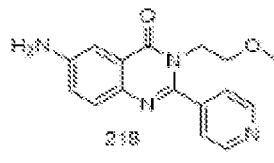
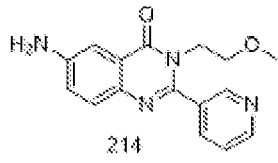
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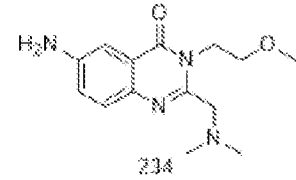
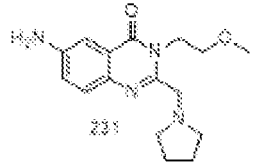
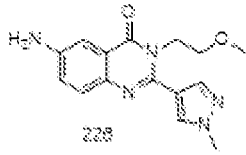
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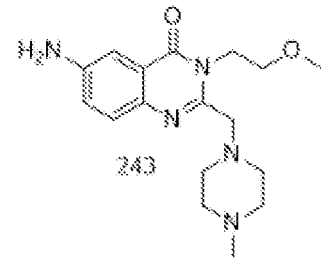
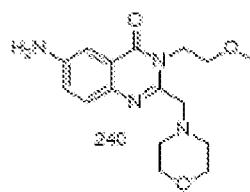
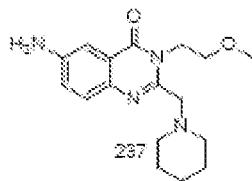
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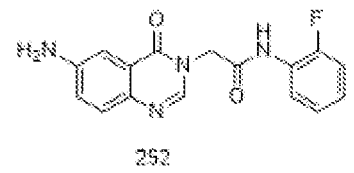
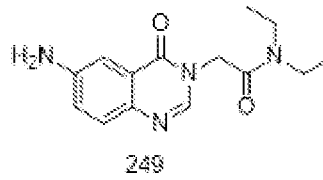
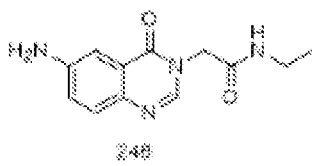
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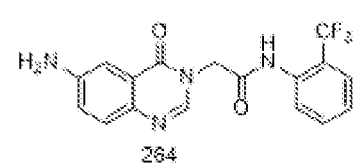
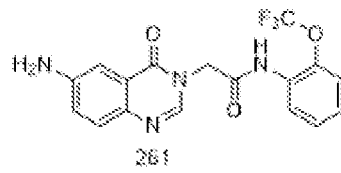
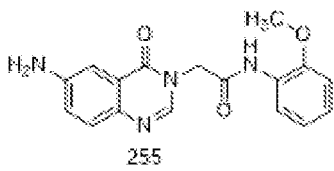
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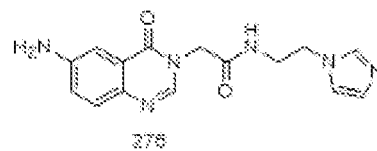
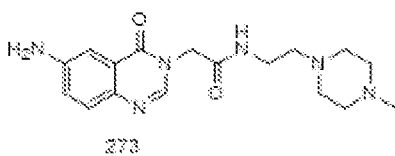
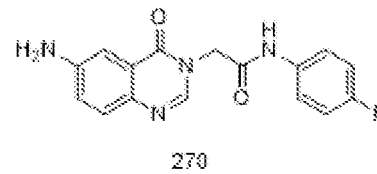
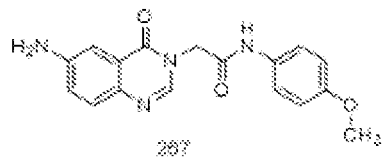
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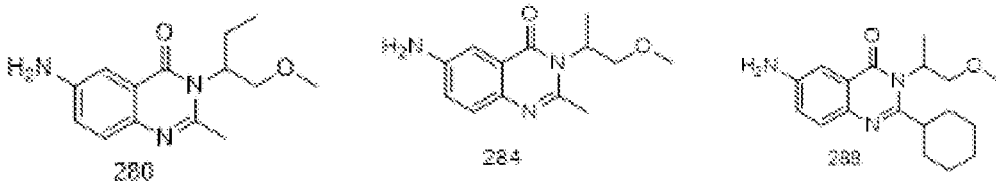
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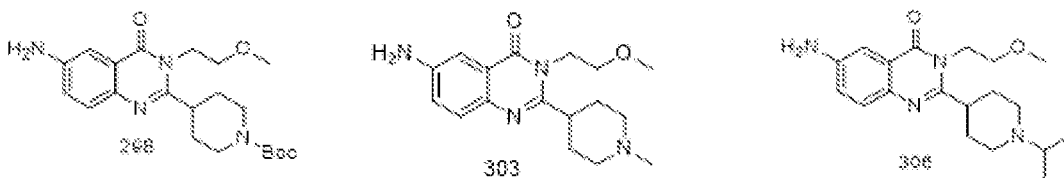
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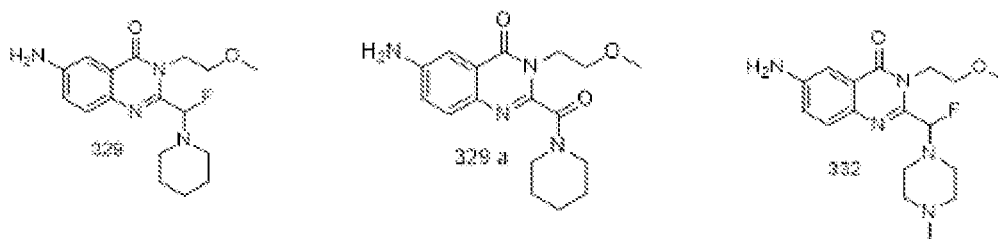
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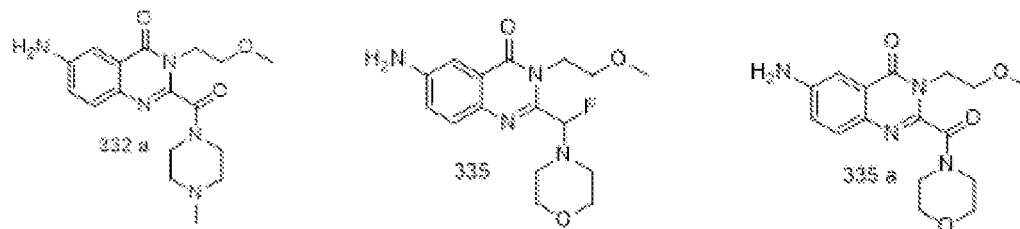
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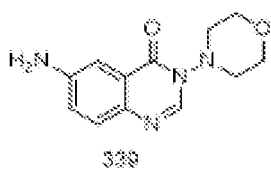
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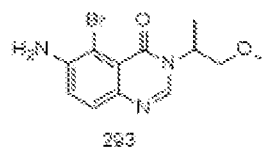
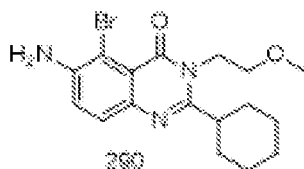
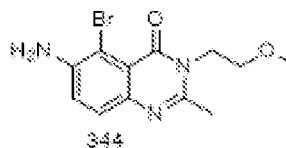
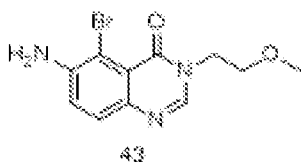


(xvii) reducing the compound selected from **205** or, **257** obtained in step (ix) and (x) using $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ to obtain the compound selected from **206** or **258**;

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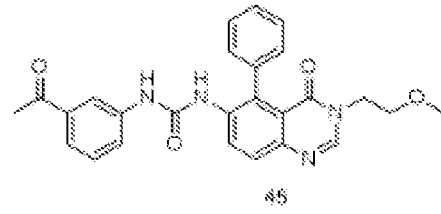
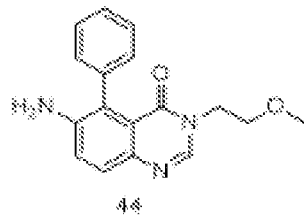


(xviii) brominating the compound selected from the group consisting of **4**, **106**, **122**, and **178** obtained in step (xvi) diluted in dichloromethane or chloroform solution by carrying out reaction in acetic acid medium followed by drop wise addition of liquid bromine on the compound at room temperature for 3-4 hours to obtain a compound selected from the group consisting of **43**, **344**, **290**, and **293**;

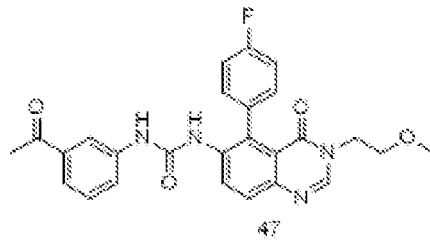
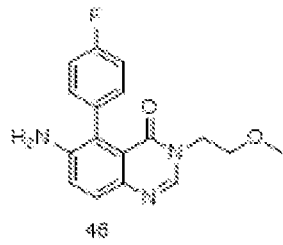


(xix) carrying out Suzuki reaction on a compound selected from the group consisting of **43**, **290**, and **293** obtained in step (xviii) by Pd₂(dba)₃ or Pd(PPh₃)₄ in presence of Cs₂CO₃ or 2M Na₂CO₃ solution in dioxane and X-Phos as a ligand at 100 °C over a period of 10-12 hours along with a boronic acid selected from the group consisting of benzenboronic acid, 4-fluorobenzeneboronic acid, pyridine-2-boronic acid, pyridine-3-boronic acid, pyridine-4-boronic acid, 6-methoxypyridine-3-boronic acid, 2-methoxypyridine-3-boronic acid, (1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)boronic acid, 4-methoxybenzeneboronic acid, 4-trifluoromethylbenzeneboronic acid, cyclohexylboronic acid, cyclopentyl boronic acid, and isopropylboronic acid to obtain a compound selected from the group consisting of **44**, **46**, **48**, **50**, **52**, **54**, **56**, **58**, **63**, **65**, **67**, **69**, **71**, **291**, and **294** which is treated with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 5-8 hours to obtain the compound having structure I selected from the group consisting of **45**, **47**, **49**, **51**, **53**, **55**, **57**, **59**, **64**, **66**, **68**, **70**, **72**, **292**, and **295**;

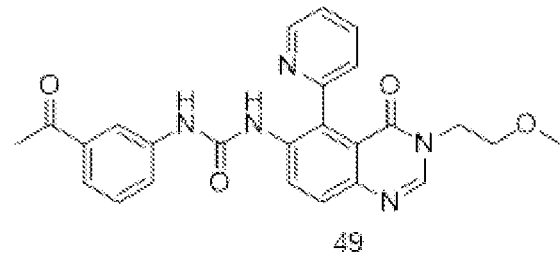
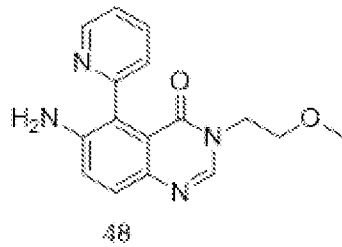
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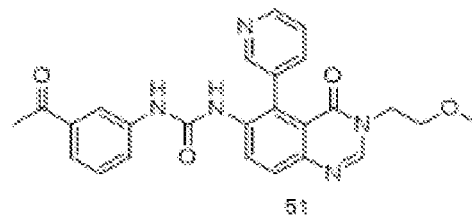
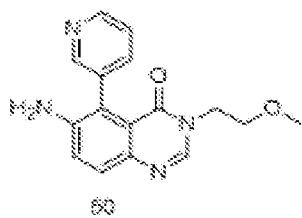
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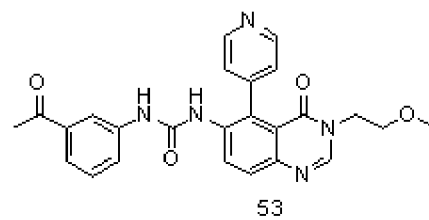
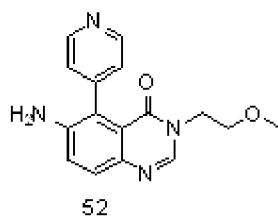
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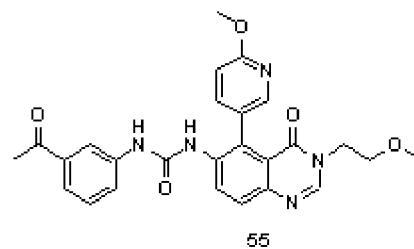
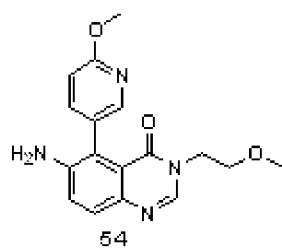
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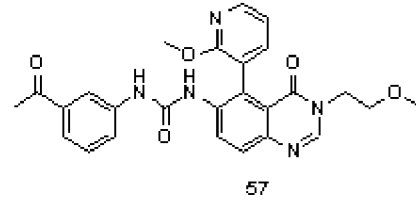
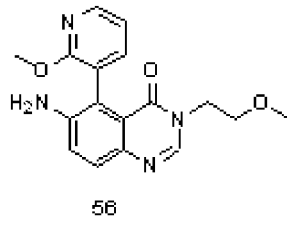
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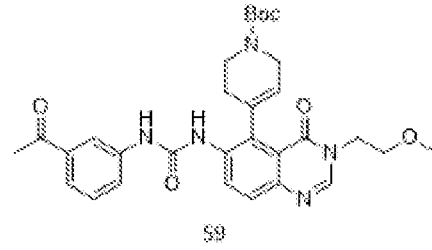
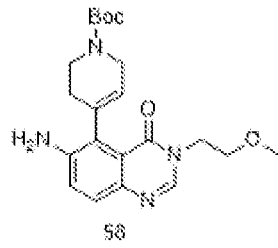
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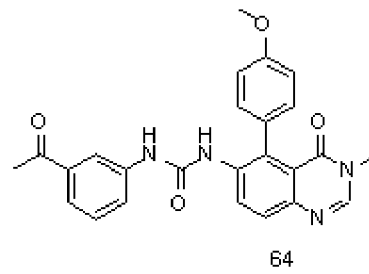
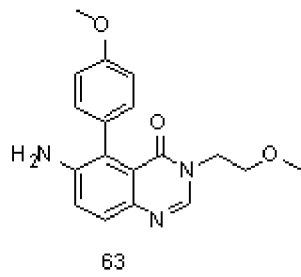
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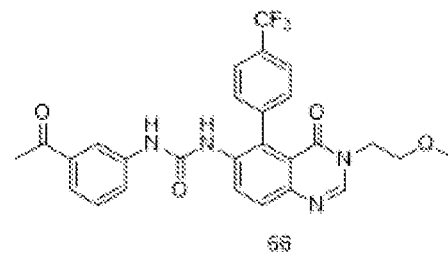
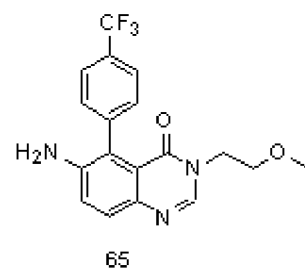
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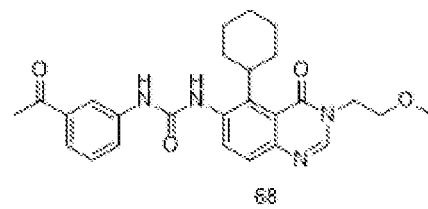
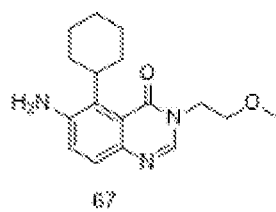


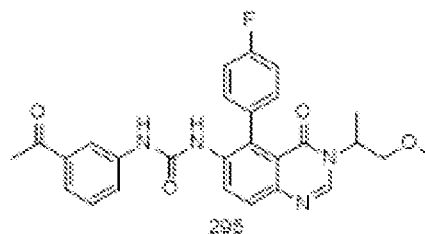
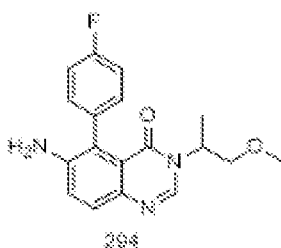
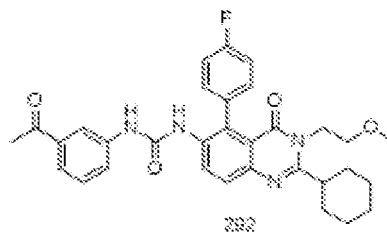
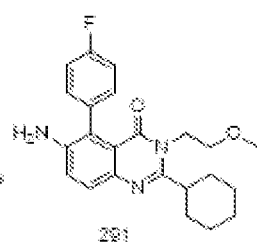
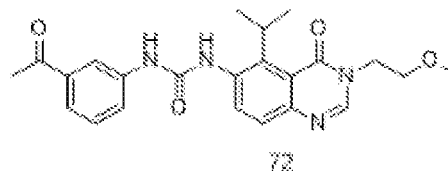
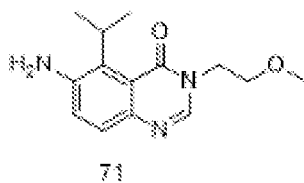
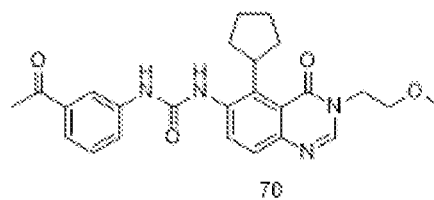
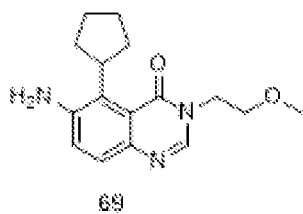
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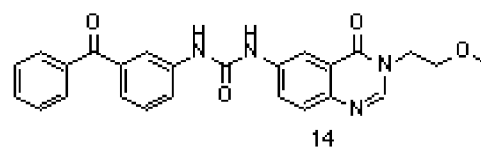
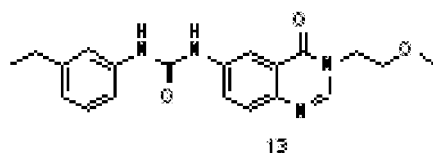
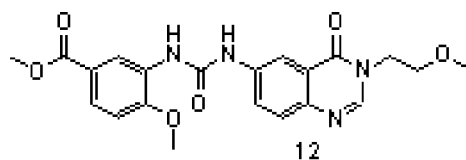
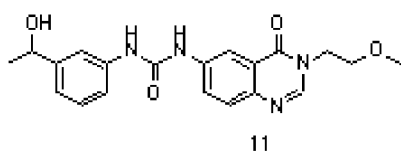
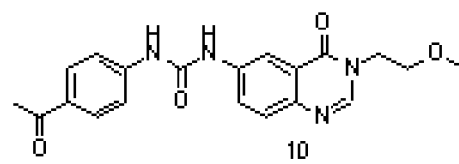
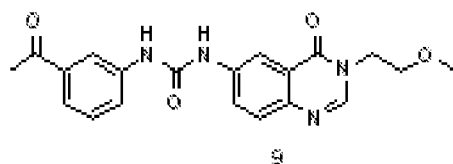
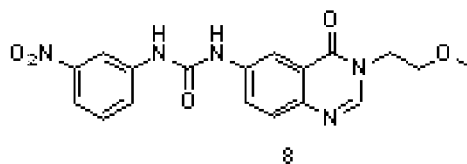
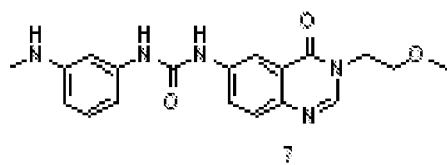
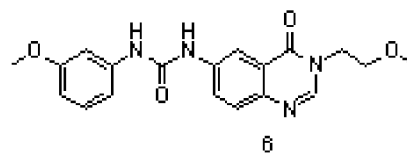
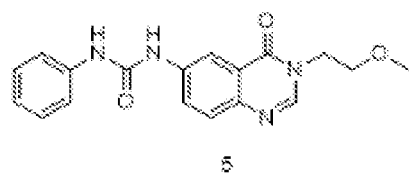


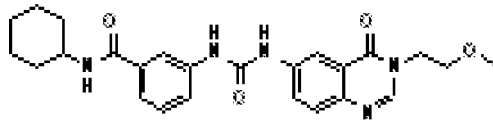
(xx) alternately, treating compound 4 obtained in step (xvi) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of aniline, m-anisidine, N1-methylbenzene-1,3-diamine, m-nitroaniline, 3-aminoacetophenone, 4-aminoacetophenone, 1-(3-aminophenyl)ethanol, methyl 3-amino-4-methoxybenzoate, 3-ethylaniline, 3'-aminobenzophenone, 3-amino-N-cyclohexylbenzamide, methyl 2-(3-aminobenzamido)-3-methylbutanoate, 3-amino-N,N-dimethylbenzamide, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 3-(benzo[d]oxazol-2-yl)aniline, N-(3-aminophenyl)acetamide, N-

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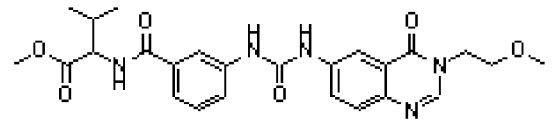
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(3-aminophenyl)-N-methylacetamide, N-(3-aminophenyl)-N-benzylacetamide, N-(3-aminobenzyl)acetamide, N-(3-aminobenzyl)-N-methylacetamide, dimethylamine, piperdine, 4-amino-1-methylpiperdine, 4-benzylpiperidine, 1-benzylpiperidin-4-amine, 1-(3-amino-4-hydroxyphenyl)ethanone, 1-(3-amino-5-chloro-2-hydroxyphenyl)ethanone, 1-(3-amino-2-hydroxy-5-methylphenyl)ethanone, and 1-(3-aminophenyl)-2,2,2-trifluoroethanol in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, and 34;**



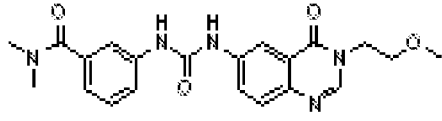


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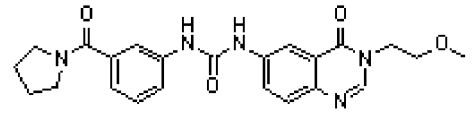


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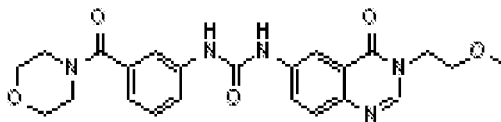


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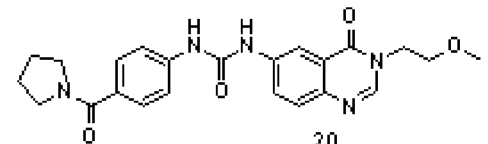


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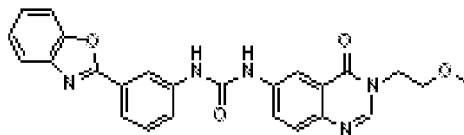
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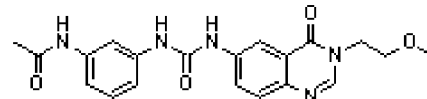
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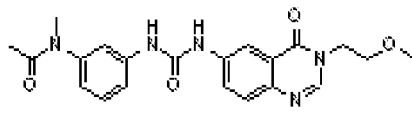


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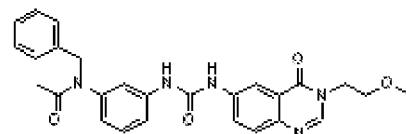


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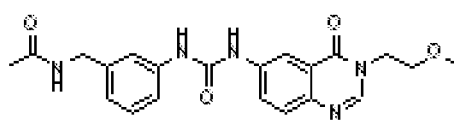


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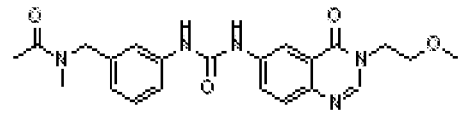


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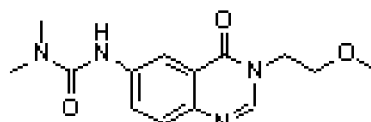


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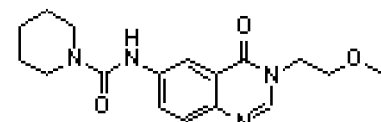


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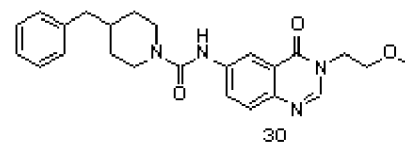
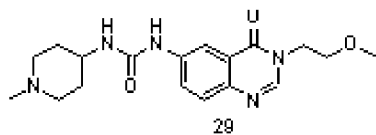
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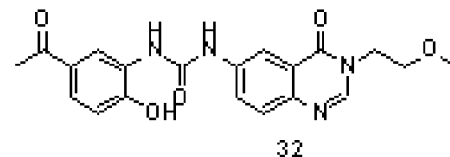
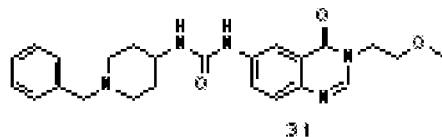
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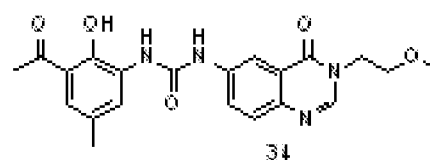
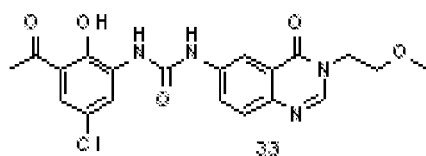
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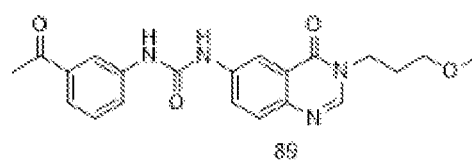
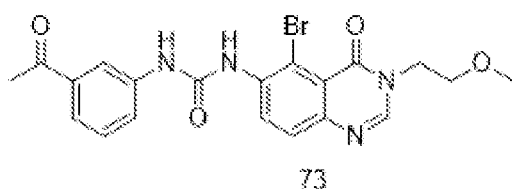


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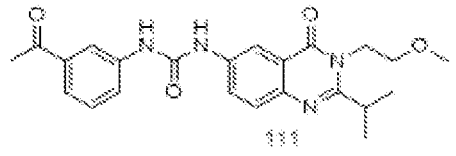
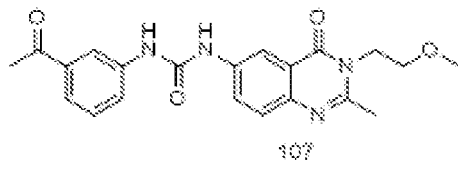
(xxi) alternately, treating the compound selected from the group consisting of **43, 88, 106, 110, 114, 118, 122, 126, 130, 138, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 191, 202, 206, 210, 214, 218, 222, 226, 231, 234, 237, 240, 243, 246, 249, 252, 255, 258, 261, 264, 267, 270, 273, 276, 280, 284, 288, 298, 303, 306, 329, 329a, 332, 332a, 335, 335a, 339, and 344** obtained in step (xvi),(xvii) and (xviii) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **73, 89, 107, 111, 115, 119, 123, 127, 131, 139, 151, 155, 159, 163, 167, 171, 175, 179, 183, 187, 192, 193, 194, 195, 196, 197, 198, 199, 203, 207, 211, 215, 219, 223, 227, 232, 235, 238, 241, 244, 247, 253, 256, 259, 262, 268, 274, 277, 281, 285, 289, 304, 307, 330, 330a, 333, 333a, 336, 336a, 340, and 345**;

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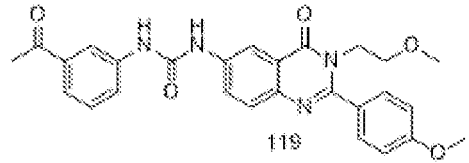
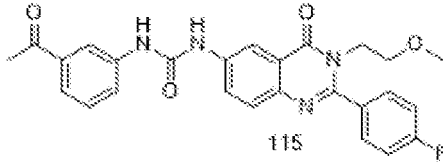
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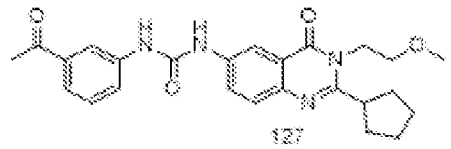
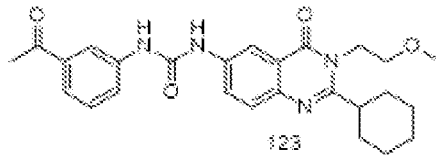
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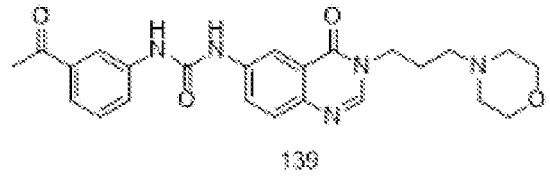
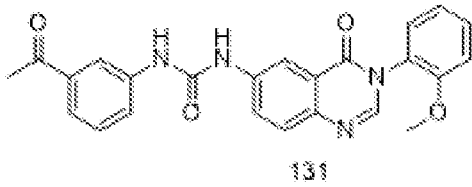
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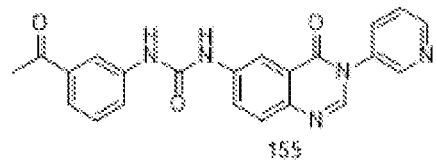
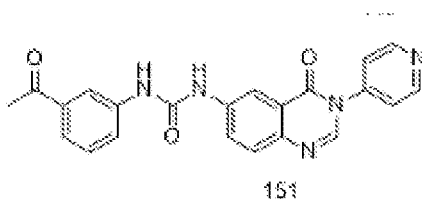
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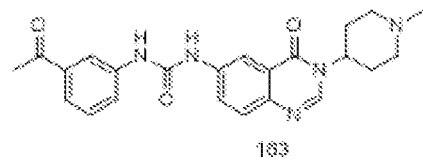
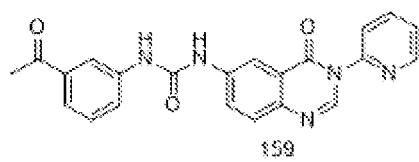
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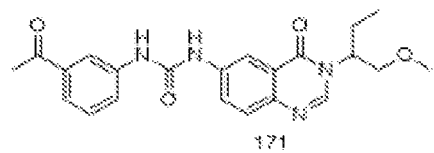
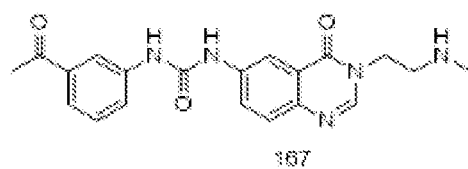
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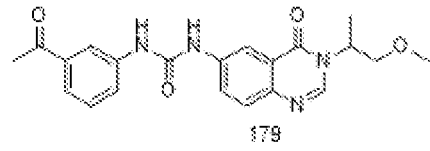
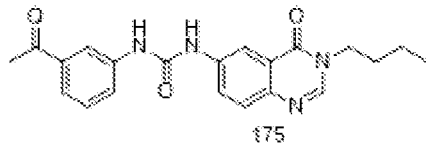


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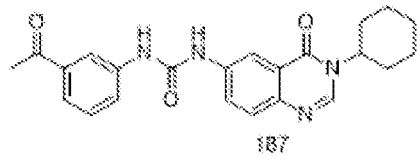
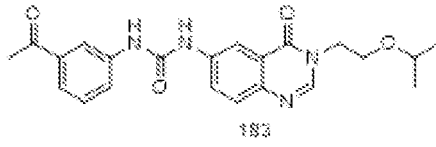


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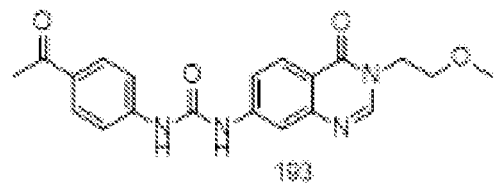
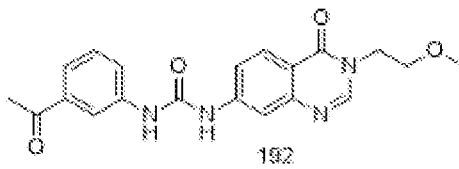




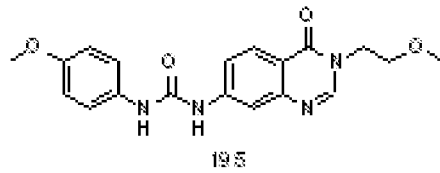
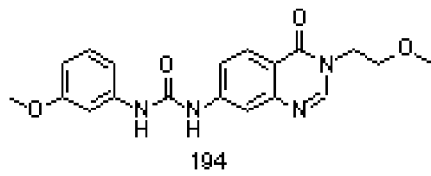
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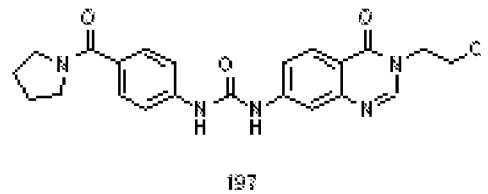
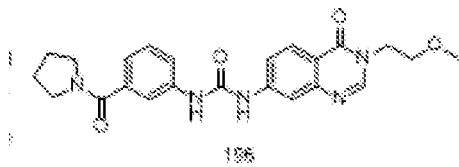
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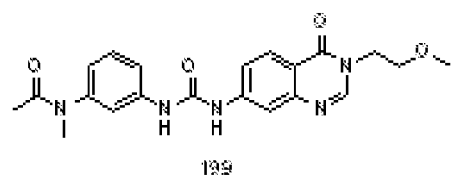
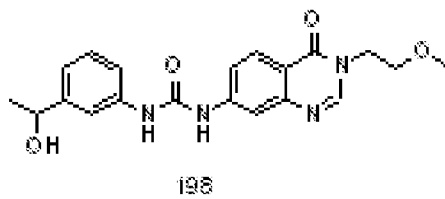
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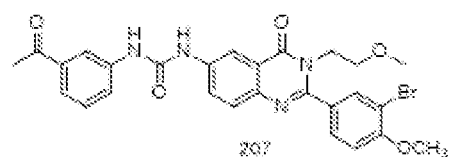
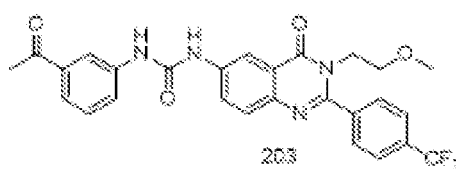
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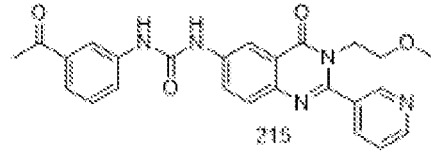
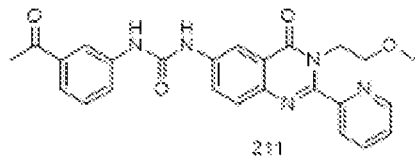


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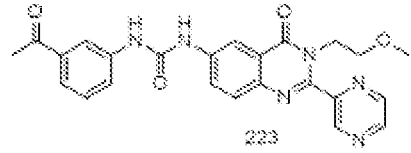
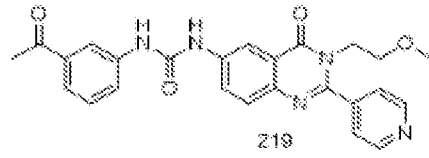


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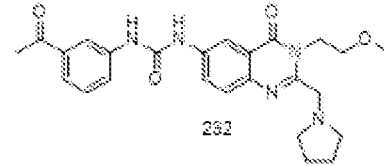
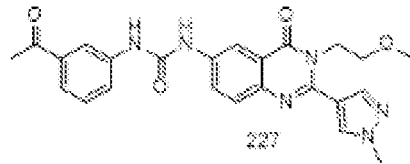




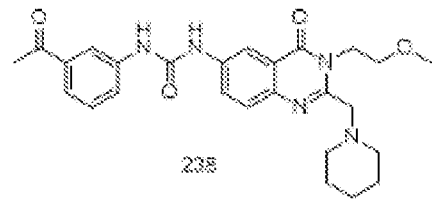
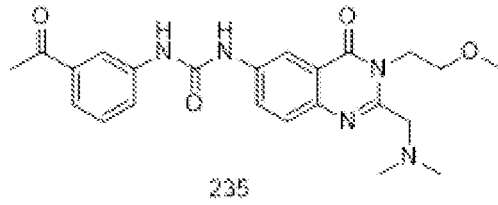
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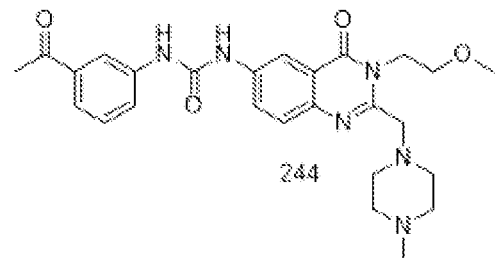
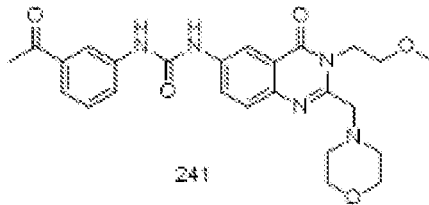
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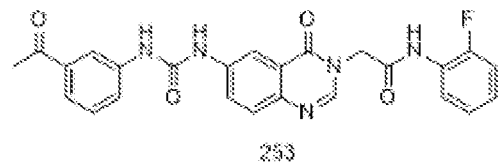
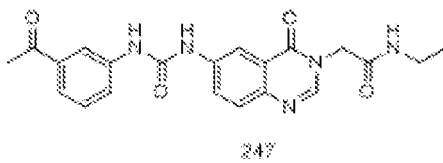
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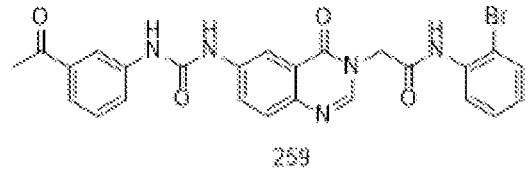
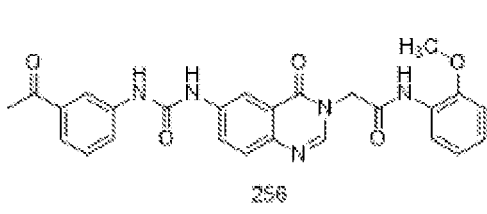


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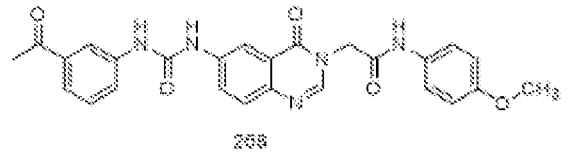
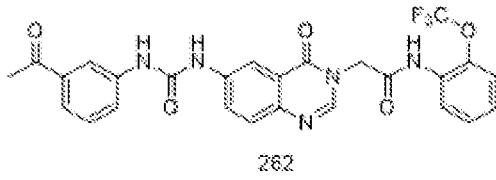


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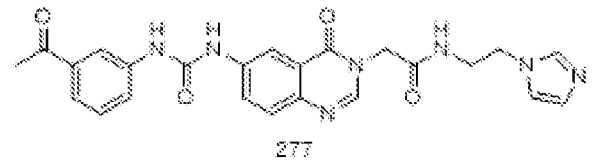
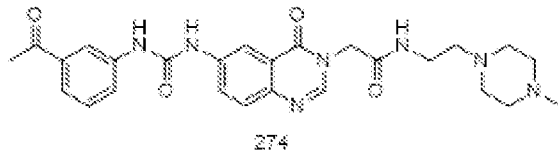
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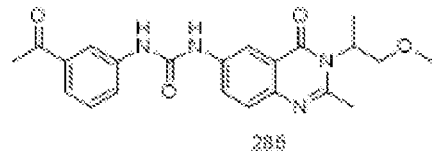
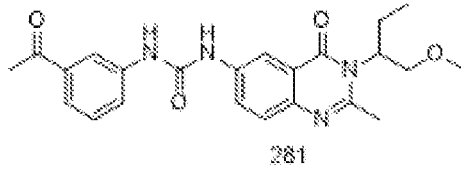
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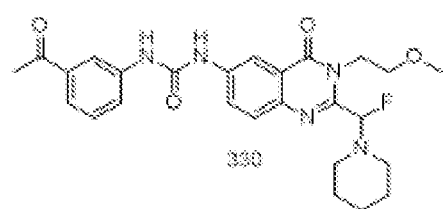
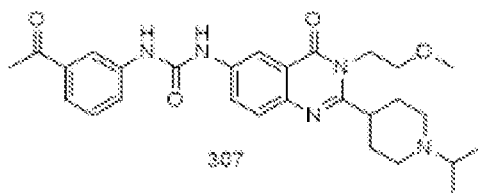
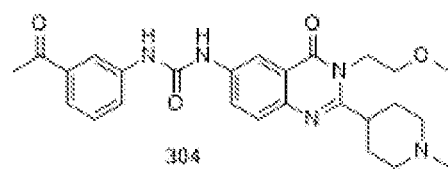
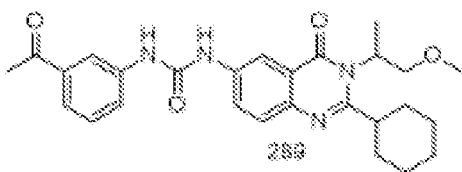
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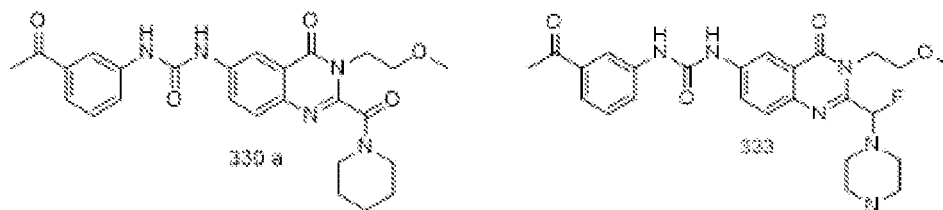


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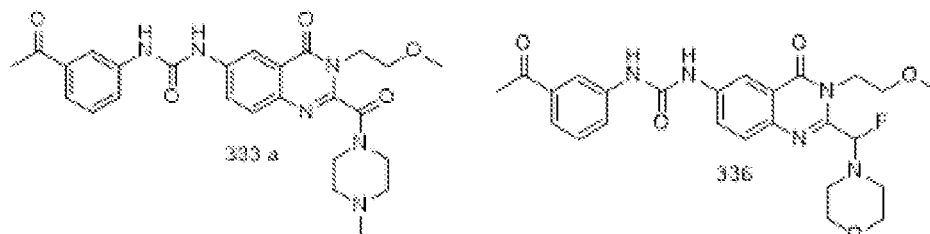


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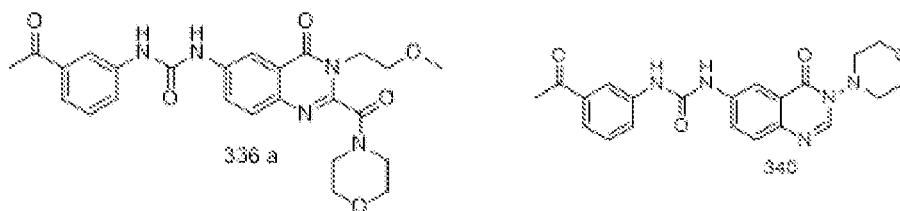




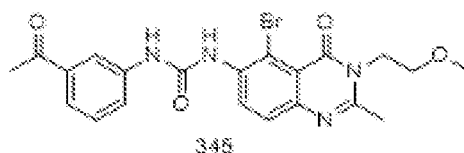
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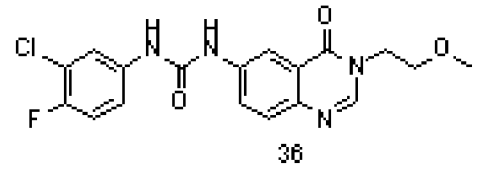
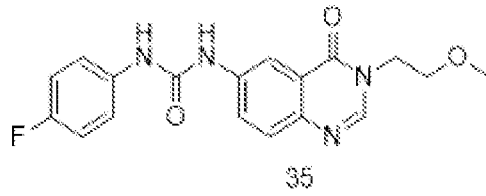
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(xxii) alternately, treating the compound selected from the group consisting of **4, 82, 92, 97, 102, 134, 142, and 146** obtained in step (xvi) with a substituted aromatic isocyanate selected from the group consisting of 4-fluorophenylisocyanate, 3-chloro-4-fluorophenylisocyanate, (4-trifluoromethoxy)phenylisocyanate, (4-trifluoromethyl)phenylisocyanate, (2-trifluoromethyl)phenylisocyanate, 4-methoxyphenylisocyanate, 2-methoxyphenylisocyanate, ethyl 3-isocyanatobenzoate, 3-acetylphenylisocyanate, and 4-acetylphenylisocyanate in presence of TEA as a base in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **35, 36, 37, 38, 39, 40, 41, 42, 83, 84, 85, 93, 94, 98, 99, 103, 135, 143, and 147;**

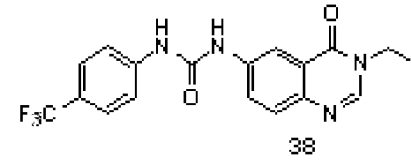
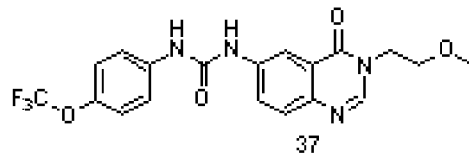
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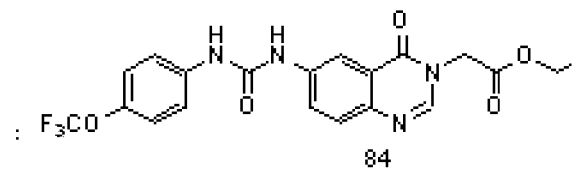
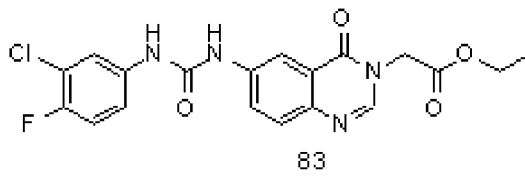
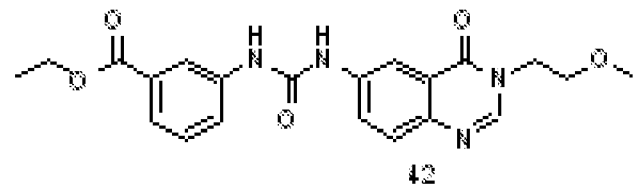
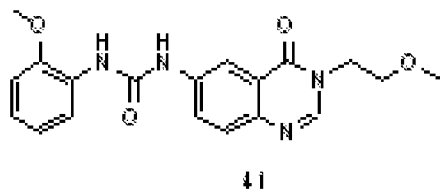
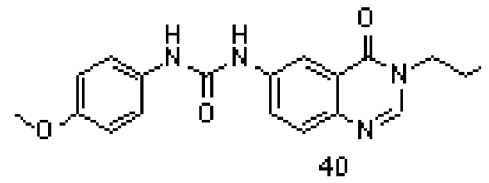
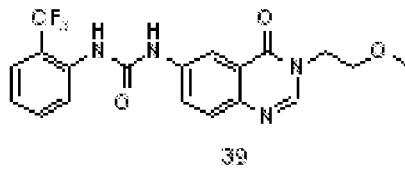
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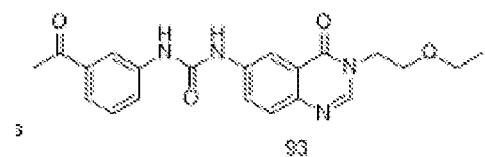
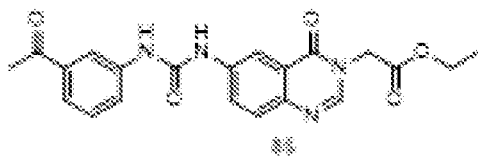
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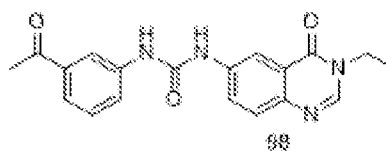
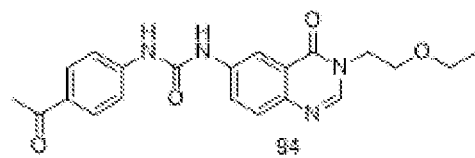
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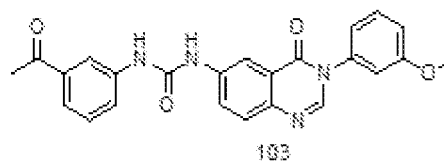
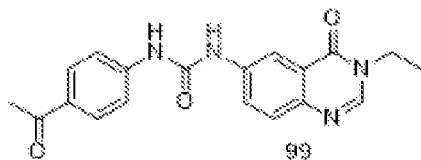
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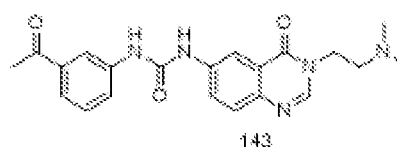
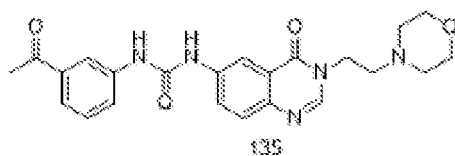
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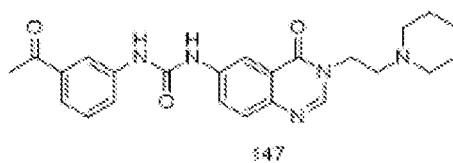
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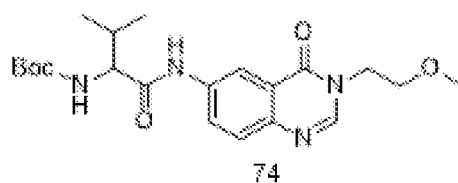
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(xxiii) alternately, reacting compound **4** obtained in step(xvi) with HATU/ TEA in DMF at room temperature with 5 hours of stirring to obtain a compound **74**;

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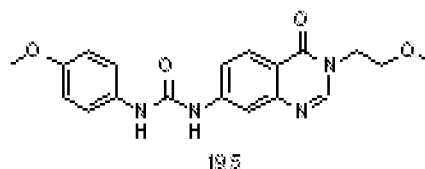
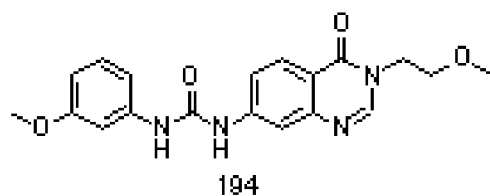


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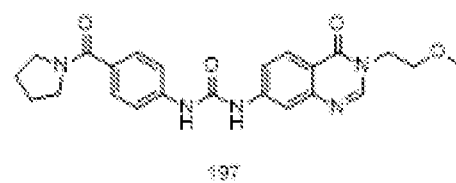
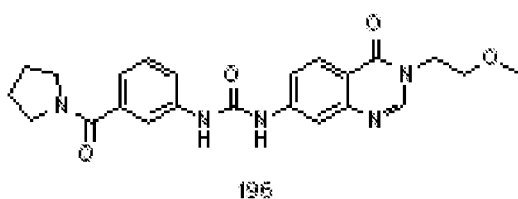
(xxiv) separately adding 3-nitrobenzoyl chloride (3-nitrobenzoic acid and Oxalyl Chloride) at 0 °C in DCM and TEA and stirring for 5 hours at room temperature to obtain a compound **77**;

aminophenyl)-2,2,2-trifluoroethanone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **194**, **195**, **196**, **197**, **198**, **199**, **308**, **309**, **310**, **311**, **312**, **313**, **314**, **315**, **316**, **317**, **318**, **319**, **320**, **321**, **322**, **323**, **324**, and **325**;

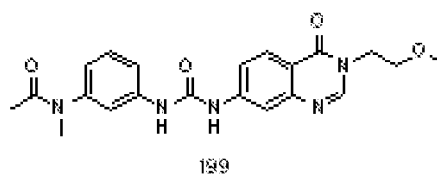
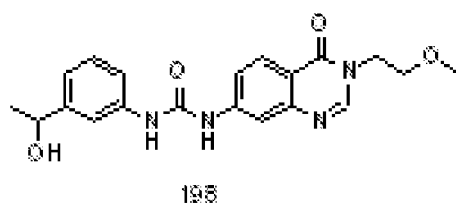
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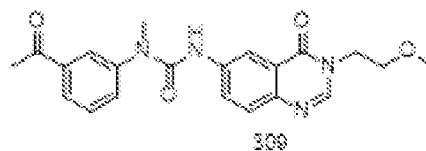
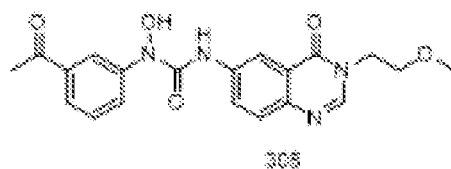
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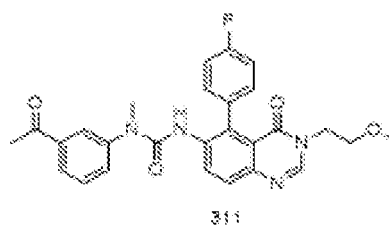
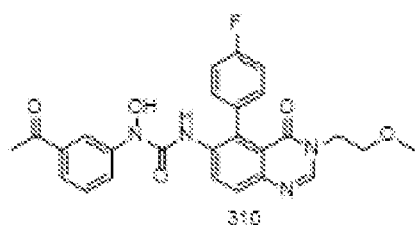
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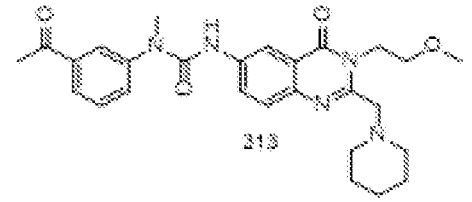
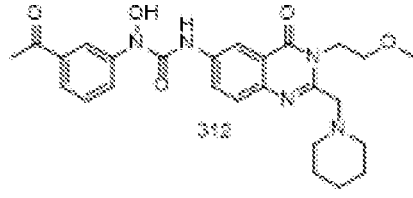
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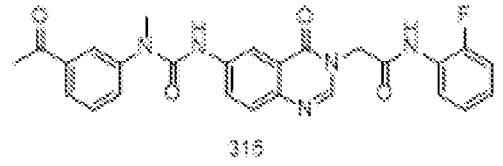
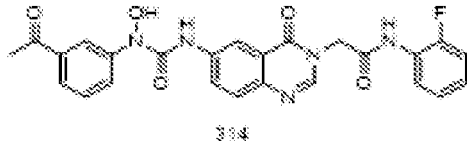
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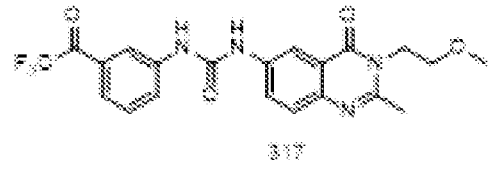
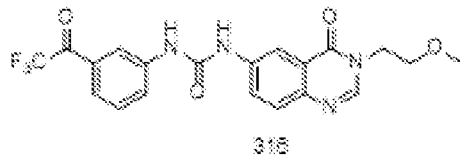
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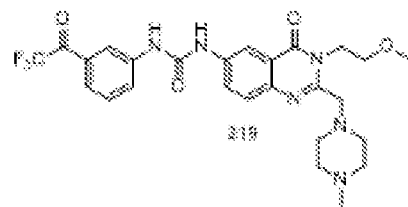
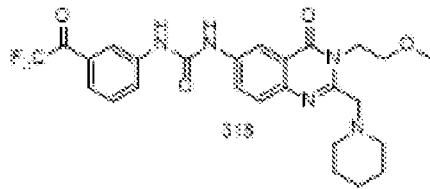
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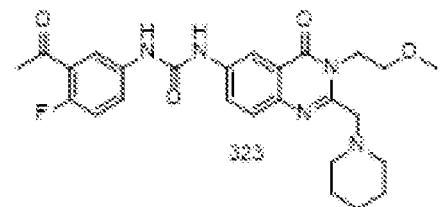
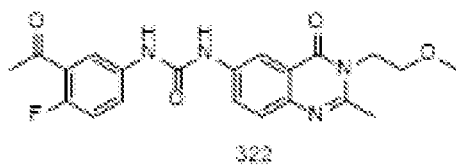
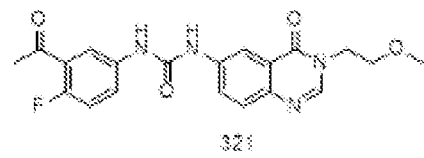
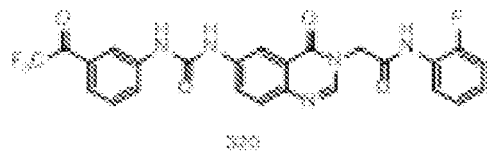
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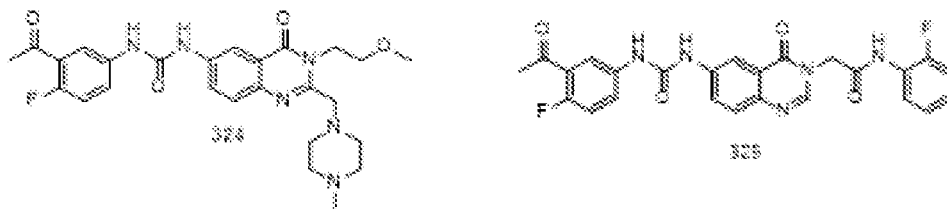
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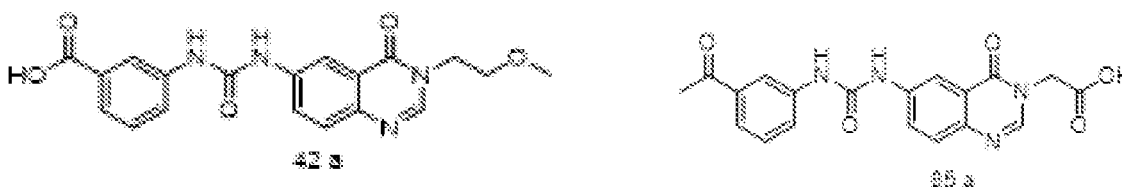
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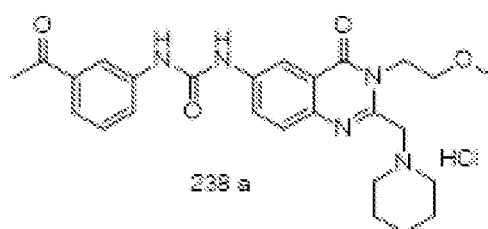
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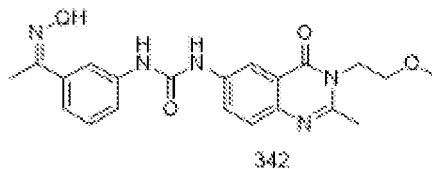
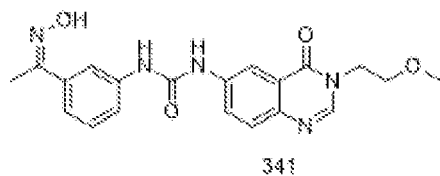
10 (xxviii) subjecting the compound selected from **42** and **85** obtained in step (xxii) to ester hydrolysis by LiOH monohydrate in presence of THF: EtOH: Water (3:2:1) proportion at room temperature for 1-2 hours to obtain the compound having structure I selected from the group consisting of **42a** and **85a**;



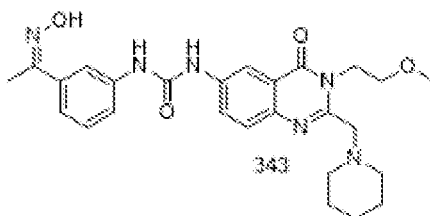
15 (xxix) reacting the compound **238** obtained in step (xxi) with 1M HCl in dioxane to obtain the compound having structure I **238a**; and



25 (xxx) reacting the compound selected from the group consisting of **9**, **107**, and **238** obtained in step (xx) and (xxi) with hydroxylamine hydrochloride ($\text{NH}_2\text{OH} \cdot \text{HCl}$) in ethanol (EtOH) at 80 °C for 12- 16 hours to obtain the compound having structure I selected from the group consisting of **341**, **342** and **343**



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4. The compound as claimed in claim 1, for use in treating diseases and disorders related to modulation of COP1 enzyme through its stabilization or modulation of ATGL.

15 5. The compound as claimed in claim 1 for use in decreasing the level of triglycerides in hepatocytes.

6. The compound as claimed in claim 1, for use in treatment of disease selected from Non-Alcoholic Fatty Liver Disease (NAFLD) or Non-Alcoholic Steatohepatitis (NASH).

20 7. A composition comprising the compound having structure I as claimed in claim 1 along with pharmaceutically acceptable excipients.

8. A method of modulation COP1 enzyme through its stabilization by compound having structure I as claimed in claim 1.

9. A method of increasing the level of ATGL by compound having structure I as claimed in claim 1.

25

2. The compound having structure I as claimed in claim 1 selected from the group consisting of:

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-phenylurea (5),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-methoxyphenyl)urea (6),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(methylamino)phenyl)urea (7),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-nitrophenyl)urea (8),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (9),

1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (10),

1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (11),

methyl 4-methoxy-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (12),

1-(3-ethylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (13),

1-(3-benzoylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (14),

N-cyclohexyl-3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamide (15),

methyl 2-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzamido)-3-methylbutanoate (16),

3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)-N,N-dimethylbenzamide (17),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (18),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(morpholine-4-carbonyl)phenyl)urea (19),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (20),

1-(3-(benzo[d]oxazol-2-yl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (21),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (22),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)-N-methylacetamide (23),

N-benzyl-N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)phenyl)acetamide (24),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)acetamide (25),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzyl)-N-methylacetamide (26),

1-(5-acetyl-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (32),

1-(3-acetyl-5-chloro-2-hydroxyphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (33),

1-(3-acetyl-2-hydroxy-5-methylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (34),

1-(4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (35),

1-(3-chloro-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (36),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea (37),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-(trifluoromethyl)phenyl)urea (38),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-(trifluoromethyl)phenyl)urea (39),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(4-methoxyphenyl)urea (40),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(2-methoxyphenyl)urea (41),

AMENDED SHEET (ARTICLE 19)

ethyl 3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoate (42),
3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)ureido)benzoic acid (42a),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-phenyl-3,4-dihydroquinazolin-6-yl)urea (45),
1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (47),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (49),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (51),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (53),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(6-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (55),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(2-methoxypyridin-3-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (57),
tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (59),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(1,2,3,6-tetrahydropyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (60),
tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-5-yl)piperidine-1-carboxylate (61),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (62),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-5-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (64),
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-5-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea (66),

AMENDED SHEET (ARTICLE 19)

1-(3-acetylphenyl)-3-(5-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (68),

1-(3-acetylphenyl)-3-(5-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (70),

1-(3-acetylphenyl)-3-(5-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (72),

1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (73),

ethyl 2-(6-(3-(3-chloro-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (83),

ethyl 2-(4-oxo-6-(3-(4-(trifluoromethoxy)phenyl)ureido)quinazolin-3(4H)-yl)acetate (84),

ethyl 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetate (85),

2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetic acid (85a),

1-(3-acetylphenyl)-3-(3-(3-methoxypropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (89),

1-(3-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (93),

1-(4-acetylphenyl)-3-(3-(2-ethoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (94),

1-(3-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (98),

1-(4-acetylphenyl)-3-(3-ethyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (99),

1-(3-acetylphenyl)-3-(3-(3-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (103),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (107),

1-(3-acetylphenyl)-3-(2-isopropyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (111),

1-(3-acetylphenyl)-3-(2-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (115),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (119),

1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (123),

AMENDED SHEET (ARTICLE 19)

1-(3-acetylphenyl)-3-(2-cyclopentyl-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (127),

1-(3-acetylphenyl)-3-(3-(2-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (131),

1-(3-acetylphenyl)-3-(3-(2-morpholinoethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (135),

1-(3-acetylphenyl)-3-(3-(3-morpholinopropyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (139),

1-(3-acetylphenyl)-3-(3-(2-(dimethylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (143),

1-(3-acetylphenyl)-3-(4-oxo-3-(2-(piperidin-1-yl)ethyl)-3,4-dihydroquinazolin-6-yl)urea (147),

1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (151),

1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (155),

1-(3-acetylphenyl)-3-(4-oxo-3-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (159),

1-(3-acetylphenyl)-3-(3-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (163),

1-(3-acetylphenyl)-3-(3-(2-(methylamino)ethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (167),

1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (171),

1-(3-acetylphenyl)-3-(3-butyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (175),

1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (179),

1-(3-acetylphenyl)-3-(3-(2-isopropoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (183),

1-(3-acetylphenyl)-3-(3-cyclohexyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (187),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (192),

1-(4-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (193),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-methoxyphenyl)urea (194),

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1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-methoxyphenyl)urea (195),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(3-(pyrrolidine-1-carbonyl)phenyl)urea (196),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea (197),

1-(3-(1-hydroxyethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)urea (198),

N-(3-(3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-7-yl)ureido)phenyl)-N-methylacetamide (199),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(4-(trifluoromethyl)phenyl)-3,4-dihydroquinazolin-6-yl)urea (203),

1-(3-acetylphenyl)-3-(2-(3-bromo-4-methoxyphenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (207),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (211),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-3-yl)-3,4-dihydroquinazolin-6-yl)urea (215),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyridin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (219),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrazin-2-yl)-3,4-dihydroquinazolin-6-yl)urea (223),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methyl-1H-pyrazol-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (227),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(pyrrolidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (232),

1-(3-acetylphenyl)-3-(2-((dimethylamino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (235),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (238),

AMENDED SHEET (ARTICLE 19)

- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholinomethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (241),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (244),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-ethylacetamide (247),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N,N-diethylacetamide (250),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (253),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-methoxyphenyl)acetamide (256),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-bromophenyl)acetamide (259),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethoxy)phenyl)acetamide (262),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(trifluoromethyl)phenyl)acetamide (265),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-methoxyphenyl)acetamide (268),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(4-fluorophenyl)acetamide (271),
- 2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide (274),
- N-(2-(1H-imidazol-1-yl)ethyl)-2-(6-(3-(3-acetylphenyl)ureido)-4-oxoquinazolin-3(4H)-yl)acetamide (277),
- 1-(3-acetylphenyl)-3-(3-(1-methoxybutan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (281),
- 1-(3-acetylphenyl)-3-(3-(1-methoxypropan-2-yl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (285),

1-(3-acetylphenyl)-3-(2-cyclohexyl-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (289),

1-(3-acetylphenyl)-3-(2-cyclohexyl-5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (292),

1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(1-methoxypropan-2-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (295),

tert-butyl 4-(6-(3-(3-acetylphenyl)ureido)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (299),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-4-yl)-3,4-dihydroquinazolin-6-yl)urea (300),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(1-methylpiperidin-4-yl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (304),

1-(3-acetylphenyl)-3-(2-(1-isopropylpiperidin-4-yl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (307),

1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (308),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea (309),

1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-hydroxyurea (310),

1-(3-acetylphenyl)-3-(5-(4-fluorophenyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-1-methylurea (311),

1-(3-acetylphenyl)-1-hydroxy-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (312),

1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-1-methylurea (313),

2-(6-(3-(3-acetylphenyl)-3-hydroxyureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (314),

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2-(6-(3-(3-acetylphenyl)-3-methylureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (315),

1-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (316),

1-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (317),

1-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (318),

1-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-3-(3-(2,2,2-trifluoroacetyl)phenyl)urea (319),

N-(2-fluorophenyl)-2-(4-oxo-6-(3-(3-(2,2,2-trifluoroacetyl)phenyl)ureido)quinazolin-3(4H)-yl)acetamide (320),

1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (321),

1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (322),

1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (323),

1-(3-acetyl-4-fluorophenyl)-3-(3-(2-methoxyethyl)-2-((4-methylpiperazin-1-yl)methyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (324),

2-(6-(3-(3-acetyl-4-fluorophenyl)ureido)-4-oxoquinazolin-3(4H)-yl)-N-(2-fluorophenyl)acetamide (325),

1-(3-acetylphenyl)-3-(2-(fluoro(piperidin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (330),

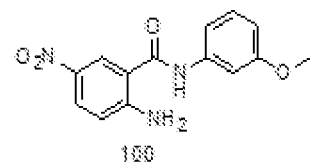
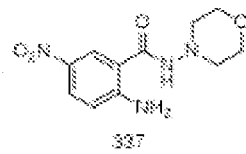
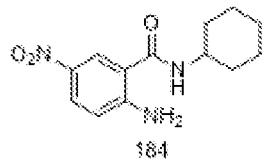
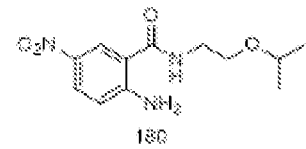
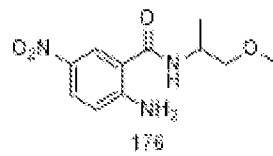
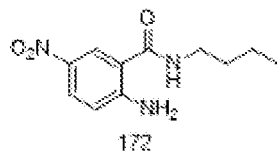
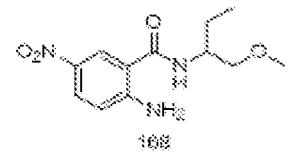
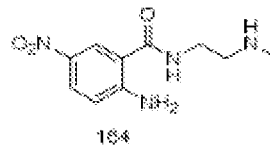
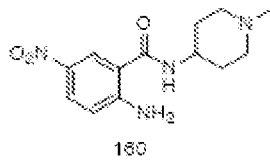
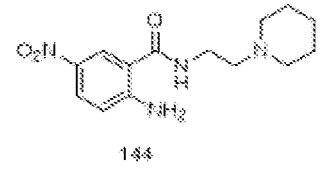
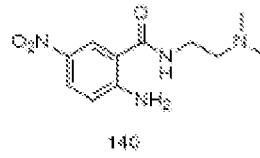
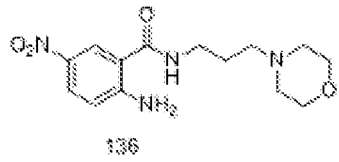
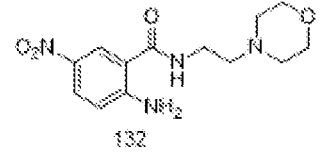
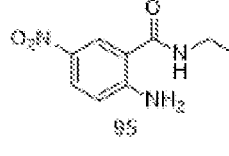
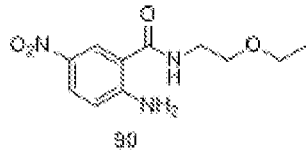
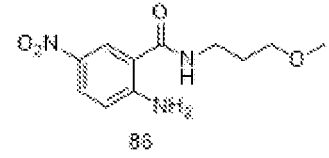
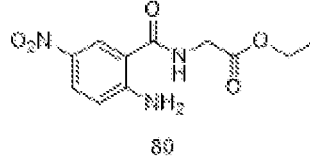
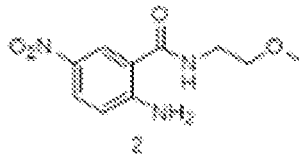
1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidine-1-carbonyl)-3,4-dihydroquinazolin-6-yl)urea (330a),

1-(3-acetylphenyl)-3-(2-(fluoro(4-methylpiperazin-1-yl)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333),

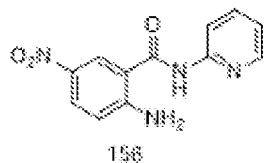
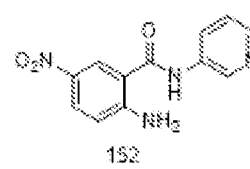
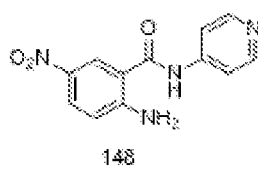
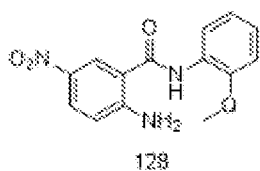
AMENDED SHEET (ARTICLE 19)

- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(4-methylpiperazine-1-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (333 a),
- 1-(3-acetylphenyl)-3-(2-(fluoro(morpholino)methyl)-3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (336),
- 1-(3-acetylphenyl)-3-(3-(2-methoxyethyl)-2-(morpholine-4-carbonyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (336 a),
- 1-(3-acetylphenyl)-3-(3-morpholino-4-oxo-3,4-dihydroquinazolin-6-yl)urea (340),
- (Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)urea (341),
- (Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (342),
- (Z)-1-(3-(1-(hydroxyimino)ethyl)phenyl)-3-(3-(2-methoxyethyl)-4-oxo-2-(piperidin-1-ylmethyl)-3,4-dihydroquinazolin-6-yl)urea (343), and
- 1-(3-acetylphenyl)-3-(5-bromo-3-(2-methoxyethyl)-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)urea (345).
3. A process for preparation of the compound having structure I as claimed in claim 1, the process steps comprising:
- (i) reacting 2-amino-5-nitrobenzoic acid (**compound 1**) with an aliphatic or an aromatic amine selected from the group consisting of 2-methoxyethylamine, glycine ethylester hydrochloride, 3-methoxypropylamine, 2-ethoxyethylamine, ethylamine 2M in THF, 4-(2-aminoethyl)morpholine, 3-(4-morpholinyl)propylamine, N,N-dimethylethylenediamine, 1-(2-aminoethyl)piperidine, 4-amino-1-methylpiperidine, N-methylethylenediamine, 2-amino-1-methoxybutane, 1-butylamine, 1-methoxy-2-propylamine, 2-aminoethyl isopropyl ether, cyclohexylamine, 4-aminomorpholine, m-anisidine, o-anisidine, 4-aminopyridine, 3-aminopyridine, and 2-aminopyridine in presence of HATU/DMF followed by TEA as a base at room temperature for 1-3 hours to obtain an amide compound selected from the group consisting of **2, 80, 86, 90, 95, 132, 136, 140, 144, 160, 164, 168, 172, 176, 180, 184, 337, 100, 128, 148, 152, and 156**;

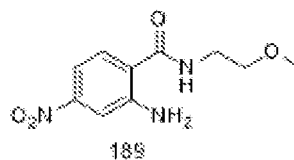
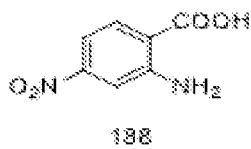
AMENDED SHEET (ARTICLE 19)



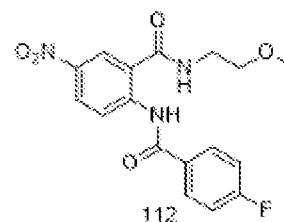
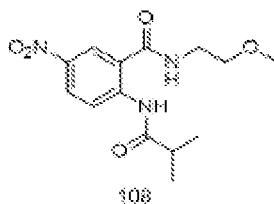
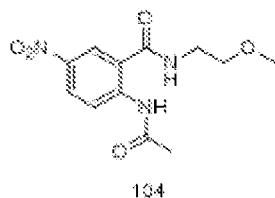
AMENDED SHEET (ARTICLE 19)

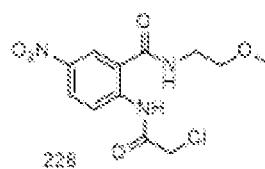
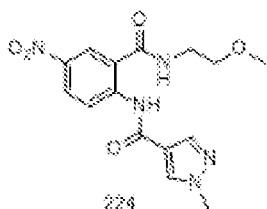
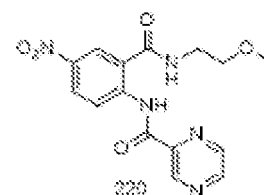
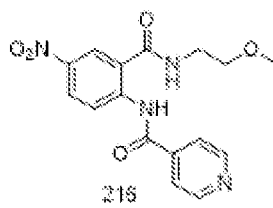
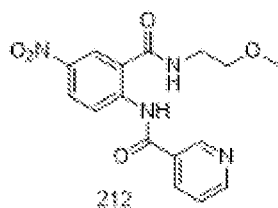
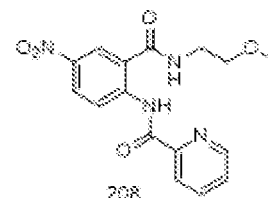
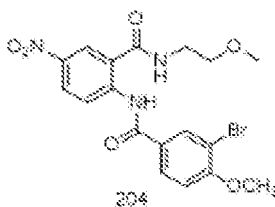
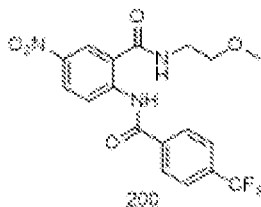
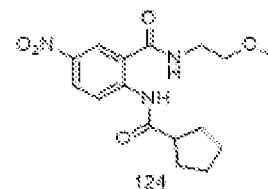
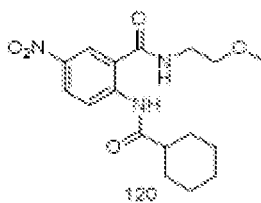
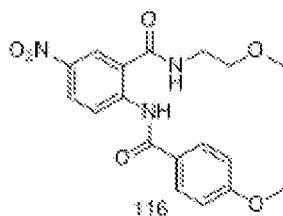


- (ii) separately, reacting 2-amino-4-nitrobenzoic acid (**compound 188**) with 2-methoxyethylamine in presence of HATU/ DMF followed by TEA as a base at room temperature for 1 hour to obtain a compound **189**;

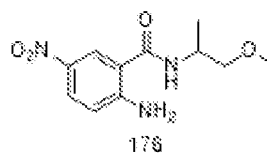
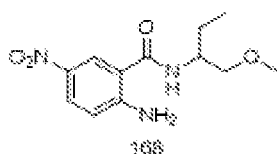


- (iii) adding an acid chloride selected from the group consisting of acetyl chloride, isopropyl chloride, 4-fluorobenzoyl chloride, 4-methoxybenzoyl chloride, cyclohexanecarbonyl chloride, cyclopentanecarbonyl chloride, 4-(trifluoromethyl)benzoyl chloride, 3-Bromo-4-methoxybenzoyl chloride, Picolinoyl chloride, Nicotinoyl chloride, Isonicotinoyl chloride, Pyrazinecarbonyl chloride, 1-methyl-1H-pyrazole-4-carbonyl chloride, and 2-chloroacetyl chloride to compound **2** obtained in step (i) in DCM at a temperature range from 0 °C to room temperature for 1-8 hours to obtain a compound selected from the group consisting of **104**, **108**, **112**, **116**, **120**, **124**, **200**, **204**, **208**, **212**, **216**, **220**, **224**, and **228**;

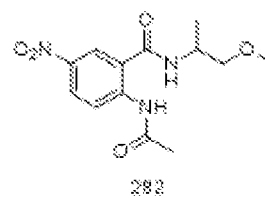
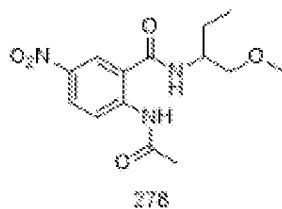




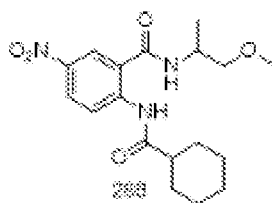
- (iv) acetylating a compound selected from the group consisting of **168**, and **176** obtained in step (i) using acetyl chloride and triethylamine (TEA) as a base in DCM at a temperature range of 0 °C to room temperature for 8 hours to obtain a compound selected from the group consisting of **278** and **282**;



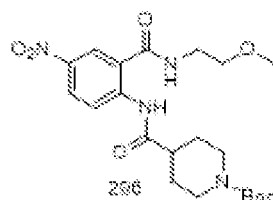
AMENDED SHEET (ARTICLE 19)



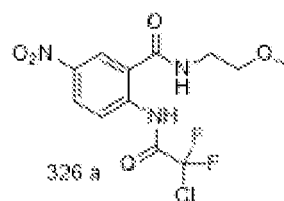
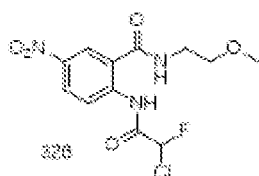
- (v) alternately, adding cyclohexanecarbonyl chloride to compound **176** obtained in step (i) to obtain a compound **286**;



- (vi) alternately, adding tert-butyl 4-(chlorocarbonyl)piperidine-1-carboxylate to compound **2** obtained in step (i) to obtain a compound **296**;



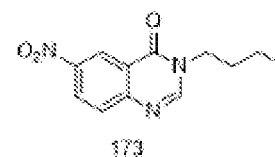
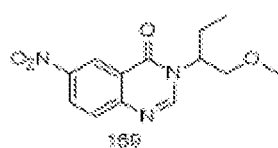
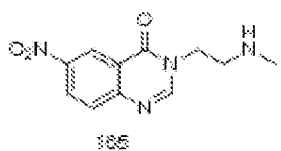
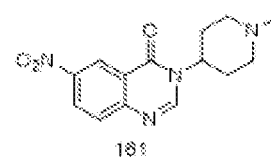
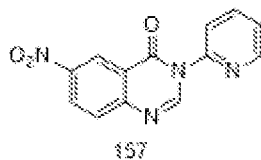
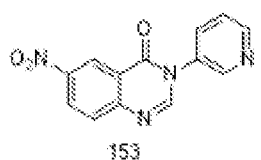
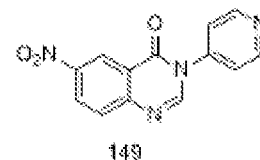
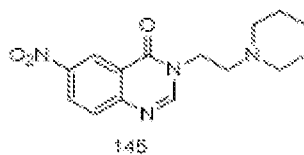
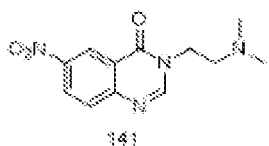
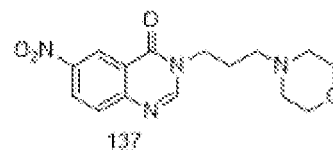
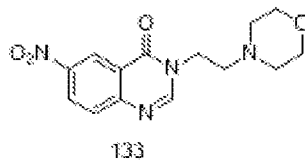
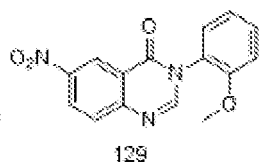
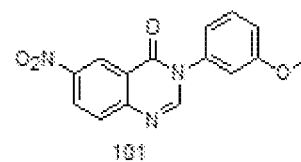
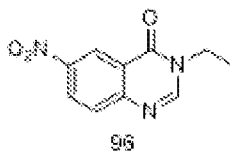
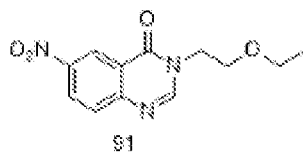
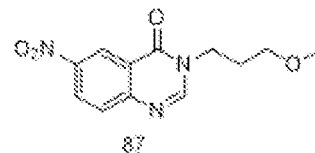
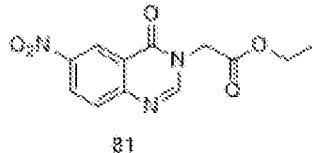
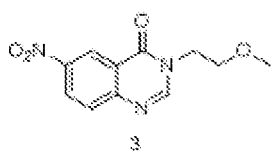
- (vii) alternately, treating compound **2** obtained in step (i) with 2-chloro-2-fluoroacetic acid or 2-chloro-2-difluoroacetic acid along with POCl₃ in pyridine solvent to obtain a compound selected from the group consisting of **326** and **326a**;



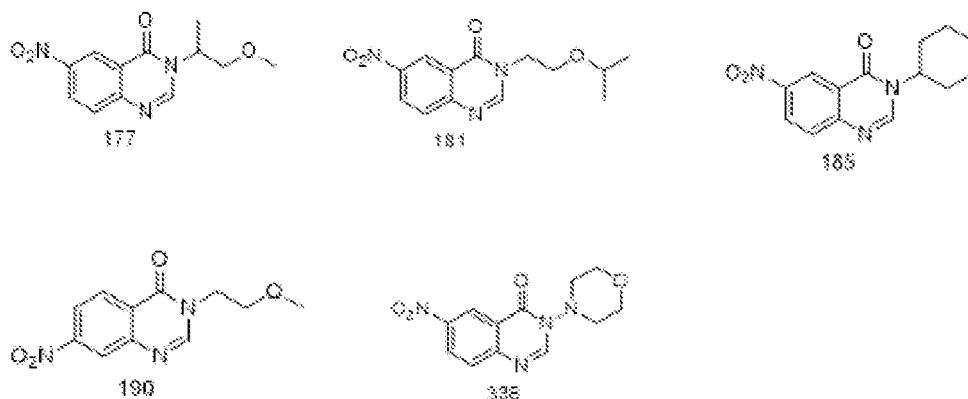
- (viii) cyclizing the compound selected from the group consisting of **2**, **80**, **86**, **90**, **95**, **100**, **128**, **132**, **136**, **140**, **144**, **148**, **152**, **156**, **160**, **164**, **168**, **172**, **176**, **180**, **184**, **189**, and **337** obtained in step (i) and (ii) using a cyclizing agent selected from trimethylorthoformate or triethylorthoformate at 100 °C for 12-16 hours to obtain a

AMENDED SHEET (ARTICLE 19)

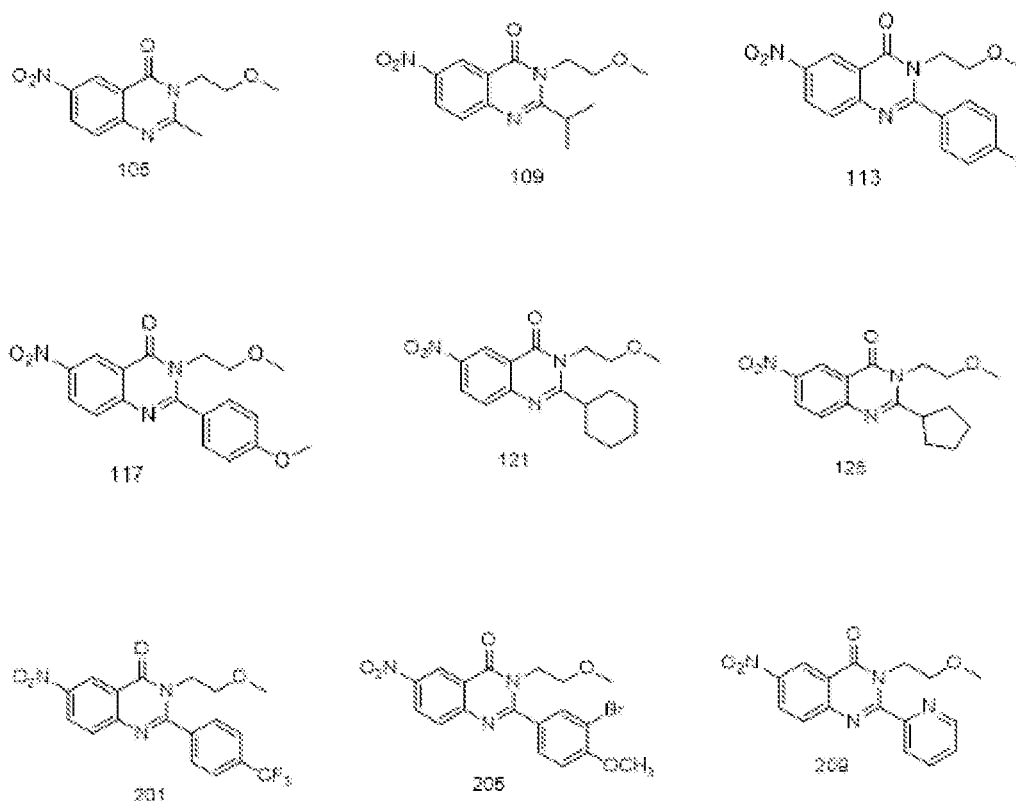
compound selected from the group consisting of **3**, **81**, **87**, **91**, **96**, **101**, **129**, **133**, **137**, **141**, **145**, **149**, **153**, **157**, **161**, **165**, **169**, **173**, **177**, **181**, **185**, **190** and **338**;



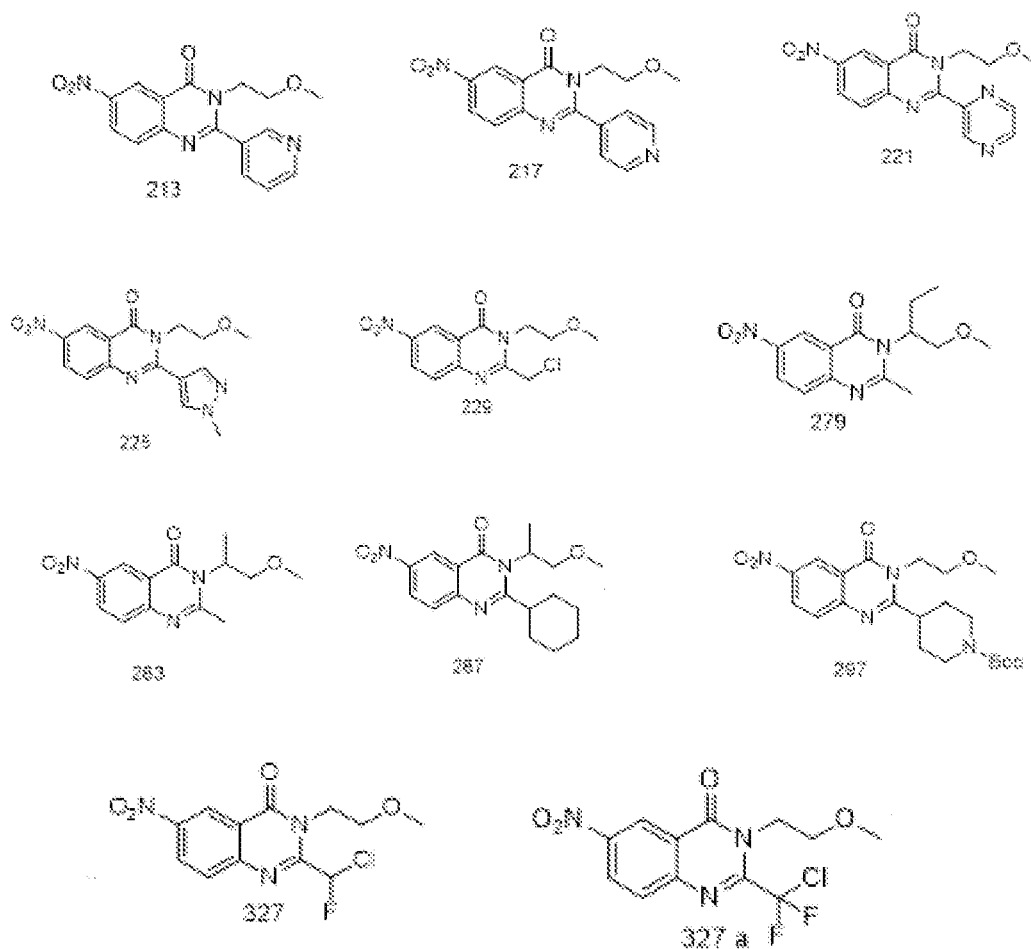
AMENDED SHEET (ARTICLE 19)



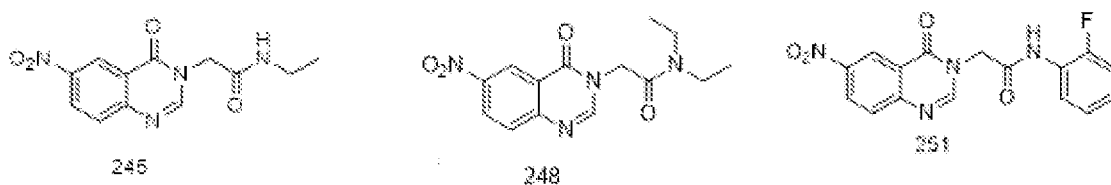
- (ix) cyclizing the compound selected from the group consisting of **104, 108, 112, 116, 120, 124, 200, 204, 208, 212, 216, 220, 224, 228, 278, 282, 286, 296, 326,** and **326a** obtained in step (iii), (iv), (v), (vi) and (vii) using a cyclizing agent $ZnCl_2$ and hexamethyldisilazane (HMDS) in DMF at 100 °C for 12 -16 hours to obtain a compound selected from the group consisting of **105, 109, 113, 117, 121, 125, 201, 205, 209, 213, 217, 221, 225, 229, 279, 283, 287, 297, 327** and **327a**;



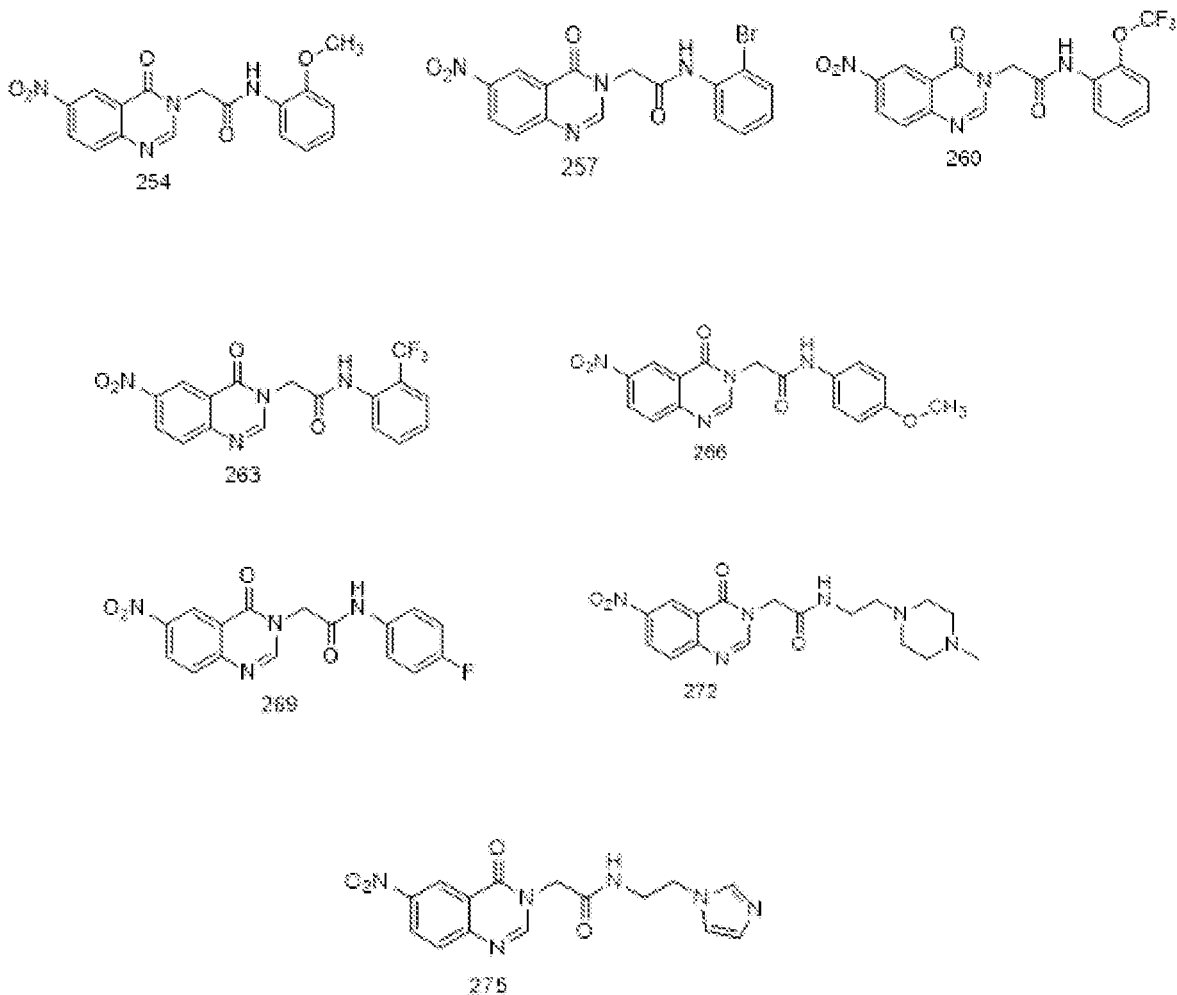
AMENDED SHEET (ARTICLE 19)



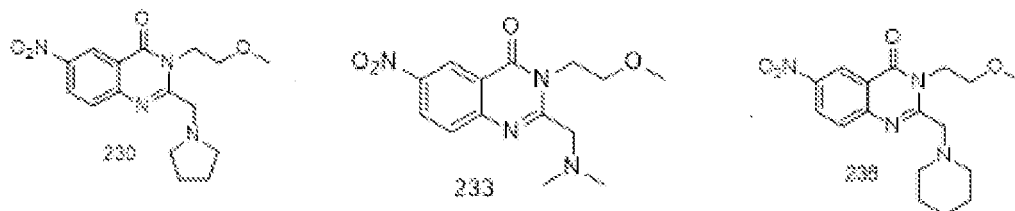
- (x) reacting the compound **81** obtained in step (viii) with an amine selected from the group consisting of ethyl amine, diethylamine, 2-fluoroaniline, *o*-anisidine, 2-bromoaniline, 2-(trifluoromethoxy)aniline, 2-(trifluoromethyl)aniline, *p*-anisidine, 4-fluoroaniline, 1-(2-aminoethyl)-4-methylpiperazine, and 1*H*-Imidazole-1-ethanamine in presence of anhydrous AlCl₃ in toluene at a temperature range from room temperature to 110 °C to obtain a compound selected from the group consisting of **245**, **248**, **251**, **254**, **257**, **260**, **263**, **266**, **269**, **272** and **275**;



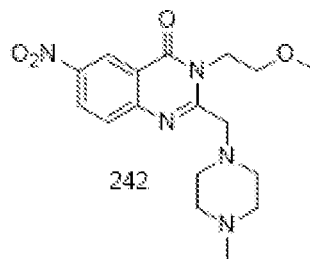
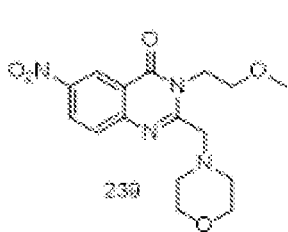
AMENDED SHEET (ARTICLE 19)



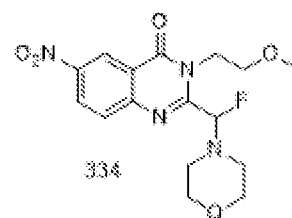
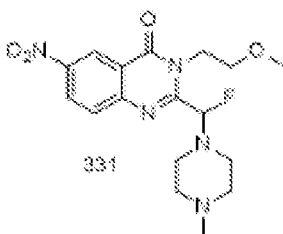
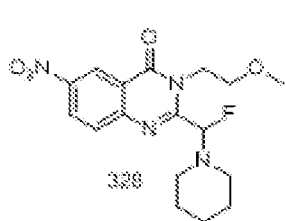
- (xi) reacting the compound **229** obtained in step (ix) with an amine selected from the group consisting of pyrrolidine, dimethylamine, piperidine, morpholine, and 1-methylpiperazine in toluene at 100 °C for 2 hours to obtain a compound selected from the group consisting of **230**, **233**, **236**, **239**, and **242**;



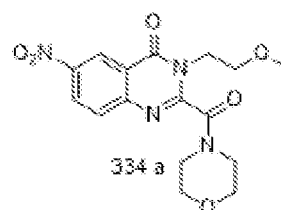
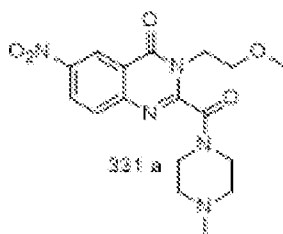
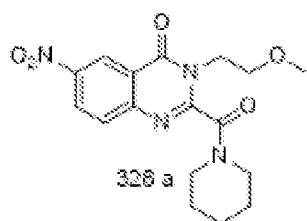
AMENDED SHEET (ARTICLE 19)



- (xii) reacting the compound **327** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of toluene to obtain a compound selected from the group consisting of **328**, **331**, and **334**;

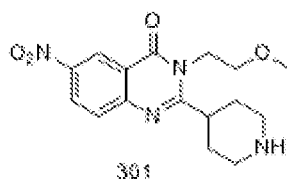


- (xiii) reacting the compound **327a** obtained in step (ix) with an amine selected from the group consisting of piperidine, 1-methylpiperazine, and morpholine in presence of a solvent selected from the group consisting of toluene, DMF, and THF in absence or presence of a base selected from K_2CO_3 , or N,N-diethylaniline to obtain a compound selected from the group consisting of **328a**, **331a**, and **334a**;

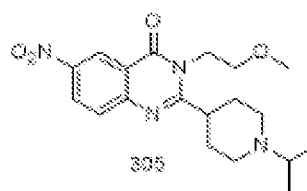
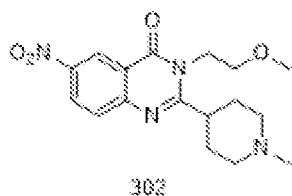


- (xiv) separately reacting the compound **297** obtained in step (ix) with trifluoroacetic acid (TFA) in DCM at a temperature range of 0 °C to room temperature for 2 hours to obtain a compound **301**;

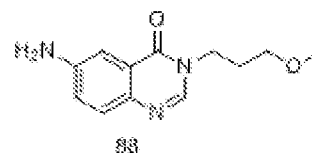
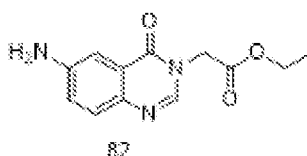
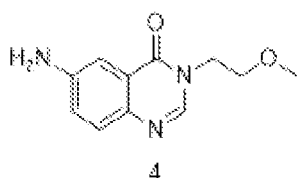
AMENDED SHEET (ARTICLE 19)



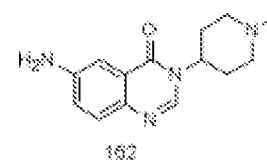
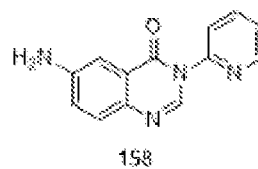
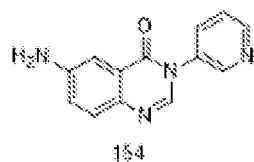
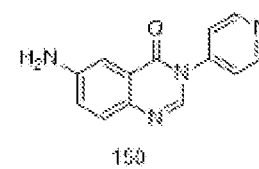
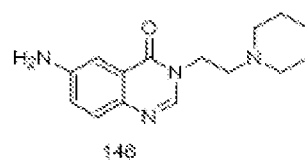
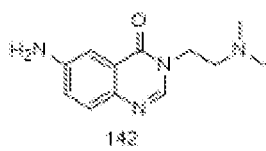
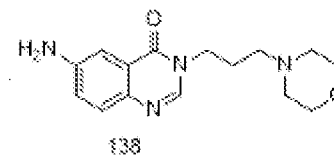
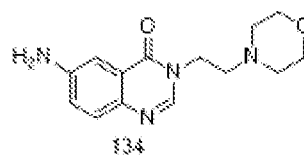
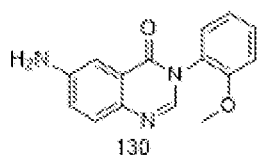
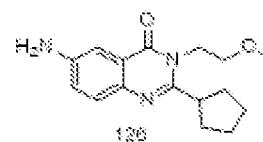
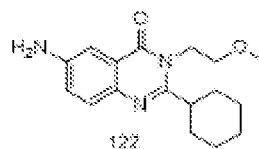
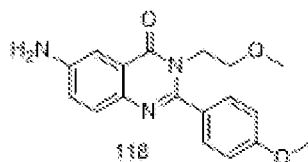
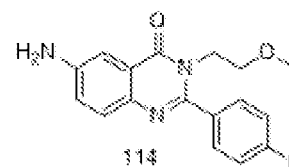
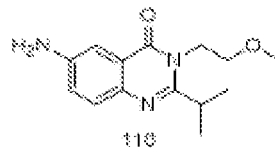
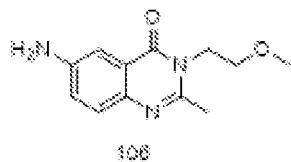
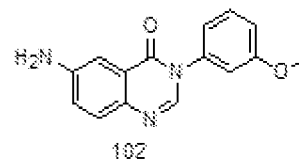
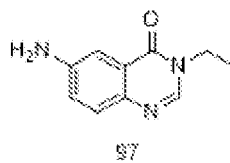
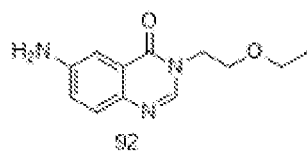
- (xv) reacting the compound **301** obtained in step (xiv) with sodium hydride (NaH) in DMF at a temperature range of 0 °C to room temperature for 3 hours with methyl iodide and 2-chloropropane, respectively to obtain a compound selected from the group consisting of **302** and **305**;



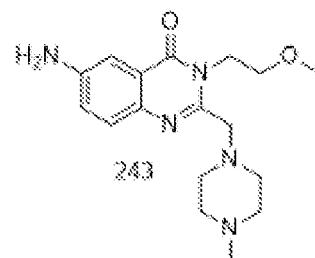
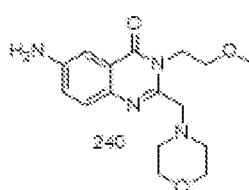
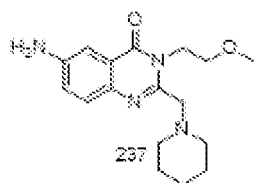
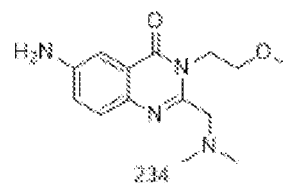
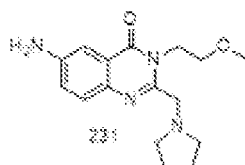
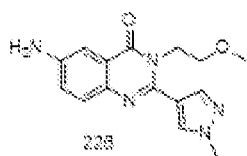
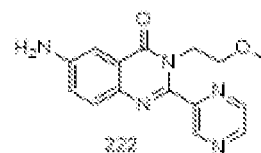
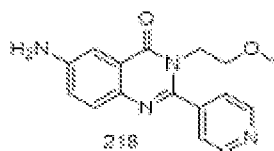
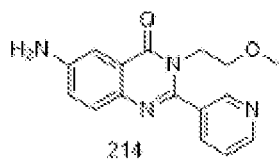
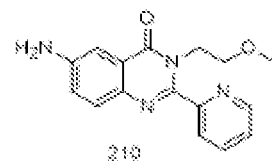
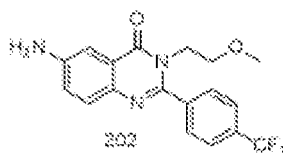
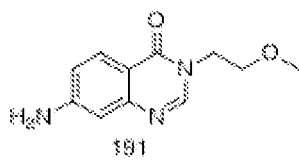
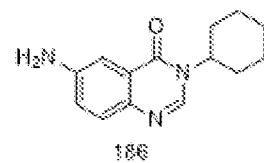
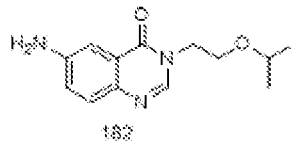
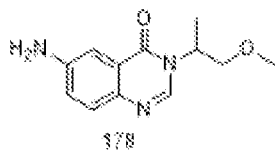
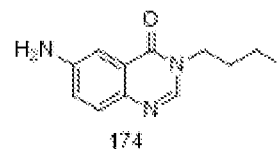
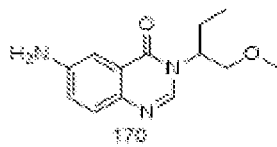
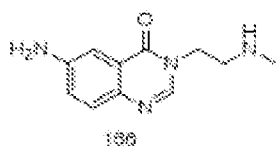
- (xvi) reducing the compound selected from the group consisting of **3, 81, 87, 91, 96, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 177, 181, 185, 190, 201, 209, 213, 217, 221, 225, 230, 233, 236, 239, 242, 245, 248, 251, 254, 260, 263, 266, 269, 272, 275, 279, 283, 287, 297, 302, 305, 328, 328a, 331, 331a, 334, 334a** and **338** obtained in steps (viii), (ix), (x), (xi), (xii), (xiii) and (xv) using Palladium-Charcoal (5% or 10 % wet) at room temperature for 3-5 hours in presence of H₂ to obtain an amine compound selected from the group consisting of **4, 82, 88, 92, 97, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 191, 202, 210, 214, 218, 222, 226, 231, 234, 237, 240, 243, 246, 249, 252, 255, 261, 264, 267, 270, 273, 276, 280, 284, 288, 298, 303, 306, 329, 329a, 332, 332a, 335, 335a, and 339**;



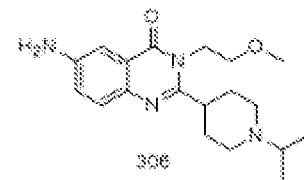
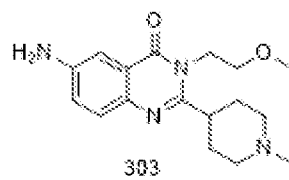
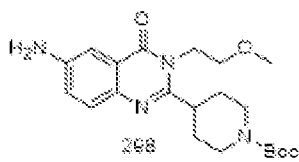
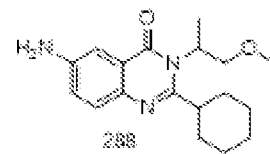
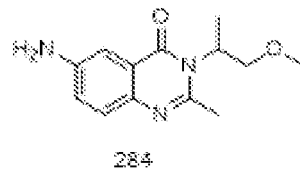
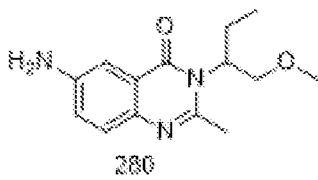
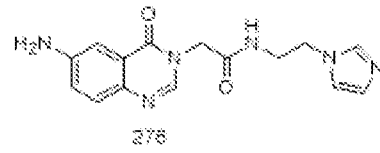
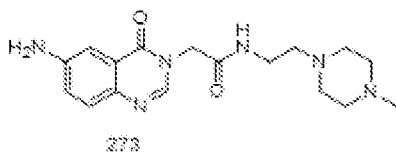
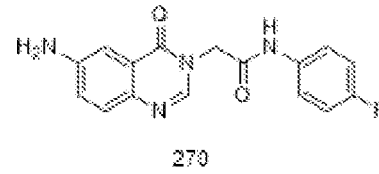
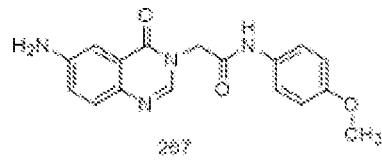
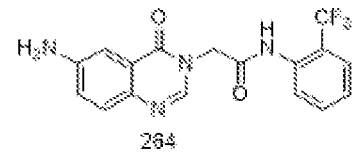
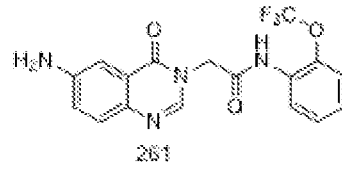
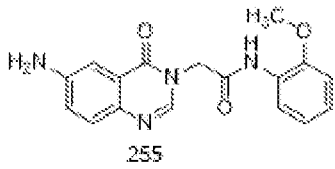
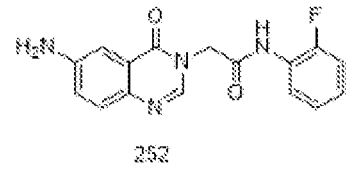
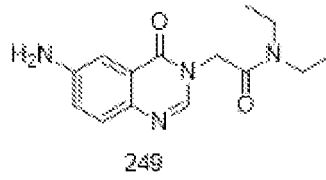
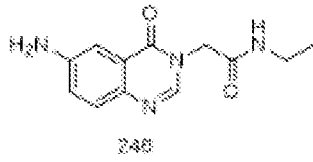
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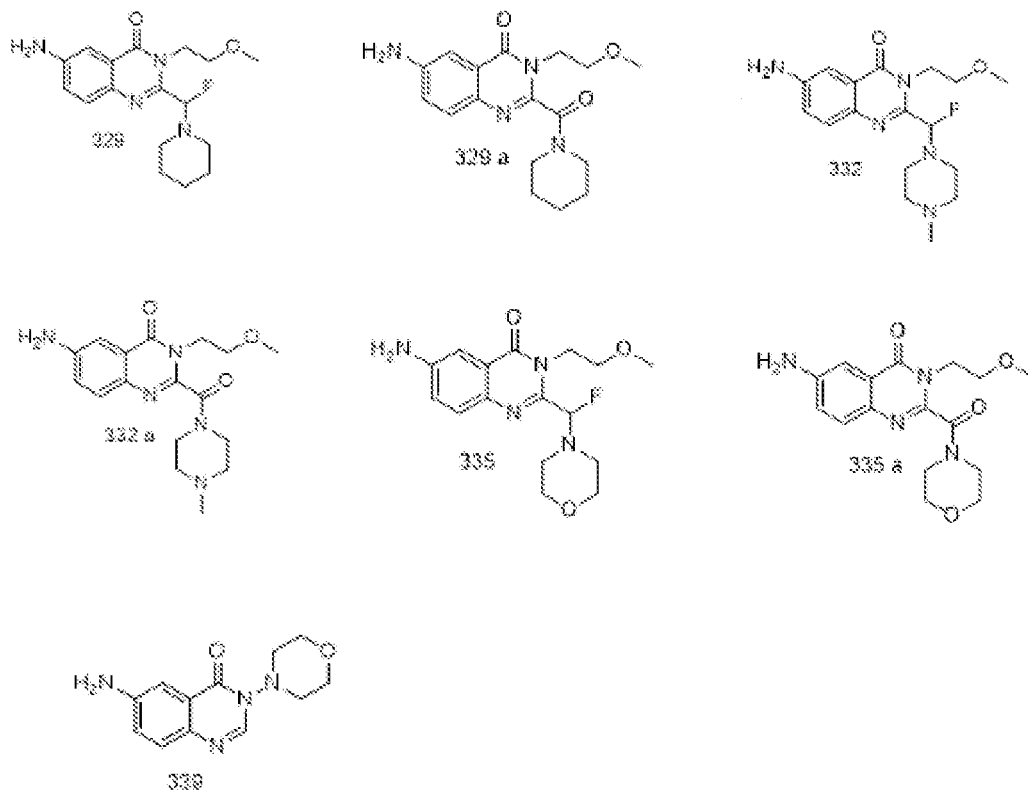
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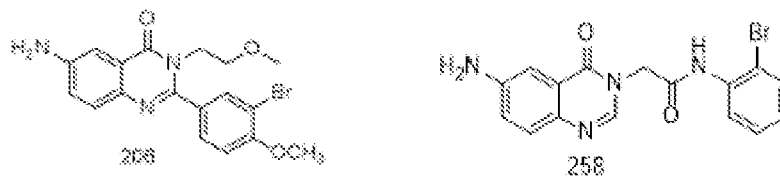
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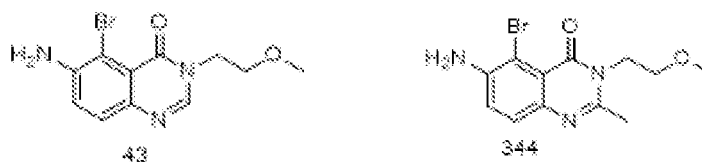
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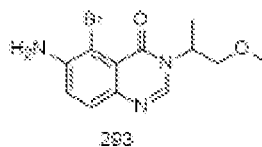
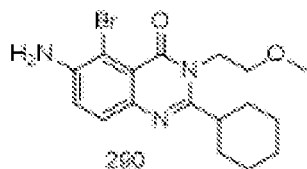
(xvii) reducing the compound selected from **205** or **257** obtained in step (ix) and (x) using $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ to obtain the compound selected from **206** or **258**;



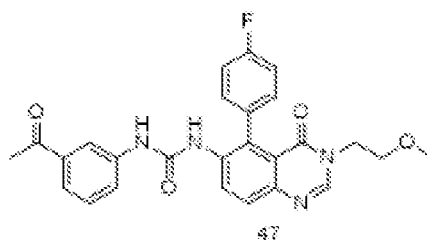
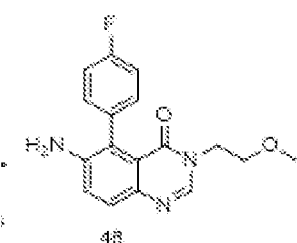
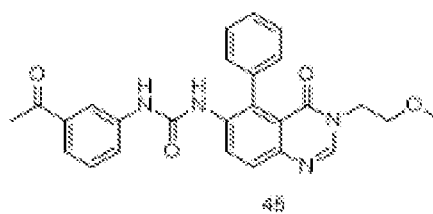
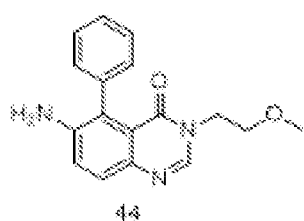
(xviii) brominating the compound selected from the group consisting of **4**, **106**, **122**, and **178** obtained in step (xvi) diluted in dichloromethane or chloroform solution by carrying out reaction in acetic acid medium followed by drop wise addition of liquid bromine on the compound at room temperature for 3-4 hours to obtain a compound selected from the group consisting of **43**, **344**, **290**, and **293**;



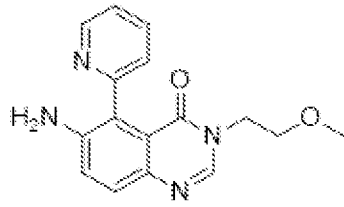
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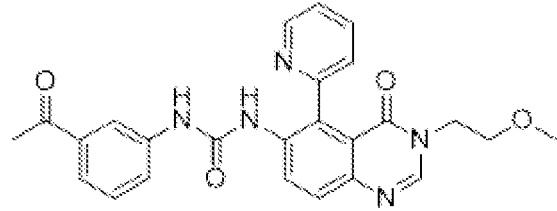
- (xix) carrying out Suzuki reaction on a compound selected from the group consisting of **43**, **290**, and **293** obtained in step (xviii) by $\text{Pd}_2(\text{dba})_3$ or $\text{Pd}(\text{PPh}_3)_4$ in presence of Cs_2CO_3 or 2M Na_2CO_3 solution in dioxane and X-Phos as a ligand at 100 °C over a period of 10-12 hours along with a boronic acid selected from the group consisting of benzenboronic acid, 4-fluorobenzenboronic acid, pyridine-2-boronic acid, pyridine-3-boronic acid, pyridine-4-boronic acid, 6-methoxypyridine-3-boronic acid, 2-methoxypyridine-3-boronic acid, (1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)boronic acid, 4-methoxybenzenboronic acid, 4-trifluoromethylbenzenboronic acid, cyclohexylboronic acid, cyclopentyl boronic acid, and isopropylboronic acid to obtain a compound selected from the group consisting of **44**, **46**, **48**, **50**, **52**, **54**, **56**, **58**, **63**, **65**, **67**, **69**, **71**, **291**, and **294** which is treated with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 5-8 hours to obtain the compound having structure I selected from the group consisting of **45**, **47**, **49**, **51**, **53**, **55**, **57**, **59**, **64**, **66**, **68**, **70**, **72**, **292**, and **295**;



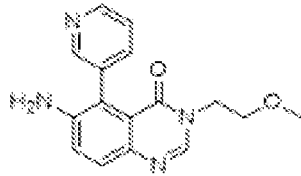
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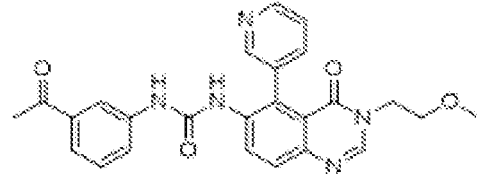
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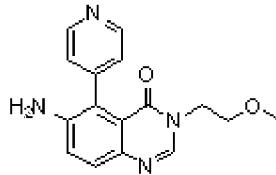
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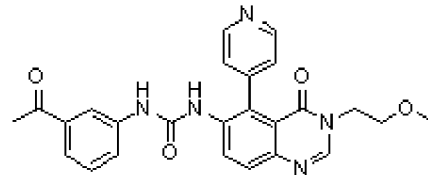
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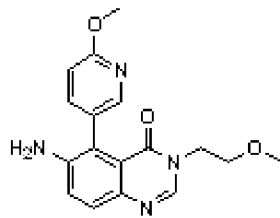
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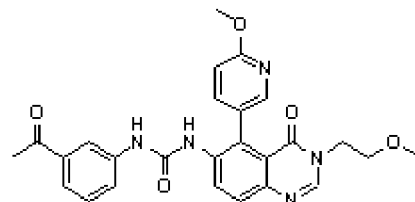
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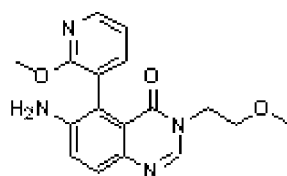
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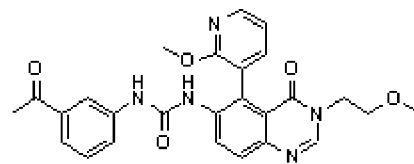
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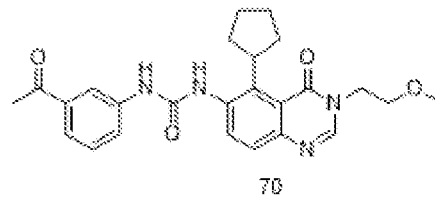
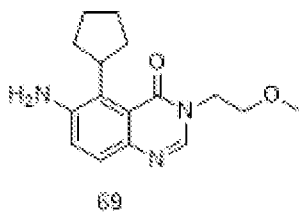
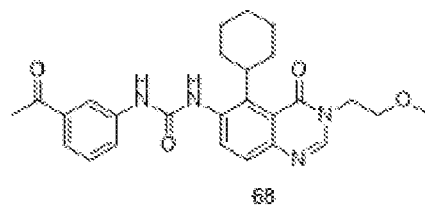
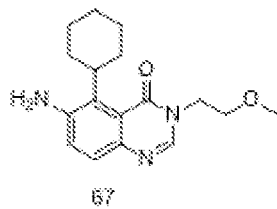
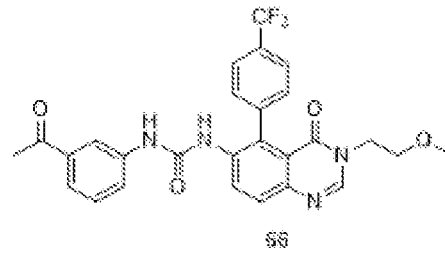
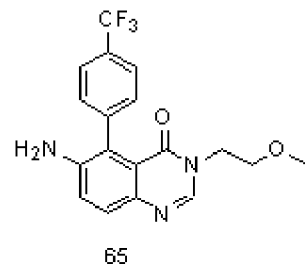
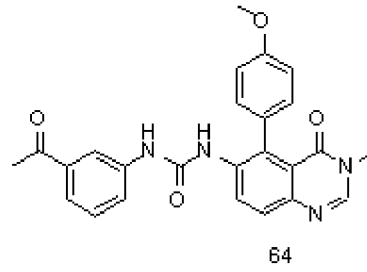
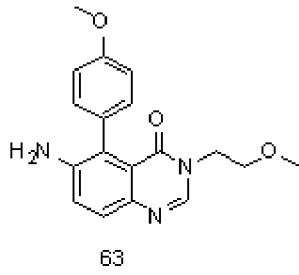
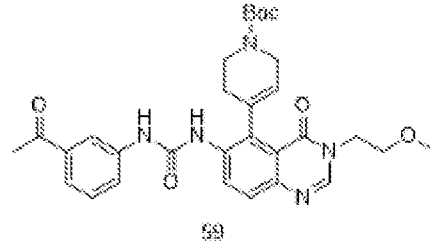
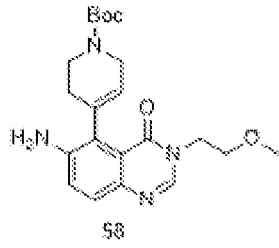


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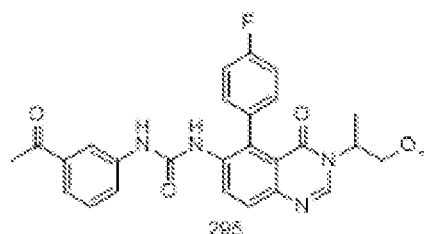
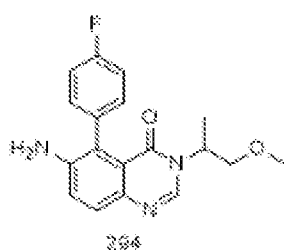
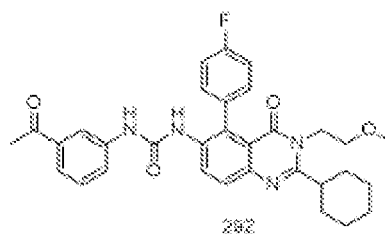
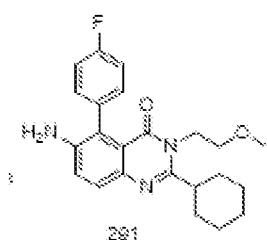
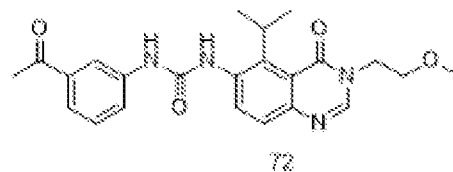
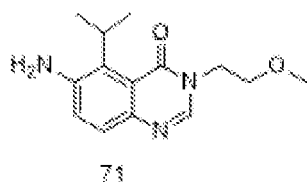


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AMENDED SHEET (ARTICLE 19)



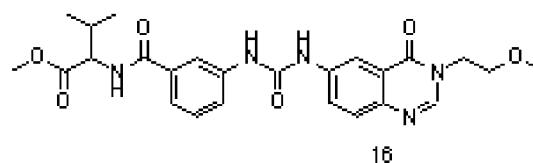
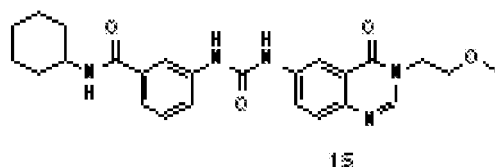
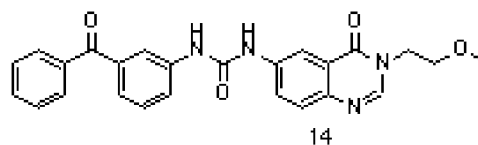
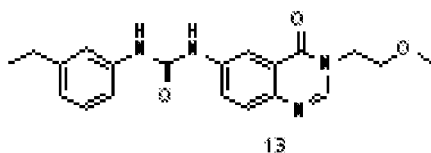
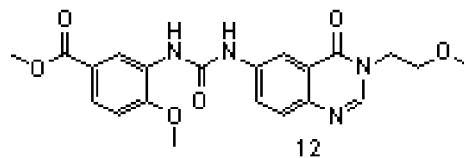
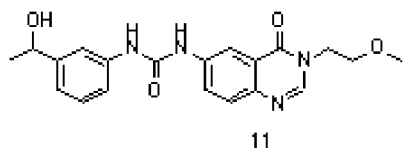
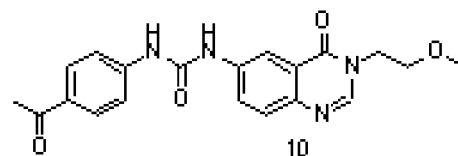
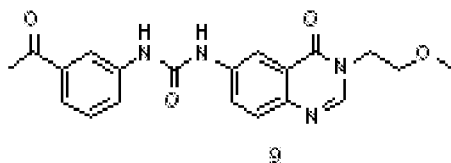
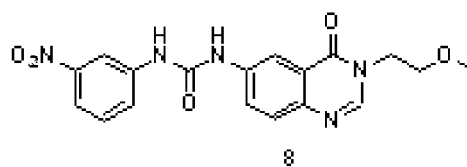
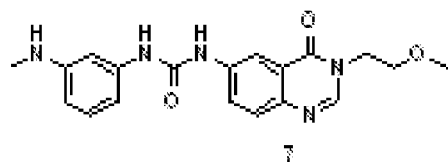
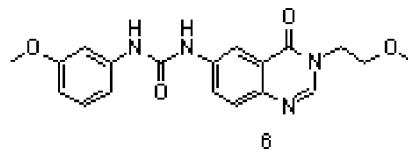
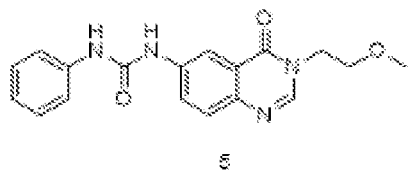
AMENDED SHEET (ARTICLE 19)



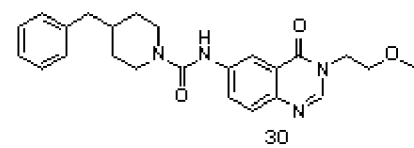
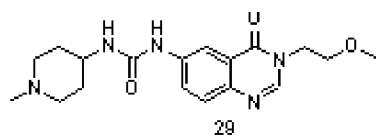
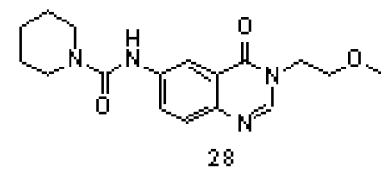
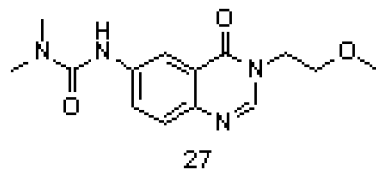
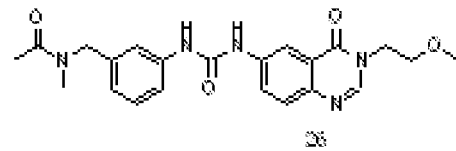
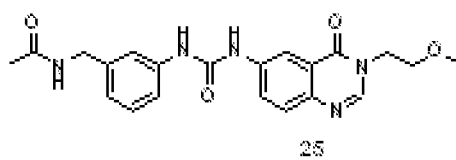
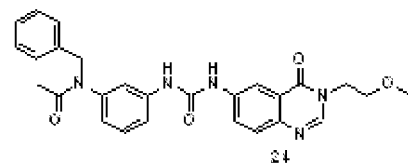
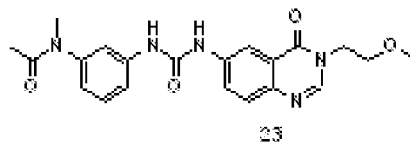
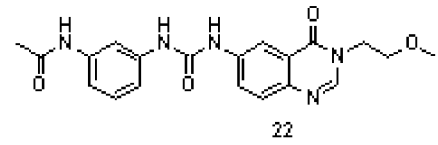
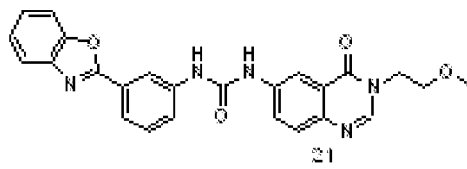
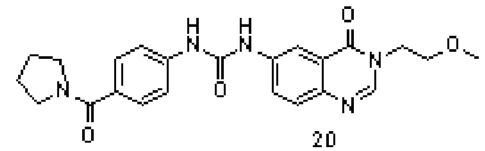
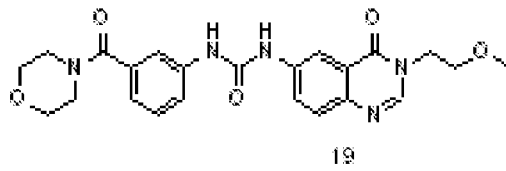
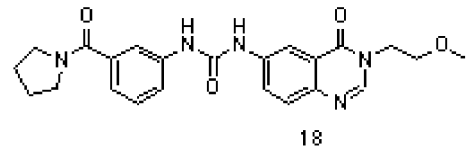
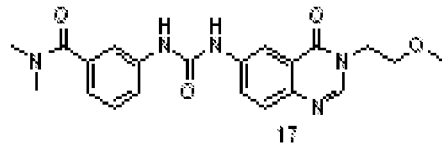
- (xx) alternately, treating compound **4** obtained in step (xvi) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of aniline, m-anisidine, N1-methylbenzene-1,3-diamine, m-nitroaniline, 3-aminoacetophenone, 4-aminoacetophenone, 1-(3-aminophenyl)ethanol, methyl 3-amino-4-methoxybenzoate, 3-ethylaniline, 3'-aminobenzophenone, 3-amino-N-cyclohexylbenzamide, methyl 2-(3-aminobenzamido)-3-methylbutanoate, 3-amino-N,N-dimethylbenzamide, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 3-(benzo[d]oxazol-2-yl)aniline, N-(3-aminophenyl)acetamide, N-(3-aminophenyl)-N-methylacetamide, N-(3-aminophenyl)-N-benzylacetamide, N-(3-aminobenzyl)acetamide, N-(3-aminobenzyl)-N-methylacetamide, dimethylamine, piperidine, 4-amino-1-methylpiperidine, 4-benzylpiperidine, 1-benzylpiperidin-4-amine, 1-(3-amino-4-hydroxyphenyl)ethanone, 1-(3-amino-5-chloro-2-hydroxyphenyl)ethanone, 1-(3-amino-2-hydroxy-5-methylphenyl)ethanone, and 1-

AMENDED SHEET (ARTICLE 19)

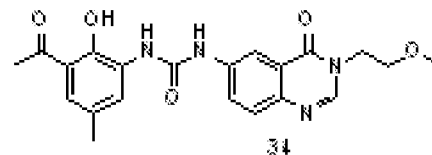
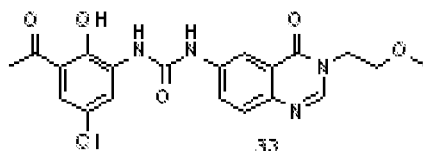
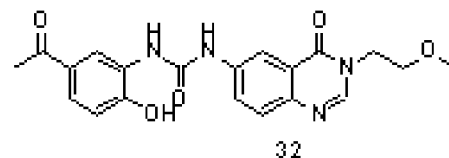
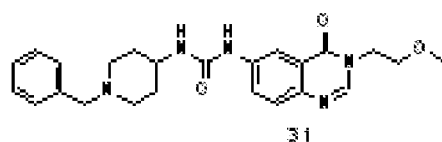
(3-aminophenyl)-2,2,2-trifluoroethanol in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, and 34;



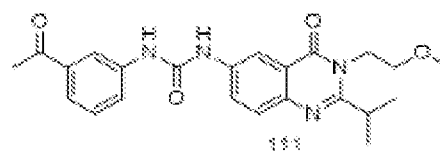
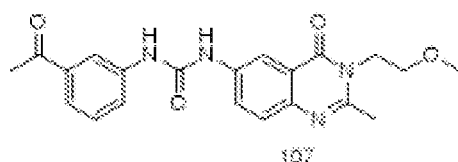
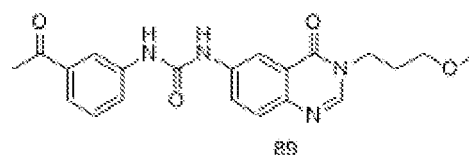
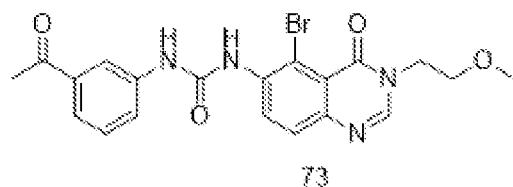
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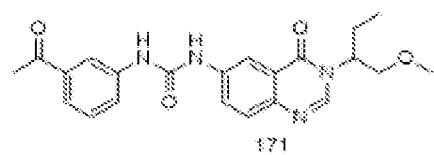
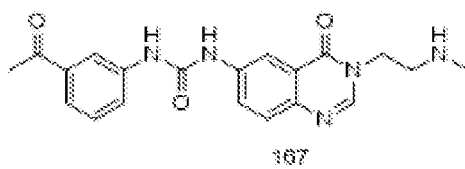
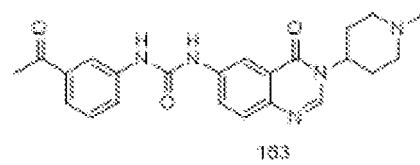
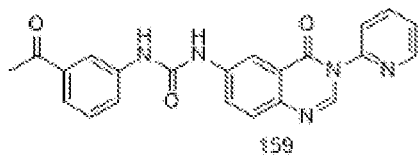
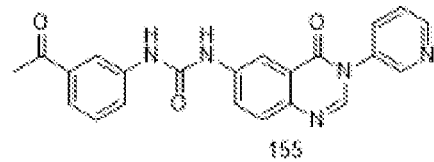
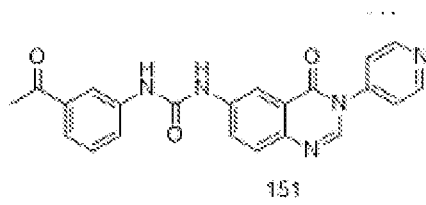
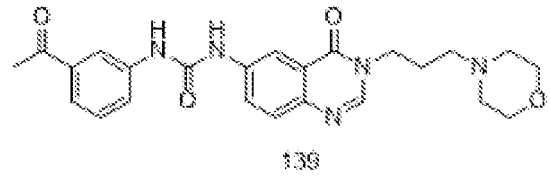
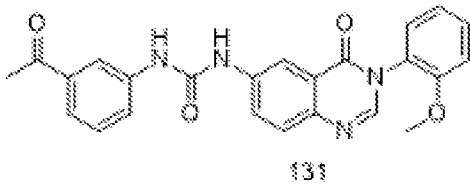
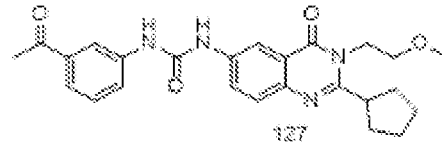
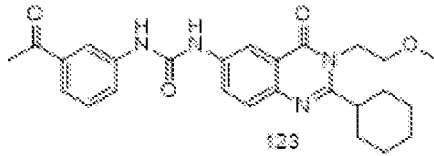
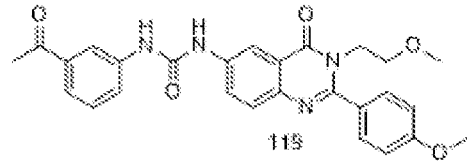
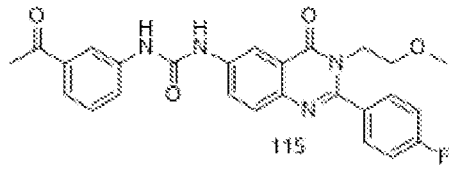
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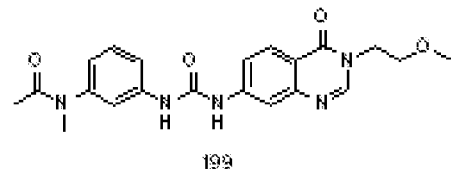
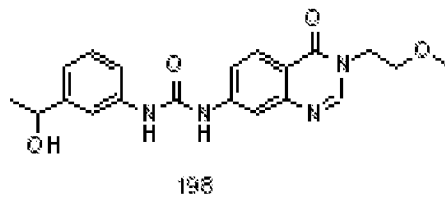
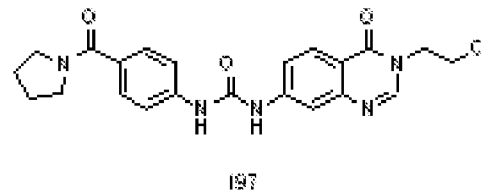
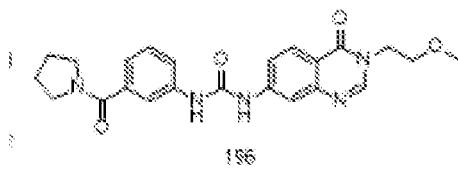
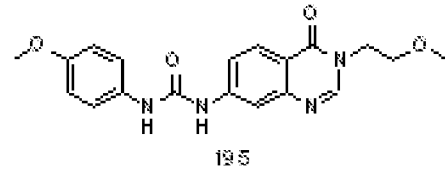
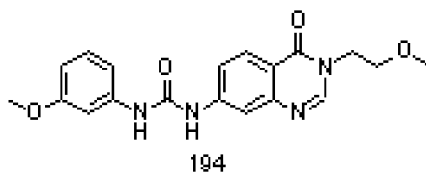
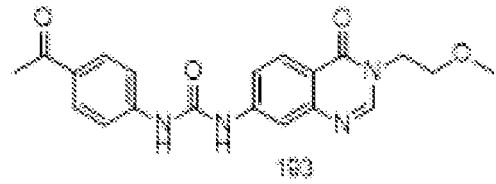
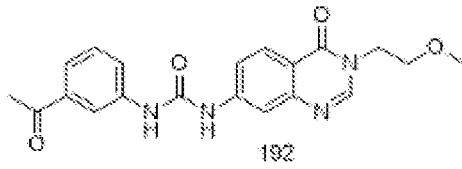
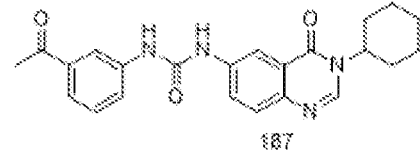
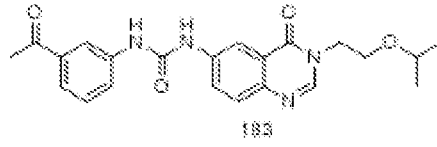
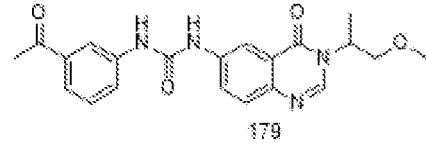
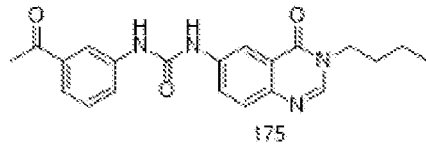
(xxi) alternately, treating the compound selected from the group consisting of **43, 88, 106, 110, 114, 118, 122, 126, 130, 138, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 191, 202, 206, 210, 214, 218, 222, 226, 231, 234, 237, 240, 243, 246, 249, 252, 255, 258, 261, 264, 267, 270, 273, 276, 280, 284, 288, 298, 303, 306, 329, 329a, 332, 332a, 335, 335a, 339, and 344** obtained in step (xvi),(xvii) and (xviii) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with 3-aminoacetophenone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **73, 89, 107, 111, 115, 119, 123, 127, 131, 139, 151, 155, 159, 163, 167, 171, 175, 179, 183, 187, 192, 193, 194, 195, 196, 197, 198, 199, 203, 207, 211, 215, 219, 223, 227, 232, 235, 238, 241, 244, 247, 253, 256, 259, 262, 268, 274, 277, 281, 285, 289, 304, 307, 330, 330a, 333, 333a, 336, 336a, 340, and 345**;



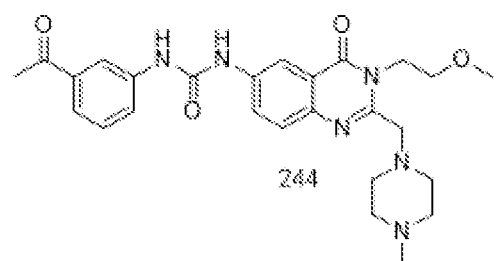
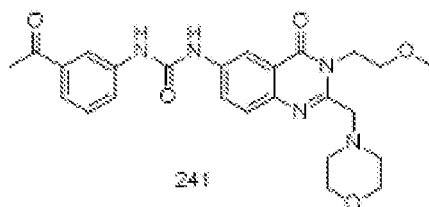
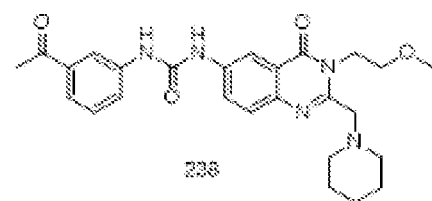
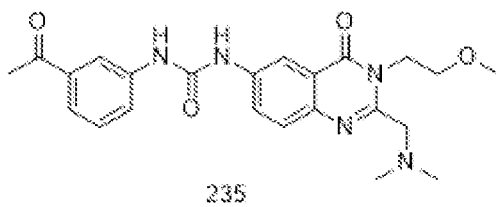
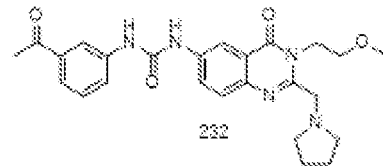
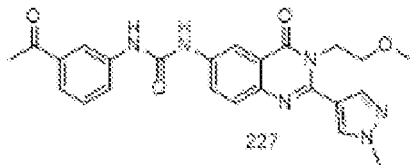
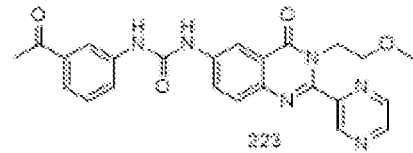
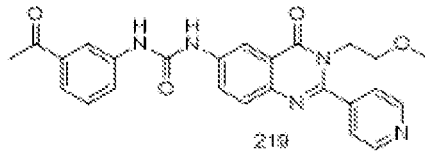
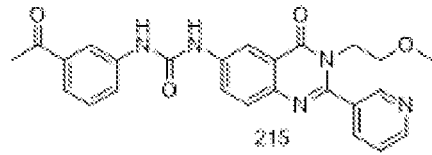
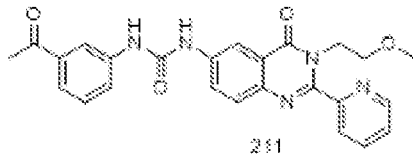
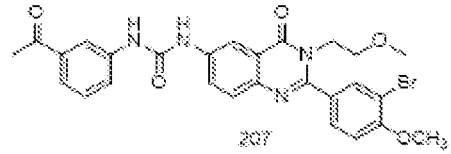
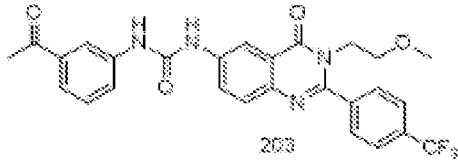
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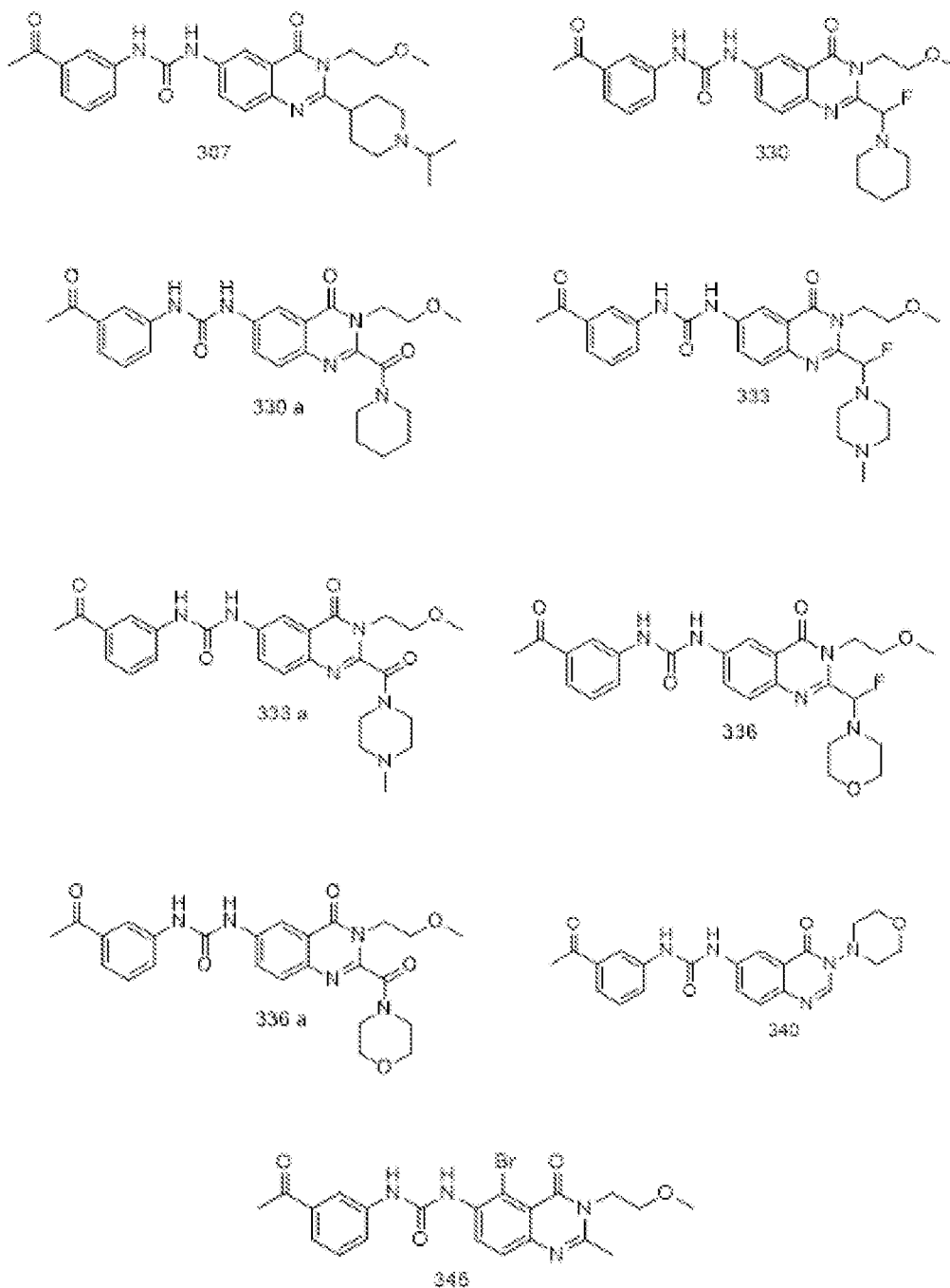
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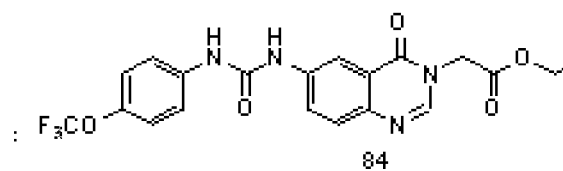
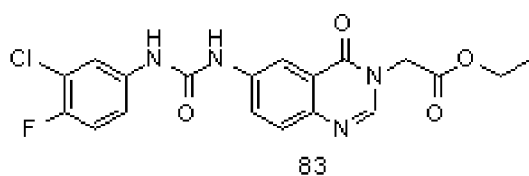
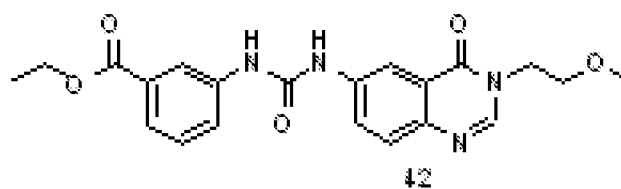
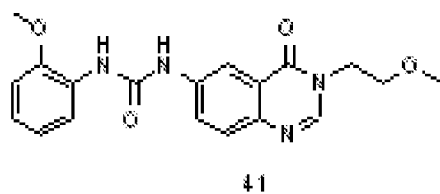
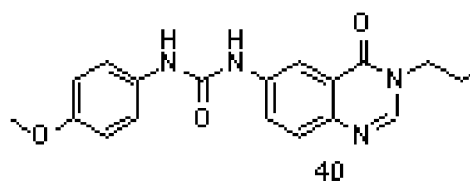
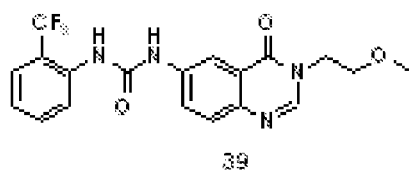
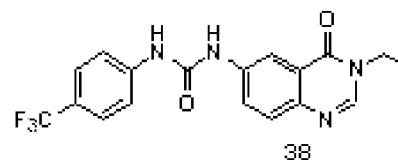
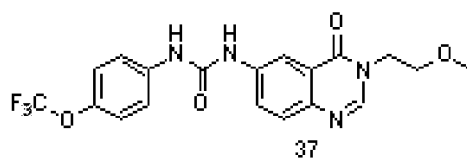
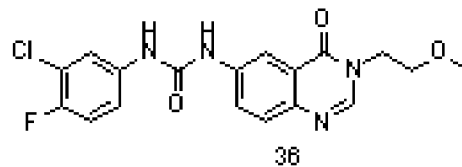
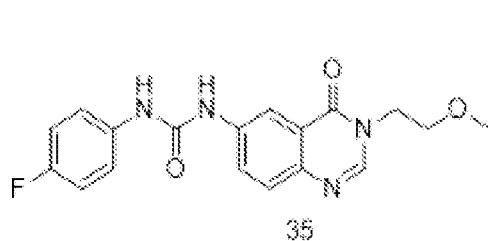


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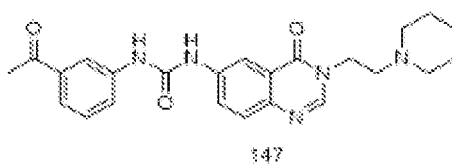
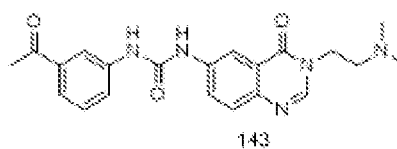
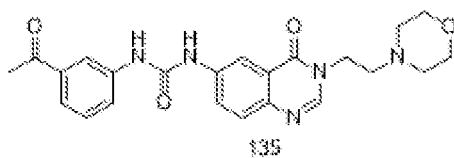
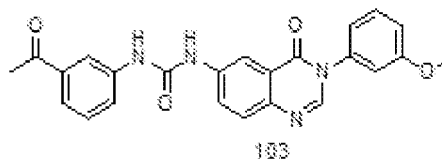
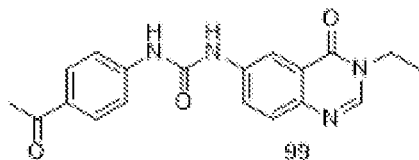
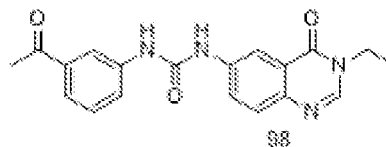
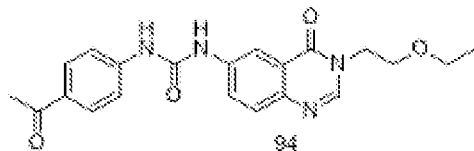
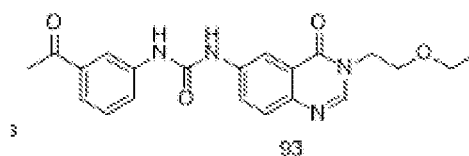
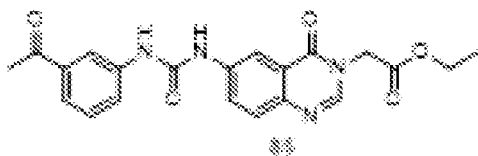


- (xxii) alternately, treating the compound selected from the group consisting of **4**, **82**, **92**, **97**, **102**, **134**, **142**, and **146** obtained in step (xvi) with a substituted aromatic isocyanate selected from the group consisting of 4-fluorophenylisocyanate, 3-chloro-4-fluorophenylisocyanate, (4-trifluoromethoxy)phenylisocyanate, (4-trifluoromethyl)phenylisocyanate, (2-trifluoromethyl)phenylisocyanate, 4-methoxyphenylisocyanate, 2-methoxyphenylisocyanate, ethyl 3-

isocyanatobenzoate, 3-acetylphenylisocyanate, and 4-acetylphenylisocyanate in presence of TEA as a base in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **35**, **36**, **37**, **38**, **39**, **40**, **41**, **42**, **83**, **84**, **85**, **93**, **94**, **98**, **99**, **103**, **135**, **143**, and **147**;

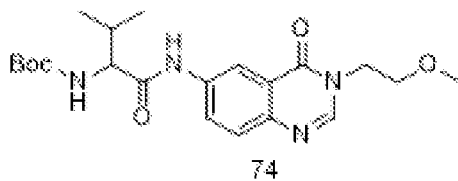


AMENDED SHEET (ARTICLE 19)

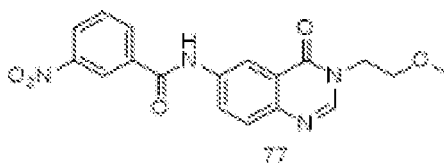


(xxiii) alternately, reacting compound **4** obtained in step(xvi) with HATU/ TEA in DMF at room temperature with 5 hours of stirring to obtain a compound **74**;

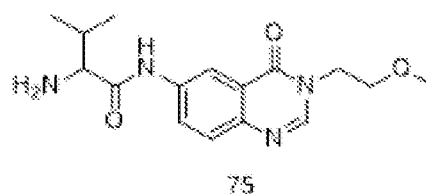
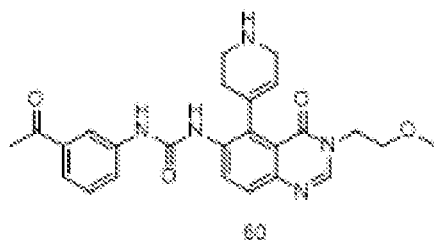
AMENDED SHEET (ARTICLE 19)



(xxiv) separately adding 3-nitrobenzoyl chloride (3-nitrobenzoic acid and Oxalyl Chloride) at 0 °C in DCM and TEA and stirring for 5 hours at room temperature to obtain a compound **77**;

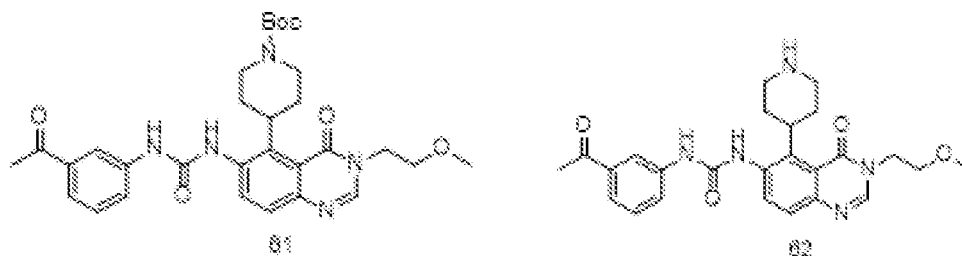


(xxv) separately Boc deprotecting the compound **59** obtained in step (xix) and the compound **74** obtained in step (xxiii) by TFA at room temperature for 2 hours to obtain a compound selected from **60** or **75**;

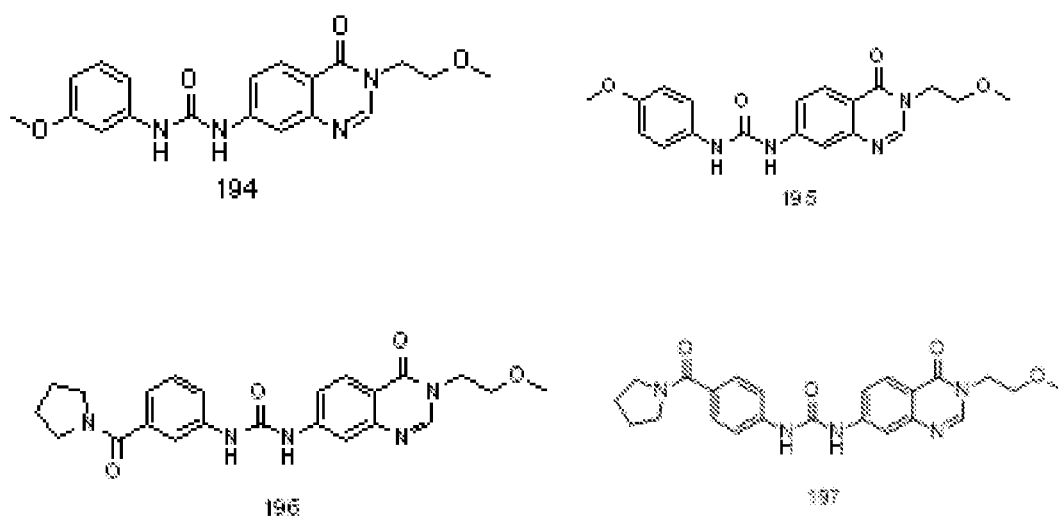


(xxvi) treating the compound **59** obtained in step (xix) and compound **60** obtained in step (xxv) with H₂/ Pd-C (5% wet) to obtain the compound having structure I selected from the group consisting of **61** and **62**;

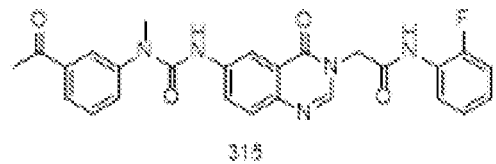
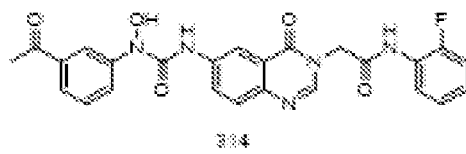
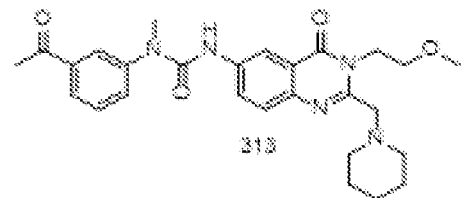
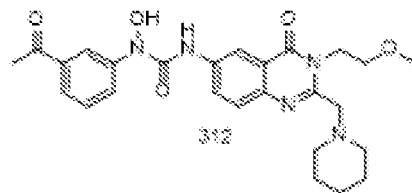
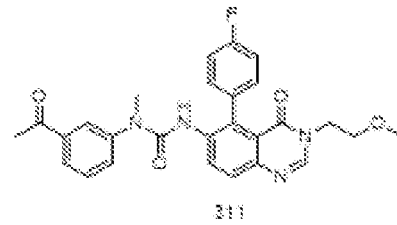
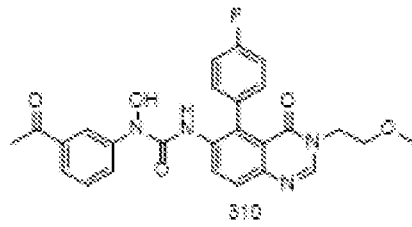
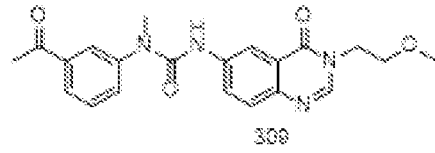
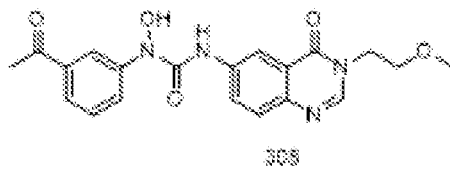
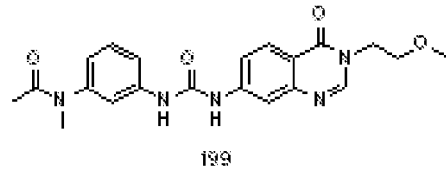
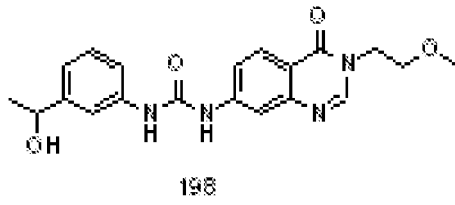
AMENDED SHEET (ARTICLE 19)



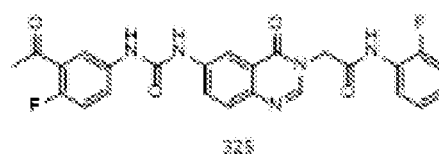
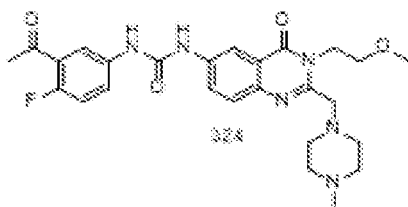
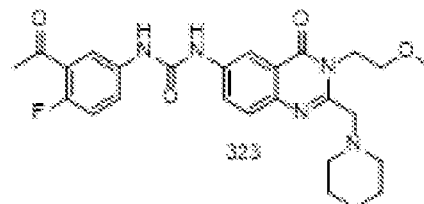
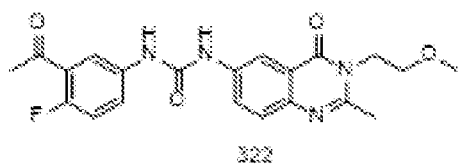
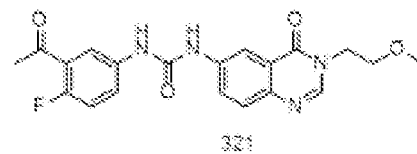
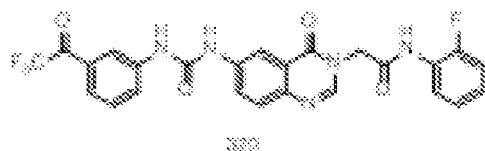
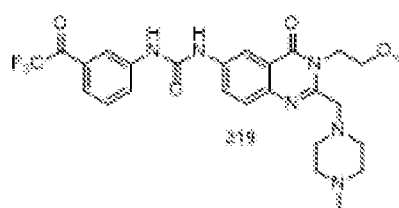
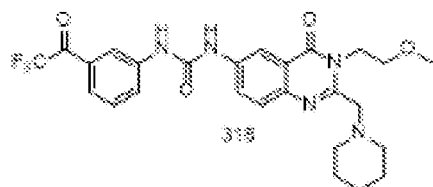
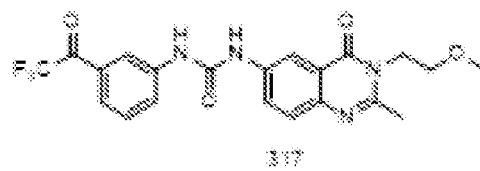
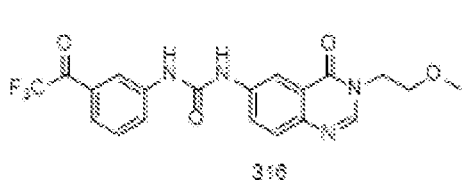
(xxvii) alternately, treating the compound selected from the group consisting of **191, 4, 46, 237, 249, 106, 243, and 252** obtained in step (xvi) and (xix) with 4-nitrophenylchloroformate in presence of TEA as a base followed by reaction with an amine selected from the group consisting of 3-aminoacetophenone, 4-aminoacetophenone, m-anisidine, p-anisidine, (3-aminophenyl)(pyrrolidin-1-yl)methanone, (4-aminophenyl)(pyrrolidin-1-yl)methanone, 1-(3-aminophenyl)-2,2,2-trifluoroethanol, -(3-aminophenyl)-N-methylacetamide, 1-(3-(hydroxyamino)phenyl)ethanone, 1-(3-(methylamino)phenyl)ethanone, and 1-(3-aminophenyl)-2,2,2-trifluoroethanone in dry THF at room temperature for 3-8 hours to obtain the compound having structure I selected from the group consisting of **194, 195, 196, 197, 198, 199, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, and 325**;



AMENDED SHEET (ARTICLE 19)

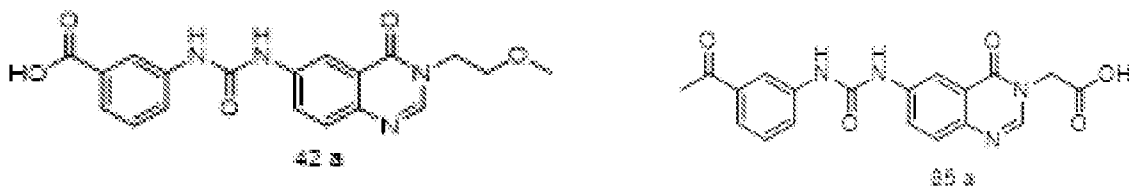


AMENDED SHEET (ARTICLE 19)

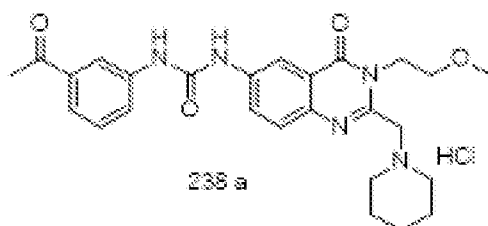


(xxviii)subjecting the compound selected from **42** and **85** obtained in step (xxii) to ester hydrolysis by LiOH monohydrate in presence of THF: EtOH: Water (3:2:1) proportion at room temperature for 1-2 hours to obtain the compound having structure I selected from the group consisting of **42a** and **85a**;

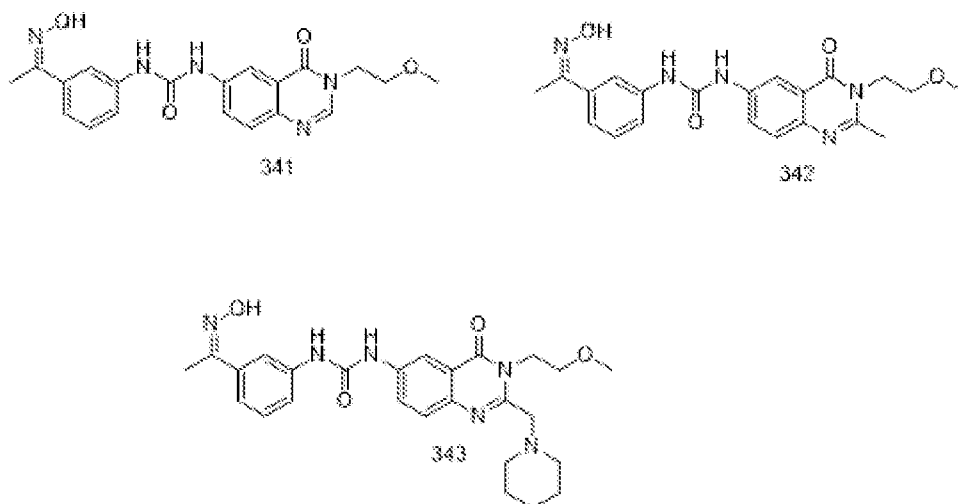
AMENDED SHEET (ARTICLE 19)



(xxix) reacting the compound **238** obtained in step (xxi) with 1M HCl in dioxane to obtain the compound having structure I **238a**; and



(xxx) reacting the compound selected from the group consisting of **9**, **107**, and **238** obtained in step (xx) and (xxi) with hydroxylamine hydrochloride ($\text{NH}_2\text{OH} \cdot \text{HCl}$) in ethanol (EtOH) at 80 °C for 12- 16 hours to obtain the compound having structure I selected from the group consisting of **341**, **342** and **343**



AMENDED SHEET (ARTICLE 19)

4. The compound as claimed in claim 1, for use in treating diseases and disorders related to modulation of COP1 enzyme through its stabilization or modulation of ATGL.
5. The compound as claimed in claim 1 for use in decreasing the level of triglycerides in hepatocytes.
6. The compound as claimed in claim 1, for use in treatment of disease selected from Non-Alcoholic Fatty Liver Disease (NAFLD) or Non-Alcoholic Steatohepatitis (NASH).
7. A composition comprising the compound having structure I as claimed in claim 1 along with pharmaceutically acceptable excipients.
8. A method of modulation COP1 enzyme through its stabilization by compound having structure I as claimed in claim 1.
9. A method of increasing the level of ATGL by compound having structure I as claimed in claim 1.

STATEMENT UNDER ARTICLE 19(1)

With reference to the search report and Written Opinion of the International Searching Authority [ISA/IN], we are suitably amending the claims to overcome the objection of clarity.

1. Claim 1 has been suitably amended to add “H” as a substituent group in the position R1, R3 and R4. Support for same is provided in structures of compounds : 1-103, 192-199, 247-277, 295, 308-311, 314-316, 321, 325, 340, 341 provided in as filed specification.
2. Any additions in the claims have been indicated by underline and any deletions in the claims have been indicated by strike through.

The amended claims do not go beyond the disclosure of the international application as filed and have no impact on the description and drawings as filed.

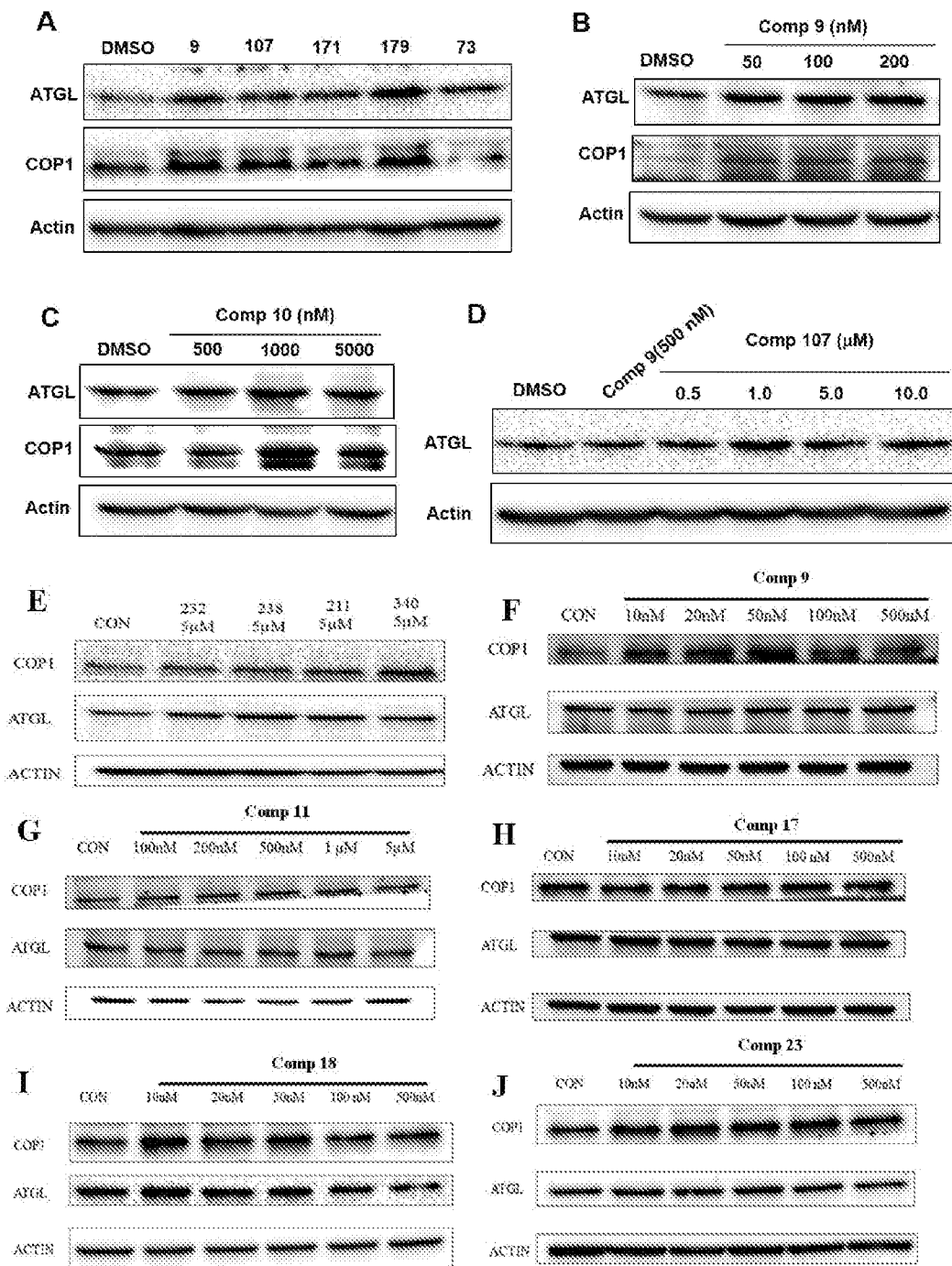


Fig. 1 (Continue..)

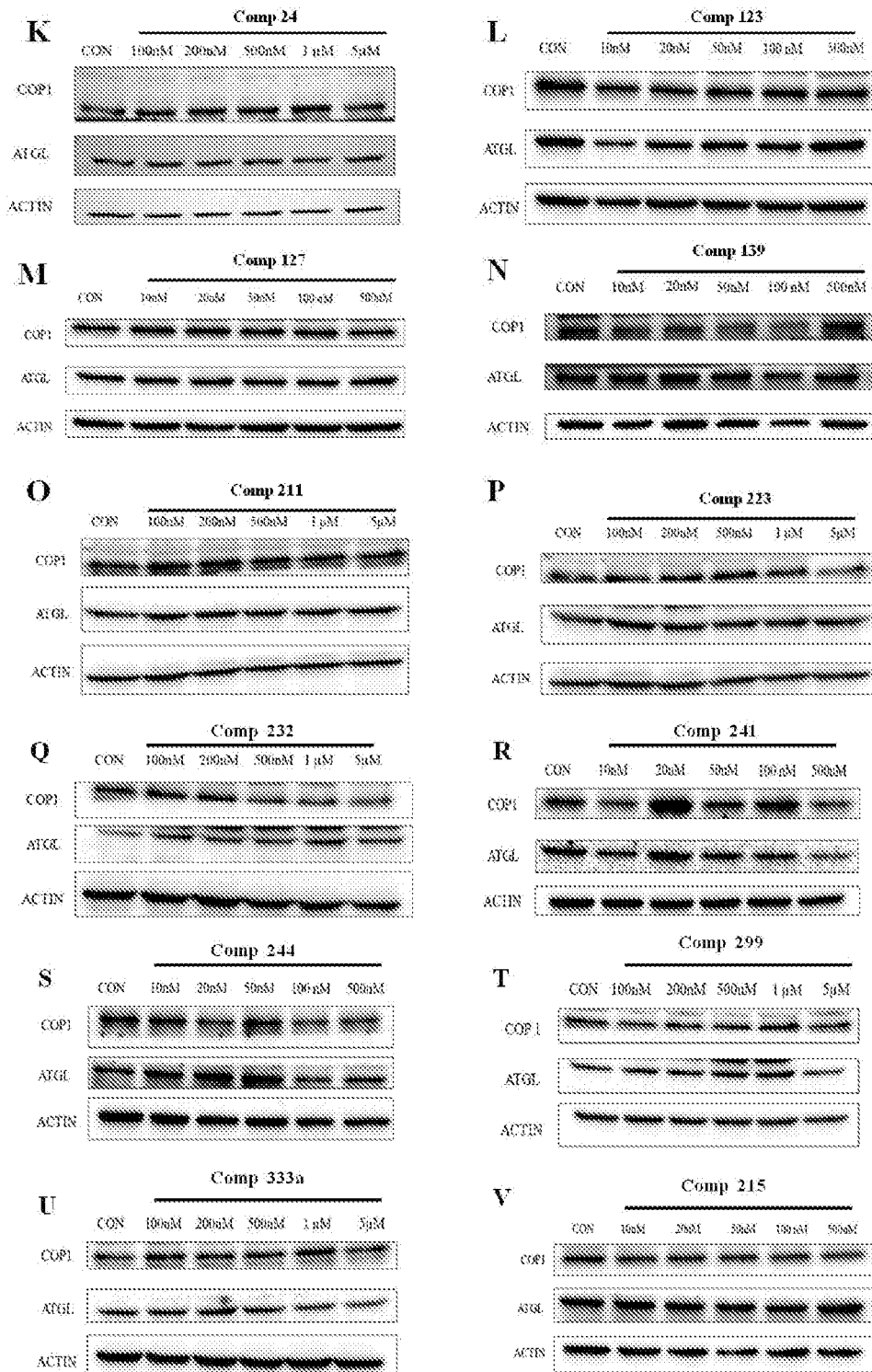


Fig. 1 (Continue..)

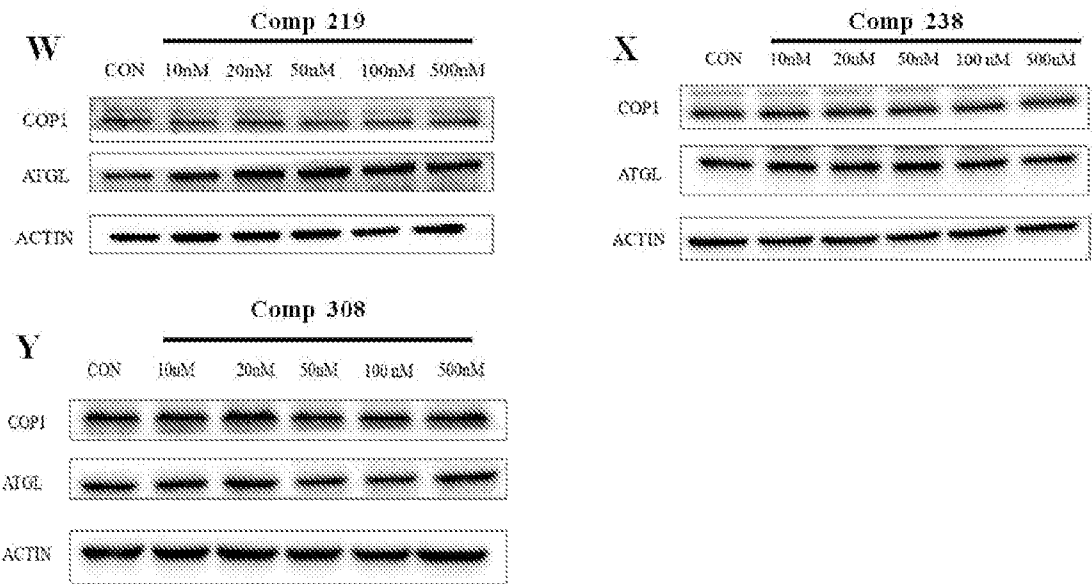


Fig. 1

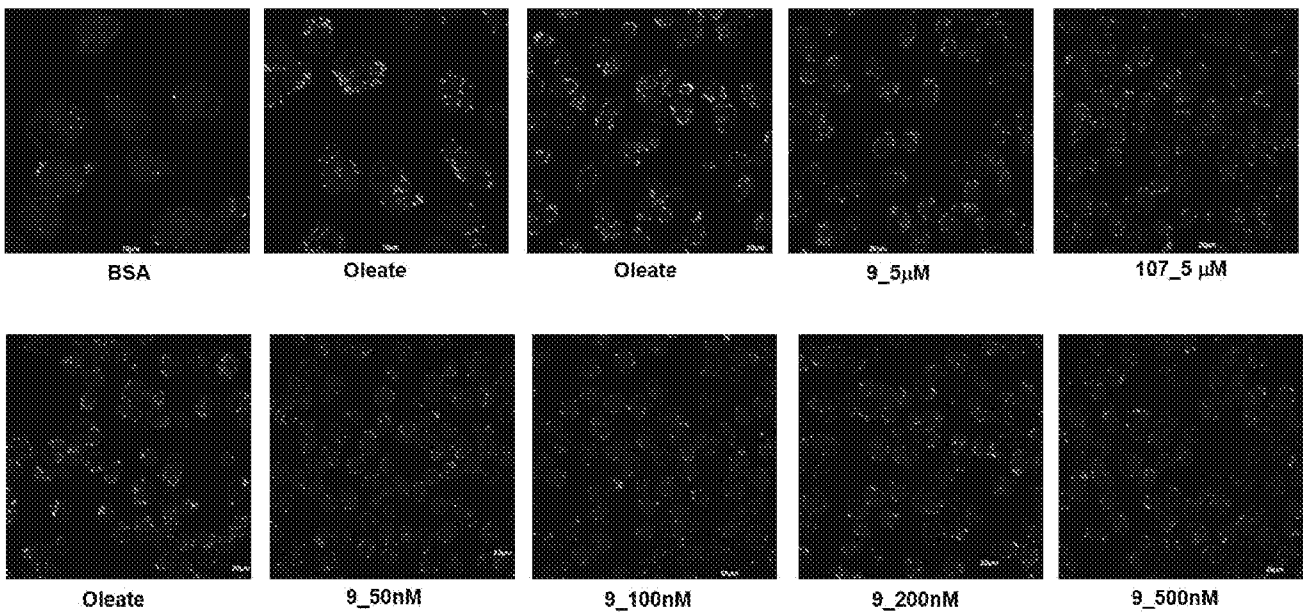


Fig. 2

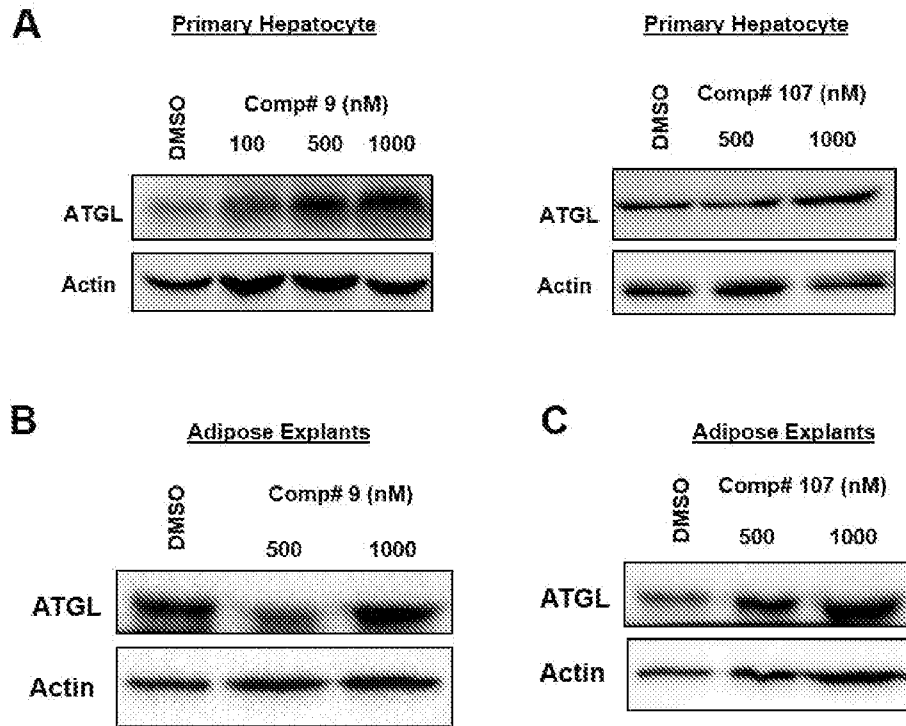


Fig. 3

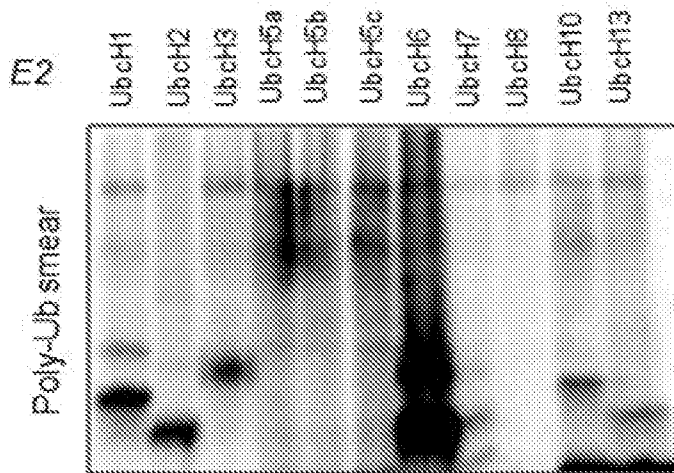


Fig. 4

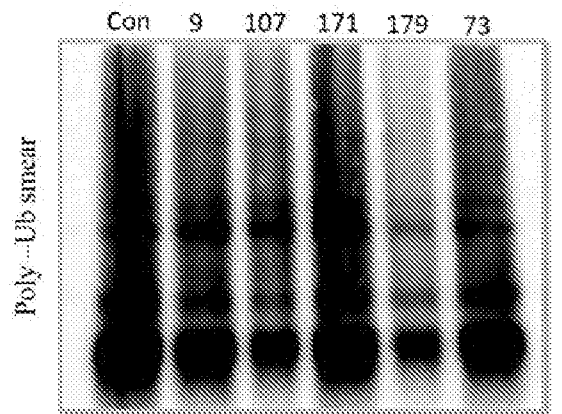


Fig. 5

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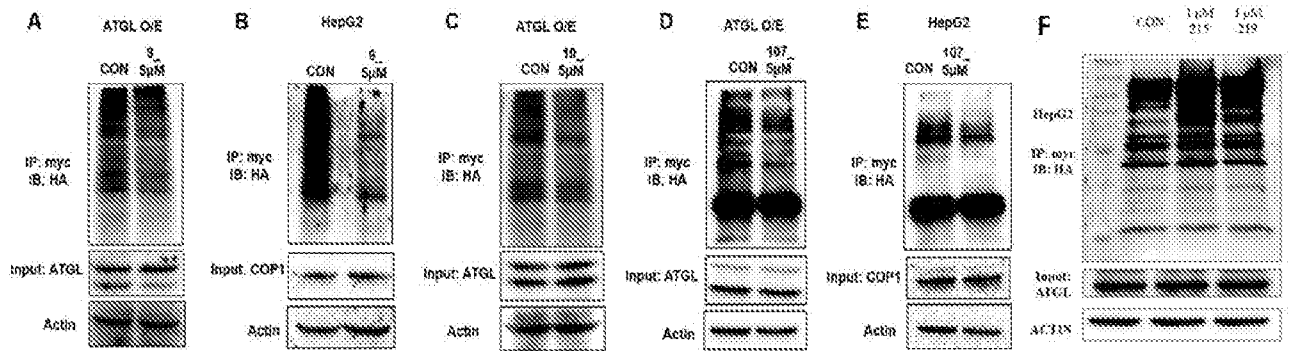


Fig. 6

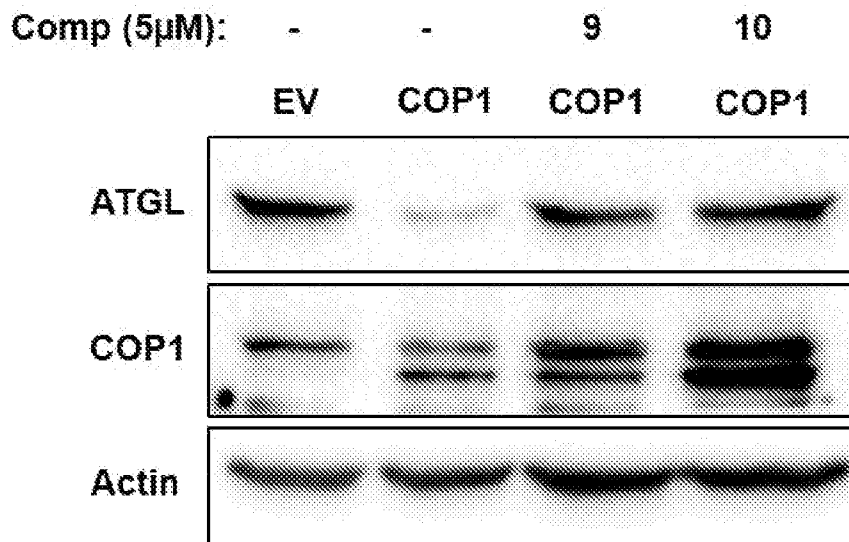


Fig. 7

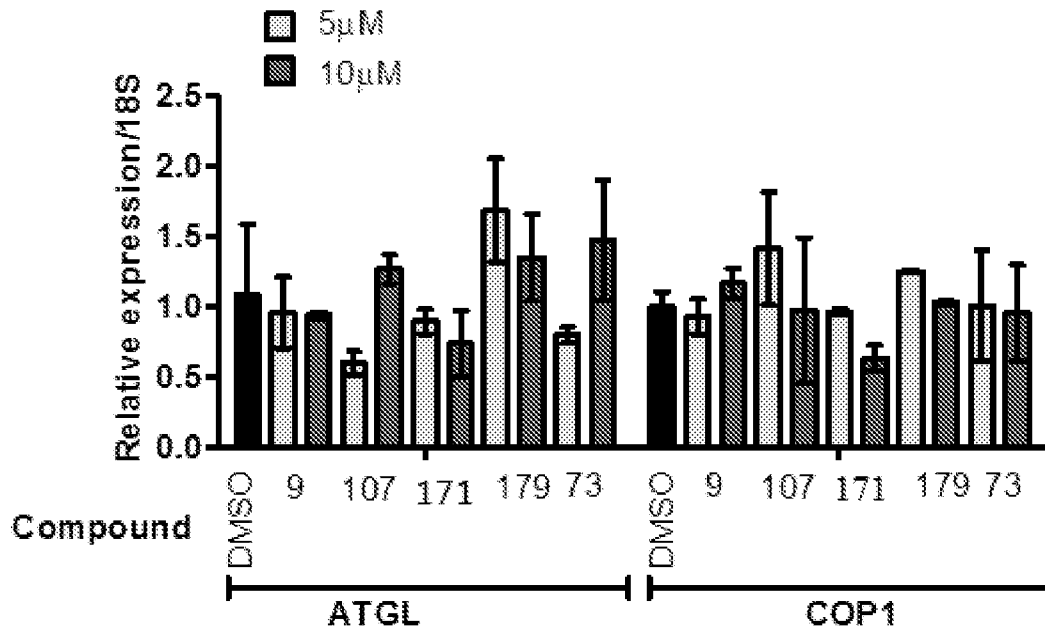


Fig. 8

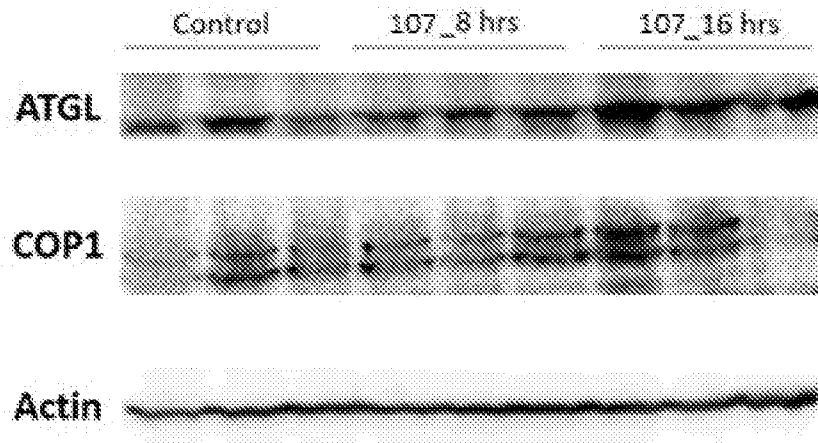


Fig. 9

7/8

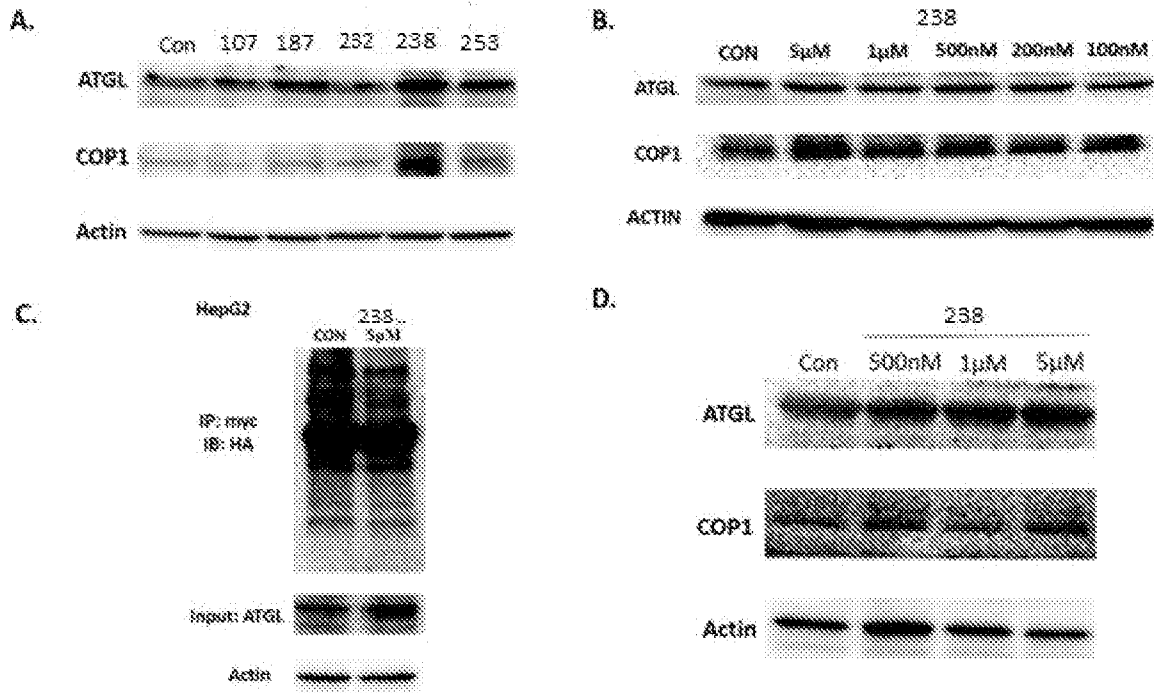


Fig. 10

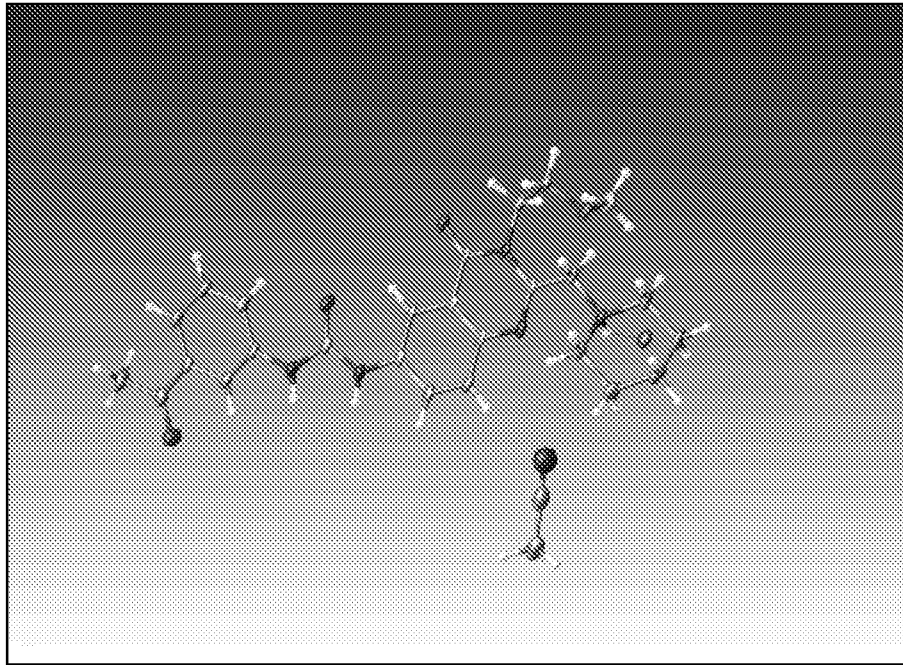


Fig. 11

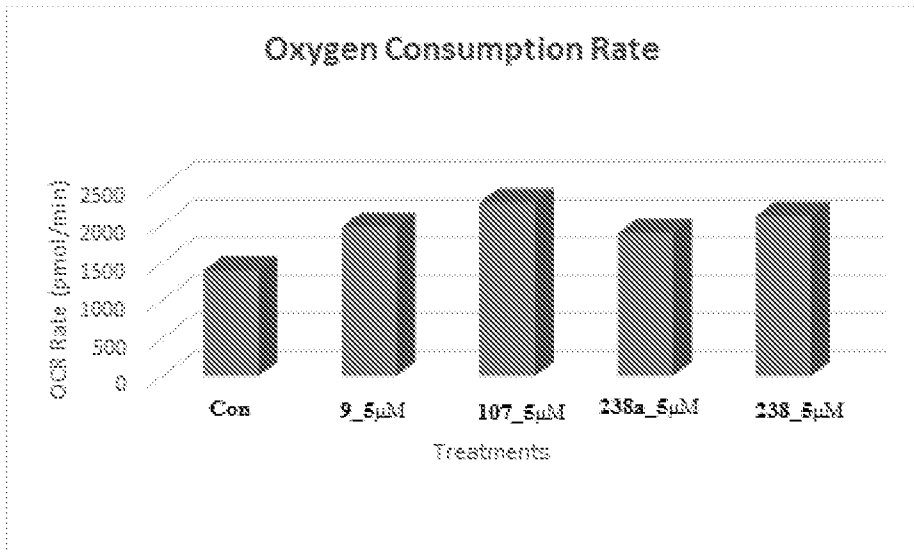


Fig. 12