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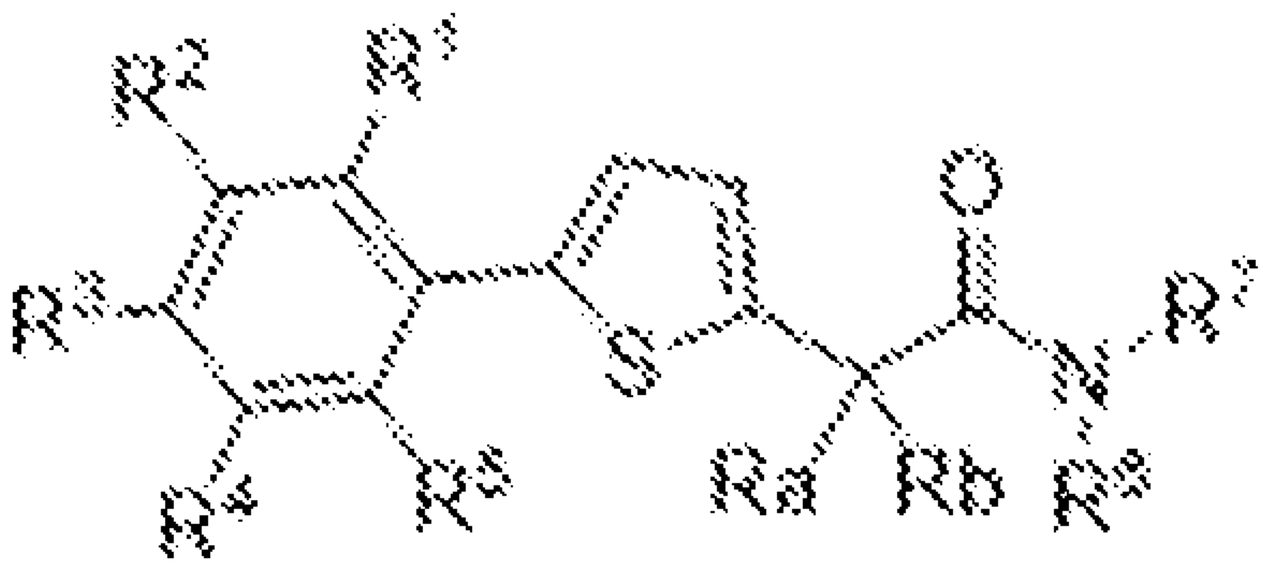
(54) Titre : NOUVEAUX COMPOSES DE THIOPHENE, PROCEDE DE SYNTHESE ET D'UTILISATION DE CEUX-CI
(54) Title: NOVEL THIOPHENE COMPOUNDS, PROCESS FOR SYNTHESIS AND USE THEREOF



Formula I

(57) Abrégé/Abstract:
The present invention relates to novel thiophene compounds of general Formula I, and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof along with process for their preparation. The present invention discloses compounds that are useful in the treatment and prevention of autoimmune diseases.

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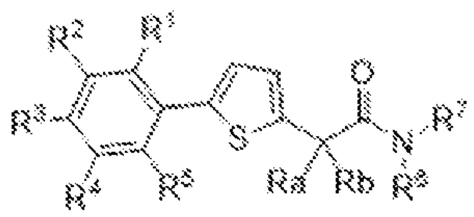
(54) **Title:** NOVEL THIOPHENE COMPOUNDS, PROCESS FOR SYNTHESIS AND USE THEREOF

(57) **Abstract:** The present invention relates to novel thiophene compounds of general Formula I, and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof along with process for their preparation. The present invention discloses compounds that are useful in the treatment and prevention of autoimmune diseases.



Formula I

WO 2019/043642 A1

NOVEL THIOPHENE COMPOUNDS, PROCESS FOR SYNTHESIS AND USE THEREOF

FIELD OF THE INVENTION:

[0001] The present invention relates to novel thiophene compounds of general Formula 1 and the process for the preparation thereof. The present invention discloses compounds that are useful in the treatment and prevention of cellular stress-mediated diseases involving systemic and /or organ-specific immunity.

BACKGROUND OF THE INVENTION:

[0002] The immune system is a collection of special cells and chemicals that fight infection-causing agents such as bacteria and viruses. An autoimmune disorder occurs when a person's immune system mistakenly attacks their own body cells and tissues. Autoimmune disorders are broadly grouped into two categories – 'organ-specific' meaning only one organ is affected, while in 'systemic' disorders, multiple organs or body systems may be affected.

[0003] There are a large number of autoimmune disorders ranging in severity from mild to disabling, depending on which system of the body is under attack and to what degree. It has also been observed that, women are more susceptible than men, particularly during their childbearing years. It is thought that sex hormones may be at least partly responsible.

[0004] Autoimmune diseases are characterized by an abnormal immune response involving either cells or antibodies, that are in either case directed against normal autologous tissues. Both adaptive immune response, comprising T-cell mediated immunity and humoral immune response, involving antibody-mediated immunity is involved in the trigger and spread of autoimmune diseases.

[0005] The triggers of autoimmunity are not well understood. Till recent years, studies on etiopathogenesis of autoimmune diseases have focused on the role of immune components.

However, several studies have now highlighted the synergistic role of target tissues in spread of autoimmunity. A common pathway that has emerged in these studies is endoplasmic reticulum stress (ER stress). ER is a major cellular organelle that is associated with critical functions involving cellular homeostasis including protein synthesis, folding and quality control, antigen processing and presentation, calcium control and redox balance. The physiological activity of the ER is tightly controlled by cell intrinsic as well as extrinsic processes. Disturbance in the functioning of ER triggers a stress response called ER stress that activates intracellular signaling pathways, constituting the unfolded protein response (UPR) targeted to manage stress conditions. However, inability to manage ER stress is implicated in a number of pathological conditions including cancers, metabolic, dermatological, cardiovascular and neurodegenerative diseases. In addition, aberrant regulation of ER stress is associated with early autoimmune events. For instance, misfolding of proteins and alteration in antigen processing can lead to immunogenic neoantigen formation. Further, stressed cells could be inadequate to support tolerance mechanisms in autoreactive cells, which are less susceptible to programmed cell death, perpetuating autoimmunity in diseases including type I diabetes, rheumatoid arthritis, psoriatic arthritis, multiple sclerosis, lupus, celiac disease, pernicious anaemia. ER stress mechanisms attain special interest in the physiology of skin, an organ that is constantly exposed to the external environment. In fact, deregulation of ER stress mechanisms are associated with several skin autoimmune diseases, including Vitiligo, psoriasis, SLE, pemphigus, scleroderma. Targeting ER stress mechanisms thus represents a potential therapeutic approach for autoimmune diseases.

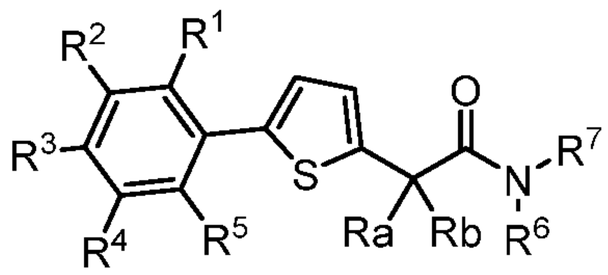
[0006] It has been observed that most of the existing therapies for autoimmune disorders aim to provide only symptomatic benefit to patients as there is little by way of targeted and effective therapy. Administration of steroids is one of the most common approach for treatment. However, the non-specific nature and side-effects associated with long-term steroid usage limits their usefulness. As an example, Vitiligo is an autoimmune disease where dysregulation of immune functions takes place with increased levels of inflammatory cytokines in the lesion. Hence, topical corticosteroids become the most common first line therapy. Patients are also advised to expose themselves to sunlight in order to increase the melanin synthesis. Phototherapy (narrowband UVB or 311 nm laser)

is generally included with topical steroids to achieve better results. However, a number of patients don't achieve the desired level of pigmentation which adds to their psychological burden. At times, dermatologists are unable to tell the possible success of the therapy being administered, hence patients remain uncertain about the duration and outcome of treatment. Clearly, new therapies targeting relevant pathways involved in triggering autoimmune responses are need of the hour.

[0007] The embodiments of the present invention provide for chemical entities that modulate cellular stress. More specifically, the chemical entities rescue cells from stress mediated death and thus impede cascade of events leading to aberrant regulation of immunity. These chemical entities thus offer potential for prevention and treatment of immune-related disorders and diseases.

SUMMARY OF THE INVENTION:

[0008] The compounds of the present invention have the general Formula I:



Formula I

wherein

R^1, R^2, R^3, R^4, R^5 are each independently selected from hydrogen, halogen and, phenyl, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C1-C5 alkoxyalkyl, straight chain or branched C1-C5 alkoxyaryl, aryl, CF3, C_3-C_7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

any of two adjacent R groups form a 5-6 membered aromatic or aliphatic ring comprising at least one hetero atom selected from a group of O, N and S;

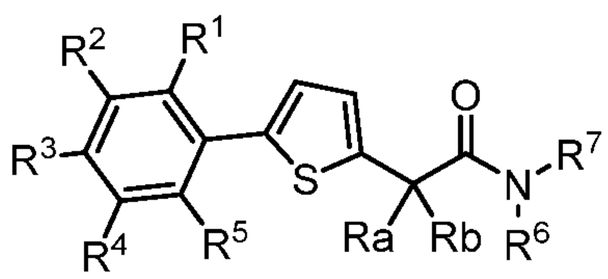
Ra and Rb are each independently selected from hydrogen, alkyl, aralkyl, alkenyl, alkynyl, or both Ra, Rb together form a 3-7 membered ring comprising at least one hetero atom selected from a group of O, N and S;

R^6 and R^7 are each independently selected from hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl,

together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N, and S, $-CH_2(CH_2)_nNR_cR_d$ wherein n is 0-3, and R_c,and R_d are both independently selected from C1-C5 alkyl or together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S; and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

[0009] The pharmaceutically acceptable salts of the compounds of present invention is selected from a group consisting of hydrochloric acid, hydrobromic acid, nitric acid, sulfuric acid, phosphoric acid, benzenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, formamidinesulfonic acid, naphthalenedisulfonic acid, formic acid, fumaric acid, acetic acid, propionic acid, lactic acid, malic acid, citric acid, maleic acid, benzoic acid, malonic acid, tartaric acid, oxalic acid succinic acid, or salts of sodium, potassium, calcium, magnesium and ammonium as an active ingredient, with one or more pharmaceutically acceptable carriers, diluents or excipients.

[0010] The present invention also relates to the process of preparation of the compounds having general Formula I:



Formula I

wherein

R^1, R^2, R^3, R^4, R^5 are each independently selected from hydrogen, halogen and, phenyl, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl, straight

chain or branched C1-C5alkoxyalkyl, straight chain or branched C1-C5 alkoxyaryl, aryl, CF3, C_3-C_7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

any of two adjacent R groups form a 5-6 membered aromatic or aliphatic ring comprising at least one hetero atom selected from a group of O, N and S;

Ra and Rb are each independently selected from hydrogen, alkyl, aralkyl, alkenyl, alkynyl, or both Ra, Rb together form a 3-7 membered ring comprising at least one hetero atom selected from a group of O, N and S;

R^6 and R^7 are each independently selected from Hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl,

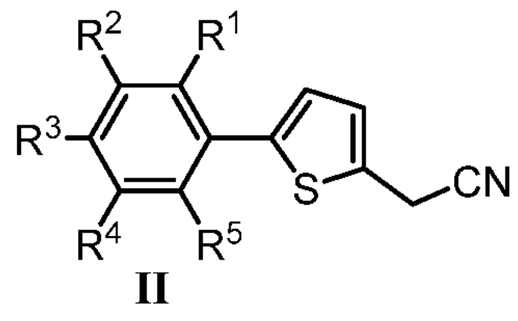
R^6 and R^7 together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N, S, $-CH_2(CH_2)_nNR_cR_d$ wherein n is 0-3, and R_c,and R_d are both independently selected from C1-C5 alkyl or together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

[0011] The process for preparation of the compounds of Formula I comprise the following steps:

a) Stirring thiophene acetonitrile in the presence of catalyst N-bromosuccinamide (NBS) in dimethylformamide (DMF) or solvents selected from dimethylsulfoxide (DMSO) Tetrahydrofuran (THF);

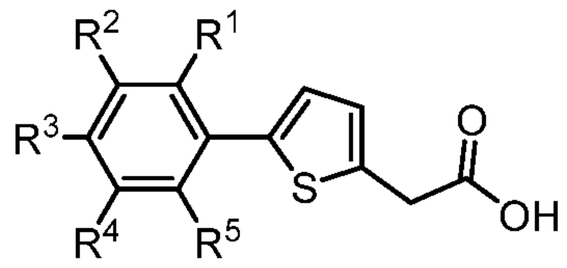
b) Reacting the resultant bromo thiophene acetonitrile obtained from Step a, with substituted phenylboronic acid in the presence of a solvent selected from a group comprising toluene, benzene, dimethyl formamide, dioxane, tertiary butanol, potassium carbonate and triphenylphosphine palladium(0) or any Palladium (0) catalyst at a temperature of about 80 °C -100°C for about 6 -24 hours to obtain compound of Formula II:



II

;

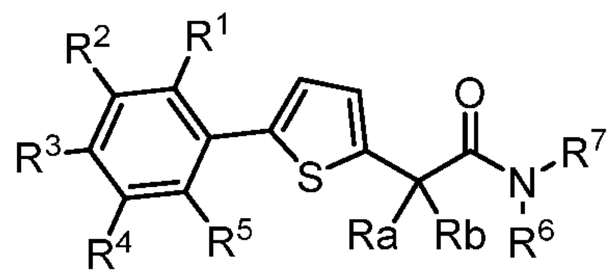
c) Refluxing the compound of Formula II after stirring it in ethanol and aqueous sodium hydroxide to obtain the compound of Formula III:



III

;

d) Coupling of compound of Formula III with amines, in the presence of a base selected from Hunigs base (N,N, Diisopropylethylamine), triethylamine, pyrrolidine, piperidine and amide coupling reagent selected from HATU, HBTU, EDC, EDC-HOBt, EDC-DMAP, DCC, DCC-DMAP, DCC-HOBt, DIC, TBTU, T3P added at 0°C to obtain Formula I:



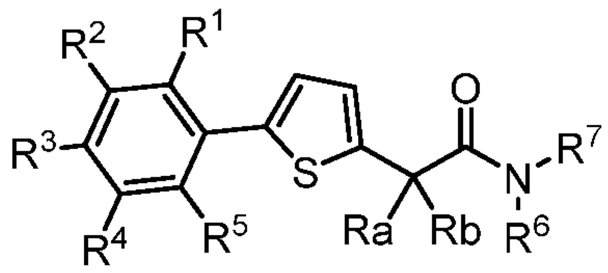
Formula I

; and

e) Optionally purifying the compound by column chromatography.

DETAILED DESCRIPTION:

[0012] The compounds of the present invention have the general Formula I:



Formula I

wherein

R1, R2, R3, R4, R5 are each independently selected from hydrogen, halogen, phenyl, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C1-C5 alkoxyalkyl, straight chain or branched C1-C5 alkoxyaryl, aryl, CF3, C3-C7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

any of two adjacent R groups form a 5-6 membered aromatic or aliphatic ring comprising at least one hetero atom selected from a group of O, N and S;

Ra and Rb are each independently selected from hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl, or both Ra, and Rb together form a 3-7 membered ring comprising at least one hetero atom selected from a group of O, N and S;

R6 and R7 are each independently selected from hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl;

-CH2(CH2)nNRcRd wherein n is 0-3, and Rc, Rd are both independently selected from straight chain or branched C1-C5 alkyl or together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S; or

both R6 and R7 may together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N and S;

and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

[0013] The pharmaceutically acceptable salts of the compounds of the present invention is selected from a group consisting of hydrochloric acid, hydrobromic acid, nitric acid,

sulfuric acid, phosphoric acid, benzenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, formamidinesulfonic acid, naphthalenedisulfonic acid, formic acid, fumaric acid, acetic acid, propionic acid, lactic acid, malic acid, citric acid, maleic acid, benzoic acid, malonic acid, tartaric acid,oxalic acid succinic acid, or salts of sodium, potassium, calcium, magnesium and ammoniumas an active ingredient, with one or more pharmaceutically acceptable carriers, diluents or excipients.

[0014] In the context of this invention, the term “alkyl” designates a hydrocarbon radical that is saturated, linear, branched, or cyclic, halogenated or not, having particularly from 1 to 5 carbon atoms. Such as methyl, trifluoromethyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tertbutyl, sec-butyl, pentyl.

[0015] The term “alkenyl” refers to a hydrocarbon radical that is unsaturated having one or more carbon-carbon double bond, linear, branched, halogenated, or cyclic having particularly from 2 to 5 carbon atoms.

[0016] The term “alkynyl” refers to a hydrocarbon radical that is unsaturated having one or more carbon-carbon triple bond, linear, branched, halogenated, or cyclic having particularly from 2 to 5 carbon atoms.

[0017] The term “alkoxyalkyl” refers to an alkyl chain linked to an oxygen atom forming an ether bond. The alkyl chain corresponds to the previously expressed definition and includes alkyl groups such as methoxy, trifluoromethoxy, ethoxy, n-propyloxy, isopropyloxy, n-butoxy, iso-butoxy, tertio-butoxy, sec-butoxy.

[0018] The term “aralkyl” refers to aryl-substituted alkyl hydrocarbon radical where the hydrocarbon radical comprises about 1-5 carbon atoms.

[0019] The term “cycloalkyl” designates an alkyl group as defined above and forms at least one cycle (e.g. cycloalkyl groups having 3 to 8 carbon atoms: cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl).

[0020] The term “aryl” refers to aromatic groups comprising preferably from 6-10 carbon atoms, possibly interrupted by one or several heteroatoms selected among N, O, or S (more specifically call “heteroaryl”). They are generally mono- or bi-cyclical and comprise preferably from 6 to 14 carbon atoms, such as phenyl, α-naphtyl, β-naphtyl.

[0021] The term “alkoxyaryl” refers to an alkyl group having bonded to an oxygen atom to form an ether bond attached to an aryl group.

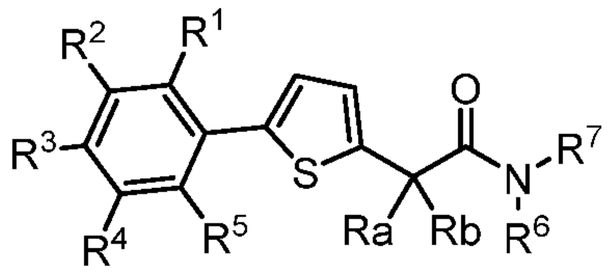
[0022] The term “heterocycle” refers to any a cycloalkyl group as defined above interrupted by one or more heteroatoms chosen among O, N and S being aliphatic or aromatic rings being preferably 3-7 membered rings.

[0023] The term “halogen” refers to an atom of fluorine, chlorine, bromine or iodine.

[0024] The term “effective amount”, “pharmaceutically effective amount” or “therapeutically effective amount” refers to any amount which will cause an improvement or change in the condition for which it is applied. The amount is sufficient to prevent or treat a disorder, disease or condition or one or more of its symptoms and/or to prevent the occurrence of the disease or disorder and can be determined by standard clinical techniques. The amount may vary with the condition being treated, the stage of advancement of the condition, the body surface area affected with the clinical condition, and the type and concentration of formulation administered.

[0025] TThe acronym “HATU” refers to 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate, Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium; the acronym “HBTU” refers to 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate, Hexafluorophosphate Benzotriazole Tetramethyl Uronium; the acronym “EDC” refers to 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide; the acronym “EDC-HOBt” refers to 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide- Hydroxybenzotriazole; the acronym “EDC-DMAP” refers to 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide-Dimethylaminopyridine; the acronym “DCC” refers to N,N'-Dicyclohexylcarbodiimide; the acronym “DCC-DMAP” refers to N,N'-Dicyclohexylcarbodiimide- 4-Dimethylaminopyridine; the acronym “DCC-HOBt” refers to N,N'-Dicyclohexylcarbodiimide -Hydroxybenzotriazole; the acronym “DIC” refers to N,N'-Diisopropylcarbodiimide; the acronym “TBTU” refers to 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate; the acronym “T3P” refers to Propylphosphonic Anhydride; the acronym “NBS” refers to N-bromosuccinamide; the acronym “DMF” refers to dimethylformamide; the acronym “DMSO” refers to dimethyl sulfoxide; the acronym “THF” refers to Tetrahyydrofuran; the acronym “DIPEA” refers to N,N-Diisopropylethylamine also known as Hunig’s base.

[0026] The present invention further discloses process the preparation of the compounds of general Formula I:



Formula I

wherein

R^1, R^2, R^3, R^4, R^5 are each independently selected from hydrogen, halogen and, phenyl, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C1-C5 alkoxyalkyl, straight chain or branched C1-C5 alkoxyaryl, aryl, CF3, C_3-C_7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

any of two adjacent R groups can form a 5-6 membered aromatic or aliphatic ring comprising at least one hetero atom selected from a group of O, N and S;

Ra and Rb are each independently selected from hydrogen, alkyl, aralkyl, alkenyl, alkynyl, or both Ra, Rb together form a 3-7 membered ring comprising at least one hetero atom selected from a group of O, N and S;

R^6 and R^7 are each independently selected from Hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl,

R^6 and R^7 together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N, S, $-CH_2(CH_2)_nNR_cR_d$ wherein n is 0-3, and

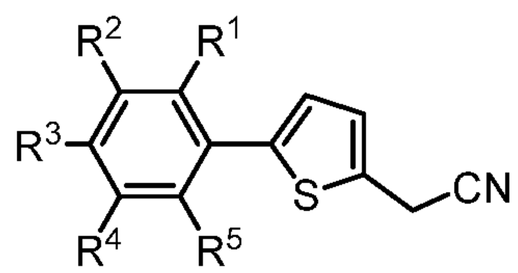
R_c,and R_d are both independently selected from C1-C5alkyl or together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

And their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

[0027] A process for preparation of the compounds of Formula I, comprising the steps of

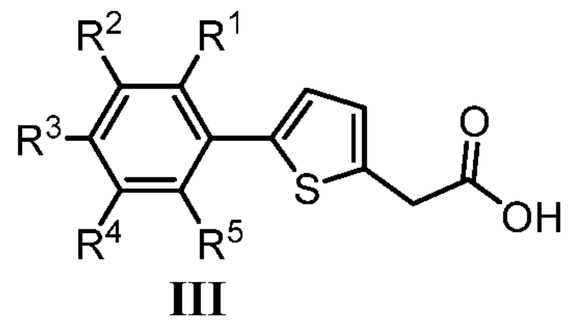
a) Stirring thiophene acetonitrile in the presence of catalyst N-bromosuccinamide (NBS) in dimethylformamide (DMF) or solvents selected from dimethylsulfoide (DMSO) Tetrrahydrofuran(THF);

b) Reacting the resultant bromo thiophene acetonitrile obtained from Step a, with substituted phenylboronic acid in the presence of solvent selected from a group comprising toluene, benzene, dimethyl formamide, dioxane, tertiary butanol, potassium carbonate and triphenylphosphine palladium(0) or any Palladium (0) catalyst at a temperature of about 80 °C -100°C for about 6 -24 hours to obtain compound of Formula II:



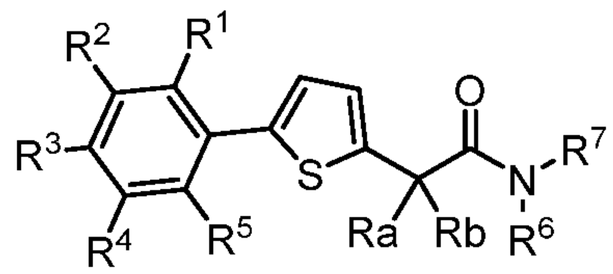
II ;

c) Refluxing the compound of Formula II after stirring it in ethanol and aqueous sodium hydroxide to obtain the compound of Formula III:



III ;

d) Coupling of compound of Formula III with amines, in the presence of a base selected from Hunigs base (N,N, Diisopropylethylamine), triethylamine, pyrrolidine, piperidine and amide coupling reagent selected from HATU, HBTU, EDC, EDC-HOBt, EDC-DMAP, DCC, DCC-DMAP, DCC-HOBt, DIC, TBTU, T3P added at 0°C to obtain Formula I:



Formula I ; and

e) Optionally purifying the compound by column chromatography.

[0028] Further, the present invention discloses the compounds of Formula I and their stereoisomers including diastereoisomers and enantiomers, pure or mixed racemic mixture, geometrical isomers, tautomers, salts, hydrates, solvates, solid forms, deuterated or any other isotopic forms and mixtures thereof.

[0029] The present invention discloses compounds of general Formula I, wherein R^1, R^2, R^3, R^4 and R^5 are independently selected from hydrogen, halogen and, phenyl, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C1-C5 alkoxyalkyl, straight chain or branched C1-C5 alkoxyaryl, aryl, CF3, a C_3-C_7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S; any of two adjacent R groups can forming a 5-6 membered aromatic or aliphatic ring comprising at least one hetero atom selected from a group of O, N and S.

[0030] The present invention discloses compounds of general Formula I, wherein a 5 or 6 membered cyclic ring having one or two hetero atoms from among O, N, and S is formed by any 2 adjacent groups selected from R^1, R^2, R^3, R^4 and R^5.

[0031] The compounds of Formula I wherein R6 and R7, together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N, S further wherein the heterocycle is optionally substituted with any substituent selected from the group comprising halogen, CF3, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5alkenyl or straight chain or branched C1-C5alkoxy. Further, wherein the heterocycle is monosubstituted, disubstituted or trisubstituted.

[0032] Compounds of Formula I wherein any two adjacent substituents selected from R1, R2, R3, R4 and R5, combine to form naphthalene.

[0033] Without being bound by theory the inventors of the present invention have contemplated novel and inventive methods for modulating ER stress pathways in cells and/or in vivo.

[0034] Accordingly, the present invention discloses compounds of general Formula I that have been unexpectedly found to be successful in influencing the ER stress pathways in cells. Going further, the inventors envisage that the compounds of general Formula I to be useful in the treatment and prevention of diseases associated with deregulation of cellular stress pathways, more specifically ER stress. The diseases include but are not limited to

cancers, tumors, metabolic disorders, neurodegeneration, cardiovascular, pulmonary, ophthalmic and dermatological disorders.

[0035] In addition, embodiments of the present invention relate to treatment and prevention of diseases/disorders involving the deregulation of immune system, including, but not limited to, Atopic Dermatitis, Urticaria, Rosacea, Actinic Keratosis and Alopecia

[0036] In another embodiment, the present invention relates to the treatment and prevention of autoimmune diseases including, but not limited to, Type I Diabetes, Rheumatoid Arthritis, Lupus, Celiac Disease, Psoriatic Arthritis, Multiple Sclerosis, Pernicious Anemia, Sjogren's syndrome, Grave's Disease, Inflammatory bowel disease.

[0037] In another embodiment, the present invention relates to the treatment and prevention of autoimmune diseases related to skin including, but not limited to, Vitiligo, Psoriasis, lichen-planus, Scleroderma, Pemphigus, Bullous, Epidermolysis bullosa, Systemic lupus erythematosus, dermatomiositis, Alopecia areata.

[0038] The present invention discloses compounds of Formula I, that are useful for treatment and prevention of ER stress related diseases. The compounds of the present invention can be used by way of a formulation or a composition for therapeutics as well as prophylactic applications for the treatment of ER stress related diseases via all modes of administration.

[0039] For example, it is suitable for oral, parenteral, topical, transdermal, intravenous, rectal, sublingual and nasal administration. It is further envisaged that in the treatment of ER stress related diseases, the disclosed compounds of Formula I, may also be administered via intramuscular, subcutaneous, intravenous and peridural administration.

[0040] The compositions comprising the compounds of Formula I as active ingredients, are intended to be administered by any suitable route, including orally, parenterally, rectally, topically, intranasal, transdermal, sublingual, ocular and local administration. They may also be typically formulated and administered in unit-dosage forms such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil-water emulsions containing suitable quantities of the active ingredient or multiple-dosage forms.

[0041] Suitable pharmaceutical preparations may also be prepared such as solutions, suspensions, tablets, dispersible tablets, pills, capsules, powders, sustained release

formulations or elixirs, for oral administration or in sterile solutions or suspensions for any suitable mode of administration, as well as transdermal patch preparation and dry powder inhalers.

[0042] The present invention further envisages pharmaceutical composition, wherein the composition is in the form of a formulation that is administered in unit-dosage forms such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, injections, syrup, liquid, microemulsion, topical creams, ointments, suppositories, sachets, troches and lozenges and oil-water emulsions containing suitable quantities of the compound of Formula I or multiple-dosage forms.

[0043] An embodiment of the present invention is directed towards treatment of the subject displaying symptoms of ER stress related diseases, comprising steps of administering a therapeutically effective amount of one or more of the compounds of general Formula I , their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

[0044] Yet another embodiment of the present invention is directed towards treatment of autoimmune diseases of skin , by reducing the immune mediated cell death , comprising the steps of administering a therapeutically effective amount of one or more of the compounds of general Formula I or their physiologically acceptable salts, and still further, their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, , hydrates, solvates, solid forms and mixtures thereof.

[0045] Another embodiment of the present invention is directed towards the treatment of skin autoimmune diseases particularly, by reducing the autoimmune mediated cell death of melanocytes, comprising administering a therapeutically effective amount of a pharmaceutical composition or formulation comprising essentially of one or more compounds of Formula I. Another embodiment of the invention is directed to a method of treating a subject who has developed vitiligo, with a pharmaceutically effective amount the one or more compound of Formula I or, their stereoisomers (diastereoisomers,

enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

[0046] The present invention envisages treatment of autoimmune diseases by administering one or more the compounds of general Formula I by way of a pharmaceutical composition comprising an effective amount of tone or more of the said compounds and a pharmaceutically acceptable carrier.

[0047] The present invention further envisages the process of preparing a pharmaceutical composition by mixing an effective amount of the one or more of the said compounds and a pharmaceutically acceptable carrier.

[0048] Particularly, a further embodiment of the present invention is directed towards the preparation of a pharmaceutical composition comprising an effective amount of one or more of the said compounds and a pharmaceutically acceptable carrier further adapted to be administered by any suitable mode of administration including oral, parenteral, rectal, topical, intranasal, transdermal, sublingual, ocular and any other local mode of administration.

[0049] The present invention envisages application of the compounds of general Formula I, their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof in any process including medicinal, prophylactic, curative, diagnostic, therapeutic or surgical in order to prevent or treat ER stress related diseases.

[0050] The present invention also envisages the application of the compounds of general Formula I or their physiologically acceptable salts, and still further, their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, , hydrates, solvates, solid forms and mixtures thereof, to effect prophylactic or maintenance therapy in a subject that may have a genetic propensity towards ER stress related diseases and such subjects who have been treated for such disease and undergone disease regression.

[0051] A preferred embodiment of the present invention is directed towards compounds of the general Formula I as provided below:

N-butyl-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-isopropoxypropyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(pyrrolidin-1-yl)ethan-1-one

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-(pyrrolidin-1-yl)ethyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(3,5-dimethylmorpholino)ethan-1-one

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-cyclopentylacetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-(trifluoromethyl)phenyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3,5-difluorobenzyl)acetamide

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide

2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide

2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(dimethylamino)ethyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide hydrochloride

2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methyl-1-(4-methylpiperazin-1-yl)propan-1-one

2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methyl-N-(2-(piperidin-1-yl)ethyl)propanamide

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methylpropanamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4,4-difluoropiperidin-1-yl)ethan-1-one

2-(5-(4-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one

N-(4-fluorophenethyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide

2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

1-(4-methylpiperazin-1-yl)-2-(5-phenylthiophen-2-yl)ethan-1-one

N-(4-fluorophenethyl)-2-(5-phenylthiophen-2-yl)acetamide

N-(2-morpholinoethyl)-2-(5-phenylthiophen-2-yl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide

2-(5-phenylthiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-phenylthiophen-2-yl)acetamide

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(2,4-dichlorophenyl)thiophen-2-yl)acetamide

2-(5-(3-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one

2-(5-(3-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide

2-(5-(3-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one

2-(5-(3-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(4-methoxyphenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

N-(2-morpholinoethyl)-2-(5-(4-(trifluoromethyl)phenyl)thiophen-2-yl)acetamide

2-(5-(3-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide

2-(5-(3-bromophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

N-(2-morpholinoethyl)-2-(5-(3-morpholinophenyl)thiophen-2-yl)acetamide

2-(5-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(3-(1-methyl-1H-pyrrol-2-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

N-(2-morpholinoethyl)-2-(5-(3-(pyrazin-2-yl)phenyl)thiophen-2-yl)acetamide

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one

2-(5-(3-(1-methyl-1H-imidazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-(4-(4-fluorophenyl)piperidin-1-yl)ethan-1-one

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide

2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl) acetamide

2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(piperidin-1-yl)acetamide

(1-(5-(4-chlorophenyl)thiophen-2-yl)cyclopropyl)(4-methylpiperazin-1-yl)methanone

(1-(5-(4-chlorophenyl)thiophen-2-yl)cyclobutyl)(4-methylpiperazin-1-yl)methanone

(3-(5-(4-chlorophenyl)thiophen-2-yl)oxetan-3-yl)(4-methylpiperazin-1-yl)methanone

(1-(5-(4-fluorophenyl)thiophen-2-yl)cyclopropyl)(4-methylpiperazin-1-yl)methanone

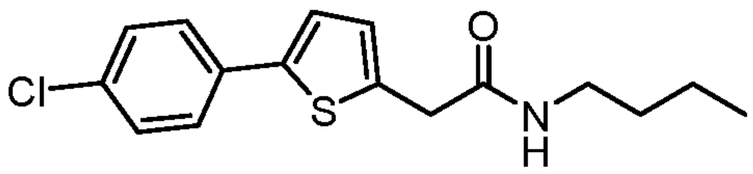
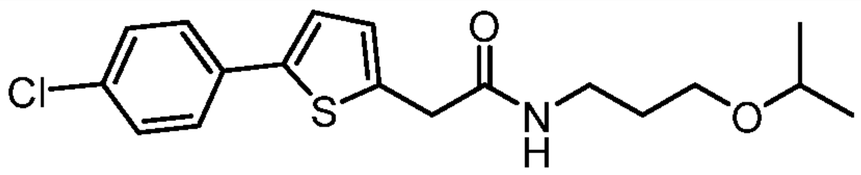
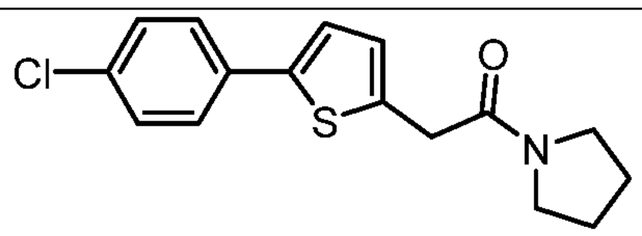
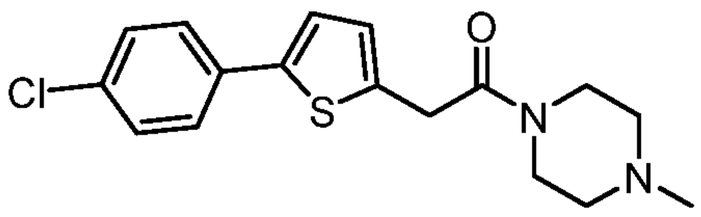
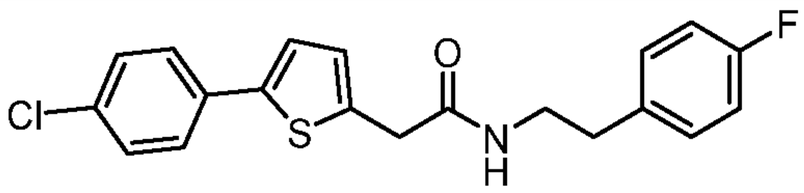
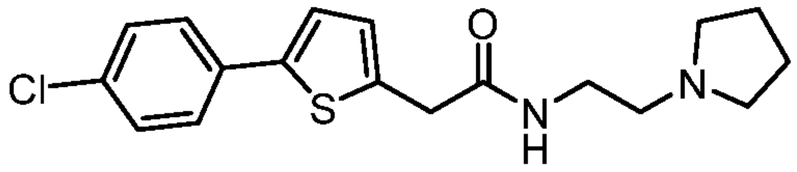
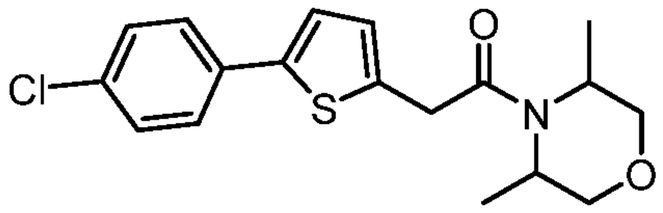
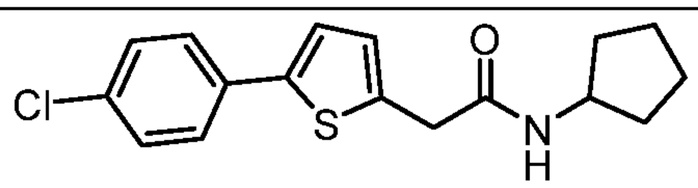
(1-(5-(4-fluorophenyl)thiophen-2-yl)cyclobutyl)(4-methylpiperazin-1-yl)methanone

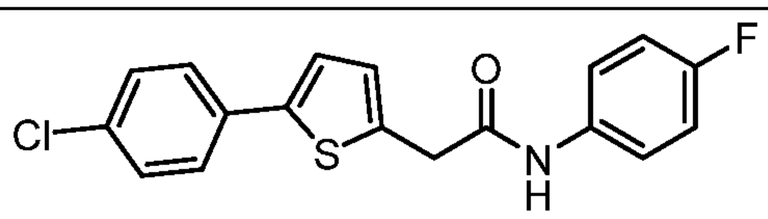
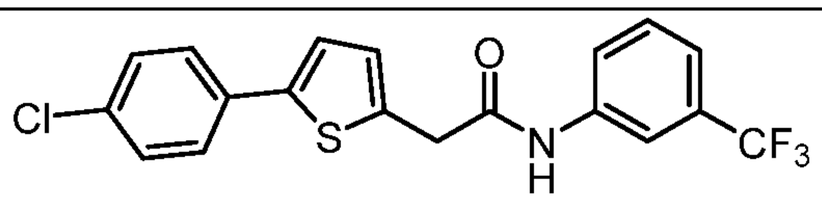
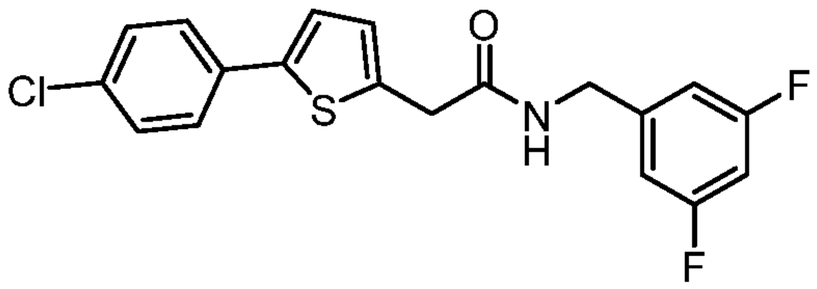
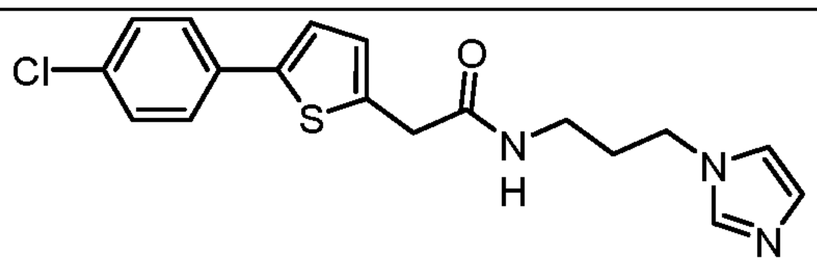
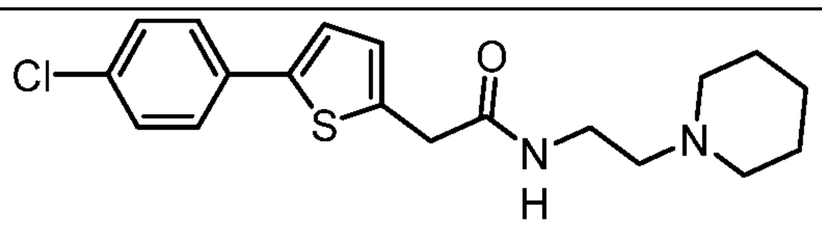
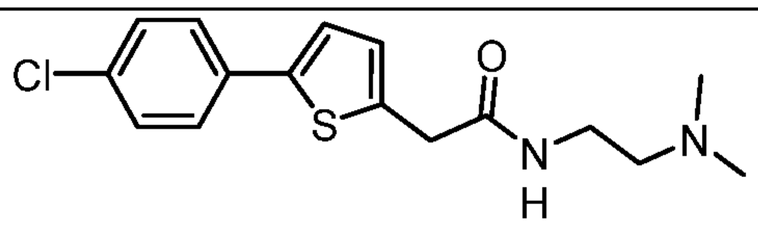
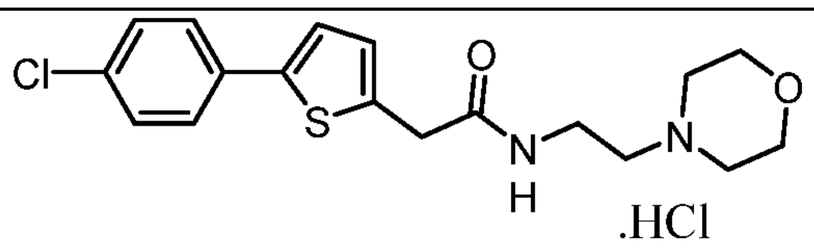
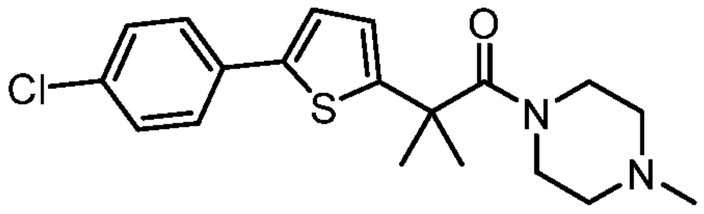
(3-(5-(4-fluorophenyl)thiophen-2-yl)oxetan-3-yl)(4-methylpiperazin-1-yl)methanone

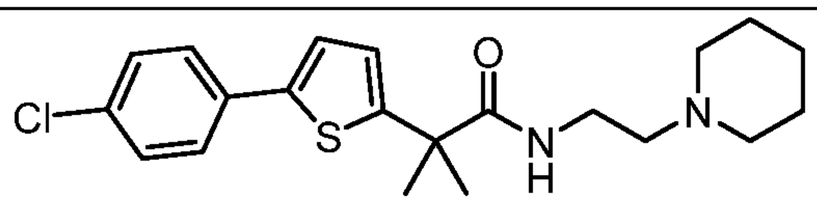
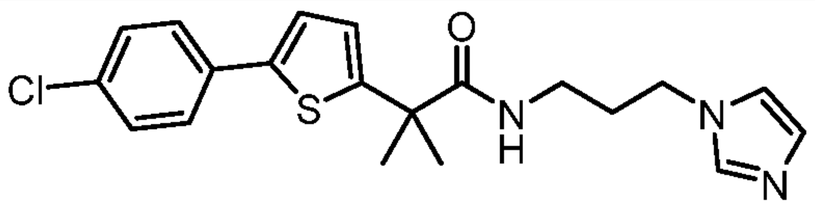
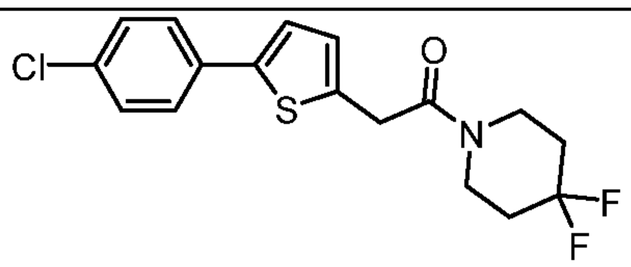
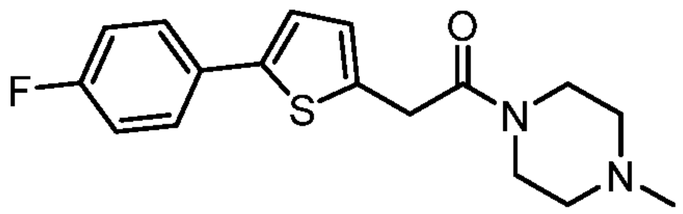
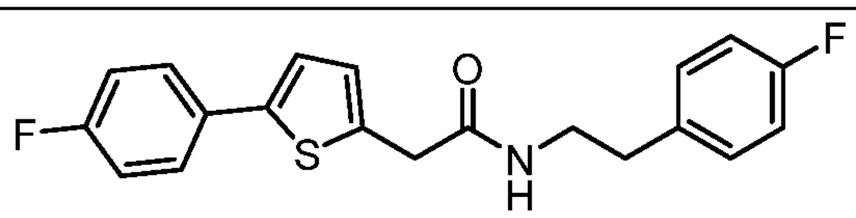
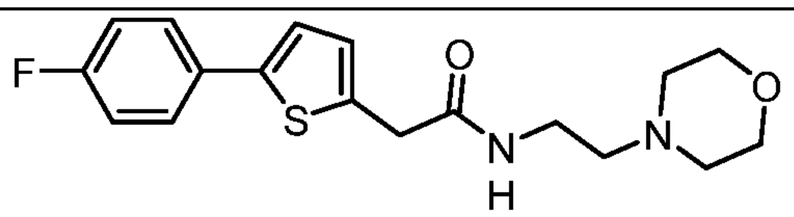
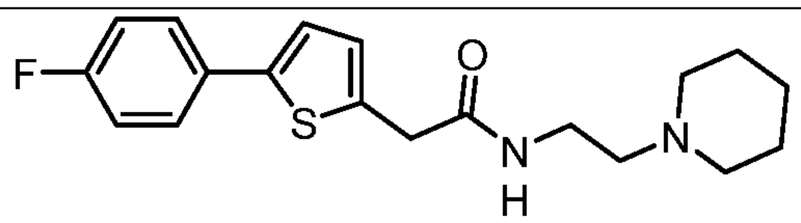
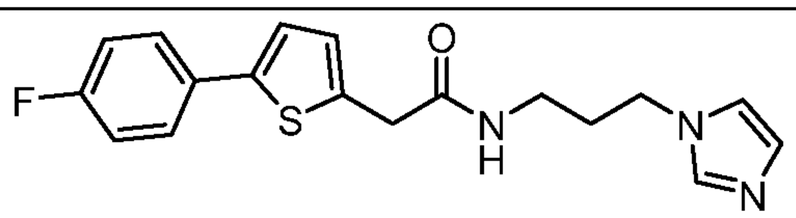
N-butyl-2-(5-(naphthalen-1-yl)thiophen-2-yl)acetamide

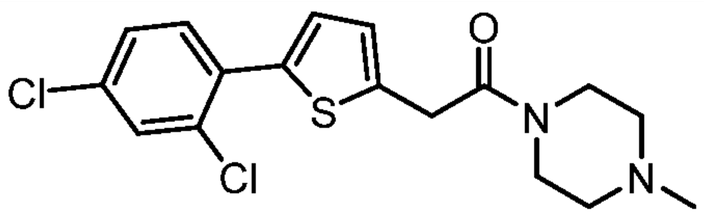
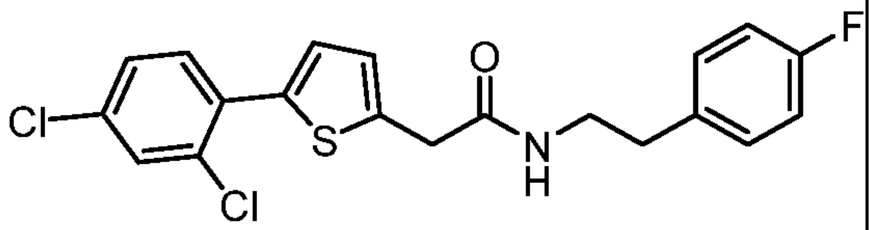
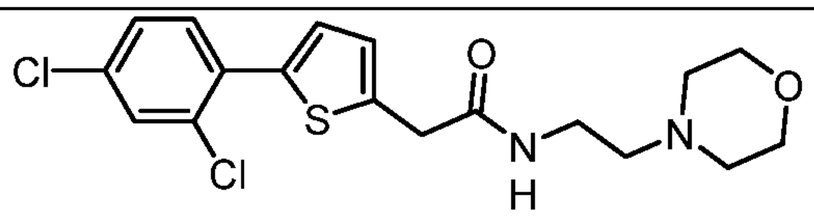
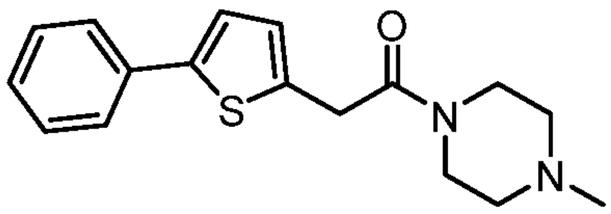
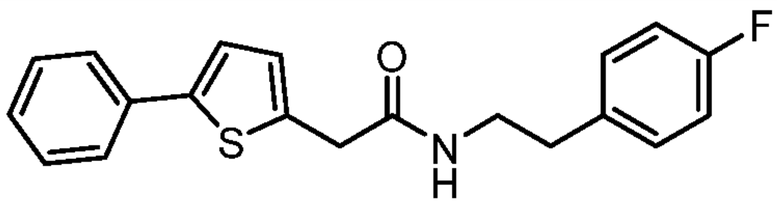
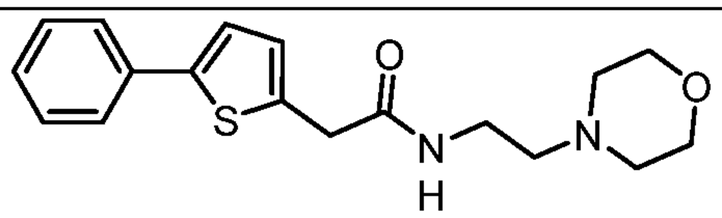
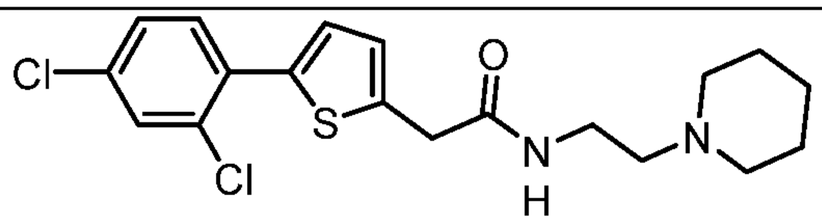
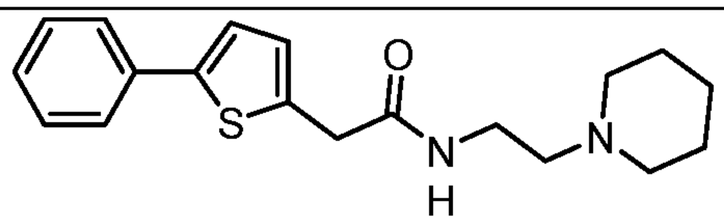
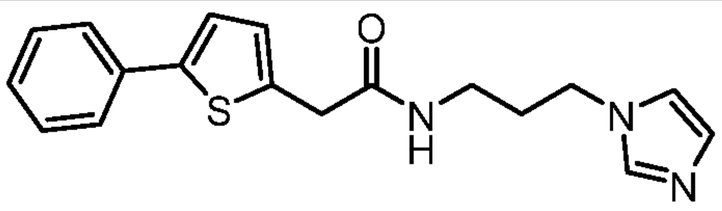
2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide

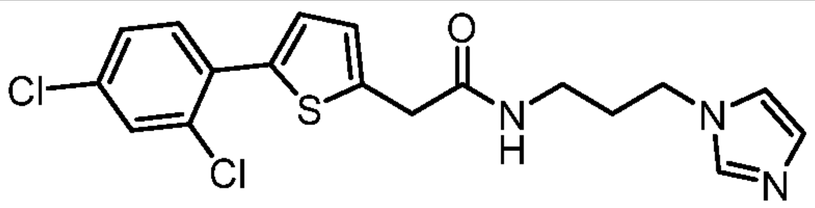
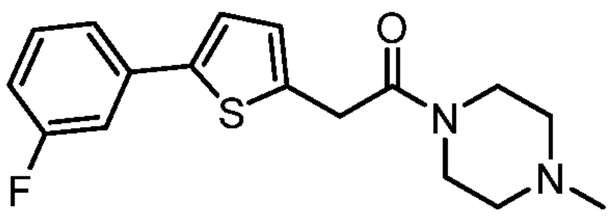
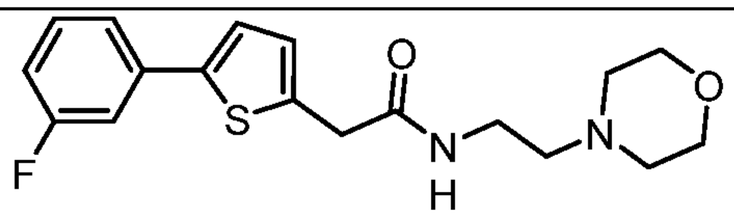
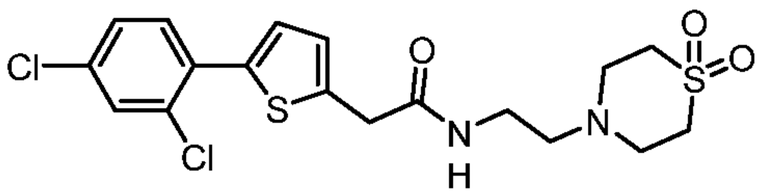
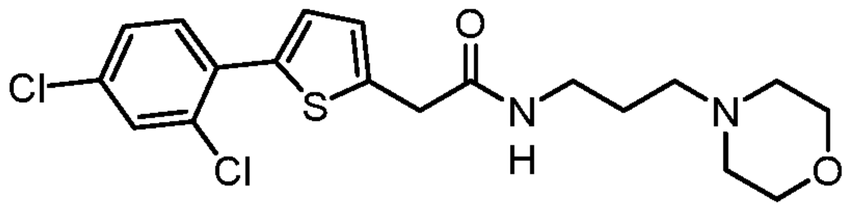
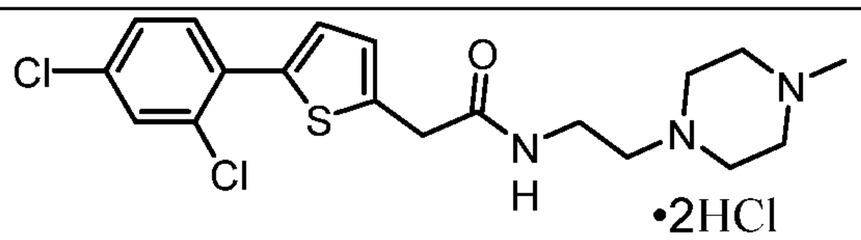
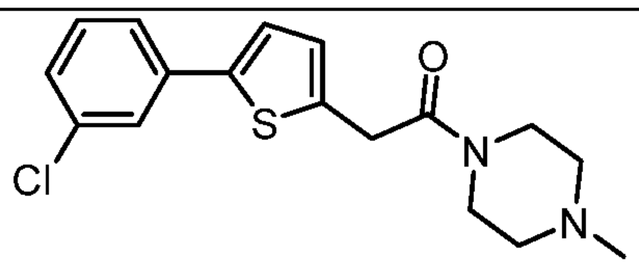
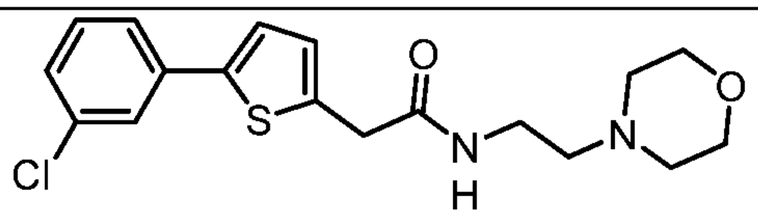
[0052] Without limiting the scope of the invention, an another advantageous embodiment of the present invention is directed towards preferred compounds chosen from among the following:

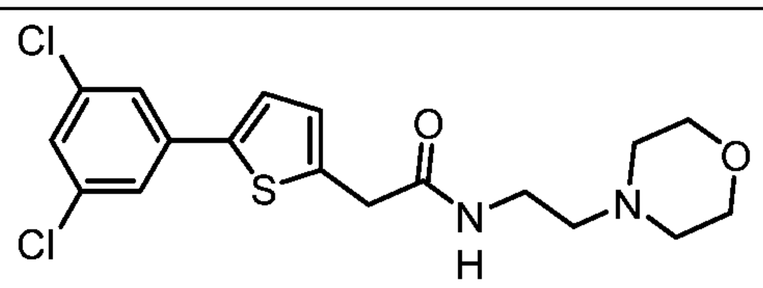
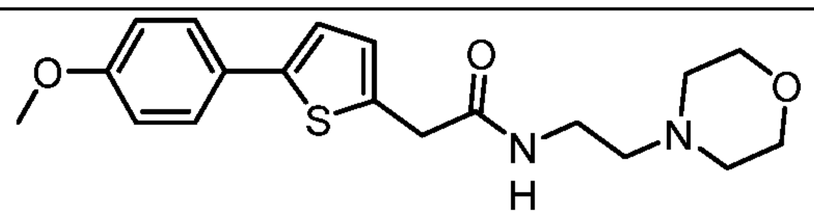
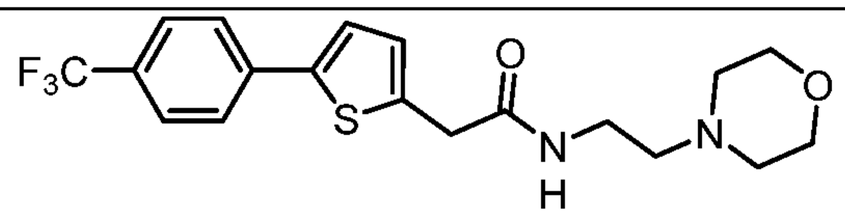
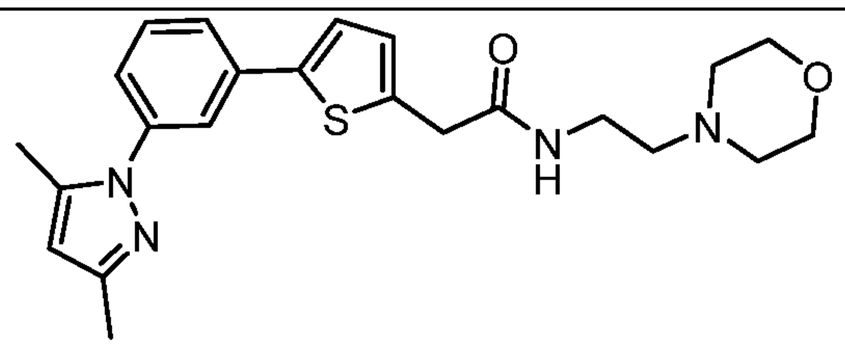
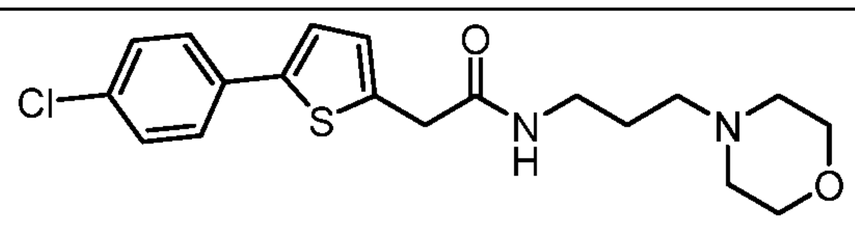
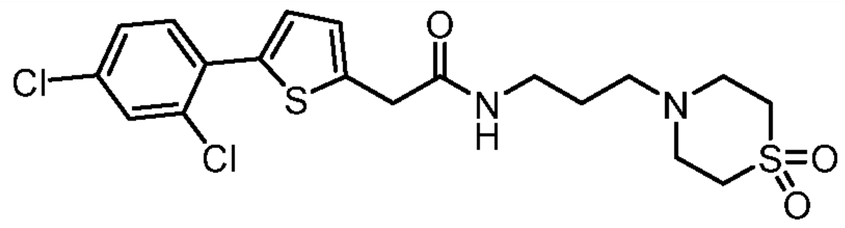
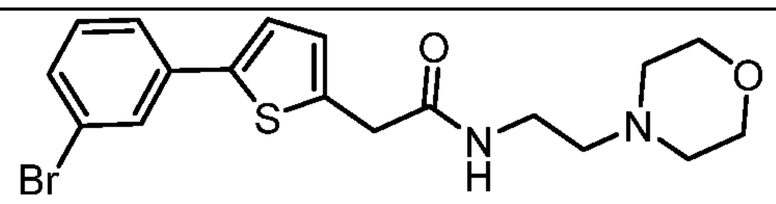
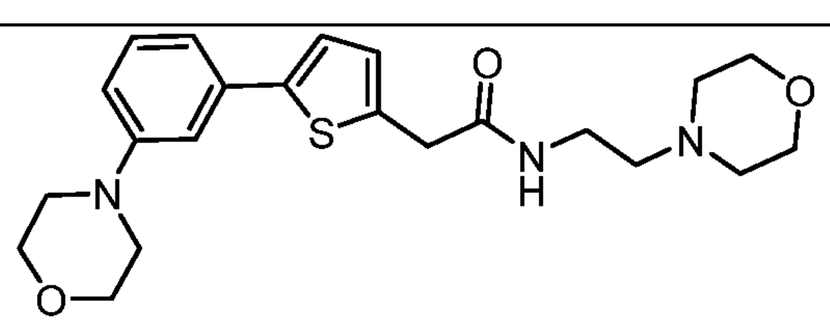
	Compound No	Structure	IUPAC name
1.	AB1010		N-butyl-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide
2.	AB1012		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-isopropoxypropyl)acetamide
3.	AB1013		2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(pyrrolidin-1-yl)ethan-1-one
4.	AB1014		2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one
5.	AB1015		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide
6.	AB1016		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-(pyrrolidin-1-yl)ethyl)acetamide
7.	AB1018		2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(3,5-dimethylmorpholino)ethan-1-one
8.	AB1019		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-cyclopentylacetamide

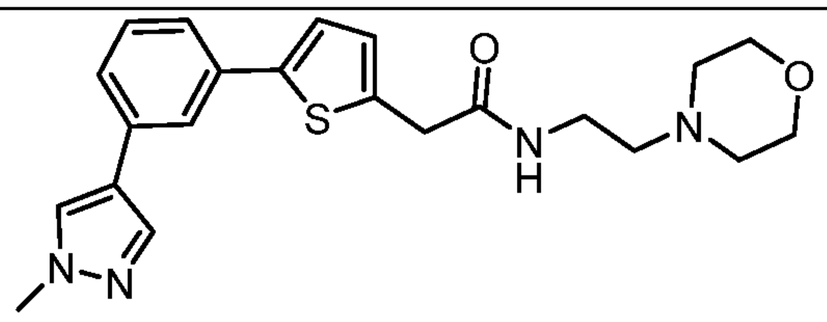
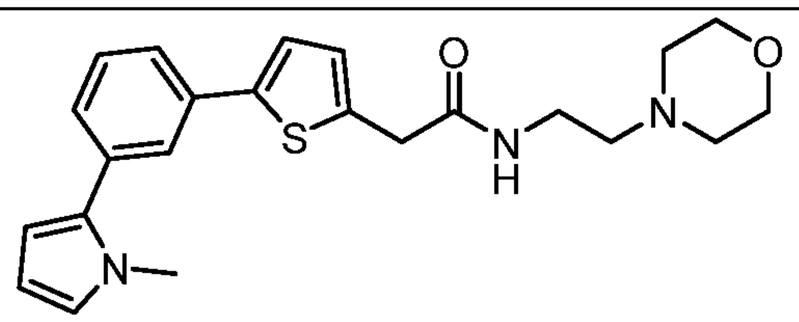
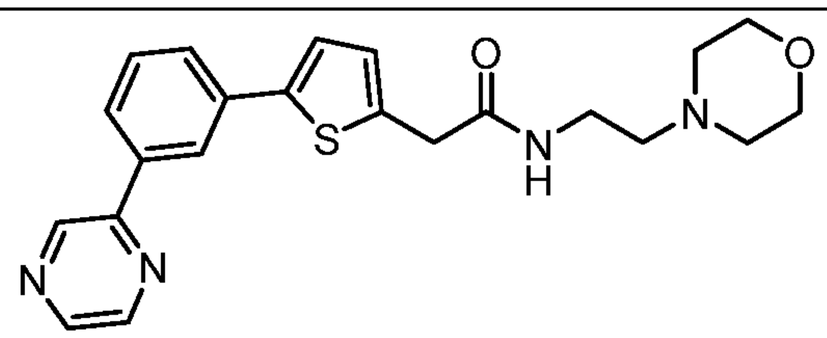
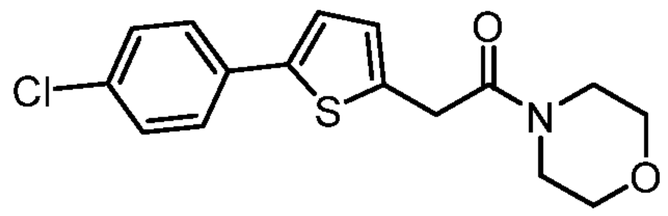
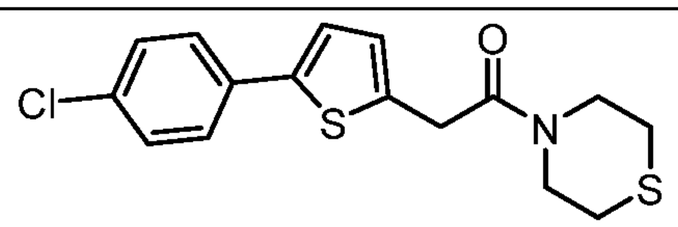
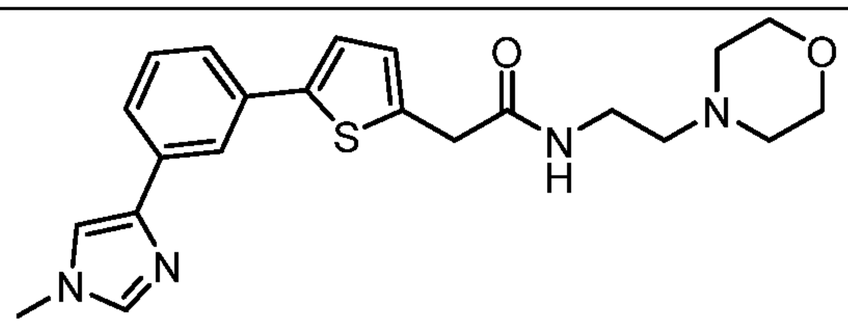
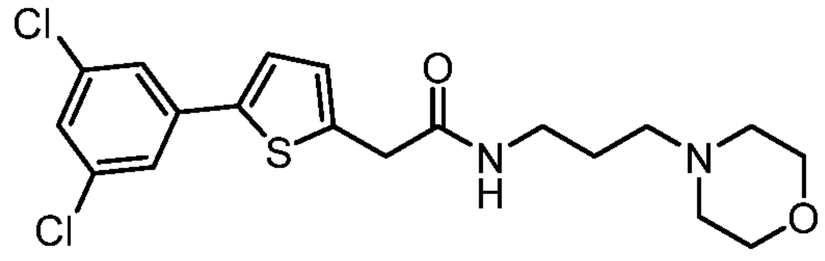
9.	AB1020		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenyl)acetamide
10	AB1021		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-(trifluoromethyl)phenyl)acetamide
11	AB1022		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3,5-difluorobenzyl)acetamide
12	AB1045		N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide
13	AB1047		2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide
14	AB1051		2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(dimethylamino)ethyl)acetamide
15	AB1062	 .HCl	2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide hydrochloride
16	AB1078		2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methyl-1-(4-methylpiperazin-1-yl)propan-1-one

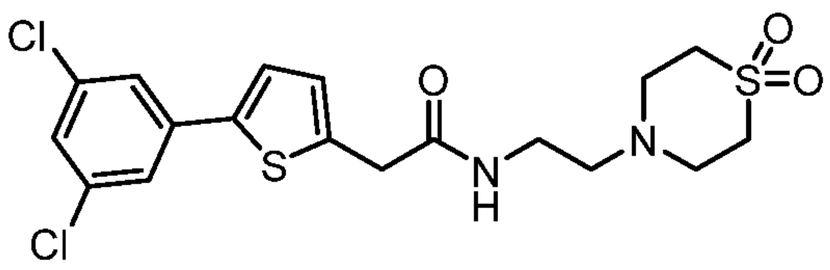
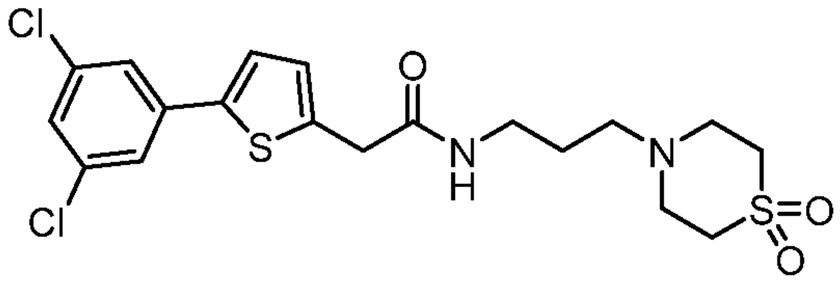
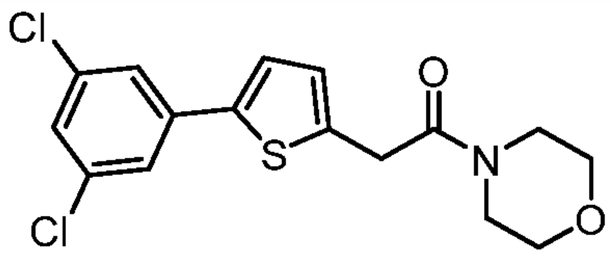
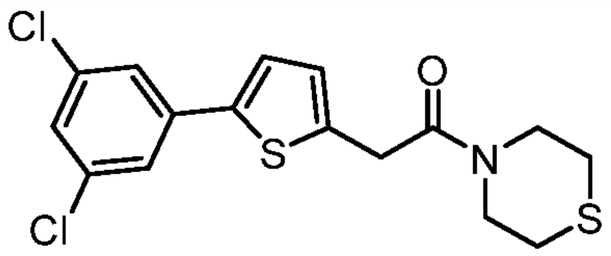
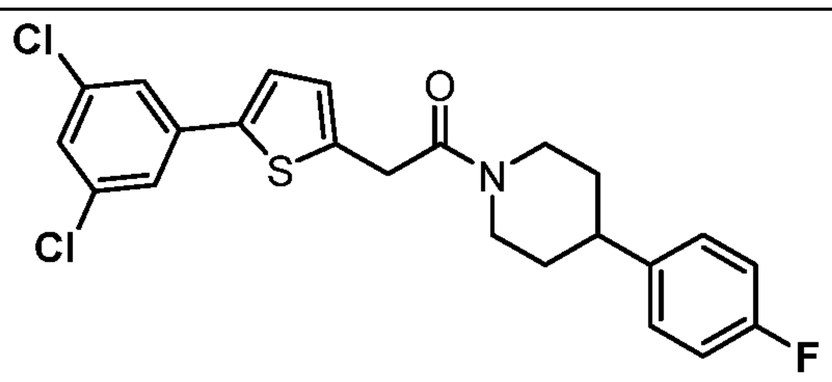
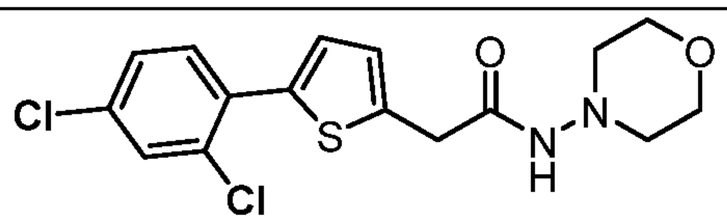
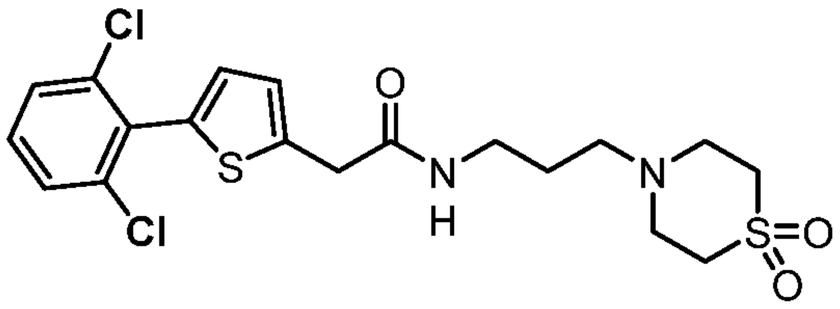
17	AB1079		2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methyl-N-(2-(piperidin-1-yl)ethyl)propanamide
18	AB1080		N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methylpropanamide
19	AB1090		2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4,4-difluoropiperidin-1-yl)ethan-1-one
20	AB1091		2-(5-(4-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one
21	AB1092		N-(4-fluorophenethyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide
22	AB1093		2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
23	AB1094		2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide
24	AB1095		N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide

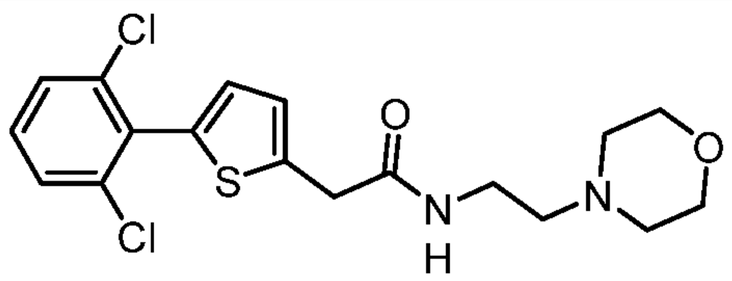
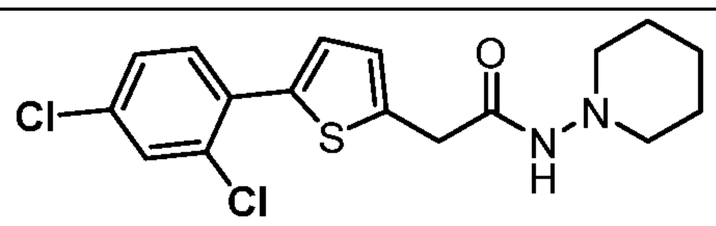
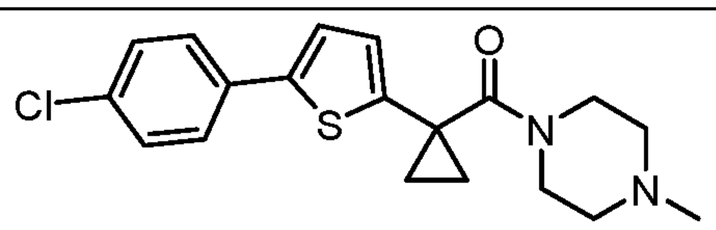
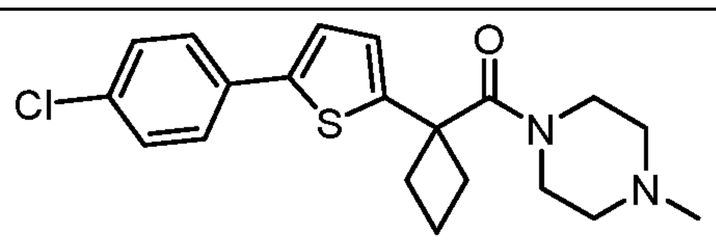
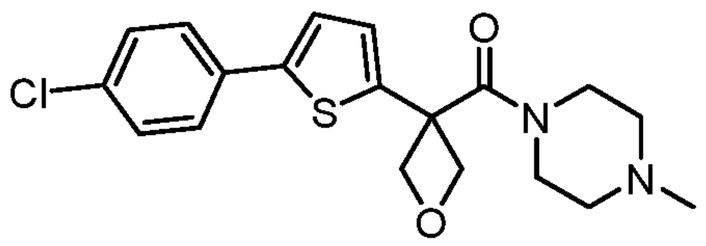
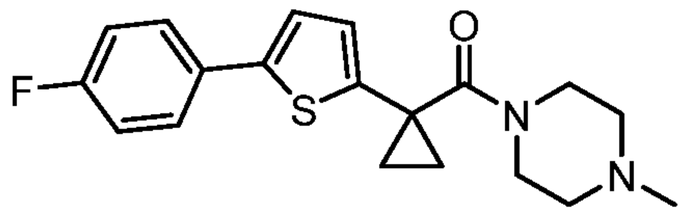
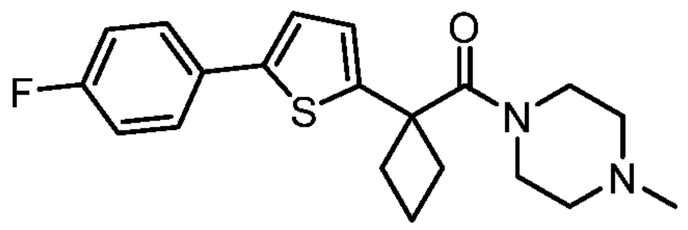
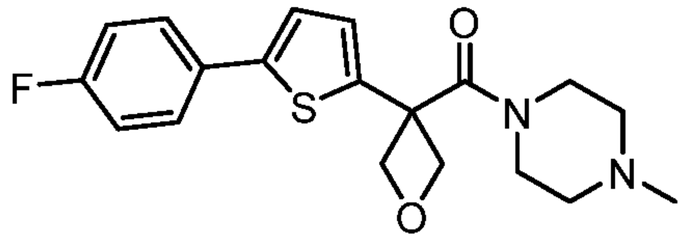
25	AB1097		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one
26	AB1098		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide
27	AB1099		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
28	AB1100		1-(4-methylpiperazin-1-yl)-2-(5-phenylthiophen-2-yl)ethan-1-one
29	AB1101		N-(4-fluorophenethyl)-2-(5-phenylthiophen-2-yl)acetamide
30	AB1102		N-(2-morpholinoethyl)-2-(5-phenylthiophen-2-yl)acetamide
31	AB1103		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide
32	AB1104		2-(5-phenylthiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide
33	AB1105		N-(3-(1H-imidazol-1-yl)propyl)-2-(5-phenylthiophen-2-yl)acetamide

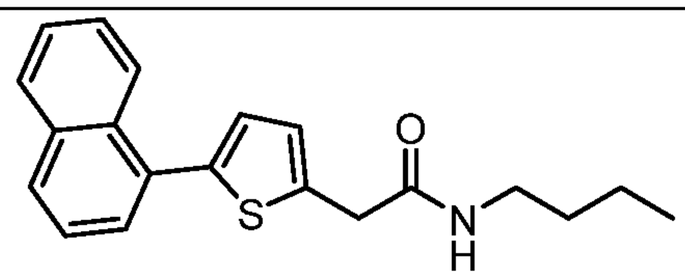
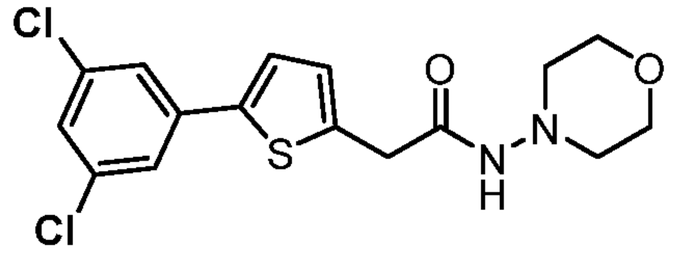
34	AB1106		N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(2,4-dichlorophenyl)thiophen-2-yl)acetamide
35	AB1107		2-(5-(3-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one
36	AB1108		2-(5-(3-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
37	AB1109		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide
38	AB1110		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-*N*-(3-morpholinopropyl)acetamide
39	AB1111		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide hydrochloride
40	AB1112		2-(5-(3-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one
41	AB1113		2-(5-(3-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide

42	AB1114		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
43	AB1115		2-(5-(4-methoxyphenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
44	AB1116		N-(2-morpholinoethyl)-2-(5-(4-(trifluoromethyl)phenyl)thiophen-2-yl)acetamide
45	AB1117		2-(5-(3-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
46	AB1118		2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide
47	AB1119		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide
48	AB1120		2-(5-(3-bromophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
49	AB1122		N-(2-morpholinoethyl)-2-(5-(3-morpholinophenyl)thiophen-2-yl)acetamide

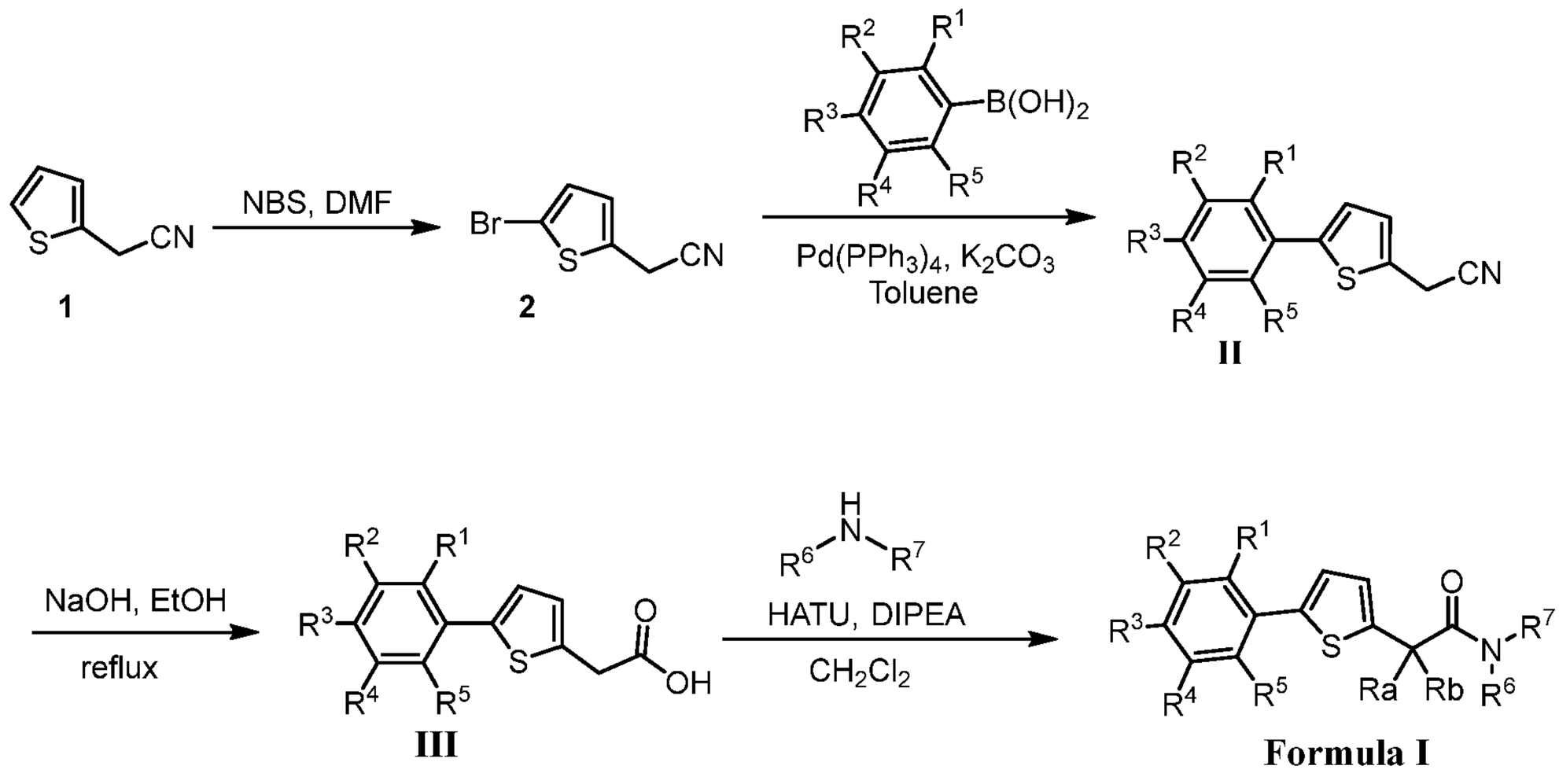
50	AB1123		2-(5-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
51	AB1146		2-(5-(3-(1-methyl-1H-pyrrol-2-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
52	AB1147		N-(2-morpholinoethyl)-2-(5-(3-(pyrazin-2-yl)phenyl)thiophen-2-yl)acetamide
53	AB1151		2-(5-(4-chlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one
54	AB1152		2-(5-(4-chlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one
55	AB1153		2-(5-(3-(1-methyl-1H-imidazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
56	AB1162		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide

57	AB1163		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide
58	AB1164		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide
59	AB1176		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one
60	AB1177		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one
61	AB1178		2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-(4-(4-fluorophenyl)piperidin-1-yl)ethan-1-one
62	AB1179		2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide
63	AB1180		2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl) acetamide

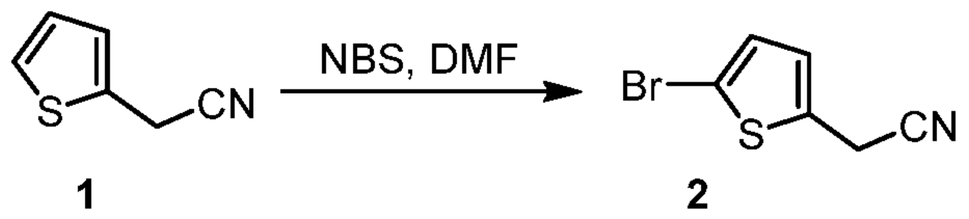
64	AB1181		2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide
65			2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(piperidin-1-yl)acetamide
66			(1-(5-(4-chlorophenyl)thiophen-2-yl)cyclopropyl)(4-methylpiperazin-1-yl)methanone
67			(1-(5-(4-chlorophenyl)thiophen-2-yl)cyclobutyl)(4-methylpiperazin-1-yl)methanone
68			(3-(5-(4-chlorophenyl)thiophen-2-yl)oxetan-3-yl)(4-methylpiperazin-1-yl)methanone
69			(1-(5-(4-fluorophenyl)thiophen-2-yl)cyclopropyl)(4-methylpiperazin-1-yl)methanone
70			(1-(5-(4-fluorophenyl)thiophen-2-yl)cyclobutyl)(4-methylpiperazin-1-yl)methanone
71			(3-(5-(4-fluorophenyl)thiophen-2-yl)oxetan-3-yl)(4-methylpiperazin-1-yl)methanone

72			N-butyl-2-(5-(naphthalen-1-yl)thiophen-2-yl)acetamide
73			2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide

[0053] The present invention further describes novel and inventive process for the preparation of the compounds of the present invention. The compounds of general Formula I have been synthesized by a novel process having the general scheme as given below:

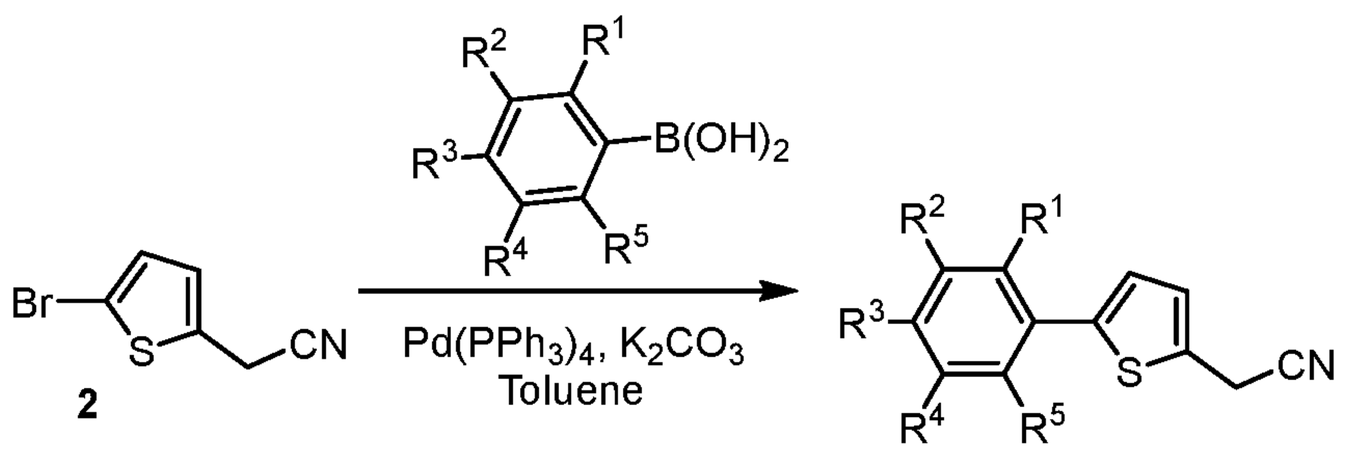


[0054] Further to the general scheme of preparation, the present invention incorporates all such conventional reaction mechanisms and parameters that would result in the preparation of the disclosed compounds as known through prior art.



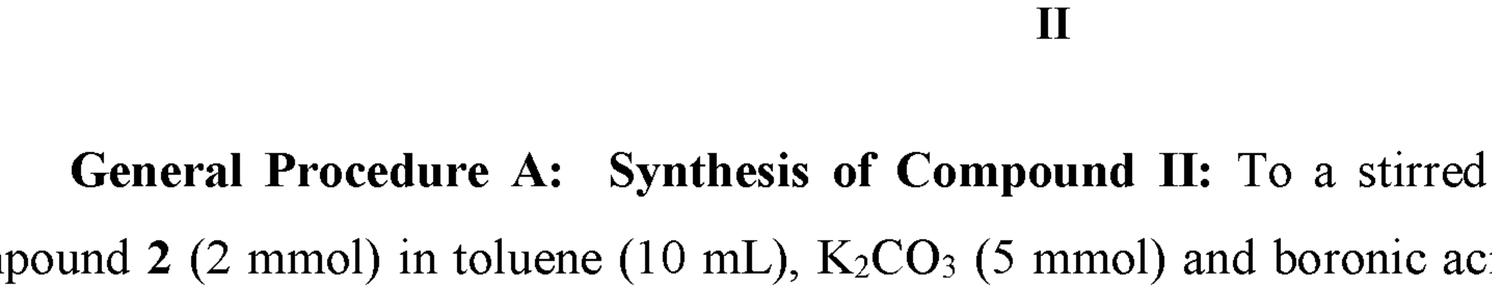
1 2

[0055] **2-(5-Bromothiophen-2-yl)acetonitrile (2):** To a stirred solution of 2-(thiophen-2-yl)acetonitrile 1 (15g, 121.7 mmol) in DMF (110 mL), NBS (22.7g, 127.8 mmol) was added portion wise for 2 h. The reaction mixture was stirred in the dark under nitrogen for 24 h. Diethyl ether (100 mL) was added to the reaction mixture and washed with water (50 mL) and brine (30 mL). Organic layer was concentrated and purified by column chromatography (silica gel 100-200 mesh, 5% ethyl acetate in pet ether) to afford compound 2 (15g, 86%) as a pale yellow solid. ^{1}H NMR (400MHz, $CDCl_3$,): 6.95(d, J = 4.1 1H), 6.84(m, 1H), 3.84 (s, 2H).

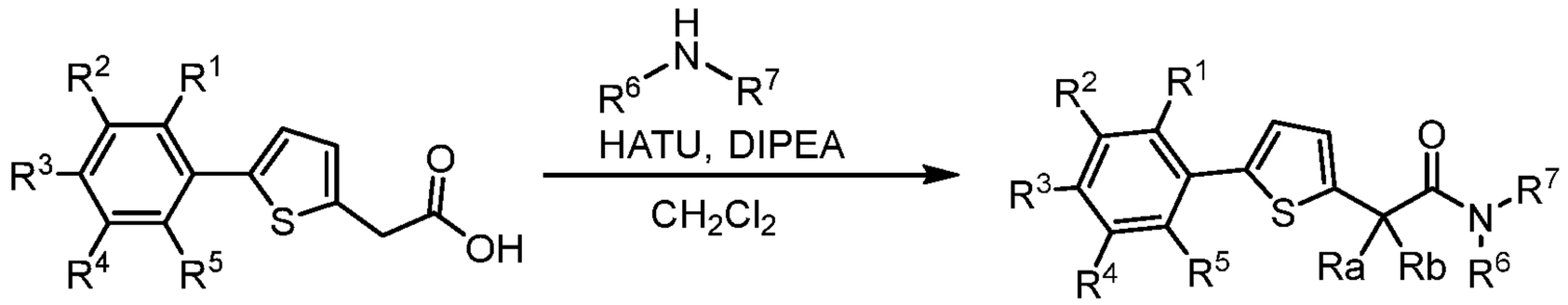


II

[0056] **General Procedure A: Synthesis of Compound II:** To a stirred solution of compound **2** (2 mmol) in toluene (10 mL), K_2CO_3 (5 mmol) and boronic acid (4 mmol) were added and purged with argon for 20 min. $Pd(PPh_3)_4$ (0.1mmol) was added and heated at 100 °C for 18 h. Cooled the reaction mixture to room temperature, concentrated and diluted with ethyl acetate (30 mL) washed with water (10 mL) and brine (10 mL). Organic layer was dried over Na_2SO_4 concentrated and purified by column chromatography to afford compound II.



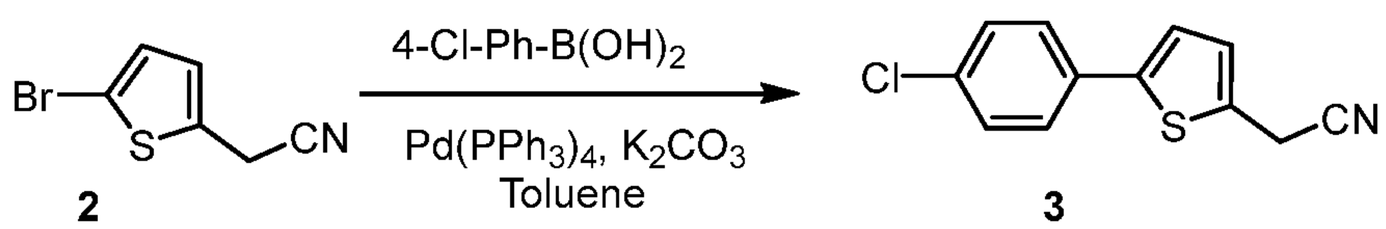
[0057] **General Procedure B: Synthesis of Compound III:** To a stirred solution of compound **II** (1 mmol) in ethanol (10 mL). NaOH (4mmol, dissolved in 3 ml of water) was added and refluxed for 4 h. concentrated the reaction mixture acidified to $P^H \sim 3$ with conc. HCl and extracted with ethyl acetate (20mL X 3). Combined the organic fractions dried over Na_2SO_4 concentrated to give compound **III**.



III **Formula I**

[0058] General Procedure C: Synthesis of Formula I:

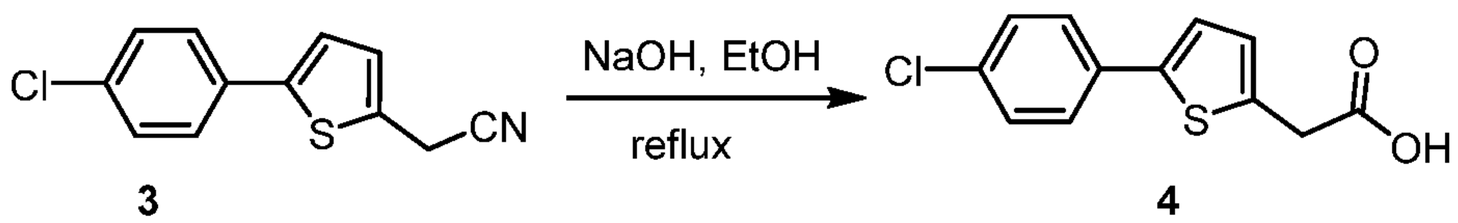
To a stirred solution of compound **III** (1 mmol) in CH_2Cl_2 (10 mL), HATU (1.1 mmol) and DIPEA (2 mmol) were added at 0 °C followed by Amine (1 mmol) was added and stirred for 20 h at room temperature. Concentrated the reaction mixture diluted with ethyl acetate (20 mL) organic fraction was washed with saturated $NaHCO_3$ (5 mL) followed by brine (10 mL). Organic fraction was dried over Na_2SO_4 concentrated and purified by column chromatography.



2 **3**

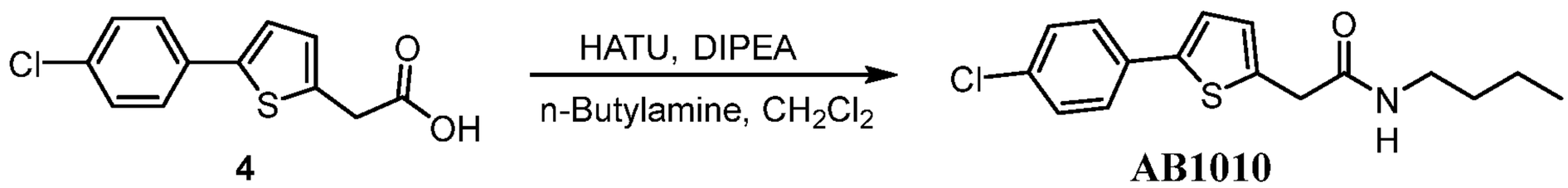
[0059] Examples of compounds and their preparation:

2-(5-(4-Chlorophenyl)thiophen-2-yl)acetonitrile (3): compound **3** (2.3 gm, 50%) synthesized from compound **2** by following general procedure **A**. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 - 7.69 (m, 2H), 7.39 - 7.51 (m, 3H), 7.09 (d, J = 3.42 Hz, 1H), 4.32 (s, 2H).



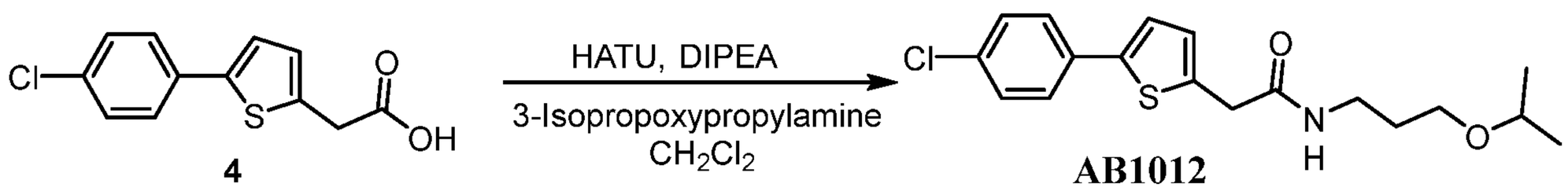
3 4

2-(5-(4-chlorophenyl)thiophen-2-yl)acetic acid (4) : Compound **4** (1.8 g, 92%) Synthesized from compound **3** by following General procedure **B**. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.64 (brs., 1H), 7.58 - 7.70 (m, 2H), 7.42 - 7.49 (m, 2H), 7.34 - 7.40 (m, 1H), 6.96 (d, J = 3.91 Hz, 1H), 3.84 (s, 2H).



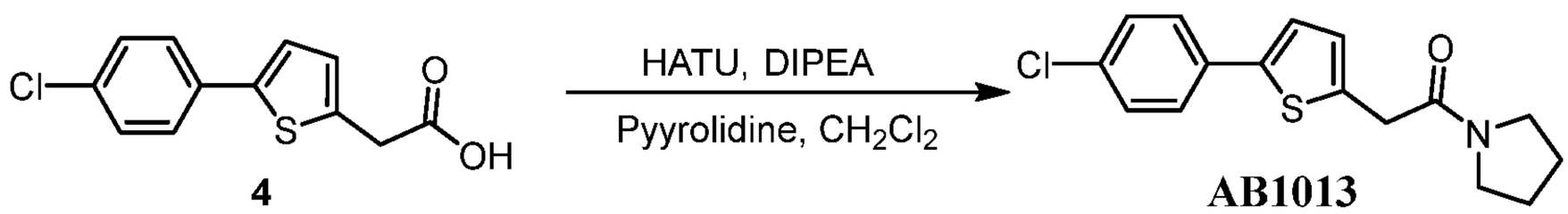
4 **AB1010**

***N*-butyl-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide (AB1010):** Compound **AB1010** (25 mg, 14%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.52 (m, 2H), 7.32 - 7.40 (m, 2H), 7.06 - 7.21 (m, 1H), 6.90 (d, J = 3.42 Hz, 1H), 5.63 (s, 1H), 3.75 (s, 2H), 3.20 - 3.31 (m, 2H), 1.38 - 1.50 (m, 2H), 1.20 - 1.35 (m, 2H), 0.85 - 0.96 (m, 3H). MS: 308 $(M+H)^+$.



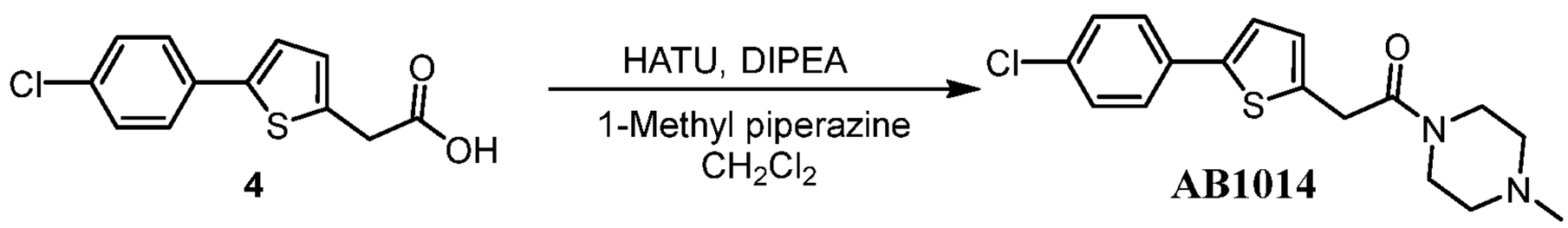
4 **AB1012**

2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-(3-isopropoxypropyl)acetamide (AB1012): Compound **AB1012** (103 mg, 50%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 - 7.51 (m, J = 8.80 Hz, 2H), 7.30 - 7.35 (m, J = 8.31 Hz, 2H), 7.14 (d, J = 3.42 Hz, 1H), 6.89 (d, J = 3.91 Hz, 1H), 6.33 (brs., 1H), 3.73 (s, 2H), 3.43 - 3.50 (m, 3H), 3.38 (q, J = 5.87 Hz, 2H), 1.68 - 1.77 (m, 2H), 1.05 (d, J = 5.87 Hz, 6H). MS: 352 $(M+H)^+$.



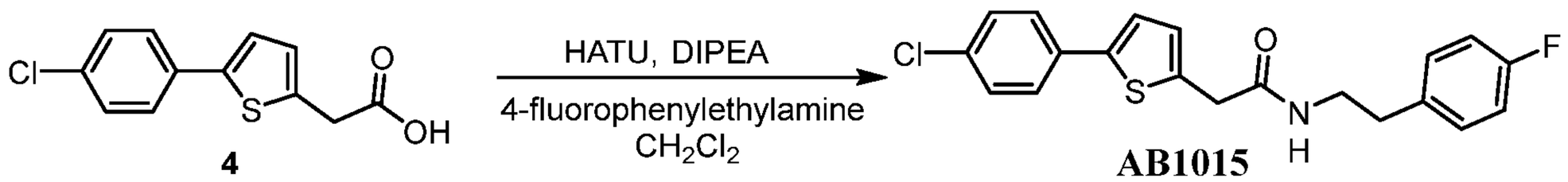
4 AB1013

2-(5-(4-Chlorophenyl)thiophen-2-yl)-1-(pyrrolidin-1-yl)ethan-1-one (AB1013): Compound **AB1013** (105 mg, 58%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.52 (m, *J* = 8.31 Hz, 2H), 7.28 - 7.34 (m, *J* = 8.31 Hz, 2H), 7.12 (d, *J* = 3.42 Hz, 1H), 6.88 (d, *J* = 3.42 Hz, 1H), 3.83 (s, 2H), 3.52 (t, *J* = 6.85 Hz, 4H), 1.97 (quin, *J* = 6.85 Hz, 2H), 1.87 (quin, *J* = 6.73 Hz, 2H). MS: 306 $(M+H)^+$.



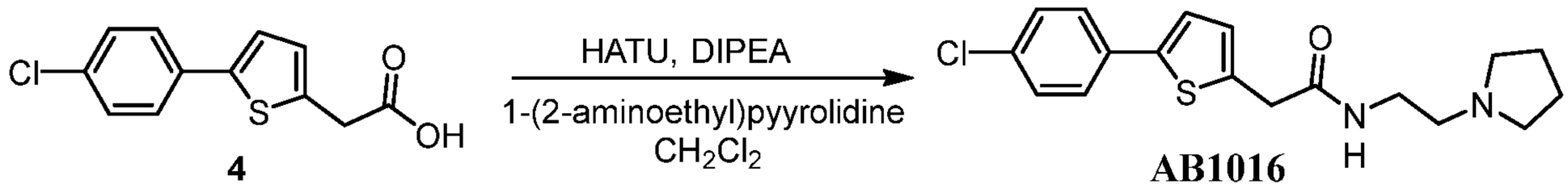
4 AB1014

2-(5-(4-Chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one (AB1014): Compound **AB1014** (93 mg, 47%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.54 (m, 2H), 7.30 - 7.37 (m, 2H), 7.12 (d, *J* = 3.91 Hz, 1H), 6.85 (d, *J* = 3.42 Hz, 1H), 3.90 (s, 2H), 3.64 - 3.72 (m, 2H), 3.51 - 3.62 (m, 2H), 2.38 (td, *J* = 5.07, 15.28 Hz, 4H), 2.29 (s, 3H). MS; 335 $(M+H)^+$. MS: 335 $(M+H)^+$. HPLC: 98.9%



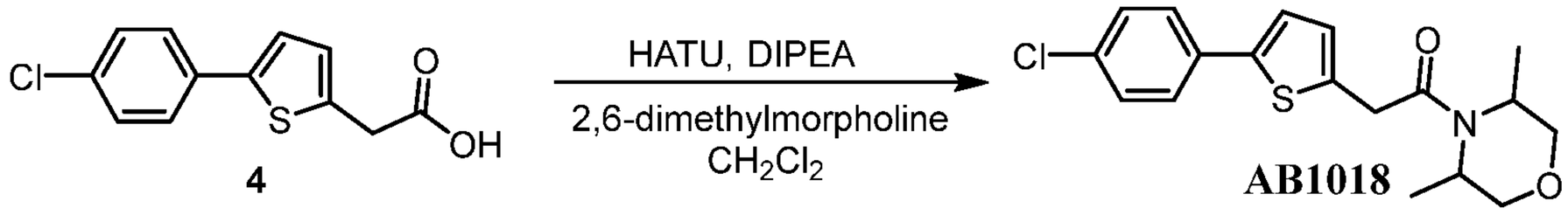
4 AB1015

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide (AB1015): Compound **AB1015** (80 mg, 33%) was synthesized from compound **4** by following general procedure **C.**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.50 (m, 2H), 7.33 - 7.38 (m, 2H), 7.12 (d, *J* = 3.91 Hz, 1H), 7.04 (dd, *J* = 5.38, 8.31 Hz, 2H), 6.90 (t, *J* = 8.56 Hz, 2H), 6.81 (d, *J* = 3.42 Hz, 1H), 5.62 (br. s., 1H), 3.72 (s, 2H), 3.48 (q, *J* = 6.52 Hz, 2H), 2.75 (t, *J* = 6.85 Hz, 2H). MS: 374 $(M+H)^+$.



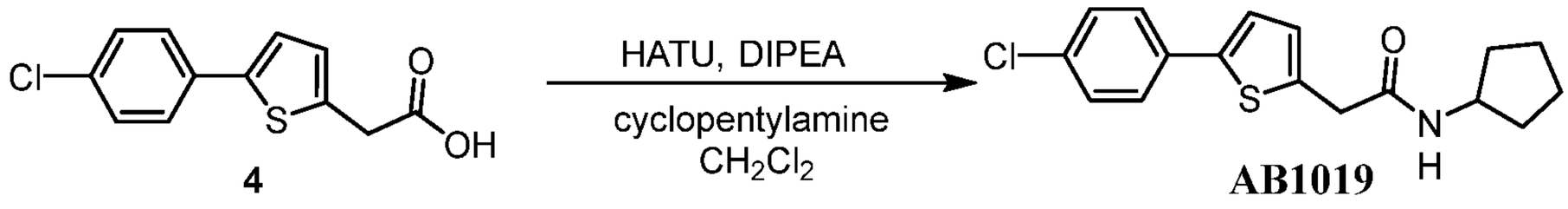
4 AB1016

2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(pyrrolidin-1-yl)ethyl)acetamide (AB1016): Compound AB1016 (80 mg, 38%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.51 (m, 2H), 7.31 - 7.37 (m, 2H), 7.17 (d, J = 3.42 Hz, 1H), 6.91 (d, J = 3.91 Hz, 1H), 6.42 (brs., 1H), 3.77 (s, 2H), 3.52 - 3.61 (m, 4H), 3.34 (q, J = 5.87 Hz, 2H), 2.48 (t, J = 6.11 Hz, 2H), 2.36 - 2.43 (m, 4H). MS: 349 $(M+H)^+$.



4 AB1018

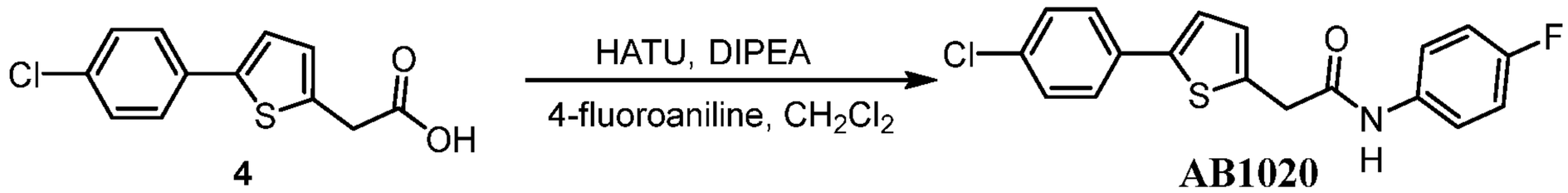
2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(3,5-dimethylmorpholino)ethan-1-one (AB1018): Compound **AB1018** (75 mg, 36%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.51 (m, 2H), 7.30 - 7.35 (m, 2H), 7.13 (d, J = 3.91 Hz, 1H), 6.85 (d, J = 3.91 Hz, 1H), 4.48 (d, J = 13.21 Hz, 1H), 3.90 (d, J = 3.91 Hz, 2H), 3.70 (d, J = 13.21 Hz, 1H), 3.35 - 3.60 (m, 2H), 2.84 (dd, J = 10.76, 13.21 Hz, 1H), 2.36 (dd, J = 10.76, 13.21 Hz, 1H), 1.18 (t, J = 7.09 Hz, 6H). MS: 350 $(M+H)^+$.



4 AB1019

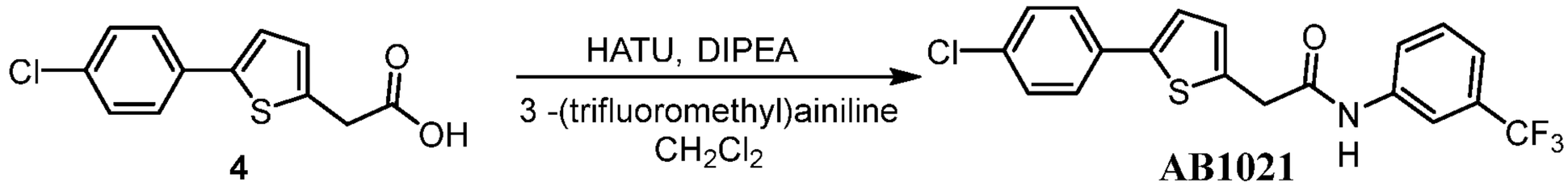
2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-cyclopentylacetamide (AB1019): Compound **AB1019** (79 mg, 42%) was synthesized from compound **4** by following general procedure **C.**^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 - 7.52 (m, 2H), 7.30 - 7.37 (m, 2H), 7.16 (d, J = 3.58 Hz, 1H), 6.88 (d, J =

3.58 Hz, 1H), 5.58 (brs., 1H), 4.08 - 4.33 (m, 1H), 3.73 (s, 2H), 1.87 - 2.09 (m, 2H), 1.46 - 1.75 (m, 4H), 1.11 - 1.41 (m, 2H). MS: 320 $(M+H)^+$.



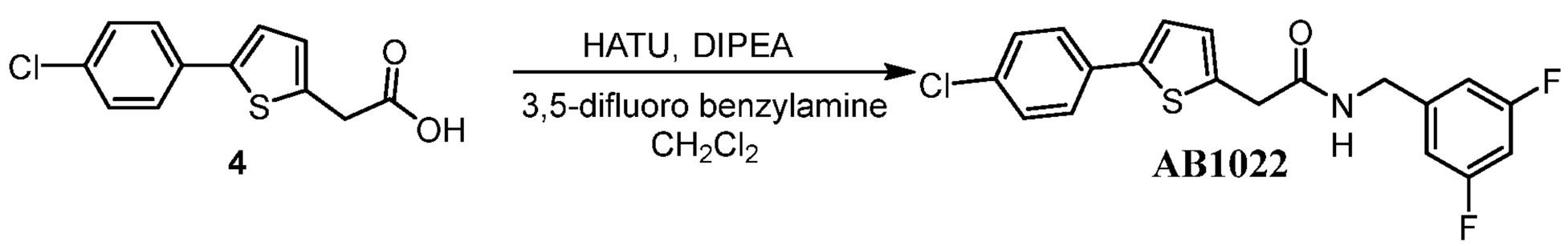
4 AB1020

2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-(4-fluorophenyl)acetamide (AB1020): Compound **AB1020** (104 mg, 51%) was synthesized from compound **4** by following general procedure **C.** ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 - 7.54 (m, 2H), 7.39 - 7.45 (m, 2H), 7.32 - 7.38 (m, 2H), 7.21 (d, *J* = 3.58 Hz, 1H), 6.92 - 7.05 (m, 3H), 3.93 (s, 2H). MS: 344 (M-H).



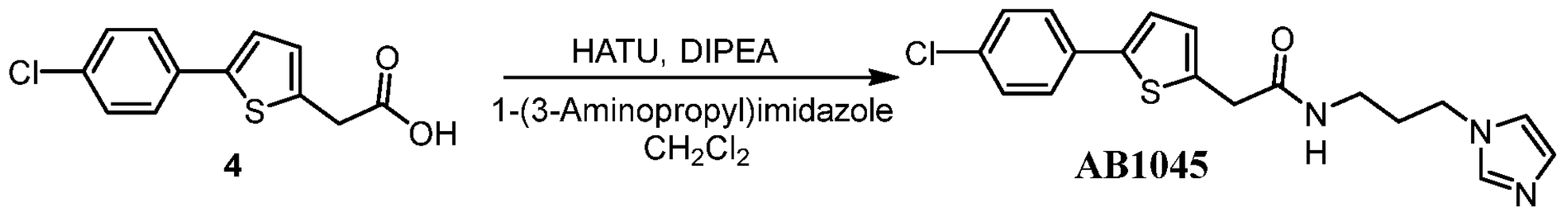
4 AB1021

2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-(3-(trifluoromethyl)phenyl)acetamide (AB1021): Compound **AB1021** (120 mg, 51%) was synthesized from compound **4** by following general procedure **C.** ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.69 (d, *J* = 8.19 Hz, 1H), 7.47 - 7.55 (m, 3H), 7.40 - 7.47 (m, 1H), 7.31 - 7.40 (m, 3H), 7.22 (d, *J* = 3.58 Hz, 1H), 7.01 (d, *J* = 3.58 Hz, 1H), 3.96 (s, 2H). MS: 394 (M-H).



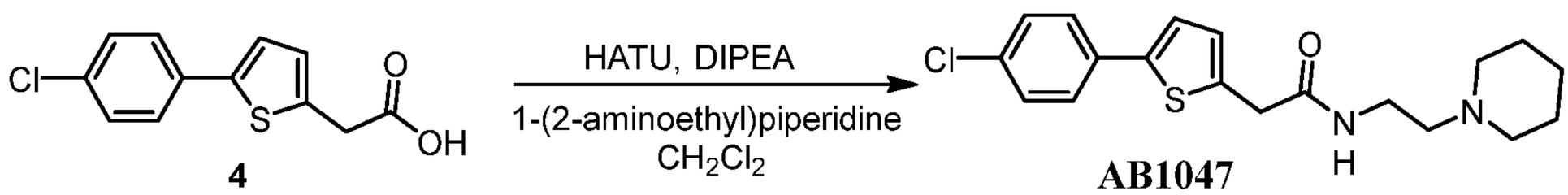
4 AB1022

2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-(3,5-difluorobenzyl)acetamide (AB1022): Compound AB1022 (103 mg, 46%) was synthesized from compound **4** by following general procedure **C.**^1H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.53 (m, 2H), 7.32 - 7.41 (m, 2H), 7.17 (d, *J* = 3.58 Hz, 1H), 6.93 (d, *J* = 3.58 Hz, 1H), 6.62 - 6.81 (m, 3H), 4.43 (d, *J* = 6.14 Hz, 2H), 3.79 - 3.91 (m, 2H). MS: 376 (M-H).



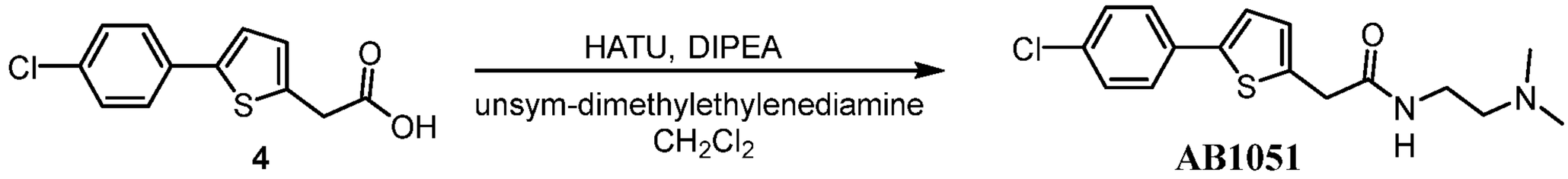
N-(3-(1*H*-Imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide (AB1045):

Compound **AB1045** (140 mg, 66%) was synthesized from compound **4** by following general procedure **C.**^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.47 (m, 3H), 7.34 (d, J = 8.4 Hz, 2H), 7.16 (d, J = 3.3 Hz, 1H), 7.05 (s, 1H), 6.91(d, J = 7.4 Hz, 2H), 5.90 (s, 1H), 3.97 (t, J = 6.9 Hz, 2H), 3.75 (s, 2H), 3.27 (q, J = 6.5 Hz, 2H), 2.02-1.85 (m, 2H); MS; 360 $(M+H)^+$. HPLC: 98.3%



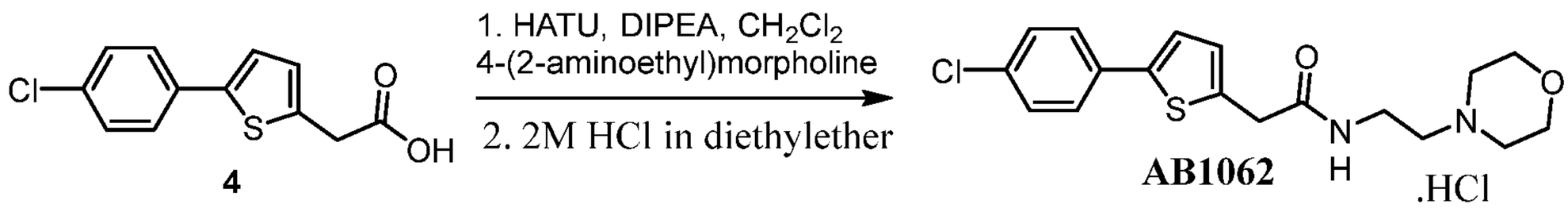
2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-(2-(piperidin-1-yl)ethyl)acetamide (AB1047):

Compound **AB1047** (76 mg, 36%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 3.6 Hz, 1H), 6.93 (d, J = 3.4 Hz, 2H), 3.77 (s, 2H), 3.39 (q, J = 5.2 Hz, 2H), 2.56 (s, 2H), 2.48 (brs, 4H), 1.55 (s, 4H), 1.41 (d, J = 5.7 Hz, 2H). MS: 363 $(M+H)^+$.



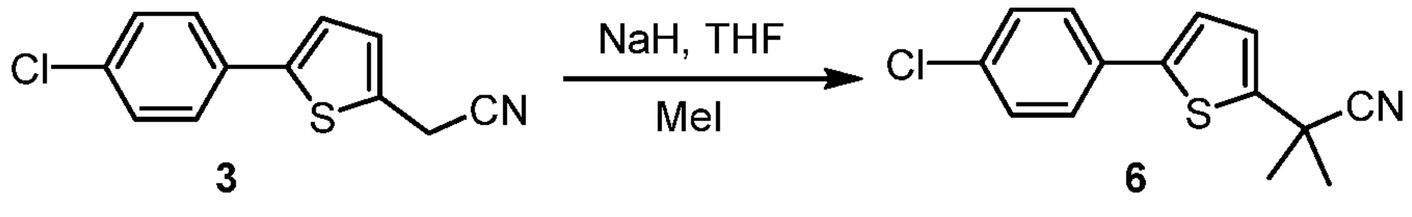
2-(5-(4-Chlorophenyl)thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)acetamide (AB1051):

Compound **AB1051** (40 mg, 21%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.46 (m, 2H), 7.33-7.31 (m, 2H), 7.14 (d, J = 3.4 Hz, 1H), 6.90 (d, J = 3.6 Hz, 1H), 6.50 (brs., 1H), 3.75 (s, 2H), 3.39 (q, J = 5.7 Hz, 2H), 2.53 (t, J = 5.9 Hz, 2H), 2.30 (s, 6H). MS: 323 $(M+H)^+$.



4 AB1062

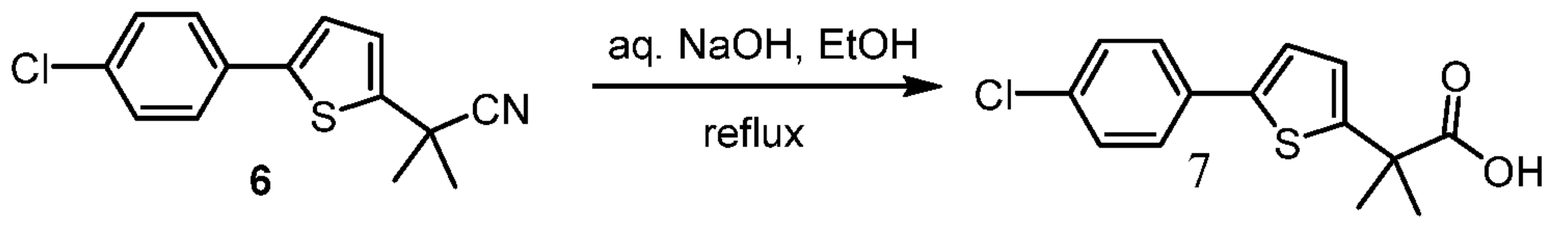
2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide hydrochloride (AB1062): To a stirred solution of compound 4 (150 mg, 0.59 mmol) in CH_2Cl_2 (5 mL), HATU (270 mg, 0.71 mmol) and DIPEA (0.2 mL) were added at 0 °C followed by 4-(2-aminoethyl)morpholine (94 µL, 0.71 mmol) was added and stirred for 20 h at room temperature. Concentrated the reaction mixture diluted with ethyl acetate (20 mL) organic fraction was washed with saturated $NaHCO_3$ (5 mL) followed by brine (10 mL). Organic fraction was dried over Na_2SO_4 concentrated and purified by column chromatography (silica gel 100-200 mesh, 5% MeOH in CH_2Cl_2) to afford compound 2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (122 mg, 56%) as off white color solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 - 7.55 (m, 2H), 7.29 - 7.40 (m, 2H), 7.14 (d, J = 3.91 Hz, 1H), 6.89 (d, J = 3.42 Hz, 1H), 3.75 (s, 2H), 3.36 (q, J = 5.87 Hz, 2H), 2.59 (t, J = 6.11 Hz, 2H), 2.48 (brs., 4H), 1.71 (td, J = 3.24, 6.73 Hz, 4H). 55mg of this compound was treated with 2M HCl in diethyl ether (3 mL) for 3h. Concentrated the reaction mixture to give AB1062 in quantitative yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.02 (s, 1H), 8.59 (t, J = 5.5 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 7.37 (d, J = 3.6 Hz, 1H), 6.95 (d, J = 3.6 Hz, 1H), 3.94 (m, 2H), 3.82 (t, J = 11.7 Hz, 2H), 3.69 (s, 2H), 3.50 (q, J = 6.1 Hz, 2H), 3.45 (d, J = 12.1 Hz, 2H), 3.18 (dd, J = 11.3 Hz, 5.9Hz, 2H), 3.11-3.04 (m, 2H); MS; 365 $(M+H)^+$. HPLC:97.7%



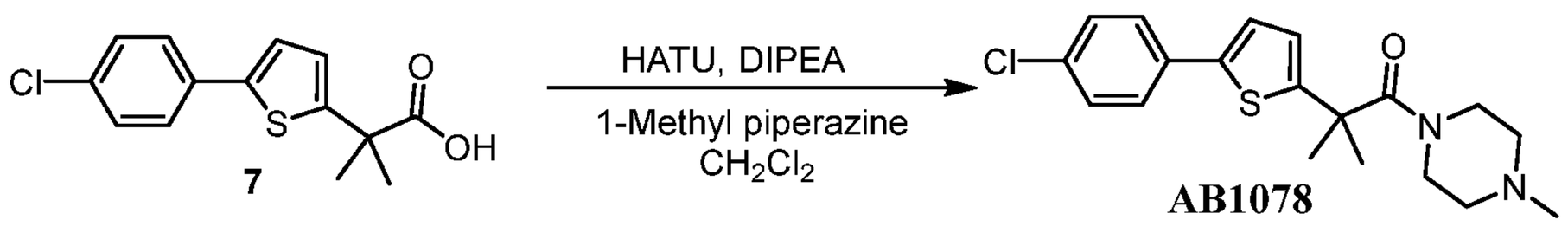
3 6

2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methylpropanenitrile (6): To a stirred solution of compound **4** (1.8gm, 7.7 mmol) in THF (30 mL), NaH (302 mg, 16.9 mmol, 60% in mineral oil) was added portion wise at 0 °C followed by MeI (1.93 mL, 30.8 mmol) was added and stirred for 3 h. Reaction was quenched with ice cold water (15 mL) and extracted with ethyl acetate (50 mL x 3). Organic layer was dried over Na_2SO_4 concentrated and purified by column chromatography (silica gel 100-200 mesh, 6-8% ethyl acetate in pet ether) to afford compound 6 (1.7 gm, 84%) as

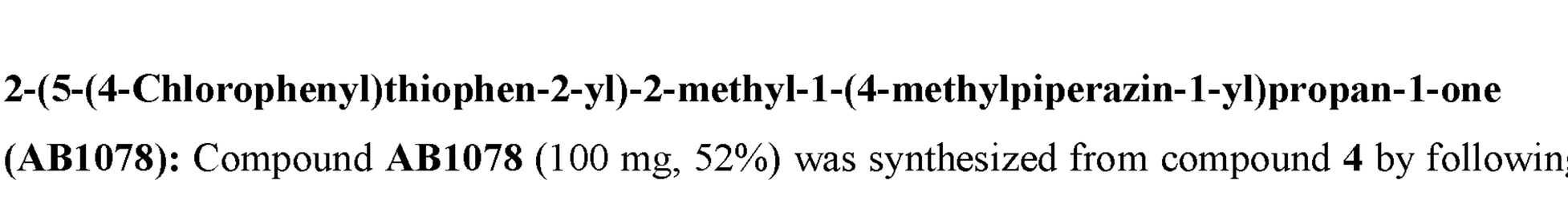
yellow color solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.13 (d, *J* = 3.6 Hz, 1H), 7.07 (d, *J* = 3.6 Hz, 1H), 1.82 (s, 6H).



2-(5-(4-Chlorophenyl)thiophen-2-yl)-2-methylpropanoic acid (7): Compound 7 (700 mg, 38%) was synthesized from compound **6** by following general procedure **B.** . ^{1}H NMR (DMSO-d_6, 500MHz): δ 12.66 (s, 1H), 7.64 (d, *J*=8.3Hz, 2H), 7.45 (d, *J*=9.0, 2H), 7.38 (d, *J*=4.1Hz, 1H), 7.00 (d, *J*=3.4Hz, 1H), 1.57 (s, 6H).

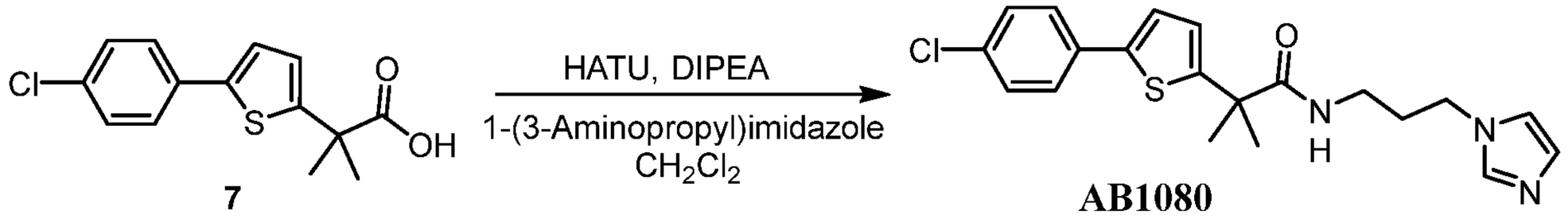


2-(5-(4-Chlorophenyl)thiophen-2-yl)-2-methyl-1-(4-methylpiperazin-1-yl)propan-1-one (AB1078): Compound **AB1078** (100 mg, 52%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 3.6 Hz, 1H), 6.77 (d, *J* = 3.6 Hz, 1H), 3.49 (brs., 4H), 2.26 (brs., 4H), 1.63 (s, 6H). MS: 363 $(M+H)^+$.



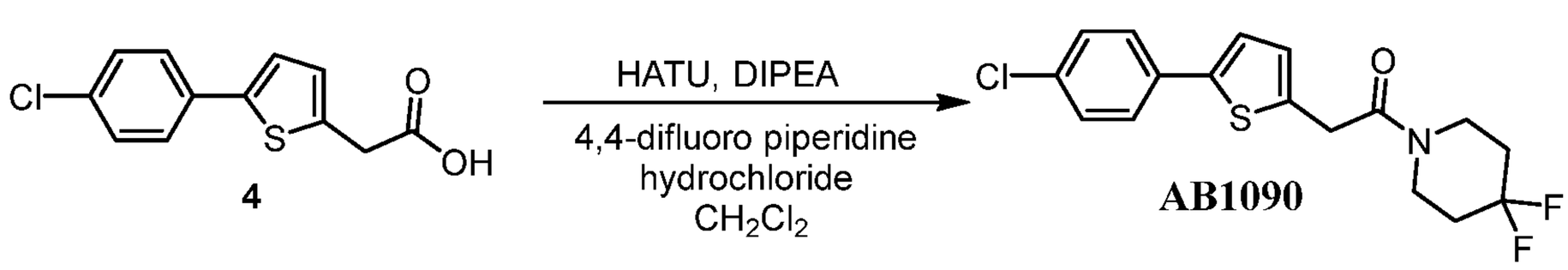
2-(5-(4-Chlorophenyl)thiophen-2-yl)-2-methyl-*N*-(2-(piperidin-1-yl)ethyl)propanamide (AB1079): Compound **AB1079** (85 mg, 41%) was synthesized from compound **4** by following

general procedure **C.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 3.4 Hz, 1H), 7.09 (s, 1H), 7.03(d, J = 3.4 Hz, 1H), 3.55 (d, J = 3.4 Hz, 2H), 3.18 (brs., 4H), 3.0 (brs., 2H), 1.82 (6H), 1.69 (s, 6H); MS; 391 $(M+H)^+$. MS: 391 $(M+H)^+$. HPLC: 98.9%



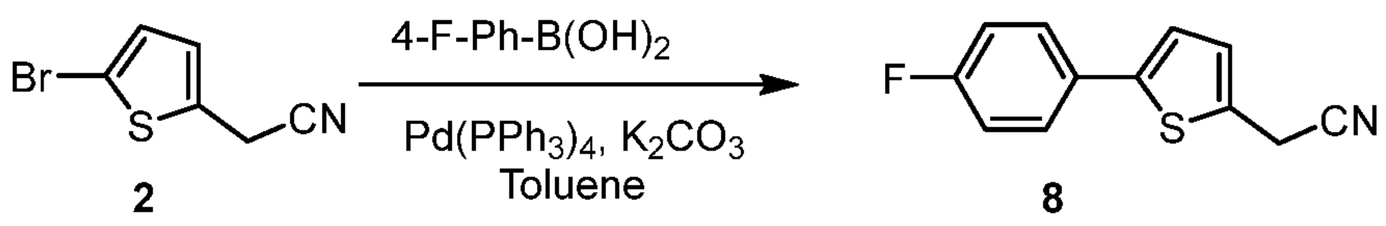
7 **AB1080**

***N*-(3-(1*H*-Imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methylpropanamide (AB1080):** Compound **AB1080** (83 mg, 40%) was synthesized from compound **7** by following general procedure **C.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 3.6 Hz, 1H), 7.04 (s, 1H), 6.96 (d, J = 3.4 Hz, 1H), 6.90 (s, 1H), 5.71 (brs., 1H), 3.92 (t, J = 6.9 Hz, 2H), 3.19 (q, J = 6.5 Hz, 2H), 1.97 - 1.93 (m, 2H), 1.66 (s, 6H). MS: 388 $(M+H)^+$.



4 **AB1090**

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4,4-difluoropiperidin-1-yl)ethan-1-one (AB1090): Compound **AB1090** (118 mg, 60%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 3.6 Hz, 1H), 6.86 (d, J = 3.6 Hz, 1H), 3.93 (s, 2H), 3.77 (t, J = 6.9 Hz, 2H), 3.64 (t, J = 6.9 Hz, 2H), 1.99-1.86 (m, 4H). MS: 356 $(M+H)^+$.



2 **8**

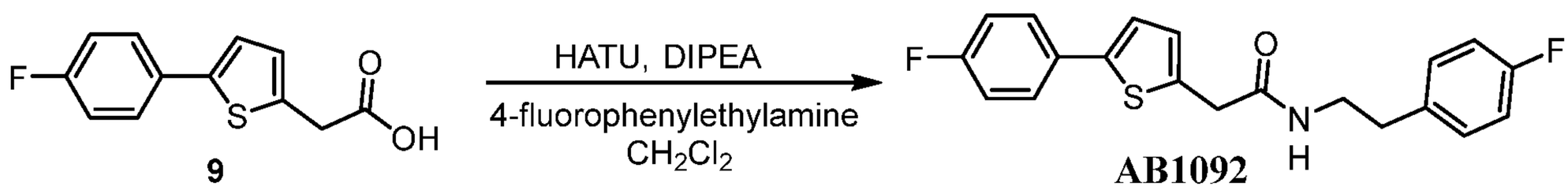
2-(5-(4-fluorophenyl)thiophen-2-yl)acetonitrile) (8): Compound **8** (1.5 gm, 71%) was synthesized from compound **2** by following general procedure A.^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 - 7.49 (m, 2H), 7.09 - 7.05 (m, 4H), 3.91 (s, 2H).

8 **9**

2-(5-(4-fluorophenyl)thiophen-2-yl)acetic acid (9): Compound **9** (1.45 g) was synthesized from compound **8** by following general procedure **B.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 - 7.49 (m, 2H), 7.09 - 7.03 (m, 3H), 6.92 (d, *J* = 3.6 Hz, 1H), 3.88 (s, 2H).

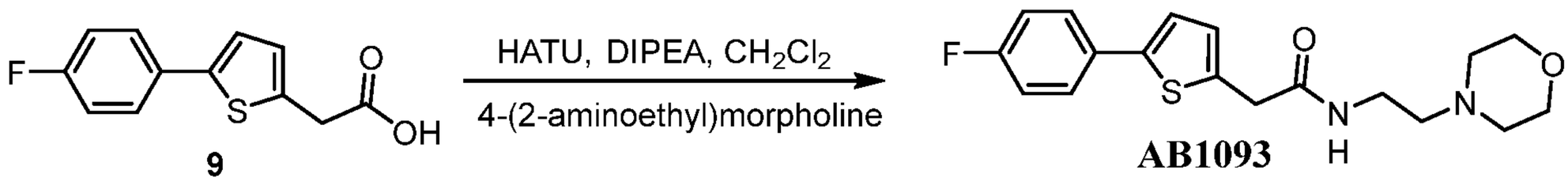
9 **AB1091**

2-(5-(4-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one (AB1091): Compound **AB1091** (78 mg, 48%) was synthesized from compound **9** by following general procedure **C.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-5.30(m, 2H), 7.07-7.03(m, 3H), 6.84(d, *J*= 3.6Hz, 1H), 3.90(s, 2H), 3.68(t, *J*= 4.9Hz, 2H), 3.56(t, *J*= 5.1Hz, 2H), 2.40(t, *J*= 5.2Hz, 2H), 2.36(t, *J*= 5.0Hz, 2H), 2.29(s, 3H). MS: 319 $(M+H)^+$.



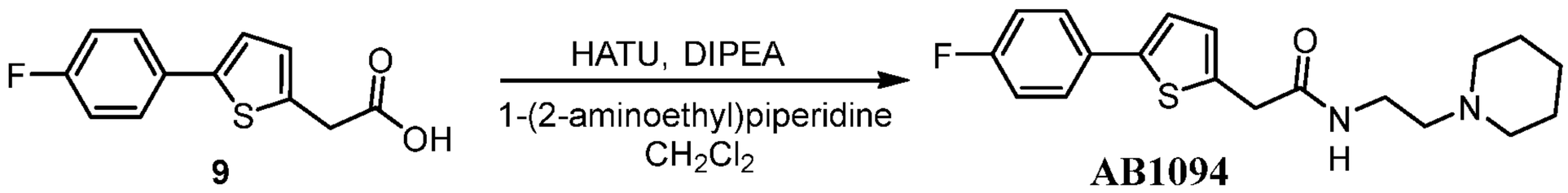
9 **AB1092**

N-(4-fluorophenethyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamideAB (1092): Compound **AB1092** (110mg, 60%) was synthesized from compound **9** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.52-7.49 (m, 2H), 7.49-7.04 (m, 5H), 6.92-6.88 (2H, m), 6.80 (d, *J*= 3.6Hz,1H), 5.62 (s, 1H), 3.72 (s, 2H), 3.48 (q, *J= 6.5Hz, 2H*), 2.75 (t, *J*= 6.9Hz, 2H). MS: 358 $(M+H)^+$.



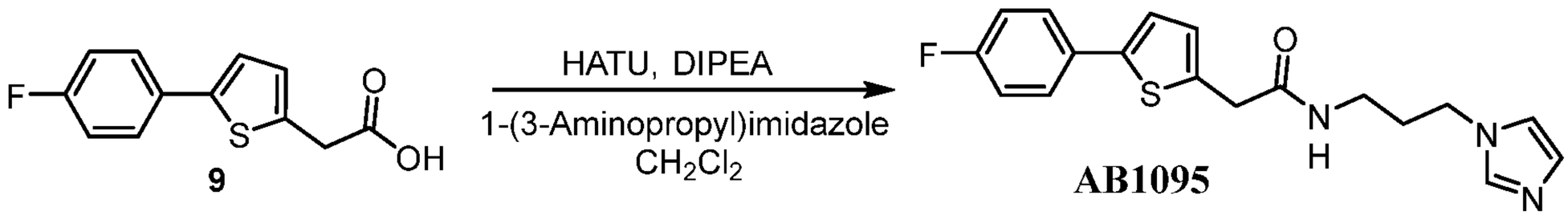
9 AB1093

2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide AB (1093): Compound **AB1093** (140mg, 79%) was synthesized from compound **9** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.53-7.50 (m, 2H), 7.13 (d, *J*= 3.6Hz, 1H), 7.08-7.05 (m, 2H), 6.91 (d, *J*= 3.6Hz, 1H), 6.37 (s, 1H), 3.77 (s, 2H), 3.55 (t, *J*= 4.4Hz, 4H), 3.33 (q, *J*= 5.6Hz, 2H), 2.45 (t, *J*= 6.0Hz, 2H), 2.37 (t, *J*= 4.0Hz, 4H). MS: 349 $(M+H)^+$.



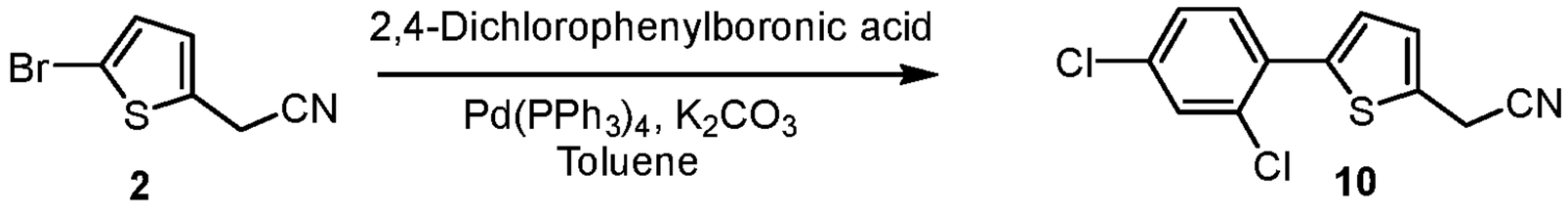
9 AB1094

2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide (AB1094): Compound **AB1094** (31mg, 10%) was synthesized from compound **9** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.53-7.50 (m, 2H), 7.11 (d, *J*= 3.4Hz, 1H), 7.11-7.04 (m, 2H), 6.90 (d, *J*= 3.6Hz, 1H), 6.64 (s, 1H), 3.76 (s, 2H), 3.32 (q, *J*= 5.6Hz, 2H), 2.44 (t, *J*= 6.0, 2H), 2.34 (s, 4H), 1.46-1.42 (m, 4H), 1.35 (d, *J*= 5.3, 2H). MS: 347 $(M+H)^+$.



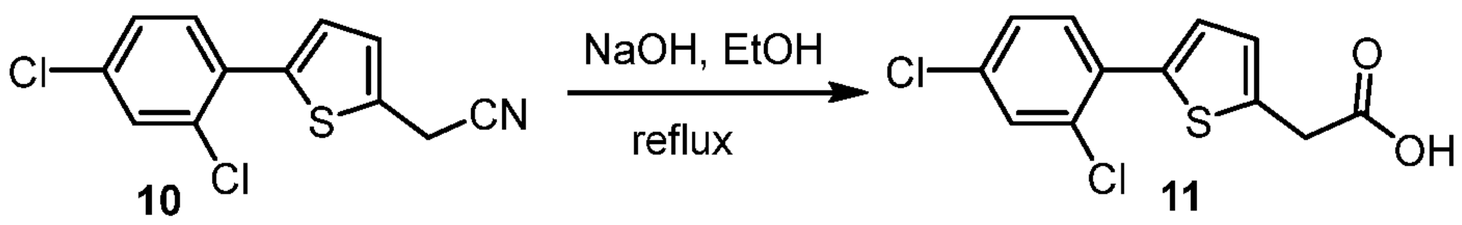
9 AB1095

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide AB(1095): Compound **AB1095** (35mg,12%) was synthesized from compound **9** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.52 (dd, *J*= 8.6Hz, 2H), 7.45 (s, 1H), 7.11-7.04 (m, 4H), 6.90-6.88 (m, 2H), 5.94 (s. 1H), 3.96 (t, *J*= 6.9Hz, 2H), 3.75 (s, 2H), 3.26 (q, *J*= 6.4Hz, 2H), 2.01-1.96 (m, 2H). MS: 344 $(M+H)^+$.

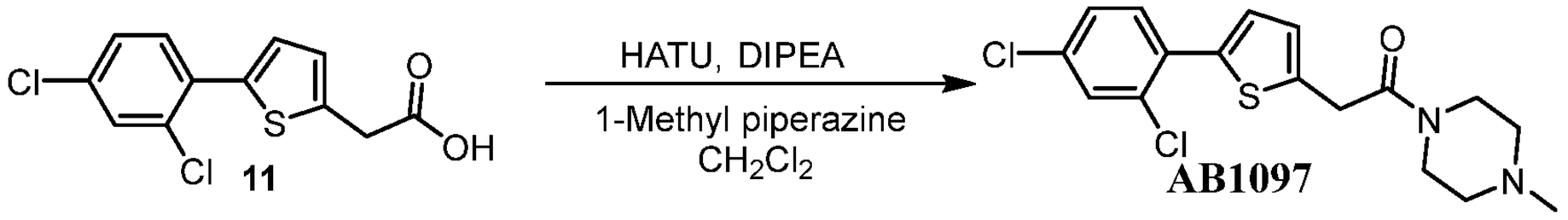


2 10

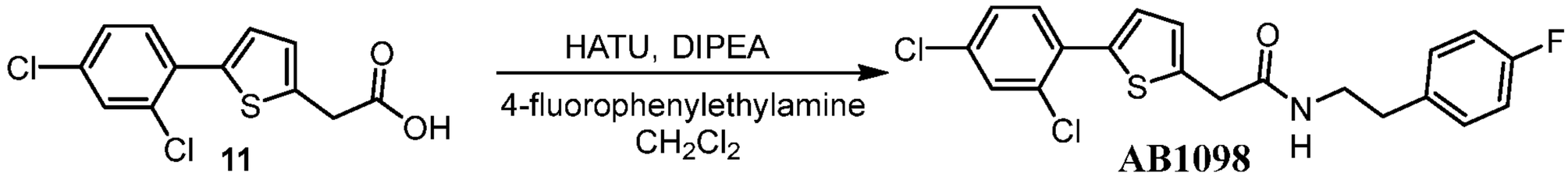
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)acetonitrile (10): compound **10** (2.4 gm, 70%) synthesized from compound **2** by following general procedure **A**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.76 (dd, *J*=12.1Hz, 10.0Hz, 1H), 7.67 (t, *J*=7.2Hz, 1H), 7.51-7.48 (m, 1H), 7.37 (q, *J*=3.4Hz, 1H), 7.14 (d, *J*=3.4Hz, 1H), 4.36 (s, 2H).



2-(5-(2,4-dichlorophenyl)thiophen-2-yl)acetic acid (11): Compound **11** (2 g, 81%) Synthesized from compound **10** by following General procedure **B**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 12.65 (bs, 1H), 7.74(s, 1H), 7.64 (d, *J* =8.3Hz, 1H), 7.49 (dd, *J*= 9.0Hz, 2.1Hz, 1H), 7.32 (d, *J* =3.4Hz, 1H), 7.01 (d, *J* =3.4Hz, 1H), 3.88 (s, 2H).

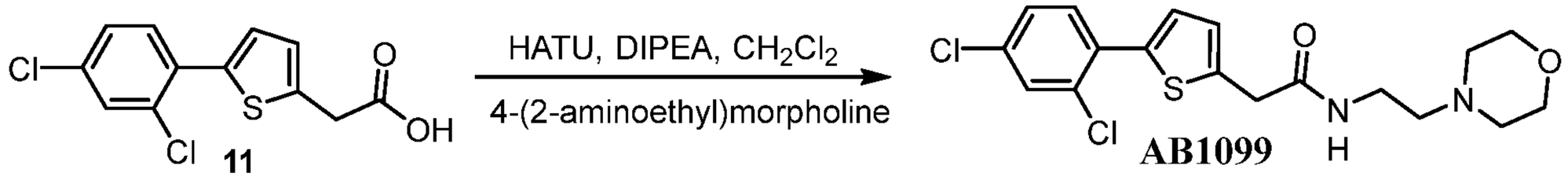


2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one (AB1097): Compound **AB1097** (62mg, 24%) was synthesized from compound **11** by following general procedure **C.** δ ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.73 (d, *J*=2.8Hz, 1H), 7.63 (d, *J*=8.3Hz, 1H), 7.48 (dd, *J*=8.3Hz, 2.1Hz, 1H), 7.31 (d, *J*=3.4Hz, 1H), 6.97 (d, *J*=3.4Hz, 1H), 4.00 (s, 2H), 3.53 (t, *J*=4.8Hz, 2H), 3.47 (s, 2H), 2.27 (t, ,*J*=5.9Hz, 4H), 2.17 (s, 3H). MS: 369 $(M+H)^+$.

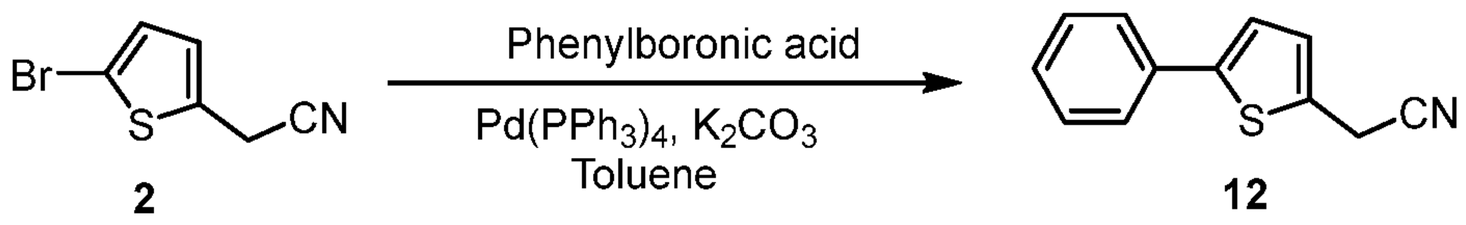


2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide (AB1098): Compound **AB1098** (61mg, 21%) was synthesized from compound **11** by following general

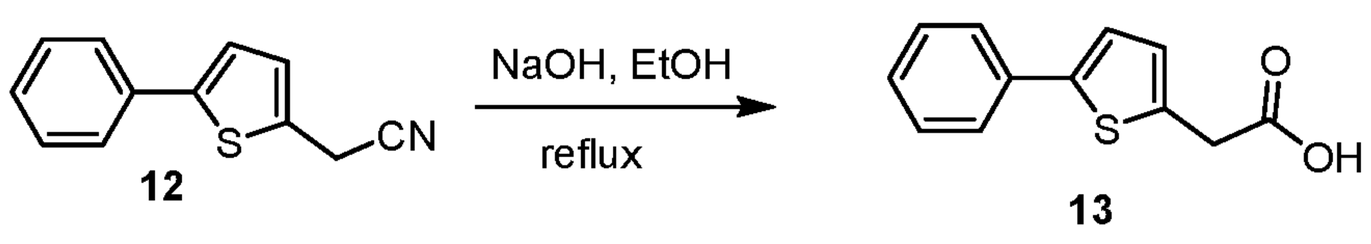
procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.55-7.52 (1H, m), 7.41 (d, *J*= 8.3, 1H), 7.30-7.27 (1H, m), 7.24-7.20 (1H, m), 7.07-7.00 (2H, m), 6.94 (q, *J*= 8.6Hz, 2H), 6.86 (dd, *J*= 13.8Hz, 3.4Hz, 1H), 5.64 (1H, s), 3.75 (d, *J*= 12.1Hz, 2H), 3.51-3.43 (2H, m), 2.77-2.71(2H, m). MS: 408 $(M+H)^+$.



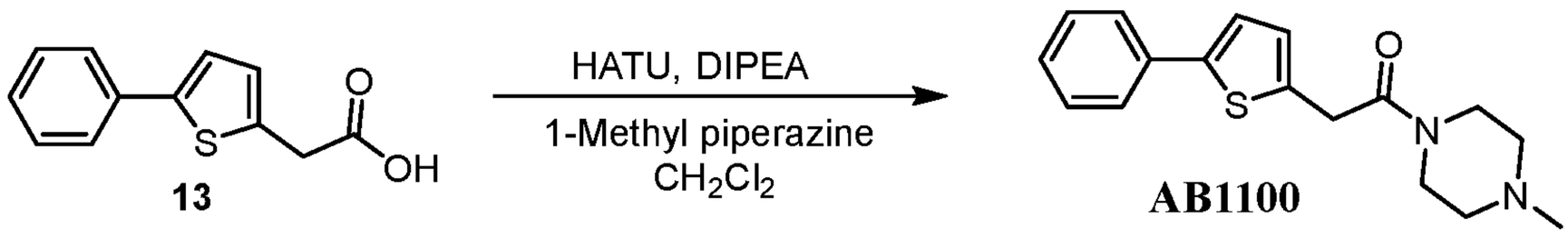
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamideAB (1099): Compound **AB1099** (4.5g, 82%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz); δ 7.49 (d, *J*= 2.1Hz, 1H), 7.43 (d, *J*= 9.0, 1H), 7.28 (d, *J*= 2.1Hz, 1H), 7.25 (1H, s), 6.96 (d, *J*= 3.4Hz, 1H), 6.39 (1H, s), 3.80 (2H, s), 3.60 (t, *J*= 4.5Hz, 4H),3.36 (q, *J*= 5.5Hz, 2H), 2.50 (t, *J*= 5.9Hz, 2H), 2.43 (4H, s). MS: 399 $(M+H)^+$. HPLC: 99.2%.



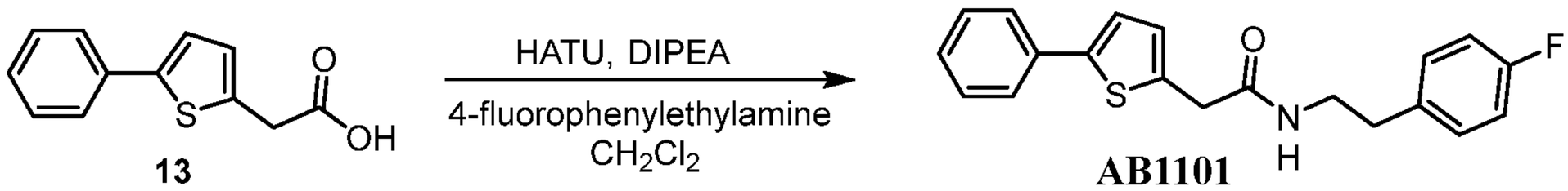
2-(5-phenylthiophen-2-yl)acetonitrile (12): compound **12** (1.6gm) synthesized from compound **2** by following general procedure **A**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.56–7.54 (m, 2H), 7.40-7.32 (m, 2H), 7.31-7.28 (m, 1H), 7.17-7.16 (m, 1H), 7.03-7.02 (m,1H), 3.92 (s, 2H).



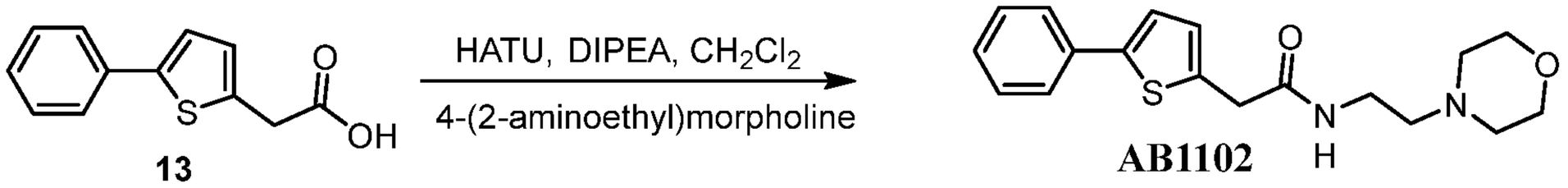
2-(5-phenylthiophen-2-yl)acetic acid (13): Compound **13** (1.3 g) Synthesized from compound **13** by following General procedure **B**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 12.61 (bs, 1H), 7.61–7.59 (m, 2H), 7.41-7.38 (m, 2H), 7.34 (d, *J* =3.4Hz, 1H), 7.30-7.27 (m, 1H), 6.95 (d, *J* =3.4Hz, 1H), 3.83 (s, 2H).



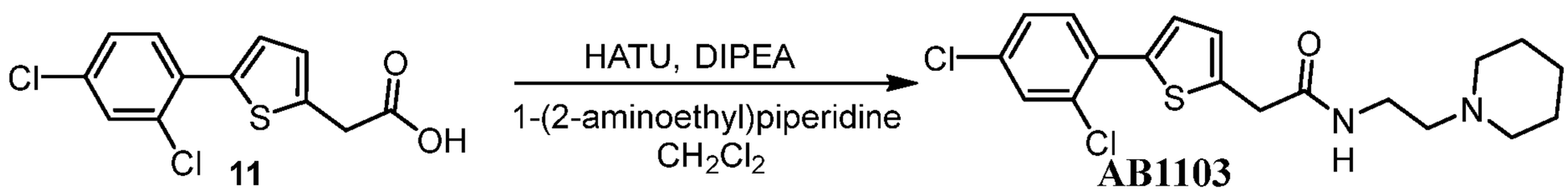
1-(4-methylpiperazin-1-yl)-2-(5-phenylthiophen-2-yl)ethan-1-one (AB1100): Compound **AB1100** (65mg, 23%) was synthesized from compound **13** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.57-7.55 (m, 2H), 7.37-7.34 (m, 2H), 7.27 (t, *J*= 1.1Hz, 1H), 7.15 (d, *J*= 3.6Hz, 1H), 6.86 (dd, *J*=3.6Hz, 0.9Hz, 1H), 3.90 (d, *J*= 0.7Hz, 2H), 3.68 (t, *J*= 4.9Hz, 2H), 3.55 (t, *J*= 5.1Hz, 2H), 2.39 (t, *J*= 5.2Hz, 2H), 2.34 (t, *J*= 5.1Hz, 2H), 2.28 (s, 3H). MS: 301 $(M+H)^+$.



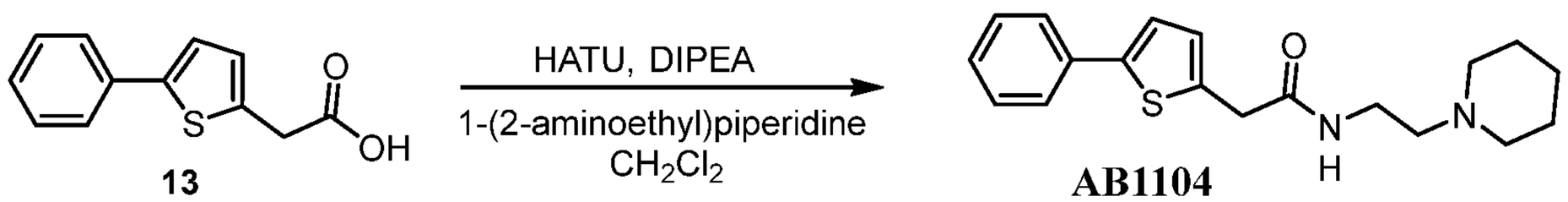
N-(4-fluorophenethyl)-2-(5-phenylthiophen-2-yl)acetamide (AB1101): Compound **AB1101** (125mg, 40%) was synthesized from compound **13** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.55 (d, *J*= 7.3Hz, 2H), 7.39 (t, *J*= 7.3Hz, 2H), 7.30 (t, *J*= 6.82Hz, 1H), 7.15 (d, *J*= 3.4Hz, 1H), 7.04 (q, *J*= 5.3Hz, 2.9Hz, 2H), 6.90 (t, *J*= 8.78Hz, 2H), 6.80 (d, *J*=3.7Hz, 1H), 3.79 (s, 2H), 3.47 (q, *J*= 6.3Hz, 2H), 2.74 (t, *J*= 6.82Hz, 2H). MS: 340 $(M+H)^+$.



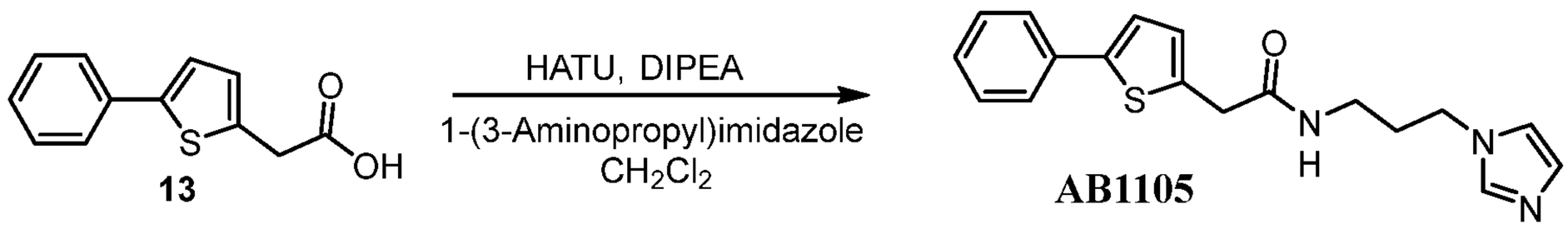
N-(2-morpholinoethyl)-2-(5-phenylthiophen-2-yl)acetamide(AB1102): Compound **AB1102** (102mg, 34%) was synthesized from compound **13** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.56 (d, *J*= 4.87Hz, 2H), 7.37 (t, *J*= 5.36Hz, 2H), 7.30 (t, 1H), 7.20 (d, 1H), 6.41(s, 1H), 3.78 (s, 2H), 3.55 (t, *J*= 4.87Hz, 4H), 3.34 (q, *J*= 5.8, 2H), 2.45 (t, *J*= 6.34Hz, 2H), 2.38 (t, *J*= 4.39Hz, 4H). MS: 331 $(M+H)^+$.



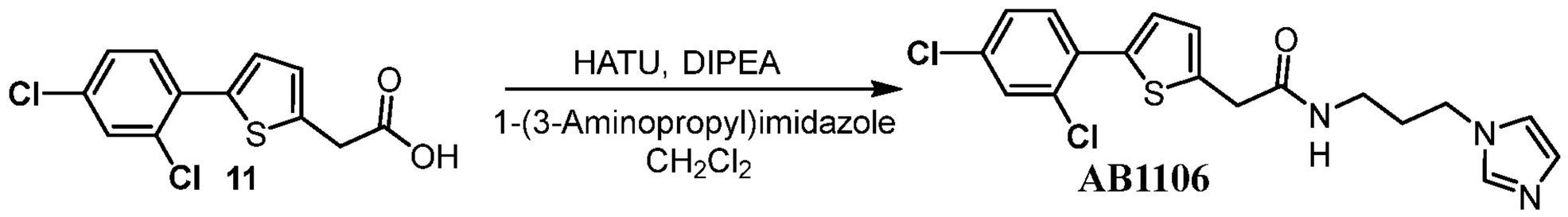
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide (AB1103): Compound **AB110** (35mg, 13%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.19 (s, 1H), 7.73 (d, *J*=2.1Hz, 1H), 7.62 (d, *J*=8.3Hz, 1H), 7.48 (dd, *J*=8.6Hz, 2.4Hz, 1H), 7.30 (d, *J*=3.4Hz, 1H), 6.97 (d, *J*=4.2Hz, 1H), 3.70 (s, 2H), 3.27 (s, 2H), 2.53 (s, 2H), 1.55 (s, 4H), 1.40 (s, 2H), 1.25-1.22 (m, 4H). MS: 397 $(M+H)^+$.



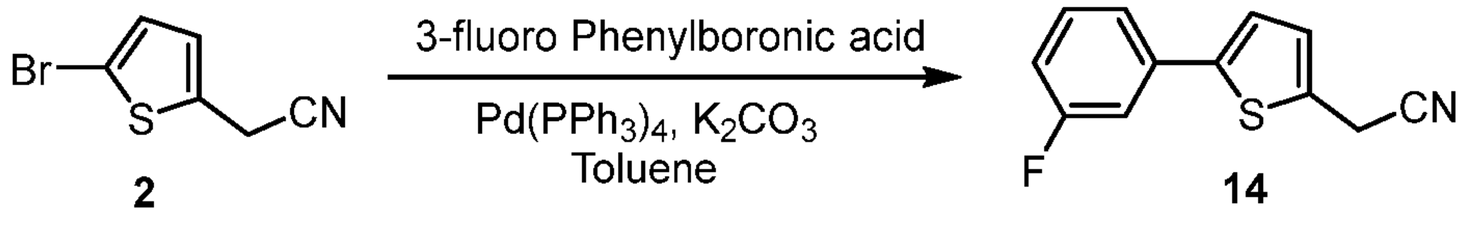
2-(5-phenylthiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide (AB1104): Compound **AB1104** (165mg, 55%) was synthesized from compound **13** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.41 (s, 1H), 7.59 (d, *J*= 7.6Hz, 2H), 7.40 (t, *J*= 7.9Hz, 2H), 7.34 (d, *J*=3.4Hz, 1H), 7.29 (t, *J*=7.2Hz, 1H), 6.93 (d, *J*=4.1Hz, 1H), 3.70 (s, 2H), 3.43 (s, 2H), 3.05 (s, 2H), 2.87 (s, 2H), 1.69 (s, 4H), 1.27 – 1.22 (m, 2H). MS: 329 $(M+H)^+$.



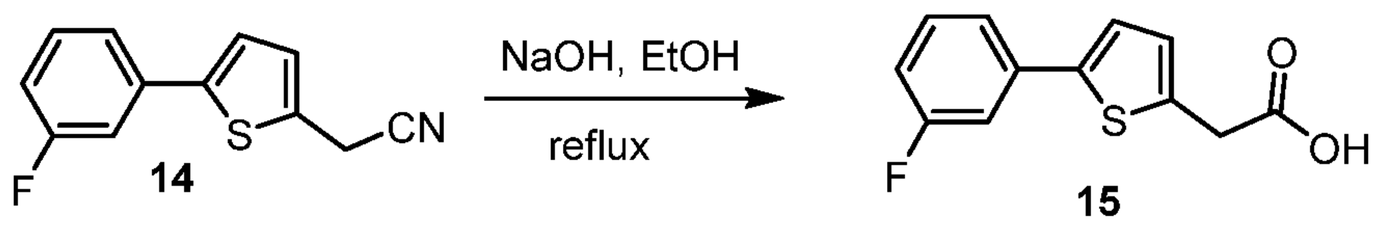
N-(3-(1H-imidazol-1-yl)propyl)-2-(5-phenylthiophen-2-yl)acetamide (AB1105): Compound **AB1105** (22mg, 11%) was synthesized from compound **13** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.57-7.55 (m, 2H), 7.53 (s, 1H), 7.39-7.36 (m, 2H), 7.30-7.27 (m, 1H), 7.19 (d, *J*= 3.6Hz, 1H), 7.04 (s, 1H), 6.90 (dd, *J*= 2.4Hz, 0.9Hz, 2H), 5.97 (s, 1H), 3.96 (t, *J*= 6.9Hz, 2H), 3.77 (s, 2H), 3.26 (q, *J*= 6.5Hz, 2H), 2.00-1.96 (m, 2H). MS: 326 $(M+H)^+$.



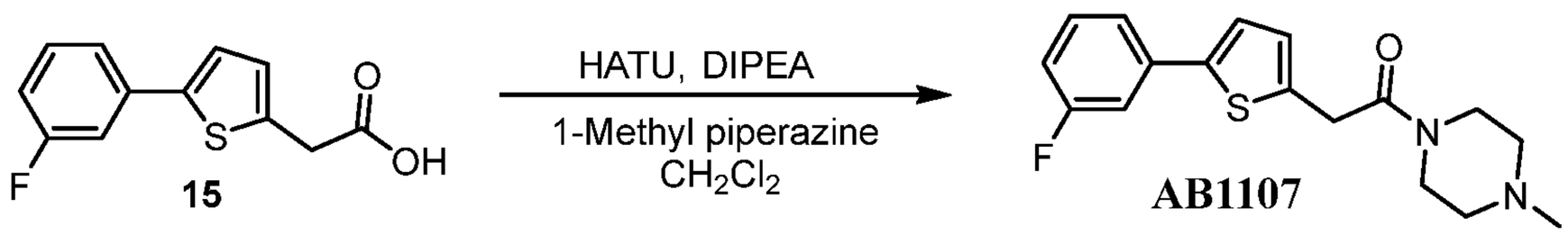
N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(2,4-dichlorophenyl)thiophen-2-yl)acetamide (AB1106): Compound **AB1106** (105mg, 38%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 1.84 (t, *J*=5.5Hz, 1H), 7.73 (d, *J*=2.1Hz, 1H), 7.66 (s, 1H), 7.62 (d, *J*=8.3Hz, 1H), 7.48 (dd, *J*=8.3Hz, 2.1Hz, 1H), 7.31 (d, *J*=3.4Hz, 1H), 7.18 (s, 1H), 6.97 (d, *J*=3.4Hz, 1H), 6.92 (s, 1H), 3.97 (t, *J*=6.9Hz, 2H), 3.70 (s, 2H), 3.04 (q, *J*=6.2Hz, 2H), 1.88-1.82 (m, 2H). MS: 394 $(M+H)^+$.



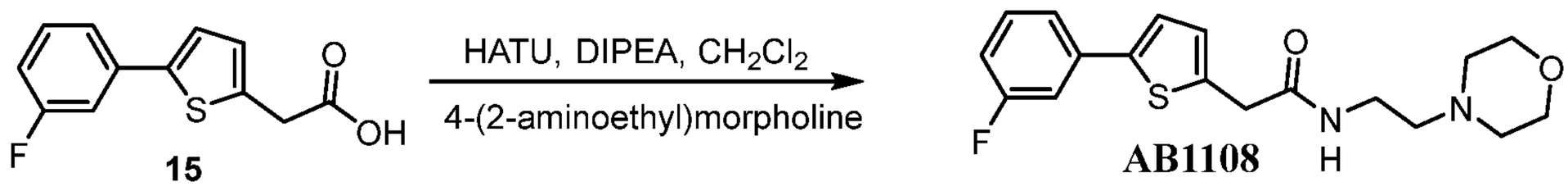
2-(5-(3-fluorophenyl)thiophen-2-yl)acetonitrile (14): compound **12** (3.1gm) synthesized from compound **2** by following general procedure **A**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.52–7.50 (m, 2H), 7.48–7.43 (m, 2H), 7.17–7.12 (m, 1H), 7.10 (d, *J*=3.4Hz, 1H), 4.34 (s, 2H).



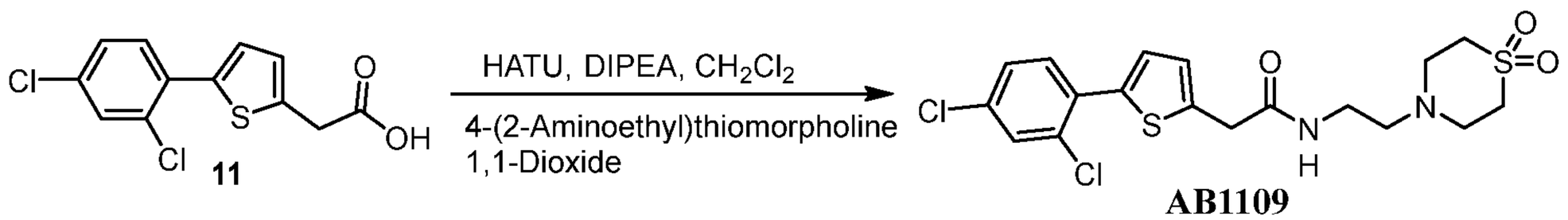
2-(5-(3-fluorophenyl)thiophen-2-yl)acetic acid (15): Compound **15** (1.7 g) Synthesized from compound **13** by following General procedure **B**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 12.64 (bs, 1H), 7.48–7.42 (m, 4H), 7.13-7.10 (m, 1H), 6.97 (d, *J* =3.4Hz, 1H), 3.85 (s, 2H).



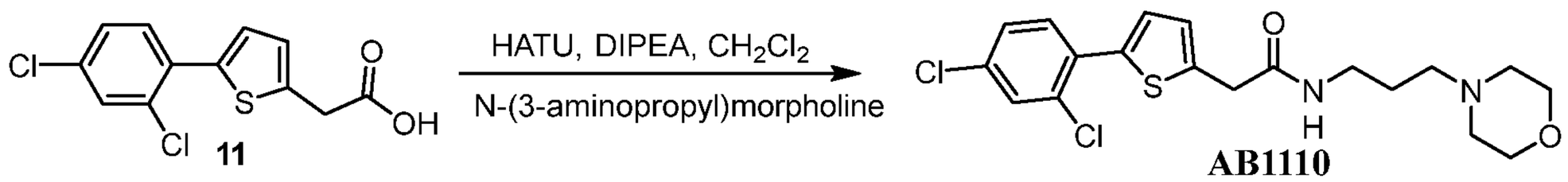
2-(5-(3-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one(AB1107): Compound **AB1107** (115mg, 71%) was synthesized from compound **15** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.34-7.31 (m, 2H), 7.24 (t, *J*= 2.0Hz, 1H), 7.16 (d, *J*=3.8Hz, 1H), 6.95 (m, 1H), 6.97-6.94 (m, 1H), 6.87 (dt, *J*= 3.6Hz, 0.9Hz, 1H), 3.90 (d, *J*= 0.9Hz, 2H), 3.69 (t, *J*= 5.0Hz, 2H), 3.56 (t, *J*= 5.1Hz, 2H), 2.38 (dt, *J*= 20.3Hz, 5.1Hz, 4H), 2.29 (s, 3H). MS: 319 $(M+H)^+$.



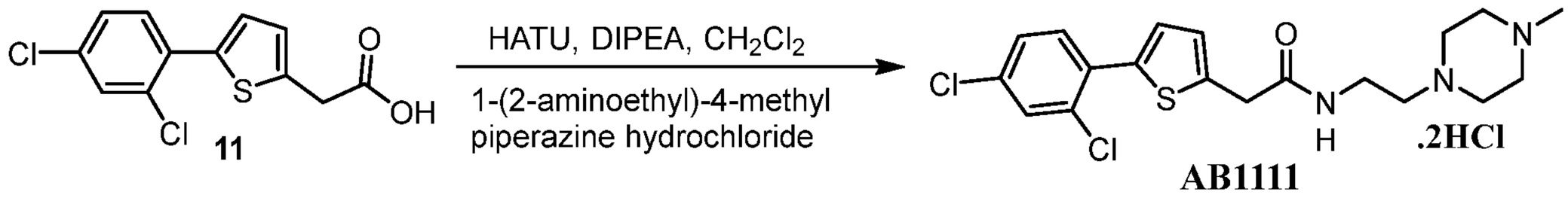
2-(5-(3-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide(AB1108): Compound **AB1108** (102mg, 58%) was synthesized from compound **15** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.34-7.32 (m, 2H), 7.24 (m, 1H), 7.21(d, *J*= 3.6Hz, 1H), 6.99-6.96 (m, 1H), 6.93 (d, *J*= 3.6Hz, 1H), 6.35 (s, 1H), 3.78(s, 2H), 3.55 (t, *J*= 4.5Hz, 4H), 3.33 (q, *J*= 5.7Hz, 2H), 2.44 (t, *J*= 6.0Hz, 2H), 2.37 (t, *J*= 4.4Hz, 4H). MS: 349 $(M+H)^+$.



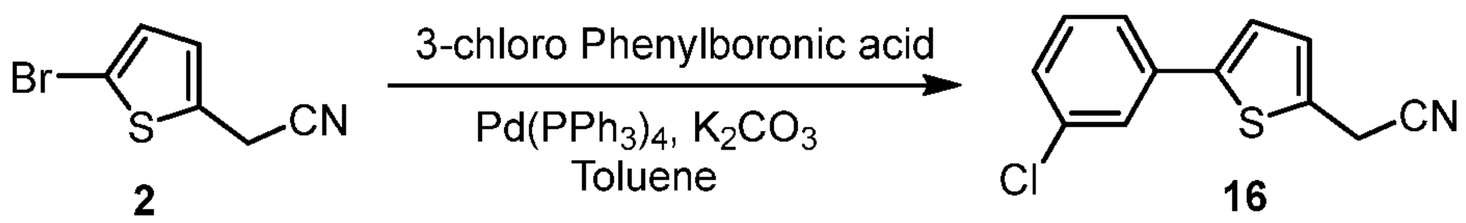
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide (AB1109): Compound **AB1109** (531mg, 57%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.08 (t, *J*= 5.5Hz, 1H), 7.73 (d, *J*= 2.1Hz, 1H), 7.62 (d, *J*= 8.3Hz, 1H), 7.48 (dd, *J*= 8.3Hz, 2.1Hz, 1H), 7.30 (d, *J*= 4.1Hz, 1H), 6.96 (d, *J*= 3.4Hz, 1H), 3.69 (s, 2H), 3.19 (q, *J*= 6.2Hz, 2H), 3.04 (d, *J*= 10.3Hz, 4H), 2.91 (d, *J*= 4.8Hz, 4H), 2.55 (t, *J*= 6.5Hz, 2H). MS: 447 $(M+H)^+$. HPLC: 98%



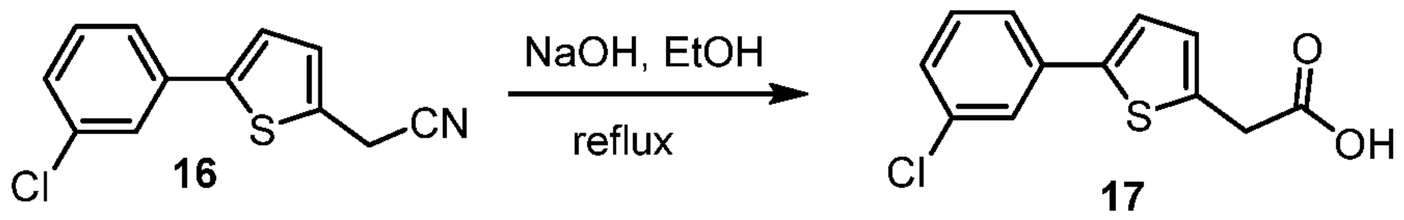
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide (AB1110): Compound **AB1110** (470mg, 33%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.15 (t, *J*= 5.5Hz, 1H), 7.73 (d, *J*= 2.1Hz, 1H), 7.62 (d, *J*= 8.3Hz, 1H), 7.48 (dd, *J*= 8.3Hz, 2.1Hz, 1H), 7.30 (d, *J*= 4.1Hz, 1H), 6.95 (d, *J*= 4.1Hz, 1H), 3.67 (s, 2H), 3.10 (q, *J*= 6.4Hz, 2H), 2.31-2.25 (m, 6H), 1.59-153 (m, 2H). MS: 413 $(M+H)^+$. HPLC:99.5%



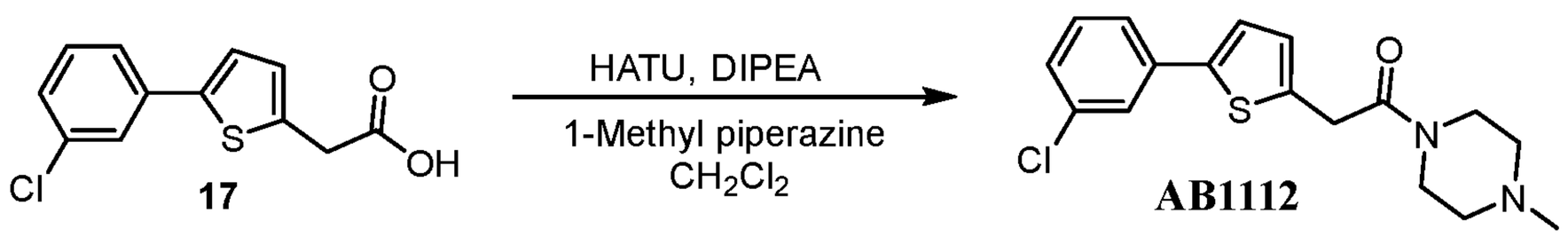
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide hydrochloride (AB1111): Compound **AB1111** (37mg) was synthesized from compound **11** by following general used for the synthesis of AB1062**.** ^{1}H NMR(dmso-d6, 500MHz): δ 8.43 (s, 1H), 7.74 (d, *J* = 2.21Hz, 1H), 7.63 (d, *J* = 8.3Hz, 1H), 7.49 (dd, *J* = 8.3Hz, 2.1Hz, 1H), 7.31 (d, *J* = 4.1Hz, 1H), 6.98 (d, *J* = 3.4Hz, 1H), 3.75 (s, 2H), 3.60-3.20 (m, 8H), 2.5 (s, 3H).



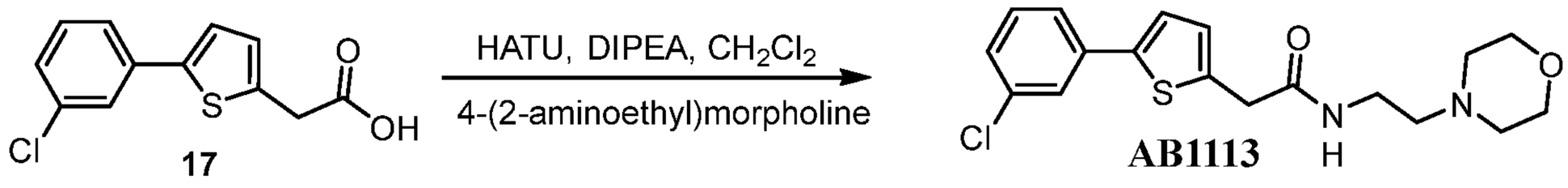
2-(5-(3-chlorophenyl)thiophen-2-yl)acetonitrile (16): compound **16** (5.6gm) synthesized from compound **2** by following general procedure **A**. ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.72 (t, *J*= 2.1Hz, 1H), 7.59-7.57 (m, 1H), 7.52 (d, *J*= 4.1Hz, 1H), δ 7.45 (t, *J*= 7.9Hz, 1H), 7.38 (dd, *J*= 9.0Hz, 2.1Hz, 1H), 7.10 (d, *J* =3.4Hz, 1H), 4.34 (s, 2H).



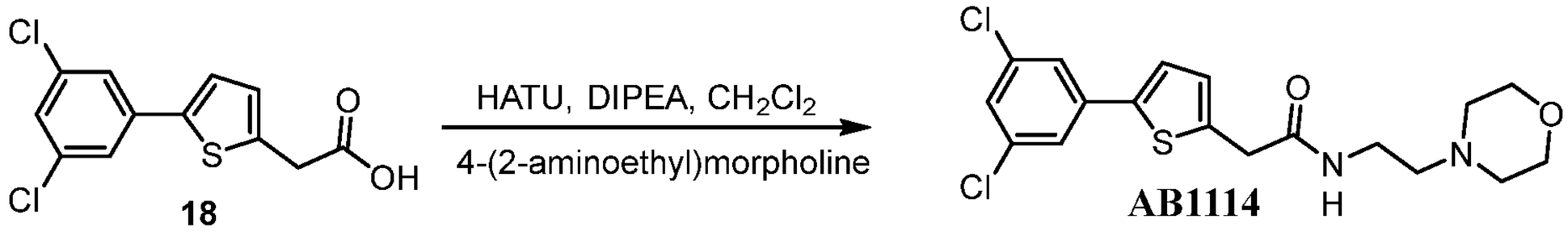
2-(5-(3-chlorophenyl)thiophen-2-yl)acetic acid (17): Compound **17** (1.7 g) Synthesized from compound **16** by following General procedure **B.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 12.64 (bs, 1H), 7.68 (t, *J*= 2.1Hz, 1H), 7.57-7.55 (m, 1H), 7.46-7.40 (m, 2H),7.34 (dd, *J*= 9.0Hz, 2.1Hz, 1H), 6.97 (d, *J* =3.4Hz, 1H), 3.86 (s, 2H).



2-(5-(3-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one (AB1112): Compound **AB1112** (155mg, 78%) was synthesized from compound **17** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.55 (t, *J*= 1.9Hz, 1H), 7.43-7.42 (m, 1H), 7.28 (t, *J*= 7.9Hz, 1H), 7.22 (dq, *J*= 8.0Hz, 1.0Hz, 1H), 7.16 (d, *J*= 3.6Hz, 1H), 6.87 (dt, *J*= 3.6Hz, 0.9Hz, 1H), 3.90 (d, *J*= 0.7Hz, 2H), 3.68 (t, *J*= 4.9Hz, 2H), 3.55 (t, *J*= 5.1Hz, 2H), 2.38 (dt, *J*= 20.4Hz, 5.1Hz, 4H), 2.29 (s, 3H). MS: 335 $(M+H)^+$.

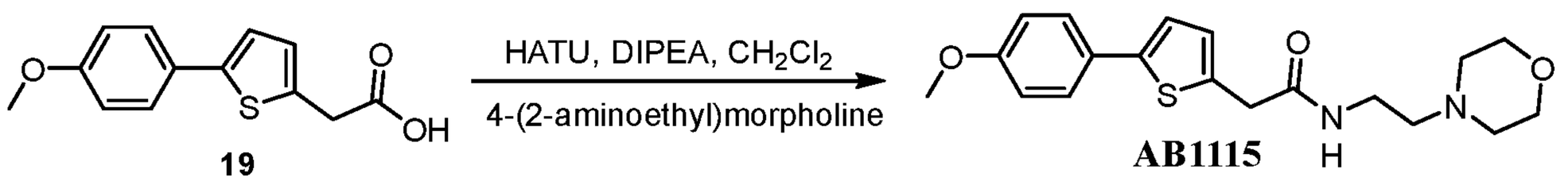


2-(5-(3-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1113): Compound **AB1113** (65mg, 30%) was synthesized from compound **17** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.54(t, *J*= 1.8Hz, 1H), 7.43(dt, *J*= 7.7Hz, 1.4Hz, 1H), 7.30(t, *J*= 7.8Hz, 1H), 7.30-7.25(m, 1H), 7.21, *J*= *3.6*Hz, 1H), 6.92(d, *J*= 3.6Hz, 1H), 6.35(s, 1H), 3.77(s, 2H), 3.56(t, *J*= 4.6Hz, 4H), 3.34(q, *J*= 5.6Hz, 2H), 2.45(t, *J*= 6.0Hz, 2H), 2.38(t, *J*= 4.5Hz, 4H). MS: 365 $(M+H)^+$.



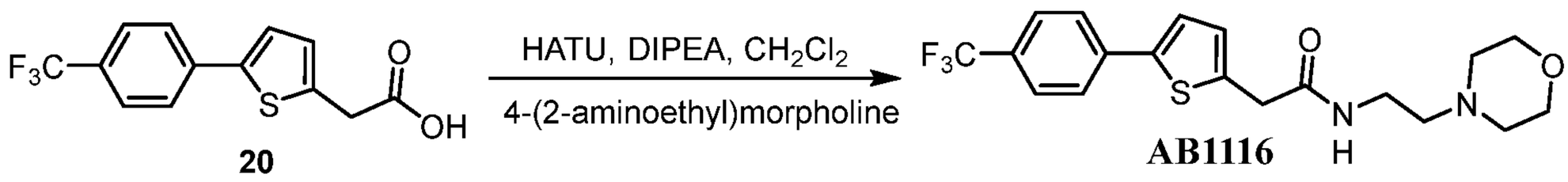
2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1114):

Compound **AB1114** (42mg, 30%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.42 (d, *J*= 1.7Hz, 2H), 7.26-7.25 (m, 1H), 7.22 (d, *J*= 3.6Hz, 1H), 6.93 (d, *J*= 3.6Hz, 1H), 6.30 (s, 1H), 3.78 (s, 2H), 3.58 (t, *J*= 4.4Hz, 4H), 3.35 (q, *J*= 5.6Hz, 2H), 2.46 (t, *J*= 6.0Hz, 2H), 2.39 (t, *J*=4.4Hz, 4H). MS: 399 $(M+H)^+$.



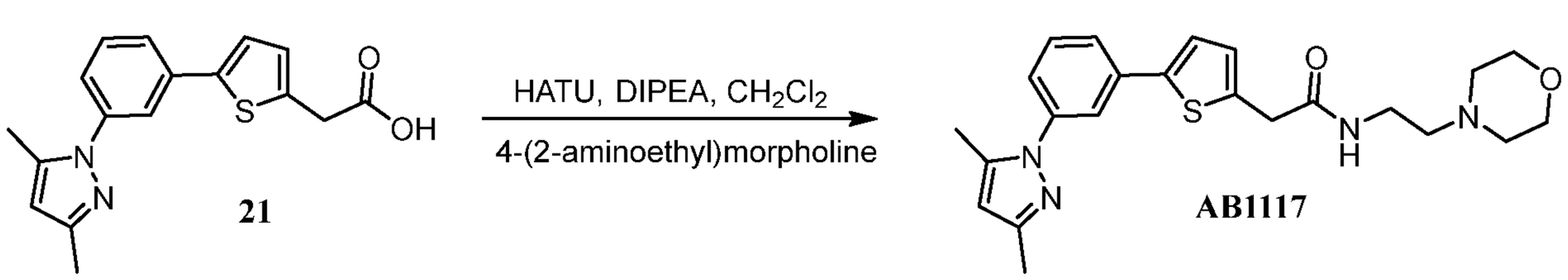
2-(5-(4-methoxyphenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1115):

Compound **AB1115** (35mg,75%) was synthesized from compound **19** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.48 (d, 2H), 7.07 (d, 1H), 6.91 - 6.88 (m, 3H), 3.38 (s, 3H), 3.76 (s, 2H), 3.57 (s, 3H), 3.34 (bd, 2H), 2.45 (bd, 6H). MS: 361 $(M+H)^+$.

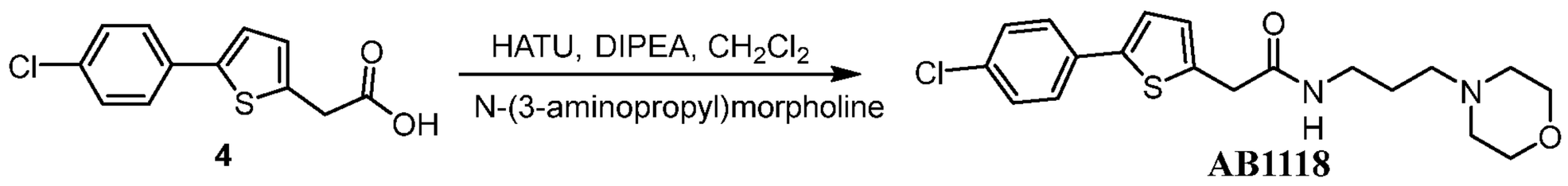


N-(2-morpholinoethyl)-2-(5-(4-(trifluoromethyl)phenyl)thiophen-2-yl)acetamide (AB1116):

Compound **AB1116** (33mg, 69%) was synthesized from compound **20** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.63 (q, 4H), 7.27 (t, 1H), 6.95 (d, 1H), 6.45 (bs, 1H), 3.79 (s, 2H), 3.59 (s, 4H), 3.36 (q, 2H), 2.49 (t, 2H), 2.42 (bs, 4H). MS: 399 $(M+H)^+$.

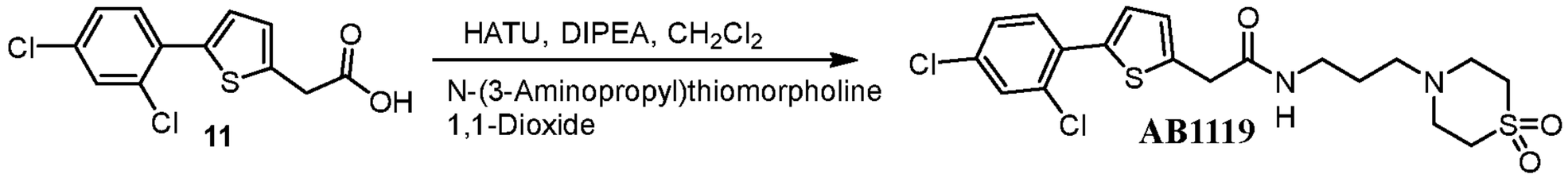


2-(5-(3-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl) acetamide (AB 1117): Compound **AB1117** (28mg, 45%) was synthesized from compound **21** by following general procedure **C**. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.63 (s, 1H), 7.52 (d, 1H), 7.44 (t, 1H), 7.32 (d, 1H), 7.26 – 7.24 (m, 1H), 6.92 (s, 1H), 6.45 (bs, 1H), 6.01 (s, 1H), 3.77 (s, 2H), 3.58 (bs, 4H), 3.35 (q, 2H), 2.48 (t, 2H), 2.41 (bs, 4H), 2.33 (s, 3H), 2.30 (s, 3H). MS: 425 $(M+H)^+$.



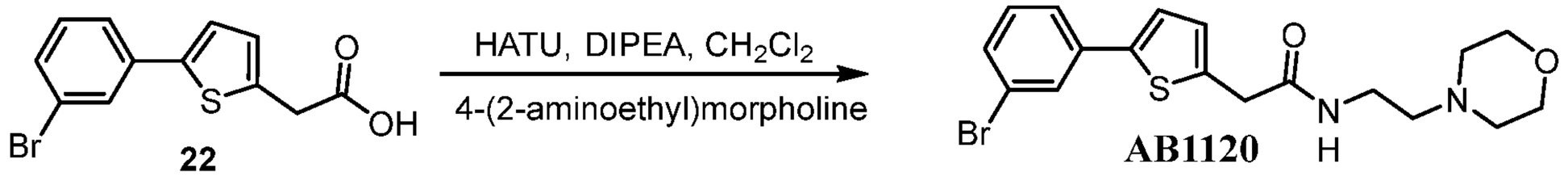
4 **AB1118**

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide (AB1118): Compound **AB1118** (65mg) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 500MHz): δ 7.48 (dt, *J*= 9.0 Hz, 2.3 Hz, 2H), 7.35 -7.23 (m, 2H), 7.15 (d, *J*=3.6Hz, 1H), 6.90 (d, *J* = 3.4Hz, 1H), 6.75 (s,1H), 3.74 (s, 2H), 3.61 (t, *J* = 4.6Hz, 4H), 3.37 (q, *J* = 6.0 Hz, 2H), 2.39 (t, *J* = 6.4 Hz, 6H), 1.69 – 1.64 (m, 2H). MS: 379 $(M+H)^+$.



11 **AB1119**

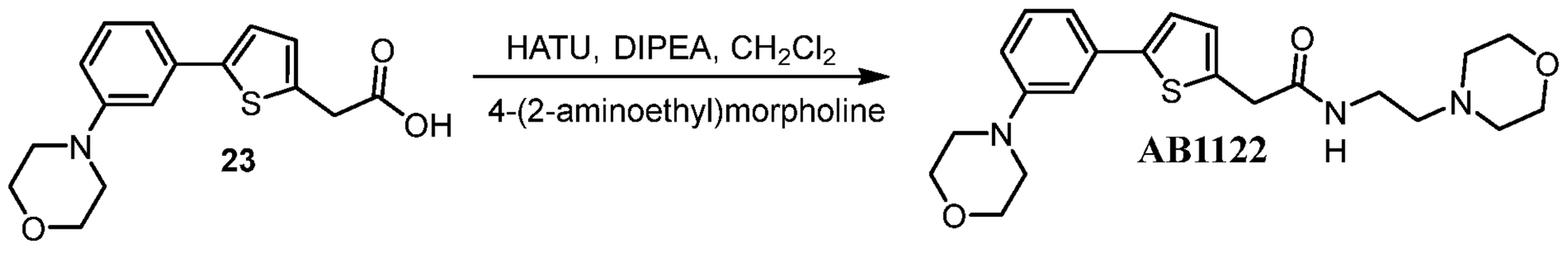
2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide (AB1119): Compound **AB1119** (1.86g, 50%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.12 (t, *J*= 5.5Hz, 1H), 7.73 (d, *J*= 2.1Hz, 1H), 7.62 (d, *J*= 8.3Hz, 1H), 7.48 (dd, *J*= 8.3Hz, 2.1Hz, 1H), 7.30 (d, *J*= 3.4Hz, 1H), 6.95 (d, *J*= 3.4Hz, 1H), 3.67 (s, 2H), 3.10 (q ,*J*= 6.4Hz, 2H), 3.06 (t, *J*= 6.4Hz, 2H), 2.84 (dd, *J*= 6.2Hz, 4.1Hz, 4H), 2.45 (t, *J*= 6.9Hz, 2H), 1.75 (q, *J*= 6.9Hz, 2H). MS: 461 $(M+H)^+$. HPLC: 99.45%.



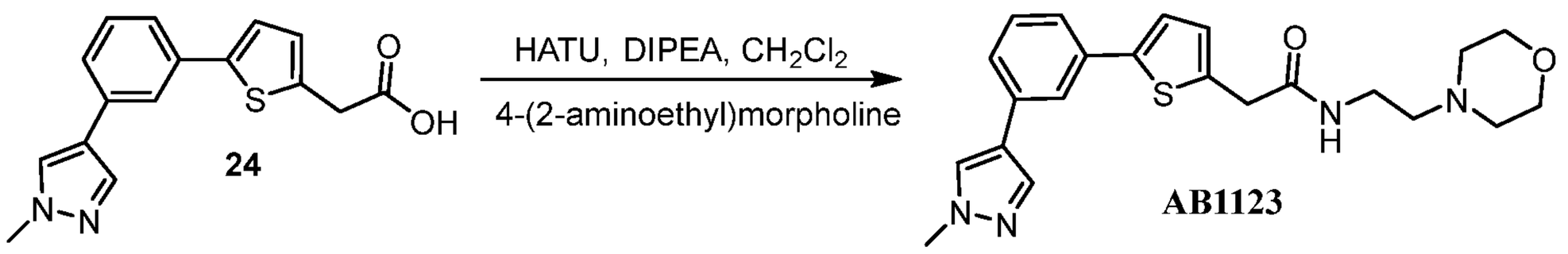
22 **AB1120**

2-(5-(3-bromophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1120): Compound **AB1120** (1.2g, 78%) was synthesized from compound **22** by following general

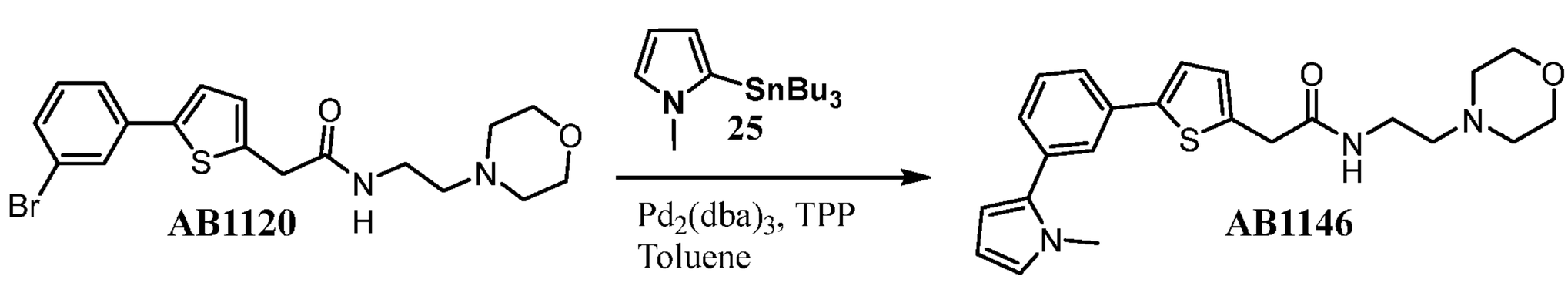
procedure **C.** ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.70 (s, 1H), 7.47 (d, 2H), 7.40 (d, 1H), 7.26 - 7.19 (m, 2H), 6.91 (d, 1H), 6.34 (s, 1H), 3.78 (s, 2H), 3.56 (t, 4H), 3.33 (q, 2H), 2.46 - 2.37 (m, 6H), 1.69 (s, 2H). MS: 409 $(M+H)^+$.



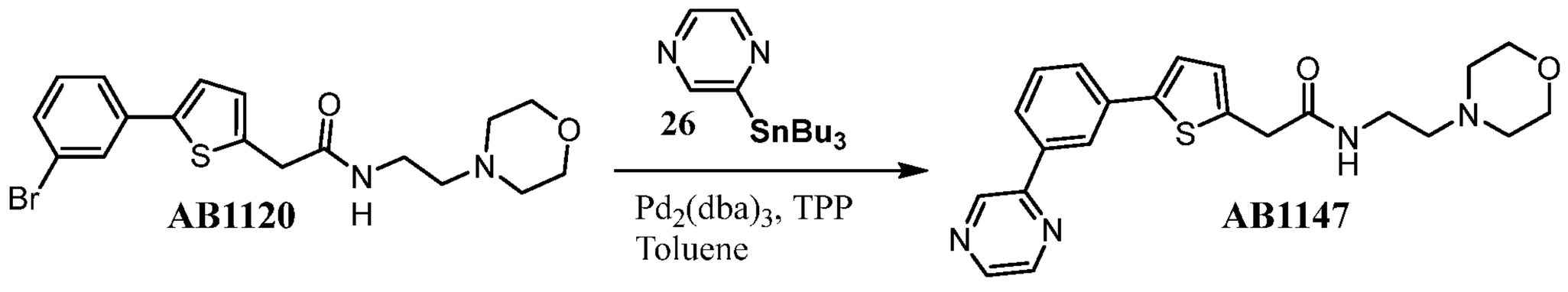
N-(2-morpholinoethyl)-2-(5-(3-morpholinophenyl)thiophen-2-yl)acetamide (AB1122): Compound **AB1122** (46mg, 70%) was synthesized from compound **23** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.29 - 7.26 (m, 1H), 7.18 (d, 1H), 7.09 – 7.07 (m, 2H), 6.90 (d, 1H), 6.86 - 6.84 (m, 1H), 6.37 (bs, 1H), 3.87 (t, 4H), 3.77 (s, 2H), 3.55 (t, 4H), 3.31 (q, 2H), 3.19 (t, 4H), 2.43 (t, 2H), 2.36 (t, 4H). MS: 416 $(M+H)^+$.



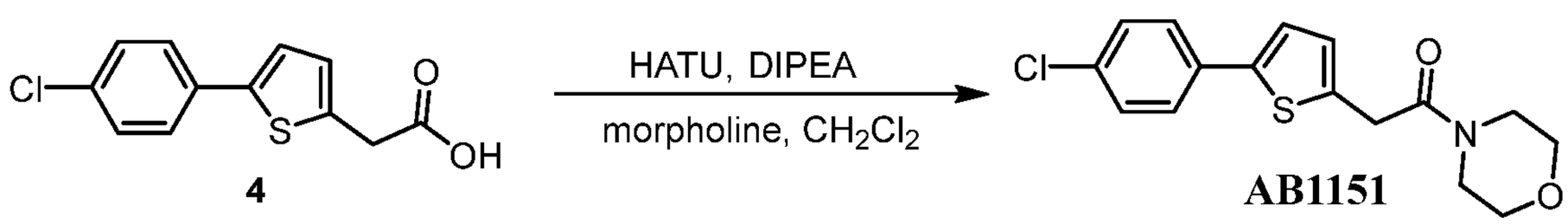
2-(5-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1123): Compound **AB1123** (25mg, 66%) was synthesized from compound **24** by following general procedure **C.** ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.81-7.25 (m, 7H), 6.96 (s, 1H), 6.45 (s, 1H), 3.98 (bs, 2H), 3.81(s, 2H), 3.60 (s, 3H), 3.37 (bs, 2H), 2.49-241 (m,5H), 1.75-1.74 (m, 2H). MS: 411 $(M+H)^+$.



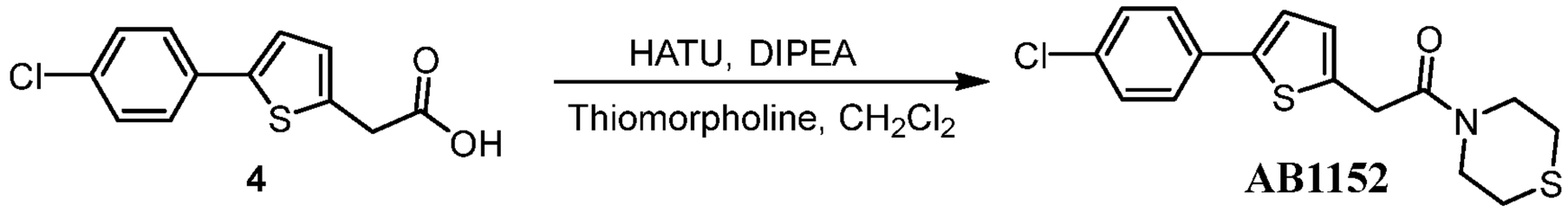
2-(5-(3-(1-methyl-1H-pyrrol-2-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1146): To a stirred solution of Compound **AB1120** (100mg, 0.24 mmol) in 10mL toluene. TPP (32mg, 0.12) followed by 1-Methyl-2-(tributylstannyl)pyrrole **(25)** (99mg, 0.26mmol) and $Pd_2(dba)_3$ (11mg, 0.012mmol) were added and stirred at 80°C for 8 hr. concentrated the reaction mixture purified by column chromatography to afford compound **AB1146** (65mg, 65%) as off white solid. ^{1}H NMR (DMSO-d6, 500MHz): δ 8.05 (d, 5.5Hz, 1H), 7.60 (s, 1H), 7.50 (d, *J*= 7.6Hz, 1H), 7.44-7.39 (m, 2H), 7.35 (d, *J*= 7.6Hz, 1H), 6.92 (d, *J*= 3.4Hz, 1H), 6.87 (t, *J*= 2.4Hz, 1H), 6.23 (q, *J*= 1.8Hz, 1H), 6.08 (t, *J*= 3.1Hz, 1H), 3.68 (t, *J*= 14.1Hz, 6H), 3.54 (q, *J*= 4.8Hz, 5H), 3.19 (q, *J*= 6.2Hz, 2H), 2.35 (t, *J*= 6.5Hz, 7H). MS: 410 $(M+H)^+$.



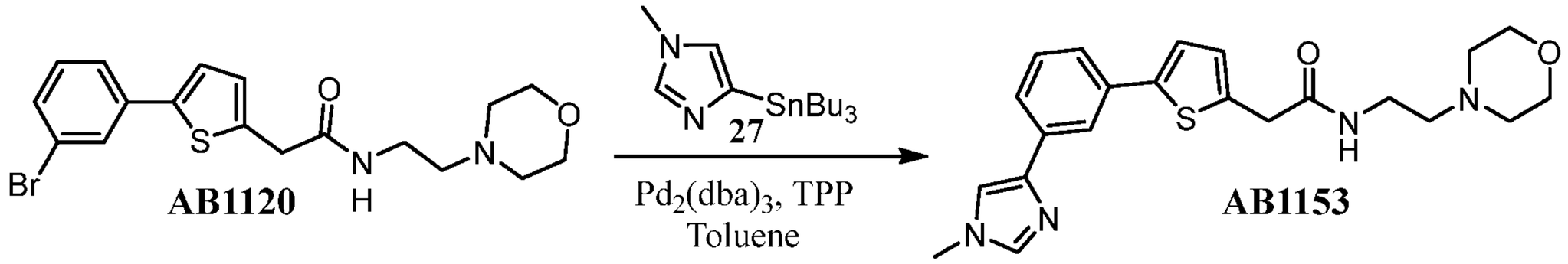
N-(2-morpholinoethyl)-2-(5-(3-(pyrazin-2-yl)phenyl)thiophen-2-yl)acetamide (AB1147): To a stirred solution of Compound **AB1120** (100mg, 0.24 mmol) in 10mL toluene. TPP (32mg, 0.12) followed by 2-(tributylstannyl)pyrazine **26** (84µL, 0.26mmol) and $Pd_2(dba)_3$ (11mg, 0.012mmol) were added and stirred at 80°C for 8 hr. concentrated the reaction mixture purified by column chromatography to afford compound **AB1147** (46mg, 46%) as off white solid**.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 9.35 (d, *J*= 1.4Hz, 1H), 8.76 (t, *J*= 2.1Hz, 1H), 8.66 (d, *J*= 2.1Hz, 1H), 8.35 (s, 1H), 8.05 (d, *J*= 7.6Hz, 2H), 7.73 (d, *J*= 8.3Hz, 1H), 7.57 (t, *J*= 7.9Hz, 1H), 7.49 (d, *J*= 3.4Hz, 1H), 6.96 (d, *J*= 3.4Hz, 1H), 3.68 (s, 2H), 3.55 (t, *J*= 4.5Hz, 4H), 3.20 (q, *J*= 6.4Hz, 2H), 2.36 (t, *J*= 6.5Hz, 6H). MS: 409 $(M+H)^+$.



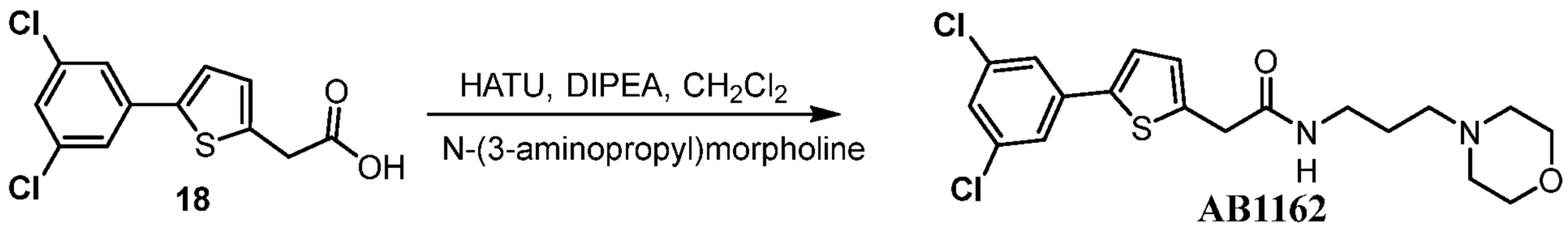
2-(5-(4-chlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one (AB1151): Compound **AB1151** (128mg, 50%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.63-7.61 (m, 2H), 7.45-7.44 (m, 2H), 7.37 (d, *J*= 3.4Hz, 1H), 6.93 (d, *J*= 3.4Hz, 1H), 3.98 (s, 2H), 3.56-3.54 (m, 6H), 3.47 (t, *J*= 3.4Hz, 1H). MS: 322 $(M+H)^+$.



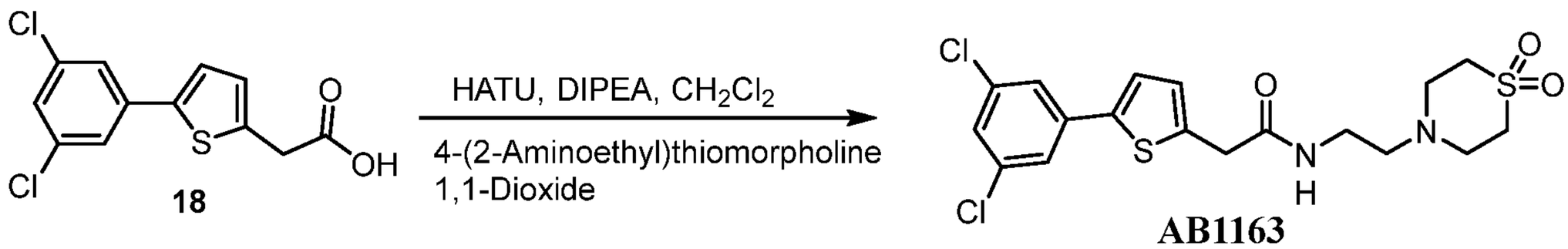
2-(5-(4-chlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one (AB1152): Compound **AB1152** (140mg, 58%) was synthesized from compound **4** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.63-7.61 (m, 2H), 7.45 (dd, *J*= 8.6Hz, 2.4Hz), 7.38 (d, *J*= 3.4Hz, 1H), 6.94 (d, *J*= 3.4Hz, 1H), 3.99 (s, 2H), 3.76 (dt, *J*= 23.9Hz, 5.0Hz, 4H), 2.55-2.54 (m, 4H). MS: 338 $(M+H)^+$.



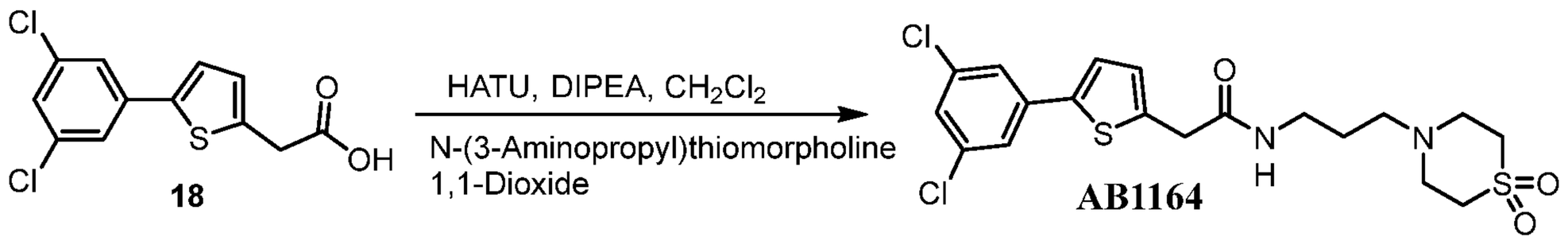
2-(5-(3-(1-methyl-1H-imidazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB 1153): Compound **AB1153** (10mg, 6%) was synthesized from compound **AB1120** by following general procedure for the synthesis of **AB1146.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.04 (t, *J*= 5.5Hz, 1H), 7.96 (s, 1H), 7.67 (d, *J*= 20.0Hz, 2H), 7.63 (d, *J*= 7.6Hz, 1H), 7.42 (d, *J*= 7.6Hz, 1H), 7.37-7.34 (m, 2H), 6.93 (d, *J*= 3.4Hz, 1H), 3.66 (s, 2H), 3.55 (t, *J*= 4.5Hz, 4H), 3.20 (q, *J*= 6.2Hz, 2H), 2.36 (t, *J*= 4.1Hz, 6H). MS: 411 $(M+H)^+$.



2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide (AB1162): Compound **AB1162** (82mg, 39%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.13 (t, *J*= 5.2Hz, 1H), 7.63 (d, *J*= 1.4Hz, 2H), 7.54 (d, *J*=3.4Hz, 1H), 7.50 (t, *J*= 1.7Hz, 1H), 6.93 (d, *J*= 3.4Hz, 1H), 3.66 (s, 2H), 3.54 (t, *J*= 4.8Hz, 4H), 3.09 (q, *J*= 6.7Hz, 2H), 2.30 (s, 4H), 2.26 (t, *J*= 7.2Hz, 2H), 1.58-1.53 (m, 2H). MS: 413 $(M+H)^+$.

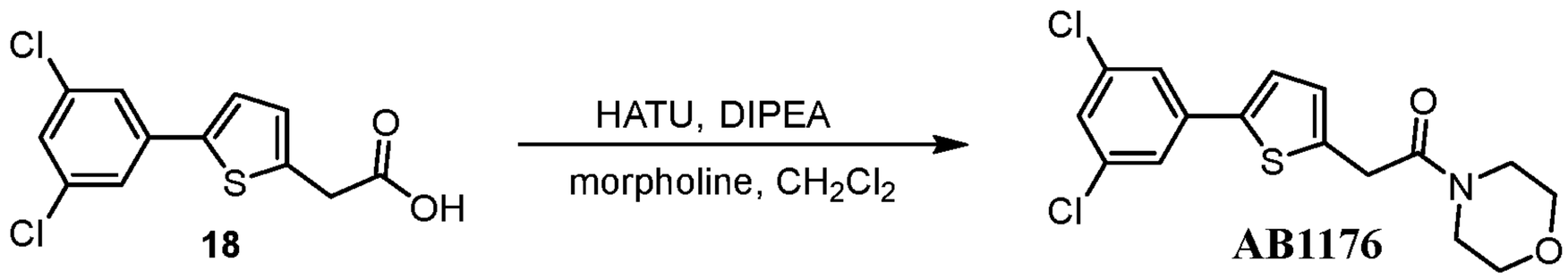


2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide (AB1163): Compound **AB1163** (142mg, 65%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR (DMSO-d6, 500MHz): δ 8.06 (t, *J*= 5.5Hz, 1H), 7.63 (d, *J*=2.1Hz, 2H), 7.54 (d, *J*= 4.1Hz, 1H), 7.49 (t, *J*= 1.7Hz, 1H), 6.95 (1H, d), 3.58 (s, 2H), 3.20-3.16 (m, 2H), 3.04 (t, *J*= 4.8Hz, 4H), 2.90 (t, *J*= 5.2Hz, 4H), 2.54 (t, *J*= 6.5Hz, 2H). MS: 447 $(M+H)^+$.

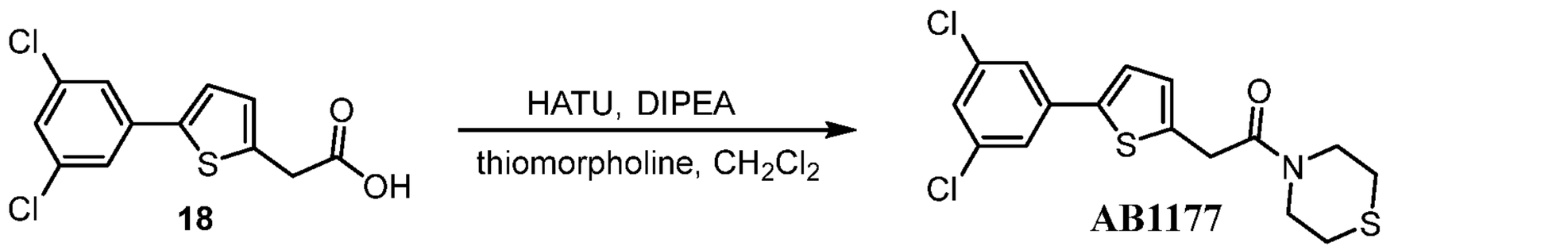


2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide (AB1164): Compound **AB1164** (149g, 61%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 8.11 (t, *J*= 5.5Hz, 1H), 7.63 (d, *J*= 2.1Hz, 2H), 7.54 (d, *J*= 3.4Hz, 1H), 7.50 (t, *J*= 1.7Hz, 1H), 6.94 (d, *J*= 3.4Hz, 1H), 3.66 (s, 2H), 3.09 (q,

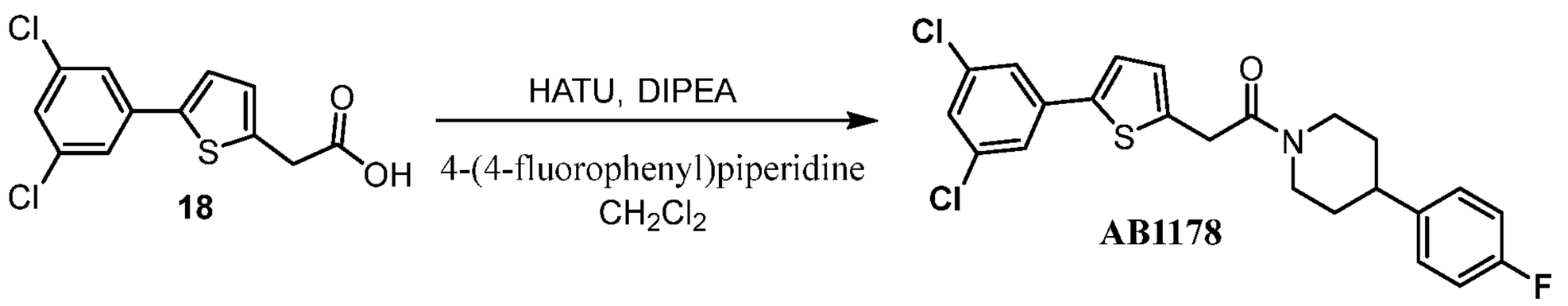
J= 6.4Hz, 2H), 3.05 (t, *J*= 4.8Hz, 4H), 2.84 (t, *J*= 4.8, 4H), 2.45 (t, *J*= 7.2Hz, 2H), 1.58-1.33 (m, 2H). MS: 461 $(M+H)^+$. HPLC: 99.2%.



2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-morpholinoethanone (AB1176): Compound **AB1176** (56mg, 38%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.65 (d, *J*= 2.1Hz, 2H), 7.55 (d, *J*= 3.4Hz, 1H), 7.50 (t, *J*=2.1Hz, 1H), 6.96 (d, *J*= 3.4Hz, 1H), 4.01 (s, 2H), 3.55 (d, *J*= 4.1Hz, 6H), 3.47 (t, *J*= 4.8Hz, 2H). MS: 356 $(M+H)^+$.

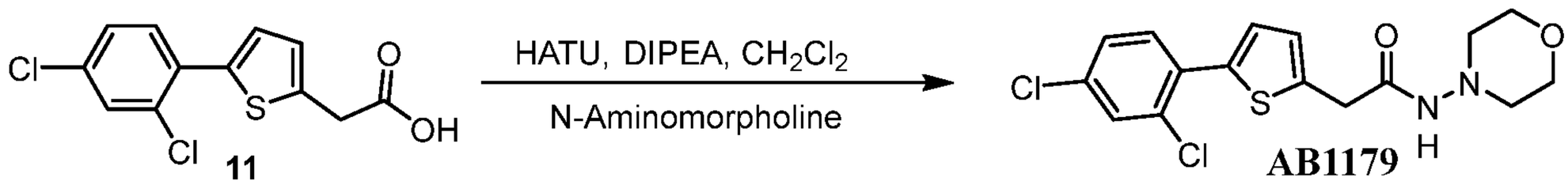


2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-thiomorpholinoethanone (AB1177): Compound **AB1177** (85mg, 54%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.65 (d, *J*=1.4Hz, 2H), 7.56 (d, *J*= 3.4Hz, 1H), 7.50 (t, *J*= 1.7Hz, 1H), 6.98 (d, *J*= 4.1Hz, 1H), 4.01 (s, 4H), 3.77 (dt, *J*= 23.6Hz, 5.2Hz, 4H), 2.56 (q, 4H). MS: 371 $(M+H)^+$.

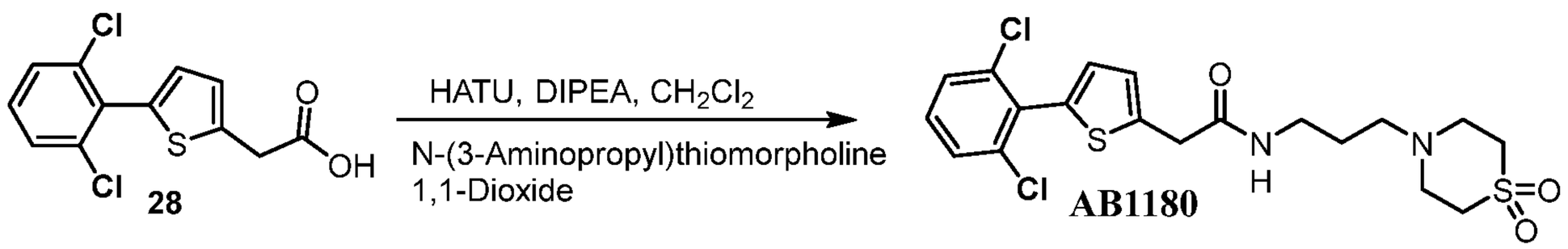


2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-(4-(4-fluorophenyl)piperidin-1-yl)ethan-1-one (AB1178): Compound **AB1178** (78mg, 50%) was synthesized from compound **18** by following general procedure **C.** ^{1}H NMR (DMSO-d_6, 500MHz): δ 7.66 (d, *J*=2.1Hz, 2H), 7.56 (d, *J*=4.1Hz,

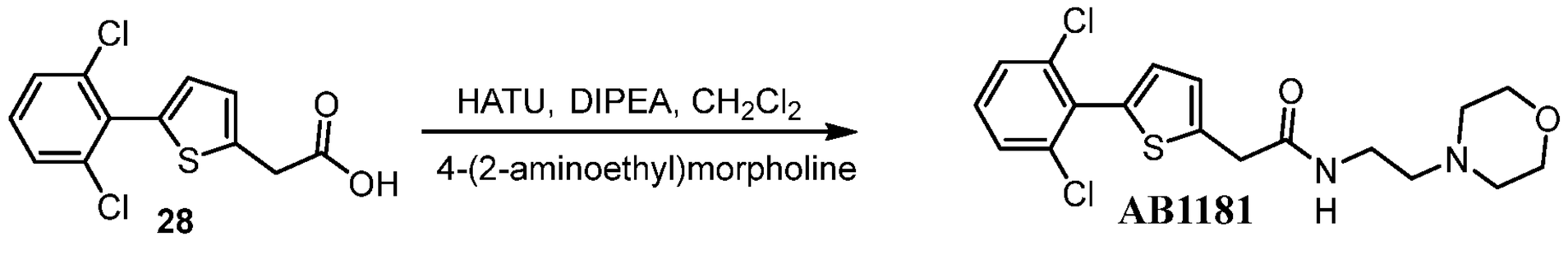
1H), 7.51 (t, *J*=1.7Hz, 1H), 7.27-7.24m, 2H), 7.09 (t, *J*=9.0Hz, 2H), 6.99 (d, *J*=3.4Hz, 1H), 4.55 (d, *J*=13.1Hz, 1H), 4.12 (d, *J*=13.1Hz, 1H), 4.04 (s, 2H), 3.15 (t, *J*=12.1Hz, 1H), 2.81-2.77 (m, 1H), 2.65 (t, *J*=11.7Hz, 1H), 1.77 (d, *J*=12.4Hz, 2H). MS: 448 $(M+H)^+$.



2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide (AB1179): Compound **AB1179** (100mg, 52%) was synthesized from compound **11** by following general procedure **C.** ^{1}H NMR($CDCl_3$, 500MHz): δ 7.44 –7.41 (m, 2H), 7.19 (d, *J*=3.4Hz, 1H), 6.96-6.94 (m, 2H), 6.20 (s, 1H), 4.02 (s, 2H), 3.81-3.79 (m, 4H), 2.83 (t, *J*=4.8Hz, 4H). MS: 371 $(M+H)^+$.



2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide (AB1180): Compound **AB1180** (177mg) was synthesized from compound **28** by following general procedure **C.** ^{1}H NMR($CDCl_3$, 500MHz): δ 7.41 (d, *J* = 8.3Hz, 2H), 7.29 (d, *J* = 2.1, 1H), 6.95 (dd, *J* = 25.5Hz, 3.4Hz, 2H), 3.82 (s, 2H), 3.35-3.32 (m, 2H), 3.01 (d, *J* = 4.8Hz, 4H), 2.95 (s, 4H), 2.50 (t, *J* = 6.9Hz, 2H), 1.68-1.64 (m, 2H).



2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide (AB1181): Compound **AB1181** (248mg) was synthesized from compound **28** by following general procedure **C.** ^{1}H NMR($CDCl_3$, 500MHz): δ 7.41 (d, *J* = 7.6Hz, 2H), 7.25 (d, *J* = 9.0Hz, 1H), 6.98 (d, *J*=3.4Hz, 1H), 6.93 (d, 1H), 6.36 (s, 1H), 3.64-3.62 (m, 2H), 3.37 (dd, *J* = 11.7Hz, 5.5Hz, 2H), 2.47-2.45 (m, 2H), 2.40 (bs, 4H).

[0060] EXPERIMENTAL DATA

Compounds as described in the present invention were synthesized and screened for their ability to rescue cells from stress induced death. The results obtained establish the remarkable effect of compounds of the present invention and show a promise towards the utility of these novel compounds in the treatment of ER stress related diseases, more specifically, autoimmune diseases.

[0061] Particularly, in-vitro studies were performed on mouse B16F10 and human A375 cells (cells of melanocyte origin) which showed that cells treated with tunicamycin suffered loss of cell viability. When they were treated with compounds of the present invention, cell viability was recovered to significant level, demonstrating the potential of compounds of present invention as efficacious compounds for utilization in treatment of skin autoimmune diseases including Vitiligo.

[0062] The table I below mentions the % recovery of cells by the compound at specific dose.

TABLE I: List of Compounds and their potency at 10 µM concentration in mouse B16F10 cells

	Compound No	B16F10 % Recovery
1.	AB1014	32
2.	AB1045	46
3.	AB1051	22
4.	AB1062	21
5.	AB1078	59
6.	AB1080	44
7.	AB1094	48
8.	AB1097	57

9.	AB1099	37
10	AB1109	26
11	AB1110	50
12	AB1114	21
13	AB1117	21
14	AB1118	44
15	AB1119	30
16	AB1120	23
17	AB1151	23
18	AB1152	27
19	AB1162	71
20	AB1164	45

TABLE II: List of Compounds and their potency at 10 µM concentration in human A375 cells

	Compound No	A375 % Recovery
1.	AB1090	24
2.	AB1097	47
3.	AB1098	28
4.	AB1099	45
5.	AB1101	22
6.	AB1110	23
7.	AB1114	32
8.	AB1119	27

9.	AB1120	30
10.	AB1151	27
11.	AB1152	23
12.	AB1162	58
13.	AB1163	37
14.	AB1164	50
15.	AB1176	25
16.	AB1177	31
17.	AB1179	20

[0063] Table III and Table IV describe potency of the compounds as effective concentration 50 (EC_{50}) which means the dose of compound needed to achieve 50% of maximum effect.

TABLE III: EC50 (μM) of NCEs in mouse B16F10 cells

Sr No	**NCE**	**B16F10** **EC50 (μM)**
1	AB1010	6.55
2	AB1062	32.1
3	AB1093	36.2
4	AB1099	10.0
5	AB1102	55.7
6	AB1108	43.7
7	AB1109	6.49
8	AB1110	6.24

9	AB1113	46.7
10	AB1114	12.5
11	AB1115	53.44
12	AB1116	13.7
13	AB1117	20.7
14	AB1118	19.5
15	AB1119	9.51
16	AB1164	9.72

TABLE IV: EC50 (μM) of NCEs in human A375 cells

Sr No	**NCE**	**A375** **EC50 (μM)**
1	AB1010	5.22
2	AB1062	48.5
3	AB1093	31.22
4	AB1099	17.3
5	AB1102	71.1
6	AB1108	34.2
7	AB1109	13.9
8	AB1110	62.7
9	AB1113	18.3
10	AB1114	4.26
11	AB1117	26.7
12	AB1118	31.6

13	AB1119	8.47
14	AB1151	10.6
15	AB1152	4.86
16	AB1162	6.02
17	AB1163	5.15
18	AB1164	3.70

[0064] **Methods used for Experimental Data :** Mouse B16F10 or human A375 cells were seeded (5000 cells per well) in 96-well plates for 24 h. Cells were then treated in quadruplicate with multiple concentrations of compounds for 6 h. The compounds were dissolved in DMSO at 1000X concentration and then diluted to final concentration directly in cell culture medium. The vehicle control (VC) contains equal amount of DMSO. Cells were then treated with tunicamycin (Tm) (300 ng/ml for B16F10 and 100 ng/ml for A375 cells) and after 72 h of treatment, MTT assay was performed. Cell growth in vehicle control was calculated as 100% and effect of the compounds over tunicamycin treatment was calculated accordingly. EC_{50} values were calculated using GraphPad Prism 7 software.

[0065] From the data provided in Table I and Table II it can be established that the compounds of the present invention are successful in rescuing cells from stress induced cell death.

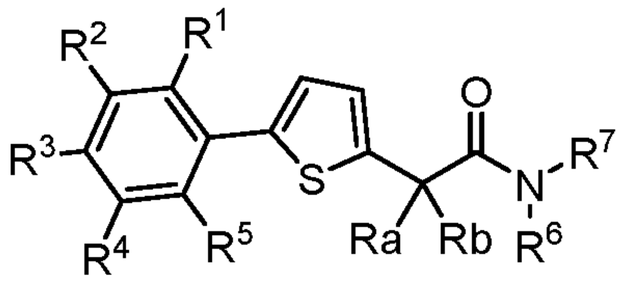
[0066] Table I and Table-II clearly reflects the effectiveness of the compounds of the present invention in recovering cell viability in mouse B16F10 and human A375 cells.

[0067] Table III and Table-IV enunciates data reflecting the EC_{50} of compounds of the present invention to achieve desired effect of recovery of cell viability.

[0068] Compounds of the present invention are therefore novel compounds that are potentially useful in applications related to the treatment and prevention of ER stress related diseases.

We Claim:

1. A compound of Formula I represented by



Formula I

wherein

R1, R2, R3, R4, R5 are each independently selected from hydrogen, halogen, phenyl, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C1-C5 alkoxyalkyl, straight chain or branched C1-C5 alkoxyaryl, aryl, CF3, C3-C7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S;

any of two adjacent R groups form a 5-6 membered aromatic or aliphatic ring comprising at least one hetero atom selected from a group of O, N and S;

Ra and Rb are each independently selected from hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl, or both Ra, and Rb together form a 3-7 membered ring comprising at least one hetero atom selected from a group of O, N and S;

R6 and R7 are each independently selected from hydrogen, straight chain or branched C1-C5 alkyl, straight chain or branched C1-C5 aralkyl, straight chain or branched C2-C5 alkenyl, straight chain or branched C2-C5 alkynyl;

-CH2(CH2)nNRcRd wherein n is 0-3, and Rc, Rd are both independently selected from straight chain or branched C1-C5 alkyl or together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S; or

both R6 and R7 may together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N and S;

and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

2. The compound of Formula I as claimed in claim 1, wherein R^1, R^2, R^3, R^4, and R^5 are each independently selected from a halogen group comprising F, Cl, Br and I.

3. The compounds of Formula I as claimed in any of claims 1 - 2, wherein at least one of the substituents selected from R1, R2, R3, R4, and R5 is a phenyl group optionally substituted by straight chain or branched C1-C5 alkyl, or straight chain or branched C1-C5 alkoxyalkyl.

4. The compound of Formula I as claimed in any of claims 1 - 3, wherein at least one of the substituents selected from R1, R2, R3, R4, and R5 is a C3-C7 aromatic or aliphatic heterocycle comprising at least one hetero atom selected from a group of O, N and S, wherein it is optionally substituted with C1-C5 alkyl, C2-C5 alkenyl or C1-C5 alkoxyalkyl.

5. The compound of Formula I as claimed in any of claims 1-4, wherein R6 and R7, together form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N and S, further wherein the heterocycle is optionally substituted with any substituent selected from the group comprising halogen, CF3, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl or straight chain or branched C1-C5 alkoxyalkyl.

6. The compound of Formula I as claimed in claim 1, wherein any two adjacent substituents selected from R1, R2, R3, R4 and R5, combine to form naphthalene.

7. The compound of Formula I as claimed in claim 1 wherein Rc, and Rd form a 3-7 membered aromatic or aliphatic heterocycle comprising at least one hetero atom selected from O, N and S, further wherein the heterocycle is optionally substituted with any substituent selected from the group of halogen, CF3, straight chain or branched C1-C5 alkyl, straight chain or branched C2-C5 alkenyl or straight chain or branched C1-C5 alkoxyalkyl.

8. The compound of Formula I as claimed in claim 1, wherein Rc, and Rd together form a heterocycle dioxidothiomorpholine.

9. The compound of Formula I and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof, as claimed in any of claims 1-8 selected from:

N-butyl-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-isopropoxypropyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(pyrrolidin-1-yl)ethan-1-one,

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-(pyrrolidin-1-yl)ethyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(3,5-dimethylmorpholino)ethan-1-one,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-cyclopentylacetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(4-fluorophenyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-(trifluoromethyl)phenyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3,5-difluorobenzyl)acetamide,

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)acetamide,

2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide,

2-(5-(4-Chlorophenyl)thiophen-2-yl)-N-(2-(dimethylamino)ethyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide hydrochloride,

2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methyl-1-(4-methylpiperazin-1-yl)propan-1-one,

2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methyl-N-(2-(piperidin-1-yl)ethyl)propenamide,

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-chlorophenyl)thiophen-2-yl)-2-methylpropanamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-(4,4-difluoropiperidin-1-yl)ethan-1-one,

2-(5-(4-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one,

N-(4-fluorophenethyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide,

2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(4-fluorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide,

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(4-fluorophenethyl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

1-(4-methylpiperazin-1-yl)-2-(5-phenylthiophen-2-yl)ethan-1-one,

N-(4-fluorophenethyl)-2-(5-phenylthiophen-2-yl)acetamide,

N-(2-morpholinoethyl)-2-(5-phenylthiophen-2-yl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide,

2-(5-phenylthiophen-2-yl)-N-(2-(piperidin-1-yl)ethyl)acetamide,

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-phenylthiophen-2-yl)acetamide,

N-(3-(1H-imidazol-1-yl)propyl)-2-(5-(2,4-dichlorophenyl)thiophen-2-yl)acetamide,

2-(5-(3-fluorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one,

2-(5-(3-fluorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(2-(4-methylpiperazin-1-yl)ethyl)acetamide,

2-(5-(3-chlorophenyl)thiophen-2-yl)-1-(4-methylpiperazin-1-yl)ethan-1-one,

2-(5-(3-chlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(4-methoxyphenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

N-(2-morpholinoethyl)-2-(5-(4-(trifluoromethyl)phenyl)thiophen-2-yl)acetamide,

2-(5-(3-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide,

2-(5-(3-bromophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

N-(2-morpholinoethyl)-2-(5-(3-morpholinophenyl)thiophen-2-yl)acetamide,

2-(5-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(3-(1-methyl-1H-pyrrol-2-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

N-(2-morpholinoethyl)-2-(5-(3-(pyrazin-2-yl)phenyl)thiophen-2-yl)acetamide,

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one,

2-(5-(4-chlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one,

2-(5-(3-(1-methyl-1H-imidazol-4-yl)phenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-morpholinopropyl)acetamide,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(2-(1,1-dioxidothiomorpholino)ethyl)acetamide,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl)acetamide,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-morpholinoethan-1-one,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-thiomorpholinoethan-1-one,

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-1-(4-(4-fluorophenyl)piperidin-1-yl)ethan-1-one,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide,

2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(3-(1,1-dioxidothiomorpholino)propyl) acetamide,

2-(5-(2,6-dichlorophenyl)thiophen-2-yl)-N-(2-morpholinoethyl)acetamide,

2-(5-(2,4-dichlorophenyl)thiophen-2-yl)-N-(piperidin-1-yl)acetamide,

(1-(5-(4-chlorophenyl)thiophen-2-yl)cyclopropyl)(4-methylpiperazin-1-yl)methanone

(1-(5-(4-chlorophenyl)thiophen-2-yl)cyclobutyl)(4-methylpiperazin-1-yl)methanone,

(3-(5-(4-chlorophenyl)thiophen-2-yl)oxetan-3-yl)(4-methylpiperazin-1-yl)methanone,

(1-(5-(4-fluorophenyl)thiophen-2-yl)cyclopropyl)(4-methylpiperazin-1-yl)methanone,

(1-(5-(4-fluorophenyl)thiophen-2-yl)cyclobutyl)(4-methylpiperazin-1-yl)methanone,

(3-(5-(4-fluorophenyl)thiophen-2-yl)oxetan-3-yl)(4-methylpiperazin-1-yl)methanone,

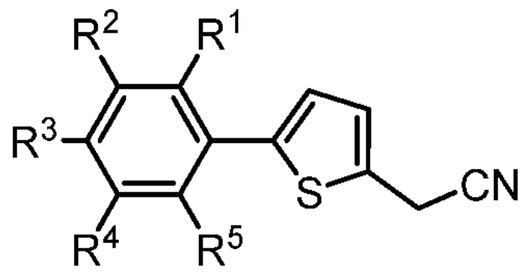
N-butyl-2-(5-(naphthalen-1-yl)thiophen-2-yl)acetamide and

2-(5-(3,5-dichlorophenyl)thiophen-2-yl)-N-morpholinoacetamide.

10. A process for the preparation of the compounds of Formula I as claimed in claims 1-9, comprising the steps of:

a) Stirring thiophene acetonitrile in the presence of catalyst N-bromosuccinamide (NBS) in solvents selected from a group comprising dimethylformamide (DMF), dimethylsulfoxide (DMSO) and Tetrahydrofuran(THF);
b) Reacting the resultant bromo thiophene acetonitrile obtained from Step a, with substituted phenylboronic acid in the presence of a solvent selected from toluene, benzene, dimethyl formamide, dioxane, tertiary butanol, potassium carbonate and

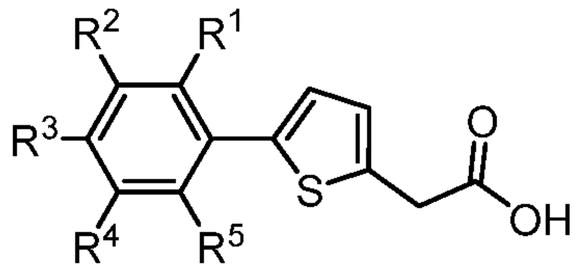
triphenylphosphine palladium(0) or any Palladium (0) catalyst at a temperature of about 80 °C -100°C for about 6 -24 hours to obtain compounds of Formula II:



II

;

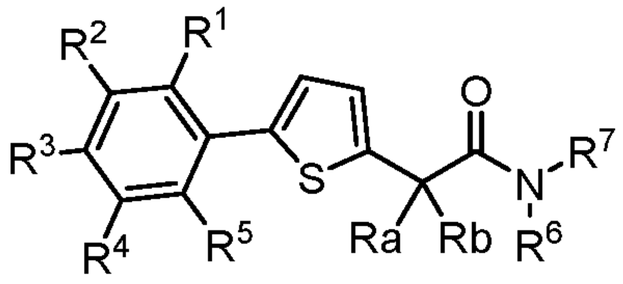
c) Refluxing the compound of Formula II after stirring it in ethanol and aqueous sodium hydroxide to obtain the compounds of Formula III:



III

;

d) Coupling of compound of Formula III with amines, in the presence of a base selected from Hunigs base (N,N, Diisopropylethylamine), triethylamine, pyrrolidine, piperidine and amide coupling reagent selected from a group comprising HATU, HBTU, EDC, EDC-HOBt, EDC-DMAP, DCC, DCC-DMAP, DCC-HOBt, DIC, TBTU, and T3P added at 0°C to obtain compounds of Formula I:



and

e) Optionally purifying the compound by column chromatography.

11. A pharmaceutical composition comprising an effective amount of one or more of the compounds as claimed in any of claims 1-10, and their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof, as an active ingredient along with a pharmaceutically acceptable carrier

12. The process for preparing a pharmaceutical composition as claimed in claim 11, comprising the step of mixing at least one of the compounds of Formula I, with a pharmaceutically acceptable carrier.

13. Use of compound of Formula I as claimed in any one of claims 1-10, for the treatment or prevention of autoimmune diseases.

14. A method of treating autoimmune diseases comprising administering a therapeutically effective amount of the compounds of Formula I as claimed in any of claims 1-10 or their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

15. A method of treating skin autoimmune diseases as claimed in claim 14, comprising administering a therapeutically effective amount of a pharmaceutical composition or formulation comprising essentially of a compound of Formula I, or their stereoisomers (diastereoisomers, enantiomers), pure or mixed, racemic mixtures, geometrical isomers, tautomers, pharmaceutically acceptable salts, hydrates, solvates, solid forms and mixtures thereof.

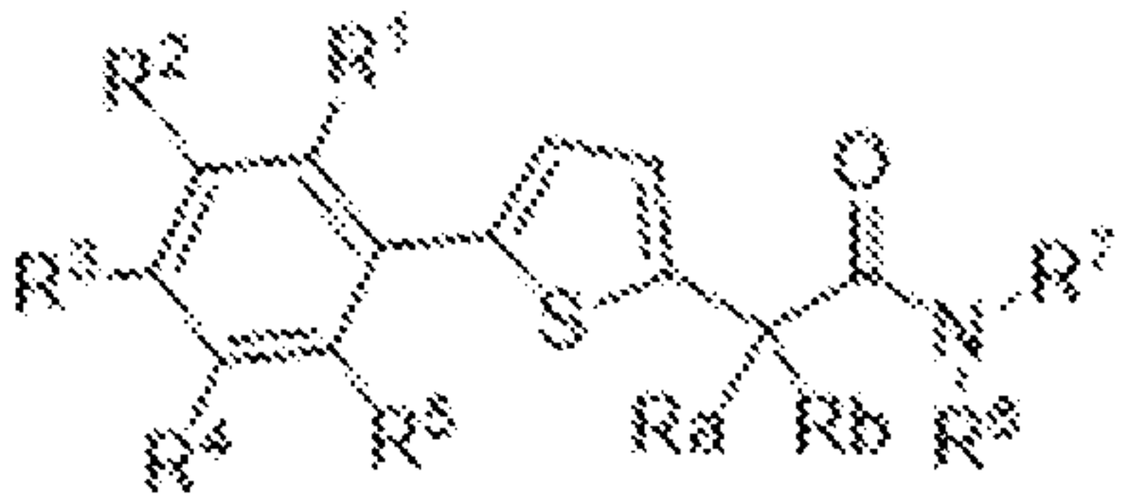
16. The method of treating autoimmune diseases as claimed in claim 14, wherein the autoimmune diseases include but are not limited to type I diabetes, rheumatoid arthritis, multiple sclerosis, lupus, celiac diseases and pernicious anaemia.

17. The method of treating skin autoimmune diseases as claimed in claim 15, wherein the skin autoimmune diseases are from a group comprising psoriasis, lupus, vitiligo, scleroderma, dermatomyositis, epidermolysis bullosa, bullous pemphigoid, leukoderma, dermatitis, Koebner's phenomenon and any other skin autoimmune disease.

18. The method of treating skin autoimmune diseases as claimed in claim 17, wherein the disease is vitiligo.

19. The method of treating autoimmune diseases as claimed in any of claims 14-18, wherein the mode of administration may be selected from a group comprising of oral, parenteral, topical, transdermal, intravenous, rectal, sublingual and nasal, intramuscular, subcutaneous, intravenous and peridural administration.

20. The pharmaceutical composition as claimed in claim 11, wherein the composition is in the form of a formulation that is administered in unit-dosage forms such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, injections, syrup, liquid, microemulsion, topical creams, ointments, suppositories, sachets, troches and lozenges and oil-water emulsions containing suitable quantities of the compound of Formula I or multiple-dosage forms.



Formula I