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(54) Title: NOVEL THIENO [2,3-D]PYRIMIDIN-4(3H)-ONE COMPOUNDS WITH ANTIMYCOBACTERIAL PROPERTIES

(57) Abstract: The present invention discloses novel thieno [2,3-d]pyrimidin-4(3H)-one compounds of Formula-I or its pharmaceutically acceptable salts with significant anti-mycobacterial activity and the pharmaceutical composition thereof.

NOVEL THIENO [2,3-D]PYRIMIDIN-4(3H)-ONE COMPOUNDS WITH ANTIMYCOBACTERIAL PROPERTIES

FIELD OF THE INVENTION

[0001] The present invention relates to a novel thieno [2,3-d]pyrimidin-4(3H)-one compounds of Formula-I or its pharmaceutically acceptable salts, having significant anti-myco bacterial activity. The invention further relates to a pharmaceutical composition comprising the same.

BACKGROUND OF THE INVENTION

[0002] In recent age tuberculosis (TB) is a major global health problem and causes millions of fatalities each year. *Mycobacterium tuberculosis* is more fatal for human than any other single microbial species.

[0003] Although there are anti-tubercular agents that are reasonably effective in treating tuberculosis (TB), the misuse of these agents has led to an increasing prevalence of multiple-drug resistant strains and extensively drug resistant (XDR) strains of *Mycobacterium tuberculosis* (Mtb) which necessitates new strategies for targeting this pathogen.

[0004] The first-line anti tubercular drugs pyrazinamide and isoniazid and some compounds given below in Figure 1 that contain amide, hydrazide or sulfonamide linkages show encouraging antitubercular activity.

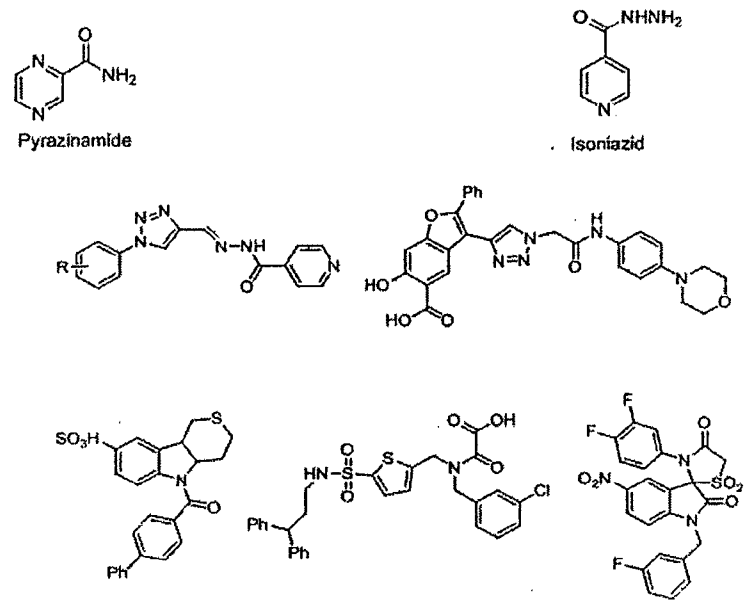


Fig 1

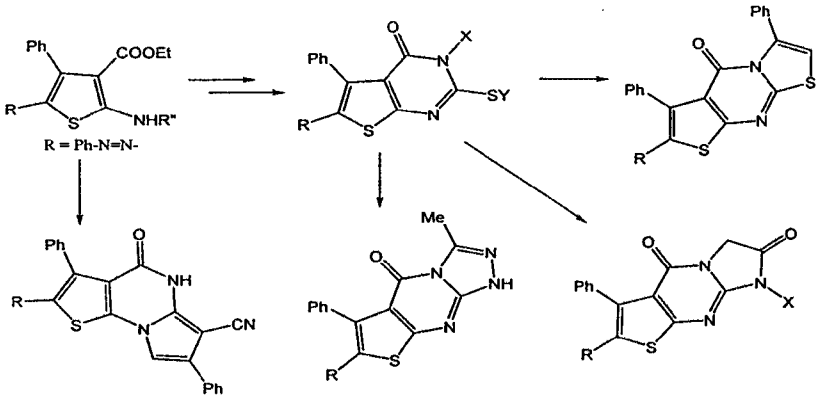
[0005] Since an estimated 9.6% of multidrug resistant tuberculosis (MDR-TB) cases have extensively drug-resistant TB (XDR-TB) according to WHO report, the search for new scaffolds to overcome the resistance to current TB drugs is still much desired.

[0006] Thieno pyrimidinones having 4-oxothienopyrimidine core structure are class of biologically active compounds known to possess both antibacterial and antifungal activity. There is ample literature available on biologically active thieno pyrimidinones and for the process of synthesis thereof.

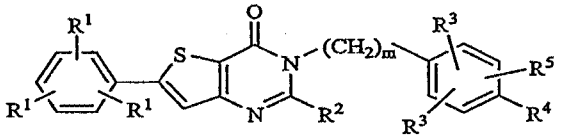
[0007] J.P. DUPIN *et al.* in *Journal of physiology and pharmacology* 2002, 53, 4, 625–634 reports the six-step synthesis of a series of benzothienopyrimidinone derivatives evaluated for potent thrombolytic activity. Further biological and biochemical screening of amino acid thienopyrimidinone derivatives for potential radioprotective character and screening of antimicrobial activity thereof, is reported in *Phosphorus, Sulfur, and Silicon and the related elements* volume 131, issue 1, 1997.

[0008] T.B. Hadda *et al*, in *Medicinal Chemistry Research* (Impact Factor: 1.61) 01/2013 discloses efficient strategy to identify pharmacophores and anti-pharmacophores sites in thienopyrimidinone derivatives for anti-bacterial/antifungal activity using Petra, Osiris and Molinspiration (POM) analyses.

[0009] Further Ekkati AR *et al.* in *Tetrahedron Letters,* 2011, 52(17):2228-2231 discloses aryl extensions of thienopyrimidinones as fibroblast growth factor receptor 1 kinase inhibitors. Regioselective synthesis and antimicrobial studies of bridgehead nitrogen heterocycles containing the thienopyrimidinone skeleton is reported by Hatem Moustafa Gaber *et al.* in *European Journal of Chemistry* 01/2011; 2(2):251-259 as described in below scheme.

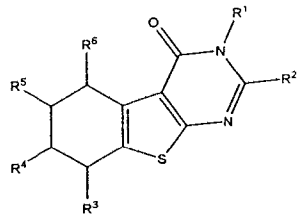


[0010] **WO2007050726** provides thienopyrimidinones compounds of Formula II, for treating a patient suffering from an MCHR-1 modulated disease or disorder such as, for example, obesity, diabetes, depression or anxiety.



Formula-II

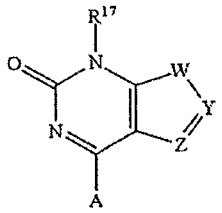
[0011] **WO 2005032527** relates to benzo (4, 5) thieno (2, 3-d) pyrimidin-4-one compounds, their 5,6-dihydro and 5, 6, 7, 8-tetrahydro derivatives of Formula III.



Formula III

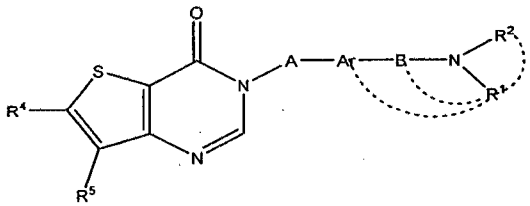
Further it discloses the use of said compounds for treatment of a steroid hormone dependent disease or disorder, preferably for a steroid hormone dependent disease or disorder requiring the inhibition of a 17-hydroxysteroid dehydrogenase enzyme, most preferably of the 17-beta HSD type 1, type 2 or type 3 enzymes.

[0012] US 7928111 disclose compounds including substituted thienopyrimidinone derivatives of formula IV, useful as sweet taste enhancers in comestible or medicinal compositions. It also provides screening methods for identifying modifiers of chemosensory receptors and their ligands.



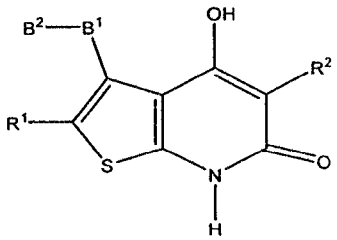
Formula IV

[0013] US2010069362 discloses thienopyrimidone compound of Formula-V having an MCH receptor antagonistic action.



Formula-V

[0014] EP 2280952 relates to thienopyridone derivatives of Formula-VI that are activators of AMPK-activated protein kinase (AMPK).



Formula-VI

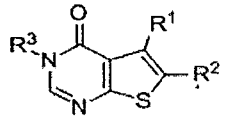
[0015] Additionally synthesis of thienopyrimidines and triazolothienopyrimidines and antimicrobial and antifungal activity thereof is reported by Nitinkumar S. Shetty *et al.* in *J. Chem. Sci.*, Vol. 121, No. 3, May 2009, pp. 301–307. These compounds are prepared by employing Gewald reaction.

[0016] Thus, the promising biological activity and easy synthesis of thieno pyrimidinone compounds inspired the present inventors to explore these novel class of compounds against mycobacterial infections which is a need in the art.

OBJECTIVES OF THE INVENTION

[0017] The main objective of the present invention is to provide a novel scaffold comprising thieno pyrimidinone necessary to overcome the resistance to current TB drugs.

[0018] Another objective of the present invention is to provide a novel thieno[2,3-*d*]pyrimidin-4(3*H*)-ones compounds of Formula-I or its pharmaceutically acceptable salts, enantiomers, analogues thereof having anti-myco bacterial activity comprising;



Formula I

wherein, R^1 and R^2 may be same or different and independently selected from the group consisting of hydrogen, halogen, (un)substituted aryl, (un)substituted C_1-C_{15} linear or branched alkyl group optionally substituted with hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy group; (un)substituted C_1-C_{15} linear or branched alkenyl; (un)substituted C_1-C_{15} linear or branched alkynyl group;

or R^1 and R^2 together form a 5 to 12 membered carbocyclic ring which may be substituted or unsubstituted;

R^3 is selected from the group consisting of hydrogen, (un)substituted (C_1-C_{15}) linear or branched alkyl; (un)substituted C_1-C_{15} linear or branched alkenyl; (un)substituted (C_1-C_{15}) linear or branched alkynyl; -CH_2-COOEt; -CH_2-COOH; $CH_2COCH_2R^4$; $CH_2CH(OH)CH_2R^4$ wherein R^4 is selected from the group consisting of (un)substituted triazol-1-yl, halogen, hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy, (un)substituted-aryl; CHR^5COAr wherein R^5 represents hydrogen or (C_1-C_4) alkyl and Ar represents (un)substituted aryl; $(CH_2)_nR^6$ or $(CH_2)_n R^{7+}X^-$ where n=1 to 7, wherein R^6 is selected from the group consisting of hydrogen, (un)substituted (C_1-C_4)alkyl, (un)substituted aryl, (un)substituted triazol-1-yl, halogen, -OH, N_3, CN, (un)substituted 2*H*-benzo[b][1,4]oxazin-3(4*H*)-on-4-yl, 3,5,6,7,8,9-hexahydro-*4H*-cyclohepta[4,5]thieno [2,3-*d*]pyrimidin-4(3*H*)-onyl, and wherein R^7 represents NMe_3 or pyridin-1-yl or 4-dimethylaminopyridin-1-yl, and X represents F, Br, I and Cl; with an exclusion, when R^1 and R^3 is H, and R^2 is selected from H, (C_1-C_3) alkyl, linear or branched (C_5-C_{10}) alkyl, propyl benzyloxy or Br; and when R^1 is methyl or ethyl, R^2 is selected from H, Br and R^3 is selected from H, n-propyl, isobutyl;

with an exclusion, when R^3 is H, R^1 and R^2 together form 5-7 membered saturated carbocyclic ring.

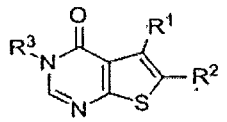
[0019] Yet another objective of the present invention is to provide a novel thieno[2,3-*d*]pyrimidin-4(3*H*)-ones compounds of Formula-I, having significant anti-mycobacterial activity.

[0020] Still another objective of the present invention is to provide a pharmaceutical composition comprising an effective amount of compound of formula-I in association with one or more pharmaceutical excipients for treatment of bacterial infections including tuberculosis.

SUMMARY OF INVENTION

[0021] To fulfill the objective, the present invention focusses on novel scaffold comprising thieno pyrimidinone necessary to overcome the resistance to current TB drugs.

[0022] In one aspect, the invention provides a novel thieno[2,3-*d*]pyrimidin-4(3*H*)-ones compounds of Formula-I or its pharmaceutically acceptable salts, enantiomers, analogues thereof having anti-myco bacterial activity comprising;



Formula I

wherein, R^1 and R^2 may be same or different and independently selected from the group consisting of hydrogen, halogen, (un)substituted aryl, (un)substituted C_1-C_{15} linear or branched alkyl group optionally substituted with hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy group; (un)substituted C_1-C_{15} linear or branched alkenyl; (un)substituted C_1-C_{15} linear or branched alkynyl group;

or R^1 and R^2 together form a 5 to 12 membered carbocyclic ring which may be substituted or unsubstituted;

R^3 is selected from the group consisting of hydrogen, (un)substituted (C_1-C_{15}) linear or branched alkyl; (un)substituted C_1-C_{15} linear or branched alkenyl; (un)substituted (C_1-C_{15}) linear or branched alkynyl; -CH_2-COOEt; .CH_2-COOH; $CH_2COCH_2R^4$; $CH_2CH(OH)CH_2R^4$ wherein R^4 is selected from the group consisting of (un)substituted triazol-1-yl, halogen, hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy, (un)substituted-aryl; CHR^5COAr wherein R^5 represents hydrogen or (C_1-C_4) alkyl and Ar represents (un)substituted aryl; $(CH_2)_nR^6$ or $(CH_2)_n R^{7+}X^-$ where n=1 to 7, wherein R^6 is selected from the group consisting of hydrogen, (un)substituted (C_1-C_4)alkyl, (un)substituted aryl, (un)substituted triazol-1-yl, halogen, -OH, N_3, CN, (un)substituted 2*H*-benzo[b][1,4]oxazin-3(4*H*)-on-4-yl, 3,5,6,7,8,9-hexahydro-4*H*-cyclohepta[4,5]thieno [2,3-*d*]pyrimidin-4(3*H*)-onyl, and wherein R^7 represents NMe_3 or pyridin-1-yl or 4-dimethylaminopyridin-1-yl, and X represents F, Br, I and Cl;

with an exclusion, when R^1 and R^3 is H, and R^2 is selected from H, (C_1-C_3) alkyl, linear or branched (C_5-C_{10}) alkyl, propyl benzyloxy or Br; and when R1 is methyl or ethyl, R^2 is selected from H, Br and R3 is selected from H, n-propyl, isobutyl;

with an exclusion, when R^3 is H, R^1 and R^2 together form 5-7 membered saturated carbocyclic ring.

[0023] In other aspect the invention provides a novel thieno[2,3-*d*]pyrimidin-4(3*H*)-ones compounds of Formula-I, having significant anti-mycobacterial activity.

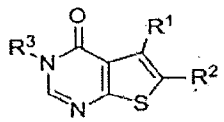
[0024] Further the invention provides a pharmaceutical composition comprising an effective amount of compound of formula-

[0025] I in association with one or more pharmaceutical excipients for treatment of bacterial infections including tuberculosis.

DETAILED DESCRIPTION OF THE INVENTION

[0026] The invention will now be described in detail in connection with certain preferred and optional embodiments, so that various aspects thereof may be more fully understood and appreciated.

[0027] In a preferred embodiment, the invention relates to a novel thieno[2,3-*d*] pyrimidin-4(3*H*)-ones with general Formula-I or its pharmaceutically acceptable salts thereof having anti-mycobacterial activity comprising;,



Formula I

wherein, R^1 and R^2 may be same or different and independently selected from the group consisting of hydrogen, halogen, (un)substituted aryl, (un)substituted or substituted C_1-C_{15} linear or branched alkyl group optionally substituted with hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy group; (un)substituted or substituted C_1-C_{15} linear or branched alkenyl; (un)substituted or substituted C_1-C_{15} linear or branched alkynyl group;

or R^1 and R^2 together form a 5 to 12 membered carbocyclic ring which may be substituted or unsubstituted;

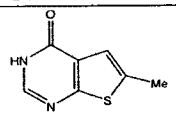
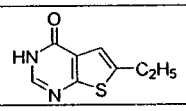
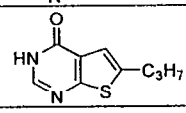
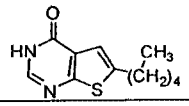
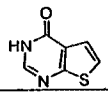
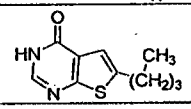
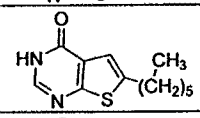
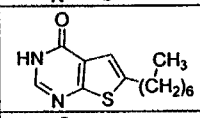
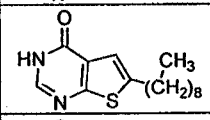
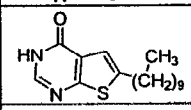
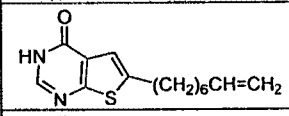
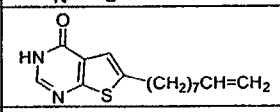
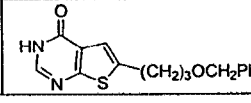
R^3 is selected from the group consisting of hydrogen, (un)substituted or substituted (C_1-C_{15}) linear or branched alkyl; (un)substituted or substituted C_1-C_{15} linear or branched alkenyl; (un)substituted or substituted (C_1-C_{15}) linear or branched alkynyl; $-CH_2$-COOEt; $-CH_2$-COOH; $CH_2COCH_2R^4$; $CH_2CH(OH)CH_2R^4$ wherein R^4 is selected from the group consisting of (un)substituted or substituted triazolyl, halogen, hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy, (un)substituted or substituted aryl; CHR^5COAr wherein R^5 represents hydrogen or (C_1-C_4) alkyl and Ar represents (un)substituted or substituted aryl; $(CH_2)_nR^6$ or $(CH_2)_n R^{7+}X^-$ where n=1 to 7, wherein R^6 is selected from the group consisting of hydrogen, (un)substituted or substituted (C_1-C_4)alkyl, (un)substituted or substituted aryl, (un)substituted or substituted triazolyl, halogen, -OH, N_3, CN, (un)substituted or substituted 2*H*-benzo[b][1,4]oxazin-3(4*H*)-on-4-yl, 3,5,6,7,8,9-hexahydro-4*H*-cyclohepta[4,5]thieno [2,3-*d*]pyrimidin-4(3*H*)-onyl, and wherein R^7 represents NMe_3 or pyridin-1-yl or 4-dimethylaminopyridin-1-yl, and X represent F, Br, I and Cl;

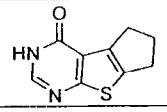
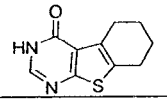
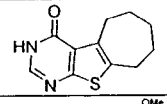
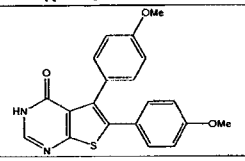
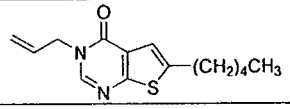
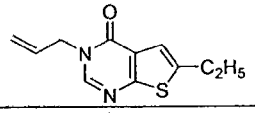
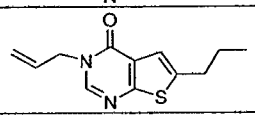
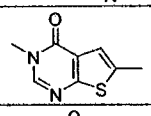
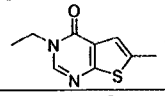
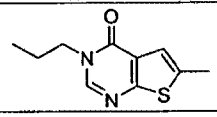
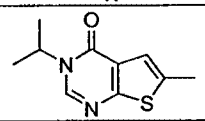
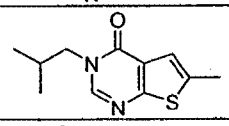
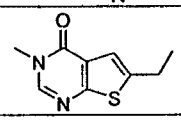
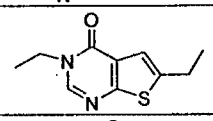
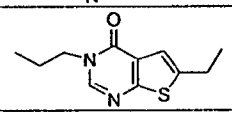
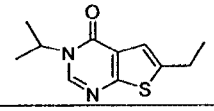
with an exclusion, when R^1 and R^3 is H, and R^2 is selected from H, (C_1-C_3) alkyl, linear or branched (C_5-C_{10}) alkyl, propyl benzyloxy or Br; and when R^1 is methyl or ethyl, R^2 is selected from H, Br and R^3 is selected from H, n-propyl, isobutyl;

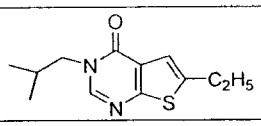
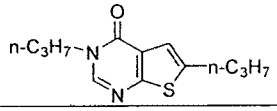
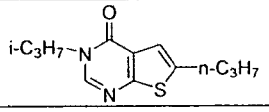
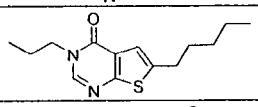
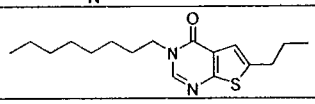
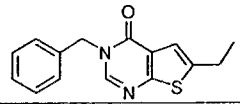
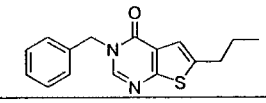
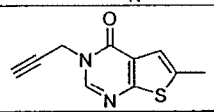
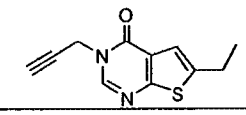
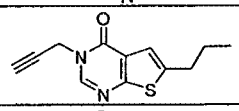
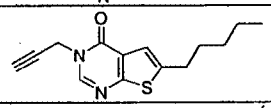
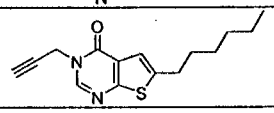
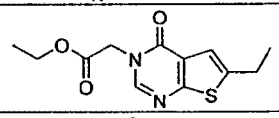
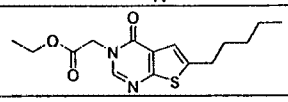
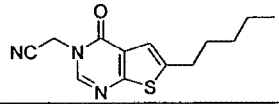
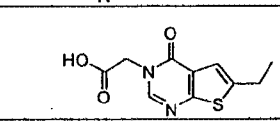
with an exclusion, when R^3 is H, R^1 and R^2 together form 5-7 membered saturated carbocyclic ring.

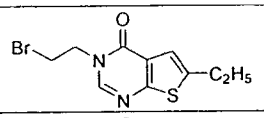
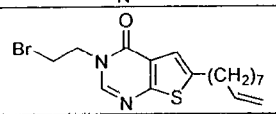
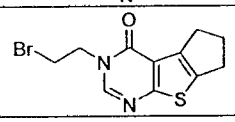
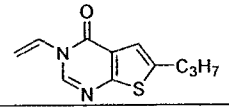
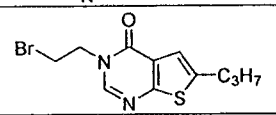
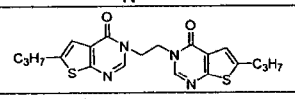
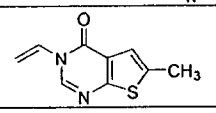
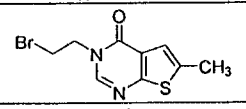
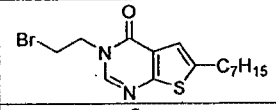
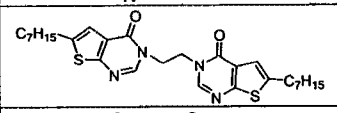
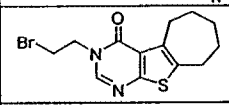
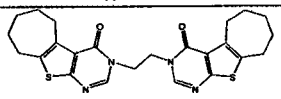
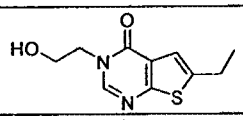
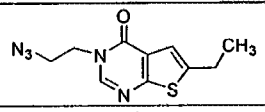
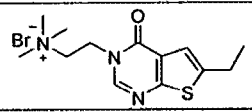
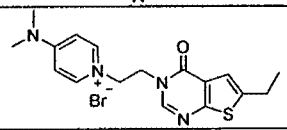
[0028] In an embodiment, the antimycobacterial thieno[2,3-*d*]pyrimidin-4(3*H*)-ones compounds of Formula-I, encompasses library of compounds as given below in Table-1.

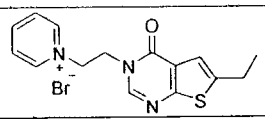
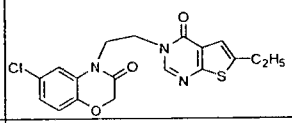
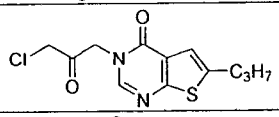
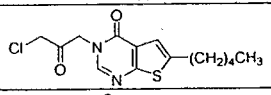
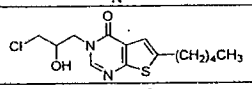
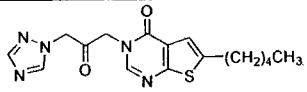
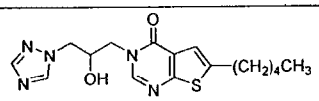
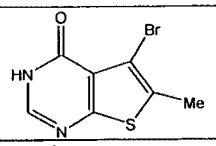
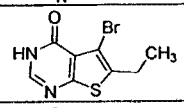
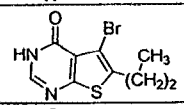
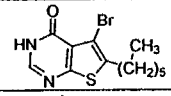
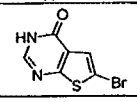
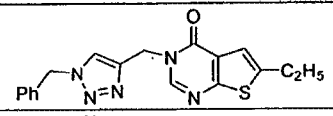
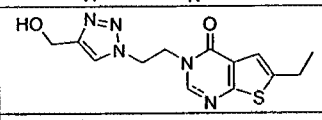
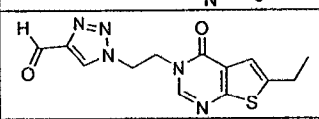
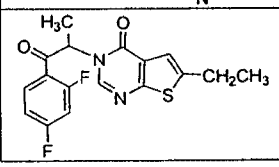
Table 1: Antimycobacterial thieno[2,3-*d*]pyrimidin-4(3*H*)-ones compounds of Formula-I,

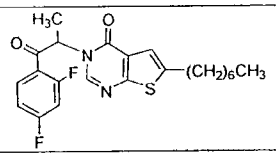
Compound No.	Structure	IUPAC Name
1		6-methylthieno[2,3-*d*]pyrimidin-4(3*H*)-one
2		6-ethylthieno[2,3-d]pyrimidin-4(3H)-one
3		6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one
4		6-(n-pentyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one
5		Thieno[2,3-*d*]pyrimidin-4(3*H*)-one
6		6-(n-Butyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one
7		6-(n-Hexyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one
8		6-(n-Heptyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one
9		6-(n-Nonyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one
10		6-(n-Decyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one
11		6-(Oct-7-en-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one
12		6-(Non-8-en-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one
13		6-(3-Benzyloxypropyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one

14		3,5,6,7-Tetrahydrocyclopenta[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one
15		5,6,7,8-Tetrahydrobenzothieno[2,3-*d*]pyrimidin-4(3*H*)-one
16		3,5,6,7,8,9-Hexahydro-4H-cyclo hepta [4,5] thieno [2,3-*d*]pyrimidin-4-one
17		5,6-bis(4-methoxy phenyl) thieno[2,3-d]pyrimidin-4(3H)-one
18		3-allyl-6-pentyl thieno [2,3-*d*] pyrimidin-4(3*H*)-one
19		3-Allyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one
20		3-Allyl-6-propyl thieno [2,3-d]pyrimidin-4(3H)-one
21		3,6-Dimethylthieno[2,3-*d*]pyrimidin-4(3H)-one
22		3-Ethyl-6-methyl thieno [2,3-*d*]pyrimidin-4(3H)-one
23		6-Methyl-3-propyl thieno [2,3-d]pyrimidin-4(3H)-one
24		3-Isopropyl-6-methyl thieno[2,3-d]pyrimidin-4(3H)-one
25		3-Isobutyl-6-methyl thieno[2,3-d]pyrimidin-4(3H)-one
26		6-Ethyl-3-methyl thieno[2,3-d]pyrimidin-4(3H)-one
27		3,6-Diethylthieno[2,3-d]pyrimidin-4(3H)-one
28		6-Ethyl-3-propyl thieno[2,3-d]pyrimidin-4(3H)-one
29		6-Ethyl-3-isopropyl thieno[2,3-d]pyrimidin-4(3H)-one

30		6-Ethyl-3-isobutyl thieno[2,3-d]pyrimidin-4(3H)-one
31		3,6-Dipropylthieno[2,3-d]pyrimidin-4(3H)-one
32		3-Isopropyl-6-propyl thieno[2,3-d]pyrimidin-4(3H)-one
33		6-Pentyl-3-propyl thieno[2,3-d]pyrimidin-4(3H)-one
34		3-Octyl-6-propyl thieno[2,3-d]pyrimidin-4(3H)-one
35		3-Benzyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one
36		3-Benzyl-6-propyl thieno[2,3-d]pyrimidin-4(3H)-one
37		6-Methyl-3-(prop-2-yn-1-yl)thieno[2,3-d] pyrimidin-4(3H)-one
38		6-Ethyl-3-(prop-2-yn-1-yl)thieno[2,3-d] pyrimidin-4(3H)-one
39		3-(Prop-2-yn-1-yl)-6-propyl thieno[2,3-d] pyrimidin-4(3H)-one
40		3-(Prop-2-yn-1-yl)-6-pentylthieno[2,3-d] pyrimidin-4(3H)-one
41		3-(Prop-2-yn-1-yl)-6-hexylthieno[2,3-d] pyrimidin-4(3H)-one
42		Ethyl 2-(6-ethyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) acetate
43		Ethyl 2-(6-pentyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) acetate
44		2-(4-oxo-6-pentyl thieno[2,3-d]pyrimidin-3 (4H)-yl)acetonitrile
45		2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3(4H)-yl)acetic acid

46		3-(2-bromoethyl-6-ethyl thieno[2,3-*d*]primidin-4 (3*H*)-one
47		3-(2-Bromoethyl)-6-(non-8-enyl)thieno[2,3-d] pyrimidin-4(3H)-one
48		3-(2-Bromoethyl)-3,5,6,7-tetrahydro-4H-cyclo penta [4,5]thieno[2,3-d] pyrimidin-4-one
49		6-propyl-3-vinyl thieno[2,3-*d*]pyrimidin-4 (3*H*)-one
50		3-(2-bromoethyl)-6-propyl thieno[2,3-*d*] primidin-4(3*H*)-one
51		3,3'-(ethane-1,2-diyl)bis(6-propyl thieno[2,3-d]pyrimidin-4 (3H)-one
52		6-methyl-3-vinyl thieno[2,3-*d*]pyrimidin-4(3*H*)-one
53		3-(2-bromoethyl)-6-methylthieno[2,3-*d*]primidin-4(3*H*)-one
54		3-(2-Bromoethyl-6-heptylthieno[2,3-*d*] primidin-4(3*H*)-one
55		3,3'-(Ethane-1,2-diyl)bis(6-heptyl thieno[2,3-d]pyrimidin-4 (3H)-one)
56		3-(2-Bromoethyl)-3,5,6,7,8,9-hexahydro-4H-cyclo hepta [4,5] thieno[2,3-d]pyrimidin-4-one
57		3,3'-(Ethane-1,2-diyl) bis(6-heptylthieno[2,3-d] pyrimidin-4(3H)-one)
58		6-ethyl-3-(2-hydroxy ethyl) thieno[2,3-d] pyrimidin-4(3H)-one
59		3-(2-Azidoethyl)-6-ethyl thieno[2,3-d]pyrimidin-4 (3H)-one
60		2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3(4H)-yl)-N,N,N-trimethylethan-1-aminium bromide
61		4-(dimethylamino)-1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl) ethyl)pyridin-1-ium bromide

62		1-(2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3 (4H)-yl)ethyl)pyridin-1-ium bromide
63		6-chloro-4-(2-(6-ethyl-4-oxothieno[2,3-*d*] pyrimidin-3(4*H*)-yl) ethyl)-2*H*-benzo [b] [1,4] oxazin-3(4*H*)-one
64		3-(3-chloro-2-oxopropyl)-6-propylthieno[2,3-*d*] pyrimidin-4(3*H*)-one
65		3-(3-chloro-2-oxopropyl)-6-pentylthieno[2,3-*d*] pyrimidin-4(3*H*)-one
66		3-(3-chloro-2-hydroxy propyl)-6-pentyl thieno [2,3-*d*]pyrimidin-4(3*H*)-one
67		3-(2-oxo-3-(1*H*-1,2,4-triazol-1-yl)propyl-6-pentylthieno[2,3-*d*] pyrimidin-4(3*H*)-one
68		3-(2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propyl)-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one
69		5-bromo-6-methyl thieno[2, 3-d] pyrimidin-4(3*H*)-one
70		5-Bromo-6-ethyl thieno [2,3-*d*]pyrimidin-4(3*H*)-one
71		5-Bromo-6-propyl thieno[2,3-*d*]pyrimidin-4 (3*H*)-one
72		5-Bromo-6-hexyl thieno[2,3-*d*]pyrimidin-4 (3*H*)-one
73		6-Bromothieno[2,3-d]pyrimidin-4(3H)-one
74		3-((1-Benzyl-1H-1,2,3-triazol-4-yl)methyl)-6-ethylthieno[2,3-d] pyrimidin-4(3H)-one
75		6-ethyl-3-(2-(4-(hydroxy methyl)-1H-1,2,3-triazol-1-yl)ethyl)thieno[2,3-d] pyrimidin-4(3H)-one
76		1-(2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)-1H-1,2,3-triazole-4-carbaldehyde
77		3-(1-(2,4-difluorophenyl)-1-oxopropan-2-yl)-6-ethylthieno[2,3-*d*] pyrimidin-4(3*H*)-one

78		3-(1-(2,4-Difluoro phenyl)-1-oxopropan-2-yl)-6-heptylthieno[2,3-*d*] pyrimidin-4(3*H*)-one

[0029] In another embodiment, the present invention relates to a synthesis of antimycobacterial thieno[2,3-d]pyrimidin-4(3H)-ones compounds of Formula-I , which can be prepared by the process known in the art.

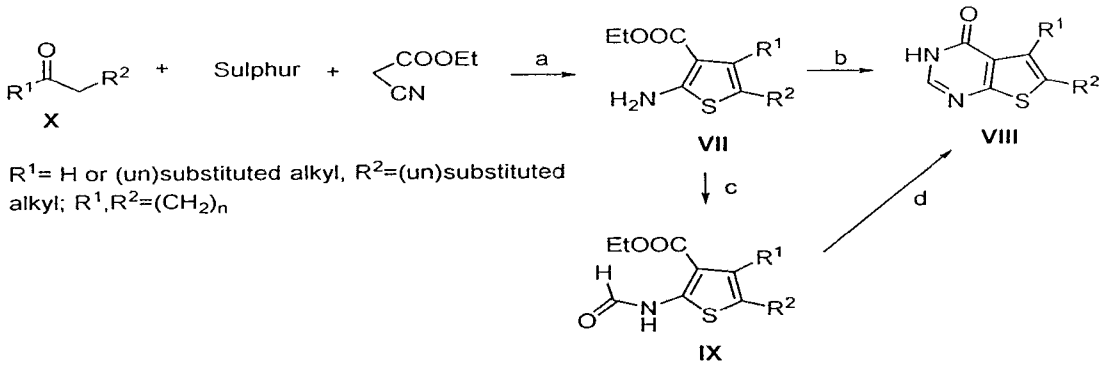
[0030] The process comprises the steps of:, a) preparing substituted 2-aminothiophene-3-carboxylates (Formula VII) by employing Gewald synthesis; b) preparing thieno[2,3-d]pyrimidin-4(3H)-ones (Formula VIII) in one step from substituted ethyl 2-aminothiophene-3-carboxylates (Formula VII) by heating with formamide and ammonium acetate or alternatively reacting ethyl 2-aminothiophene-3-carboxylates (Formula VII) with formic acid and ammonium acetate to obtain ethyl 2-formylaminothiophene-3-carboxylates (Formula IX) followed by treatment with formamide and ammonium formate to get the desired thieno [2,3-d]pyrimidin-4(3H)-ones (Formula VIII); and c) synthesizing variously substituted thieno[2,3-d]pyrimidin-4(3H)-one of formula (I) from compound of formula (Formula VIII).

[0031] According to the process, Gewald reaction is carried out by condensing aldehyde or ketone Formula X) with ethyl cyanoacetate in the presence of elemental sulfur and organic base, in a suitable solvent to obtain substituted 2-aminothiophene-3-carboxylates (Formula VII).

[0032] The organic base is selected from the group consisting of triethylamine, diethylamine, pyridine, quinoline and the like; solvent is selected from DMF, DMSO, THF, acetone, acetonitrile or ethanol either alone or mixtures thereof.

[0033] The reaction of substituted 2-aminothiophene-3-carboxylates (Formula VII) with formamide and ammonium acetate is carried out at temperature range 140° to 160°C. After completion of the reaction, reaction mixture is cooled to room temperature and crushed ice is added followed by filtration, washing and drying under vacuum to obtain thieno[2, 3-*d*]pyrimidin-4(3*H*)-one (compound of Formula VIII).

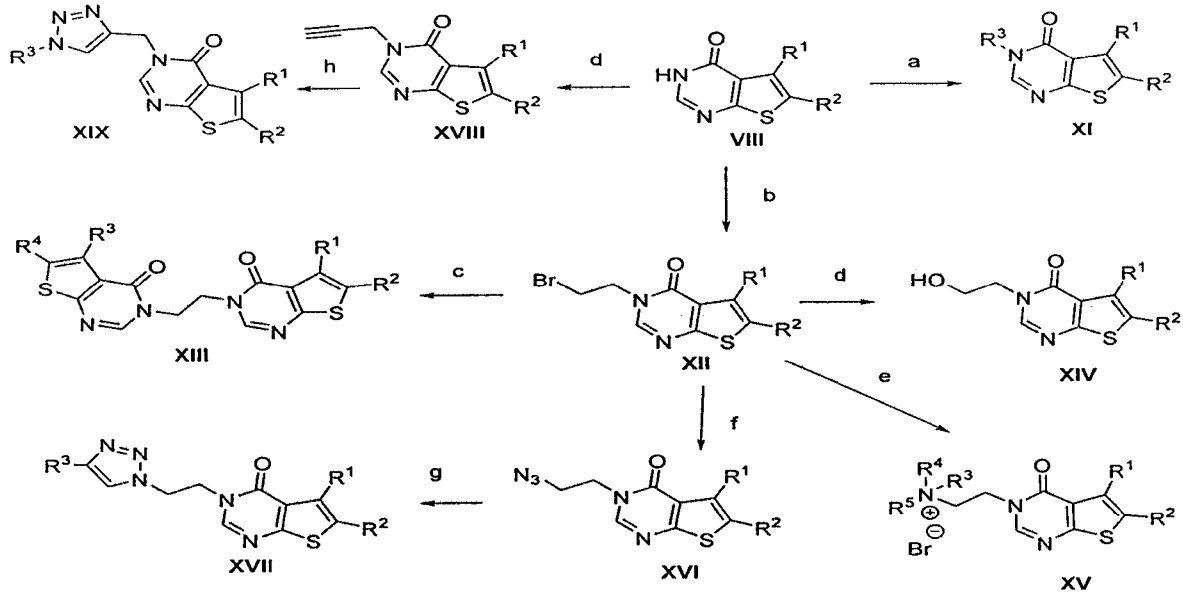
[0034] The preparation of thieno [2,3-*d*]pyrimidin-4(3*H*)-one (Formula VIII) from aldehyde or ketone (X) by Gewald process is shown below in Scheme 1.



Scheme 1. Synthesis of thienopyrimidinones **VIII**

Reagents and conditions: a. Et_3N, DMF or quinoline, EtOH; b. Formamide, ammonium acetate; c. Formic acid, ammonium acetate; d. Formamide, ammonium formate

[0035] The number of variously substituted thieno [2,3-d]pyrimidin-4(3H)-ones with general structures XI to XIX were obtained from compound of formula (VIII) as shown in Scheme 2.



Scheme 2. Synthesis of thienopyrimidinones with general structures **XI** to **XIX**

Reagents and conditions: a. R^3X, K_2CO_3, DMF or acetonitrile, RT; b. $BrCH_2CH_2Br$, K_2CO_3, DMF, RT; c. Required thienopyrimidinone, K_2CO_3, DMF, RT; d. K_2CO_3, DMF, RT; e. $NR^3R^4R^5$, MeOH, sealed tube, 50°C; f. NaN_3, DMF, 80°C; g. Propargyl alcohol, t-BuOH, water, $CuSO_4.5H_2O$, sodium ascorbate, RT; h. Benzyl azide, t-BuOH, water, $CuSO_4.5H_2O$, sodium ascorbate, RT.

[0036] Thus, reaction of thieno [2,3-d]pyrimidin-4(3H)-one (VIII) with required (un)substituted alkyl/alkenyl/alkynyl halides in the presence of potassium carbonate afforded substituted thieno [2,3-d]pyrimidin-4(3H)-ones, 18 to 44 (refer Table 1 for structures). The acid 45 was prepared from the corresponding ester 42. The bromide XII was obtained by reacting thieno [2,3-d]pyrimidin-4(3H)-one (VIII) with dibromoethane in DMF in the presence of potassium carbonate. The bromide XII served as intermediate for a number of substituted thieno [2,3-d] pyrimidin-4(3H)-ones XIII, XIV, XV, XVI

etc. The reaction of bromide XII with thieno [2,3-d]pyrimidin-4(3H)-one (VIII) in DMF in the presence of potassium carbonate afforded dimeric thieno [2,3-d]pyrimidin-4(3H)-one XIII while stirring; the bromide XII with potassium carbonate in DMF afforded alcohol XIV. The reaction of bromide XII with tertiary amine in methanol resulted in the formation of water-soluble salts XV. Azide XVI was obtained by treating bromide XII with sodium azide in DMF at 80°C. Click reaction of azide XVI with propargyl alcohol afforded triazol-1-yl-thieno [2,3-d]pyrimidin-4(3H)-one XVII. The thieno [2,3-d]pyrimidin-4(3H)-one (VIII) on reaction with propargyl bromide in DMF in the presence of potassium carbonate provided acetylenic thieno [2,3-d]pyrimidin-4(3H)-one XVIII which on Click reaction afforded 3-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-6-(un)substituted alkylthieno[2,3-d]pyrimidin-4(3H)-one, XIX.

[0037] In an embodiment, the compounds prepared in the present invention can be subjected further to various reactions to get a large number of compounds for optimization of biological activity.

[0038] In another embodiment, the compounds of the present invention are characterized by spectral analysis such as NMR, IR, Mass and UV, elemental analysis and melting point etc.

[0039] The bacterial infections according to the invention may be caused due to gram negative, gram positive bacteria preferably Mycobacterium smegmatis MC2155 strain, Mycobacterium bovis BCG and Mycobacterium tuberculosis H37Rv strain.

[0040] In another embodiment, the thieno[2,3-d]pyrimidin-4(3H)-ones compounds of Formula-I exhibit anti-mycobacterial activity that inhibits the growth of *Mycobacterium smegmatis MC2155, Mycobacterium bovis BCG* or *Mycobacterium tuberculosis H37Rv* among other mycobacterium species/strains. In case of some of the compounds, the percentage inhibition ranges from about 40 to 68% e.g. compounds 2, 20, 29, 39, 64 and 65. The thieno [2,3-d] pyrimidin-4(3H)-ones comprising compounds 26, 38, 40, 41, 43, 44 and 58–exhibited significant activity against *Mycobacterium smegmatis/ Mycobacterium bovis BCG* (inhibition in the range of 30-40% at 30 μM). One of the thieno [2,3-d] pyrimidin-4(3H)-one 40 was screened against *Mycobacterium tuberculosis H37Rv* and exhibited antitubercular activity with MIC equal to 8 μg/mL

[0041] In yet another embodiment, the present invention provides a pharmaceutical composition comprising of the active ingredient of Formula I or its pharmaceutically acceptable salts, along with pharmaceutically acceptable excipients or carriers, for the treatment of infections caused due to *Mycobacterium smegmatis MC²155 strain, Mycobacterium bovis BCG* and *Mycobacterium tuberculosis $H_{37}R_v$ strain.* in a subject.

[0042] In another embodiment, the present invention provides a pharmaceutical composition for treating or preventing tuberculosis in a subject, comprising anti mycobacterial compounds of Formula 1 in association with at least one pharmaceutically acceptable excipient.

[0043] The excipients or carriers are selected from diluents, glidants, lubricants, solubilizers, stabilizer, preservatives, sugar, coating agent, flavors, fillers and other inactive ingredients.

[0044] The quantity of the compounds of Formula I used in pharmaceutical compositions of the present invention will vary depending upon the body weight of the patient and the mode of administration and can be of any effective amount to achieve the desired therapeutic effect. The compound of the present invention can also be administered optionally with other antibacterial actives depending on the disease conditions.

[0045] The pharmaceutical composition according to the invention can be in the form of a solid such as pills, powders, granules, tablets, capsules, pellets, beads etc. or can be present in the liquid form such as solutions, emulsions, suspensions, syrup etc. or can be used in the form of inhalants or parenteral injection.

According to the invention, the pharmaceutical compositions containing compounds of Formula I may be administered using an effective amount, along with pharmaceutically acceptable excipients for the treatment of tuberculosis. Generally, the quantity of active compound of Formula-I is in the range between 0.9% to 99% by weight of the composition.

[0046] In yet another embodiment, the invention provides method of treating or preventing the growth of bacterial infections in a subject comprising administering an effective amount of compound of Formula I or its pharmaceutical salt in association with one or more pharmaceutical excipients.

[0047] The pharmaceutical composition can be administered by any means that delivers the active pharmaceutical ingredient(s) to the site of the body whereby it can exert a therapeutic effect on the patient.

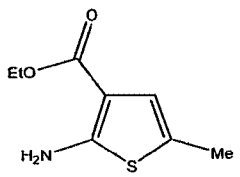
[0048] In another embodiment, the present invention relates to the use of compounds of Formula 1 for the preparation of medicament useful for treatment or prevention of tuberculosis

[0049] The following examples, which include preferred embodiments, will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of examples and for purpose of illustrative discussion of preferred embodiments of the invention only and are not limiting the scope of the invention.

EXAMPLES

[0050] Example 1: Preparation of 6-methyl-thieno[2,3-d]pyrimidin-4(3*H*)-one (1):

a) Preparation of ethyl 2-amino-5-methylthiophene-3-carboxylate:



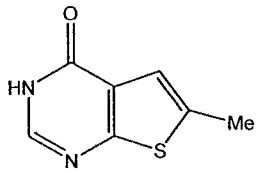
Propanal (25 g, 0.431 mole), ethyl cyanoacetate (45.09 ml, 0.431 mole) and sulphur (13.79 g, 0.431 mole) were taken in two necked R.B. flask containing 250 ml dry DMF. Reaction mixture was stirred for 15 min followed by addition of TEA (30.15 ml, 0.215 moles) drop wise with constant stirring. After complete addition, the reaction mixture was stirred at 50 ^{0}C for 12 hrs. Reaction was monitored

by TLC. After completion of the reaction, reaction mixture was cooled to room temperature and water was added to it. The reaction mixture was extracted with ethyl acetate (3 x 100 ml) and the extract was dried and concentrated to obtain ethyl 2-amino-5-methyl- thiophene-3-carboxylate (40 g, 50.16 %) as a brownish sticky liquid.

IR ($CHCl_3$): 3334, 1667 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ 1.33 (t, J = 8 Hz, 3H), 2.26 (s, 3H), 4.25 (q, J= 8 Hz, 2H), 5.47 (s, 2H), 6.62 (s, 1H).

b) Preparation of 6-methylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (1) from ethyl 2-amino-5-methylthiophene-3-carboxylate:



Ethyl 2-amino-5-methylthiophene-3-carboxylate (30 g, 0.1621 mole) and ammonium acetate (16.23 g, 0.2103 mole) were taken in two necked R.B. flask containing 114 ml formamide. Reaction mixture was stirred at 150 ^0C for 20 h. After completion of the reaction, reaction mixture was cooled to room temperature and crushed ice was added in it. The solid product formed was filtered, washed with water and dried under vacuum to obtain 6-methylthieno [2, 3-*d*]pyrimidin-4(3*H*)-one (16.35 g, 54 %) as a white solid, M.P. 269 ^0C.

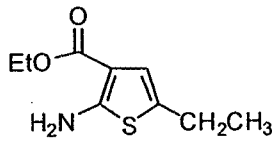
IR ($CHCl_3$): 1655 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$+DMSO-d_6): δ 2.57 (s, 3H), 7.15 (s, 1H), 8.00 (s, 1H), 11.65 (s, 1H).

^{13}C NMR (50MHz, $CDCl_3$+DMSO-d_6): δ 15.61, 118.62, 125.23, 137.54, 143.31, 157.90, 206.78.

[0051] Example 2: Preparation of 6-ethylthieno[2,3-d]pyrimidin-4(3H)-one (2):

a) Ethyl 2-amino-5-ethylthiophene-3-carboxylate

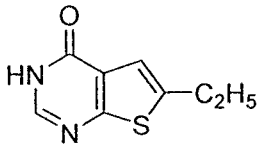


In a two-necked round bottom flask, butanal (10 ml, 0.138 mol), ethyl cyanoacetate (15.6 ml, 0.138 mol), DMF (100 ml) and sulphur (4.4 g, 0.138 mol) were taken and the mixture was flushed with argon. Triethyl amine (6.31 ml, 0.069 mol) was added and the reaction mixture was stirred at 50-55°C for 12 hrs. Reaction was monitored by TLC. After completion of reaction, water (200 ml) was added to reaction. It was extracted with DCM (3 X 200 ml). The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain ethyl 2-amino-5-ethylthiophene-3-carboxylate as brown thick liquid (8.0 g, 80.2%);

IR ($CHCl_3$): 3419, 3309, 2931, 1674, 1598, 1506, 1387 cm^{-1};

^1H NMR (200 MHz, $CDCl_3$): δ 1.23 (t, J = 7 Hz, 3H), 1.34 (t, J = 7 Hz, 3H), 2.62 (q, J = 7 Hz, 2H), 4.26 (q, J = 7 Hz, 2H), 4.62 (bs, 2H), 6.64 (s, 1H).

b) Preparation of 6-ethylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (2) from ethyl 2-amino-5-ethylthiophene-3-carboxylate:



The ethyl 2-amino-5-ethylthiophene-3-carboxylate (8.00 g, 0.0417 mol), ammonium acetate (3.01 g, 0.0417 mol) and formamide (32.00 ml, 0.803 mol) were taken in two necked RB flask equipped with condenser and stirred at 140-150 °C for 10 h. The reaction mixture was then cooled to room temperature, ice was added and stirred for 30 min and the white solid obtained was filtered, washed with water followed by washing with ethyl acetate in pet ether (3 X 20 ml) to get 6-ethylthieno[2,3-*d*]pyrimidin-4(3*H*)-one as white powder, 6.4 g (80 %).

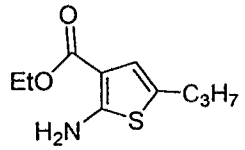
IR ($CHCl_3$): 2925, 2855, 1664, 1583, 1459, 1377 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ 1.22 (t, *J* = 8 Hz, 3H), 2.81 (q, *J* = 8 Hz, 2H), 7.07 (s, 1H), 8.02 (s, 1H), 12.40 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 15.21, 23.11, 117.30, 124.76, 144.22, 144.95, 157.00, 162.75.

[0052] Example 3: Preparation of 6-propyl thieno[2,3-*d*]pyrimidin-4(3*H*)-one (3):

a) Preparation of ethyl 5-propyl-2-aminothiophene-3-carboxylate:



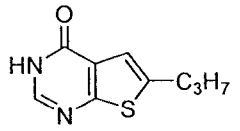
In a two-necked round bottom flask, pentanal (10 ml, 0.016 mol), ethyl cyanoacetate (13.71 ml, 0.016 mol), DMF (100 ml) and sulphur (3.71 g, 0.016 mol) were taken and the mixture was flushed with argon. Triethyl amine (6.31 ml, 0.058 mol) was added and the reaction mixture was stirred at 50-55 °C for 12 h. Reaction was monitored by TLC (ethyl acetate- pet ether, 20:80). After completion of reaction, water (200 ml) was added to reaction. It was then extracted with DCM (3 X 200 ml). The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain ethyl 2-amino-5-pentyl-thiophene-3-carboxylate as brown thick liquid (11.00 g, 89.3%).

IR ($CHCl_3$): 3445, 3338, 2932, 1668, 1587 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): 0.94 (t, *J* = 7 Hz, 3H), 1.32 (t, *J* = 8 Hz, 3H), 1.54-1.63 (m, 2H), 2.53 (t, J = 7 Hz, 2H), 4.24 (q, J = 8 Hz, 2H), 5.87 (bs, 2H), 6.62 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 13.34, 14.35, 24.11, 31.57, 59.39, 105.88, 121.34, 126.35, 161.37, 165.28.

b) Preparation of 6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (3) from ethyl 5-propyl-2-aminothiophene-3-carboxylate:



The ethyl 2-amino-5-propylthiophene-3-carboxylate (11.00 g, 0.051 mol), ammonium acetate (3.87 g, 0.051 mol) and formamide (41.13 ml, 1.032 mol) were taken in two necked RB flask equipped with condenser and stirred at 140-150 °C for 10 h. The reaction mixture was then cooled to room temperature, ice was added and stirred for 30 min and the white solid obtained was filtered, washed with water followed by washing with ethyl acetate in pet ether (3 X 20 ml) to get 6-propylthieno[2,3-d]pyrimidin-4(3H)-one as white powder, 8.9 g, (80. 90 %) .

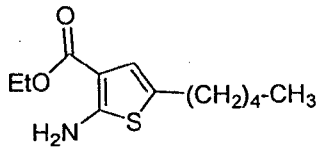
IR ($CHCl_3$): 2922, 1661, 1463, cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.02 (t, *J*= 7 Hz, 3H), 1.72-1.82 (m, 2H), 2.86 (t, *J* = 6 Hz, 2H), 7.17 (s, 1H), 8.05 (s, 1H), 12.86 (bs, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 13.52, 24.24, 32.60, 117.60, 124.85, 142.85, 144.74, 159.84, 164.48.

[0053] Example 4: Preparation of 6-(n-pentyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (4)

a) Preparation of ethyl 5-pentyl-2-aminothiophene-3-carboxylate:



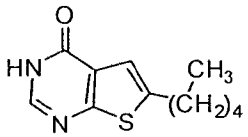
In a two-necked round bottom flask, heptanal (12.22 ml, 0.087 moles), ethyl cyanoacetate (9.33 ml, 0.08757 moles), DMF (100 ml) and sulphur (2.80 gm, 0.08757 mole) were taken and the mixture was flushed with argon. Triethyl amine (6.31 ml, 0.04378 moles) was added and the reaction mixture was stirred at 50-55 °C for 12 h. Reaction was monitored by TLC (ethyl acetate- pet ether, 20:80). After completion of reaction, water (200 ml) was added to reaction. It was then extracted with DCM (3 X 200 ml). The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain ethyl 2-amino-5-pentyl-thiophene-3-carboxylate as brown thick liquid (21.67 gm, 72.4%).

IR ($CHCl_3$): 3441, 3334, 2929, 1674, 1588, 1504 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 0.90 (t, *J* = 7 Hz, 3H), 1.25-1.38 (m, 6H), 1.58 (quint, *J* = 7 Hz, 2H), 2.57 (t, *J* = 7 Hz, 2H), 4.26 (q, *J* = 7 Hz, 2H), 5.78 (bs, 2H), 6.63 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 14.01, 14.54, 22.42, 29.70, 30.77, 31.16, 59.59, 106.12, 121.35, 126.90, 161.40, 165.45.

b) Preparation of 6-(n-pentyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (4) from ethyl 5-pentyl-2-aminothiophene-3-carboxylate:



A mixture of ethyl 2-amino-5-n-pentylthiophene-3-carboxylate (100 g, 0.41 mol), ammonium acetate (31.95 g, 0.41 mol) and formamide (330 ml, 8.3 mol) was taken in a two necked round bottom flask equipped with reflux condenser and a guard tube and stirred at 145-150 °C for 10 h. The reaction mixture was then cooled to room temperature, diluted with chilled water (800 ml) and stirred for 30 min to obtain a white solid product which was filtered, washed with water (3 X 300 ml) followed by washing with 20 % ethyl acetate in pet-ether (3 x 20 ml) to obtain 6-(n-pentyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one as off-white solid (74.89 g, 81.3 %).

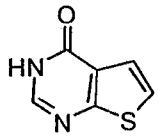
MP: 170-173 °C; **IR** (Chloroform): 3434, 1663 cm^{-1};

^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, *J* = 6 Hz, 3H), 1.31-1.38 (m, 4H), 1.65-1.75 (m, 2H), 2.84 (t, *J* = 8 Hz, 2H), 7.13 (s, 1H), 8.07 (s, 1H), 12.9 (bs, 1H);

^{13}C NMR (50 MHz, $CDCl_3$): δ 13.8, 22.2, 30.4, 30.5, 31.0, 117.3, 124.7, 142.9, 144.9, 159.8, 164.2.

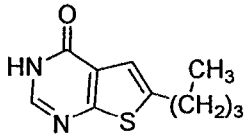
[0054] The following thieno[2,3-d] pyrimidin-4(3H)-ones were prepared by using procedures similar to those described in **Examples 1-4** from substituted 2-aminothiophene-3-carboxylates (which can be prepared by Gewald synthesis as described in **Examples 1-4** starting with appropriate aldehydes/ketones) by reaction with ammonium acetate and formamide.

[0055] Example 5: Thieno[2,3-*d*]pyrimidin-4(3*H*)-one (5)



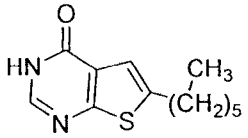
Nature: White solid; **MP:** 220-222 °C; **Yield:** 91.8 %; **IR** (Chloroform): 3387, 1676 cm^{-1}; **^{1}H NMR** (200 MHz, DMSO-d_6): δ 7.41 (d, *J* = 6 Hz, 1H), 7.60 (d, *J* = 6 Hz, 1H), 8.15 (s, 1H), 12.54 (bs, 1H); **^{13}C NMR** (50 MHz, DMSO-d_6): δ 121.9, 124.1, 124.9, 145.8, 157.8, 164.5.

[0056] Example 6: Preparation of 6-(n-Butyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6)



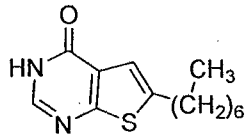
^{1}H NMR (200 MHz, $CDCl_3$): *δ* 0.96 (t, *J* = 7 Hz, 3H), 1.32-1.53 (m, 2H), 1.64-1.81 (m, 2H), 2.88 (t, *J* = 8 Hz, 2H), 7.17 (s, 1H), 8.05 (s, 1H).

[0057] Example 7: 6-(n-Hexyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7)



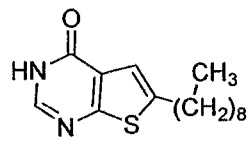
Nature: Dark brown solid; **MP:** 181 °C; **Yield:** 84.6 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.90 (t, J = 6 Hz, 3H), 1.21-1.50 (m, 6H), 1.61-1.86 (m, 2H), 2.87 (t, J = 8 Hz, 2H), 7.15 (s, 1H), 8.03 (s, 1H), 12.80 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.9, 22.5, 28.8, 30.5, 30.9, 31.6, 117.4, 124.8, 143.0, 145.0, 159.6, 163.9; **IR** (Chloroform): 3388, 1664 cm^{-1}; **MS** (ESI) *m/z*: 237.1471 (M + 1).

[0058] Example 8: 6-(n-Heptyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (8)



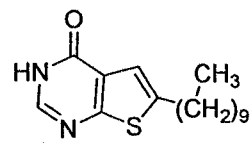
Nature: Off-white solid; **MP:** 170-171 °C; **Yield:** 91.5 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.89 (t, J = 6 Hz, 3H), 1.26-1.37 (m, 8H), 1.69-1.76 (m, 2H), 2.87 (t, J = 6 Hz, 2H), 7.17 (s, 1H), 8.05 (s, 1H), 12.82 (bs, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.7, 22.2, 28.6 (2C), 30.3, 30.6, 31.3, 117.1, 124.5, 142.6, 144.6, 159.6, 164.1; **IR** (Chloroform): 3319, 1664 cm^{-1}.

[0059] Example 9: 6-(n-Nonyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (9)



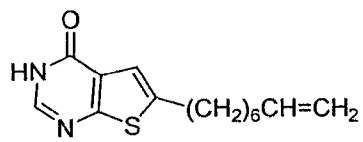
Nature: White solid; **MP:** 167 °C; **Yield:** 88.0 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.91 (t, J = 6 Hz, 3H), 1.14-1.55 (m, 12H), 1.65-1.92 (m, 2H), 2.89 (t, J = 6 Hz, 2H), 7.19 (s, 1H), 8.09 (s, 1H), 12.96 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.3, 21.9, 28.2, 28.5 (2C), 28.7, 29.9, 30.3, 31.1, 116.8, 124.2, 142.4, 144.4, 159.0, 163.4; **IR** (Chloroform): 3319, 1663 cm^{-1}.

[0060] Example 10: 6-(n-Decyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (10)



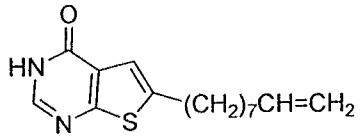
Nature: Off-white solid; **MP:** 158 °C; **Yield:** 85.1 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.88 (t, J = 6 Hz, 3H), 1.24-1.35 (m, 14H), 1.66-1.80 (m, 2H), 2.86 (t, J = 6 Hz, 2H), 7.17 (s, 1H), 8.15 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 15.3, 23.9, 30.2, 30.5 (2C), 30.7, 30.8, 31.8, 32.2, 33.1, 118.7, 142.3, 145.7, 146.3, 158.7, 163.7; **IR** (Chloroform): 3386, 1677 cm^{-1}.

[0061] Example 11: 6-(Oct-7-en-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (11)



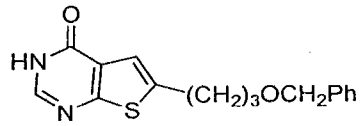
[0062] **Nature:** White solid; **MP:** 156 °C; **Yield:** 78.5 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.24-1.45 (m, 6H), 1.65-1.76 (m, 2H), 2.00-2.11 (m, 2H), 2.86 (t, *J* = 6 Hz, 2H), 4.90-5.09 (m, 2H), 5.70-5.90 (m, 1H), 7.15 (s, 1H), 8.05 (s, 1H), 12.79 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 28.5 (3C), 30.4, 30.7, 33.5, 114.1, 117.3, 124.7, 138.7, 143.0, 144.6, 159.4, 164.1; **IR** (Chloroform): 3382, 1666 cm^{-1}.

Example 12: 6-(Non-8-en-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (12)



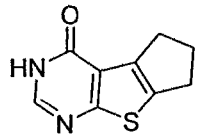
Nature: Grey solid; **MP:** 130-132 °C; **Yield:** 74.7 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.24-1.36 (m, 8H), 1.66-1.80 (m, 2H), 1.99-2.10 (m, 2H), 2.87 (t, *J* = 6 Hz, 2H), 4.91-5.04 (m, 2H), 5.71-5.90 (m, 1H), 7.17 (s, 1H), 8.16 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 28.6, 28.7, 28.8, 28.9, 30.4, 30.8, 33.5, 114.0, 117.3, 124.7, 138.9, 142.9, 144.7, 159.5, 164.1; **IR** (Chloroform): 3375, 1665 cm^{-1}.

[0063] Example 13: 6-(3-Benzyloxypropyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (13)



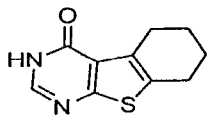
Nature: Pale yellow solid; **MP:** 161-163 °C; **Yield:** 78.7 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.91-2.12 (m, 2H), 3.01 (t, *J* = 6 Hz, 2H), 3.53 (t, *J* = 6 Hz, 2H), 4.51 (s, 2H), 7.17 (s, 1H), 7.33 (bs, 5H), 8.03 (s, 1H), 12.84 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$, CCl_4): δ 27.3, 31.0, 68.6, 73.0, 117.9, 124.8, 127.6 (3C), 128.4 (2C), 138.2, 143.0, 143.8, 159.8, 164.6; **IR** (Chloroform): 3318, 1665, 1100 cm^{-1}.

[0064] Example 14: 3,5,6,7-Tetrahydrocyclopenta[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (14)



Nature: Grey solid; **MP:** 249 °C; **Yield:** 81.4 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.21-1.50 (m, 2H), 2.12-2.68 (m, 2H), 2.73-2.87 (m, 2H), 8.02 (s, 1H), 12.80 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 25.6, 28.9, 31.4, 117.7, 125.1, 139.1, 145.9, 158.6, 165.4; **IR** (Chloroform): 3369, 1662 cm^{-1}.

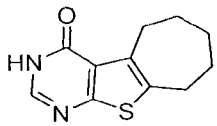
[0065] Example 15: 5,6,7,8-Tetrahydrobenzothieno[2,3-*d*]pyrimidin-4(3*H*)-one (15)



Nature: Yellow solid; **MP:** 253 °C; **Yield:** 89.4 %; **^{1}H NMR** (200 MHz, $CDCl_3$ + CCl_4 + DMSO-d_6): δ 1.36-1.52 (m, 4H), 2.31-2.40 (m, 2H), 2.51-2.62 (m, 2H), 7.45 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$ + CCl_4 + DMSO-d_6): δ 22.2, 22.9, 25.0, 25.7, 123.3, 131.3, 132.8, 144.1, 158.5, 163.0; **IR** (Chloroform): 3271, 1662 cm^{-1}.

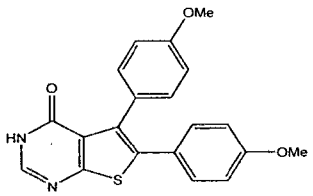
[0066] Example 16: 3,5,6,7,8,9-Hexahydro-4H-cyclohepta[4,5]thieno[2,3-*d*]pyrimidin-4-one

(16)



^{1}H NMR (200 MHz, $CDCl_3$): δ 1.70-1.79 (m, 4H), 1.86-2.00 (m, 2H), 2.88 (t, J = 5 Hz, 2H), 3.36 (t, J = 5 Hz, 2H), 7.98 (s, 1H), 12.24 (s, 1H).

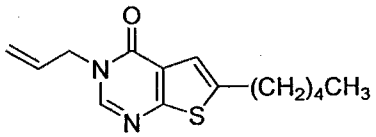
[0067] Example 17: Preparation of 5,6-bis(4-methoxyphenyl)thieno[2,3-d]pyrimidin-4(3H)-one (17)



^{1}H NMR (200 MHz, $CDCl_3$ + DMSO-d_6): δ 3.71 (s, 3H), 3.75 (s, 3H), 6.71-6.83 (m, 4H), 6.95-7.17 (m, 4H), 7.97 (s, 1H), 12.25 (s, 1H).

The 3-substituted thieno[2,3-*d*]pyrimidin-4(3H)-ones were prepared from the corresponding thieno[2,3-*d*]pyrimidin-4(3H)-ones by reaction with required (un)substituted alkyl halides in presence of base.

[0068] Example 18: Preparation of 3-allyl-6-pentylthieno[2,3-*d*] pyrimidin-4(3*H*)-one (18)



In a two-necked round bottom flask thieno[2,3-d] pyrimidin-4(3H)-one compound **4** (9 gm, 0.0404 moles), K_2CO_3 (13.85 gm, 0.0404 moles) and TBAB (6.44 g, 0.02 mol) were taken and the mixture was flushed with argon. Allyl bromide (1.23 ml, 0.0144 moles) in ethyl acetate (100 ml) was added by cannula. This reaction mixture was refluxed at 80 ^{0}C for 12 hr. Reaction was monitored by TLC (ethyl acetate- pet ether, 50:50). After completion of reaction, water (200 ml) was added to reaction. It was then extracted with ethyl acetate (3 X 200 ml). The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain, 5-allyl-2-pentylthieno[2,3-d]pyrimidin-4(5H)-one (**18**) as white powder, m.p. 64 ^{0}C (7.81 g, 73%).

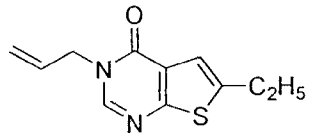
IR ($CHCl_3$): 2927, 1670, 1570, 1448 cm^{-1}.

^{1}**H NMR** (200 MHz, $CDCl_3$): δ 0.89 (t, J= 6 Hz, 3H), 1.30-1.39 (m, 4H), 1.71 (quintet, *J* = 8 Hz, 2H), 2.83 (t, *J* = 8 Hz, 2H), 4.61-4.65 (m, 2H), 5.19-5.32 (m, 2H), 5.79-6.05 (m, 1H), 7.15 (s, 1H), 7.92 (s, 1H).

^{13}**C NMR** (50 MHz, $CDCl_3$): δ 13.90, 22.27, 30.53, 30.67, 31.01, 48.06, 118.24, 118.80, 124.67, 131.93, 144.75, 145.30, 156.97, 162.33.

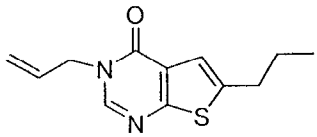
[0069] Thieno[2,3-d] pyrimidin-4(3H)-ones **19** and **20** were prepared from **2** and **3** respectively by using procedure similar to 3-allyl-6-pentylthieno[2,3-*d*] pyrimidin-4(3*H*)-one **(18).**

[0070] Example 19: 3-Allyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one (19)



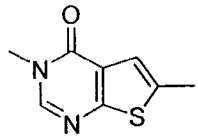
^{1}**H NMR (200 MHz, $CDCl_3$):** δ 1.35 (t, J = 7 Hz, 3H), 2.88 (q, J = 8 Hz, 2H), 4.60-4.68 (m, 2H), 5.18-5.34 (m, 2H), 5.87-6.10 (m, 1H), 7.18 (s, 1H), 7.93 (s, 1H).

[0071] Example 20: 3-Allyl-6-propylthieno[2,3-d]pyrimidin-4(3H)-one (20)



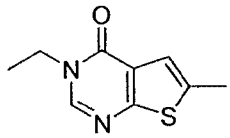
^{1}**H NMR (200 MHz, $CDCl_3$):** δ 0.99 (t, J = 7 Hz, 3H), 1.62-1.88 (m, 2H), 2.82 (t, J =7 Hz, 3H), 4.61–4.66 (m, 2H), 5.19–5.33 (m, 2H), 5.88–6.08 (m, 1H), 7.16 (s, 1H), 7.92 (s, 1H).

[0072] Example 21: 3,6-dimethylthieno[2,3-*d*]pyrimidin-4(3H)-one (21)



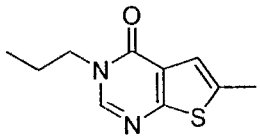
^{1}**H NMR (200 MHz, $CDCl_3$):** δ 2.54 (s, 3H), 3.59 (s, 3H), 7.13 (s, 1H), 7.96 (s, 1H).

[0073] Example 22: 3-Ethyl-6-methylthieno[2,3-*d*]pyrimidin-4(3H)-one (22)



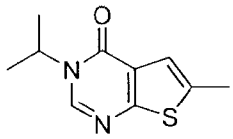
^{1}**H NMR (200 MHz, $CDCl_3$):** δ 1.41 (t, J= 7 Hz, 3H), 2.54 (s, 3H), 4.07 (q, J= 7 Hz, 2H), 7.14 (s, 1H), 7.95 (s, 1H).

[0074] Example 23: 6-Methyl-3-propylthieno[2,3-d]pyrimidin-4(3H)-one (23)



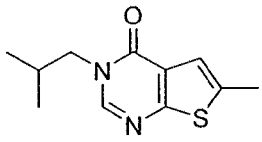
^{1}**H NMR (200 MHz, $CDCl_3$):** δ 0.99 (t, J= 4 Hz, 3H), 1.72-1.82 (m, 2H), 2.54 (s, 3H), 3.96 (t, J= 4 Hz, 2H), 7.13 (s, 1H), 8.05 (s, 1H).

[0075] Example 24: 3-Isopropyl-6-methylthieno[2,3-d]pyrimidin-4(3H)-one (24)



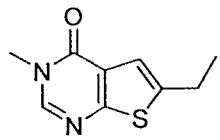
[0076] ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.46 (d, J= 7 Hz, 6H), 2.54 (s, 3H), 5.12-5.30 (m, 1H), 7.13 (s, 1H), 8.00 (s, 1H).

[0077] Example 25: 3-Isobutyl-6-methylthieno[2,3-d]pyrimidin-4(3H)-one (25)



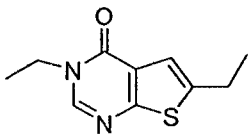
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.97 (d, J= 8 Hz, 6H), 2.10-2.28 (m, 1H), 2.54 (s, 3H), 3.80 (d, J= 8 Hz, 2H), 7.13 (s, 1H), 7.88 (s, 1H).

[0078] Example 26: 6-Ethyl-3-methylthieno[2,3-d]pyrimidin-4(3H)-one (26)



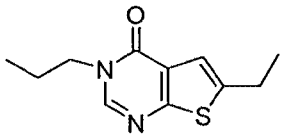
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (t, J= 8 Hz, 3H), 2.87 (q, J= 8 Hz, 2H), 3.58 (s, 3H), 7.15 (s, 1H), 7.95 (s, 1H).

[0079] Example 27: 3,6-Diethylthieno[2,3-d]pyrimidin-4(3H)-one (27)



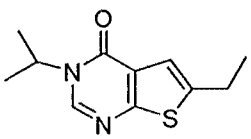
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (t, J =8 Hz, 3H), 1.41 (t, J = 7 Hz, 3H), 2.88 (q, J= 8 Hz, 2H), 4.07 (q, J = 7 Hz, 2H), 7.17 (s, 1H), 7.95 (s, 1H).

[0080] Example 28: 6-Ethyl-3-propylthieno[2,3-d]pyrimidin-4(3H)-one (28)



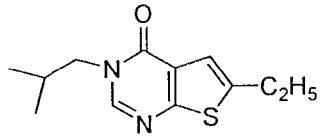
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99 (t, J = 8 Hz, 3H), 1.35 (t, J = 8 Hz, 3H), 1.72-1.92 (m, 2H), 2.88 (q, J = 8 Hz, 2H), 3.97 (t, J = 7 Hz, 2H), 7.17 (s, 1H), 7.93 (s, 1H).

[0081] Example 29: 6-Ethyl-3-isopropylthieno[2,3-d]pyrimidin-4(3H)-one (29)



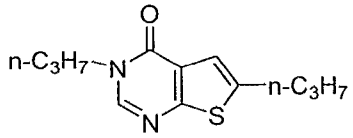
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.29 (t, J = 7 Hz, 3H), 1.40 (d, J = 7 Hz, 6H), 2.82 (q, J =7 Hz, 2H), 5.07-5.25 (m, 1H), 7.10 (s, 1H), 7.97 (s, 1H).

[0082] Example 30: 6-Ethyl-3-isobutylthieno[2,3-d]pyrimidin-4(3H)-one (30)



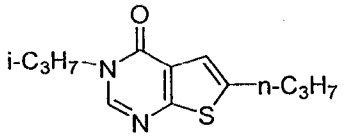
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99 (d, J =7 Hz, 6H), 1.36 (t, J = 8 Hz, 3H), 2.14-2.25 (m, 1H), 2.88 (q, J = 8 Hz, 2H), 3.81 (d, J = 8 Hz, 2H), 7.17 (s, 1H), 7.88 (s, 1H).

[0083] Example 31: 3,6-Dipropylthieno[2,3-d]pyrimidin-4(3H)-one (31)



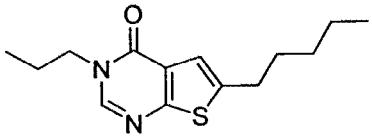
^{1}H NMR (200 MHz, $CDCl_3$): δ0.98 (t, J = 7 Hz, 6H), 1.62-1.92 (m, 4H), 2.81 (t, J = 7 Hz, 2H), 3.96 (t, J = 7 Hz, 2H), 7.15 (s, 1H), 7.92 (s, 1H).

[0084] Example 32: 3-Isopropyl-6-propylthieno[2,3-d]pyrimidin-4(3H)-one (32)



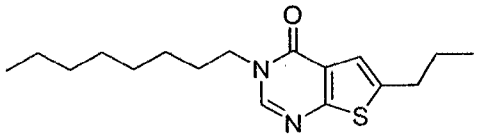
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99 (t, J =7 Hz, 3H), 1.49 (d, J =7 Hz, 6H), 1.63-1.85 (m, 2H), 2.82 (t, J = 8 Hz, 2H), 5.13-5.31 (m, 1H), 7.15 (s, 1H), 8.01 (s, 1H).

[0085] Example 33: 6-Pentyl-3-propylthieno[2,3-d]pyrimidin-4(3H)-one (33)



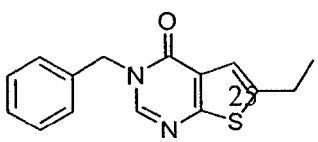
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88-1.05 (m, 6H), 1.30-1.42 (m, 4H), 1.66-1.90 (m, 5H), 2.84 (t, J= 7 Hz, 2H), 3.98 (t, J= 7 Hz, 2H), 7.16 (s, 1H), 8.01 (s, 1H).

[0086] Example 34: 3-Octyl-6-propylthieno[2,3-d]pyrimidin-4(3H)-one (34)



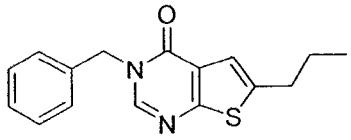
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.87 (t, J = 7 Hz, 3H), 1.00 (t, J = 7 Hz, 3H), 1.12-1.44 (m, 10 H), 1.64-1.85 (m, 4H), 2.82 (t, J = 7 Hz, 2H), 3.99 (t, J = 7 Hz, 2H), 7.16 (s, 1H), 7.93 (s, 1H).

[0087] Example 35: 3-Benzyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one (35)



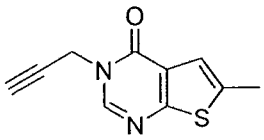
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (t, J= 7 Hz, 3H), 2.87 (q, J= 7 Hz, 2H), 5.21 (s, 2H), 7.19 (s, 1H), 7.29-7.38 (m, 5H), 8.01 (s, 1H).

[0088] Example 36: 3-Benzyl-6-propylthieno[2,3-d]pyrimidin-4(3H)-one (36)



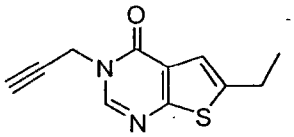
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, J = 7 Hz, 3H), 1.66-1.88 (m, 2H), 2.82 (t, J =7 Hz, 2H), 5.21 (s, 2H), 7.17 (s, 1H), 7.35 (s, 5H), 8.02 (s, 1H).

[0089] Example 37: 6-Methyl-3-(prop-2-yn-1-yl)thieno[2,3-d]pyrimidin-4(3H)-one (37)



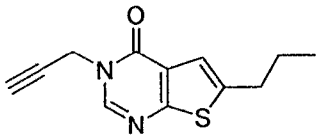
^{1}H NMR (200 MHz, $CDCl_3$): δ 2.42-2.50 (m, 4H), 4.81 (d, J= 1 Hz, 2H), 7.14 (s, 1H), 8.25 (s, 1H).

[0090] Example 38: 6-Ethyl-3-(prop-2-yn-1-yl)thieno[2,3-d]pyrimidin-4(3H)-one (38)



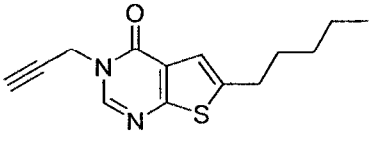
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (t, J = 8 Hz, 3H), 2.51 (t, J = 3 Hz, 1H), 2.89 (q, J = 8 Hz, 2H), 4.82 (d, J = 3 Hz, 2H), 7.17 (s, 1H), 8.24 (s, 1H).

[0091] Example 39: 3-(Prop-2-yn-1-yl)-6-propylthieno[2,3-d]pyrimidin-4(3H)-one (39)



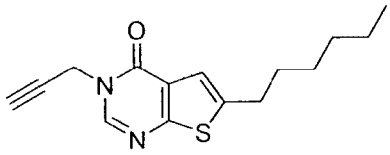
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99 (t, J= 7 Hz, 3H), 1.74 (q, J= 7 Hz, 2H), 2.51 (t, J= 3 Hz, 1H), 2.01 (t, J= 7 Hz, 2H), 4.81 (d, J= 2 Hz, 2H), 7.17 (s, 1H), 8.25 (s, 1H).

[0092] Example 40: 3-(Prop-2-yn-1-yl)-6-pentylthieno[2,3-d]pyrimidin-4(3H)-one (40)



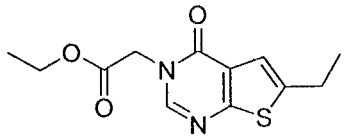
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, J = 7 Hz, 3H), 1.26–1.45 (m, 4H), 1.63-1.72 (m, 2H), 2.51 (t, J =3 Hz, 1H), 2.84 (t, J = 7 Hz, 2H), 4.81 (d, J =3 Hz, 2H), 7.16 (s, 1H), 8.23 (s, 1H).

[0093] Example 41: 3-(Prop-2-yn-1-yl)-6-hexylthieno[2,3-d]pyrimidin-4(3H)-one (41)



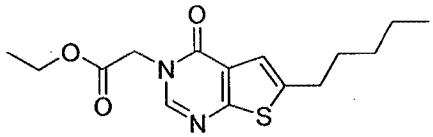
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, J = 7 Hz, 3H), 1.25–1.42 (m, 6H), 1.71 (quintet, J=7 Hz, 2H), 2.51 (t, J =3 Hz, 1H), 2.84 (t, J = 7 Hz, 2H), 4.81 (d, J =3 Hz, 2H), 7.16 (s, 1H), 8.24 (s, 1H).

[0094] Example 42: Ethyl 2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)acetate (42)



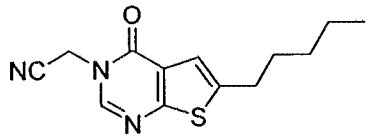
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.30 (t, J= 7 Hz, 3H), 1.35 (t, J= 7 Hz, 3H), 2.88 (q, J= 7 Hz, 2H), 4.26 (q, J= 7 Hz, 2H), 4.71 (s, 2H), 7.17 (s, 1H), 7.90 (s, 1H).

[0095] Example 43: Ethyl 2-(6-pentyl-4-oxothieno [2,3-d]pyrimidin-3(4H)-yl)acetate (43)



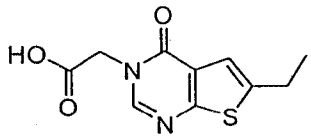
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.83 (t, J = 7 Hz, 3H), 1.18-1.35 (m, 7H), 1.60-1.74 (m, 4H), 2.84 (t, J =7 Hz, 2H), 4.28 (q, J =7 Hz, 2H), 4.71 (s, 1H), 7.15 (s, 1H), 7.90 (s, 1H).

[0096] Example 44: Preparation of 2-(4-oxo-6-pentylthieno[2,3-d]pyrimidin-3(4H)-yl)acetonitrile (44)



^{1}H NMR (200 MHz, $CDCl_3$): δ0.91 (t, J = 7 Hz, 3H), 1.31-1.41 (m, 4H), 1.65-1.78 (m, 2H), 2.86 (t, J=7 Hz, 2H), 4.92 (s, 2H), 7.18 (s, 1H), 8.05 (s, 1H).

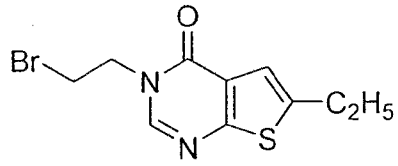
[0097] Example 45: Preparation of 2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)acetic acid (45)



45 was prepared from compound **42** by stirring with ethanolic sodium hydroxide at room temperature.

^{1}H NMR (200 MHz, $CDCl_3$+MeOH-d_4): δ 1.15 (t, J= 8 Hz, 3H), 2.68 (q, J= 8 Hz, 2H), 4.54 (s, 2H), 6.94 (s, 1H), 7.83 (s, 1H).

[0098] Example 46: Preparation of 3-(2-bromoethyl-6-ethylthieno[2,3-*d*]primidin-4(3*H*)-one (46):



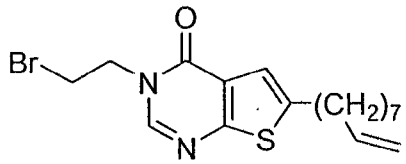
In a two-necked round bottom flask, potassium carbonate was dried by heating (2.07 g, 0.066 mol) and thieno[2,3-d] pyrimidin-4(3H)-one **2** (1.00 g, 0.022 mol) were taken and DMF (20 ml) was added. Mixture was flushed with argon. Further the reaction mixture was stirred at room temperature for 30 min. Dibromoethane (2.086 ml, 0.044 mol) was added dropwise for 10 min. Reaction was monitored by TLC (ethyl acetate-pet ether 40:60). After 16 hrs reaction mixture was quenched by adding water, extracted with DCM. The organic layer was dried over Na_2SO_4 concentrated and purified by column chromatography to obtain 3-(2-bromoethyl-6-propylthieno [2,3-*d*]primidin-4(3*H*)-one **46** as white solid. 2.4 g (60%).

IR ($CHCl_3$): 3019, 1674, 1574, 1538, 1430 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.36 (t, J = 7 Hz, 3H), 2.90 (q, J = 7 Hz, 2H), 3.77 (t, J = 6 Hz, 2H), 4.38 (t, J = 6 Hz, 2H), 7.18 (s, 1H), 7.99 (s, 1H).

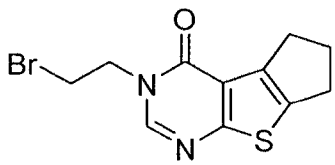
^{13}C NMR (50 MHz, $CDCl_3$): δ 15.29, 24.01, 29.82, 48.75, 117.38, 124.58, 145.80, 146.46, 157.06, 162.74.

[0099] Example 47: 3-(2-Bromoethyl)-6-(non-8-enyl)thieno[2,3-d]pyrimidin-4(3H)-one (47)



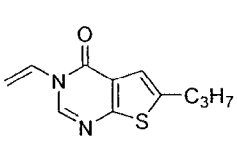
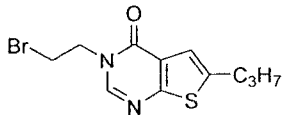
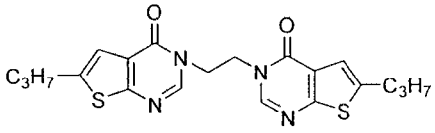
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20-1.46 (m, 8H), 1.62-1.80 (m, 2H), 1.96-2.13 (m, 2H), 2.85 (t, J= 8 Hz, 2H), 3.77 (t, J = 6 Hz, 2H), 4.38 (t, J = 6 Hz, 2H), 4.88-5.06 (m, 2H), 5.70-5.92 (m, 1H), 7.16 (s, 1H), 8.00 (s, 1H).

[00100] Example 48: 3-(2-Bromoethyl)-3,5,6,7-tetrahydro-4H-cyclopenta[4,5]thieno[2,3-d]pyrimidin-4-one (48)

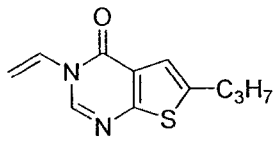


^{1}H NMR (200 MHz, $CDCl_3$): δ 2.40-2.57 (m, 2H), 2.93-3.13 (m, 4H), 3.77 (t, J = 6 Hz, 2H), 4.28-4.41 (m, 2H), 7.94 (s, 1H).

[00101] **Example 49: Preparation of 6-propyl-3-vinylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (49), 3-(2-bromoethyl)-6-propylthieno[2,3-*d*]primidin-4(3*H*)-one (50) and 3,3'-(ethane-1,2-diyl)bis(6-propylthieno[2,3-d]pyrimidin-4(3H)-one) (51)**


and

and


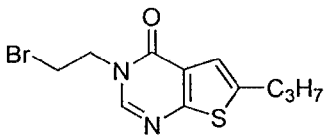
In a two-necked round bottom flask, potassium carbonate (6.38 g, 0.0463 mol) was taken and dried by heating under vacuum, thieno[2,3-d] pyrimidin-4(3H)-one **3** (3 g, 0.0154 mol) and DMF (120 ml) were added under argon. This reaction mixture was stirred at room temp for 30 min. Dibromoethane (2.18 ml, 0.0309 mol) was added dropwise over 10 min. Reaction was monitored by TLC (ethyl acetate-pet ether 40:60). After 16 h, reaction mixture was quenched by adding water and extracted with DCM. The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain 6-propyl-3-vinylthieno [2,3-*d*]pyrimidin-4(3*H*)-one **49** as white solid; 0.5 g (16.66 %);



IR ($CHCl_3$):3418, 2918, 1678, 1566, 1537, 1249, 775, cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J*=8Hz 3H), 1.67-181 (m, 2H), 2.83 (t, *J*=8Hz, 2H), 5.24 (dd, 1H), 5.45 (dd, 1H), 7.18 (s, 1H), 7.35-7.48 (dd, 1H) 8.16 (s, 1H).

Further elution afforded 3-(2-bromoethyl)-6-propylthieno[2,3-*d*]primidin-4(3*H*)-one **50** as white solid; 1.8 g (60%); M. P. 94 °C

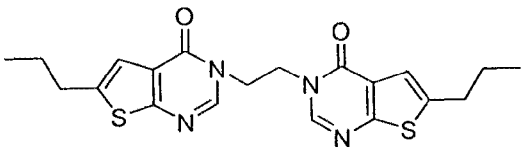


IR ($CHCl_3$): 2925, 1676, 1571, 1429 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J*= 7 Hz, 3H), 1.70-1.84 (m, 2H), 2.83 (t, *J*= 8 Hz, 2H), 3.76 (t, *J*= 6 Hz, 2H), 4.38 (t, *J*= 6 Hz, 2H), 7.16 (s, 1H), 7.99 (s, 1H).

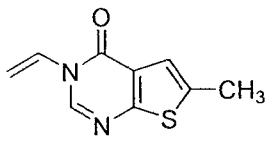
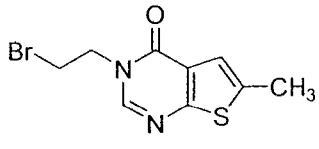
^{13}C NMR (50 MHz, $CDCl_3$): δ 13.54, 24.32, 29.80, 32.64, 48.76, 118.20, 124.58, 144.79, 145.75, 157.06, 162.83.

Further elution afforded 3,3'-(ethane-1,2-diyl)bis(6-propylthieno[2,3-d]pyrimidin-4(3H)-one) **(51)**



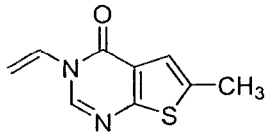
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.01 (t, J = 7 Hz, 6H), 1.65-1.85 (m, 4H), 2.83 (t, J = 7 Hz, 4H), 4.42 (s, 4H), 7.16 (s, 2H), 7.69 (s, 2H).

[00102] Example 50: Preparation of 6-methyl-3-vinylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (52) and 3-(2-bromoethyl)-6-methylthieno[2,3-*d*]primidin-4(3*H*)-one (53) :


and


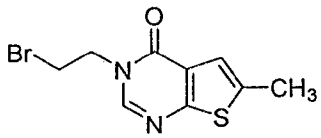
These compounds were prepared by reacting compound **1** with dibromoethane using procedure described above.

[00103] Example 51: 6-Methyl-3-vinylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (52):



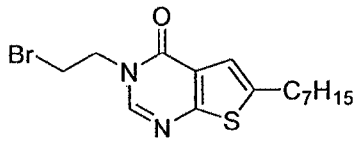
^{1}H NMR (200 MHz, $CDCl_3$): δ 2.55 (s, 3H), 5.25 (d, J = 8 Hz, 1H), 5.46 (d, J = 16 Hz, 1H), 7.16 (s, 1H), 7.38-7.44 (m, 1H), 8.16 (s, 1H).

[00104] Example 52: 3-(2-Bromoethyl)-6-methylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (53) :



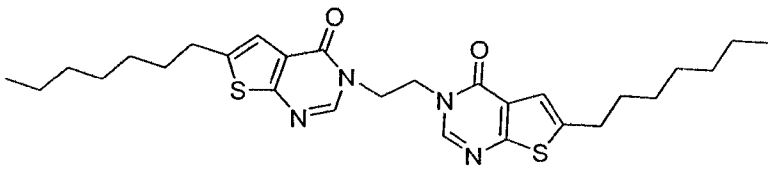
^{1}H NMR (200 MHz, $CDCl_3$): δ 2.55 (s, 3H), 3.76 (t, J = 6 Hz, 2H), 4.38 (t, J = 6 Hz, 2H), 7.13 (s, 1H), 7.99 (s, 1H).

[00105] Example 53: 3-(2-Bromoethyl-6-heptylthieno[2,3-*d*]primidin-4(3*H*)-one (54):



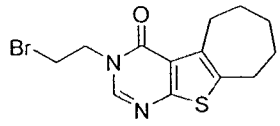
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, J =7 Hz, 3H), 1.27-1.35 (m, 8H), 1.71(t, J = 7 Hz, 2H), 2.84 (t, J = 7 Hz,2H), 3.76(t, J = 5 Hz,2H), 4.38(t, J = 5 Hz,2H) 7.15(s, 1H), 7.99 (s,1H).

[00106] Example 54: 3,3'-(Ethane-1,2-diyl)bis(6-heptylthieno[2,3-d]pyrimidin-4(3H)-one) (55)



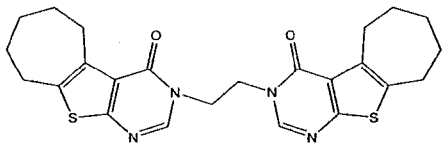
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (s, 6H), 1.12-1.50 (m, 16H), 1.62-1.90 (m, 4H), 2.85 (t, *J* = 7 Hz, 4H), 4.43 (s, 4H), 7.16 (s, 2H), 7.70 (s, 2H).

[00107] Example 55: 3-(2-Bromoethyl)-3,5,6,7,8,9-hexahydro-4H-cyclohepta[4,5]thieno[2,3-d] pyrimidin-4-one (56)



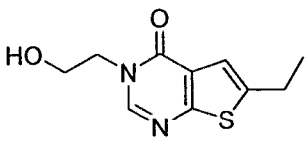
^{1}H NMR (200 MHz, $CDCl_3$): *δ* 1.68-1.72 (m, 4H), 1.88-1.91 (m, 2H), 2.81-2.86 (m, 2H), 3.30-3.33 (m, 2H), 3.75 (t, J = 5 Hz, 2H), 4.34 (t, J = 5 Hz, 2H), 7.95 (s, 1H).

[00108] Example 56: 3,3'-(Ethane-1,2-diyl)bis(6-heptylthieno[2,3-d]pyrimidin-4(3H)-one) (57)



^{1}H NMR (200 MHz, $CDCl_3$): *δ* 1.55-1.77 (m, 8H), 1.80-2.01 (m, 4H), 2.83-2.90 (m, 4H), 3.31-3.38 (m, 4H), 4.37 (br s, 4H), 7.69 (s, 2H); **MS** (AB Sciex TOF/TOF, m/z): 467.2186 (M+1), 489.2083 (M+Na).

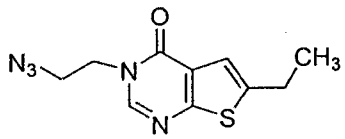
[00109] Example 57: Preparation of 6-ethyl-3-(2-hydroxyethyl)thieno[2,3-d]pyrimidin-4(3H)-one (58)



Compound **58** was prepared by stirring compound **46** with potassium carbonate in DMF at room temperature.

^{1}H NMR (200 MHz, $CDCl_3$): *δ* 1.38 (t, *J*= 7 Hz, 3H), 2.89 (q, *J*= 7 Hz, 2H), 3.18 (s, 1H), 4.01 (t, *J*= 5 Hz, 2H), 4.17 (t, *J*= 5 Hz, 2H), 7.10 (s, 1H), 8.02 (s, 1H).

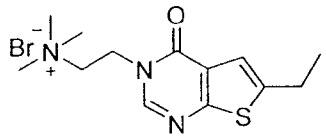
[00110] Example 58: 3-(2-Azidoethyl)-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one (59)



Compound **59** was prepared from compound **46** by reaction with sodium azide in DMF at 80°C.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.36 (t, J = 7 Hz, 3H), 2.90 (q, *J* = 7 Hz, 2H), 3.76 (t, *J* = 5 Hz, 2H), 4.13 (t, *J* = 5 Hz, 2H), 7.17 (s, 1H), 7.95 (s, 1H).

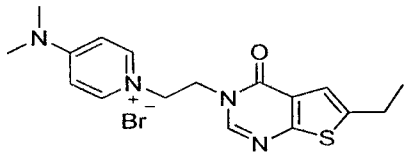
[00111] Example 59: Preparation of 2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)-N,N,N-trimethylethan-1-aminium bromide (60)



A mixture of 3-(2-bromoethyl)-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one **46** (0.4 gm, 1.39 mmoles), methanol (4 ml) and liquid trimethyl amine (0.821 gm, 13.9 mmoles) was taken in a sealed tube with screw cap and stirred in oil bath at 50°C for 12 h. Methanol was then evaporated with the help of rotavapor. Then pet ether was added in reaction mixture and it was filtered through Whatman filter paper with the help of Buchner funnel to obtain 2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)-N,N,N-trimethylethan-1-aminium bromide **(60)** as white solid (240 mg, 49.8%).

^{1}H NMR (200 MHz, DMSO-d_6): δ 1.26 (t, J= 8 Hz, 3H), 2.86 (q, J= 8 Hz, 2H), 3.67 (t, J= 6 Hz, 2H), 4.45 (t, J= 6 Hz, 2H), 7.15 (s, 1H), 8.48 (s, 1H).

[00112] Example 60: Preparation of 4-(dimethylamino)-1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)pyridin-1-ium bromide (61)

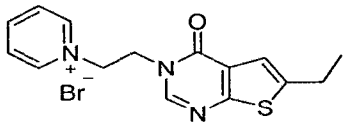


3-(2-Bromoethyl)-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one **46** (0.400 gm, 1.39 mmoles) was taken in two neck round bottom flask. Then methanol (5 ml) was added in it under dry condition. Then 4-dimethylaminopyridine (0.170 gm, 1.39 mmoles) was added in reaction mixture. Then the reaction mixture was stirred in oil bath at 50°C for 12 h. Reaction was monitored by TLC.

Methanol was evaporated with the help of rotavapor. It was then diluted with ethyl acetate-pet ether (50:50), organic layer decanted, ethyl acetate (15 ml) was added and the reaction mixture was filtered through Whatman filter paper with the help of Buchner funnel to get 4-(dimethylamino)-1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)pyridin-1-ium bromide **(61)** as a white solid (416 mg, 80%).

^{1}H NMR (200 MHz, MeOH-d_4): δ 1.34 (t, J= 7 Hz, 3H), 2.95 (q, J= 7 Hz, 2H), 3.23 (s, 6H), 4.52-4.60 (m, 4H), 6.96 (d, J= 6 Hz, 2H), 7.10 (s, 1H), 8.08 (d, J= 6 Hz, 2H), 8.12 (s, 1H).

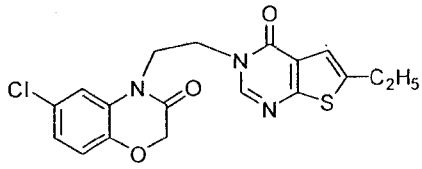
[00113] Example 61: Preparation of 1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)pyridin-1-ium bromide (62)



Compound **62** was prepared by the procedure described for 4-(dimethylamino)-1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)pyridin-1-ium bromide **(61).**

^{1}H NMR (200 MHz MeOH-d_4): δ 1.36 (t, *J*= 7 Hz, 3H), 2.93 (q, *J*= 7 Hz, 2H), 4.76 (t, *J* = 6 Hz 2H), 5.14 (t, *J*= 6 Hz, 2H), 7.06 (s, 1H), 8.15 (t, *J*= 7 Hz, 1H), 8.31 (s, 1H), 8.68 (t, *J*= 7 Hz, 1H), 9.05 (d, *J*= 5Hz,1H).

[00114] Example 62: Preparation of 6-chloro-4-(2-(6-ethyl-4-oxothieno[2,3-*d*]pyrimidin-3(4*H*)-yl)ethyl)-2*H*-benzo[b][1,4]oxazin-3(4*H*)-one (63) :

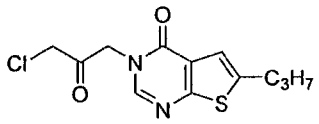


In a two-necked round bottom flask, potassium carbonate (0.5 g, 0.00174 mol) was taken and dried by heating, tetrabutylammonium bromide (0.56 g, 0.00174 mol), 6-chloro-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (0.44 g, 0.00264 mol) and DMF (15 ml) were added. Mixture was flushed with argon. The reaction mixture thus obtained was stirred at room temp for 30 min. 3-(2-Bromoethyl)-6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one **46** (0.5 g, 0.00174 mol) in DMF was added dropwise followed by KI (0.26 g, 0.00174 mol). Reaction was monitored by TLC (ethyl acetate-pet ether 40:60). After 24 hrs, reaction mixture was quenched by adding water, extracted with DCM, the organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain 6-chloro-4-(2-(6-ethyl-4-oxothieno[2,3-*d*]pyrimidin-3(4*H*)-yl)ethyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one **63** as white solid; 0.21g (42%).

IR ($CHCl_3$): 3019, 1662, 1572, 1329, 1217, 770 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.41 (t, *J*= 8 Hz, 3H), 2.93 (q, *J*= 8 Hz, 2H), 3.43 (s, 2H), 4.29 (t, *J*= 6 Hz, 2H), 4.43 (t, *J*= 6 Hz, 2H), 7.09-7.14 (m, 2H), 7.27-7.31 (m, 2H), 7.89 (s, 1H).

[00115] Example 63: Preparation of 3-(3-chloro-2-oxopropyl)-6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (64)



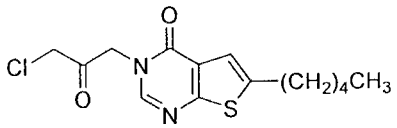
In two necked round flask, thieno[2,3-*d*]pyrimidin-4(3*H*)-one **3** (2.00 g, 0.0093 mol) and K_2CO_3 (27.5 g, 0.2 mol) were taken and the mixture was flushed with argon. Dichloroacetone (6.8 g, 0.053 mol) dissolved in CH_3CN (10 ml) was added by cannula. Further the reaction mixture was stirred at 70 ^{0}C for 6 hr. Reaction was monitored by TLC. After completion of reaction, acetonitrile was evaporated, ethyl acetate was added and the reaction mixture was filtered through Buckner funnel, ethyl acetate layer was concentrated and purified by column chromatography to obtain 3-(3-chloro-2-oxopropyl)-6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (**64**) as yellow solid; 1.43 g (47.6 %).

IR ($CHCl_3$): 3684, 3020, 2400, 1676, 1523, 1423, 669 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J* = 7 Hz, 3H), 1.65-1.85 (m, 2H), 2.83 (t, *J* = 7 Hz, 2H), 4.30 (s, 2H), 4.99 (s, 2H), 7.14 (s, 1H), 7.85 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 18.28, 29.02, 34.27, 51.68, 57.02, 122.91, 128.90, 149.09, 151.43, 161.52, 200.56.

[00116] Example 64: Preparation of 3-(3-chloro-2-oxopropyl)-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (65)



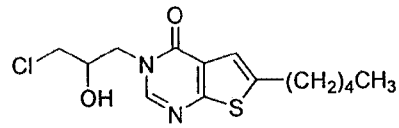
In a two-necked round bottom flask, thieno[2,3-d]pyrimidin-4(3H)-one **4** (1 gm, 4.5 mmoles) and K_2CO_3 (14 gm, 101 mmole) were taken and the mixture was flushed with argon. Dichloroacetone (3 gm, 26.98 mmoles) dissolved in CH_3CN (80 ml) was added by cannula. Further the reaction mixture was stirred at 70 ^{0}C for 6 hr. Reaction was monitored by TLC (ethyl acetate- pet ether, 30:70). After completion of reaction, CH_3CN was evaporated, ethyl acetate was added (50 ml) and the reaction mixture was filtered through Buckner funnel, ethyl acetate layer was concentrated and purified by column chromatography to obtain 3-(3-chloro-2-oxopropyl)-6-pentylthieno [2, 3-d] pyrimidin-4(3H)-one as yellow solid (0.44 g, 31.42%).

IR ($CHCl_3$): 3021, 2930, 1738, 1667, 1573, 1536 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, J= 7 Hz, 3H), 1.26-1.42 (m, 4H), 1.72 (quintet, J = 7 Hz, 2H), 2.84 (t, J = 7 Hz, 2H), 4.30 (s, 2H), 4.99 (s, 2H), 7.13 (s, 1H), 7.85 (s, 1H).

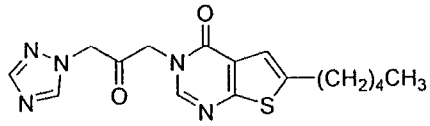
^{13}C NMR (50 MHz, $CDCl_3$+ DMSO-d_6): δ 12.62, 20.79, 28.05, 28.98, 29.53, 45.75, 51.00, 116.64, 122.62, 143.19, 145.64, 155.40, 161.26, 194.62.

[00117] Example 65: Preparation of 3-(3-chloro-2-hydroxypropyl)-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (66)



^{1}H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, J= 6 Hz, 3H), 1.26-1.42 (m, 4H), 1.62-1.78 (m, 2H), 2.84 (t, J = 8 Hz, 2H), 3.63 (d, J= 6 Hz, 2H), 3.81 (d, J= 4 Hz, 1H, D_2O exchangeable), 3.95-4.08 (m, 1H), 4.15-4.30 (m, 1H), 4.35-4.45 (m, 1H), 7.12 (s, 1H), 8.01 (s, 1H).

[00118] Example 66: Preparation of 3-(2-oxo-3-(1*H*-1,2,4-triazol-1-yl)propyl-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (67)



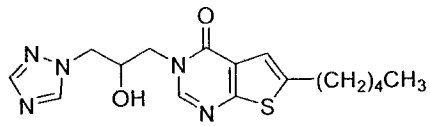
In a two-necked round bottom flask, 1,2,4-triazole (1 gm, 15 mmol), compound **65** (1 gm, 3.2 mmol), and $NaHCO_3$ (1.68 gm, 20 mmol) were taken and the mixture was flushed with argon. Toluene (100 ml) was added by cannula. This reaction mixture was refluxed at 110 ^{0}C for 4 hr. Reaction was monitored by TLC (ethyl acetate- pet ether, 35:65). After completion of reaction, toluene was evaporated and the residue was extracted with ethyl acetate (3 x 50 ml). The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain 3-(2-oxo-3-(1H-1,2,4-triazol-1-yl)propyl-6-pentylthieno[2,3-d]pyrimidin-4(3H)-one (**67**) (0.44 g, 40%).

IR ($CHCl_3$): 3448, 2925, 1740, 1681 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, J = 7 Hz, 3H), 1.29-1.42 (m, 4H), 1.71 (quintet, J = 7 Hz, 2H), 2.84 (t, J = 7 Hz, 2H), 4.69 (s, 2H), 5.27 (s, 2H), 7.12 (s, 1H), 7.85 (s, 1H), 8.04 (s, 1H), 8.27 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 13.93, 22.33, 29.69, 30.61, 30.72, 31.07, 52.37, 56.52, 117.92, 124.21, 144.99, 145.83, 152.70, 156.96, 163.05, 195.32.

[00119] Example 67: Preparation of 3-(2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propyl)-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (68):



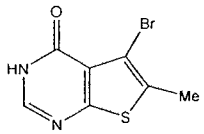
In a two-necked round bottom flask 3-(oxiran-2-ylmethyl)-6-pentylthieno[2,3-d] pyrimidin-4(3*H*)-one (prepared from **4** by reaction with epichlorohydrin) (8 gm, 0.028 moles), K_2CO_3 (9.66 gm, 0.07 moles) and TBAB (4.51 g, 0.014 mole) were taken and the mixture was flushed with argon. 1,2,4-Triazole (1.8 gm, 0.028 moles) dissolved in ethyl acetate (100 ml) was added by cannula. This reaction mixture was stirred at 60 ^{0}C for 12 hr. Reaction was monitored by TLC (ethyl acetate). After completion of reaction, water (200 ml) was added to reaction. It was then extracted with ethyl acetate (3 X 200 ml). The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography to obtain 3-(2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl)-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (**68**) (yellow solid, m.p.137 ^{0}C, 5.98 g, 60%).

IR ($CHCl_3$): 3382, 2932, 1674, 1573, 1537 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, J = 7 Hz, 3H), 1.24-1.38 (m, 4H), 1.68 (quintet, J = 7 Hz, 2H), 2.80 (t, J = 7 Hz, 2H), 3.88-4.46 (m, 5H), 5.43 (bs, 1H), 7.03 (s, 1H), 7.80 (s, 1H), 8.04 (s, 1H), 8.12 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 13.84 22.19, 30.42 30.58, 30.98, 49.41, 52.98, 67.29, 117.71, 124.07, 144.12, 144.98, 146.57, 151.35, 157.50, 162.40.

[00120] Example 68: Preparation of 5-bromo-6-methylthieno[2, 3-d] pyrimidin-4(3*H*)-one (69):



6-Methyl-thieno[2, 3-d]pyrimidin-4(3*H*)-one **1** (5 g, 0.0301 mole) was taken in two necked R.B. flask with guard tube, acetic acid (25 ml) was added, stirred for 10 min and bromine (1.8 ml, 0.0331 mole) in acetic acid (18 ml) was added drop wise. After complete addition, the reaction mixture was stirred at 60 ^{0}C till reaction was completed. Reaction was monitored by TLC. After completion of the reaction, reaction mixture was cooled to room temperature and diluted with water. The solid obtained was filtered and dried to obtain 5-bromo-6-methylthieno[2, 3-d]pyrimidin-4(3*H*)-one (4.0 g, 54.20 %) as a white solid, M.P. 255-7 ^{0}C.

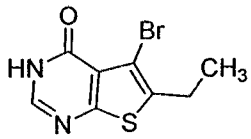
IR ($CHCl_3$): 1686, 1593, cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$ + DMSO-d_6): δ 2.33 (s, 3H), 7.77 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6): δ 13.98, 102.89, 130.85, 143.95, 156.05, 161.09, 178.87.

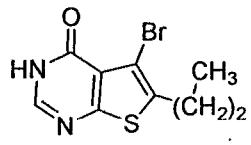
[00121] Compounds **70, 71, 72** and **73** were prepared by bromination of the corresponding thieno[2,3-*d*]pyrimidin-4(3*H*)-ones **2, 3, 7** and **5** using the procedure given for the compound **69**.

[00122] **Example 69: 5-Bromo-6-ethylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (70)**



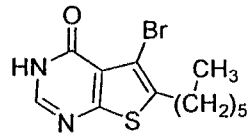
Nature: Grey solid; **MP:** 242 °C; **Yield:** 58.1 %; **^{1}H NMR** (200 MHz, $CDCl_3$ + DMSO-d_6): δ 1.20 (t, J = 8 Hz, 3H), 2.77 (q, J = 8 Hz, 2H), 7.81 (s, 1H), 12.16 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$ + DMSO-d_6): δ 13.8, 22.1, 101.8, 121.2, 138.3, 144.1, 156.4, 161.2; **IR** (Chloroform): 3393, 1657 cm^{-1}.

[00123] **Example 70: 5-Bromo-6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (71)**



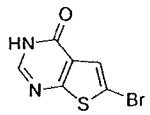
Nature: Pale yellow solid; **MP:** 205 °C; **Yield:** 53.7 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.03 (t, J = 6 Hz, 3H), 1.71-1.77 (m, 2H), 2.87 (t, J = 6 Hz, 2H), 8.13 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.5, 23.5, 31.3, 138.9, 143.9, 148.1, 149.0, 153.0, 158.5; **IR** (Chloroform): 3400, 1662 cm^{-1}.

[00124] **Example 71: 5-Bromo-6-hexylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (72)**



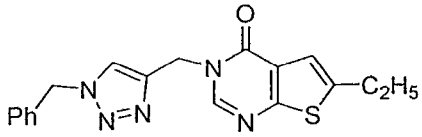
Nature: Off-white solid; **MP:** 147-148 °C; **Yield:** 55.0 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.90 (t, J = 6 Hz, 3H), 1.28-1.45 (m, 6H), 1.63-1.78 (m, 2H), 2.88 (t, J = 8 Hz, 2H), 8.12 (s, 1H), 12.47 (bs, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.9, 22.4, 28.6, 29.3, 30.0, 31.3, 102.9, 121.6, 139.1, 144.1, 158.5, 162.5; **IR** (Chloroform): 3370, 1655 cm^{-1}.

[00125] Example 72: 6-Bromothieno[2,3-d]pyrimidin-4(3H)-one (73)



^{1}H NMR (200 MHz, $CDCl_3$): δ 7.51 (s, 1H), 8.70 (s, 1H).

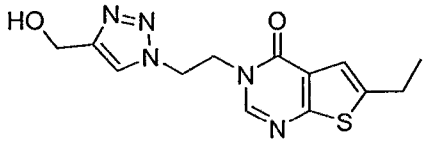
[00126] Example 73: 3-((1-Benzyl-1H-1,2,3-triazol-4-yl)methyl)-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one (74):



6-Ethyl-3-(prop-2-yn-1-yl)thieno[2,3-d]pyrimidin-4(3H)-one **19** (436 mg, 1.99 mmoles) and (azidomethyl)benzene (318 mg, 2.39 mmoles) were dissolved in mixture of water and t-butyl alcohol (1:1, 5 ml). Copper sulphate (6 mg, 0.0.398 mmoles) already dissolved in water was added to the reaction mixture. Then sodium ascorbate (6 mg, 0.0398 mmoles) was added to the reaction mixture and the reaction mixture was stirred at room temperature for 8 h. After completion of reaction, the reaction mixture was extracted with ethyl acetate, washed with water, dried over sodium sulphate, concentrated and purified by column chromatography to obtain 3-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one **74** (625 mg, 89%).

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.33 (t, J = 7 Hz, 3H), 2.85 (q, J = 7 Hz, 2H), 5.24 (s, 2H), 5.48 (s, 2H), 7.12 (s, 1H), 7.28-7.39 (m, 6H), 7.67 (s, 1H), 8.26 (s, 1H).

[00127] Example 74: Preparation of 6-ethyl-3-(2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)ethyl)thieno[2,3-d]pyrimidin-4(3H)-one (75)

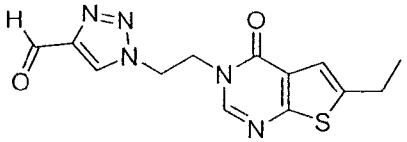


3-(2-Azidoethyl)-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one (2 gm, 8 mmoles) and propargyl alcohol (538 mg, 9.6 mmoles) were dissolved in mixture of water and t-butyl alcohol (1:1, 10 ml). Copper sulphate ($CuSO_4$, $5H_2O$) (25 mg, 0.16 mmoles) already dissolved in water was added to the reaction mixture. Then sodium ascorbate (237 mg, 1.2 mmoles) was added to the reaction mixture and the reaction mixture was stirred at room temperature for 7 h. After completion of reaction, the reaction mixture was extracted with ethyl acetate, washed with water, dried over sodium sulphate,

concentrated and purified by column chromatography to obtain 6-ethyl-3-(2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)ethyl)thieno[2,3-d]pyrimidin-4(3H)-one 75 (2 g, 81.9%).

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (t, J = 8 Hz, 3H), 2.88 (q, J = 8 Hz, 2H), 4.55 (t, J = 6 Hz, 2H), 4.73 (s, 2H), 4.79 (t, J = 6 Hz, 2H), 7.16 (s, 1H), 7.42 (s, 1H), 7.50 (s, 1H).

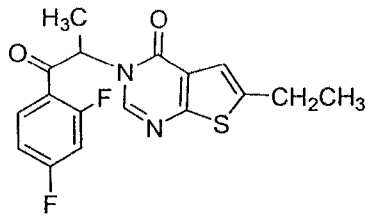
[00128] Example 75: Preparation of 1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)-1H-1,2,3-triazole-4-carbaldehyde (76)



Compound **76** was prepared from **75** by oxidation with IBX in DMSO at RT for 3 h.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.36 (t, J = 8 Hz, 3H), 2.89 (q, J = 8 Hz, 2H), 4.60 (t, J = 6 Hz, 2H), 4.90 (t, J = 6 Hz, 2H), 7.16 (s, 1H), 7.55 (s, 1H), 8.01 (s, 1H), 10.10 (s, 1H).

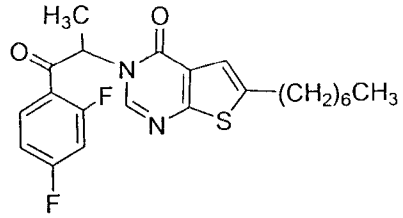
[00129] Example 76: Preparation of 3-(1-(2,4-difluorophenyl)-1-oxopropan-2-yl)-6-ethylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (77)



Sodium hydride (1.44 g, 0.06 mol) was taken in two necked round bottom flask equipped with guard tube, DMF (50 ml) was added to it and cooled to 0 °C. 6-Ethyl-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**2**) (9 g, 0.05 mmol) in DMF (50 ml) was added over a period of 10 min and stirred at same temperature for 1 h. 2-Bromo-1-(2,4-difluorophenyl)propan-1-one (**87**) (12.45 g, 0.05 mol) was added slowly and the whole reaction mixture was stirred at room temperature for 3 h. It was then diluted with water (200 ml), extracted with ethyl acetate (3 X 100 ml), dried over Na_2SO_4 and concentrated under vacuum on rotary evaporator. Purification by column chromatography yielded pure product as brown semisolid (12.7 g, 73 %).

Nature: Brown semisolid; **Yield:** 73 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.34 (t, J = 8 Hz, 3H), 1.77 (d, J = 6 Hz, 3H), 2.87 (q, J = 8 Hz, 2H), 6.08 (q, J = 8 Hz, 1H), 6.83-7.13 (m, 2H), 7.10 (s, 1H), 7.91-8.03 (m, 1H), 8.22 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 15.1, 15.9, 23.9, 58.4, 104.7 (t), 112.8 (d), 117.4, 120.1 (d), 124.1, 133.5 (d), 144.2, 146.4, 156.5, 161.6, 162.2 (dd), 166.6 (dd), 192.9; **IR** (Chloroform): 1671 (b) cm^{-1}; **MS** (ESI) *m/z*: 371.5112 (M + Na), 387.5271 (M + K).

[00130] Example 77: 3-(1-(2,4-Difluorophenyl)-1-oxopropan-2-yl)-6-heptylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (78)



Compound of **8** (0.05 mmol) was stirred with sodium hydride (0.06 mol) and 2-bromo-1-(2,4-difluorophenyl)propan-1-one (0.05 mol) in DMF (50 ml) at room temperature for 3 h. It was then diluted with water (200 ml), extracted with ethyl acetate (3 X 100 ml), dried over Na_2SO_4 and concentrated under vacuum on rotary evaporator. Purification by column chromatography yielded pure product.

Nature: Off-white semisolid; **Yield:** 73 %; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.88 (t, J = 6 Hz, 3H), 1.24-1.33 (m, 8H), 1.65-1.78 (m, 5H), 2.81 (t, J = 6 Hz, 2H), 6.03 (q, J = 8 Hz, 1H), 6.81-6.99 (m, 2H), 7.07 (s, 1H), 7.90-7.98 (m, 1H), 8.04 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.9, 15.8, 22.4, 28.8, 30.4 (2C), 30.9, 31.5, 58.4, 104.7 (t), 112.8 (d), 118.0, 120.2 (d), 124.0, 133.3 (d), 144.1, 144.8, 156.6, 162.3, 162.7 (dd), 165.6 (dd), 192.9; **IR** (Chloroform): 1666 (b) cm^{-1}.

Experimental:

ANTI- MYCOBACTERIAL ACTIVITY ASSAY:

[00131] *Mycobacterium smegmatis* and *Mycobacterium bovis* BCG share considerable homology with *Mycobacterium tuberculosis* and were considered as appropriate models for study of anti-tubercular activity of compounds of formula I. Accordingly, the compounds synthesized were evaluated to ascertain their anti-mycobacterial capacity on *M. smegmatis* (*MC*^{2} 155) strain/*Mycobacterium bovis* BCG strain. Primarily the activity was determined in the form of percentage inhibition following which the MIC was calculated for the compounds showing 30% or more growth inhibition. Initially, 10mM stock concentrations of the compounds were diluted with the required 100% (v/v) DMSO solution to achieve a working concentration of 1.5 mM. The assay was performed in a 96 well format plate. 100 µl of inoculum was incubated with 2% of working solution (1.5 mM of compound), making the final concentration of compound as 30 µM. The inoculum of *M. smegmatis/ M. bovis* BCG was maintained in Middlebrook 7H9 broth supplemented with ADS (Albumin-Dextrose-Saline) or OADC respectively. Prior to assay the inoculum was diluted 1:1000 times.

[00132] To ascertain the activity of the compounds, controls like DMSO were taken as a growth control, media control (Blank) as well as Rifampicin and Isoniazid as positive controls of inhibition of *Mycobacterium smegmatis* (*MC*^{2} 155) as well as *M. bovis* BCG. All the experiments were conducted as triplicates. After incubation for 48 h, the growth of the bacteria was studied by turbidometry by measuring the absorbance at 600 nm using a Multi Mode Reader (Perkin Elmer). Percentage growth inhibition was determined against DMSO (the compound dilutions were prepared in DMSO) and those compounds which showed inhibition at 30% or more were further analyzed to

determine their MIC values. In order to attain this objective, the inhibition was tested at increasing concentrations of compound from 6.25 µM to 100 µM. After the period of incubation, from the absorbance of the inoculum observed at 600 nm, MIC values were calculated as the lowest drug concentration, which showed 90% growth inhibition of the bacteria.

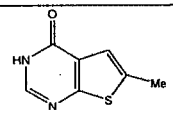
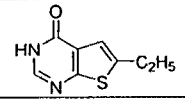
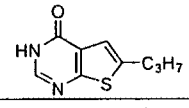
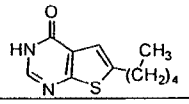
[00133] As the compounds were targeted towards *M. tuberculosis*, the activity of the compounds showing promising MICs against *M. smegmatis/M. bovis* BCG were evaluated against *M. tuberculosis* (H37Rv) using Alamar blue assay. The assay was performed in 96 well formats. 100 µL of inoculum diluted in 7H9 broth was added to the wells containing serially diluted test compound prepared in concentration series from 0.125 µg/mL to 64 µg/mL in 100 µL of Mtb inoculum with 2% DMSO taken as control. All experiments were performed in triplicates.

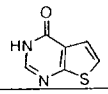
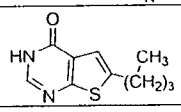
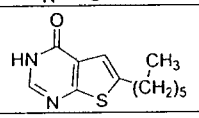
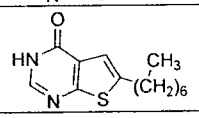
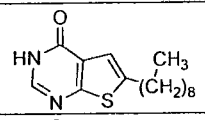
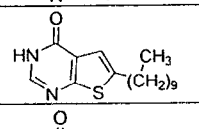
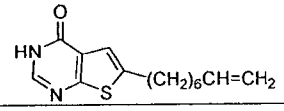
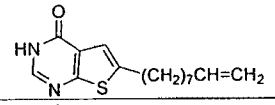
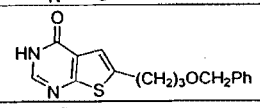
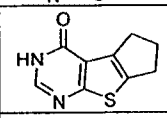
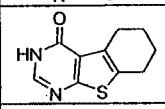
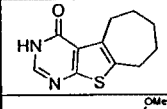
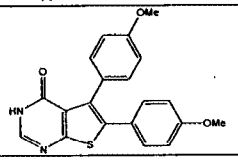
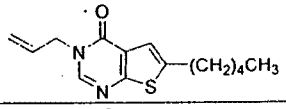
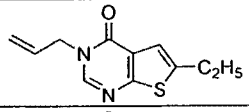
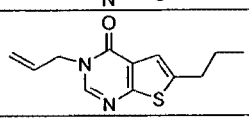
[00134] Peripheral wells of assay plate were filled with sterile distilled water to avoid evaporation in assay wells. The plates were sealed with parafilm and were incubated at 37°C for 7 days. On the day of termination of assay, 5 µL of a freshly prepared Alamar Blue reagent was added to all assay wells. The assay plates were further incubated at 37°C for 24 h. Then the plates were observed visibly for conversion of dye. Appearance of blue color in the well was interpreted as no growth and a pink color was scored as growth. From the observation of growth in comparison to the control, the MIC was defined, as the lowest drug concentration required which inhibits color change from blue to pink. As internal standards for assay, Rifampicin and Isoniazid were chosen.

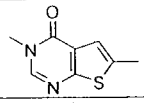
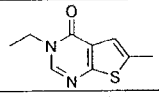
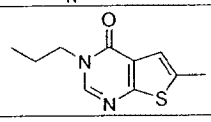
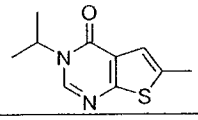
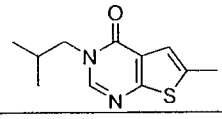
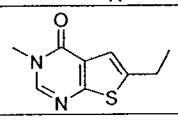
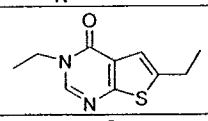
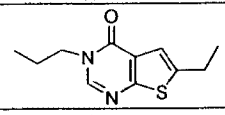
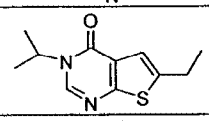
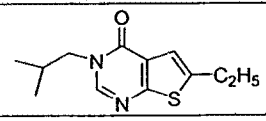
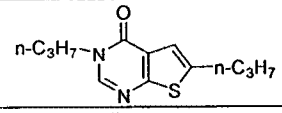
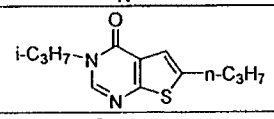
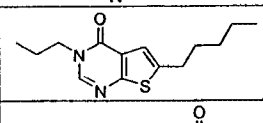
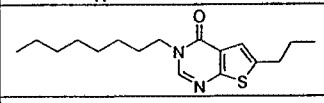
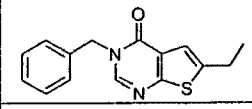
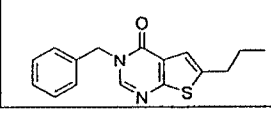
Conclusion:

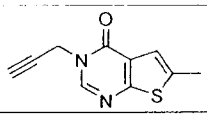
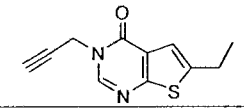
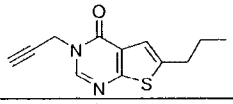
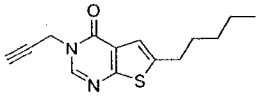
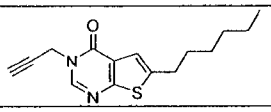
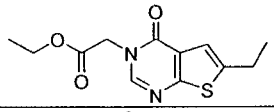
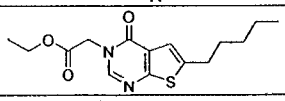
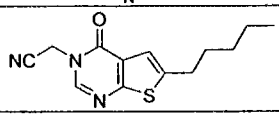
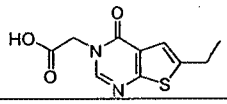
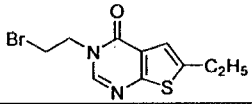
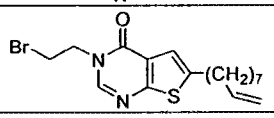
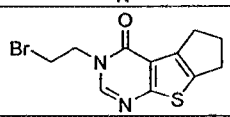
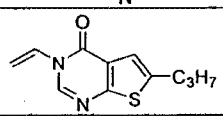
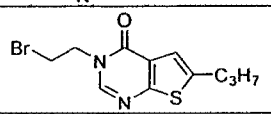
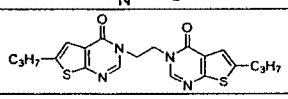
[00135] The antimycobacterial activity against *Mycobacterium smegmatis* (*MC2 155)/Mycobacterium bovis BCG* is provided in Table 2 below:

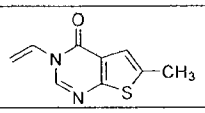
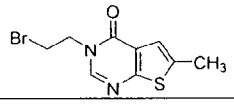
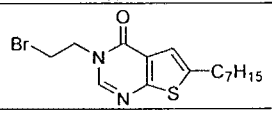
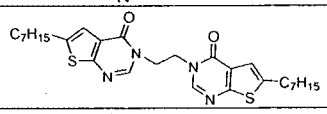
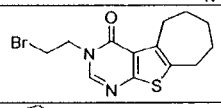
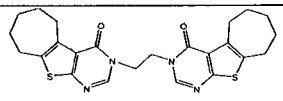
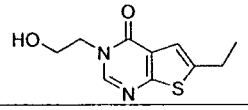
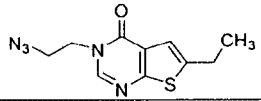
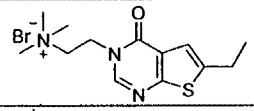
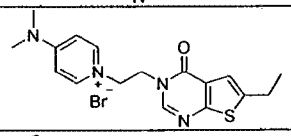
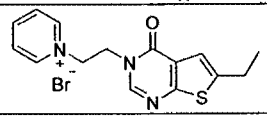
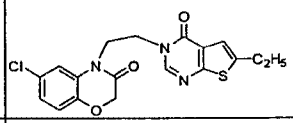
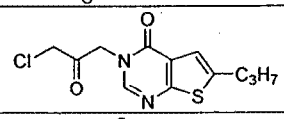
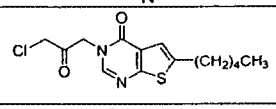
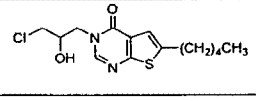
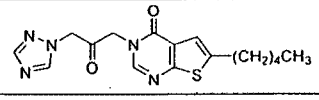
Table 2: Antimycobacterial activity of thieno[2,3-d]pyrimidin-4(3H)-ones of Formula I

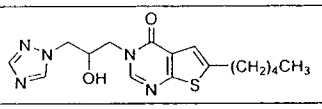
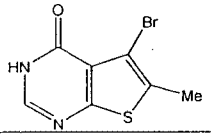
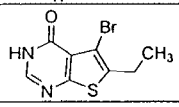
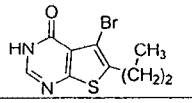
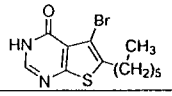
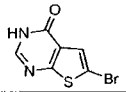
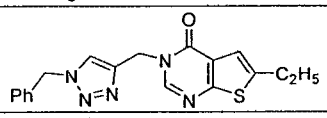
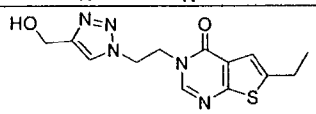
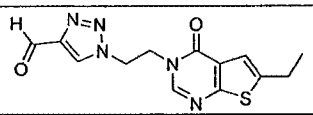
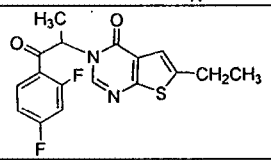
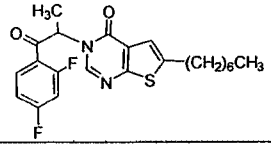
Compound No.	Structure	IUPAC Name	% inhibition at 30 µM
1		6-methylthieno[2,3-*d*]pyrimidin-4(3*H*)-one	12.5
2		6-ethylthieno[2,3-d]pyrimidin-4(3H)-one	41.5
3		6-propylthieno[2,3-*d*]pyrimidin-4(3*H*)-one	1.0
4		6-(n-pentyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	-9.7

5		Thieno[2,3-*d*]pyrimidin-4(3*H*)-one	11.6
6		6-(n-Butyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	10.6
7		6-(n-Hexyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	-11.2
8		6-(n-Heptyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	14.2
9		6-(n-Nonyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	13.2
10		6-(n-Decyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	16.1
11		6-(Oct-7-en-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one	23.3
12		6-(Non-8-en-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one	21.5
13		6-(3-Benzyloxypropyl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-one	14.9
14		3,5,6,7-Tetrahydrocyclopenta[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one	16.1
15		5,6,7,8-Tetrahydrobenzothieno[2,3-*d*]pyrimidin-4(3*H*)-one	27.0
16		3,5,6,7,8,9-Hexahydro-4H-cyclo hepta [4,5] thieno [2,3-*d*]pyrimidin-4-one	18.6
17		5,6-bis(4-methoxy phenyl) thieno[2,3-d]pyrimidin-4(3H)-one	-5.4*
18		3-allyl-6-pentyl thieno [2,3-*d*] pyrimidin-4(3*H*)-one	--
19		3-Allyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one	13.7
20		3-Allyl-6-propyl thieno [2,3-d]pyrimidin-4(3H)-one	40.4

21		3,6-Dimethylthieno[2,3-*d*]pyrimidin-4(3H)-one	22.2
22		3-Ethyl-6-methyl thieno [2,3-*d*]pyrimidin-4(3H)-one	25.6
23		6-Methyl-3-propyl thieno [2,3-d]pyrimidin-4(3H)-one	8.0
24		3-Isopropyl-6-methyl thieno[2,3-d]pyrimidin-4(3H)-one	-0.5
25		3-Isobutyl-6-methyl thieno[2,3-d]pyrimidin-4(3H)-one	24.6
26		6-Ethyl-3-methyl thieno[2,3-d]pyrimidin-4(3H)-one	30.4
27		3,6-Diethylthieno[2,3-d]pyrimidin-4(3H)-one	16.4
28		6-Ethyl-3-propyl thieno[2,3-d]pyrimidin-4(3H)-one	9.9
29		6-Ethyl-3-isopropyl thieno[2,3-d]pyrimidin-4(3H)-one	41.4
30		6-Ethyl-3-isobutyl thieno[2,3-d]pyrimidin-4(3H)-one	28.5
31		3,6-Dipropylthieno[2,3-d]pyrimidin-4(3H)-one	25.1
32		3-Isopropyl-6-propyl thieno[2,3-d]pyrimidin-4(3H)-one	28.5
33		6-Pentyl-3-propyl thieno[2,3-d]pyrimidin-4(3H)-one	18.7*
34		3-Octyl-6-propyl thieno[2,3-d]pyrimidin-4(3H)-one	27.8
35		3-Benzyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one	19.0
36		3-Benzyl-6-propyl thieno[2,3-d]pyrimidin-4(3H)-one	24.3

37		6-Methyl-3-(prop-2-yn-1-yl)thieno[2,3-d] pyrimidin-4(3H)-one	12.4*
38		6-Ethyl-3-(prop-2-yn-1-yl)thieno[2,3-d] pyrimidin-4(3H)-one	29.7
39		3-(Prop-2-yn-1-yl)-6-propyl thieno[2,3-d] pyrimidin-4(3H)-one	43.1*
40		3-(Prop-2-yn-1-yl)-6-pentylthieno[2,3-d] pyrimidin-4(3H)-one	40.0 (MIC 25 µM against M. tuberculosis H37Rv)
41		3-(Prop-2-yn-1-yl)-6-hexylthieno[2,3-d] pyrimidin-4(3H)-one	35.8
42		Ethyl 2-(6-ethyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) acetate	9.2
43		Ethyl 2-(6-pentyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) acetate	34.5
44		2-(4-oxo-6-pentyl thieno[2,3-d]pyrimidin-3 (4H)-yl)acetonitrile	30.7*
45		2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3(4H)-yl)acetic acid	-2.6
46		3-(2-bromoethyl-6-ethyl thieno[2,3-*d*]primidin-4 (3*H*)-one	24.1
47		3-(2-Bromoethyl)-6-(non-8-enyl)thieno[2,3-d] pyrimidin-4(3H)-one	21.5
48		3-(2-Bromoethyl)-3,5,6,7-tetrahydro-4H-cyclo penta [4,5]thieno[2,3-d] pyrimidin-4-one	28.0
49		6-propyl-3-vinyl thieno[2,3-*d*]pyrimidin-4 (3*H*)-one	--
50		3-(2-bromoethyl)-6-propyl thieno[2,3-*d*] primidin-4(3*H*)-one	6.4
51		3,3'-(ethane-1,2-diyl)bis(6-propyl thieno[2,3-d]pyrimidin-4 (3H)-one	--

52		6-methyl-3-vinyl thieno[2,3-*d*]pyrimidin-4(3*H*)-one	3.6
53		3-(2-bromoethyl)-6-methylthieno[2,3-*d*]primidin-4(3*H*)-one	3.3
54		3-(2-Bromoethyl-6-heptylthieno[2,3-*d*] primidin-4(3*H*)-one	Not active
55		3,3'-(Ethane-1,2-diyl)bis(6-heptyl thieno[2,3-d]pyrimidin-4 (3H)-one)	17.7*
56		3-(2-Bromoethyl)-3,5,6,7,8,9-hexahydro-4H-cyclo hepta [4,5] thieno[2,3-d]pyrimidin-4-one	27.2
57		3,3'-(Ethane-1,2-diyl) bis(6-heptylthieno[2,3-d] pyrimidin-4(3H)-one)	--
58		6-ethyl-3-(2-hydroxy ethyl) thieno[2,3-d] pyrimidin-4(3H)-one	35.0
59		3-(2-Azidoethyl)-6-ethyl thieno[2,3-d]pyrimidin-4 (3H)-one	12.2
60		2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3(4H)-yl)-N,N,N-trimethylethan-1-aminium bromide	-3.6
61		4-(dimethylamino)-1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl) ethyl)pyridin-1-ium bromide	9.4
62		1-(2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3 (4H)-yl)ethyl)pyridin-1-ium bromide	2.1
63		6-chloro-4-(2-(6-ethyl-4-oxothieno[2,3-*d*] pyrimidin-3(4*H*)-yl) ethyl)-2*H*-benzo [b] [1,4] oxazin-3(4*H*)-one	2.8
64		3-(3-chloro-2-oxopropyl)-6-propylthieno[2,3-*d*] pyrimidin-4(3*H*)-one	50.1
65		3-(3-chloro-2-oxopropyl)-6-pentylthieno[2,3-*d*] pyrimidin-4(3*H*)-one	67.1
66		3-(3-chloro-2-hydroxy propyl)-6-pentyl thieno [2,3-*d*]pyrimidin-4(3*H*)-one	24.9
67		3-(2-oxo-3-(1*H*-1,2,4-triazol-1-yl)propyl-6-pentylthieno[2,3-*d*] pyrimidin-4(3*H*)-one	3.3

68		3-(2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propyl)-6-pentylthieno[2,3-*d*]pyrimidin-4(3*H*)-one	4.0
69		5-bromo-6-methyl thieno[2, 3-d] pyrimidin-4(3*H*)-one	--
70		5-Bromo-6-ethyl thieno [2,3-*d*]pyrimidin-4(3*H*)-one	25.5
71		5-Bromo-6-propyl thieno[2,3-*d*]pyrimidin-4 (3*H*)-one	20.8
72		5-Bromo-6-hexyl thieno[2,3-*d*]pyrimidin-4 (3*H*)-one	-8.4
73		6-Bromothieno[2,3-d]pyrimidin-4(3H)-one	-0.9
74		3-((1-Benzyl-1H-1,2,3-triazol-4-yl)methyl)-6-ethylthieno[2,3-d] pyrimidin-4(3H)-one	11.0
75		6-ethyl-3-(2-(4-(hydroxy methyl)-1H-1,2,3-triazol-1-yl)ethyl)thieno[2,3-d] pyrimidin-4(3H)-one	14.0
76		1-(2-(6-ethyl-4-oxo thieno[2,3-d]pyrimidin-3(4H)-yl)ethyl)-1H-1,2,3-triazole-4-carbaldehyde	10.8
77		3-(1-(2,4-difluorophenyl)-1-oxopropan-2-yl)-6-ethylthieno[2,3-*d*] pyrimidin-4(3*H*)-one	9.8
78		3-(1-(2,4-Difluoro phenyl)-1-oxopropan-2-yl)-6-heptylthieno[2,3-*d*] pyrimidin-4(3*H*)-one	25.3

[00136] The % inhibition was recorded at 30 µM concentration against *Mycobacterium smegmatis*.

#The % inhibition was recorded at 30 µM concentration against *Mycobacterium bovis* BCG.

Controls- Rifampicin-*M. smegmatis* 1.87 µg/ML, *M. bovis* BCG 0.25 µg/ML and *M. tuberculosis* (H37Rv) 0.06 µg/ML; Isoniazid- *M. smegmatis* 16 µg/ML, *M. bovis* BCG 1 µg/ML and *M. tuberculosis* (H37Rv) 0.03 µg/ML

[00137] The thieno[2,3-d] pyrimidin-4(3H)-one **40** was screened against *Mycobacterium tuberculosis* MtbH37Rv and was found to have MIC equal to 8 µg/mL. The compound **2** exhibited significant antimycobacterial activity. Compounds with carbocyclic ring attached to the thiophene

group such as compound **15, 48** and **56** showed moderate antimycobacterial activity. N-alkylation of compound **2** afforded corresponding alkylated products out of which compound **29** was equally active as compound **2**. Conversion of **2** into **35** and **42**, by reaction with benzyl bromide and ethyl bromoacetate respectively, decreased the activity while **45** prepared by hydrolysis of **42** exhibited no activity. The bromide **46** prepared by reaction of compound **2** with 1,2-dibromoethane exhibited moderate activity, the corresponding water-soluble quaternary ammonium salt **60** had no activity while **58** prepared from **46** showed significant antimycobacterial activity. The 6-(n)-pentylthieno[2,3-d]pyrimidin-4(3H)-one as such did not exhibit antimycobacterial activity but compounds **43** and **44** prepared by its reaction with ethyl bromoacetate and bromoacetonitrile exhibited significant antimycobacterial activity. The compounds **38, 39** and **40** prepared from the corresponding thieno[2,3-d]pyrimidin-4(3H)-one **(2)** also exhibited significant antimycobacterial activity.

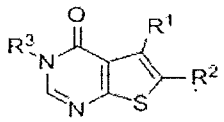
In sum, a number of thieno[2,3-d]pyrimidin-4(3H)-one with different structural features were synthesized and evaluated for their antimycobacterial activity. The thieno [2,3-d] pyrimidin-4(3H)-ones comprising compounds 2, 20, 26, **29, 38, 39, 40, 41, 43, 44, 58, 64 and 65** ~~**38, 39 and 40**~~ exhibited significant activity against *Mycobacterium smegmatis/ Mycobacterium bovis BCG* (inhibition in the range of 30-4068% at 30 μM). One of the thieno [2,3-d] pyrimidin-4(3H)-ones (**40**) was screened against *Mycobacterium tuberculosis H37Rv* and exhibited antitubercular activity with MIC equal to 8 μg/mL.

ADVANTAGES OF THE PRESENT INVENTION

[00138] The present invention provides novel thieno[2,3-d]pyrimidin-4(3H)-one compounds of general formula (I) which show great potential as antitubercular agents against *Mycobacterium tuberculosis H37Rv and* multi drug resistant tubercular bacteria. The compounds of the present invention are easy to synthesize and can be prepared by the processes known in the art.

WE CLAIM

1. A novel anti-mycobacterial thieno [2,3-d]pyrimidin-4(3H)-ones compounds of Formula-I or its pharmaceutically acceptable salts thereof;



Formula I

wherein, R^1 and R^2 may be same or different and independently selected from the group consisting of hydrogen, halogen, (un)substituted aryl, (un)substituted C_1-C_{15} linear or branched alkyl group optionally substituted with hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy group; (un)substituted C_1-C_{15} linear or branched alkenyl; (un)substituted C_1-C_{15} linear or branched alkynyl group;

or R^1 and R^2 together form a 5 to 12 membered carbocyclic ring which may be substituted or unsubstituted;

R^3 is selected from the group consisting of hydrogen, (un)substituted (C_1-C_{15}) linear or branched alkyl; (un)substituted C_1-C_{15} linear or branched alkenyl; (un)substituted (C_1-C_{15}) linear or branched alkynyl; -CH_2-COOEt; -CH_2-COOH; $CH_2COCH_2R^4$; $CH_2CH(OH)CH_2R^4$ wherein R^4 is selected from the group consisting of (un)substituted triazol-1-yl, halogen, hydroxy, amino, nitrile, nitro, carboxyl, carbonyl, ester, alkoxy, (un)substituted aryl; CHR^5COAr wherein R^5 represents hydrogen or (C_1-C_4) alkyl and Ar represents (un)substituted aryl; $(CH_2)_nR^6$ or $(CH_2)_n$ $R^{7+}X^-$ where n=1 to 7, wherein R^6 is selected from the group consisting of hydrogen, (un)substituted (C_1-C_4)alkyl, (un)substituted aryl, (un)substituted triazol-1-yl, halogen, -OH, N_3, CN, (un)substituted 2*H*-benzo[b][1,4]oxazin-3(4*H*)-on-4-yl, 3,5,6,7,8,9-hexahydro-*4H*-cyclohepta[4,5]thieno [2,3-*d*]pyrimidin-4(3*H*)-onyl, and wherein R^7 represents NMe_3 or pyridin-1-yl or 4-dimethylaminopyridin-1-yl, and X represents F, Br, I and Cl;

with an exclusion, when R^1 and R^3 is H, and R^2 is selected from H, (C_1-C_3) alkyl, linear or branched (C_5-C_{10}) alkyl, propyl benzyloxy or Br; and when R^1 is methyl or ethyl, R^2 is selected from H, Br and R^3 is selected from H, n-propyl, isobutyl;

with an exclusion, when R^3 is H, R^1 and R^2 together form 5-7 membered saturated carbocyclic ring.

2. The anti -mycobacterial compounds of Formula 1 according to claim 1, selected from a group consisting of;

6-(n-Butyl)-thieno[2,3-d]pyrimidin-4(3H)-one;

6-(Oct-7-en-1-yl)thieno[2,3-d]pyrimidin-4(3H)-one;

6-(Non-8-en-1-yl)thieno[2,3-d]pyrimidin-4(3H)-one;
5,6-Bis(4-methoxy phenyl) thieno[2,3-d]pyrimidin-4(3H)-one;
3-Allyl-6-pentylthieno[2,3-d] pyrimidin-4(3H)-one;
3-Allyl-6-ethylthieno[2,3-d]pyrimidin-4(3H)-one;
3-Allyl-6-propylthieno[2,3-d] pyrimidin-4(3H)-one;
3,6-Dimethylthieno[2,3-d] pyrimidin-4(3H)-one;
3-Ethyl-6-methyl thieno [2,3-d]pyrimidin-4(3H)-one;
6-Methyl-3-propyl thieno [2,3-d]pyrimidin-4 (3H)-one;
3-Isopropyl-6-methyl thieno[2,3-d]pyrimidin-4 (3H)-one;
3-Isobutyl-6-methyl thieno [2,3-d]pyrimidin-4 (3H)-one;
6-Ethyl-3-methyl thieno [2,3-d]pyrimidin-4 (3H)-one;
3,6-Diethylthieno[2,3-d] pyrimidin-4(3H)-one;
6-Ethyl-3-isopropyl thieno [2,3-d]pyrimidin-4(3H)-one;
3,6-Dipropylthieno[2,3-d] pyrimidin-4(3H)-one;
3-Isopropyl-6-propyl thieno[2,3-d]pyrimidin-4 (3H)-one;
6-Pentyl-3-propyl thieno[2,3-d]pyrimidin-4 (3H)-one;
3-Octyl-6-propyl thieno[2,3-d]pyrimidin-4 (3H)-one;
3-Benzyl-6-ethyl thieno[2,3-d]pyrimidin-4 (3H)-one;
3-Benzyl-6-propyl thieno[2,3-d]pyrimidin-4 (3H)-one;
6-Methyl-3-(prop-2-yn-1-yl)thieno[2,3-d]pyrimidin-4(3H)-one;
6-Ethyl-3-(prop-2-yn-1-yl)thieno[2,3-d]pyrimidin-4 (3H)-one;
3-(Prop-2-yn-1-yl)-6-propyl thieno[2,3-d] pyrimidin-4(3H)-one;
3-(Prop-2-yn-1-yl)-6-pentyl thieno[2,3-d] pyrimidin-4(3H)-one;
3-(Prop-2-yn-1-yl)-6-hexyl thieno[2,3-d] pyrimidin-4(3H)-one;
Ethyl 2-(6-ethyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) acetate;
Ethyl 2-(6-pentyl-4-oxothieno [2,3-d] pyrimidin-3(4H)-yl) acetate;
2-(4-~~o~~Oxo-6-pentyl thieno[2,3-d]pyrimidin-3 (4H)-yl)acetonitrile;
2-(6-Ethyl-4-oxo thieno [2,3-d]pyrimidin-3 (4H)-yl) acetic acid;
3-(2-Bromoethyl-6-ethyl thieno[2,3-d]primidin-4 (3H)-one;
3-(2-Bromoethyl)-6-(non-8-enyl)thieno[2,3-d]pyrimidin-4(3H)-one;
3-(2-Bromoethyl)-3,5,6,7-tetrahydro-4H-cyclopenta[4,5]thieno[2,3-d] pyrimidin-4-one;
6-Propyl-3-vinyl thieno[2,3-d]pyrimidin-4(3H)-one;
3-(2-Bromoethyl)-6-propylthieno[2,3-d] primidin-4(3H)-one;
3,3'-(Ethane-1,2-diyl) bis(6-propylthieno[2,3-d] pyrimidin-4(3H)-one;
6-Methyl-3-vinyl thieno[2,3-d]pyrimidin-4 (3H)-one;
3-(2-Bromoethyl)-6-methylthieno[2,3-d] pyrimidin-4(3H)-one;
3-(2-Bromoethyl-6-heptyl thieno[2,3-d] primidin-4(3H)-one;

3,3'-(Ethane-1,2-diyl) bis(6-heptylthieno[2,3-d]pyrimidin-4(3H)-one;
3-(2-Bromoethyl)-3,5,6,7,8,9-hexahydro-4H-cyclohepta[4,5] thieno[2,3-d] pyrimidin-4-one;
3'-(Ethane-1,2-diyl) bis(6-heptyl thieno [2,3-d]pyrimidin-4(3H)-one);
6-Ethyl-3-(2-hydroxy ethyl)thieno[2,3-d] pyrimidin-4(3H)-one;
3-(2-Azidoethyl)-6-ethyl thieno[2,3-d]pyrimidin-4 (3H)-one;
2-(6-Ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)-N,N,N-trimethylethan-1-aminium bromide;
4-(Dimethylamino)-1-(2-(6-ethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)ethyl pyridin-1-ium bromide;
1-(2-(6-Ethyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) ethyl)pyridin-1-ium bromide;
6-Chloro-4-(2-(6-ethyl-4-oxothieno[2,3-d] pyrimidin-3(4H)-yl) ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one;
3-(3-Chloro-2-oxo propyl)-6-propyl thieno[2,3-d] pyrimidin-4(3H)-one;
3-(3-Chloro-2-oxopropyl)-6-pentyl thieno[2,3-d] pyrimidin-4(3H)-one;
3-(3-Chloro-2-hydroxypropyl)-6-pentylthieno[2,3-d] pyrimidin-4(3H)-one;
3-(2-Oxo-3-(1H-1,2,4-triazol-1-yl) propyl-6-pentylthieno[2,3-d] pyrimidin-4(3H)-one;
3-(2-Hydroxy-3-(1H-1,2,4-triazol-1-yl)propyl)-6-pentyl thieno[2,3-d] pyrimidin-4(3H)-one;
5-Bromo-6-ethyl thieno[2,3-d] pyrimidin-4(3H)-one;
5-Bromo-6-propyl thieno[2,3-d] pyrimidin-4(3H)-one;
5-Bromo-6-hexyl thieno[2,3-d] pyrimidin-4(3H)-one;
3-((1-Benzyl-1H-1,2,3-triazol-4-yl) methyl)-6-ethyl thieno[2,3-d] pyrimidin-4 (3H)-one;
6-Ethyl-3-(2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)ethyl)thieno[2,3-d]pyrimidin-4(3H)-one;
1-(2-(6-Ethyl-4-oxo thieno[2,3-d] pyrimidin-3(4H)-yl) ethyl)-1H-1,2,3-triazole-4-carbaldehyde;
3-(1-(2,4-Difluoro phenyl)-1-oxo propan-2-yl)-6-ethylthieno[2,3-d] pyrimidin-4(3H)-one;
3-(1-(2,4-Difluoro phenyl)-1-oxo propan-2-yl)-6-heptylthieno[2,3-d] pyrimidin-4(3H)-one.

3. A pharmaceutical composition for treating or preventing tuberculosis in a subject, comprising anti mycobacterial compounds of Formula 1 in association with at least one pharmaceutically acceptable excipient.
4. A method of treating or preventing tuberculosis in a subject, comprising administering an effective amount of compound of Formula 1 in association with pharmaceutical excipients.
5. Use of compounds of Formula 1 for the preparation of medicament useful for treatment or prevention of tuberculosis.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2015/000054

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/519 A61P31/06
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, FSTA, INSPEC, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EKINS SEAN ET AL: "Combining Computational Methods for Hit to Lead Optimization in Mycobacterium Tuberculosis Drug Discovery", PHARMACEUTICAL RESEARCH (DORDRECHT), vol. 31, no. 2, 17 October 2013 (2013-10-17), pages 414-435, XP002739895, figure 2 page 420, right-hand column, paragraph 3 ----- -/--	1,3-5

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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Date of the actual completion of the international search	Date of mailing of the international search report
21 May 2015	11/06/2015

Name and mailing address of the ISA/	Authorized officer
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2

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EKINS SEAN ET AL: "Enhancing Hit Identification in Mycobacterium tuberculosis Drug Discovery Using Validated Dual-Event Bayesian Models", PLOS ONE, vol. 8, no. 5, E63240, May 2013 (2013-05), pages 1-8, XP002739896, figure 1 abstract	1,3-5
Y	SEGURA-CABRERA A ET AL: "Structure-based prediction of Mycobacterium tuberculosis shikimate kinase inhibitors by high-throughput virtual screening", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, AMSTERDAM, NL, vol. 18, no. 11, 1 June 2008 (2008-06-01), pages 3152-3157, XP022711187, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2008.05.003 [retrieved on 2008-05-04] table 1	1-5
Y	RASHMI P ET AL: "Thienopyrimidines as Novel Inhibitors of Mycobacterium tuberclosis: Synthesis and In-vitro Studies", ARCHIV DER PHARMAZIE (WEINHEIM), vol. 344, no. 7, July 2011 (2011-07), pages 459-465, XP002739897, table 1	1-5
Y	LLUÍS BALLELL ET AL: "Fueling Open-Source Drug Discovery: 177 Small-Molecule Leads against Tuberculosis", CHEMMEDCHEM, vol. 8, no. 2, 10 February 2013 (2013-02-10), pages 313-321, XP055105573, ISSN: 1860-7179, DOI: 10.1002/cmdc.201200428 table 1	1-5
X	AZAB M. E.: "Utility of the Enaminonitrile Moiety in the Synthesis of Some Biologically Active Thenopyrimidine Derivatives", PHOSPHORUS, SULFUR, AND SILICON, vol. 183, 2008, pages 1766-1782, XP002739898, Schemes 1 and 2	1,3

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HILL PAMELA J ET AL: "Selective Inhibitors of Bacterial t-RNA-(N(1)G37) Methyltransferase (TrmD) That Demonstrate Novel Ordering of the Lid Domain", JOURNAL OF MEDICINAL CHEMISTRY, vol. 56, no. 18, September 2013 (2013-09), pages 7278-7288, XP002739899, table 2 -----	1,3