The invention relates to chemical compounds, or pharmaceutically acceptable salts thereof of the formula (I): which have bacterial Murl inhibitory activity and are accordingly useful for their treatment and prophylaxis of bacterial infection, e.g., *E. faecalis* or *E. faecium* infection. Further, the invention relates to methods of treatment of the human or animal body. The invention also relates to processes for the manufacture of the compounds, to pharmaceutical compositions containing them, and to their use in the manufacture of medicaments of use in the treatment and prevention of various bacterial diseases in a warm-blooded animals such as man.
DERIVATIVES OF ADENINE AND 8-AZA-ADENINE AND USES THEREOF

Field of the Invention

The present invention relates to novel derivatives of adenine and 8-aza-adenine, their pharmaceutical compositions and methods of use. In addition, the present invention relates to the use of derivatives of adenine and 8-aza-adenine for treatment and prevention of various diseases caused by bacteria, for example, Enterococcus faecalis or Enterococcus faecium infection.

Background of the Invention

Most bacteria, especially Gram positive bacteria, utilize a cell wall comprised of crosslinked peptidoglycan units to maintain shape and resist high osmotic pressure potentials. Bacterial cell wall biosynthesis is a validated target for antimicrobial activity; cephalosporins, penicillins and glycopeptides are antimicrobial agents, which block cell wall biosynthesis (Walsh, C., Molecular mechanisms that confer antibacterial resistance. Nature, 2000, 406: p. 775-781). Cell wall biosynthesis requires the enzyme Murl, a glutamate racemase, and therefore this enzyme is essential for bacterial viability (Doublet, P., et al., The murl gene of Escherichia coli is an essential gene that encodes a glutamate racemase activity. Journal of Bacteriology, 1993, 175(10): p. 2970-9).

As bacteria are constantly evolving to develop resistance to widely used antibiotics, there is a continuing need for new antibacterial compounds having different mechanisms of action to treat bacterial infections. Infections by multidrug resistant Gram positive cocci, for example, such as staphylococcal, streptococcal or enterococcal infections, are a serious problem, especially in children, the elderly, and hospitalized patients.

Summary of the Invention

The present invention describes novel derivatives of adenine and 8-aza-adenine, which inhibit bacterial Murl, e.g., E. faecalis Murl or E. faecium Murl, and compositions of such compounds and methods of use. The compounds disclosed herein represent a valuable contribution to the development of therapies directed to diseases resulting from bacterial infection, e.g., Gram positive bacterial infection, e.g., infection caused by Gram positive cocci such as staphylococcal, streptococcal or enterococcal infections or, for example, E. faecalis, or...
E. faecium infection. The compounds are of particular interest to treat infections that are resistant to conventional antibiotics, such as penicillin and cephalosporin.

In one embodiment, the invention relates to compounds represented by formula (I):

![Chemical structure](image)

or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein:

X₁ is a divalent C₆alkyl, a divalent C₆alkenyl or a divalent C₆alkynyl, wherein the divalent alkyl, alkenyl or alkynyl may be optionally substituted with one or more substituent selected from the group consisting of halo, cyano, nitro, hydroxy, =O, =S, C₁₋₄alkoxy, C₆alkyl, 4alkylsulfanyl, amino, C₁₋₄alkylamino, and C₁₋₄diarylamino;

X₂ is -O-, -S-, or -NR₄⁻, wherein R₄ is hydrogen or a C₁₋₄alkyl;

X₃ is CR₁₀ or N;

R₁ is a C₃₋₄carbocycle, morpholinyl, quinolinyl, benzodioxinyl, benzodioxolyl, 1H-pyrazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 2-oxo-2,3-dihydro-1,3-benzoxazolyl, tetrahydro-1H-pyran, 1-benzothiophenyl, furanyl, thiazolyl, isoxazolyl, and oxetanyl, or oxetanyl are optionally substituted on one or more carbon atom with one or more R₅; and wherein each =N- of the quinolinyl, pyrazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, thiazolyl, and isoxazolyl, may be each independently optionally substituted with an oxo; and wherein the -NH- of morpholinyl, 1H-pyrazolyl, and 2-oxo-2,3-dihydro-1,3-benzoxazolyl may be optionally substituted with R₆;

R₂ is a C₆alkyl, C₆alkenyl, C₆alkynyl, C₃₋₄carbocycle, heterocycle, C₃₋₄carbocycleCi₆alkyl, or heterocycleCi₆alkyl, wherein the alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl may be optionally substituted on one or more carbon atoms with one or more R₆, and wherein if R₂ is a heterocycle or a heterocyclealkyl comprising one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₂ is a heterocycle or a
heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently
optionally substituted with Rs;

R₃ and R₄ are each, independently, hydrogen, Cᵢ₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₁₄carbocycle, heterocycle, C₃₋₁₄carbocycleC₁₋₆alkyl, or heterocycloCᵢ₋₆alkyl, wherein the

alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocycloalkyl may be optionally substituted on one or more carbon atoms with one or more R₇, and wherein if R₃ or R₄ is a heterocycle or a heterocycloalkyl comprising one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₃ or R₄ is a heterocycle or a heterocycloalkyl that contains one or more -NH-, each -NH- may be independently optionally substituted with R₉; or R₃ and R₄ taken together with the nitrogen atom to which they are attached form a heterocycle which may be optionally substituted on one or more carbon atoms with one or more R₇, wherein if the heterocycle comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with R₉;

R₅, R₆, and R₇, for each occurrence, are independently selected from the group consisting of a halo, nitro, cyano, C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₄carbocycle, heterocycle, C₃₋₁₄carbocycleC₁₋₆alkyl, heterocycleC₁₋₆alkyl, C₁₋₆haloalkyl, -ORn, -SRn, -NR₁₂R₃₋₁₃, -C(O)R₁₁, -C(O)OR₁₁, -C(O)NR₁₂R₃₋₁₃, -NR₁₁C(O)R₁₁, -OC(O)R₁₁, -NR₁₁C(O)OR₁₁, -OC(O)NR₁₂R₃₋₁₃, -NR₁₁C(O)NR₁₂R₃₋₁₃, -NR₁₁C(NR₁₋₆)NR₁₂R₃₋₁₃, -S(O)ₚRₙ, -NR₁₁S(0)ₚRₙ, and -S(O)ₚNR₁₂Rₙ, wherein if R₅, R₆ or R₇ is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocycloalkyl, it may be optionally further substituted on one or more carbon atoms with one or more R₅; and wherein if R₅, R₆ or R₇ is a heterocycle or a heterocycloalkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₅, R₆ or R₇ is a heterocycle or a heterocycloalkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R₁₆;

R₈, R₉, or R₁₇, for each occurrence, are independently selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₁₄carbocycle, heterocycle, C₃₋₁₄carbocycleC₁₋₆alkyl, heterocycleC₁₋₆alkyl, C₁₋₆haloalkyl, -C(O)R₁₁, -C(O)OR₁₁, -
C(O)NR\textsubscript{2}Rn, -S(O)pRn, and -S(O)\textsubscript{p}NR\textsubscript{2}Ri\textsubscript{3}, wherein if \( R_{8}, R_{9} \) or \( R_{17} \) is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be optionally substituted on one or more carbon atoms with one or more \( R_{i5} \); and wherein if \( R_{8}, R_{9} \) or \( R_{17} \) is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if \( R_{8}, R_{9} \) or \( R_{17} \) is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with \( R_{i6} \);

\( R_{i6} \) is hydrogen, a C\textsubscript{1}\textsubscript{o}alkyl, a heterocycleC\textsubscript{1}\textsubscript{o}alkyl, -NR\textsubscript{2}Rn, -C(O)Rn, -C(O)ORn, -C(O)NR\textsubscript{2}Ri\textsubscript{13}, -OC(O)Rn, -OC(O)NR\textsubscript{2}Ri\textsubscript{13}, -NRnC(NR\textsubscript{i4})NR\textsubscript{2}Ri\textsubscript{3}, -S(O)pRn, -NRnS(O)pRn, and -S(O)pNR\textsubscript{2}Ri\textsubscript{3};

\( R_{n} \), for each occurrence, is independently selected from the group consisting of hydrogen, C\textsubscript{1}\textsubscript{6}alkyl, C\textsubscript{2}\textsubscript{6}alkenyl, C\textsubscript{2}\textsubscript{6}alkynyl, C\textsubscript{3}\textsubscript{i4}carbocycle, heterocycle, C\textsubscript{3}\textsubscript{i4}carbocycleC\textsubscript{1}oalkyl, heterocycleC\textsubscript{1}oalkyl, wherein if \( R_{n} \) is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more \( R_{i5} \); and wherein if \( R_{n} \) is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if \( R_{n} \) is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with \( R_{i6} \);

\( R_{i2} \) and \( R_{i3} \), for each occurrence, are independently selected from the group consisting of hydrogen, C\textsubscript{1}\textsubscript{6}alkyl, C\textsubscript{2}\textsubscript{6}alkenyl, C\textsubscript{2}\textsubscript{6}alkynyl, C\textsubscript{2}\textsubscript{i4}carbocycle, heterocycle, C\textsubscript{3}C\textsubscript{i4}carbocycleC\textsubscript{1}oalkyl, heterocycleC\textsubscript{1}oalkyl, wherein if \( R_{i2} \) or \( R_{i3} \) is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more \( R_{i5} \); and wherein if \( R_{i2} \) or \( R_{i3} \) is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if \( R_{i2} \) or \( R_{i3} \) is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with \( R_{i6} \); or \( R_{i2} \) and \( R_{i3} \) taken together with the nitrogen atom to which they are attached for a heterocycle, wherein the heterocycle may be optionally substituted on one or more carbon atoms with one or more \( R_{i5} \); and wherein if the heterocycle
comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6;

Ri5, for each occurrence, is independently selected from the group consisting of halo, nitro, cyano, C_6alkyl, C_2-6alkenyl, C_2-6alkynyl, C_3,i4carbocycle, heterocycle, C_3.

i4carbocycleC_i6alkyl, heterocycleCi_6alkyl, Ci_6haloalkyl, -ORis, -SRis, -NRi_1,Ri20, -C(O)RiS,
-C(O)ORi_8, -C(O)NRi_9Ri_20, -NRi_8C(O)Ri_8, -OC(O)Ri_8, -OC(O)NRi_8Ri_20, -NRi_8C(O)NRi_9Ri_20, -NRi_8C(NR_2i)NRi_9Ri_20, -S(O)pRi_8, -NRi_8S(O)pRi_8, and -S(O)qNRi_9Ri_20;

Ri4 and Ri_3, for each occurrence, are independently selected from the group consisting of hydrogen, a C_i6alkyl, nitro, cyano, amino, alkylamino, dialkylamino, or hydroxy;

Ri_16, for each occurrence, is independently selected from the group consisting of C_i6alkyl, C_2-6alkenyl, C_2-6alkynyl, C_3,i4carbocycle, heterocycle, C_3,i4carbocycleC_i6alkyl, heterocycleCi-ealkyl, Ci_6haloalkyl, -C(O)Ri_8, -C(O)ORi_8, -C(O)NRi_8Ri_20, -S(O)pRi_8, and -S(O)pNRi_9Ri_20;

Ri_8, for each occurrence, is independently selected from the group consisting of hydrogen, C_1-6alkyl, C_2-6alkenyl, C_2-6alkynyl, C_3,i4carbocycle, heterocycle, C_3,i4carbocycleCi_6alkyl, heterocycleC_1-6alkyl;

Ri_9 and R_20, for each occurrence, are independently selected from the group consisting of hydrogen, C_1-6alkyl, C_2-6alkenyl, C_2-6alkynyl, C_3,i4carbocycle, heterocycle, C_3,i4carbocycleC_1-6alkyl, heterocycleC_1-6alkyl; or Ri_9 and R_20 taken together with the nitrogen atom to which they are attached for a heterocycle; and

p is 1 or 2.

In some embodiments of the compounds of formula (I), one or more of the following provisos apply:

Ri is not an unsubstituted phenyl, unsubstituted biphenyl, an unsubstituted cyclopropyl, or 3-cyclopentanyloxy-4-methoxyphenyl;

when Ri is 4-chlorophenyl, 4-fluorophenyl, cyclohexyl, or furanyl, R_2 is not unsubstituted naphthyl or unsubstituted cyclopentyl;

when Ri is morpholinyl, one of R_3 and R_4 is not 4-aminobenzyl or phenylethyl;

when X_2 is NR_i8, R_2 is a C_1-6alkyl which is optionally substituted with one or more carbon atom with one or more R_6, and Ri is not 4-aminophenyl, 2-chlorophenyl, 4-methylphenyl, 3-(methoxycarbonylmethyl)-phenyl, 2-fluorophenyl, or 2,6-difluorophenyl.
when \(-X_2-R_2\) is methylsulfanyl, \(R_i\) is not 4-methylphenyl, 2-methoxyphenyl, or 2-fluorophenyl;

when \(-X_2-R_2\) is an unsubstituted n-butyloxy, \(R_i\) is not 3-(2-methoxy-2-oxoethyl)-phenyl, 3-cyanomethyl-phenyl, 3-chloromethyl-phenyl, 3-hydroxymethyl-phenyl, 4-benzyloxyphenyl, 3-cyanomethyl-4-fluoro-phenyl, 3-chloromethyl-4-fluoro-phenyl, 3-hydroxymethyl-4-fluoro-phenyl, 3-methoxycarbonyl-4-fluoro-phenyl, 4-hydroxyphenyl, or 3-(1,1,2-trimethoxy-2-oxoethyl)-phenyl; and

when \(-X-R_2\) is an unsubstituted n-butyloxy and \(-NR_3R_4\) is \(-NH_2\), \(R_i\) is not 3-methoxycarbonyl-phenyl or 4-acetoxyphenyl.

In another embodiment, the invention relates to compounds represented by formula (II):

\[
\begin{align*}
R_3 & \quad N \\
R_4 & \quad N \\
R_2 & \quad X_3 \\
R_{22} & \quad N \\
X_3 & \quad -O- \text{ or } -S-;
\end{align*}
\]

\((H)\)

or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein \(X_3, R_2, R_3,\) and \(R_4\) are defined as above, and wherein:

\(X_4\) is \(-O-\) or \(-S-;\)

\(R_{22}\) is a C3-alkyl which is optionally substituted on one or more carbon atom with one or more substituents selected from the group consisting of halo, nitro, cyano, \(-OR_n, -SR_n, -NR_2R_13, -C(O)R_n, -C(O)NR_2R_13, -NRnC(O)Rn, -OC(O)R_n, -NRnC(O)ORn, -OC(O)NR_2R_13, -NRnC(O)NR_2R_13, -NRnC(NR_4)NR_2R_13, -S(O)_pR_n, -NRnS(0)_pR_n,\) and \(-S(O)_pNR_2R_13;\) wherein \(R_n, R_{12}, R_n, RH,\) and \(p\) are defined as above.

In some embodiments of the compounds of formula (II), one or both of the following provisos apply:

when both \(R_3\) and \(R_4\) are hydrogen, \(R_2\) and \(R_{22}\) are not both n-hexyl or both n-propyl, or \(R_{22}\) is not n-propyl and \(R_2\) is not methyl; and
when R₂ is methyl, R₃ and R₄ taken together with the nitrogen atom to which they are attached are not a substituted or unsubstituted piperazino.

Compounds represented by formula (I) or (II) have bacterial, e.g., *E. faecalis* Murl, or *E. faecium* Murl, inhibitory activity and are accordingly useful for their treatment and prophylaxis of various diseases caused by bacteria expressing Murl, for example *E. faecalis* or *E. faecium* infection, and thus in methods of treatment or prophylaxis for humans and animals. The invention also relates to processes for the manufacture of compounds represented by formula (I) or (II), to pharmaceutical compositions containing compounds represented by formula (I) or (II), and to their use in the manufacture of medicaments for use in the treatment and prophylaxis of various diseases caused by bacterial infection, e.g., *E. faecalis* or *E. faecium* infection, in a warm-blooded animal such as man.

**Detailed Description of the Invention**

A. **Definitions**

Unless otherwise specified, the below terms used herein are defined as follows:

As used herein, the term "carbocycle" refers to a monocyclic or polycyclic, saturated, partially saturated or unsaturated ring system having 3 to 14 ring atoms, wherein all the ring atoms are carbon atoms. Carbocyclic ring systems can be unsubstituted or substituted with one or more independently selected substituents. Carbocyclic ring systems include aryl, cycloalkenyl, and cycloalkyl ring systems. The term "C₃₄carbocycle" refers to a carbocycle having from 3 to 14 ring carbon atoms.

As used herein, the term "aryl" means a monocyclic or polycyclic-aromatic ring system. Examples of suitable aryl groups include, but are not limited to, phenyl, tollyl, anthacenyl, fluorenyl, indenyl, azulenyl, and naphthyl, as well as benzo-fused carbocyclic moieties such as 5,6,7,8-tetrahydronaphthyl. An aryl group can be unsubstituted or substituted with one or more independently selected substituents. The term "C₆₇₄aryl" refers to an aryl group having from 6 to 14 independently selected carbon atoms. In certain embodiments, the aryl group is a monocyclic ring, wherein the ring comprises 6 carbon atoms.

As used herein, the term "cycloalkyl" means a saturated, mono- or polycyclic alkyl radical typically having from 3 to 14 carbon atoms. Representative cycloalkyls include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl, adamantyl, decahydronaphthyl, octahydrapentalene, bicycle[1.1.1]pentanyl, and
the like. Cycloalkyl groups can be unsubstituted or substituted with one or more independently selected substituents. The term "C\textsubscript{3-14} cycloalkyl" refers to a cycloalkyl group having from 3 to 14 ring carbon atoms.

As used herein, the term "cycloalkenyl" means a cyclic non-aromatic alkenyl radical having at least one carbon-carbon double bond in the cyclic system and typically having from 5 to 14 carbon atoms. Representative cycloalkenyls include cyclopentenyl, cyclopentadienyl, cyclohexenyl, cyclohexadienyl, cycloheptenyl, cycloheptadienyl, cycloheptatrienyl, cyclooctenyl, cyclooctadienyl, cyclooctatrienyl, cyclononenyl, cyclononadienyl, cyclodecenyl, cyclodecadienyl and the like. Cycloalkenyl groups can be unsubstituted or substituted with one or more independently selected substituents. The term "C\textsubscript{3-14} cycloalkenyl" refers to a cycloalkenyl group having from 3 to 14 ring carbon atoms.

As used herein, the term "alkyl" means a saturated straight chain or branched non-cyclic hydrocarbon typically having from 1 to 10 carbon atoms, preferably 1-6 carbon atoms. Representative saturated straight chain alkyls include methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl and n-decy; while saturated branched alkyls include isopropyl, sec-butyl, isobutyl, tert-butyl, isopentyl, 2-methylbutyl, 3-methylbutyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2-methylhexyl, 3-methylhexyl, 4-methylhexyl, 5-methylhexyl, 2,3-dimethylbutyl, 2,3-dimethylpentyl, 2,4-dimethylpentyl, 2,3-dimethylhexyl, 2,4-dimethylhexyl, 2,5-dimethylhexyl, 2,2-dimethylpentyl, 2,2-dimethylhexyl, 3,3-dimethylypentyl, 3,3-dimethylhexyl, 4,4-dimethylhexyl, 2-ethylpentyl, 3-ethylpentyl, 2-ethylhexyl, 3-ethylhexyl, 4-ethylhexyl, 2-methyl-2-ethylpentyl, 2-methyl-3-ethylpentyl, 2-methyl-4-ethylpentyl, 2-methyl-2-ethylhexyl, 2-methyl-3-ethylhexyl, 2-methyl-4-ethylhexyl, 2,2-diethylpentyl, 3,3-diethylhexyl, 2,2-diethylhexyl, 3,3-diethylhexyl and the like. Alkyl groups included in compounds of this invention may be optionally substituted with one or more independently selected substituents. The term "Ci-6alkyl" refers to an alkyl group having from 1 to 6 carbon atoms.

As used herein, the term "alkenyl" means a straight chain or branched, hydrocarbon radical typically having from 2 to 10 carbon atoms, preferably 2-6 carbon atom, and having at least one carbon-carbon double bond. Representative straight chain and branched alkenyls include vinyl, allyl, 1-but enyl, 2-butenyl, isobutyl enyl, 1-pent enyl, 2-pent enyl, 3-methyl-1-butenyl, 1-methyl-2-butenyl, 2,3-dimethyl-2-butenyl, 1-hex enyl, 2-hex enyl, 3-hex enyl, 1-hept enyl, 2-hept enyl, 3-hept enyl, 1-oct enyl, 2-oct enyl, 3-oct enyl, 1-non enyl, 2-non enyl, 3-non enyl, 1-dec enyl, 2-dec enyl, 3-dec enyl and the like. Alkenyl groups can be unsubstituted or
substituted with one or more independently selected substituents on the saturated or unsaturated portion of the alkenyl group. The term "C_{2\_6}alkenyl" refers to an alkenyl group having from 2 to 6 carbon atoms.

As used herein, the term "alkynyl" means a straight chain or branched, hydrocarbon radical typically having from 2 to 10 carbon atoms, preferably 2-6 carbon atoms, and having at least one carbon-carbon triple bond. Representative straight chain and branched alkynyls include acetylenyl, propynyl, 1-butynyl, 2-butynyl, 1-pentylnyl, 2-pentylnyl, 3-methyl-1-butynyl, 4-pentylnyl-l-hexynyl, 2-hexynyl, 5-hexynyl, 1-heptylnyl, 2-heptynylnyl, 6-heptynylnyl, 1-octynyl, 2-octynyl, 7-octynyl, 1-nonynyl, 2-nonynyl, 8-nonynyl, 1-decynyl, 2-decynyl, 9-decynyl and the like. Alkynyl groups can be unsubstituted or substituted with one or more independently selected substituents. The term "C_{2\_6}alkynyl" refers to an alkynyl group having from 2 to 6 carbon atoms.

The term "alkylene," as used herein, refers to an alkyl group that has two points of attachment to two moieties (e.g., -CH\_2-, -CH\_2CH\_2-, etc.). Alkylene groups may be unsubstituted or substituted with one or more independently selected substituents. The term "Ci\_6alkylene" refers to an alkylene group having from 1 to 6 carbon atoms. An alkylene group is also referred to herein as a divalent alkyl group.

The term "divalent alkenyl," as used herein refers to an alkenyl group that has two points of attachment to two or more moieties (e.g., -CH=CH-, -CH\_2CH=CHCH\_2-, CH=CHCH\_2-, and the like). Divalent alkenyl groups may be unsubstituted or substituted with one or more independently selected substituents. The term "divalent Ci\_6alkenyl" refers to a divalent alkenyl group having from 1 to 6 carbon atoms.

The term "divalent alkynyl," as used herein refers to an alkynyl group that has two points of attachment to two or more moieties (e.g., -C≡C-, -CH\_2C≡CCH\_2-, -C≡CCH\_2-, and the like). Divalent alkynyl groups may be unsubstituted or substituted with one or more independently selected substituents. The term "divalent Ci\_6alkynyl" refers to a divalent alkynyl group having from 1 to 6 carbon atoms.

The term "carbocyclealkyl," as used herein, refers to a carbocycle group that is attached to another moiety via an alkylene linker. The term "C\_17\_4carbocycleCi\_4alkyl" refers to a C3\_i4carbocycle group that is attached to another moiety via a C1\_4alkylene linker. Carbocyclealkyl groups can be unsubstituted or substituted on the alkyl or carbocycle portion with one or more independently selected substituents. Representative carbocyclealkyl groups
include benzyl, cyclopropylmethyl, phenylethyl, 2-(naphth-1-yl)-propyl, 2-(fluoren-9-yl)-ethyl, 3-cyclohexyl-propyl, and the like.

The term "arylalkyl," as used herein, refers to an aryl group that is attached to another moiety via an alkylene linker. The term "Ce- ary1Ci-ealkyl" refers to a C₆e₇aryl group that is attached to another moiety via a Ci-6alkylene linker. Arylalkyl groups can be unsubstituted or substituted with one or more independently selected substituents. Representative arylalkyl groups include benzyl, phenylethyl, 2-(naphth-1-yl)-propyl, 2-(fluoren-9-yl)-ethyl, and the like.

As used herein, the term "heterocycle," refers to a monocyclic or polycyclic heterocyclic ring having 3- to 14- ring members which is either a saturated ring, an unsaturated non-aromatic ring, or an aromatic ring. A 3-membered heterocycle can contain up to 3 heteroatoms, and a 4- to 14-membered heterocycle can contain from 1 to about 8 heteroatoms. Each heteroatom is independently selected from nitrogen, which can be quaternized; oxygen; and sulfur, including sulfoxide and sulfone. The heterocycle may be attached to another moiety via a nitrogen or carbon atom. Any heteroatom in a heterocycle may be substituted with a protecting group known to those of ordinary skill in the art, for example, the hydrogen on a nitrogen may be substituted with an amine protecting group, such as a tert-butoxycarbonyl group. Furthermore, the heterocycle may be optionally substituted with one or more independently selected substituents on any carbon atom or nitrogen atom.

Only stable isomers of such substituted heterocyclic groups are contemplated in this definition. The term "heterocycle" encompasses heteroaryl rings, heterocycloalkenyl rings, and heterocycloalkyl rings.

As used herein, the term "heteroaryl" means a monocyclic or polycyclic aromatic ring system having carbon atom ring members and one or more heteroatom ring members selected from oxygen, sulfur or nitrogen. Typically, a heteroaryl ring has from 5 to about 14 ring members in which at least 1 ring member is a heteroatom selected from oxygen, sulfur and nitrogen. In another embodiment, the heteroaryl ring is a 5 or 6 membered ring and may contain from 1 to about 4 heteroatoms. In another embodiment, the heteroaryl ring has a 7 to 14 ring members and may contain from 1 to about 7 heteroatoms. Representative heteroaryls include pyridyl, furyl, thienyl, pyrrolyl, oxazolyl, imidazolyl, indoliziny1, thiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, triazopyridinyl, pyridinyl, thiadiazolyl, pyrazinyl, quinolyl, isoquinolyl, indazolyl, benzoxazolyl, benzofuryl, benzothiazolyl, indolizinyl, imidazopyridinyl, isothiazolyl, tetrazolyl, benzimidazolyl,
benzoxazolyl, benzothiazolyl, benzothiadiazolyl, benzoxadiazolyl, indolyl, tetrahydroindolyl, azaindolyl, imidazopyridyl, quinzaolinyl, purinyl, pyrrolo[2,3]pyrimidyl, pyrazolo[3,4]pyrimidyl or benzo(b)thienyl and the like. Heteroaryl groups may be optionally substituted on carbon or nitrogen ring atoms with one or more independently selected substituents.

The term "heterocycloalkyl" refers to a saturated, monocyclic or polycyclic ring system having carbon atom ring members and one or more heteroatom ring members selected from oxygen, sulfur or nitrogen. Heterocycloalkyl groups may be optionally substituted on a carbon or a nitrogen ring atom with one or more independently selected substituents. A heterocycloalkyl has from 3 to 14 ring members. Representative heterocycloalkyl groups include morpholinyl, thiomorpholinyl, pyrrolidinyl, piperidinyl, piperazinyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, and the like.

The term "heterocycloalkenyl" refers to a partially unsaturated, non-aromatic, monocyclic or polycyclic ring system having carbon atom ring members and one or more heteroatom ring members selected from oxygen, sulfur or nitrogen. Heterocycloalkenyl groups may be optionally substituted on a carbon or a nitrogen ring atom with one or more independently selected substituents. A heterocycloalkenyl has from 3 to 14 ring members. Representative heterocycloalkenyl groups include 4H-pyranyl, tetrahydropyridinyl, dihydropyridinyl, and the like.

A heterocyclealkyl group refers to a heterocycle that is attached to another moiety via an alkylene linker. The term "heterocycleCi-alkyl" refers to a heterocycle group that is attached to another moiety via an alkylene having from 1 to 6 carbon atoms. Heterocyclealkyl groups can be unsubstituted or substituted on the heterocycle or alkyl portion with one or more independently selected substituents.

The term "alkoxy," as used herein, refers to an alkyl group which is linked to another moiety though an oxygen atom. The term "Ci-alkoxy" refers to an alkoxy group that has from 1 to 6 carbon atoms. Alkoxy groups can be substituted or unsubstituted with one or more independently selected substituents.

The term "alkylsulfanyl," as used herein, refers to an alkyl group which is linked to another moiety though a divalent sulfur atom. The term "Ci-alkylsulfanyl" refers to an alkylsulfanyl group that has from 1 to 6 carbon atoms. Alkylsulfanyl groups can be substituted or unsubstituted with one or more independently selected substituents.
The term "arylsulfanyl," as used herein, refers to an aryl group which is linked to another moiety through a divalent sulfur atom. The term "Ce-14arylsulfanyl" refers to an arylsulfanyl group that has from 6-14 ring carbon atoms. Arylsulfanyl groups can be substituted or unsubstituted with one or more independently selected substituents.

The term "amino" refers to -NH₂. The term "alkylamino," as used herein, refers to an amino group in which one hydrogen atom attached to the nitrogen has been replaced by an alkyl group. The term "Ci.6alkylamino," refers to an alkylamino group in which the alkyl portion has from 1 to 6 carbon atoms. The term "dialkylamino," as used herein, refers to an amino group in which two hydrogen atoms attached to the nitrogen have been replaced by alkyl groups, in which the alkyl groups can be the same or different. The term "C₁₆6dialkylamino," refers to a dialkylamino group in which each alkyl group, independently, has from 1 to 6 carbon atoms. Alkylamino groups and dialkylamino groups can be substituted or unsubstituted with one or more independently selected substituents.

As used herein, the term "halogen" or "halo" means fluoro, chloro, bromo, or iodo.

As used herein, the term "haloalkyl" means an alkyl group in which one or more -H is replaced with a halo group. The term "Ci.6haloalkyl," refers to a haloalkyl that has 1-6 carbon atoms. Representative haloalkyl groups include -CF₃, -CHF₂, -CCl₃, -CH₂CH₂Br, -CH₂CH(CH₂CH₂Br)CH₃, -CHICH₃, and the like.

As used herein, the term "hydroxyalkyl" means an alkyl group in which one or more -H is replaced with an -OH group. The term "Ci.6hydroxyalkyl," refers to a hydroxyalkyl that has 1-6 carbon atoms. Representative hydroxyalkyl groups include -CH₂OH, -CH(OH)₂, -CH₂CH₂OH, -CH₂CH(CHOH)₂CH₃, -CH(OH)CH₃, and the like.

As used herein, the term "lower" refers to a group having up to four carbon atoms. For example, a "lower alkyl" refers to an alkyl radical having from 1 to 4 carbon atoms, and a "lower alkenyl" or "lower alkynyl" refers to an alkenyl or alkynyl radical having from 2 to 4 carbon atoms, respectively. A lower alkoxy or a lower alkylsulfanyl refers to an alkoxy or an alkylsulfanyl having from 1 to 4 carbon atoms. Lower substituents are typically preferred.

As used herein, the term "compound(s) of this invention" and similar terms refers to a compound of formula (I) or (II), or any exemplified compound disclosed herein, or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

The term "displaceable group," refers to a group which can be displaced by a nucleophile under the reaction condition specified. Skilled artisan can select displaceable
groups which can be displaced by a particular nucleophile under particular reaction conditions. Preferred displaceable groups are halo groups.

As used herein and unless otherwise indicated, the term "prodrug" means a derivative of a compound that can hydrolyze, oxidize, or otherwise react under biological conditions (in vitro or in vivo) to provide a compound of this invention. Prodrugs may only become active upon such reaction under biological conditions, but they may have activity in their unreacted forms. Examples of prodrugs contemplated in this invention include, but are not limited to, analogs or derivatives of compounds of formulas (I) or (II), or any of the exemplified compounds disclosed herein that comprise biohydrolyzable moieties such as biohydrolyzable amides, biohydrolyzable esters, biohydrolyzable carbamates, biohydrolyzable carbonates, biohydrolyzable ureides, and biohydrolyzable phosphate analogues. Other examples of prodrugs include derivatives of compounds of formulas (I) or (II), or any of the exemplified compounds disclosed herein that comprise -NO, -NO₂, -ONO, or -ONO₂ moieties. Prodrugs can typically be prepared using well-known methods, such as those described by 1 BURGER'S MEDICINAL CHEMISTRY AND DRUG DISCOVERY (1995) 172-178, 949-982 (Manfred E. Wolff ed., 5.sup.th ed), the entire teachings of which are incorporated herein by reference.

As used herein and unless otherwise indicated, the terms "biohydrolyzable amide", "biohydrolyzable ester", "biohydrolyzable carbamate", "biohydrolyzable carbonate", "biohydrolyzable ureide" and "biohydrolyzable phosphate analogue" mean an amide, ester, carbamate, carbonate, ureide, or phosphate analogue, respectively, that either: 1) does not destroy the biological activity of the compound and confers upon that compound advantageous properties in vivo, such as uptake, duration of action, or onset of action; or 2) is itself biologically inactive but is converted in vivo to a biologically active compound.

Examples of biohydrolyzable amides include, but are not limited to, lower alkyl amides, cc-amino acid amides, alkoxyacetyl amides, and alkylaminoalkylcarbonyl amides. Examples of biohydrolyzable esters include, but are not limited to, lower alkyl esters, alkoxyacyloxy esters, alkyl acylamino alkyl esters, and choline esters. Examples of biohydrolyzable carbamates include, but are not limited to, lower alkylamines, substituted ethylenediamines, aminoacids, hydroxyalkylamines, heterocycle amines, and polyether amines.

In one embodiment, a biohydrolyzable ester of a compound of the invention containing carboxy or hydroxy group is, for example, a pharmaceutically acceptable ester which is hydrolyzed in the human or animal body to produce the parent acid or alcohol.
Suitable pharmaceutically acceptable esters for carboxy include d-ealkoxymethyl esters for example methoxymethyl, d-ealkanoyloxymethyl esters for example pivaloyloxymethyl, phthalidyl esters, C₃₋₅cycloalkoxy carbonyloxyC₆aryl esters for example 1-cyclohexylcarbonyloxyethyl; 1,3-dioxolen-2-onylmethyl esters for example 5-methyl-1,3-dioxolen-2-onylmethyl; and C₁₋₅alkoxycarbonyloxyethyl esters for example 1-methoxycarbonyloxyethyl and may be formed at any carboxy group in the compounds of this invention.

In another embodiment, a biohydrolyzable ester of a compound of the invention containing a hydroxy group includes inorganic esters such as phosphate esters and e

-acyloxyalkyl ethers and related compounds which as a result of the in vivo hydrolysis of the ester breakdown to give the parent hydroxy group. Examples of α-acyloxyalkyl ethers include acetoxymethoxy and 2,2-dimethylpropionyloxy-methoxy. A selection of in vivo hydrolyzable ester forming groups for hydroxy include alkanoyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl, alkoxycarbonyl (to give alkyl carbonate esters), dialkylcarbamoyl and N-(dialkylaminoethyl)-7V-alkylcarbamoyl (to give carbamates), dialkylaminoacetyl and carboxyacetyl. Examples of substituents on benzoyl include morpholino and piperazino linked from a ring nitrogen atom via a methylene group to the 3- or 4- position of the benzoyl ring.

As used herein, the term "pharmaceutically acceptable salt," is a salt formed from an acid and a basic group of a compound of the invention. Illustrative salts include, but are not limited, to sulfate, citrate, acetate, oxalate, chloride, bromide, iodide, nitrate, bisulfate, phosphate, acid phosphate, isonicotinate, lactate, salicylate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, genticinate, fumarate, gluconate, glucaronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, and pamoate (i.e., 1,l'-methylene-bis-(2-hydroxy-3-naphthoate)) salts. The term "pharmaceutically acceptable salt" also refers to a salt prepared from a compound of the invention having an acidic functional group, such as a carboxylic acid functional group, and a pharmaceutically acceptable inorganic or organic base. Suitable bases include, but are not limited to, hydroxides of alkali metals such as sodium, potassium, and lithium; hydroxides of alkaline earth metal such as calcium and magnesium; hydroxides of other metals, such as aluminum and zinc; ammonia, and organic amines, such as unsubstituted or hydroxy-substituted mono-, di-, or trialkylamines; dicyclohexylamine; tributyl amine; pyridine; N-methyl,N-ethylamine; diethylamine;
triethylamine; mono-, bis-, or tris-(2-hydroxy-lower alkyl amines), such as mono-, bis-, or tris-(2-hydroxyethyl)-amine, 2-hydroxy-tert-butylamine, or tris-(hydroxymethyl)methylamine, N,N-di-lower alkyl-N-(hydroxy lower alkyl)-amines, such as N,N-dimethyl-N-(2-hydroxyethyl)-amine, or tri-(2-hydroxyethyl)amine; N-methyl-D-glucamine; and amino acids such as arginine, lysine, and the like. The term "pharmacologically acceptable salt" also refers to a salt prepared from a compound of the invention having a basic functional group, such as an amino functional group, and a pharmacologically acceptable inorganic or organic acid. Suitable acids include, but are not limited to, hydrogen sulfate, citric acid, acetic acid, oxalic acid, hydrochloric acid, hydrogen bromide, hydrogen iodide, nitric acid, phosphoric acid, isonicotinic acid, lactic acid, salicylic acid, tartaric acid, ascorbic acid, succinic acid, maleic acid, besylic acid, fumaric acid, gluconic acid, glucaronic acid, saccharic acid, formic acid, benzoic acid, glutamic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulphonic acid, and p-toluenesulfonic acid.

As used herein, the term "pharmacologically acceptable solvate," is a solvate formed from the association of one or more solvent molecules to one or more molecules of a compound of a compound of the invention. The term solvate includes hydrates (e.g., hemihydrate, mono-hydrate, dihydrate, trihydrate, tetrahydrate, and the like).

Some compounds of the invention may have chiral centres and/or geometric isomeric centres (e.g., E- and Z- isomers), and it is to be understood that the invention encompasses all such optical, diastereoisomers and geometric isomers that possess E. faecalis Murl or E. faecium Murl inhibitory activity.

The invention relates to any and all tautomeric forms of the compounds of the invention that possess E. faecalis Murl or E. faecium Murl inhibitory activity.

A "subject," as used herein, refers to a mammal, preferably a human, but can also be an animal in need of veterinary treatment, e.g., companion animals (e.g., dogs, cats, and the like), farm animals (e.g., cows, sheep, pigs, horses, and the like) and laboratory animals (e.g., rats, mice, guinea pigs, and the like).

As noted above, one embodiment of the present invention is directed to treating or preventing diseases caused by bacterial infections, wherein the bacteria comprise a Murl enzyme for cell wall biosynthesis, such as E. faecalis and E. faecium infections. "Treating a subject with a disease caused by a bacterial infection" includes achieving, partially or substantially, one or more of the following: the reducing or amelioration of the progression, severity and/or duration of the infection, arresting the spread of an infection, ameliorating or
improving a clinical symptom or indicator associated with a the infection (such as tissue or serum components), and preventing the reoccurrence of the infection.

As used herein, the terms "preventing a bacterial infection" refer to the reduction in the risk of acquiring the infection, or the reduction or inhibition of the recurrence of the infection. In a preferred embodiment, a compound of the invention is administered as a preventative measure to a patient, preferably a human, before a surgical procedure is performed on the patient to prevent infection.

As used herein, the term "effective amount" refers to an amount of a compound of this invention for treating or preventing a bacterial infection is an amount which is sufficient to prevent the onset of an infection, reduce or ameliorate the severity, duration, or progression, of an infection, prevent the advancement of an infection, cause the regression of an infection, prevent the recurrence, development, onset or progression of a symptom associated with an infection, or enhance or improve the prophylactic or therapeutic effect(s) of another therapy.

B. Compounds of the Invention

In one embodiment, the present invention provides a compound of formula (I):

```
   R_3
   N       N       N
   |       |       |
   X_1  -N=N-  X_2
   |       |       |
   X_3
```

or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein:

\( X_1 \) is a divalent \( C^aUcyl \), a divalent \( C_6^i\)alkenyl or a divalent \( C_6^i\)alkynyl, wherein the divalent alkyl, alkenyl or alkynyl may be optionally substituted with one or more substituent selected from the group consisting of halo, cyano, nitro, hydroxy, =O, =S, \( C_{1,4}^i\)alkoxy, \( C_{4}^i\)alkylsulfanyl, amino, \( C_{1,4}^i\)alkylamino, and \( C_{1,4}^i\)dialkylamino;

\( X_2 \) is \(-O-, -S-, \) or \(-NR^a-, \) wherein \( R^a \) is hydrogen or a \( C_{1,4}^i\)alkyl;

\( X_3 \) is \( CR_{10} \) or \( N; \)

\( R^i \) is a \( C_{3,4}^i\)carbocycle, morpholinyl, quinolinyl, benzodioxinyl, benzodioxolyl, 1-H-pyrazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 2-oxo-2,3-dihydro-1,3-benzoxazolyl, tetrahydro-1H-pyran, 1-benzothiophenyl, furanyl, thiazolyl, isoxazolyl, or oxetanyl, wherein the carbocycle, morpholinyl, quinolinyl, benzodioxinyl, benzodioxolyl, 1-H-pyrazolyl, 1,3,4-
oxadiazolyl, 1,2,4-oxadiazolyl, 2-oxo-2,3-dihydro-1,3-benzoazolyl, tetrahydro-lH-pyran, 1-
benzo thiophenyl, furanyl, thiazolyl, isoxazolyl, or oxetanyl is optionally substituted on one or
more carbon atom with one or more R₅; and wherein each =N- of the quinolinyl, pyrazolyl,
1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, thiazolyl, and isoxazolyl, may be each independently
optionally substituted with an oxo; and wherein the -NH- of morpholinyl, 1-H-pyrazolyl, and
2-0X0-2,3-dihydro-1,3-benzoazo 1y1 may be optionally substituted with Rn;
R₂ is a C₃₋₆ alkyl, C₅₋₆ alkenyl, C₅₋₆ alkynyl, C₃₋₄ carbocycle, heterocycle, C₃₋₄
carbocycleC₅₋₆ alkyl, or heterocycleC₅₋₆ alkyl, wherein the alkyl, alkenyl, alkynyl, carbocycle,
heterocycle, carbocyclealkyl, or heterocyclealkyl may be optionally substituted on one or
more carbon atoms with one or more R₆, and wherein if R₂ is a heterocycle or a
heterocyclealkyl comprising one or more -S-, =N- or both, each -S- may be independently
optionally substituted with one or two oxo groups and each =N- may be independently
optionally substituted with one oxo group; and wherein if R₂ is a heterocycle or a
heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently
optionally substituted with Rs;
R₃ and R₄ are each, independently, hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₄
heterocycle, heterocycle, C₃₋₄ carbocycleC₁₋₆ alkyl, or heterocycloc₃₋₄ alkyl, wherein the
alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclocyclealkyl may be
optionally substituted on one or more carbon atoms with one or more R₇, and wherein if R₃ or
R₄ is a heterocycle or a heterocyclealkyl comprising one or more -S-, =N- or both, each -S-
may be independently optionally substituted with one or two oxo groups and each =N-
may be independently optionally substituted with one oxo group; and wherein if R₃ or R₄ is a
heterocycle or a heterocyclealkyl that contains one or more -NH-, each -NH- may be
independently optionally substituted with R₉; or R₃ and R₄ taken together with the nitrogen
atom to which they are attached form a heterocycle which may be optionally substituted on
one or more carbon atoms with one or more R₇, wherein if the heterocycle comprises one or
more -S-, =N- or both, each -S- may be independently optionally substituted with one or two
oxo groups and each =N- may be independently optionally substituted with one oxo group;
and wherein if the heterocycle comprises one or more -NH-, each -NH- may be
independently optionally substituted with R₉;
R₅, R₆ and R₇, for each occurrence, are independently selected from the group
consisting of a halo, nitro, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₄ carbocycle,
heterocycle, C₃₋₄ carbocycleC₁₋₆ alkyl, heterocycleC₁₋₆ alkyl, C₁₋₆ haloalkyl, -ORn, -SRn, -
NR \_1\_2R\_1\_3,-C(O)R\_1\_1,-C(O)OR\_1\_1,-C(O)NR\_1\_2R\_1\_3,-NR\_1\_1C(O)R\_1\_1,-OC(O)R\_1\_1,-NR\_1\_1C(O)OR\_1\_1,-OC(O)NR\_1\_2R\_1\_3,-NR\_1\_1C(O)NR\_1\_2R\_1\_3,-NR\_1\_1C(NR\_1\_4)NR\_1\_2R\_1\_3,-S(0)\_pR\_n,-NR\_1\_1S(O)\_pR\_1\_1, and -S(O)\_pNR\_1\_2R\_1\_3, wherein if R\_5, R\_6 or R\_7 is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be optionally further substituted on one or more carbon atoms with one or more R\_5\_6; and wherein if R\_5, R\_6 or R\_7 is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R\_5, R\_6 or R\_7 is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R\_5\_6.

Rs, R\_9, or R\_1\_7, for each occurrence, are independently selected from the group consisting of C\_1\_6alkyl, C\_2\_6alkenyl, C\_2\_6alkynyl, C\_3\_4carbocycle, heterocycle, C\_3\_1\_4carbocycleC\_1\_6alkyl, heterocycleC\_1\_6alkyl, C\_1\_6haloalkyl, -C(O)R\_1\_1,-C(O)OR\_1\_1,-C(O)NR\_1\_2R\_1\_3,-S(0)\_pR\_n, and -S(O)\_pNR\_1\_2R\_1\_3, wherein if R\_8, R\_9 or R\_1\_7 is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be optionally substituted on one or more carbon atoms with one or more R\_5\_6; and wherein if R\_8, R\_9 or R\_1\_7 is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R\_8, R\_9 or R\_1\_7 is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R\_5\_6.

R\_1\_10 is hydrogen, a C\_1\_6alkyl, a heterocycleC\_1\_6alkyl, -NR\_1\_1R\_1\_3,-C(O)R\_1\_1,-C(O)OR\_1\_1,-C(O)NR\_1\_2R\_1\_3,-NR\_1\_1C(O)R\_1\_1,-OC(O)R\_1\_1,-NR\_1\_1C(O)OR\_1\_1,-OC(O)NR\_1\_2R\_1\_3,-NR\_1\_1C(NR\_1\_4)NR\_1\_2R\_1\_3,-S(0)\_pR\_n,-NR\_1\_1S(O)\_pR\_1\_1, and -S(O)\_pNR\_1\_2R\_1\_3.

R\_1\_11, for each occurrence, is independently selected from the group consisting of hydrogen, C\_1\_6alkyl, C\_2\_6alkenyl, C\_2\_6alkynyl, C\_3\_4carbocycle, heterocycle, C\_3\_1\_4Ca\^{+}OCyCl\_ealkyl, heterocycleC\_1\_6alkyl, wherein if R\_1\_1 is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more R\_5\_6, and wherein if R\_1\_1 is heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R\_1\_1 is a heterocycle
or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R_{i6};

R_{i2} and R_{n}, for each occurrence, are independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-14} carbocycle, heterocycle, C_{3-14} carbocycleC_{1-6} alkyl, heterocycleC_{1-6} alkyl, wherein if R_{i2} or R_{n} is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more R_i5, and wherein if R_{i2} or R_{n} is heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R_{i2} or R_{n} is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R_{i6}; or R_{i2} and R_{n} taken together with the nitrogen atom to which they are attached for a heterocycle, wherein the heterocycle may be optionally substituted on one or more carbon atoms with one or more R_i5, and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally selected from the group consisting of halo, nitro, cyano, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-14} carbocycle, heterocycle, C_{3-14} carbocycleC_{1-6} alkyl, heterocycleC_{1-6} alkyl, C_{1-6} haloalkyl, -OR_{18}, -SR_{18}, -NR_{i19}R_{20}, -C(O)RiS, -C(O)ORi g, -C(O)NRi gR_{20}, -NRi gC(O)Ri g, -OC(O)Ri g, -NRi gC(O)ORi g, -OC(O)NRi gR_{20}, -NRi gC(O)NRi gR_{20}, -NRi gC(NR_{2-1})NRi gR_{20}, -S(O)_{p}Ri g, -NRi gS(O)_{p}Ri g, and -S(O)_{p}NRi gR_{20};

R_{i4} and R_{2-1}, for each occurrence, are independently selected from the group consisting of hydrogen, a C_{1-6} alkyl, nitro, cyano, amino, alkylamino, dialkylamino, or hydroxy;

R_{i6}, for each occurrence, is independently selected from the group consisting of C_{i-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-14} carbocycle, heterocycle, C_{3-14} carbocycleC_{1-6} alkyl, heterocycleC_{i-6} alkyl, C_{i-6} haloalkyl, -C(O)Ri g, -C(O)ORi g, -C(O)NRi gR_{20}, -S(O)_{p}Ri g, and -S(O)_{p}NRi gR_{20};

R_{i8}, for each occurrence, is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-14} carbocycle, heterocycle, C_{3-14} carbocycleC_{1-6} alkyl.
R\textsubscript{19} and R\textsubscript{20}, for each occurrence, are independently selected from the group consisting of hydrogen, C\textsubscript{1-6}alkyl, C\textsubscript{2-6}alkenyl, C\textsubscript{2-6}alkynyl, C\textsubscript{3-14}carbocycle, heterocycle, C\textsubscript{3-14}carbocycleC\textsubscript{1-6}alkyl, heterocycleC\textsubscript{1-6}alkyl; or R\textsubscript{19} and R\textsubscript{20} taken together with the nitrogen atom to which they are attached for a heterocycle; and

p is 1 or 2.

In some embodiments of the compounds of formula (I), one or more (including all) of the following provisos apply:

- R\textsubscript{i} is not an unsubstituted phenyl, unsubstituted biphenyl, an unsubstituted cyclopropyl, or 3-cyclopentyloxy-4-methoxyphenyl;
- when R\textsubscript{i} is 4-chlorophenyl, 4-fluorophenyl, cyclohexyl, or furanyl, R\textsubscript{2} is not unsubstituted naphthyl or unsubstituted cyclopentyl;
- when R\textsubscript{i} is morpholinyl, one of R\textsubscript{3} and R\textsubscript{4} are not 4-aminobenzyl or phenylethyl;
- when X\textsubscript{2} is -NR\textsubscript{a} -, R\textsubscript{2} is a C\textsubscript{1-4}alkyl which is optionally substituted with one or more carbon atom with one or more R\textsubscript{6}, and R\textsubscript{i} is not 4-aminophenyl, 2-chlorophenyl, 4-methylphenyl, 3-(methoxycarbonylmethyl)-phenyl, 2-fluorophenyl, or 2,6-difluorophenyl.
- when -X\textsubscript{2}-R\textsubscript{2} is methylsulfanyl, R\textsubscript{i} is not 4-methylphenyl, 2-methoxyphenyl, or 2-fluorophenyl;
- when -X\textsubscript{2}-R\textsubscript{2} is an unsubstituted n-butyloxy, R\textsubscript{i} is not 3-(2-methoxy-2-oxoethyl)-phenyl, 3-cyanomethyl-phenyl, 3-chloromethyl-phenyl, 3-hydroxymethyl-phenyl, 4-benzzyloxyphenyl, 3-cyanomethyl-4-fluoro-phenyl, 3-chloromethyl-4-fluoro-phenyl, 3-hydroxymethyl-4-fluoro-phenyl, 3-methoxycarbonyl-4-fluoro-phenyl, 2-methoxy-5-cyanomethyl-phenyl, 2-methoxy-5-chloromethyl-phenyl, 2-methoxy-5-hydroxymethyl-phenyl, 2-methoxy-5-methoxycarbonyl-phenyl, 3,4-di-(methoxycarbonyl)-phenyl, 4-hydroxyphenyl, or 3-(1,1,2-trimethoxy-2-oxoethyl)-phenyl; and
- when -X-R\textsubscript{2} is an unsubstituted n-butyloxy and -NR\textsubscript{3}R\textsubscript{4} is -NH\textsubscript{2}, R\textsubscript{i} is not 3-methoxycarbonyl-phenyl or 4-acetoxyphenyl.

In another embodiment, the invention relates to compounds represented by formula (II):
or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein X_3, R_2, R_3, and R_4 are defined as above, and wherein:

5 \( X_4 \) is -O- or -S-;

R_22 is a C_3,6alkyl which is optionally substituted on one or more carbon atom with one or more substituents selected from the group consisting of halo, nitro, cyano, -ORn, -SRn, -NR_{12}R_{13}, -C(O)R_{11}, -C(O)OR_{11}, -C(O)NR_{12}R_{13}, -NR_{11}C(O)R_{11}, -OC(O)R_{11}, -NR_{11}C(O)OR_{11}, -OC(O)NR_{12}R_{13}, -NR_{11}C(O)NR_{12}R_{13}, -NR_{11}C(NR_{14})NR_{12}R_{13}, -S(O)_{p}R_{n}, -NR_{n}S(0)_{p}R_{n}, and

10 -S(O)_{p}NR_{12}R_{13}; wherein R_{11}, R_{i2}, R_{i3}, RH, and p are defined as above.

In some embodiments of the compounds of formula (II), one or both of the following provisos apply:

when both R_3 and R_4 are hydrogen, R_2 and R_22 are not both n-hexyl or both n-propyl, or R_22 is not n-propyl and R_2 is not methyl; and

15 when R_2 is methyl, R_3 and R_4 taken together with the nitrogen atom to which they are attached are not a substituted or unsubstituted piperazino.

In one embodiment of the compounds of formula (I), R_i is a C_3,14carbocycle which is optionally substituted on one or more carbon atoms with one or more independently selected R_5. In one aspect of this embodiment, R_i is phenyl which is optionally substituted with one or more independently selected R_5. In another aspect of this embodiment, R_5, for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-yloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-yloxy, ethoxycarbonyl, carboxy, ethyl,

20 carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenoxy, 4-fluorophenoxy, and 1-methyl-ethyl. In another aspect of this embodiment, R_i has one R_5 substituent. In another aspect of this embodiment, R_i has
two independently selected \( R_5 \) substituents. In another aspect of this embodiment, \( R_i \) has three independently selected \( R_5 \) substituents.

In another embodiment of the compounds represented by formula (I), \( R_i \) is morpholinyl which is optionally substituted on one or more carbon atom with one or more independently selected \( R^5 \), and wherein if the morpholinyl comprises -NH-, it may be optionally substituted on the nitrogen atom with \( R_n \). In another aspect of this embodiment, \( R_5 \), for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-enyl, ethoxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-ynyl, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenyl, 4-fluorophenyl, and 1-methyl-ethyl. In another aspect of this embodiment, \( R_i \) has one \( R_5 \) substituent. In another aspect of this embodiment, \( R_i \) has two independently selected \( R_5 \) substituents. In another aspect of this embodiment, \( R_i \) has three independently selected \( R_5 \) substituents. In another aspect of this embodiment, \( R_{17} \) is selected from the group consisting of \( C_{1-4} \)alkyl, benzyl, acetyl, \( C_{1-4} \)alkoxycarbonyl, carbamoyl, \( N-C_{1-4} \)alkylcarbamoyl, \( N,N-C_{1-4} \)dialkylcarbamoyl, \( C_{1-4} \)alkylsulfonyl.

In another embodiment of the compounds represented by formula (I), \( R_i \) is benzodioxinyl or benzodioxolyl, which can be optionally substituted on one or more carbon atom with one or more independently selected \( R_5 \). In another aspect of this embodiment, \( R_5 \), for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-enyl, ethoxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-ynyl, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenyl, 4-fluorophenyl, and 1-methyl-ethyl. In another aspect of this embodiment, \( R_i \) has one \( R_5 \) substituent. In another aspect of this embodiment, \( R_i \) has two independently selected \( R_5 \) substituents. In another aspect of this embodiment, \( R_i \) has three independently selected \( R_5 \) substituents.

In another embodiment of the compounds represented by formula (I), \( R_i \) is quinolinyl which is optionally substituted with one or more independently selected \( R^5 \) and which is
optionally substituted on the nitrogen atom with an oxo. In another aspect of this embodiment, \( R_5 \), for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-yloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-yloxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenoxy, 4-fluorophenoxyloxy, and 1-methyl-ethyl. In another aspect of this embodiment, \( R_i \) has one \( R_5 \) substituent. In another aspect of this embodiment, \( R_i \) has two independently selected \( R_5 \) substituents. In another aspect of this embodiment, \( R_i \) has three independently selected \( R_5 \) substituents.

- In another embodiment of the compounds represented by formula (I), \( X_i \) is CH₂⁻.
- In another embodiment of the compounds represented by formula (I), \( X_i \) is C(O)CH₂⁻, CH₂C(O)⁻, -C(O)⁻, -CH(OH)CH₂⁻, or -CH₂CH₂⁻.

In another embodiment of the compounds represented by formula (I), \( X_2 \) is O⁻.
- In another embodiment of the compounds represented by formula (I), \( X_2 \) is S⁻.
- In another embodiment of the compounds represented by formula (I), \( X_2 \) is -NR⁻. In one aspect of this embodiment, \( R^a \) is H. In another aspect of this embodiment, \( R^a \) is a C₃₆alkyl. In another aspect of this embodiment, \( R^a \) is methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, or tert-butyl.

- In one embodiment of the compounds represented by formula (II), \( R_{22} \) is an unsubstituted C₃₆alkyl group.
- In another embodiment of the compounds represented by formula (II), \( R_{22} \) is propyl, butyl, 2,3-dihydroxy-propyl, 3-cyanopropyl, 2-methyl-propyl, 3-phenoxy-2-hydroxy-propyl, 2-hydroxy-2-methyl-propyl, 2-hydroxy-3-methoxy-propyl, 4,4,4-trifluoro-butyl, 2-hydroxybutyl, 2-ethyl-butyl, 4-cyanobutyl, or isopentyl.
- In another embodiment of the compounds represented by formula (II), \( X_4 \) is O⁻.
- In another embodiment of the compounds represented by formula (II), \( X_4 \) is S⁻.
- In another embodiment of the compounds represented by formula (I) or (II), \( R_2 \) is C₃₆alkyl which is optionally substituted on one or more carbon atoms with one or more \( R_6 \). In one aspect of this embodiment, \( R_2 \) is a C₃₆alkyl selected from the group consisting of methyl, ethyl, n-propyl, n-butyl, n-pentyl, isobutyl, isopentyl, and 2-methylbutyl, wherein the C₃₆alkyl may be optionally substituted on one or more carbon atom with one or more \( R_6 \). In one
aspect of this embodiment, R₆, for each occurrence, is independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, N,N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I) or (II), R₂ is a 5 C₃₋₄ Cycloalkyl which may be optionally substituted on one or more carbon atom with one or more R₆. In one aspect of this embodiment, R₂ is cyclopentyl or cyclohexyl which may be optionally substituted on one or more carbon atom with one or more R₆. In one aspect of this embodiment, R₆, for each occurrence, is independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, N,N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I) or (II), R₂ is decahydrornaphthalenyl, phenyl, but-2-en-1-yl, pent-2-yn-1-yl, but-2-yn-1-yl, or phenyl, each of which may be optionally substituted on one or more carbon atom with one or more R₆. In one aspect of this embodiment, R₆, for each occurrence, is independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, N,N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I) or (II), R₂ is piperidinyl which may be optionally substituted on one or more carbon atom with one or more R₆, and wherein if the piperidinyl group comprises -NH-, it may be substituted with Rₛ. In one aspect of this embodiment, R₆, for each occurrence, is independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, N,N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl. In one aspect of this embodiment, Rₛ is methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, tert-butyl, acetyl, or methylsulfonyl.

In another embodiment of the compounds represented by formula (I) or (II), R₃ and R₄ are both hydrogen.

In another embodiment of the compounds represented by formula (I) or (II), one of R₃ or R₄ is hydrogen and the other is methyl, n-butyl, morpholinoethyl, (furan-3-yl)-methyl, (5-methyl-furan-2-yl)-methyl, benzyl, 2,6-difluorobenzyl, cyclopropyl, 2-phenyl-cyclopropyl, or benzoimidazol-2-yl.

In another embodiment of the compounds represented by formula (I) or (II), R₃ or R₄ are both methyl.
In another embodiment of the compounds represented by formula (I) or (II), R and R together with the nitrogen atom to which they are attached form morpholino.

In another embodiment of the compounds represented by formula (I) or (II), X₃ is CRio. In one aspect of this embodiment, Rio is H. In another aspect of this embodiment, Rio is selected from the group consisting of 2-piperizino-ethylamino, 2-(4-methyl-piperazino)-ethylamino, 2-morpholo-ethylamino, 2-hydroxyethylamino, 2-(diethylamino)-ethylamino, morpholo, piperazine, methyl, carboxy, and ethoxycarbonyl.

In another embodiment of the compounds represented by formula (I) or (II), X₃ is N.

In another embodiment of the compounds represented by formula (I), Ri is phenyl which is optionally substituted with from one to three independently selected R₅; R₂ is a C₆ alkyl which is optionally substituted with from one to three independently selected R₆; and X₁ is -CH₂-. In one aspect of this embodiment, R₅, for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-lyloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-lyloxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxo, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethylamino, acetoxy, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyroxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenyl, 4-fluorophenyl, and 1-methyl-ethyl. In another aspect of this embodiment, Ri has one R₅ substituent. In another aspect of this embodiment, Ri has two independently selected R₅ substituents. In another aspect of this embodiment, Ri has three independently selected R₅ substituents. In another aspect of this embodiment, R₂ is unsubstituted. In another aspect of this embodiment, R₂ is substituted with from one to three independently selected R₆ which are independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, N,N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I), Ri is phenyl which is optionally substituted with from one to three independently selected R₅; R₂ is a C₆ alkyl which is optionally substituted with from one to three independently selected R₆; X₁ is -CH₂-; and R₃ and R₄ are both hydrogen. In one aspect of this embodiment, R₅, for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-lyloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-lyloxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxo, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-
methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenoxy, 4-fluorophenoxy, and 1-methyl-ethyl. In another aspect of this embodiment, R_i has one R_5 substituent. In another aspect of this embodiment, R_i has two independently selected R_5 substituents. In another aspect of this embodiment, R_i has three independently selected R_5 substituents. In another aspect of this embodiment, R_2 is unsubstituted. In another aspect of this embodiment, R_2 is substituted with from one to three R_6 which are independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, 7V,7V-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I), R_i is phenyl which is optionally substituted with from one to three independently selected R_5; R_2 is a Ci_6 alkyl which is optionally substituted with from one to three independently selected R_6; X_i is CH_2-; and one of R_3 or R_4 is hydrogen and the other is 2-morpholinoethyl. In one aspect of this embodiment, R_5, for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-ynoxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-ynoxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenoxy, 4-fluorophenoxy, and 1-methyl-ethyl. In another aspect of this embodiment, R_i has one R_5 substituent. In another aspect of this embodiment, R_i has two independently selected R_5 substituents. In another aspect of this embodiment, R_i has three independently selected R_5 substituents. In another aspect of this embodiment, R_2 is unsubstituted. In another aspect of this embodiment, R_2 is substituted with from one to three R_6 which are independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, 7V,7V-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I), R_i is phenyl which is optionally substituted with from one to three independently selected R_5; R_2 is a Ci_6 alkyl which is optionally substituted with from one to three independently selected R_6; X_i is CH_2-; R_3 and R_4 are both hydrogen; and X_5 is CH. In one aspect of this embodiment, R_5, for each occurrence, is independently selected from the group consisting of nitro, methoxy,
methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-yloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-yloxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenoxo, 4-fluorophenoxo, and 1-methyl-ethyl. In another aspect of this embodiment, $R_{i}$ has one $R_{5}$ substituent. In another aspect of this embodiment, $R_{i}$ has two independently selected $R_{5}$ substituents. In another aspect of this embodiment, $R_{i}$ has three independently selected $R_{5}$ substituents. In another aspect of this embodiment, $R_{2}$ is unsubstituted. In another aspect of this embodiment, $R_{2}$ is substituted with from one to three $R_{6}$ which are independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, 7V,7V-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (I), $R_{i}$ is phenyl which is optionally substituted with from one to three independently selected $R_{5}$; $R_{2}$ is a $C_{6}$ alkyl which is optionally substituted with from one to three independently selected $R_{6}$; $X_{i}$ is -CH$_{2}$_; $R_{3}$ and $R_{4}$ are both hydrogen; and $X_{3}$ is $C_{10}$ wherein $R_{i0}$ is -NR$_{2}$R$_{3}$. In one aspect of this embodiment, $R_{5}$, for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-yloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-yloxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfonyl, 4-chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy, phenyl, aminomethyl, 2-fluorophenoxo, 4-fluorophenoxo, and 1-methyl-ethyl. In another aspect of this embodiment, $R_{i}$ has one $R_{5}$ substituent. In another aspect of this embodiment, $R_{i}$ has two independently selected $R_{5}$ substituents. In another aspect of this embodiment, $R_{i}$ has three independently selected $R_{5}$ substituents. In another aspect of this embodiment, $R_{2}$ is unsubstituted. In another aspect of this embodiment, $R_{2}$ is substituted with from one to three $R_{6}$ which are independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, $N,N$-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl. In another aspect of this embodiment, -NR$_{2}$R$_{3}$ is selected from the group consisting of 2-piperizino-ethylamino,
2-(4-methyl-piperazino)-ethylamino, 2-morpholino-ethylamino, 2-hydroxyethylamino, 2-
(diethylamino)-ethylamino, morpholino, and piperazine.

In another embodiment of the compounds represented by formula (I), Ri is phenyl
which is optionally substituted with from one to three independently selected R5; R2 is a C3,
14cycloalkyl which is optionally substituted with from one to three independently selected R6;
and Xi is -CH2-. In one aspect of this embodiment, R2 is a cyclopentyl or cyclohexyl which
is optionally substituted with one or more independently selected R6. In one aspect of this
embodiment, R5, for each occurrence, is independently selected from the group consisting of
nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-
10yloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-yloxy, ethoxycarbonyl,
carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl, tetrazole-
5-yl, 2-(N-methyl-piperazino)-ethyl-amino, acetamido, hydroxy, aminosulfanyl, 4-
chlorophenyl, 2-methoxyphenyl, phenylsulfonylmethyl, butyloxy, cyclopropylmethoxy,
phenyl, aminomethyl, 2-fluorophenyl, 4-fluorophenyl,ox, and 1-methyl-ethyl. In another
aspect of this embodiment, Ri has one R5 substituent. In another aspect of this embodiment,
Ri has two independently selected R5 substituents. In another aspect of this embodiment, Ri
has three independently selected R5 substituents. In another aspect of this embodiment, R2 is
unsubstituted. In another aspect of this embodiment, R2 is substituted with from one to three
R6 which are independently selected from the group consisting of cyclopropyl, cyclobutyl,
20cyclopentyl, cyclohexyl, methoxy, methyl, 2V,7V-dimethylamino, acetamido, fluoro, hydroxy,
phenyl, and methylsulfonyl.

In another embodiment of the compounds represented by formula (II), R2 is a C1,
6alkyl which is optionally substituted with from one to three independently selected R6; X3 is
CH; and R3 and R4 are both hydrogen. In one aspect of this embodiment, R2 is unsubstituted.
25In another aspect of this embodiment, R2 is substituted with from one to three R6 which are
independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl,
cyclohexyl, methoxy, methyl, 2V,7V-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and
methylsulfonyl.

In another embodiment of the compounds represented by formula (II), R2 is a C1,
306alkyl which is optionally substituted with from one to three independently selected R6; X3 is
CH; and one of R3 or R4 is hydrogen and the other is 2-morpholinoethyl. In one aspect of this
embodiment, R2 is unsubstituted. In another aspect of this embodiment, R2 is substituted with
from one to three R6 which are independently selected from the group consisting of
cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, N,N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

In another embodiment, the invention provides compounds selected from the group consisting of:

2-(butylthio)-9-(3-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[3-(trifluoromethyl)benzyl]-9H-purin-6-amine;
2-(butylthio)-9-(3-chlorobenzyl)-9H-purin-6-amine;
3-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]benzonitrile;
2-(butylthio)-9-(3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,4-dichlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-methoxy-5-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-chloro-4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,6-dichlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-chloro-5-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine;
methyl 3-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]benzoate;
2-(butylthio)-9-(4-chloro-2-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[2-fluoro-6-(trifluoromethyl)benzyl]-9H-purin-6-amine;
2-(butylthio)-9-(2-fluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[4-(methylsulfonyl)benzyl]-9H-purin-6-amine;
2-(butylthio)-9-(2-chloro-5-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,4-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(4,5-dimethoxy-2-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(5-chloro-2-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-chloro-2,6-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-dimethoxybenzyl)-9H-purin-6-amine;
2-(butylthio)-9-{2-[(phenylsulfonyl)methyl]benzyl}-9H-purin-6-amine;
2-(butylthio)-9-(4-fluoro-3-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(4-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,4-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,5-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-chlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-chloro-4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-chloro-4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-dimethylbenzyl)-9H-purin-6-amine;
2-\{6-amino-2-(butylthio)-9H-purin-9-yl\}methylbenzonitrile;
4-\{6-amino-2-(butylthio)-9H-purin-9-yl\}methylbenzonitrile;
9-(4-bromo-2-fluorobenzyl)-2-(butylthio)-9H-purin-6-amine;
2-(butylthio)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,5-dichlorobenzyl)-9H-purin-6-amine;
methyl 4-\{6-amino-2-(butylthio)-9H-purin-9-yl\}methyl-3-methoxybenzoate;
2-(butylthio)-9-(3-fluoro-4-methylbenzyl)-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-2-(isobutylthio)-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-2-\{(3-methylbutyl)thio\}-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-2-\{(2-methylbutyl)thio\}-9H-purin-6-amine;
2-(cyclopentylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine;
2-(cyclohexylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-2-(2-methoxyethoxy)-9H-purin-6-amine;
2-(butylthio)-9-(cyclobutylmethyl)-9H-purin-6-amine;
2-(butylthio)-9-(cyclohexylmethyl)-9H-purin-6-amine;
2-(butylthio)-9-(tetrahydro-2H-pyran-2-ylmethyl)-9H-purin-6-amine;
9-(3-chloro-2,6-difluorobenzyl)-\textit{N}-(2-morpholin-4-ylethyl)-2-(4,4,4-trifluorobutoxy)-9H-purin-6-amine;
2-(butylthio)-9-(2,3-dichlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-\{(5-chloro-1-benzothien-3-yl)methyl\}-9H-purin-6-amine;
2-(butyl{9-(3-chloro-2,6-difluorobenzyl)-6-{[(2-morpholin-4-ylethyl)amino]-9 \textit{H}-purin-2-yl}} amino)ethanol;
2-butoxy-9-(2,3-dichlorobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-[4-(methylsulfonyl)benzyl]-7\textit{V}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(2-methoxy-5-nitrobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
3-({2-butoxy-6-{[(2-morpholin-4-ylethyl)amino]-9 \textit{H}-purin-9-yl}methyl}benzonitrile;
9-(5-amino-2-methoxybenzyl)-2-butoxy- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
9-(2,6-difluorobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-2-phenoxy-9 \textit{H}-purin-6-amine;
5-(butylthio)-3-(3-chloro-2,6-difluorobenzyl)-3 \textit{H}-[1,2,3]triazolo[4,5-\textit{d}]pyrimidin-7-amine;
5-(butylthio)-3-(2,6-difluoro-3-methylbenzyl)-3 \textit{H}-[1,2,3]triazolo[4,5-\textit{d}]pyrimidin-7-amine;
2-(butylthio)-9-bis(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-(cyclopropylmethoxy)-9-[3-(trifluoromethyl)benzyl]-9 \textit{H}-purin-6-amine;
2-(cyclopentylmethoxy)-9-[3-(trifluoromethyl)benzyl]-9 \textit{H}-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-(pentyloxy)-9 \textit{H}-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-{[(3-methylcyclopentyl)oxy]-9 \textit{H}-purin-6-amine;
2-(benzyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-(cyclobutylmethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-(cyclopentyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-(l-cyclopropylethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine; 
9-(2,6-difluoro-3-methylbenzyl)-2-[(l-methylcyclopropyl)methoxy]-9 \textit{H}-purin-6-amine; 
2-(cyclopropylmethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine 
9-(2,6-difluoro-3-methylbenzyl)-2-methoxy-9 \textit{H}-purin-6-amine; 
9-(2,6-difluoro-3-methylbenzyl)-2-propoxy-9 \textit{H}-purin-6-amine; 
2-(cyclohexyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine; 
9-(2,6-difluoro-3-methylbenzyl)-2-isobutoxy-9 \textit{H}-purin-6-amine; 
9-(2,6-difluoro-3-methylbenzyl)-N,\textit{N}^2-dimethyl-9\textit{H}-purine-2,6-diamine; 
9-(2,6-difluoro-3-methylbenzyl)-2-[2-(dimethylamino)ethoxy]-9 \textit{H}-purin-6-amine; 
N-(2-{{6-amino-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-2-yl}oxy}ethyl)acetamide; 
9-(2,6-difluoro-3-methylbenzyl)-2-[(4,4,5,5,5-pentafluoropentyl)oxy]-9 \textit{H}-purin-6-amine; 
2-[[6-amino-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-2-yl][methyl]amino]ethanol; 
9-(2,6-difluoro-3-methylbenzyl)-2-(4,4,4-trifluorobutoxy)-9 \textit{H}-purin-6-amine; 
2-(decahydro-naphthalen-2-yloxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine / 2-(decahydronaphthalen-1-yloxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine; 
\textit{N}^2\textit{N}^6-butyl-9-(2,6-difluoro-3-methylbenzyl)-\textit{N}^6-(2-morpholin-4-ylethyl)-\textit{N}^2-propyl-9\textit{H}-purine-2,6-diamine; 
\textit{N}^2\textit{N}^6-butyl-9-(2,6-difluoro-3-methylbenzyl)-\textit{N}^6-methyl-\textit{N}^2-(2-morpholin-4-ylethyl)-9\textit{H}-purine-2,6-diamine; 
2-butoxy-9-[3-(trifluoromethyl)benzyl]-9\textit{H}-purin-6-amine; 
3-[(6-amino-2-butoxy-9\textit{H}-purin-9-yl)methyl]benzoic acid; 
2-butoxy-9-(2,6-difluorobenzyl)-9 \textit{H}-purin-6-amine; 
2-butoxy-9-(2,6-difluorobenzyl)-\textit{N},\textit{N}dimethyl-9\textit{H}-purin-6-amine; 
\textit{N}^2\textit{n}butyl-9-(2,6-difluorobenzyl)-9 \textit{H}-purine-2,6-diamine; 
2-butoxy-9-(2,6-difluorobenzyl)-\textit{N}-methyl-9\textit{H}-purin-6-amine; 
2-butoxy-9-(2-butoxy-6-fluorobenzyl)-\textit{N}-methyl-9\textit{H}-purin-6-amine; 
2-(cyclopropylmethoxy)-9-[2-(cyclopropylmethoxy)-6-fluorobenzyl]-\textit{N}-methyl-9\textit{H}-
purin-6-amine;
9-(2,6-difluorobenzyl)-N-methyl-2-[2-(methylsulfonyl)ethoxy]-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-N-methyl-2-(2-methylbutoxy)-9H-purin-6-amine;
2-(cyclobutylmethoxy)-9-(2,6-difluorobenzyl)-N-methyl-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-N-methyl-2-(pentyloxy)-9H-purin-6-amine;
2-(cyclopentylxyloxy)-9-(2,6-difluorobenzyl)-N-methyl-9H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-N-ethyl-9H-purin-6-amine;
N-benzyl-2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
N-benzyl-9-(2,6-difluoro-3-methylbenzyl)-2-(pentyloxy)-9H-purin-6-amine;
2-butoxy-N-cyclopropyl-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[2-(6-difluorophenyl)acetyl]-9H-purin-6-amine;
2-(butylthio)-9-(2,6-difluorobenzoyl)-9H-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzoyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzoyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
1-[6-amino-2-(butylthio)-9H-purin-9-yl]-2-(2,6-difluorophenyl)ethanol;
3-[(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-1-oxido-9H-purin-9-ylmethyl)benzamide;
3-[(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-ylmethyl)benzamide;
2-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]-4-nitrophenol;
4-[(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-1-oxido-9H-purin-9-ylmethyl)benzamide;
4-[(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-ylmethyl)benzamide;
1-[4-[(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-yl]methyl]phenyl]ethanone;
2-butoxy-9-(2,6-difluorobenzyl)-8-methyl-9H-purin-6-amine;
2-butoxy-9-(2,6-difluorobenzyl)-N°-(2-morpholin-4-ylethyl)-9H-purine-6,8-diamine;
2-butoxy-9-(2,6-difluorobenzyl)-8-(4-methylpiperazin-1-yl)-9H-purin-6-amine;
2-butoxy-N°-[2-(diethylamino)ethyl]-9-(2,6-difluorobenzoyl)-9H-purine-6,8-diamine;
2-[[6-amino-2-butoxy-9-(2,6-difluorobenzyl)-9H-purin-8-yl]amino]ethanol;
2-butoxy-9-(2,6-difluorobenzyl)-8-morpholin-4-yl-9H-purin-6-amine;
2-butoxy-9-(2,6-difluorobenzyl)-N°-[2-(4-methylpiperazin-1-yl)ethyl]-9H-purine-
6,8-diamine;
2-butoxy-9-(2-fluoro-6-[(2-(4-methylpiperazin-1-yl)ethyl]amino)benzyl)-N\textsuperscript{8}-(2-(4-methylpiperazin-1-yl)ethyl]-9\textsubscript{H}-purine-6,8-diamine;
2-butoxy-9-(2,6-difluorobenzyl)-N\textsuperscript{8}-(2-piperazin-1-ylethyl)-9 \textsubscript{H}-purine-6,8-diamine;
2-butoxy-N\textsuperscript{7}-(2,6-difluorobenzyl)-9-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-N\textsuperscript{7}-(5-methyl-2-furyl)methyl]-9-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(2,3-difluorobenzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-N\textsuperscript{7}-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetrafluorobenzyl)-9 \textsubscript{H}-purin-6-amine;
9-[3,5-bis(trifluoromethyl)benzyl]-2-butoxy-N\textsuperscript{7}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-N\textsuperscript{7}-(2-morpholin-4-ylethyl)-9-(2,3,4,5-tetrafluorobenzyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-N\textsuperscript{7}-(3,4-difluorobenzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-N\textsuperscript{7}-(2-chloro-5-(trifluoromethyl)benzyl]-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-N\textsuperscript{7}-(2-fluoro-4-(trifluoromethyl)benzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(4-bromo-2-fluorobenzyl)-2-butoxy-N\textsuperscript{7}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-[2-fluoro-4-(trifluoromethyl)benzyl]-N\textsuperscript{7}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(3,4-difluorobenzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(3-chloro-2-fluorobenzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(4-fluoro-3-methylbenzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(3-(2-fluorophenoxy)benzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-(2-fluoro-6-methylbenzyl)-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-amine;
2-butoxy-9-[3-(2-fluorophenoxy)benzyl]-N\textsuperscript{8}-(2-morpholin-4-ylethyl)-9 \textsubscript{H}-purin-6-
amine;
9-(1,3-benzodioxol-5-ylmethyl)-2-butoxy- Α -[(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
2-butoxy-9-[3-chloro-2-fluoro-5-(trifluoromethyl)benzyl]- Α -[(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
2-butoxy-9- [3-(4-fluorophenoxy)benzyl] -7V-(2-morpholin-4-yethyl)-9 Η -purin-6-amine;
2-butoxy-9-[3-fluoro-2-(trifluoromethyl)benzyl]- Α -[(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
2-butoxy-9-(2,3-dichlorobenzyl)- Α -[(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
methyl 4-([2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9 Η -purin-9-yl]methyl)-3-methoxybenzoate;
methyl 3-([2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9 Η -purin-9-yl]methyl)benzoate;
4-((2-butoxy-9-(2-morpholin-4-yethyl)-9 Η -purin-6-yl)amino)methylbenzenesulfonamide;
4-((2-butoxy-6-2-morpholin-4-yethyl)amino)-9 Η -purin-9-yl)methyl)-3-methoxybenzoic acid;
2-butoxy-7V-(2-morpholin-4-yethyl)-9- [2-(trifluoromethyl)benzyl] -9Η -purin-6-amine;
[4-((2-butoxy-6-[2-morpholin-4-ylethyl)amino]-9 Η -purin-9-yl]methyl)phenylmethano 1;
2-butoxy- Α -(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetrafluoro-4-methylbenzyl)-9 Η -purin-6-amine;
2-butoxy-9-(4-chloro-2-nitrobenzyl)- Α -(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
2-butoxy-9-(2-methyl-3-nitrobenzyl)- Α -(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
9-[(1-bromo-2-naphthyl)methyl]-2-butoxy- Α -(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
2-butoxy-9-[(6-fluoro-4 Η -1,3-benzodioxin-8-yl)methyl]- Α -(2-morpholin-4-ylethyl)-9 Η -purin-6-amine;
Α -[4-((2-butoxy-6-[2-morpholin-4-ylethyl)amino]-9 Η -purin-9-yl]methyl)phenylacetamide;
9-(4-bromobenzyl)-2-butoxy-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(3-chlorobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-\(N\)-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetramethylbenzyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(2-fluoro-6-nitrobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(5-methyl-2-nitrobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 9-(2-bromo-5-methoxybenzyl)-2-butoxy-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(2,5-dimethoxybenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(2,4-dichlorobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(3-methoxybenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 4-({2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9\(H\)-purin-9-yl}methyl)phenylacetate; 2-butoxy-9-(3-fluorobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-\(N\)-(2-morpholin-4-ylethyl)-9-(2-nitrobenzyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(2-chloro-4-fluorobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-7\(V\)-(2-morpholin-4-ylethyl)-9-{4-\([E\]-2-phenylvinyl\]benzyl)-9\(H\)-purin-6-amine; 2-butoxy-\(N\)-(2-morpholin-4-ylethyl)-9-(2,4,6-triisopropylbenzyl)-9\(H\)-purin-6-amine; ethyl 3-({2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9\(H\)-purin-9-yl}methyl)benzoate; 2-butoxy-9-(mesitylmethyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-[5-chloro-2-(trifluoromethyl)benzyl]-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-\(N\)-(2-morpholin-4-ylethyl)-9-(2,3,5-trifluorobenzyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(2,3-dimethoxybenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 2-butoxy-9-(2-chloro-6-fluorobenzyl)-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine; 9-[2-fluoro-6-(pent-2-yn-1-yloxy)benzyl]-\(N\)-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-ylxyloxy)-9\(H\)-purin-6-amine; 2-[\((2E)\)-but-2-en-1-ylxyloxy]-9-\[2-\{\((2E)\)-but-2-en-1-ylxyloxy\}-6-fluorobenzyl\]-\(N\)-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-(hex-2-yn-1-yloxy)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yloxy)-9H-purin-6-amine;
2-(allyloxy)-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-[(2E)-but-2-en-1-yloxy]-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-[(3-methylbut-2-en-1-yl)oxy]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-(but-2-yn-1-yloxy)-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
ethyl 2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9H-purine-8-carboxylate;
2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9H-purine-8-carboxylic acid;
N-(1H-benzimidazol-2-ylmethyl)-2-butoxy-9-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-[4-(aminomethyl)benzyl]-2-butoxy-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine; and pharmaceutically acceptable salt, solvate, or prodrug thereof.

In another embodiment the invention provides compounds selected from the group consisting of:
2-(butylthio)-9-(4,4,4-trifluorobutyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-ethylbutyl)-9H-purin-6-amine;
2-(butylthio)-9-propyl-9H-purin-6-amine;
2-(butylthio)-9-(3-methylbutyl)-9H-purin-6-amine;
2-(butylthio)-9-isobutyl-9H-purin-6-amine;
4-[6-amino-2-(butylthio)-9H-purin-9-yl]butanenitrile;
5-[6-amino-2-(butylthio)-9H-purin-9-yl]pentanenitrile;
2-(benzyloxy)-9-butyl-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-butyl-N-(2-morpholin-4-ylethyl)-2-phenoxy-9H-purin-6-amine;
9-butyl-N-(2-morpholin-4-ylethyl)-2-(pyridin-2-yloxy)-9H-purin-6-amine;
9-butyl-2-[(4-methylpyridin-2-yl)oxy]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
and pharmaceutically acceptable salt, solvate, or prodrug thereof.

Where a particular substituent, such as an alkyl substituent, occurs multiple times in a given structure or moiety, the identity of the substituent is independent in each case and may be the same as or different from other occurrences of that substituent in the structure or moiety. Furthermore, individual substituents in the specific embodiments and exemplary compounds of this invention are preferred in combination with other such substituents in the compounds of this invention, even if such individual substituents are not expressly noted as being preferred or not expressly shown in combination with other substituents.

C. METHODS OF PREPARING COMPOUNDS OF THE INVENTION

In another embodiment, the present invention provides a process for preparing a compound of formula (I) or (II), or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

An adenine derivative, represented by formula (I) or (II) in which $X_2$ or $X_4$, respectively, is $-\text{S-}$ can be prepared by reacting a 4,6-diaminopyrimidine-2-thiol with an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl that has a displaceable group, such as a halo, in the presence of a base, such as NaOH, KOH or LiOH and a polar solvent, such as an alcohol, to form intermediate (i). Intermediate (i) is then converted to a nitroso compound by reacting it with sodium nitrite in the presence of acetic acid and water to form intermediate (ii). Intermediate (ii) is hydrogenated using platinum(IV)oxide and H₂ gas to convert the nitroso group to an amine group, forming intermediate (iii). Typically, this reaction is carried out in an alcoholic solvent such as ethanol. Intermediate (iii) is converted to a purine by refluxing it in formamide to form intermediate (iv). Intermediate (iv) can be reacted in the presence of a carbonate, such as cesium carbonate or MP carbonate™, with an alkyl, a carbocyclealkyl, or a heterocyclealkyl that comprises a displaceable group to form a compound of formula (I) or (II) (see Scheme A).

Scheme A
In another embodiment, compounds of the invention represented by formula (I) or (II) can be prepared by heating 2,6-dichloro-9H-purine with aqueous ammonia or with a primary or secondary amine to form intermediate (vi). The chloro substituent of intermediate (vi) can then be displaced by a thiol substituent of an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl in the presence of cesium carbonate and heat to form a compound of intermediate (vii). Alternatively, the chloro group of intermediate (vi) can be displaced by a hydroxy substituent or an amine substituent of an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl in the presence of a strong base, such as NaOH, and heat to form intermediate (viii) (see Scheme B). Intermediate (vii) or (viii) can be reacted in the presence of a carbonate, such as cesium carbonate or MP carbonate™, with an alkyl, a carbocyclealkyl, or a heterocyclealkyl that comprises a displaceable group to form a compound of formula (I) or (II), as shown in Scheme A.
Compounds of the invention in which X is nitrogen can be prepared by reacting a 2-substituted-4,5,6-triaminopyrimidine with sodium nitrite in acetic acid and water to form intermediate (ix). The reaction is generally carried out at about -20 °C to about 10 °C (see Scheme C). Similarly to the reaction shown in Scheme A, intermediate (ix) can be reacted in the presence of a carbonate, such as cesium carbonate or MP carbonate™, with an alkyl, a carbocyclealkyl, or a heterocyclealkyl that comprises a displaceable group to form a compound of formula (I) or (II) wherein X is nitrogen.

Scheme C
It will be appreciated that certain of the various ring substituents in the compounds of the present invention may be introduced by standard aromatic substitution reactions or generated by conventional functional group modifications either prior to or immediately following the processes mentioned above, and as such are included in the process aspect of the invention. Such reactions and modifications include, for example, introduction of a substituent by means of an aromatic substitution reaction, reduction of substituents, alkylation of substituents and oxidation of substituents. The reagents and reaction conditions for such procedures are well known in the chemical art. Particular examples of aromatic substitution reactions include the introduction of a nitro group using concentrated nitric acid, the introduction of an acyl group using, for example, an acyl halide and Lewis acid (such as aluminium trichloride) under Friedel Crafts conditions; the introduction of an alkyl group using an alkyl halide and Lewis acid (such as aluminium trichloride) under Friedel Crafts conditions; and the introduction of a halogen group. Particular examples of modifications include the reduction of a nitro group to an amino group by for example, catalytic hydrogenation with a nickel catalyst or treatment with iron in the presence of hydrochloric acid with heating; oxidation of alkylthio to alkylsulphinyl or alkylsulphonyl.

It will also be appreciated that in some of the reactions mentioned herein it may be necessary/desirable to protect any sensitive groups in the compounds. The instances where protection is necessary or desirable and suitable methods for protection are known to those skilled in the art. Conventional protecting groups may be used in accordance with standard practice (for illustration see T.W. Green, Protective Groups in Organic Synthesis, John Wiley and Sons, 1991). Thus, if reactants include groups such as amino, carboxy or hydroxy it may be desirable to protect the group in some of the reactions mentioned herein.

A suitable protecting group for an amino or alkylamino group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an alkoxy carbonyl group, for example a methoxycarbonyl, ethoxycarbonyl or t-butoxycarbonyl group, an arylmethoxycarbonyl group, for example benzyloxy carbonyl, or an aroyl group, for example benzoyl. The deprotection conditions for the above protecting groups necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or alkoxy carbonyl group or an aryl group may be removed for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an acyl group such as a t-butoxycarbonyl group may be removed, for example, by treatment with a suitable acid such as hydrochloric, sulphuric or phosphoric acid or trifluoroacetic acid and an
aryl methoxycarbonyl group such as a benzylloxycarbonyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon, or by treatment with a Lewis acid for example boron tris(trifluoroacetate). A suitable alternative protecting group for a primary amino group is, for example, a phthaloyl group which may be removed by treatment with an alkylamine, for example dimethylaminopropylamine, or with hydrazine.

A suitable protecting group for a hydroxy group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an aroyl group, for example benzoyl, or an arylmethyl group, for example benzyl. Other suitable protecting groups for an alcohol include alkyl silyl group such as trimethylsilyl or t-butyl-dimethylsilyl. The deprotection conditions for the above protecting groups will necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or an aroyl group may be removed, for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an arylmethyl group such as a benzyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

Alkylsilyl groups may be removed by treatment with a fluoride such as tetra-n-butylammonium fluoride or by treatment with an acid such as aqueous HCl.

A suitable protecting group for a carboxy group is, for example, an esterifying group, for example a methyl or an ethyl group which may be removed, for example, by hydrolysis with a base such as sodium hydroxide, or for example a t-butyl group which may be removed, for example, by treatment with an acid, for example an organic acid such as trifluoroacetic acid, or for example a benzyl group which may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

The protecting groups may be removed at any convenient stage in the synthesis using conventional techniques well known in the chemical art.

D. METHODS OF USE

As stated hereinbefore the compounds defined in the present invention have Murl inhibitory activity and are useful for treating or preventing bacterial infection. These properties may be assessed, for example, using the procedure described in Example 221.

**LGDH Coupled Enzyme Assay**

Compounds of the invention were tested for inhibition of glutamate racemase using a coupled enzyme assay as previously described (Lundqvist et al, "Exploitation of structural and regulatory diversity in glutamate racemases" Nature, 2007, in press). Assays were
performed in 96-well polystyrene flat-bottom black plates (FLUOTRAC 200) in 102µL reactions containing 2µL compound dissolved in dimethylsulfoxide, 85µL Enzyme Working Solution (final concentrations were 100mM Tris pH 8.0, 0.03% PEG 8000, 0.03mg/mL bovine serum albumin, 15U/mL L-glutamate dehydrogenase (LGDH), 5mM dithiothreitol, 10mM NAD⁺ and either 80mM E.faecalis Murl or 100mM E.faecium Murl or 1µM S.aureus Murl) and 15µL 6.67mM D-glutamate to initiate the reaction (final concentration was 1mM).

Purification of E. faecalis Murl, E. faecium Murl and S. aureus Murl was carried out as follows.

The frozen cell paste was resuspended in 50mL of Lysis Buffer [20mM Tris/HCl, pH 7.5, 5mM DL-Glutamate, 1 EDTA-free protease inhibitor cocktail tablet (Roche Molecular Biochemical)]. Cells were disrupted by French press at 18,000psi twice at 4°C, and the crude extract was centrifuged at 20,000rpm (45Ti rotor, Beckman) for 30min at 4°C. The supernatant was loaded at a flow rate of 2.0mL/min onto a 5mL HiTrap Ni²⁺ chelating column (GE Healthcare Lifebioscences) pre-equalibrated with Buffer A (20mM Tris/HCl, pH 7.5, 5mM DL-Glu). The column was then washed with Buffer A, and the protein was eluted by a linear gradient from 0 to 0.5M Imidazole in Buffer A. Fractions containing Murl were pooled, and solid (NHL)₂SO₄ (0.4g/mL) was added to precipitate all the proteins and mixed on ice for 1h. The sample was centrifuged at 25,000rpm for 30min at 4°C (45Ti rotor, Beckman); the pellet was then dissolved in 9mL of Buffer A. The 5mL sample was applied at a flow rate of 1.0mL/min to a 320mL Sephacryl S-200 (HR 26/60) (GE Healthcare Lifebioscincses) pre-equalibrated with Buffer A. The fractions containing Murl were pooled and dialyzed against IL Storage buffer (10mM Tris/HCl, pH 7.5, 0.1mM EGTA, 150mM NaCl, 1mM TCEP, 5mM DL-Glu, 50% Glycerol). The protein was characterized by SDS-PAGE analysis and analytical LC-MS and judged to be at 95% purity. The protein was stored at -20°C.

E.faecalis reactions were incubated at rt for 60min and S.aureus reactions were incubated at rt for 120min before reactions were quenched by addition of 50µL 1.5% acetic acid (final concentration was 0.5%). Quenched plates were centrifuged at rt for 30min at 3000rpm and supernatants transferred to clear flat-bottom polystyrene 96 well plates (Costar 9017) for HPLC. Chiral separation of D and L-glutamate was performed using a Phenomenex Chirex (D)-Penicillamine column (50 x 4.6mM) with 95% 2mM CuSO₄, 5% methanol as the eluent and a flow rate of 1.5mL/min at 50°C. Data were reported as the
increase in peak area for L-glutamate. Compound potency was based on IC50 measurements determined from reactions performed in the presence of different compound concentrations. Assay artifacts due to insoluble compounds under assay conditions were assessed using nephelometry to measure turbidity.

The compounds of the invention described herein have a measured IC50 in this assay against at least one isozyme of Murl (e.g., E. faecalis Murl, E. faecium Murl or S. aureus Murl) of <400 μM or the compounds inhibit the glutamate racemase reaction by >20% at the limit of their solubility in the assay medium. Solubility is determined under assay conditions using a nephelometer to detect a change in turbidity as the concentration of compound increases. The limit of solubility is defined as the maximum concentration before a detectable increase in turbidity is measured.

According to a further aspect of the present invention there is provided a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, as defined hereinbefore for use in a method of treatment of the human or animal body by therapy.

We have found that the compounds defined in the present invention, or a pharmaceutically acceptable salt thereof, are effective anti-bacterial agents which property is believed to arise from their Murl inhibitory properties. Accordingly, the compounds of the present invention are expected to be useful for treating or preventing diseases or medical conditions resulting in whole or in part from an infection caused by bacteria expressing Murl.

In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Acinetobacter spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Bacteroides spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Burkholderia spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Campylobacter spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Chlamydia spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Chlamydophila spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Clostridium spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Enterobacter spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Enterococcus spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an
infection caused by Escherichia spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Gardnerella spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Haemophilus spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Helicobacter spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Klebsiella spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Legionella spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Moraxella spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Morganella spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Mycoplasma spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Neisseria spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Peptostreptococcus spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Proteus spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Pseudomonas spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Salmonella spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Serratia spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Staphylococcus spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Streptococcus spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Stenotrophomonas spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Ureaplasma spp. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by aerobes. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by obligate anaerobes. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by facultative anaerobes. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by gram-positive bacteria. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by gram-negative bacteria. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by gram-
variable bacteria. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by atypical respiratory pathogens.

In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Acinetobacter baumanii. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Acinetobacter haemolyticus. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Acinetobacter junii. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Acinetobacter johnsonii. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Acinetobacter Iwoffii. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Bacteroides bivius. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Bacteroides fragilis. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Burkholderia cepacia. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Campylobacter jejuni. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Chlamydia pneumoniae. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Chlamydia urealyticus. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Chlamyphila pneumoniae. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Clostridium difficile. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Enterobacter aerogenes. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Enterobacter cloacae. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Enterococcus faecalis. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Enterococcus faecium. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Escherichia coli. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Gardnerella vaginalis. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Haemophilus parainfluenzae. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Haemophilus influenzae. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Helicobacter pylori. In one aspect of the invention an "infection" or "bacterial infection" refers to an
infection caused by *Klebsiella pneumoniae*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Legionella pneumophila*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Methicillin-resistant *Staphylococcus aureus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Mycoplasma pneumoniae*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Neisseria gonorrhoeae*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Penicillin-resistant *Streptococcus pneumoniae*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus magnus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus micros*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus anaerobius*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus asaccharolyticus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus prevotii*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus tetradius*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Peptostreptococcus vaginalis*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Proteus mirabilis*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Pseudomonas aeruginosa*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Quinolone-Resistant *Staphylococcus aureus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Quinolone-Resistant *Staphylococcus epidermis*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Salmonella typhi*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Salmonella paratyphi*. In
one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Salmonella enteritidis*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Salmonella typhimurium*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Serratia marcescens*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Staphylococcus aureus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Staphylococcus epidermidis*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Staphylococcus saprophyticus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Streptococcus agalactiae*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Streptococcus pneumoniae*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Streptococcus pyogenes*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Stenotrophomonas maltophilia*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by *Ureaplasma urealyticum*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Vancomycin-Resistant *Enterococcus faecium*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Vancomycin-Resistant *Enterococcus faecalis*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Vancomycin-Resistant *Staphylococcus aureus*. In one aspect of the invention an "infection" or "bacterial infection" refers to an infection caused by Vancomycin-Resistant *Staphylococcus epidermis*.

In one aspect of the invention "infection" or "bacterial infection" refers to a gynecological infection. In one aspect of the invention "infection" or "bacterial infection" refers to a respiratory tract infection (RTI). In one aspect of the invention "infection" or "bacterial infection" refers to a sexually transmitted disease. In one aspect of the invention "infection" or "bacterial infection" refers to a urinary tract infection. In one aspect of the invention "infection" or "bacterial infection" refers to acute exacerbation of chronic bronchitis (ACEB). In one aspect of the invention "infection" or "bacterial infection" refers to acute otitis media. In one aspect of the invention "infection" or "bacterial infection" refers to acute sinusitis. In one aspect of the invention "infection" or "bacterial infection" refers to an infection caused by drug resistant bacteria. In one aspect of the invention "infection" or "bacterial infection" refers to catheter-related sepsis. In one aspect of the invention
"infection" or "bacterial infection" refers to chancroid. In one aspect of the invention "infection" or "bacterial infection" refers to chlamydia. In one aspect of the invention "infection" or "bacterial infection" refers to community-acquired pneumonia (CAP). In one aspect of the invention "infection" or "bacterial infection" refers to complicated skin and skin structure infection. In one aspect of the invention "infection" or "bacterial infection" refers to uncomplicated skin and skin structure infection. In one aspect of the invention "infection" or "bacterial infection" refers to endocarditis. In one aspect of the invention "infection" or "bacterial infection" refers to febrile neutropenia. In one aspect of the invention "infection" or "bacterial infection" refers to gonococcal cervicitis. In one aspect of the invention "infection" or "bacterial infection" refers to gonococcal urethritis. In one aspect of the invention "infection" or "bacterial infection" refers to hospital-acquired pneumonia (HAP). In one aspect of the invention "infection" or "bacterial infection" refers to osteomyelitis. In one aspect of the invention "infection" or "bacterial infection" refers to sepsis. In one aspect of the invention "infection" or "bacterial infection" refers to syphilis.

In a particular aspect, the invention provides a method of treatment or prophylaxis of bacterial infection, e.g., Gram positive bacterial infection, e.g., infection caused by Gram positive cocci such as staphylococcal, streptococcal or enterococcal infections for example, E. faecalis or E. faecium infection, e.g. treatment or prophylaxis of antibiotic resistant infection, or in treatment of pneumonia, septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial meningitis, or post-operative infection, in a patient in need of such treatment or prophylaxis, comprising administering to the patient an effective amount of a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as defined hereinbefore.

Thus according to this aspect of the invention there is provided a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as defined hereinbefore for use as a medicament.

According to a further aspect of the invention there is provided the use of a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as defined hereinbefore in the manufacture of a medicament for use in the production of a compound having a bacterial Murl inhibitory effect, e.g., a E. faecalis or E. faecium Murl inhibitory effect in a warm-blooded animal such as man.
According to this aspect of the invention there is provided the use of a compound of
the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically
acceptable salt, solvate or prodrug thereof, as defined hereinbefore in the manufacture of a
medicament for use in the treatment or prophylaxis of bacterial infection, e.g., infection by
a Murl expressing bacteria, e.g., Gram positive bacterial infection, e.g., infection caused by
Gram positive cocci such as staphylococcal, streptococcal or enterococcal infections, for
example, E._faecalis or E._faecium infection; for example in the treatment of pneumonia,
septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial
meningitis, or post-operative infection; for example in the treatment or prophylaxis of
antibiotic resistant infection; in a warm-blooded animal, e.g., man.

According to a further feature of this aspect of the invention there is provided a
method for producing a bacterial Murl inhibitory effect, e.g., a E._faecalis or E._faecium
inhibitory effect, in a warm-blooded animal, such as man, in need of such treatment which
comprises administering to said animal an effective amount of a compound of formula (I),
(II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt,
solvate or prodrug thereof, as defined above.

According to a further feature of this aspect of the invention there is provided a
method for producing an antibacterial effect in a warm-blooded animal, such as man, in need
of such treatment which comprises administering to said animal an effective amount of a
compound of formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically
acceptable salt, solvate or prodrug thereof, as defined above.

According to a further aspect of the invention there is provided the use of a compound
of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically
acceptable salt, solvate or prodrug thereof, as defined hereinbefore for production of a
bacterial Murl inhibitory effect in a warm-blooded animal such as man.

According to another aspect of the invention there is provided the use of a compound
of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically
acceptable salt, solvate or prodrug thereof, as defined hereinbefore for production of an
antibacterial effect in a warm-blooded animal such as man.

According to a further feature of the invention, there is provided the use of a
compound of the formula (I), (II), or any of the embodiments disclosed herein, or a
pharmaceutically acceptable salt, solvate or prodrug thereof, as defined hereinbefore for use
in the treatment or prophylaxis of bacterial infection, e.g., infection by Murl expressing
bacteria, e.g., Gram positive bacterial infection, e.g., infection caused by Gram positive cocci such as staphylococcal, streptococcal or enterococcal infections, for example, *E. faecalis* or *E. faecium* infection; for example in the treatment of pneumonia, septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial meningitis, or post-operative infection; for example in the treatment or prophylaxis of antibiotic resistant infection; in a warm-blooded animal, e.g., man.

The compounds of the invention described herein may be applied as a sole therapy or may involve, in addition to a compound of the invention, one or more other substances and/or treatments. Such conjoint treatment may be achieved by way of the simultaneous, sequential or separate administration of the individual components of the treatment. Where the administration is sequential or separate, the delay in administering the second component should not be such as to lose the beneficial effect of the combination. Suitable classes and substances may be selected from one or more of the following:

i) other antibacterial agents for example macrolides e.g. erythromycin, azithromycin or clarithromycin; quinolones e.g. ciprofloxacin or levofloxacin; β-lactams e.g. penicillins e.g. amoxicillin or piperacillin; cephalosporins e.g. ceftriaxone or ceftazidime; carbapenems, e.g. meropenem or imipenem etc; aminoglycosides e.g. gentamicin or tobramycin; or oxazolidinones; and/or

ii) anti-infective agents for example, an antifungal triazole e.g. or amphotericin; and/or

iii) biological protein therapeutics for example antibodies, cytokines, bactericidal/permeability-increasing protein (BPI) products; and/or

iv) efflux pump inhibitors.

Therefore, in a further aspect of the invention there is provided a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof and a chemotherapeutic agent selected from:

i) one or more additional antibacterial agents; and/or

ii) one or more anti-infective agents; and/or

iii) biological protein therapeutics for example antibodies, cytokines, bactericidal/permeability-increasing protein (BPI) products; and/or

iv) one or more efflux pump inhibitors.
Such conjoint treatment may be advantageous because, for example, the bacterial attack may involve organisms better treated by such conjoint treatment. Other advantageous conjoint treatment may arise from a need to treat, for example, bacterial attack together with a need to treat a parallel infection or disease such as diabetes.

E. PHARMACEUTICAL COMPOSITIONS

According to a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvates, or prodrugs thereof, as defined hereinbefore, in association with a pharmaceutically-acceptable diluent or carrier.

In a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as defined herein before in association with a pharmaceutically-acceptable diluent or carrier for use in the production of a Murl inhibitory effect, e.g., a E. faecalis or E. faecium Murl inhibitory effect in a warm-blooded animal such as man.

In a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as defined herein before in association with a pharmaceutically-acceptable diluent or carrier for use in the production of an antibacterial effect in a warm-blooded animal such as man.

In a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the formula (I), (II), or any of the embodiments disclosed herein, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as defined herein before in association with a pharmaceutically-acceptable diluent or carrier for use in the treatment or prophylaxis of bacterial infection, e.g., infection by Murl expressing bacteria, e.g., Gram positive bacterial infection, e.g., infection caused by Gram positive cocci such as staphylococcal, streptococcal or enterococcal infections, for example, E. faecalis or E. faecium infection; for example in the treatment of pneumonia, septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial meningitis, or post-operative infection; for example in the treatment or prophylaxis of antibiotic resistant infection; in a warm-blooded animal, e.g., man.
The compositions of the invention may be in a form suitable for oral use (for example as tablets, lozenges, hard or soft capsules, aqueous or oily suspensions, emulsions, dispersible powders or granules, syrups or elixirs), for topical use (for example as creams, ointments, gels, or aqueous or oily solutions or suspensions), for administration by inhalation (for example as a finely divided powder or a liquid aerosol), for administration by insufflation (for example as a finely divided powder) or for parenteral administration (for example as a sterile aqueous or oily solution for intravenous, subcutaneous, intramuscular or intramuscular dosing or as a suppository for rectal dosing).

The compositions of the invention may be obtained by conventional procedures using conventional pharmaceutical excipients well known in the art. Thus, compositions intended for oral use may contain, for example, one or more coloring, sweetening, flavoring and/or preservative agents.

Suitable pharmaceutically acceptable excipients for a tablet formulation include, for example, inert diluents such as lactose, sodium carbonate, calcium phosphate or calcium carbonate; granulating and disintegrating agents such as corn starch or algenic acid; binding agents such as starch; lubricating agents such as magnesium stearate, stearic acid or talc; preservative agents such as ethyl or propyl/?-hydroxybenzoate; and anti-oxidants, such as ascorbic acid. Tablet formulations may be uncoated or coated either to modify their disintegration and the subsequent absorption of the active ingredient within the gastrointestinal tract, or to improve their stability and/or appearance, in either case, using conventional coating agents and procedures well known in the art.

Compositions for oral use may be in the form of hard gelatin capsules in which the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules in which the active ingredient is mixed with water or an oil such as peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions generally contain the active ingredient in finely powdered form or in the form of nano or micronized particles together with one or more suspending agents, such as sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethylcellulose, sodium alginate, polyvinyl-pyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents such as lecithin or condensation products of an alkylene oxide with fatty acids (for example polyoxethylene stearate), or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxyctanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as
polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with long
chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products
of ethylene oxide with partial esters derived from fatty acids and a hexitol such as
polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial
esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan
monooleate. The aqueous suspensions may also contain one or more preservatives such as
ethyl or propyl p-hydroxybenzoate; anti-oxidants such as ascorbic acid); colouring agents;
flavouring agents; and/or sweetening agents such as sucrose, saccharine or aspartame.

Oily suspensions may be formulated by suspending the active ingredient in a
vegetable oil such as arachis oil, olive oil, sesame oil or coconut oil or in a mineral oil such as
liquid paraffin. The oily suspensions may also contain a thickening agent such as beeswax,
hard paraffin or cetyl alcohol. Sweetening agents such as those set out above, and flavouring
agents may be added to provide a palatable oral preparation. These compositions may be
preserved by the addition of an anti-oxidant such as ascorbic acid.

Dispersible powders and granules suitable for preparation of an aqueous suspension
by the addition of water generally contain the active ingredient together with a dispersing or
wetting agent, suspending agent and one or more preservatives. Suitable dispersing or
wetting agents and suspending agents are exemplified by those already mentioned above.
Additional excipients such as sweetening, flavouring and colouring agents, may also be
present.

The pharmaceutical compositions of the invention may also be in the form of
oil-in-water emulsions. The oily phase may be a vegetable oil, such as olive oil or arachis oil,
or a mineral oil, such as for example liquid paraffin or a mixture of any of these. Suitable
emulsifying agents may be, for example, naturally-occurring gums such as gum acacia or gum
tragacanth, naturally-occurring phosphatides such as soya bean, lecithin, an esters or partial
esters derived from fatty acids and hexitol anhydrides (for example sorbitan monooleate) and
condensation products of the said partial esters with ethylene oxide such as polyoxyethylene
sorbitan monooleate. The emulsions may also contain sweetening, flavoring and preservative
agents.

Syrups and elixirs may be formulated with sweetening agents such as glycerol,
propylene glycol, sorbitol, aspartame or sucrose, and may also contain a demulcent,
preservative, flavoring and/or coloring agent.
The pharmaceutical compositions may also be in the form of a sterile injectable aqueous or oily suspension, which may be formulated according to known procedures using one or more of the appropriate dispersing or wetting agents and suspending agents, which have been mentioned above. A sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example a solution in 1,3-butanediol.

Compositions for administration by inhalation may be in the form of a conventional pressurized aerosol arranged to dispense the active ingredient either as an aerosol containing finely divided solid or liquid droplets. Conventional aerosol propellants such as volatile fluorinated hydrocarbons or hydrocarbons may be used and the aerosol device is conveniently arranged to dispense a metered quantity of active ingredient.

For further information on formulation the reader is referred to Chapter 25.2 in Volume 5 of Comprehensive Medicinal Chemistry (Corwin Hansch; Chairman of Editorial Board), Pergamon Press 1990.

The amount of active ingredient that is combined with one or more excipients to produce a single dosage form will necessarily vary depending upon the host treated and the particular route of administration. For example, a formulation intended for oral administration to humans will generally contain, for example, from 0.5 mg to 2 g of active agent compounded with an appropriate and convenient amount of excipients which may vary from about 5 to about 98 percent by weight of the total composition. Dosage unit forms will generally contain about 1 mg to about 500 mg of an active ingredient. Accordingly the optimum dosage may be determined by the practitioner who is treating any particular patient. For further information on Routes of Administration and Dosage Regimes the reader is referred to Chapter 25.3 in Volume 5 of Comprehensive Medicinal Chemistry (Corwin Hansch; Chairman of Editorial Board), Pergamon Press 1990.

In the above other pharmaceutical composition, process, method, use and medicament manufacture features, the alternative and preferred embodiments of the compounds of the invention described herein also apply.

F. RESEARCH TOOLS

In addition to their use in therapeutic medicine, the compounds of formula (I) or (II) and pharmaceutically acceptable salts, solvates or prodrugs thereof are also useful as pharmacological tools in the development and standardization of in vitro and in vivo test
systems for the evaluation of the effects of inhibitors of Murl in bacteria, e.g., *E.faecalis* or *E. faecium* Murl, in laboratory animals such as cats, dogs, rabbits, monkeys, rats and mice, as part of the search for new therapeutic agents.

5 **Examples**

The invention will now be illustrated by the following non-limiting examples in which, unless stated otherwise:

(i) temperatures are given in degrees Celsius (°C); operations that were carried out at room or ambient temperature ("rt") were at a temperature in the range of 18-25°C;

(ii) organic solutions were dried over anhydrous sodium sulphate; evaporation of solvent was carried out using a rotary evaporator under reduced pressure (600-4000 Pascals; 4.5-30 mmHg) with a bath temperature of up to 60 °C;

(iii) in general, the course of reactions was followed by thin layer chromatography (TLC) and reaction times are given for illustration only;

(iv) final products had satisfactory proton nuclear magnetic resonance (NMR) spectra and/or mass spectral (MS) data;

(v) yields are given for illustration only and are not necessarily those which can be obtained by diligent process development; preparations were repeated if more material was required;

(vii) when given, NMR data is in the form of delta values for major diagnostic protons, given in parts per million (ppm) relative to tetramethylsilane (TMS) as an internal standard, determined at 400 MHz using perdeuterio dimethyl sulphoxide (DMSO-d$_6$) as solvent unless otherwise indicated;

(vii) chemical symbols have their usual meanings; SI units and symbols are used;

(viii) solvent ratios are given in volume:volume (v/v) terms; and

(ix) mass spectra were run with an electron energy of 70 electron volts in the chemical ionization (CI) mode using a direct exposure probe; where indicated ionization was effected by electron impact (EI), fast atom bombardment (FAB) or electrospray (ESP); values for m/z are given; generally, only ions which indicate the parent mass are reported; and unless otherwise stated, the mass ion quoted is (MH)$^+$;

(x) where a synthesis is described as being analogous to that described in a previous example the amounts used are the millimolar ratio equivalents to those used in the previous example;
(xi) the following abbreviations have been used:

- **HATU** O-(7-Azabenzotriazol-1-yl)-N,N',N''-tetramethyluronium hexafluorophosphate;
- **THF** tetrahydrofuran;
- **DMF** N,N-dimethylformamide;
- **EtOAc** ethyl acetate;
- **DIEA** N,N-diisopropylethylamine;
- **DCM** dichloromethane;
- **DMSO** dimethylsulphoxide;
- **MeCN** acetonitrile;
- **NBS** N-bromosuccinimide; and
- **MeOH** methanol;

(xii) "ISCO" refers to normal phase flash column chromatography using 12 g and 40 g pre-packed silica gel cartridges used according to the manufacturers instruction obtained from ISCO, Inc, 4700 superior street Lincoln, NE, USA; and

(xiii) "Gilson HPLC" refers to a YMC-AQC 18 reverse phase HPLC Column with dimension 20 mm/100 and 50 mm/250 in water/MeCN with 0.1% TFA as mobile phase, obtained

(xiv) Parr Hydrogenator or Parr shaker type hydrogenators are systems for treating chemicals with hydrogen in the presence of a catalyst at pressures up to 5 atmospheres (60 psig) and temperatures to 80 °C.

**Preparation of Starting Materials**
Intermediate 1: 4,6-diaminopyrimidine-2-thiol

Intermediate 2: 2-(butylthio)pyrimidine-4,6-diamine

To a suspension of commercially available 4,6-diaminopyrimidine-2-thiol (5g, 35mmol) in methanol (70mL) was added IN sodium hydroxide (35mL). The resulting solution was stirred for 1h at rt then evaporated to give a tan solid. The tan solid and 1-bromobutane (4.1mL, 38.5mmol) were combined in DMF (50mL) and stirred at rt overnight. The DMF was evaporated to yield a brown oil, 6.9g. \textbf{MS (ESP)}: 199 (MH$^+$) for C$_8$H$_{14}$N$_4$S

Intermediate 3: 2-(butylthio)-5-nitrosopyrimidine-4,6-diamine

A solution of 2-(butylthio)pyrimidine-4,6-diamine (Intermediate 2, 6.9g, 35 mmol) in acetic acid (138 mL) and water (30 mL) was cooled to 0°C and treated dropwise, over 20 min, with sodium nitrite (4.4g, 63 mmol) in water (30mL). The reaction mixture turned dark brown and a bright pink solid formed. After 30 min the pink solid was collected by filtration and washed with cold water (400 mL) to yield a bright blue solid, 6.8g. \textbf{MS (ESP)}: 228 (MH$^+$) for C$_8$H$_{14}$N$_5$OS
**Intermediate 4: 2-(butythio)pyrimidine-4,5,6-triamine**

A suspension of 2-(butythio)-5-nitrosopyrimidine-4,6-diamine (Intermediate 3, 6.8g, 30 mmol) in ethanol (100mL) was flushed with N₂ and platinum(IV) oxide (0.34g, 1.5mmol) was added. The reaction was stirred under a H₂ balloon at rt overnight. The reaction mixture was filtered through celite and evaporated to yield a green solid, 6.5g. **MS (ESP):** 214 (MH⁺) for C₈H₁₅N₅S

**Intermediate 5: 2-(butythio)-9 H-purin-6-amine**

2-(butythio)pyrimidine-4,5,6-triamine (Intermediate 4, 5.8g, 27mmol) was dissolved in formamide (130mL) and refluxed for 5h. The reaction mixture was cooled to rt and water (150 mL) was added. The orange precipitate was collected by filtration, 4.9g. **MS (ESP):** 224 (MH⁺) for C₉H₁₅N₅S

**Scheme II: Intermediates 6-8**

**Intermediate 6: 2,6-dichloro-9 H-purine**

Commercially available.

**Intermediate 7: 2-chloro-9 H-purin-6-amine**

Commercially available 2,6-dichloro-9 H-purine (1g, 5.2mmol) was dissolved in 7N ammonia/methanol (10mL) and heated in microwave reactor for 50 min at 120°C. The reaction was filtered to collect a yellow solid, 0.75g. **MS (ESP):** 170 (MH⁺) for C₅H₄ClN₅

**Intermediate 8: 2-chloro-9-[3-(trifluoromethyl)benzyl]-9 H-purin-6-amine**

2-chloro-9 H-purin-6-amine (Intermediate 7, 0.56g, 3.3mmol), cesium carbonate (1.3g, 4mmol) and 3-(trifluoromethyl)benzyl bromide (0.56mL, 3.6mmol) were combined in DMF (25mL) and stirred at rt overnight. The reaction mixture was poured into water and the off-white precipitate was collected by filtration, 0.95g. **MS (ESP):** 328 (MH⁺)

Intermediates 24 and 25 were prepared using an analogous method to that used to prepare Intermediate 8:
**Intermediate 24:** 2-chloro-9-[3-cyanobenzyl]-9\(H\)-purin-6-amine

The **Intermediate 24** was prepared by alkylation of 2-chloro-9\(H\)-purin-6-amine (**Intermediate 7**) with 3-cyanobenzyl bromide. **MS (ES):** \(285(MH^+)\) for \(C_{13}H_{9}N_{6}Cl\)

**Intermediate 25:** 2-chloro-9-[2,6-difluorobenzyl]-9\(H\)-purin-6-amine

2-chloro-9-[2,6-difluorobenzyl]-9\(H\)-purin-6-amine was prepared by alkylation of 2-chloro-9\(H\)-purin-6-amine (**Intermediate 7**) with 2,6-difluorobenzyl bromide. **MS (ES):** \(296(MH^+)\) for \(C_{12}H_{8}N_{3}F_{2}\)

**Scheme III: Intermediates 9-14:**

**Intermediate 9:** 2-(isobutylthio)-9\(H\)-purin-6-amine

In a pressure tube, 2-chloro-9\(H\)-purin-6-amine (**Intermediate 7**, 0.1g, 0.6mmol), 2-methyl-1-propanethiol (0.32mL, 3mmol) and cesium carbonate (0.38g, 1.2mmol) were combined in DMF (2mL) and heated at 150°C overnight. The reaction mixture was cooled to rt and poured into water. The resulting off-white precipitate was collected by filtration, 0.1g. **MS (ESP):** \(224(MH^+)\) for \(C_{9}H_{13}N_{5}S\).
Intermediate 10: 2-[(3-methylbutyl)thiol-9 H-purin-6-amine

In a pressure tube, 2-chloro-9 H-purin-6-amine (Intermediate 7, 0.1g, 0.6mmol), 3-methyl-1-butanol (0.36mL, 3mmol) and cesium carbonate (0.38g, 1.2mmol) were combined in DMF (2mL) and heated at 150°C overnight. The reaction mixture was cooled to rt and poured into water. The resulting white precipitate was collected by filtration, 0.07 g. MS (ESP): 238 (MH⁺) for C₁₀H₁₅N₅S

Intermediate 11: 2-[(2-methylbutyl)thiol-9 H-purin-6-amine

In a pressure tube, 2-chloro-9 H-purin-6-amine (Intermediate 7, 0.2g, 1.2mmol), 2-methyl-1-butanol (0.72mL, 6mmol) and cesium carbonate (0.77g, 2.4mmol) were combined in DMF (4mL) and heated at 150°C overnight. The reaction was not complete. More cesium carbonate (leq) and 2-methyl-1-butanol (5eq) were added and the reaction mixture was heated at 150°C overnight. The reaction mixture was cooled to rt and poured into water. The resulting white precipitate was collected by filtration, 0.2g. MS (ESP): 238 (MH⁺) for C₁₀H₁₅N₅S

Intermediate 12: 2-(cyclopentylthio)-9 H-purin-6-amine

In a pressure tube, 2-chloro-9 H-purin-6-amine (Intermediate 7, 0.2g, 1.2mmol), cyclopentanethiol (0.63mL, 6mmol) and cesium carbonate (0.77g, 2.4mmol) were combined in DMF (4mL) and heated at 150°C overnight. The reaction was not complete. More cesium carbonate (leq) and cyclopentanethiol (5eq) were added and the reaction mixture was heated at 150°C overnight. The reaction mixture was cooled to rt and poured into water. The resulting white precipitate was collected by filtration, 0.188 g. MS (ESP): 236 (MH⁺) for C₁₀H₁₅N₅S

Intermediate 13: 2-(cyclohexylthio)-9 H-purin-6-amine

In a pressure tube, 2-chloro-9 H-purin-6-amine (Intermediate 7, 0.2g, 1.2mmol), cyclohexanethiol (0.72mL, 6mmol) and cesium carbonate (0.77g, 2.4 mmol) were combined in DMF (4mL) and heated at 150°C overnight. The reaction was not complete. More cesium carbonate (leq) and cyclohexanethiol (5eq) were added and the reaction mixture was heated at 150°C overnight. The reaction mixture was cooled to rt and poured into water. The resulting white precipitate was collected by filtration, 0.114g. MS (ESP): 250 (MH⁺) for C₁₄H₂₁N₅S
Intermediate 14: 2-(2-methoxyethoxy)-9 H-purin-6-amine

2-chloro-9 H-purin-6-amine (Intermediate 7, 0.1g, 0.6mmol), 2-methoxyethanol (3mL) and sodium hydroxide (~0.1g) were heated in a pressure tube at 150°C overnight. The excess 2-methoxyethanol was evaporated to give a brown oil, 0.1lg crude. MS (ESP): 210 (MH⁺) for C₈H₁₅N₅O₂

Scheme IV: Intermediate 15

Intermediate 15: 2-chloro-9-(2,6-difluoro-3-methylbenzyl)-9 H-purin-6-amine

2-chloro-9 H-purin-6-amine (Intermediate 7, 1g, 6.4mmol), 2,6-difluoro-3-methylbenzyl bromine (1.7g, 7.6mmol) and cesium carbonate (2.5g, 7.6mmol) were combined in DMF (10mL) and stirred at rt overnight. The reaction mixture was poured into water and the off-white precipitate was collected by filtration, 2g. MS (ESP): 310 (MH⁺) for C₁₃H₁₀ClF₂N₅

Scheme V: Intermediates 16 and 17

Intermediate 16: 2-chloro-A-(2,6-morpholin-4-ylethyl)-9 H-purin-6-amine

Commercially available 2,6-dichloro-9 H-purine (0.7g, 3.7mmol) and 4-(2-aminoethyl)morpholine (0.63mL, 4.8mmol) were combined in THF (4mL) and heated in microwave reactor for 30min at 120°C. The resulting tan solid was collected by filtration, 0.85g. MS (ESP): 283 (MH⁺) for C₁₅H₁₅ClN₆O
Intermediate 17: 2-butoxy-9\textsuperscript{H}-purin-6-amine

2-chloro-9\textsuperscript{H}-purin-6-amine (Intermediate 16, 0.2g, 0.7mmol), 1-butanol (3mL) and sodium hydroxide (~0.1g) were heated in a pressure tube at 150°C overnight. The excess 1-butanol was evaporated to give a tan oil, 0.22g crude. **MS (ESP):** 321 (MH\textsuperscript{+}) for C\textsubscript{5}H\textsubscript{24}N\textsubscript{6}O\textsubscript{2}

Scheme VI: Intermediate 18

[Diagram of the reaction]

Intermediate 18: 9-butyl-2-chloro-9\textsuperscript{H}-purin-6-amine

2-chloro-9\textsuperscript{H}-purin-6-amine (Intermediate 16, 1.2g, 4.4mmol), 1-bromobutane (0.52mL, 4.8mmol) and cesium carbonate (1.6g, 4.8mmol) were combined in DMF (10mL) and heated at 60°C overnight. The DMF was evaporated and the resulting oil was dissolved in water and extracted twice with chloroform. The organic layers were dried over magnesium sulfate and evaporated to give an orange oil. **Silica gel chromatography (dichloromethane/methanol) afforded desired product, 0.95g. MS (ESP):** 339 (MH\textsuperscript{+}) for C\textsubscript{5}H\textsubscript{23}ClIN\textsubscript{6}O

Scheme VII: Intermediate 19

[Diagram of the reaction]

Intermediate 19: N\textsuperscript{2}-(2-morpholin-4-ylethyl)-2-(4,4,4-trifluoro-butoxy)-9\textsuperscript{H}-purin-6-amine

2-chloro-N\textsuperscript{2}-(2-morpholin-4-ylethyl)-9\textsuperscript{H}-purin-6-amine (Intermediate 16, 0.2g, 0.7mmol), 4,4,4-trifluoro-1-butanol (2mL) and sodium hydroxide (~0.2g) were heated in a
pressure tube at 150°C overnight. The excess alcohol was evaporated to yield a brown oil, 0.26 g crude. **MS (ESP):** 375 (MH⁺) for C₁₅H₂₁IF₃N₆O₂

**Scheme VIII: Intermediate 20**

![Scheme VIII: Intermediate 20](image)

**Intermediate 20: 2-chloro-9-(2,6-difluoro-3-methylbenzyl)-N′-(2-morpholin-4-ylethyl)-9H-purin-6-amine**

2-chloro-Ν-(2-morpholin-4-ylethyl)-9H-purin-6-amine (Intermediate 16, 0.2 g, 0.7 mmol), 2,6-difluoro-3-methylbenzyl bromine (0.18 g, 0.84 mmol) and cesium carbonate (0.27 g, 0.84 mmol) were combined in DMF (2 mL) and stirred at 60°C overnight. The reaction mixture was filtered and evaporated to yield an orange oil, 0.29 g crude. **MS (ESP):** 423 (MH⁺) for C₁₉H₂IClF₂N₆O

**Intermediate 26: 2-chloro-9-(^,6-difluorobenzyl)-Ν'-dimethyl-9H-purin-6-amine**

The titled intermediate was prepared by alkylation of 2-chloro-7V,7V-dimethyl-9H-purin-6-amine [JACS (1958) 80 404-408] with 2,6-difluorobenzyl bromide. **MS (ES):** 324 (MH⁺) for C₁₄H₁₂F₂N₅
The titled intermediate was obtained by alkylation of 2-chloro-7V-methyl-9H-purin-6-amine (prepared as described in JACS (1958) 80 404-408) with 2,6-difluorobenzyl bromide.

**Intermediate 28: 2-chloro-9-(^,6-difluoro-3-methylbenzyl)- N-ethyl-9H-purin-6-amine**

The titled intermediate was obtained by alkylation of 2-chloro-7V-ethyl-9H-purin-6-amine (prepared as described in WO 2001/009134) with 2,6-difluoro-3-methyl-benzyl bromide.

**Intermediate 29: A'-benzyl-2-chloro-9-(2,6-difluoro-3-methylbenzyl)-9 H-purin-6-amine**

The titled intermediate was prepared by alkylation of 7V-benzyl-2-chloro-9H-purin-6-amine (prepared as described in Tet. Letters (1998) 39 (13) 1827-1830) with 2,6-difluoro-3-methyl-benzyl bromide.

**Intermediate 30: 2-chloro-A'-cyclopropyl-9-(2,6-difluoro-3-methylbenzyl)-9 H-purin-6-amine**
The titled intermediate was prepared by alkylation of 2-chloro-7\textsuperscript{V}-cyclopropyl-9\textsuperscript{H}-purin-6-amine (prepared as described in J. Med. Chem. (1997) 40(20) 3207-3216) with 2,6-difluoro-3-methyl-benzyl bromide. \textbf{MS (ES)}: 350(MH\textsuperscript{+}) for C\textsubscript{16}H\textsubscript{14}ClF\textsubscript{2}N\textsubscript{5}

**Scheme IX: Intermediate 21**

**Intermediate 21**: 2-(butyl\{6-[(2-morpholin-4-ylethyl)amino]-9\textsuperscript{H}-purin-2-yl\}amino)ethanol

2-Chloro-\textit{N}-(2-morpholin-4-ylethyl)-9\textit{H}-purin-6-amine (Intermediate 16, 0.2g, 0.7mmol), N,N-butylethanolamine (2mL) and sodium hydroxide (~0.1g) were heated in a pressure tube at 150°C overnight. The excess alcohol was evaporated and the resulting oil was dissolved in 0.25M sodium hydroxide and extracted with ethyl acetate. The organic extracts were dried over magnesium sulfate and evaporated to yield a green oil, 0.12g. \textbf{MS (ESP)}: 364 (MH\textsuperscript{+}) for C\textsubscript{17}H\textsubscript{29}N\textsubscript{7}O\textsubscript{2}

**Scheme X: Intermediate 22**
**Intermediate 22**: \( \text{N-}f_2\text{-morpholin-4-ylethyl)-2-phenoxy-9 } H\text{-purin-6-amine} \)

2-Chloro- \( \text{N-}f_2\text{-morpholin-4-ylethyl)-9 } H\text{-purin-6-amine} \) (Intermediate 16, 0.22g, 0.78mmol), phenol (~lg) and sodium hydroxide (~0.1g) were combined in a pressure tube and heated at 150°C for 4h. The cooled reaction mixture was diluted with chloroform and washed with water. Silica gel chromatography (dichloromethane/methanol) afforded desired product, 0.17g. **MS (ESP)**: 341 (MH⁺) for \( \text{C}_{17}\text{H}_{20}\text{N}_{6}\text{O}_2 \)

**Scheme XI: Intermediate 23**

**Intermediate 23**: 5-(butylthio)-3 \( H\text{-[1,2,3] triazolo[4,5-c]pyrimidin-7-amine} \)

2-(butylthio)pyrimidine-4,5,6-triamine (Intermediate 4, Ig, 4.7mmol) was dissolved in water (30mL) and acetic acid (10mL) at 0°C. A solution of sodium nitrite (0.4g, 5.6mmol) in water (15mL) was added dropwise. After 30 min a green solid was collected by filtration and washed with water, Ig. **MS (ESP)**: 225 (MH⁺) for \( \text{C}_{9}\text{H}_{12}\text{N}_{6}\text{S} \)
Scheme XII: Intermediates 31-35
**Intermediate 31:** 6-amino-8-bromo-9-(2,6-difluorobenzyl)-9₉H-purin-2-ol

A mixture of 5-amino-2-bromo-l-(2,6-difluorobenzyl)-l H-imidazole-4-carbonitrile (1.58g, 5.05mmol) [Intermediate 32] and urea (3.0g, 65.2mmol) were heated at 160°C for 16h. Water (15mL) was added to the hot reaction. After cooling to rt, the precipitate was filtered, washed with acetone and dried under vacuum to obtain a solid (2.76g). MS (ESP) M/z= 356 (MH+) for C₁₂H₈BrF₂N₅O

**Intermediate 32:** 5-amino-2-bromo-l-(^,6-difluorobenzyl)-l H-imidazole-4-carbonitrile

To a solution of 5-amino 1-(2,6-difluorobenzyl)-l H-imidazole-4-carbonitrile (2.5g, 10.7mmol) (Intermediate 33) in THF (50mL) was added dropwise a solution of N-bromo succinimide (2.47g, 13.9mmol) in THF (40mL). The reaction was allowed to stir for 10 min. The reaction mixture was partitioned between ethylacetate and sodium bicarbonate (saturated solution). The organic phase was washed with brine, dried over MgSO₄ and evaporated to obtain a solid (1.58g, 47%). MS (ESP) M/z= 313 (MH+) for CnH₂BrF₂N₄

**Intermediate 33:** 5-amino 1-(2,6-difluorobenzyl)-l H-imidazole-4-carbonitrile

A mixture of ethyl [(Z)-2-amino-l,2-dicyanovinyl]imido formate (prepared as described in Syn Commun 31(4) 549-554) (6.5g, 39.63mmol) and anilinium chloride (0.08, 0.62mmol) in ethanol (130mL) was cooled to 0°C. 2,6- difluorobenzylamine (4.45g, 31.3mmol) was added dropwise keeping the temperature between 10-15°C. The reaction was allowed to stir at rt overnight. To the reaction mixture was added a solution of NaOH (IN, 75mL). The reaction was allowed to stir for 2h and then concentrated at reduced pressure. The residue was diluted with water (50mL) and filtered. The solid was dried overnight under vacuum. (3.8g, 52%)

MS (ESP) M/z= 235 (MH+) for CnH₈F₂N₄

**Intermediate 34:** 6-amino-8-chloro-9-(2,6-difluorobenzyl)-9₉H-purin-2-ol

A mixture of 5-amino-2-chloro-l-(2,6-difluorobenzyl)-l H-imidazole-4-carbonitrile (0.93g, 3.47mmol) (Intermediate 35) and urea (3.0g, 43.5mmol) was heated at 160°C for 16h. Water (10mL) was added to the hot reaction. After cooling to rt, the precipitate was filtered, washed with acetone and dried under vacuum to obtain a solid (1.76 g). MS (ESP) M/z= 312 (MH+) for C₁₂H₈ClF₂N₅O
**Intermediate 35: 5-amino-2-chloro-1-(^,6-difluorobenzyl)-1H-imidazole-4-carbonitrile**

To a solution of 5-amino 1-(2,6-difluorobenzyl)-1H-imidazole-4-carbonitrile (1.0g, 4.3mmol) (Intermediate 33) in THF (50mL) was added dropwise a solution of N-chloro succinimide (0.67g, 5.01mmol) in THF (40mL). The reaction was allowed to stir overnight. The reaction mixture was partitioned between ethyl acetate and sodium bicarbonate (saturated solution). The organic phase was washed with brine, dried over MgSO₄ and evaporated to obtain a solid (0.93g, 80%) MS (ESP) M/z=269 (MH+) for CnH₇ClF₂N₄

**Scheme XIII: Intermediates 36 and 37**

**Intermediate 36: 2H-benzimidazol-2-ylmethyl)-2-chloro-9H-purin-6-amine:**

A solution of 2,6-dichloropurine (1.0g, 5.3mmol) in THF (2.5mL) was treated with 2-aminomethyl benzimidazole (1.3g, 5.91mmol). The reaction was heated to reflux for 3 days.
The reaction was concentrated at reduced pressure. The residue was triturated with water, filtered, washed with hexane to yield a solid product with purity adequate for synthesis.

**Intermediate 37**: \( N'-(1H\text{-benzimidazol-2-ylmethyl})\text{-2-chloro}-9\text{-}(2\text{-morpholin-4-ylethyl})\text{-9H-purin-6-amine} \)

A solution of \( N-(1H\text{-benzimidazol-2-ylmethyl})\text{-2-chloro}-9\text{-H-purin-6-amine} \) (Intermediate 36) (1.7g, 5.3mmol) above was dissolved in DMF (15mL) and treated with Cs\(_2\)CO\(_3\) (4.9g, 15.04 mmol) and 4-(2-chloroethyl)-morpholine (1.4g, 7.53 mmol). The reaction was allowed to stir at rt overnight. The reaction mixture was diluted with dichloromethane, washed with water twice, dried over MgSO\(_4\) and evaporated to obtain the title compound as a solid (2.0g, 91%)

**Scheme XIV: Intermediates 38 and 39**

![Scheme XIV: Intermediates 38 and 39](image-url)
**Intermediate 38**: 2-chloro-\(N\)-[(5-methyl-2-furyl)methyl]-9\(H\)-purin-6-amine

A solution of 2,6-dichloropurine (1.0g, 5.3mmol) in THF (2.5mL) was treated with [(5-methyl-2-furyl)methyl]amine (0.6g, 5.38mmol). The reaction was heated to reflux for 3 days. The reaction was concentrated at reduced pressure. The residue was triturated with water, filtered, washed with hexane to yield a solid product (0.86g, 61%). Carried on without further purification. MS (ESP) M/z= 264 (MH+ ) for CnHi0ClN5O

**Intermediate 39**: 2-chloro-\(N\)-[(5-methyl-2-furyl)methyl]-9-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine

A solution of 2-chloro-\(N\)-[(5-methyl-2-furyl)methyl]-9\(H\)-purin-6-amine (Intermediate 38) (0.75g, 2.84mmol) was dissolved in DMF (10mL) and treated with Cs2CO3 (2.78g, 8.55mmol) and 4-(2-chloroethyl)-morpholine (0.795g, 4.27mmol). The reaction was allowed to stir at rt overnight. The reaction mixture was diluted with dichloromethane, washed with water twice, dried over MgSO4 and evaporated. The residue was purified by reverse phase chromatography [15-75% CH3CN/H2O, 0.1% TFA] to obtain the product as a TFA salt (1.0g, 72%).
**Intermediate 40**: 2-chloro-\(N\)-(2,6-difluorobenzyl)-9\(H\)-purin-6-amine:

A solution of 2,6-dichloropurine (1.0g, 5.3mmol) in THF (2.5mL) was treated with 2,6-difluorobenzylamine (1.135g, 7.93mmol). The reaction was heated at 120°C for 30min using microwave irradiation. The reaction was concentrated at reduced pressure. The residue was triturated with water, filtered, washed with hexane to yield a solid product (1.4g, 89%) MS (ESP) M/z= 296 (MH+) for \(\text{C}_{12}\text{H}_8\text{ClF}_2\text{N}_5\)

**Intermediate 41**: 2-chloro-\(N\)-(2,6-difluorobenzyl)-9-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine:

A solution of 2-chloro-\(N\)-(2,6-difluorobenzyl)-9\(H\)-purin-6-amine (Intermediate 40) (1.4g, 4.73mmol) was dissolved in THF (7.5mL) and treated with \(\text{Cs}_2\text{CO}_3\) (2.75g, 8.46mmol) and 4-(2-chloroethyl)morpholine (1.4g, 7.53mmol). The reaction was allowed to stir at rt overnight. The reaction mixture was diluted with dichloromethane, washed with water twice,
dried over MgSO₄ and evaporated to obtain the title compound as a solid (1.26 g, 65%) MS (ESP) M/z = 409 (MH+) for \( \text{C}_{18}\text{H}_{19}\text{ClF}_{2}\text{N}_{6}\text{O} \)

**Scheme XVI: Intermediates 42 and 43**

**Intermediate 42:** 4-[[2-chloro-9 \( H \)-purin-6-yl]aminomethyl]benzenesulfonamide

A solution of 2,6-dichloropurine (1.0g, 5.3mmol) in THF (2.5mL) was treated with 4-(aminomethyl)benzenesulfonamide (1.3g, 5.84mmol). The reaction was heated at 75°C for 2h. The reaction was concentrated at reduced pressure. The residue was triturated with water, filtered, washed with hexane to yield a solid product. (1.83g, quant.) MS (ESP) M/z = 338 (MH+) for \( \text{C}_{12}\text{H}_{11}\text{ClN}_{6}\text{O}_{2}\text{S} \)

**Intermediate 43:** 4-[[2-chloro-9 \( H \)-purin-6-yl]aminomethyl]benzenesulfonamide

A solution of 4-[[2-chloro-9 \( H \)-purin-6-yl]aminomethyl]benzenesulfonamide (Intermediate 42) (1.5g, 4.73mmol) above was dissolved in DMF (10mL) and treated with
Cs₂CO₃ (4.3g, 13.23mmol) and 4-(2-chloroethyl)-morpholine (1.25g, 6.72mmol). The reaction was allowed to stir at rt overnight. The reaction mixture was diluted with dichloromethane, washed with water twice, dried over MgSO₄ and evaporated to obtain the title compound as a solid (0.73g, 34%) MS (ESP) M/z= 452 (MH⁺) for C₁₈H₂₂ClN₇O₃S

Scheme XVII: Intermediate 44

**Intermediate 44**: 2-chloro-9-(2,6-difluorobenzyl)-A-(2-morpholin-4-yethyl)-9 H-purin-6-amine

2-chloro-N-(2-morpholin-4-yethyl)-9 H-purin-6-amine (**Intermediate 16**, 1.415g, 5.0mmol), 2,6-difluorobenzyl bromine (1.24g, 6.0mmol) and cesium carbonate (1.69g, 6.0mmol) were combined in DMF (6mL) and stirred at 60°C overnight. The reaction mixture was diluted with ethyl acetate and water. Aqueous layer was extracted twice with ethyl acetate (25mL). Combined organic extracts were washed with water (3x 25mL), dried over MgSO₄ and evaporated to yield a pale yellow oil, 0.35g crude. **MS (ESP)**: 409 (MH⁺) for C₁₈H₁ₙClF₂N₆O
Scheme XVIII: Intermediates 45-49

Intermediate 45

Intermediate 46

Intermediate 47

Intermediate 48

Intermediate 49
Intermediate 45: 4-(2,6-dichloropyrimidin-4-yl)morpholine

A solution of 2,4,6-trichloropyrimidine (3.66g, 20mmol) in dichloromethane (75 mL) was cooled to -78 °C. A mixture morpholine (1.7mL, 20mmol) and di-isopropylethylamine (0.6 mL, 22mmol) was added dropwise. The reaction was allowed to warm to rt and stir overnight. The reaction mixture was partitioned between dichloromethane and water. The organic phase was dried over MgSO₄ and evaporated to obtain a white solid. (3.25g, 70%) MS (ESP): 234 (MH⁺) for C₁₈H₁₉Cl₂N₅O₃

Intermediate 46: 4-(2-butoxy-6-chloropyrimidin-4-yl)morpholine

To a suspension of NaH (60% in oil, 0.834g, 20.8 mmol) in DMF (20mL) at O°C was added n-butanol (1.33mL, 14.6mmol). A solution of 4-(2,6-dichloropyrimidin-4-yl)morpholine (Intermediate 45) (3.25g, 13.9mmol) in DMF (20mL) was added dropwise. The reaction was allowed to stir at O°C for 3h. The reaction was allowed to warm to rt. The reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was washed with water (IX 50mL). The organic layers were combined, washed with water (4 X 40mL), dried over MgSO₄ and evaporated to obtain a white solid. Chromatography on silica gel using (4 - 10% ethyl acetate/hexane) gave the product as a white solid (2.0g, 53%) MS (ESP): 272 (MH⁺) for C₁₂H₁₈ClN₃O₂

Intermediate 47: 2-butoxy-N-(3,4-dichlorobenzyl)-6-morpholin-4-ylpyrimidin-4-amine

A mixture of 4-(2-butoxy-6-chloropyrimidin-4-yl)morpholine (2.0g, 7.35mmol) (Intermediate 46) and 3,4-dichlorobenzylamine (1.96mL, 14.7mmol) was heated at 170°C for 2h using microwave irradiation. The resultant product was dissolved in ethyl acetate and washed with IN hydrochloric acid. The organic extract was dried over MgSO₄ and evaporated to obtain a yellow solid. (2.14g, 70%) MS (ESP): 411 (MH⁺) for C₁₂H₂₄Cl₂N₄O₂

Intermediate 48: 2-butoxy-N-(3,4-dichlorobenzyl)-6-morpholin-4-yl-5-nitrosopyrimidin-4-amine

To a solution of 2-butoxy-N-(3,4-dichlorobenzyl)-6-morpholin-4-ylpyrimidin-4-amine (Intermediate 47) (2.14g, 5.19mmol) in acetic acid (20mL) and water (2mL) at O°C was added dropwise a solution of NaNO₂ (0.65g, 9.34mmol). The reaction turned a dark red color. The reaction was allowed to stir in ice for one hour, diluted with water and filtered. The blue solid was dried under vacuum at 45°C overnight. (1.76g, 75%) MS (ESP): 440 (MH⁺) for C₁₉H₂₃Cl₂N₅O₃
**Intermediate 49: 2-butoxy-Λ^-(3,4-dichlorobenzyl)-6-morpholin-4-ylpyrimidine-4,5-diamine**

A suspension of 2-butoxy-7V-(3,4-dichlorobenzyl)-6-morpholin-4-yl-5-nitrosopyrimidin-4-amine (Intermediate 48) (1.76g, 4.01mmol) in ethanol (35mL) and acetic acid (1mL) was heated to reflux. Zinc dust (1.6g, 24.6mmol) was added portionwise at a rate to maintain reflux. Once the addition was complete the reaction was heated at reflux for 1h. The reaction was allowed to cool slightly, then was filtered through a pad of Celite. The filtrate was evaporated. The crude product was carried on to the subsequent step. **MS** (ESP): 426 (MH^+) for C_{19}H_{25}Cl_2N_5O_2

![Scheme XIX: Intermediate 50](image)

**Intermediate 50: 2-butoxy-9H-purin-6-amine**

In a sealed pressure tube was charged with 6-amino-2-chloro-purine (300mg, 1.77mmol), n-butanol (12ml) and sodium hydroxide (400mg, 10mmol). The tube was heated at 120°C for 12h. The reaction mixture was then cooled to rt and excess of n-butanol was removed under reduced pressure. The residue was extracted with ethyl acetate and water. The solid in aqueous phase was filtered and dried to afford 150mg desired product (41% yield) as white solid. **MS (ES): 208(MH^+)** for C_{9}H_{13}N_{5}O

![Scheme XX: Intermediate 51](image)
Intermediate 51: 2-butoxy-N-(pyridin-3-ylmethyl)-9H-purin-6-amine

In a sealed pressure tube was charged with 2-chloro-N-(pyridin-3-ylmethyl)-9H-purin-6-amine (800mg, 3.08mmol) (prepared as described in GB patent 2392155), n-butanol (7mL) and sodium hydroxide (800mg, 20mmol). The tube was heated at 150°C for 24h. The reaction mixture was then cooled to rt and excess of n-butanol was evaporated at reduced pressure. The residue was purified by silica-gel chromatography (methanol/dichloromethane) to afford 140mg desired product (15% yield) as white solid. MS (ES): 299(MH⁺) for C₁₅H₁₈N₆O

Intermediate 52: 2-butoxy-N-(3-furylmethyl)-9H-purin-6-amine

The titled intermediate was prepared in an analogous manner to Intermediate 51 using 2-chloro-N-(3-furylmethyl)-9H-purin-6-amine (prepared as described in JACS (1959) 81, 3789-3792).

MS (ES): 288(MH⁺) for C₁₄H₁₀ClN₅O₂

Intermediate 53: 8-bromo-2-butoxy-9-(2,6-difluorobenzyl)-9H-purin-6-amine
The title compound was prepared by treating a solution of 6-amino-8-bromo-9-(2,6-difluorobenzyl)-9'H-purin-2-ol (2.5g, 7.02 mmol) [Intermediate 31] in DMF (50mL) with 1-bromobutane (2.25mL, 20.95mmol) and K2CO3 (5.8g, 42mmol). The reaction mixture was heated at 45°C overnight. The reaction was concentrated at reduced pressure, diluted with water (25mL) neutralized with NaHSO₄ (10% solution) and extracted with EtOAc. Organic extracts were dried over MgSO₄ and evaporated. Purification by reverse phase chromatography [35-50% Acetonitrile/FtO/ 0.1 % TFA] gave the title compound as solid.

1H NMR (300 MHz, DMSO-D₆) δ ppm 0.89 (t, J=7.3 Hz, 3 H) 1.27 - 1.41 (m, 2 H) 1.51 - 1.64 (m, 2 H) 4.13 (t, J=6.6 Hz, 2 H) 5.32 (s, 2 H) 7.10 (t, J=8.10 Hz, 2 H) 7.39 - 7.55 (m, 3 H)

MS (ESP) M/z= 412 (MH+) for C_{16}H_{16}BrF_{2}N_{5}O
Scheme XXII: Intermediates 54 and 55

Intermediate 54: \(N\)-(1H-benzimidazol-2-ylmethyl)-2-chloro-9\(H\)-purin-6-amine

A solution of 2,6-dichloropurine (1.0 g, 5.3 mmol) in THF (2.5 mL) was treated with 2-aminomethyl benzimidazole (1.3 g, 5.91 mmol). The reaction was heated to reflux for 3 days. The reaction was concentrated at reduced pressure. The residue was triturated with water, filtered, washed with hexane to yield a solid product (1.76 g, >100%) [Purity was adequate to proceed with the synthesis.]

Intermediate 55: \(N\)-(1H-benzimidazol-2-ylmethyl)-2-chloro-9-(2-morpholin-4-ylethyl)-9\(H\)-purin-6-amine:
A solution of \( N\)-(1\( H\)-benzimidazol-2-ylmethyl)-2-chloro-9 \( H\)-purin-6-amine (Intermediate 54) (1.7g, 5.3 mmol) above was dissolved in DMF (15mL) and treated with Cs\(_2\)CO\(_3\) (4.9g, 15.04 mmol) and 4-(2-chloroethyl)-morpholine (1.4g, 7.53 mmol). The reaction was allowed to stir at room temperature overnight. The reaction mixture was diluted with dichloromethane, washed with water twice, dried over MgSO\(_4\) and evaporated to obtain the title compound as a solid (2.0 g, 91%)

### EXAMPLES

#### Table 1 Experimental

**Example 1**: 2-fbutylthio)-9-(3-nitrobenzyl)-9 \( H\)-purin-6-amine

2-(Butylthio)-9 \( H\)-purin-6-amine (Intermediate 5, 0.22g, lmmol), 3-nitrobenzylbromide (0.22g, lmmol) and cesium carbonate (0.33g, lmmol) were combined in DMF (5mL) and stirred at rt overnight. The reaction mixture was filtered and concentrated under reduced pressure. The resulting oil was triturated with cold methanol to afforded the desired compound as a solid. **MS (ES)**: 359 (MH\(^+\)) for C\(_{16}\)H\(_{18}\)N\(_6\)O\(_2\)S. **\(^1\)H NMR Data DMSO-d6** 0.83 (t, 3H); 1.33 (m, 2H); 1.56 (m, 2H); 3.03 (t, 2H); 5.46 (s, 2H); 7.35 (bs, 2H); 7.65 (m, IH); 7.77 (m, IH); 8.16 (m, IH); 8.20 (s, IH); 8.20 (m, IH).

The examples in Table 1 below were prepared by analogous methods. The starting material is Intermediate 5 unless otherwise noted.

<table>
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<tr>
<th>Ex#</th>
<th>Name</th>
<th>MS</th>
<th>(^1)H NMR Data DMSO-d6</th>
<th>Foot Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2-(butylthio)-9-[3-(trifluoromethyl)benzyl]-9( H)-purin-6-amine</td>
<td>382 (MH(^+)) for C(<em>{17})H(</em>{18})F(_3)N(_5)S</td>
<td>0.83 (t, 3H); 1.33 (m, 2H); 1.56 (m, 2H); 3.02 (t, 2H); 5.40 (s, 2H); 7.33 (bs, 2H); 7.58 (m, 2H); 7.66 (m, 1H); 7.76 (s, 1H); 8.19 (s, 1H).</td>
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<tr>
<td>Ex#</td>
<td>Name</td>
<td>MS</td>
<td>^H NMR Data DMSO-d6</td>
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<tr>
<td>3</td>
<td>2-(butylthio)-9-(3-chlorobenzyl)-9H-purin-6-amine</td>
<td>348 (MH^+) for C_{16}H_{18}ClN_S</td>
<td>0.86 (t, 3H); 1.36 (m, 2H); 1.59 (m, 2H); 3.04 (t, 2H); 5.30 (s, 2H); 7.32 (m, 5H); 7.43 (s, 1H); 8.15 (s, 1H).</td>
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<tr>
<td>4</td>
<td>3-[(6-amino-2-(butylthio)-9H-purin-9-yl)methyl]benzonitrile</td>
<td>339 (MH^+) for C_{17}H_{18}N_S</td>
<td>0.84 (t, 3H); 1.34 (m, 2H); 1.56 (m, 2H); 3.02 (t, 2H); 5.36 (s, 2H); 7.34 (bs, 2H); 7.57 (m, 2H); 7.77 (d, 1H); 7.84 (s, 1H); 8.16 (s, 1H).</td>
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<td>5</td>
<td>2-(butylthio)-9-(3-methylbenzyl)-9H-purin-6-amine</td>
<td>328 (MH^+) for C_{17}H_{21}N_S</td>
<td>0.87 (t, 3H); 1.38 (m, 2H); 1.61 (m, 2H); 2.25 (s, 3H); 3.05 (t, 2H); 5.24 (s, 2H); 7.15 (m, 4H); 7.29 (bs, 2H); 8.12 (s, 1H).</td>
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<td>2-(butylthio)-9-(3,4-dichlorobenzyl)-9H-purin-6-amine</td>
<td>382 (MH^+) for C_{16}H_{17}ClS</td>
<td>0.84 (t, 3H); 1.33 (m, 2H); 1.56 (m, 2H); 3.02 (t, 2H); 5.31 (s, 2H); 7.25 (m, 1H); 7.34 (bs, 2H); 7.60 (d, 1H); 7.64 (s, 1H); 8.15 (s, 1H).</td>
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<tr>
<td>7</td>
<td>2-(butylthio)-9-(2-methoxy-5-nitrobenzyl)-9H-purin-6-amine</td>
<td>389 (MH^+) for C_{17}H_{20}N_S</td>
<td>0.81 (t, 3H); 1.32 (m, 2H); 1.55 (m, 2H); 3.01 (t, 2H); 3.96 (s, 3H); 5.32 (s, 2H); 7.25 (d, 1H); 7.30 (bs, 2H); 8.02 (m, 1H); 8.07 (s, 1H); 8.24 (m, 1H).</td>
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<td>8</td>
<td>2-(butylthio)-9-(2-chloro-4-fluorobenzyl)-9H-purin-6-amine</td>
<td>366 (MH^+) for C_{16}H_{17}ClFS</td>
<td>0.82 (t, 3H); 1.33 (m, 2H); 1.55 (m, 2H); 3.00 (t, 2H); 5.36 (s, 2H); 6.97 (m, 1H); 7.19 (m, 2H); 7.91 (s, 1H).</td>
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<td>9</td>
<td>2-(butylthio)-9-(2,6-dichlorobenzyl)-9H-purin-6-amine</td>
<td>382 (MH^+) for C_{16}H_{17}ClS</td>
<td>0.87 (t, 3H); 1.36 (m, 2H); 1.52 (m, 2H); 2.97 (t, 2H); 5.52 (s, 2H); 7.26 (bs, 2H); 7.44 (m, 1H); 7.52 (m, 2H); 7.91 (s, 1H).</td>
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<td>10</td>
<td>2-(butylthio)-9-(2-chloro-5-nitrobenzyl)-9H-purin-6-amine</td>
<td>393 (MH^+) for C_{16}H_{17}ClNO_S</td>
<td>0.80 (t, 3H); 1.30 (m, 2H); 1.51 (m, 2H); 2.96 (t, 2H); 5.52 (s, 2H); 7.35 (bs, 2H); 7.81 (d, 1H); 8.11 (m, 1H); 8.14 (s, 1H); 8.20 (m, 1H).</td>
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<td>11</td>
<td>2-(butylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine</td>
<td>350 (MH^+) for C_{16}H_{17}FNO_S</td>
<td>0.88 (t, 3H); 1.37 (m, 2H); 1.56 (m, 2H); 3.00 (t, 2H); 5.37 (s, 2H); 7.10 (m, 2H); 7.26 (bs, 2H); 7.44 (m, 1H); 8.05 (s, 1H).</td>
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<tr>
<td>12</td>
<td>methyl 3-{{6-amino-2-(butylthio)-9H-purin-9-yl}methyl}benzoate</td>
<td>372 (MH^+) for C_{18}H_{21}N_S</td>
<td>0.83 (t, 3H); 1.34 (m, 2H); 1.57 (m, 2H); 3.03 (t, 2H); 3.82 (s, 3H); 5.37 (s, 2H); 7.30 (bs, 2H); 7.49 (m, 1H).</td>
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<td>MS</td>
<td>$^1$H NMR Data DMSO-d6</td>
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<tr>
<td>13</td>
<td>2-(butylthio)-9-(4-chloro-2-fluorobenzyl)-9H-purin-6-amine</td>
<td>366 ($M^+\text{)}$ for $\text{C}<em>{16}\text{H}</em>{17}\text{ClF}<em>{3}\text{N}</em>{5}\text{S}$</td>
<td>0.84 (t, 3H); 1.32 (m, 2H); 1.53 (m, 2H); 2.98 (t, 2H); 5.34 (s, 2H); 7.25 (m, 2H); 7.30 (bs, 2H); 7.45 (d, 1H); 8.08 (s, 1H).</td>
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<td>2-(butylthio)-9-[2-fluoro-6-(trifluoromethyl)benzyl]-9H-purin-6-amine</td>
<td>400 ($M^+\text{)}$ for $\text{C}<em>{17}\text{H}</em>{17}\text{F}<em>{3}\text{N}</em>{3}\text{S}$</td>
<td>0.85 (t, 3H); 1.33 (m, 2H); 1.49 (m, 2H); 2.89 (t, 2H); 5.47 (s, 2H); 7.26 (bs, 2H); 7.64 (m, 3H); 7.86 (s, 1H).</td>
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<tr>
<td>15</td>
<td>2-(butylthio)-9-(3-methoxybenzyl)-9H-purin-6-amine</td>
<td>344 ($M^+\text{)}$ for $\text{C}<em>{17}\text{H}</em>{21}\text{N}_{3}\text{OS}$</td>
<td>0.86 (t, 3H); 1.37 (m, 2H); 1.60 (m, 2H); 3.05 (t, 2H); 3.71 (s, 3H); 5.25 (s, 2H); 6.85 (m, 2H); 6.92 (m, 1H); 7.23 (m, 1H); 7.29 (bs, 2H); 8.13 (s, 1H).</td>
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<tr>
<td>16</td>
<td>2-(butylthio)-9-(2-fluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>346 ($M^+\text{)}$ for $\text{C}<em>{17}\text{H}</em>{20}\text{F}<em>{3}\text{N}</em>{3}\text{S}$</td>
<td>0.85 (t, 3H); 1.35 (m, 2H); 1.57 (m, 2H); 2.22 (s, 3H); 3.02 (t, 2H); 5.33 (s, 2H); 7.03 (m, 2H); 7.23 (m, 1H); 7.30 (bs, 2H); 8.07 (s, 1H).</td>
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<tr>
<td>17</td>
<td>2-(butylthio)-9-[4-(methylsulfonyl)benzyl]-9H-purin-6-amine</td>
<td>392 ($M^+\text{)}$ for $\text{C}<em>{17}\text{H}</em>{21}\text{N}<em>{3}\text{O}</em>{2}\text{S}_{2}$</td>
<td>0.84 (t, 3H); 1.35 (m, 2H); 1.57 (m, 2H); 3.02 (t, 2H); 5.33 (s, 2H); 7.03 (m, 2H); 7.23 (m, 1H); 7.30 (bs, 2H); 8.07 (s, 1H).</td>
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<td>18</td>
<td>2-(butylthio)-9-(4-methoxy-3-nitrobenzyl)-9H-purin-6-amine</td>
<td>389 ($M^+\text{)}$ for $\text{C}<em>{17}\text{H}</em>{20}\text{O}<em>{3}\text{N}</em>{3}\text{S}$</td>
<td>0.85 (t, 3H); 1.36 (m, 2H); 1.59 (m, 2H); 3.04 (t, 2H); 3.88 (s, 3H); 5.30 (s, 2H); 7.31 (bs, 2H); 7.34 (m, 1H); 7.63 (m, 1H); 7.95 (m, 1H); 8.15 (s, 1H).</td>
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<tr>
<td>19</td>
<td>2-(butylthio)-9-{{4-chloro-2-(trifluoromethyl)quinolin-6-yl}methyl}-9H-purin-6-amine</td>
<td>467 ($M^+\text{)}$ for $\text{C}<em>{20}\text{H}</em>{18}\text{ClF}<em>{3}\text{N}</em>{6}\text{S}$</td>
<td>0.65 (t, 3H); 1.18 (m, 2H); 1.42 (m, 2H); 2.96 (t, 2H); 5.64 (s, 2H); 7.34 (bs, 2H); 7.91 (m, 1H); 8.25 (m, 4H).</td>
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<tr>
<td>20</td>
<td>2-(butylthio)-9-(2-chloro-5-fluorobenzyl)-9H-purin-6-amine</td>
<td>366 ($M^+\text{)}$ for $\text{C}<em>{16}\text{H}</em>{17}\text{ClF}<em>{3}\text{N}</em>{3}\text{S}$</td>
<td>0.82 (t, 3H); 1.31 (m, 2H); 1.53 (m, 2H); 2.98 (t, 2H); 5.39 (s, 2H); 7.00 (m, 1H); 7.24 (m, 1H); 7.34 (bs, 2H); 7.55 (m, 1H); 8.10 (s, 1H).</td>
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<tr>
<td>21</td>
<td>2-(butylthio)-9-(3-fluorobenzyl)-9H-</td>
<td>332 ($M^+\text{)}$ for $\text{C}<em>{16}\text{H}</em>{18}\text{F}<em>{3}\text{N}</em>{3}\text{S}$</td>
<td>0.84 (t, 3H); 1.35 (m, 2H); 1.57 (m, 2H); 3.02 (t, 2H);</td>
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<td>22</td>
<td>2-(butylthio)-9-(2,4-difluorobenzyl)-9H-purin-6-amine</td>
<td>350 (MH$^+$) for C$<em>{16}$H$</em>{17}$F$_2$N$_5$S</td>
<td>0.85 (t, 3H); 1.34 (m, 2H); 1.56 (m, 2H); 3.01 (t, 2H); 3.73 (s, 2H); 7.06 (m, 1H); 7.31 (m, 4H); 8.09 (s, 1H).</td>
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<td>23</td>
<td>2-(butylthio)-9-(4,5-dimethoxy-2-nitrobenzyl)-9H-purin-6-amine</td>
<td>419 (MH$^+$) for C$<em>{18}$H$</em>{22}$N$_6$O$_5$S</td>
<td>0.81 (t, 3H); 1.29 (m, 2H); 1.51 (m, 2H); 2.96 (t, 2H); 3.73 (s, 3H); 3.85 (s, 3H); 5.59 (s, 2H); 6.89 (s, 1H); 7.31 (bs, 2H); 7.67 (s, 1H); 8.01 (s, 1H).</td>
<td>1</td>
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<tr>
<td>24</td>
<td>2-(butylthio)-9-(5-chloro-2-fluorobenzyl)-9H-purin-6-amine</td>
<td>366 (MH$^+$) for C$<em>{16}$H$</em>{17}$ClFN$_5$S</td>
<td>0.85 (t, 3H); 1.35 (m, 2H); 1.58 (m, 2H); 3.02 (t, 2H); 5.35 (s, 2H); 7.26 (m, 1H); 7.31 (bs, 2H); 7.40 (m, 2H); 8.11 (s, 1H).</td>
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<tr>
<td>25</td>
<td>2-(butylthio)-9-(3-chloro-2,6-difluorobenzyl)-9H-purin-6-amine</td>
<td>384 (MH$^+$) for C$<em>{16}$H$</em>{16}$ClF$_2$N$_5$S</td>
<td>0.87 (t, 3H); 1.36 (m, 2H); 1.55 (m, 2H); 2.98 (t, 2H); 5.41 (s, 2H); 7.19 (m, 1H); 7.29 (bs, 2H); 7.65 (m, 1H); 8.10 (s, 1H).</td>
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<tr>
<td>26</td>
<td>2-(butylthio)-9-(3,5-dimethoxybenzyl)-9H-purin-6-amine</td>
<td>374 (MH$^+$) for C$<em>{18}$H$</em>{23}$N$_5$O$_2$S</td>
<td>0.87 (t, 3H); 1.37 (m, 2H); 1.62 (m, 2H); 3.06 (t, 2H); 3.69 (s, 6H); 5.20 (s, 2H); 6.42 (m, 1H); 6.49 (m, 2H); 7.30 (bs, 2H); 8.12 (s, 1H).</td>
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<td>27</td>
<td>2-(butylthio)-9-{(2-[(phenylsulfonyl)methyl]benzyl)-9H-purin-6-amine</td>
<td>468 (MH$^+$) for C$<em>{23}$H$</em>{25}$N$_5$O$_2$S$_2$</td>
<td>0.82 (t, 3H); 1.32 (m, 2H); 1.52 (m, 2H); 3.00 (t, 2H); 5.01 (s, 2H); 5.34 (s, 2H); 7.08 (m, 1H); 7.20 (m, 2H); 7.30 (m, 3H); 7.63 (m, 2H); 7.69 (m, 3H); 8.03 (s, 1H).</td>
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<tr>
<td>28</td>
<td>2-(butylthio)-9-(4-fluoro-3-nitrobenzyl)-9H-purin-6-amine</td>
<td>377 (MH$^+$) for C$<em>{16}$H$</em>{17}$FN$_6$O$_2$S</td>
<td>0.84 (t, 3H); 1.34 (m, 2H); 1.56 (m, 2H); 3.03 (t, 2H); 5.40 (s, 2H); 7.32 (bs, 2H); 7.57 (m, 1H); 7.75 (m, 1H); 8.17 (s, 1H); 8.21 (m, 1H).</td>
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<tr>
<td>29</td>
<td>2-(butylthio)-9-(4-nitrobenzyl)-9H-purin-6-amine</td>
<td>359 (MH$^+$) for C$<em>{16}$H$</em>{18}$N$_6$O$_2$S</td>
<td>0.76 (t, 3H); 1.28 (m, 2H); 1.50 (m, 2H); 3.00 (t, 2H); 5.42 (s, 2H); 7.41 (d, 2H); 8.05 (s, 1H); 8.11 (d, 2H).</td>
<td>15</td>
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<tr>
<td>30</td>
<td>2-(butylthio)-9-(3,4-</td>
<td>350 (MH$^+$)</td>
<td>0.86 (t, 3H); 1.36 (m, 2H); 1.50 (m, 2H); 3.00 (t, 2H); 5.42 (s, 2H); 7.41 (d, 2H); 8.05 (s, 1H); 8.11 (d, 2H).</td>
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<td></td>
<td>difluorobenzyl)-9H-purin-6-amine</td>
<td>C₁₆H₁₂F₂N₅S</td>
<td>1.58 (m, 2H); 3.03 (t, 2H); 5.29 (s, 2H); 7.15 (m, 1H); 7.32 (bs, 2H); 7.42 (m, 2H); 8.14 (s, 1H).</td>
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<tr>
<td>31</td>
<td>2-(butylthio)-9-(3,5-difluorobenzyl)-9H-purin-6-amine</td>
<td>350 (MH⁺) for C₁₆H₁₂F₂N₅S</td>
<td>0.85 (t, 3H); 1.36 (m, 2H); 1.58 (m, 2H); 3.03 (t, 2H); 5.33 (s, 2H); 7.05 (m, 2H); 7.19 (m, 1H); 7.34 (bs, 2H); 8.15 (s, 1H).</td>
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<tr>
<td>32</td>
<td>2-(butylthio)-9-(2,5-difluorobenzyl)-9H-purin-6-amine</td>
<td>350 (MH⁺) for C₁₆H₁₂F₂N₅S</td>
<td>0.85 (t, 3H); 1.35 (m, 2H); 1.56 (m, 2H); 3.01 (t, 2H); 5.35 (s, 2H); 7.13 (m, 1H); 7.25 (m, 2H); 7.31 (bs, 2H); 8.10 (s, 1H).</td>
<td>1</td>
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<tr>
<td>33</td>
<td>2-(butylthio)-9-(2-fluorobenzyl)-9H-purin-6-amine</td>
<td>332 (MH⁺) for C₁₆H₁₈FN₃S</td>
<td>0.85 (t, 3H); 1.35 (m, 2H); 1.56 (m, 2H); 3.01 (t, 2H); 5.36 (s, 2H); 7.18 (m, 3H); 7.31 (bs, 2H); 7.35 (m, 1H); 8.09 (s, 1H).</td>
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<tr>
<td>34</td>
<td>2-(butylthio)-9-(4-fluorobenzyl)-9H-purin-6-amine</td>
<td>332 (MH⁺) for C₁₆H₁₈FN₃S</td>
<td>0.86 (t, 3H); 1.36 (m, 2H); 1.59 (m, 2H); 3.04 (t, 2H); 5.28 (s, 2H); 7.16 (m, 2H); 7.30 (bs, 2H); 7.37 (m, 2H); 8.13 (s, 1H).</td>
<td>1</td>
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<tr>
<td>35</td>
<td>2-(butylthio)-9-(2-chlorobenzyl)-9H-purin-6-amine</td>
<td>348 (MH⁺) for C₁₆H₁₈ClN₃S</td>
<td>0.81 (t, 3H); 1.31 (m, 2H); 1.53 (m, 2H); 2.98 (t, 2H); 5.40 (s, 2H); 7.06 (m, 1H); 7.31 (m, 2H); 7.33 (bs, 2H); 7.49 (m, 1H); 8.09 (s, 1H).</td>
<td>1</td>
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<td>36</td>
<td>2-(butylthio)-9-(2-methylbenzyl)-9H-purin-6-amine</td>
<td>328 (MH⁺) for C₁₇H₂₁N₅S</td>
<td>0.84 (t, 3H); 1.34 (m, 2H); 1.57 (m, 2H); 2.37 (s, 3H); 3.01 (t, 2H); 5.30 (s, 2H); 6.98 (m, 1H); 7.13 (m, 1H); 7.19 (m, 2H); 7.31 (bs, 2H); 8.04 (s, 1H).</td>
<td>1</td>
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<tr>
<td>37</td>
<td>2-(butylthio)-9-(3-chloro-4-fluorobenzyl)-9H-purin-6-amine</td>
<td>366 (MH⁺) for C₁₆H₁₇ClFN₃S</td>
<td>0.85 (t, 3H); 1.35 (m, 2H); 1.58 (m, 2H); 3.03 (t, 2H); 5.29 (s, 2H); 7.32 (bs, 2H); 7.39 (m, 2H); 7.62 (m, 1H); 8.15 (s, 1H).</td>
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<tr>
<td>38</td>
<td>2-(butylthio)-9-(2-nitrobenzyl)-9H-purin-6-amine</td>
<td>359 (MH⁺) for C₁₆H₁₈N₆O₂S</td>
<td>0.76 (t, 3H); 1.25 (m, 2H); 1.46 (m, 2H); 2.90 (t, 2H); 5.65 (s, 2H); 6.97 (d, 1H); 7.36 (bs, 2H); 7.57 (t, 1H); 7.67 (t, 1H); 8.06 (s, 1H); 8.11 (d, 1H).</td>
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<tr>
<td>39</td>
<td>2-(butylthio)-9-(3-</td>
<td>366 (MH⁺) for</td>
<td>0.85 (t, 3H); 1.35 (m, 2H);</td>
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<tr>
<td>40</td>
<td>2-(butylthio)-9-(3,5-dimethylbenzyl)-9H-purin-6-amine</td>
<td>C$<em>{18}$H$</em>{22}$N$_6$S</td>
<td>342 (MH$^+$) for C$<em>{18}$H$</em>{22}$N$_6$S 0.87 (t, 3H); 1.38 (m, 2H); 1.63 (m, 2H); 2.20 (s, 6H); 3.06 (t, 2H); 5.19 (s, 2H); 6.90 (s, 1H); 6.94 (s, 2H); 7.28 (bs, 2H); 8.11 (s, 1H).</td>
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<tr>
<td>41</td>
<td>2-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]benzonitrile</td>
<td>C$<em>{17}$H$</em>{18}$N$_6$S</td>
<td>339 (MH$^+$) for C$<em>{17}$H$</em>{18}$N$_6$S 0.80 (t, 3H); 1.30 (m, 2H); 1.48 (m, 2H); 2.96 (t, 2H); 5.52 (s, 2H); 7.23 (d, 1H); 7.35 (bs, 2H); 7.50 (t, 1H); 7.65 (t, 1H); 7.88 (d, 1H); 8.14 (s, 1H).</td>
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<td>42</td>
<td>4-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]benzonitrile</td>
<td>C$<em>{17}$H$</em>{18}$N$_6$S</td>
<td>339 (MH$^+$) for C$<em>{17}$H$</em>{18}$N$_6$S 0.81 (t, 3H); 1.29 (m, 2H); 1.50 (m, 2H); 2.97 (t, 2H); 5.39 (s, 2H); 7.33 (bs, 2H); 7.41 (d, 2H); 7.80 (d, 2H); 8.14 (s, 1H).</td>
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<td>43</td>
<td>9-(4-bromo-2-fluorobenzyl)-2-(butylthio)-9H-purin-6-amine</td>
<td>C$<em>{16}$H$</em>{17}$BrF$_5$NS</td>
<td>410 (MH$^+$) for C$<em>{16}$H$</em>{17}$BrF$_5$NS 0.84 (t, 3H); 1.32 (m, 2H); 1.53 (m, 2H); 2.99 (t, 2H); 5.33 (s, 2H); 7.17 (m, 1H); 7.32 (bs, 2H); 7.38 (m, 1H); 7.58 (m, 1H); 8.09 (s, 1H).</td>
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<td>44</td>
<td>2-(butylthio)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>C$<em>{17}$H$</em>{19}$F$_2$N$_6$S</td>
<td>364 (MH$^+$) for C$<em>{17}$H$</em>{19}$F$_2$N$_6$S 0.88 (t, 3H); 1.37 (m, 2H); 1.57 (m, 2H); 2.17 (s, 3H); 3.01 (t, 2H); 5.36 (s, 2H); 7.00 (m, 1H); 7.27 (bs, 2H); 7.30 (m, 1H); 8.04 (s, 1H).</td>
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<td>45</td>
<td>2-(butylthio)-9-(2,5-dichlorobenzyl)-9H-purin-6-amine</td>
<td>C$<em>{16}$H$</em>{17}$Cl$_2$N$_6$S</td>
<td>382 (MH$^+$) for C$<em>{16}$H$</em>{17}$Cl$_2$N$_6$S 0.83 (t, 3H); 1.32 (m, 2H); 1.55 (m, 2H); 2.99 (t, 2H); 5.39 (s, 2H); 7.25 (m, 1H); 7.34 (bs, 2H); 7.44 (m, 1H); 7.53 (m, 1H); 8.11 (s, 1H).</td>
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<td>46</td>
<td>methyl 4-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]-3-methoxybenzoate</td>
<td>C$<em>{19}$H$</em>{23}$N$_5$O$_3$S</td>
<td>402 (MH$^+$) for C$<em>{19}$H$</em>{23}$N$_5$O$_3$S 0.81 (t, 3H); 1.30 (m, 2H); 1.53 (m, 2H); 2.98 (t, 2H); 3.83 (s, 3H); 3.91 (s, 3H); 5.30 (s, 2H); 7.02 (d, 1H); 7.29 (bs, 2H); 7.49 (m, 2H); 8.04 (s, 1H).</td>
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<td>47</td>
<td>2-(butylthio)-9-(3-fluoro-4-methylbenzyl)-9H-purin-6-amine</td>
<td>C$<em>{17}$H$</em>{20}$FN$_6$S</td>
<td>346 (MH$^+$) for C$<em>{17}$H$</em>{20}$FN$_6$S 0.85 (t, 3H); 1.36 (m, 2H); 1.58 (m, 2H); 2.16 (s, 3H); 3.03 (t, 2H); 5.25 (s, 2H); 7.03 (m, 1H); 7.13 (m, 1H).</td>
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<td>48</td>
<td>9-(2,6-difluorobenzyl)-2-(isobutylthio)-9H-purin-6-amine</td>
<td>350 (MH⁺) for C₁₆H₁₇F₂N₅S</td>
<td>0.94 (d, 6H); 1.82 (m, 1H); 2.94 (d, 2H); 5.37 (s, 2H); 7.10 (m, 2H); 7.26 (bs, 2H); 7.34 (m, 1H); 8.05 (s, 1H).</td>
<td>1, 5</td>
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<td>49</td>
<td>9-(2,6-difluorobenzyl)-2-[3-methylbutylthio]-9H-purin-6-amine</td>
<td>364 (MH⁺) for C₁₇H₁₉F₂N₅S</td>
<td>0.90 (d, 6H); 1.47 (m, 2H); 1.69 (m, 1H); 3.02 (t, 2H); 5.38 (s, 2H); 7.10 (m, 2H); 7.26 (bs, 2H); 7.44 (m, 1H); 8.04 (s, 1H).</td>
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<td>50</td>
<td>9-(2,6-difluorobenzyl)-2-[2-methylbutylthio]-9H-purin-6-amine</td>
<td>364 (MH⁺) for C₁₇H₁₉F₂N₅S</td>
<td>0.88 (m, 6H); 1.17 (m, 1H); 1.47 (m, 1H); 1.61 (m, 1H); 2.93 (m, 1H); 3.07 (m, 1H); 5.37 (s, 2H); 7.10 (m, 2H); 7.27 (bs, 2H); 7.44 (m, 1H); 8.05 (s, 1H).</td>
<td>1, 7</td>
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<td>51</td>
<td>2-(cyclopentylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine</td>
<td>362 (MH⁺) for C₁₇H₁₇F₂N₅S</td>
<td>1.41 (m, 2H); 1.64 (m, 4H); 2.08 (m, 2H); 3.83 (m, 1H); 5.38 (s, 2H); 7.10 (m, 2H); 7.26 (bs, 2H); 7.44 (m, 1H); 8.06 (s, 1H).</td>
<td>1, 8</td>
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<td>52</td>
<td>2-(cyclohexylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine</td>
<td>376 (MH⁺) for C₁₈H₁₉F₂N₅S</td>
<td>1.36 (m, 5H); 1.68 (m, 3H); 1.97 (m, 2H); 3.65 (m, 1H); 5.38 (s, 2H); 7.10 (m, 2H); 7.26 (bs, 2H); 7.43 (m, 1H); 8.07 (s, 1H).</td>
<td>1, 9</td>
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<tr>
<td>53</td>
<td>9-(2,6-difluorobenzyl)-2-(2-methoxyethoxy)-9H-purin-6-amine</td>
<td>336 (MH⁺) for C₁₅H₁₅F₂N₅O₂</td>
<td>3.26 (s, 3H); 3.57 (t, 2H); 4.27 (t, 2H); 5.33 (s, 2H); 7.12 (m, 2H); 7.21 (bs, 2H); 7.44 (m, 1H); 7.96 (s, 1H).</td>
<td>3, 10</td>
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<tr>
<td>54</td>
<td>2-(butythio)-9-(cyclobutylmethyl)-9H-purin-6-amine</td>
<td>292 (MH⁺) for C₁₄H₂₁N₅S</td>
<td>0.89 (t, 3H); 1.39 (m, 2H); 1.77 (m, 8H); 2.76 (m, 1H); 3.04 (t, 2H); 4.08 (d, 2H); 7.24 (bs, 2H); 7.98 (s, 1H).</td>
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<td>55</td>
<td>2-(butythio)-9-(cyclohexylmethyl)-9H-purin-6-amine</td>
<td>320 (MH⁺) for C₁₆H₂₅N₅S</td>
<td>0.90 (t, 3H); 0.97 (m, 2H); 1.12 (m, 3H); 1.39 (m, 2H); 1.50 (m, 2H); 1.64 (m, 5H); 1.83 (m, 1H); 3.03 (t, 2H); 3.91 (d, 2H); 7.24 (bs, 2H); 7.95 (s, 1H).</td>
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<tr>
<td>56</td>
<td>2-(butythio)-9-(4,4,4-trifluorobutyl)-9H-purin-6-amine</td>
<td>334 (MH⁺) for C₁₃H₁₈F₃N₅S</td>
<td>0.89 (t, 3H); 1.39 (m, 2H); 1.63 (m, 2H); 2.04 (m, 2H); 2.26 (m, 2H); 3.05 (t, 1H).</td>
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<td>57</td>
<td>2-(butylthio)-9-(2-ethylbutyl)-9H-purin-6-amine</td>
<td>308 (MH$^+$) for C$<em>{12}$H$</em>{25}$N$_5$S</td>
<td>0.86 (m, 9H); 1.22 (m, 4H); 1.39 (m, 2H); 1.63 (m, 2H); 1.85 (m, 1H); 3.04 (t, 2H); 3.98 (d, 2H); 7.26 (bs, 2H); 7.99 (s, 1H).</td>
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<td>58</td>
<td>2-(butylthio)-9-propyl-9H-purin-6-amine</td>
<td>266 (MH$^+$) for C$<em>{12}$H$</em>{19}$N$_5$S</td>
<td>0.86 (m, 6H); 1.40 (m, 2H); 1.63 (m, 2H); 1.79 (m, 2H); 3.05 (t, 2H); 4.03 (t, 2H); 7.25 (bs, 2H); 7.99 (s, 1H).</td>
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<td>59</td>
<td>2-(butylthio)-9-(3-methylbutyl)-9H-purin-6-amine</td>
<td>294 (MH$^+$) for C$<em>{14}$H$</em>{22}$N$_5$S</td>
<td>0.90 (m, 9H); 1.41 (m, 3H); 1.67 (m, 4H); 3.05 (t, 2H); 4.09 (t, 2H); 7.25 (bs, 2H); 8.02 (s, 1H).</td>
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<td>60</td>
<td>2-(butylthio)-9-isobutyl-9H-purin-6-amine</td>
<td>280 (MH$^+$) for C$<em>{13}$H$</em>{21}$N$_5$S</td>
<td>0.83 (d, 6H); 0.89 (t, 3H); 1.39 (m, 2H); 1.63 (m, 4H); 2.16 (m, 1H); 3.03 (t, 2H); 3.88 (d, 2H); 7.25 (bs, 2H); 7.97 (s, 1H).</td>
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<td>61</td>
<td>2-(butylthio)-9-(tetrahydro-2H-pyran-2-ylmethyl)-9H-purin-6-amine</td>
<td>322 (MH$^+$) for C$<em>{15}$H$</em>{23}$N$_6$OS</td>
<td>0.90 (t, 3H); 1.16 (m, 1H); 1.40 (m, 5H); 1.64 (m, 4H); 3.05 (m, 2H); 3.25 (m, 1H); 3.66 (m, 1H); 3.83 (m, 1H); 4.07 (m, 2H); 7.26 (bs, 2H); 7.89 (s, 1H).</td>
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<td>62</td>
<td>4-[6-amino-2-(butylthio)-9H-purin-9-yl]butanenitrile</td>
<td>291 (MH$^+$) for C$<em>{13}$H$</em>{18}$N$_6$S</td>
<td>0.89 (t, 3H); 1.40 (m, 2H); 1.63 (m, 2H); 2.11 (m, 2H); 2.51 (m, 2H); 3.07 (t, 2H); 4.16 (t, 2H); 7.28 (bs, 2H); 8.00 (s, 1H).</td>
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<td>63</td>
<td>5-[6-amino-2-(butylthio)-9H-purin-9-yl]pentanenitrile</td>
<td>305 (MH$^+$) for C$<em>{14}$H$</em>{20}$N$_6$S</td>
<td>0.91 (t, 3H); 1.44 (m, 4H); 1.64 (m, 2H); 1.88 (m, 2H); 2.54 (m, 2H); 3.06 (t, 2H); 4.12 (t, 2H); 7.27 (bs, 2H); 8.02 (s, 1H).</td>
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<td>64</td>
<td>9-(3-chloro-2,6-difluorobenzyl)-N-(2-morpholin-4-ylethyl)-2-(4,4,4- trifluorobutoxy)-9H-purin-6-amine</td>
<td>535 (MH$^+$) for C$<em>{22}$H$</em>{24}$ClF$_5$N$_6$O$_2$</td>
<td>1.87 (m, 2H); 2.38 (m, 8H); 3.53 (m, 6H); 4.21 (m, 2H); 5.36 (s, 2H); 7.20 (m, 1H); 7.65 (m, 2H); 8.02 (s, 1H).</td>
<td>3, 11</td>
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<td>65</td>
<td>2-(butylthio)-9-(2,3-dichlorobenzyl)-9H-purin-6-amine</td>
<td>382 (MH$^+$) for C$<em>{16}$H$</em>{17}$Cl$_2$N$_5$S</td>
<td>0.78 (t, 3H); 1.27 (m, 2H); 1.49 (m, 2H); 2.94 (t, 2H); 5.44 (s, 2H); 6.95 (m, 1H); 7.30 (m, 1H); 7.33 (bs,</td>
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<td>66</td>
<td>2-(butylthio)-9-[(5-chloro-1-benzothien-3-yl)methyl]-9H-purin-6-amine</td>
<td>404 (MH(^{+})) for C(<em>{18})H(</em>{18})ClN(<em>{5})S(</em>{2})</td>
<td>2H: 7.59 (m, 1H); 8.10 (s, 1H). 1H: 1.35 (m, 2H); 2H: 1.61 (m, 2H); 3.09 (t, 2H); 5.54 (s, 2H); 7.33 (bs, 2H); 7.43 (m, 1H); 7.80 (s, 1H); 8.04 (d, 1H); 8.18 (m, 2H).</td>
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<td>67</td>
<td>2-(butyl)[9-(3-chloro-2,6-difluorobenzyl)-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-2-yl]amino)ethanol</td>
<td>524 (MH(^{+})) for C(<em>{24})H(</em>{32})ClF(<em>{2})N(</em>{7})O(_{2})</td>
<td>2H: 1.21 (m, 3H); 2H: 1.46 (m, 2H); 2.41 (m, 4H); 2.51 (t, 2H); 3.56 (m, 12H); 5.22 (s, 2H); 6.89 (m, 1H); 7.36 (m, 1H); 7.64 (s, 1H).</td>
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<td>68</td>
<td>2-butoxy-9-(2,3-dichlorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>479 (MH(^{+})) for C(<em>{22})H(</em>{28})Cl(<em>{2})N(</em>{6})O(_{2})</td>
<td>2H: 1.38 (m, 2H); 2H: 1.64 (m, 2H); 2.48 (m, 4H); 2.59 (t, 2H); 3.63 (m, 6H); 4.22 (m, 2H); 5.38 (s, 2H); 6.94 (m, 1H); 7.16 (m, 1H); 7.42 (m, 1H); 7.83 (s, 1H).</td>
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<td>69</td>
<td>2-butoxy-9-[4-(methylsulfonyl)benzyl]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>489 (MH(^{+})) for C(<em>{23})H(</em>{32})N(<em>{6})O(</em>{2})S</td>
<td>2H: 1.36 (m, 2H); 2H: 1.62 (m, 2H); 2.45 (m, 4H); 2.56 (t, 2H); 2.96 (s, 3H); 3.59 (m, 6H); 4.21 (m, 2H); 5.33 (s, 2H); 7.42 (m, 2H); 7.80 (m, 2H); 7.87 (s, 1H).</td>
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<td>70</td>
<td>2-butoxy-9-(2-methoxy-5-nitrobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>486 (MH(^{+})) for C(<em>{23})H(</em>{31})N(<em>{5})O(</em>{5})</td>
<td>2H: 1.36 (m, 2H); 2H: 1.62 (m, 2H); 2.42 (m, 4H); 2.53 (t, 2H); 3.58 (m, 6H); 3.88 (s, 3H); 4.22 (m, 2H); 5.23 (s, 2H); 7.05 (m, 1H); 7.83 (s, 1H); 8.11 (m, 2H).</td>
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<td>71</td>
<td>3-(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-yl)methylbenzonitrile</td>
<td>436 (MH(^{+})) for C(<em>{23})H(</em>{29})N(<em>{2})O(</em>{2})</td>
<td>2H: 1.37 (m, 2H); 2H: 1.64 (m, 2H); 2.46 (m, 4H); 2.56 (t, 2H); 3.60 (m, 6H); 4.23 (t, 2H); 5.26 (s, 2H); 7.41 (m, 1H); 7.54 (m, 2H); 7.64 (m, 1H); 7.88 (s, 1H).</td>
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<td>72</td>
<td>9-(5-amino-2-methoxybenzyl)-2-butoxy-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>456 (MH(^{+})) for C(<em>{23})H(</em>{33})N(<em>{5})O(</em>{3})</td>
<td>2H: 1.39 (m, 2H); 2H: 1.66 (m, 2H); 2.46 (m, 4H); 2.56 (t, 2H); 3.60 (m, 6H); 3.67 (s, 3H); 4.25 (t, 2H); 5.08 (s, 2H); 6.50 (m, 1H); 6.59 (m, 1H); 6.69 (m, 1H); 7.68 (s, 1H).</td>
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<td>73</td>
<td>9-(2,6-difluorobenzyl)-N-(2-morpholin-4-ylethyl)-2-phenoxy-9H-purin-6-amine</td>
<td>467 (MH$^+$) for C$<em>{24}$H$</em>{22}$F$_2$N$_6$O$_2$</td>
<td>2.21 (m, 4H); 2.32 (m, 2H); 3.33 (m, 2H); 3.47 (m, 4H); 5.29 (s, 2H); 7.09 (m, 4H); 7.18 (m, 1H); 7.36 (m, 2H); 7.44 (m, 1H); 7.80 (m, 1H); 7.99 (s, 1H).</td>
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<td>74</td>
<td>5-(butylthio)-3-(3-chloro-2,6-difluorobenzyl)-3H-[1,2,3]triazolo[4,5-$d$]pyrimidin-7-amine</td>
<td>385 (MH$^+$) for C$<em>{13}$H$</em>{15}$ClF$_2$N$_6$S</td>
<td>0.88 (t, 3H); 1.37 (m, 2H); 1.58 (m, 2H); 3.02 (t, 2H); 5.75 (s, 2H); 7.22 (m, 1H); 7.70 (m, 1H).</td>
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<td>75</td>
<td>5-(butylthio)-3-(2,6-difluoro-3-methylbenzyl)-3H-[1,2,3]triazolo[4,5-$d$]pyrimidin-7-amine</td>
<td>365 (MH$^+$) for C$<em>{16}$H$</em>{18}$F$_2$N$_6$S</td>
<td>0.89 (t, 3H); 1.38 (m, 2H); 1.60 (m, 2H); 2.18 (s, 3H); 3.04 (t, 2H); 5.69 (s, 2H); 7.03 (m, 1H); 7.34 (m, 1H); 8.24 (bs, 2H).</td>
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<td>76</td>
<td>5-(butylthio)-3-(2,6-difluorobenzyl)-3H-[1,2,3]triazolo[4,5-$d$]pyrimidin-7-amine</td>
<td>351 (MH$^+$) for C$<em>{15}$H$</em>{16}$F$_2$N$_6$S</td>
<td>0.89 (t, 3H); 1.38 (m, 2H); 1.59 (m, 2H); 3.03 (t, 2H); 5.71 (s, 2H); 7.13 (m, 2H); 7.48 (m, 1H); 8.08 (bs, 1H); 8.41 (bs, 1H).</td>
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<td>77</td>
<td>2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>348(MH$^+$) for C$<em>{17}$H$</em>{19}$F$_2$N$_4$O</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 0.9 (t, 3H); 1.4(m, 2H); 1.6(m, 2H); 2.17 (s, 3H); 4.14 (t, 2H); 5.30 (s, 2H); 7.0 (t, 1H); 7.16 (s, br, 2H); 7.29 (q, 1H); 7.80 (s, 1H); 7.93(s, 1H)</td>
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<td>78</td>
<td>2-(butylthio)-9-(3-chloro-2,6-difluorobenzyl)-9H-purin-6-amine</td>
<td>384(MH$^+$) for C$<em>{16}$H$</em>{16}$ClF$_2$N$_5$S</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 0.91 (t, 3H); 1.40(m, 2H); 1.60(m, 2H); 3.00 (q, 2H); 5.45 (s, 2H); 7.20(t, 1H); 7.28 (s, br, 2H); 7.68 (q, 1H); 8.13(s, 1H)</td>
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<td>79</td>
<td>2-butoxy-9-(3-chloro-2,6-difluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>481(MH$^+$) for C$<em>{22}$H$</em>{27}$ClF$_2$N$_5$O</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 1.00(t, 3H); 1.47(m, 2H); 1.72(m, 2H); 2.60 (m, 4H); 3.64 (m, 6H); 4.24(t, 2H); 5.47(s, 2H); 7.29(t, 1H); 7.73 (s, br, 1H); 7.75 (q, 1H); 8.11(s, 1H)</td>
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<td>80</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>447(MH(^+)) for C(<em>{22})H(</em>{28})F(_2)N(_6)O(_2)</td>
<td>(^1)H NMR (DMSO-D(_6)) (\delta): 1.00 (t, 3H); 1.18 (m, 2H); 1.72 (m, 2H); 2.60 (m, 4H); 3.64 (m, 6H); 4.27 (m, 2H); 5.43 (s, 2H); 7.21 (t, 2H); 7.54 (m, 1H); 7.64 (s, br, 1H); 8.05 (s, 1H)</td>
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<td>81</td>
<td>2-butoxy-9-(3-chloro-2,6-difluorobenzyl)-N-(pyridin-3-ylmethyl)-9H-purin-6-amine</td>
<td>459(MH(^+)) for C(<em>{22})H(</em>{21})ClF(_3)N(_6)O</td>
<td>(^1)H NMR (DMSO-D(_6)) (\delta): 0.65 (t, 3H); 1.11 (m, 2H); 1.37 (m, 2H); 3.89 (s, 2H); 4.38 (d, 2H); 5.14 (s, 2H); 6.95 (dt, 1H); 7.00 (m, 1H); 7.45 (m, 2H); 7.83 (s, 1H); 8.17 (dd, 1H); 8.23 (t, 1H); 8.31 (s, 1H)</td>
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<td>82</td>
<td>2-butoxy-9-(3-chloro-2,6-difluorobenzyl)-N-(3-furylethyl)-9H-purin-6-amine</td>
<td>448(MH(^+)) for C(<em>{21})H(</em>{20})ClF(_3)N(_5)O(_2)</td>
<td>(^1)H NMR (DMSO-D(_6)) (\delta): 0.93 (t, 3H); 1.40 (m, 2H); 1.65 (m, 2H); 4.17 (t, 2H); 4.45 (s, br, 2H); 5.44 (s, 2H); 6.50 (s, 1H); 7.20 (t, 1H); 7.55 (d, 2H); 7.65 (q, 1H); 8.07 (s, 1H); 8.20 (s, br, 1H)</td>
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<td>83</td>
<td>4-([2-butoxy-6-[(2-morpholin-4-yethyl)amino]-9H-purin-9-yl]methyl)benzonitrile</td>
<td>436(MH(^+)) for C(<em>{23})H(</em>{29})N(_7)O(_2)</td>
<td>(^1)H NMR (DMSO-D(_6)) (\delta): 0.89 (t, 3H); 1.34 (m, 2H); 1.62 (m, 2H); 2.40 (m, 4H); 3.54 (m, 6H); 4.18 (t, 2H); 5.36 (s, 2H); 7.41 (d, 2H); 7.66 (s, br, 1H); 7.81 (d, 2H); 8.06 (s, 1H)</td>
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<td>84</td>
<td>2-(butylthio)-N,9-bis(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>504(MH(^+)) for C(<em>{22})H(</em>{25})F(_4)N(_5)S</td>
<td>(^1)H NMR (DMSO-D(_6)) (\delta): 0.80 (t, 3H); 1.46 (m, 2H); 1.60 (m, 2H); 2.25 (s, 6H); 3.00 (t, 2H); 5.40 (s, 2H); 6.95 (dt, 2H); 7.20 (d, 2H); 8.07 (s, 1H); 8.20 (s, br, 1H)</td>
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</tbody>
</table>

Table 1 Footnotes
1. purification by trituration with cold methanol
2. purification by reverse phase chromatography
3. purification by silica gel chromatography
4. NMR ran in methanol-d\(^4\)
Example 85: 2-fcyclopropylmethoxy)-9-[3-(trifluoromethyl)benzyl]-9H-purin-6-amine

Scheme XXIV

Intermediate 8

2-Chloro-9-[3-(trifluoromethyl)benzyl]-9H-purin-6-amine (Intermediate 8, 0.1 g, 0.32 mmol) and excess sodium hydroxide were suspended in cyclopropylmethanol in a sealed tube and heated at 70°C for 72 hours. The excess cyclopropylmethanol was evaporated and the resulting oil was triturated with water to afford the desired compound as a solid.

MS (ESP) M/z: 364 (MH+) for C_{17}H_{16}F_{3}N_{5}O

^{1}H NMR Data DMSO-d6 0.25 (m, 2H); 0.49 (m, 2H); 1.18 (m, IH); 4.01 (d, 2H); 5.35 (s, 2H); 7.24 (bs, 2H); 7.59 (m, 2H); 7.66 (m, IH); 7.77 (s, IH); 8.09 (s, IH).

The compounds in Table 2 were prepared by methods analogous to the method used to prepare Example 85.
Table 2: Starting material is Intermediate 15 unless otherwise noted

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<td>86</td>
<td>2-((cyclopentylmethoxy)-9-[3-(trifluoromethyl)benzyl]-9H-purin-6-amine</td>
<td>392 (MH^+)</td>
<td>1.22-1.70 (m, 8H); 2.23 (m, 1H); 4.06 (m, 2H); 5.36 (s, 2H); 7.24 (bs, 2H); 7.59 (m, 2H); 7.65 (m, 1H); 7.79 (m, 1H); 8.08 (s, 1H).</td>
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<td>87</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-(pentoxyloxy)-9H-purin-6-amine</td>
<td>362 (MH^+)</td>
<td>0.86 (m, 3H); 1.30 (m, 4H); 1.62 (m, 2H); 2.17 (s, 3H); 4.13 (t, 2H); 5.29 (s, 2H); 7.00 (m, 1H); 7.15 (bs, 2H); 7.29 (m, 1H); 7.92 (s, 1H).</td>
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<td>88</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-[3-methylcyclopentyl]oxy]-9H-purin-6-amine</td>
<td>374 (MH^+)</td>
<td>0.99 (m, 3H); 1.18 (m, 2H); 1.77 (m, 3H); 2.16 (m, 2H); 2.17 (s, 3H); 5.16 (m, 1H); 5.29 (s, 2H); 7.00 (m, 1H); 7.11 (bs, 2H); 7.29 (m, 1H); 7.93 (s, 1H).</td>
<td>3</td>
</tr>
<tr>
<td>89</td>
<td>2-(bentlyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>382 (MH^+)</td>
<td>2.15 (s, 3H); 5.26 (s, 2H); 5.32 (s, 2H); 7.01 (m, 1H); 7.31 (m, 8H); 7.95 (s, 1H).</td>
<td>3</td>
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<tr>
<td>90</td>
<td>2-((cyclobutylmethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>360 (MH^+)</td>
<td>1.80 (m, 4H); 2.01 (m, 2H); 2.18 (s, 3H); 2.63 (m, 1H); 4.12 (d, 2H); 5.30 (s, 2H); 7.01 (m, 1H); 7.15 (bs, 2H); 7.30 (m, 1H); 7.92 (s, 1H).</td>
<td>3, 2</td>
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<tr>
<td>91</td>
<td>2-(cyclopentyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>360 (MH^+)</td>
<td>1.58 (m, 6H); 1.84 (m, 2H); 2.17 (s, 3H); 5.20 (m, 1H); 5.30 (s, 2H); 7.01 (m, 1H); 7.11 (bs, 2H); 7.30 (m, 1H); 7.94 (s, 1H).</td>
<td>2</td>
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<tr>
<td>92</td>
<td>2-(1-cyclopropylethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>360 (MH^+)</td>
<td>0.24 (m, 2H); 0.40 (m, 2H); 1.02 (m, 1H); 1.22 (d, 3H); 2.17 (s, 3H); 4.51 (m, 1H); 5.28 (s, 2H); 7.00 (m, 1H); 7.10 (bs, 2H); 7.30 (m, 1H); 7.93 (s, 1H).</td>
<td>3</td>
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<tr>
<td>93</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-[(1-methylcyclopropyl) methoxy]-9H-purin-6-amine</td>
<td>360 (MH^+)</td>
<td>0.33 (m, 2H); 0.45 (m, 2H); 1.10 (s, 3H); 2.18 (s, 3H); 3.97 (s, 2H); 5.29 (s, 2H); 7.01 (m, 1H); 7.16 (bs, 2H); 7.30 (m, 1H); 7.92 (s, 1H).</td>
<td>4</td>
</tr>
<tr>
<td>94</td>
<td>2-</td>
<td>346 (MH^+)</td>
<td>0.26 (m, 2H); 0.50 (m, 2H)</td>
<td>3</td>
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<td>$^1$H NMR Data DMSO-d6</td>
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<td></td>
<td>(cyclopropylmethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>C$<em>{17}$H$</em>{17}$F$_2$N$_5$O</td>
<td>2H); 1.17 (m, 1H); 2.19 (s, 3H); 4.00 (d, 2H); 5.31 (s, 2H); 7.02 (m, 1H); 7.16 (bs, 2H); 7.30 (m, 1H); 7.94 (s, 1H).</td>
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<tr>
<td>95</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-methoxy-9H-purin-6-amine</td>
<td>306 (MH$^+$) for C$<em>{14}$H$</em>{13}$F$_2$N$_5$O</td>
<td>2.17 (s, 3H); 3.74 (s, 3H); 5.31 (s, 2H); 7.02 (m, 1H); 7.22 (bs, 2H); 7.30 (m, 1H); 7.94 (s, 1H).</td>
<td>4</td>
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<td>96</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-propoxy-9H-purin-6-amine</td>
<td>334 (MH$^+$) for C$<em>{16}$H$</em>{17}$F$_2$N$_5$O</td>
<td>0.91 (t, 3H); 1.63 (m, 2H); 2.17 (s, 3H); 4.09 (t, 2H); 5.29 (s, 2H); 7.00 (m, 1H); 7.17 (bs, 2H); 7.30 (m, 1H); 7.93 (s, 1H).</td>
<td>2</td>
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<tr>
<td>97</td>
<td>2-(cyclohexyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>374 (MH$^+$) for C$<em>{19}$H$</em>{21}$F$_2$N$_5$O</td>
<td>1.30 (m, 5H); 1.54 (m, 1H); 1.70 (m, 2H); 1.87 (m, 2H); 2.17 (s, 3H); 4.79 (m, 1H); 5.30 (s, 2H); 7.00 (m, 1H); 7.11 (bs, 2H); 7.29 (m, 1H); 7.95 (s, 1H).</td>
<td>3</td>
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<td>98</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-isobutoxy-9H-purin-6-amine</td>
<td>348 (MH$^+$) for C$<em>{17}$H$</em>{19}$F$_2$N$_5$O</td>
<td>0.91 (d, 6H); 1.94 (m, 1H); 2.18 (s, 3H); 3.92 (d, 2H); 5.30 (s, 2H); 7.00 (m, 1H); 7.18 (bs, 2H); 7.30 (m, 1H); 7.93 (s, 1H).</td>
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<td>99</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-N$_2$.N$_2$-dimethyl-9H-purine-2,6-diamine</td>
<td>319 (MH$^+$) for C$<em>{15}$H$</em>{16}$F$_2$N$_6$</td>
<td>2.16 (s, 3H); 3.00 (s, 6H); 5.22 (s, 2H); 6.70 (bs, 2H); 6.99 (m, 1H); 7.27 (m, 1H); 7.74 (s, 1H).</td>
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<td>100</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-[2-(dimethylamino)ethoxy]-9H-purin-6-amine</td>
<td>363 (MH$^+$) for C$<em>{17}$H$</em>{20}$F$_2$N$_6$O</td>
<td>2.17 (m, 9H); 2.51 (m, 2H); 4.24 (m, 2H); 5.31 (s, 2H); 7.01 (m, 1H); 7.19 (bs, 2H); 7.30 (m, 1H); 7.95 (s, 1H).</td>
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<td>101</td>
<td>N-2-[[6-amino-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-2-yl]oxy]ethylacetamide</td>
<td>N-(2-[[6-amino-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-2-yl]oxy]ethylacetamide</td>
<td>1.79 (s, 3H); 2.17 (s, 3H); 3.11 (m, 2H); 4.13 (m, 2H); 5.29 (s, 2H); 7.01 (m, 1H); 7.20 (bs, 2H); 7.30 (m, 1H); 7.93 (s, 1H); 8.07 (m, 1H).</td>
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<td>102</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-[4,4,5,5-pentafluoropentyl]oxy]-9H-purin-6-amine</td>
<td>452 (MH$^+$) for C$<em>{18}$H$</em>{16}$F$_7$N$_5$O</td>
<td>1.90 (m, 2H); 2.17 (s, 3H); 2.30 (m, 2H); 4.24 (m, 2H); 5.31 (s, 2H); 7.01 (m, 1H); 7.24 (bs, 2H); 7.30 (m, 1H); 7.95 (s, 1H).</td>
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<td>103</td>
<td>2-[(6-amino-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-2-yl)(methyl)amino]ethanol</td>
<td>349 ($MH^+$) for C$<em>{18}$H$</em>{18}$F$_2$N$_6$O</td>
<td>2.17 (s, 3H); 3.05 (s, 3H); 3.54 (m, 4H); 4.55 (bs, 1H); 5.21 (s, 2H); 6.68 (bs, 2H); 6.98 (m, 1H); 7.27 (m, 1H); 7.73 (s, 1H).</td>
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<td>104</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-(4,4,4-trifluorobutoxy)-9H-purin-6-amine</td>
<td>402 ($MH^+$) for C$<em>{17}$H$</em>{16}$F$_3$N$_5$O</td>
<td>1.86 (m, 2H); 2.17 (s, 3H); 2.33 (m, 2H); 4.21 (t, 2H); 5.30 (s, 2H); 7.01 (m, 1H); 7.24 (bs, 2H); 7.30 (m, 1H); 7.95 (s, 1H).</td>
<td>4</td>
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<tr>
<td>105</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-(piperidin-4-yloxy)-9H-purin-6-amine</td>
<td>375 ($MH^+$) for C$<em>{18}$H$</em>{20}$F$_2$N$_6$O</td>
<td>1.36 (m, 2H); 1.85 (m, 2H); 2.17 (s, 3H); 2.53 (m, 2H); 2.93 (m, 2H); 4.82 (m, 1H); 5.29 (s, 2H); 6.99 (m, 1H); 7.12 (bs, 2H); 7.29 (m, 1H); 7.96 (s, 1H).</td>
<td>3</td>
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<tr>
<td>106</td>
<td>2-(decahydro-naphthalen-2-yl oxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>428 ($MH^+$) for C$<em>{23}$H$</em>{27}$F$_2$N$_5$O</td>
<td>1.40 (m, 17H); 2.16 (s, 3H); 5.29 (s, 2H); 6.98 (m, 1H); 7.10 (bs, 2H); 7.28 (m, 1H); 7.95 (s, 1H).</td>
<td>3, 6</td>
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<tr>
<td>107</td>
<td>$N^2$-butyl-9-(2,6-difluoro-3-methylbenzyl)-$N^6$-(2-morpholin-4-yethyl)-$N^3$-propyl-9H-purine-2,6-diamine</td>
<td>502 ($MH^+$) for C$<em>{26}$H$</em>{37}$F$_2$N$_7$O</td>
<td>0.85 (m, 6H); 1.25 (m, 2H); 1.49 (m, 4H); 2.16 (s, 3H); 2.37 (m, 4H); 2.47 (m, 2H); 3.40 (m, 6H); 3.54 (m, 4H); 5.21 (s, 2H); 6.96 (m, 1H); 7.10 (bs, 1H); 7.27 (m, 1H); 7.73 (s, 1H).</td>
<td>5, 8</td>
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<tr>
<td>108</td>
<td>$N^2$-butyl-9-(2,6-difluoro-3-methylbenzyl)-$N^6$-methyl-$N^3$-(2-morpholin-4-yethyl)-9H-purine-2,6-diamine</td>
<td>474 ($MH^+$) for C$<em>{26}$H$</em>{33}$F$_2$N$_3$O</td>
<td>0.83 (t, 3H); 1.21 (m, 2H); 1.45 (m, 2H); 2.10 (s, 3H); 2.42 (m, 4H); 2.53 (t, 2H); 3.19 (m, 3H); 3.54 (m, 8H); 5.19 (s, 2H); 6.75 (m, 1H); 7.10 (m, 1H); 7.58 (s, 1H).</td>
<td>5, 8, 10</td>
</tr>
<tr>
<td>109</td>
<td>2-(benzyloxy)-9-buty1-$N$-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>411 ($MH^+$) for C$<em>{22}$H$</em>{36}$N$_6$O$_2$</td>
<td>0.87 (t, 3H); 1.21 (m, 2H); 1.72 (m, 2H); 2.38 (m, 4H); 2.47 (m, 2H); 3.53 (m, 6H); 4.03 (m, 2H); 5.31 (s, 2H); 7.35 (m, 5H);</td>
<td>3, 9</td>
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<td>1H NMR Data DMSO-d6</td>
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<tr>
<td>110</td>
<td>9-buty1-N-(2-morpholin-4-ylethyl)-2-phenoxy-9H-purin-6-amine</td>
<td>397 (MH⁺) for C₂₁H₂₈N₆O₂</td>
<td>0.85 (t, 3H); 1.20 (m, 2H); 1.72 (m, 2H); 2.21 (m, 4H); 2.33 (m, 2H); 3.34 (m, 2H); 3.48 (m, 4H); 4.00 (m, 2H); 7.14 (m, 3H); 7.37 (m, 2H); 7.76 (m, 1H); 7.99 (s, 1H).</td>
<td>3, 9</td>
</tr>
<tr>
<td>111</td>
<td>9-buty1-N-(2-morpholin-4-ylethyl)-2-(pyridin-2-yloxy)-9H-purin-6-amine</td>
<td>398 (MH⁺) for C₂₀H₂₇N₅O₂</td>
<td>0.87 (t, 3H); 1.24 (m, 2H); 1.75 (m, 2H); 2.39 (m, 4H); 2.53 (m, 2H); 3.53 (m, 6H); 4.11 (m, 2H); 6.26 (m, 1H); 6.43 (m, 1H); 7.49 (m, 1H); 7.68 (m, 1H); 7.99 (m, 1H); 8.26 (s, 1H).</td>
<td>5, 9</td>
</tr>
<tr>
<td>112</td>
<td>9-butyl-2-[(4-methylpyridin-2-yl)oxy]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>412 (MH⁺) for C₂₁H₂₉N₅O₂</td>
<td>0.87 (t, 3H); 1.23 (m, 2H); 1.75 (m, 2H); 2.17 (s, 3H); 2.38 (m, 4H); 2.52 (m, 2H); 3.53 (m, 6H); 4.11 (m, 2H); 6.11 (m, 1H); 6.23 (s, 1H); 7.55 (m, 1H); 7.94 (m, 1H); 8.24 (s, 1H).</td>
<td>3, 9</td>
</tr>
<tr>
<td>113</td>
<td>2-butoxy-9-[3-(trifluoromethyl)benzyl]-9H-purin-6-amine</td>
<td>366(MH⁺) for C₁₇H₁₈F₃N₃O</td>
<td>³¹H NMR (DMSO-D₆) δ: 0.9 (t, 3H); 1.4(m, 2H); 1.6(m, 2H); 4.2 (t, 2H); 5.35 (s, 2H); 7.2 (s, 2H); 7.5-7.7 (m, 3H); 7.80 (s, 1H); 8.12(s, 1H)</td>
<td>7</td>
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<tr>
<td>114</td>
<td>3-[(6-amino-2-butoxy-9H-purin-9-yl)methyl]benzoic acid</td>
<td>342(MH⁺) for C₁₇H₁₉N₃O</td>
<td>³¹H NMR (DMSO-D₆) δ: 0.85 (t, 3H); 1.20(m, 2H); 1.50(m, 2H); 4.10 (t, 2H); 5.24 (s, 2H); 7.2-8.3 (m, 7H)</td>
<td>11</td>
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<tr>
<td>115</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-9H-purin-6-amine</td>
<td>334(MH⁺) for C₁₆H₁₇F₂N₃O</td>
<td>³¹H NMR (DMSO-D₆) δ: 0.86 (t, 3H); 1.25(m, 2H); 1.55(m, 2H); 4.10 (t, 2H); 5.25 (s, 2H); 7.05 (t, 2H); 7.10 (s, br, 2H); 7.38 (m, 1H); 7.90 (s, 1H)</td>
<td>12</td>
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<tr>
<td>116</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-N,N-dimethyl-9H-purin-6-amine</td>
<td>362(MH⁺) for C₁₈H₂₁F₂N₃O</td>
<td>³¹H NMR (DMSO-D₆) δ: 0.95 (t, 3H); 1.40(m, 2H); 1.65(m, 2H); 3.5(s, 6H); 4.20 (t, 2H); 5.35 (s, 2H); 7.16 (t, 2H); 7.45 (m, 1H); 8.00 (s, 1H)</td>
<td>13</td>
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<tr>
<td>117</td>
<td>N²-buty1-9-(2,6-</td>
<td>333(MH⁺) for C₁₈H₂₁F₂N₃O</td>
<td>³¹H NMR (DMSO-D₆) δ:</td>
<td>12</td>
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<tr>
<td>118</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-N-methyl-9H-purin-6-amine</td>
<td>C_{16}H_{18} F_{2} N_{6}</td>
<td>0.95 (t, 3H); 1.40(m, 2H); 1.46(m, 2H); 3.28 (q, 2H); 5.33 (s, 2H); 6.24(t, 1H); 6.68 (s, br, 2H); 7.15 (t, 2H); 7.52 (m, 1H); 7.80(s, 1H)</td>
<td>14</td>
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<tr>
<td>119</td>
<td>2-butoxy-9-(2-butoxy-6-fluorobenzyl)-N-methyl-9H-purin-6-amine</td>
<td>C_{17}H_{19} F_{2} N_{5}O</td>
<td>348(MH^+) for C_{17}H_{19} F_{2} N_{5}O</td>
<td>^1H NMR (DMSO-D_6) δ: 0.90 (t, 3H); 1.35(m, 2H); 1.65(m, 2H); 2.80(s, 3H); 4.20 (t, 2H); 5.35 (s, 2H); 7.10 (t, 2H); 7.50 (m, 1H); 7.70 (s, br, 1H); 7.95 (s, 1H)</td>
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<tr>
<td>120</td>
<td>2-(cyclopropylmethoxy)-9-[2-(cyclopropylmethoxy)-6-fluorobenzyl]-N-methyl-9H-purin-6-amine</td>
<td>C_{21}H_{23} F N_{5}O_{2}</td>
<td>402(MH^+) for C_{21}H_{24} F N_{5}O_{2}</td>
<td>^1H NMR (DMSO-D_6) δ: 0.30 (m, 4H); 0.62(m, 4H); 1.24(m, 2H); 2.90(s, 3H); 3.90 (d, 2H); 4.08 (d, 2H); 5.24 (s, 2H); 6.80 (m, 2H); 7.30 (q, 1H); 7.65(s, br, 1H); 7.85 (s, 1H)</td>
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<td>121</td>
<td>9-(2,6-difluorobenzyl)-N-methyl-2-[2-(methylsulfonyl)ethoxy]-9H-purin-6-amine</td>
<td>C_{16}H_{17} F_{2} N_{5}O_{5}S</td>
<td>348(MH^+) for C_{16}H_{17} F_{2} N_{5}O_{5}S</td>
<td>^1H NMR (DMSO-D_6) δ: 3.10 (s, 3H); 3.35(t, 2H); 3.50(t, 2H); 4.28(s, 3H); 5.30 (s, 2H); 7.15 (t, 2H); 7.48 (m, 1H); 7.85 (s, 1H); 10.83 (s, br, 1H)</td>
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<td>122</td>
<td>9-(2,6-difluorobenzyl)-N-methyl-2-(2-methylbutoxy)-9H-purin-6-amine</td>
<td>C_{18}H_{21} F_{2} N_{5}O</td>
<td>362(MH^+) for C_{18}H_{21} F_{2} N_{5}O</td>
<td>^1H NMR (DMSO-D_6) δ: 0.78 (m, 6H); 1.02(m, 1H); 1.28 (m, 1H); 1.64(m, 1H); 2.75 (s, br, 3H); 3.85 (m, 2H); 5.18 (s, 2H); 6.95 (t, 1H); 7.26 (m, 1H); 7.50 (s, br, 1H); 7.80 (s, 1H)</td>
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<tr>
<td>123</td>
<td>2-(cyclobutylmethoxy)-9-(2,6-difluorobenzyl)-N-methyl-9H-purin-6-</td>
<td>C_{18}H_{19}F_{2} N_{5}O</td>
<td>360(MH^+) for C_{18}H_{19}F_{2} N_{5}O</td>
<td>^1H NMR (DMSO-D_6) δ: 1.78 (m, 2H); 1.92(m, 2H); 2.08 (m, 2H); 2.70(m, 1H); 2.89 (s, br, 3H); 4.20 (d, 2H); 5.40 (s, 2H); 7.15 (t,</td>
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<tr>
<td>124</td>
<td>9-(2,6-difluorobenzyl)-N-methyl-2-(pentyloxy)-9H-purin-6-amine</td>
<td>362(MH$^+$) for C$<em>{18}$H$</em>{21}$F$_2$N$_3$O</td>
<td>$^1$H NMR (CDCl$_3$) δ: 0.90 (t, 3H); 1.35(m, 4H); 1.75(m, 2H); 3.20(s, 3H); 5.30(s, 2H); 5.62 (s, 1H); 6.87 (t, 2H); 7.35 (m, 1H); 7.50(s, 1H)</td>
<td>14</td>
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<tr>
<td>125</td>
<td>2-(cyclopentyloxy)-9-(2,6-difluorobenzyl)-N-methyl-9H-purin-6-amine</td>
<td>360(MH$^+$) for C$<em>{18}$H$</em>{19}$F$_2$N$_3$O</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 1.5-2.2(m, 8H); 2.95(s, br, 3H); 5.30(m, 1H); 5.40(s, 2H); 7.20 (t, 2H); 7.50 (m, 1H); 7.75(s, br, 1H); 8.0(s, 1H)</td>
<td>14</td>
</tr>
<tr>
<td>126</td>
<td>2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-N-ethyl-9H-purin-6-amine</td>
<td>376(MH$^+$) for C$<em>{19}$H$</em>{23}$F$_2$N$_3$O</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 0.92 (t, 3H); 1.15(t, 3H); 1.40(m, 2H); 1.60(m, 2H); 2.20(s, 3H); 3.40(m, br, 2H); 4.20 (t, 2H); 5.35(s, 2H); 7.00(t, 1H); 7.31(m, 1H); 7.75(s, br, 1H); 7.95(s, 1H)</td>
<td>15</td>
</tr>
<tr>
<td>127</td>
<td>$N$-benzyl-2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>438(MH$^+$) for C$<em>{24}$H$</em>{25}$F$_2$N$_3$O</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 0.95 (t, 3H); 1.40(m, 2H); 1.65(m, 2H); 2.20(s, 3H); 4.15(t, 2H); 4.65 (d, 2H); 5.38(s, 2H); 7.05(t, 1H); 7.15-7.40(m, 6H); 8.00(s, 1H); 8.40(s, br, 1H)</td>
<td>16</td>
</tr>
<tr>
<td>128</td>
<td>$N$-benzyl-9-(2,6-difluoro-3-methylbenzyl)-2-(pentyloxy)-9H-purin-6-amine</td>
<td>452(MH$^+$) for C$<em>{25}$H$</em>{27}$F$_2$N$_3$O</td>
<td>$^1$H NMR (DMSO-D$_6$) δ: 0.78 (t, 3H); 1.30(m, 4H); 1.65(m, 2H); 2.21(s, 3H); 4.15(t, 2H); 4.64 (d, 2H); 5.35(s, 2H); 7.00(t, 1H); 7.15-7.45(m, 6H); 8.00(s, 1H)</td>
<td>16</td>
</tr>
<tr>
<td>129</td>
<td>2-butoxy-$N$-cyclopropyl-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine</td>
<td>388(MH$^+$) for C$<em>{20}$H$</em>{23}$F$_2$N$_3$O</td>
<td>$^1$H NMR (CDCl$_3$) δ: 0.69 (s, 2H); 0.85(m, 2H); 0.95(t, 3H); 1.55(m, 2H); 1.76(m, 2H); 2.21 (s, 3H); 3.20(s, br, 2H); 4.35(t, 2H); 5.29(s, 2H); 6.80(t, 1H); 7.15(q, 1H); 7.70(s, 1H)</td>
<td>17</td>
</tr>
</tbody>
</table>

Table 2 Footnotes
1. purification by trituration with water
2. purification by trituration with cold methanol
3. purification by silica gel chromatography
4. product crashed out of reaction mixture upon addition of methanol
5. purification by reverse phase chromatography
6. 2/1 mixture of isomers
7. starting material intermediate 8
8. starting material intermediate 20
9. starting material intermediate 18
10. NMR ran in methanol-d$_4$
11. starting material intermediate 24
12. starting material intermediate 25
13. starting material intermediate 26
14. starting material intermediate 27
15. starting material intermediate 28
16. starting material intermediate 29
17. starting material intermediate 30

**Example 130:** 2-(Butylthio)-9-((2,6-difluorophenyl)acetyll-9$^H$-purin-6-amine

**Scheme XXV**

2-(Butylthio)-9$^H$-purin-6-amine (Intermediate 5, 0.2 g, 0.9 mmol), (2,6-difluorophenyl)acetyl bromide (0.42 g, 1.8 mmol) and triethylamine (0.25 mL, 1.8 mmol) were combined in DMF (4 mL) and heated at 60$^\circ$C overnight. The solvent was evaporated and the resulting oil was triturated with cold methanol to afford the desired compound as a solid.

**MS (ESP) M/z:** 378 (MH$^+$) for C$_{17}$H$_{17}$F$_2$N$_5$OS

$^1$H NMR Data DMSO-d$_6$ 0.79 (t, 3H); 1.29 (m, 2H); 1.56 (m, 2H); 2.98 (t, 2H); 5.55 (s, 2H); 7.31 (m, 2H); 7.34 (bs, 2H); 7.72 (m, 1H); 8.00 (s, 1H).

Compounds in Table 3 were prepared by methods analogous to those used to prepare Example 130.
### Table 3: compounds made by acylation

<table>
<thead>
<tr>
<th>EX.</th>
<th>Name</th>
<th>MS</th>
<th>¹H NMR Data DMSO-d6</th>
<th>Foot Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>131</td>
<td>2-(butylthio)-9-(2,6-difluorobenzoyl)-9H-purin-6-amine</td>
<td>364 (M⁺) for C₁₆H₁₅F₂N₅OS</td>
<td>0.81 (t, 3H); 1.25 (m, 4H); 2.38 (m, 2H); 7.36 (t, 2H); 7.70 (bs, 2H); 7.78 (m, 1H); 8.71 (s, 1H).</td>
<td>1</td>
</tr>
<tr>
<td>132</td>
<td>2-butoxy-9-(3-chloro-2,6-difluorobenzoyl)-N-(2-morpholin-4-yl ethyl)-9H-purin-6-amine</td>
<td>495 (M⁺) for C₂₂H₂₅ClF₂N₆O₃</td>
<td>0.83 (t, 3H); 1.25 (m, 2H); 1.44 (m, 2H); 2.46 (m, 4H); 2.56 (t, 2H); 3.61 (m, 8H); 7.15 (m, 1H); 7.71 (m, 1H); 8.44 (s, 1H).</td>
<td>2, 3</td>
</tr>
<tr>
<td>133</td>
<td>2-butoxy-9-(2,6-difluoro-3-methylbenzoyl)-N-(2-morpholin-4-yl ethyl)-9H-purin-6-amine</td>
<td>475 (M⁺) for C₂₃H₂₈F₂N₆O₃</td>
<td>0.79 (t, 3H); 1.20 (m, 2H); 1.38 (m, 2H); 2.17 (s, 3H); 2.42 (m, 4H); 2.51 (t, 2H); 3.57 (m, 8H); 6.95 (m, 1H); 7.40 (m, 1H); 8.37 (s, 1H).</td>
<td>2, 3</td>
</tr>
</tbody>
</table>

**Table 3 Footnotes**
1. purification by trituration with cold methanol
2. purification by reverse phase chromatography
3. NMR ran in methanol-d4

### Table 4: Additional compounds of the invention

<table>
<thead>
<tr>
<th>Ex. #</th>
<th>Name</th>
<th>MS</th>
<th>¹H NMR Data methanol-d4</th>
<th>Foot Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>134</td>
<td>1-[6-amino-2-(butylthio)-9H-purin-9-yl]-2-(2,6-difluorophenyl)ethanol</td>
<td>380 (M⁺) for C₁₇H₁₉F₂N₅OS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>135</td>
<td>3-(2-butoxy-6-[2-morpholin-4-yl ethyl]amino]-1-oxido-9H-purin-9-yl[methyl]benzamide</td>
<td>470 (M⁺) for C₂₃H₃₁N₅O₄</td>
<td>0.86 (t, 3H); 1.37 (m, 2H); 1.63 (m, 2H); 3.10 (m, 2H); 3.47 (m, 4H); 3.69 (m, 2H); 4.05 (m, 4H); 4.24 (t, 2H); 5.25 (s, 2H); 7.34 (m, 2H); 7.67 (m, 1H); 7.76 (s, 1H); 7.84 (s, 1H).</td>
<td></td>
</tr>
<tr>
<td>136</td>
<td>3-(2-butoxy-6-[2-morpholin-4-yl ethyl]amino]-9H-purin-9-yl[methyl]benzamide</td>
<td>454 (M⁺) for C₂₃H₃₁N₅O₃</td>
<td>0.88 (t, 3H); 1.39 (m, 2H); 1.65 (m, 2H); 3.15 (m, 2H); 3.32 (m, 2H); 3.70 (m, 4H); 3.92 (m, 4H); 4.04 (m, 2H); 4.29 (m, 2H); 5.31 (m, 2H); 7.33 (m, 1H); 7.44 (m, 1H); 7.68 (m, 1H); 7.80 (m, 1H); 7.97 (m, 1H).</td>
<td></td>
</tr>
</tbody>
</table>
Table 4 Experimentals

Example 134: l-[6-amino-2-fbutylthio)-9 H-purin-9-yll-2-(2.,6-difluorophenyl)ethanol

Scheme XXVI

To a solution of 2-(butylthio)-9-[(2,6-difluorophenyl)acetyl]-9 H-purin-6-amine (Example 130, 0.05g, 0.05mmol) in THF (2mL) at 0°C was added 1M lithium aluminum hydride (0.26mL, 0.26mmol). The reaction mixture was stirred overnight at rt, then at 60°C for 48h. The reaction was quenched with methanol and saturated ammonium chloride, then filtered to remove solid. The filtrate was evaporated and triturated with cold methanol to yield a yellow solid, which was purified by reverse phase chromatography (acetonitrile/water/ammonium acetate) to give desired product.

Example 135: 3-f[2-butoxy-6-[f2-morpholin-4-ylethyl)aminol-l-oxido-9 H-purin-9-yllmethyDbenzamide

Scheme XXVII
To a solution of 3-{{2-butoxy-6-{(2-morpholin-4-ylethyl)amino}-9H-purin-9-yl}methyl}benzonitrile (Example 71, 0.16g, 0.37mmol) in ethanol (2mL) at 0°C was added 1N sodium hydroxide (1mL) and 30% hydrogen peroxide (1mL). The reaction mixture was stirred for 1h then warmed to rt and evaporated. The resulting oil was triturated with methanol and filtered to remove solid. The filtrate was evaporated to give white solid, which was purified by reverse phase chromatography (acetonitrile/water/ammonium acetate) to give the N-oxide of the desired compound.

Example 136: 3-f{2-butoxy-6-{f2-morpholin-4-ylethyl)aminol-9  H-purin-9-yl}methyl}benzamide

Scheme XXVIII

To a solution of 3-{{2-butoxy-6-{(2-morpholin-4-ylethyl)amino}-9H-purin-9-yl}methyl}benzonitrile (Example 71, 0.16g, 0.37mmol) in ethanol (2mL) at 0°C was added 1N sodium hydroxide (1mL) and 30% hydrogen peroxide (1mL). The reaction mixture was stirred for 1h then quenched with sodium bisulfite. Solution stirred for 30min, then solvent was evaporated to give an oil. The sticky oil was triturated with methanol and evaporated to yield a white foam.

Example 137: 2-{{6-amino-2-fbutylthio)-9 H-purin-9-yl}methyl}-4-nitrophenol
The titled compound was obtained by demethylation of 2-(butylthio)-9-(2-methoxy-5-nitrobenzyl)-9\(H\)-purin-6-amine (Example 7) (30.5mg, 0.0786mmol) with boron tribromide solution in dichloromethane (IM, 3mL, 3mmol) in dichloromethane (6mL) at 50°C for 24h as monitored by LC-MS. The reaction was quenched with water at room temperature and extracted with dichloromethane. After drying (MgSO\(_4\)) and removal of solvent, the desired product was purified by reverse phase HPLC (acetonitrile/Water/TFA). Yield, 5%. MS (ES): 375(MH\(^+\)) for C\(_{16}\)H\(_{18}\)N\(_6\)O\(_3\)S

\(^1\)H NMR (DMSO-Dn) \(\delta\): 0.90 (t, 3H); 1.50(m, 2H); 1.70(m, 2H); 3.25(t, 2H); 2.92 (t, 2H); 5.25 (s, 2H); 6.48(d, IH); 7.90(dd, IH); 8.15(m, 3H)

**Examples 138 and 139:** 4-f{2-butoxy-6-[f2-morpholin-4-ylethyl)aminol-l-oxido-9 \(H\)-purin-9-yl}methyl)benzamide and 4-{(2-butoxy-6-[(2-morpholin-4-ylethyl)aminol -9\(H\)-purin-9-yl)methyl]benzamide
The titled compound was prepared by oxidizing 4-((2-butoxy-6-((2-morpholin-4-yl)ethyl)amino)-9*H*-purin-9-yl)methyl)benzonitrile \textbf{(Example 83)} (2.0g, 4.60mmol) with hydrogen peroxide (10mL, 30% solution) in presence of 1M NaOH (10mL) in ethanol (5mL) at 0°C for 1h. The reaction was quenched with Na$_2$S$_2$O$_3$. After removing water and ethanol from the aqueous phase, the mixture was purified by reverse phase HPLC (NH$_4$OAc/Water). Two products were isolated. The first peak of 17mg was assigned as 4-((2-butoxy-6-((2-morpholin-4-yl)ethyl)amino)-1-oxido-9*H*-purin-9-yl)methyl)benzamide \textbf{(Example 138)} and the second peak of 1.3 mg as 4-((2-butoxy-6-((2-morpholin-4-yl)ethyl)amino)-9*H*-purin-9-yl)methyl)benzamide \textbf{(Example 139)}.
Example 138: MS (ES): 470(MH⁺) for C₂₃H₃IN₇O₄ \(^{1}H\) NMR (CDSOD-D₂) \(\delta\): 0.75 (t, 3H); 1.42(m, 2H); 1.64(m, 2H); 3.10(m, 6H); 3.50(m, 6H); 4.2(m, 3H); 4.25 (t, 2H); 5.25(s, 2H); 7.25(d, 2H); 7.76(d, 2H); 7.82(s, 1H)

Example 139: MS (ES): 454(MH⁺) for C₂₃H₃IN₇O₄ \(^{1}H\) NMR (CD30D-D₂) \(\delta\): 0.85 (t, 3H); 1.38(m, 2H); 1.65(m, 2H); 2.45(s, br, 4H); 2.55(t, 2H); 3.60(m, 6H); 4.25 (t, 2H); 5.29(s, 2H); 7.30(d, 2H); 7.76(d, 2H); 7.85 (s, 1H)

Example 140: 1-[4-f{2-butoxy-6-[f2-morpholin-4-ylethyl)amino]-9H-purin-9-yl}methyl]phenyllethanone

Scheme XXXI

The titled compound was prepared by reacting 4-((2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-yl)methyl)benzonitrile (Example 83) (280mg, 0.64mmol) with methyl magnesium bromide (3M solution in diethyl ether, 0.56mL, 1.68mmol) in diethyl ether (10mL) at -78 ⁰C. The reaction was allowed to warm to rt. The reaction was quenched with ammonium chloride and extracted with ethyl acetate. After drying (MgSO₄) and removal of solvent, the product (60mg) was isolated by silica-gel chromatography (methanol/dichloromethane) as an oil (21% yield). MS (ES): 453(MH⁺) for C₂₄H₃₂N₆O₃ \(^{1}H\) NMR (CDCl₃) \(\delta\): 0.95 (t, 3H); 1.41(m, 2H); 1.80(m, 2H); 2.52(s, 3H); 2.65(t, 2H); 3.75(m, 8H); 4.25 (t, 2H); 5.29(s, 2H); 6.30(s, br, 1H); 7.35(d, 2H); 7.68 (m, 3H)

Example 141: 2-butoxy-9-d,6-difluorobenzyl)-8-methyl-9H-purin-6-amine

Scheme XXXII
The title compound was prepared from Intermediate 53 as follows: A solution of 8-bromo-2-butoxy-9-(2,6-difluorobenzyl)-9\(H\)-purin-6-amine (100mg, 0.242mmol) in THF (5mL) was treated with triphenyl phosphine (7.0mg, 0.027mmol) and palladium dichloride (2.4mg, 0.013mmol). The reaction was allowed to stir under argon for 5min. Trimethyl aluminum (2N in hexanes, 0.27mL) was added dropwise. The reaction was heated at 150°C for 1800 sec using microwave irradiation. The reaction mixture was evaporated at reduced pressure, diluted with chloroform, filtered through Celilte, washed with brine. The organic phase was dried over MgSO\(_4\) and evaporated. Purification by reverse phase chromatography [25-60% acetonitrile/H\(_2\)O/0.1% TFA] gave the title compound as a solid. IH NMR (300 MHz, DMSO-D6) \(\delta\) ppm 0.89 (t, \(J\)=7.3 Hz, 3 H) 1.29 - 1.42 (m, 2 H) 1.54 - 1.65 (m, 2 H) 4.17 (t, \(J\)=6.6 Hz, 2 H) 5.32 (s, 2 H) 7.02 - 7.17 (m, 2 H) 7.36 - 7.51 (m, 1 H) MS (ESP) M/z= 348 (MH+) for C\(_{17}\)H\(_{19}\)F\(_2\)N\(_5\)O

**Example 142:** 2-butoxy-9-(2,6-difluorobenzyl)-\(8\)-(2-morpholin-4-ylethyl)-9\(H\)-purine-6,8-diamine

**Scheme XXXIII**

The title compound was prepared from Intermediate 53 as follows: 8-bromo-2-butoxy-9-(2,6-difluorobenzyl)-9\(H\)-purin-6-amine (100mg, 0.24mmol) was added to 4-(2-aminoethyl)morpholine (1mL, 7.63mmol). The reaction was heated to 170°C for 1800s using microwave irradiation. The reaction mixture was concentrated at reduced pressure. The
product was purified by reverse phase chromatography [5-95 % CH3CN/H2O/0.1% TFA] to
give the title compound as a TFA salt. 1H NMR (300 MHz, DMSO-D6) δ ppm 0.87 (t, J=7.3
Hz, 3 H) 1.22 - 1.38 (m, 2 H) 1.46 - 1.60 (m, 2 H) 3.29 - 3.44 (m, J=13.9 Hz, 5 H) 3.67 - 3.77
(m, 4H) 3.78 - 3.89 (m, 6H) 4.06 (t, J=6.6 Hz, 2 H) 5.18 (s, 2 H) 7.09 (t, J=8.1 Hz, 2 H) 7.39 -
5 7.49 (m, 1 H) MS(ESP) M/z= 462 (MH+) for C_{22}H_{29}F_{2}N_{7}O_{2}

**Table 5:** The Examples in Table 5 were prepared as described for Example 142 using the
appropriate amines

<table>
<thead>
<tr>
<th>EX.</th>
<th>Name</th>
<th>MS</th>
<th>1H NMR (300 MHz, DMSO-D6) δ ppm</th>
<th>Start Mat.</th>
</tr>
</thead>
<tbody>
<tr>
<td>143</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-8-(4-methylpiperazin-1-yl)-9H-purin-6-amine</td>
<td>432 (MH+) for C_{21}H_{27}F_{2}N_{7}O</td>
<td>0.87 (t, J=7.3 Hz, 3 H) 1.25 - 1.38 (m, 2 H) 1.46 - 1.58 (m, 2 H) 2.88 (s, 3 H) 3.14 - 3.25 (m, 4 H) 3.53 (d, J=9.6 Hz, 4 H) 3.86 (s, 2 H) 4.00 (t, J=6.6 Hz, 2 H) 5.23 (s, 2 H) 7.06 (t, J=8.1 Hz, 2 H) 7.35 - 7.46 (m, 1 H)</td>
<td>Intermediate 53</td>
</tr>
<tr>
<td>144</td>
<td>2-butoxy-N^8-[2-(diethylamino)ethyl]-9-(2,6-difluorobenzyl)-9H-purine-6,8-diamine</td>
<td>448 [MH+] for C_{22}H_{31}F_{2}N_{7}O</td>
<td>0.87 (t, J=7.3 Hz, 3 H) 1.13 - 1.24 (m, 6 H) 1.25 - 1.38 (m, 2 H) 1.48 - 1.60 (m, 2 H) 3.24 (q, J=7.0 Hz, 2 H) 3.36 (t, J=5.7 Hz, 2 H) 3.74 (d, J=4.5 Hz, 2 H) 4.00 (m, 3 H) 4.10 (m, 4 H) 5.21 (s, 2 H) 7.10 (t, J=8.1 Hz, 2 H) 7.31 - 7.47 (m, 1 H)</td>
<td>Intermediate 53</td>
</tr>
<tr>
<td>145</td>
<td>2-[[6-amino-2-butoxy-9-(2,6-difluorobenzyl)-9H-purin-8-yl]amino]ethanol</td>
<td>393 [MH+] for C_{18}H_{22}F_{2}N_{6}O_{2}</td>
<td>0.81 - 0.92 (m, 3 H) 1.32 (ddd, J=14.9, 7.4, 7.3 Hz, 2 H) 1.49 - 1.63 (m, 2 H) 3.48 (d, J=4.9 Hz, 3 H) 3.57 - 3.71 (m, 3 H) 4.02 - 4.17 (m, 2 H) 5.29 (s, 2 H) 7.03 - 7.19 (m, 2 H) 7.36 - 7.52 (m, 1 H)</td>
<td>Intermediate 53</td>
</tr>
<tr>
<td>146</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-8-morpholin-4-yl-9H-purin-6-amine</td>
<td>419 [MH+] for C_{20}H_{24}F_{2}N_{6}O_{2}</td>
<td>0.88 (t, J=7.3 Hz, 3 H) 1.27 - 1.38 (m, 2 H) 1.49 - 1.62 (m, 2 H) 3.06 (d, J=4.3 Hz, 4 H) 3.62 - 3.68 (m, 6 H) 4.08 (t, J=6.7 Hz, 2 H) 5.25 (s, 1 H) 7.06 (t, J=8.1 Hz, 2 H) 7.32 - 7.46 (m, 1 H)</td>
<td>Intermediate 53</td>
</tr>
<tr>
<td>147</td>
<td>2-butoxy-9-(2,6-difluorobenzyl)-N^8-[2-(4-methylpiperazin-1-yl)ethyl]-9H-purine-6,8-diamine</td>
<td>475 [MH+] for C_{23}H_{32}F_{2}N_{8}O (APCI)</td>
<td>0.89 (t, J=7.3 Hz, 3 H) 1.24 - 1.39 (m, 2 H) 1.49 - 1.59 (m, 2 H) 2.90 (s, 3 H) 3.14 - 3.27 (m, 4 H) 3.54 (d, J=9.6 Hz, 4 H) 3.88 (s, 6 H) 4.01 (t, J=6.6 Hz, 2 H)</td>
<td>Intermediate 53</td>
</tr>
</tbody>
</table>
The title compound was prepared from 2-chloro-7V-(2,6-difluorobenzyl)-9-(2-
morpholin-4-ylethyl)-9 H-purin-6-
amine (Intermediate 41) as follows: A solution of 2-
chloro-Ν-(2,6-difluorobenzyl)-9-(2-morpholin-4-ylethyl)-9 H-purin-6-
amine (Intermediate 
41)(1.26g, 3.09mmol) in n-butanol (7.5mL) was treated with sodium hydroxide pellets (1.Og, 
25mmol). The reaction was heated at 120°C for 1800s using microwave irradiation. The 
reaction was concentrated at reduced pressure, partitioned between dichloromethane and
water. The aqueous phase was extracted with CH$_2$Cl$_2$ (2 x 25 mL). The organic phases were
dried over MgSO$_4$ and evaporated to obtain the crude product. Purification by reverse phase
chromatography [5-95% CH$_3$CN/H$_2$O/0.1% TFA] gave the final compound as a TFA salt.
MS (ESP) m/z = 447 [MH$^+$] for C$_{22}$H$_{28}$F$_2$N$_6$O$_2$

Example 151: 2-butoxy- N-[(5-methyl-2-furyl)methyl]-9-q-morpholin-4-ylethyl)-9 $H$-purin-6-amine

Scheme XXXV

A solution of 2-chloro- N-[(5-methyl-2-furyl)methyl]-9-(2-morpholin-4-ylethyl)-9 $H$-purin-6-amine (Intermediate 39) (1.0g, 2.65mmol) in n-butanol (10mL) was treated with
sodium hydroxide pellets (2.0g, 50mmol). The reaction was heated in a sealed tube at 80°C
over night. The reaction was concentrated at reduced pressure to afford a light yellow solid.
The solid was dissolved in ethyl acetate, washed with water, dried over MgSO$_4$ and
evaporated to obtain the product as a solid. 1H NMR (300 MHz, DMSO-D6) $\delta$ ppm 0.80 -
0.94 (m, 3 H) 1.39 (dq, $J$=14.8, 7.4 Hz, 2 H) 1.57 - 1.71 (m, 2 H) 2.19 (s, 3 H) 2.33 - 2.45 (m,
4 H) 2.65 (t, $J$=6.1 Hz, 2 H) 3.43 - 3.56 (m, 4 H) 4.14 (t, $J$=6.1 Hz, 2 H) 4.21 (t, $J$=6.5 Hz, 2
H) 4.53 (s, 2 H) 5.94 (d, $J$=2.7 Hz, 1 H) 6.07 (d, $J$=2.7 Hz, 1 H) 7.93 (s, 1 H)  MS (ESP)
m/z= 415 [MH$^+$] for C$_{21}$H$_{30}$N$_6$O$_3$
Example 152: 2-butoxy-9-(2,3-difluorobenzyl)-A -(2-morpholin-4-ylethyl)-9 H -purin-6-
amine

Scheme XXXVI

To a solution of 2-butoxy-N-(2-morpholin-4-ylethyl)-9 H -purin-6-amine
(Intermediate 17) (200mg, 0.625mmole) in THF (3mL) was added Cs₂CO₃ (300mg 0.923mmol and 2,3-difluorobenzyl bromide (0.2mL, 1.57mmol). The reaction was heated at 60°C for 2h, diluted with water (2mL). The mixture was extracted with ethyl acetate (2 X 5mL). The organic extracts were dried over MgSO₄ and evaporated. The residue was purified by reverse phase chromatography [5-95% acetonitrile, water, 0.1 % TFA] to obtain the product as a TFA salt. ¹H NMR (300 MHz, DMSO-D6) δ ppm 0.89 (t, J=7.3 Hz, 3 H) 1.30 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.38 - 3.54 (m, 3 H) 3.61 - 3.72 (m, 3 H) 3.96 - 4.02 (m, 5 H) 4.23 (t, J=6.6 Hz, 2 H) 5.40 (s, 2 H) 7.14 - 7.28 (m, 1 H) 7.30 - 7.44 (m, 1 H) 7.59 - 7.73 (m, J=9.6 Hz, 1 H) 8.11 (s, 1 H) MS (ESP) m/z= 445 [M-H⁻] for C₂₂H₂₈F₂N₆O₂

Table 6: The Examples in Table 6 were prepared as described for Example 152 using the appropriate alkylating agent and Intermediate 17 as starting material.

<table>
<thead>
<tr>
<th>Ex</th>
<th>Name</th>
<th>MS (m/z)</th>
<th>¹H NMR (300MHz, DMSO-D6) δppm</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>153</td>
<td>2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetrafluorobenzyl)-9H-purin-6-amine</td>
<td>483 [MH⁺] for C₂₂H₂₆F₄N₆O₂</td>
<td>0.90 (t, J=7.3 Hz, 3 H) 1.29 - 1.42 (m, 2 H) 1.56 - 1.69 (m, 2 H) 3.05 - 3.15 (m, 2 H) 3.25 - 3.35 (m, 2 H) 3.57 - 3.73 (m, 4 H) 3.88 - 4.03 (m, 4 H) 4.16 (t, J=6.7 Hz, 2 H) 5.46 (s, 2 H) 7.90 (s, 1 H) 8.14 (s, 1 H)</td>
<td></td>
</tr>
<tr>
<td>154</td>
<td>9-[3,5-bis(trifluoromethyl)benzyl]-2-butoxy-N-(2-</td>
<td>547 [MH⁺] for C₂₄H₂₈F₆N₆O₂</td>
<td>0.90 (t, J=7.3 Hz, 3 H) 1.30 - 1.44 (m, 2 H) 1.66 (d, J=6.8 Hz, 2 H) 3.09 (s, 1 H) 3.34 (s, 2 H) 3.67 (s, 6 H) 3.87 - 4.02 (m, 4 H) 4.22 (t, J=6.6 Hz, 2 H) 5.50 (s,</td>
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<td>Ex</td>
<td>Name</td>
<td>MS (m/z)</td>
<td>$^1$H NMR (300MHz, DMSO-D6) $\delta$ ppm</td>
<td>Note</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------------------------------------</td>
<td>------------------</td>
<td>------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>155</td>
<td>2-butoxy-N-(2-morpholin-4-yl methyl)-9-(2,3,4,5-tetrafluorobenzyl)-9H-purin-6-amine</td>
<td>483 [MH$^+$] for C$<em>{22}$H$</em>{26}$F$_4$N$_6$O$_2$</td>
<td>0.86 - 0.94 (m, 3 H) 1.30 - 1.42 (m, 2 H) 1.59 - 1.71 (m, 2 H) 3.05 - 3.14 (m, 2 H) 3.28 - 3.40 (m, 2 H) 3.60 - 3.75 (m, 4 H) 3.90 - 4.05 (m, 2 H) 4.22 (t, J=6.7 Hz, 2 H) 5.37 (s, 2 H) 7.39 - 7.52 (m, 1 H) 8.11 (s, 1 H)</td>
<td></td>
</tr>
<tr>
<td>156</td>
<td>2-butoxy-9-(3,4-difluorobenzyl)-N-(2-morpholin-4-yl methyl)-9H-purin-6-amine</td>
<td>447 [MH$^+$] for C$<em>{22}$H$</em>{26}$F$_2$N$_6$O$_2$</td>
<td>0.90 (t, J=7.4 Hz, 3 H) 1.31 - 1.45 (m, 2 H) 1.61 - 1.74 (m, 2 H) 3.4 - 3.6 (m, 9 H) 3.9 - 4.0 (m, 4 H) 4.27 (t, J=6.4 Hz, 2 H) 5.28 (s, 2 H) 7.12 - 7.26 (m, 1 H) 7.36 - 7.51 (m, 2 H) 8.14 (s, 1 H)</td>
<td></td>
</tr>
<tr>
<td>157</td>
<td>2-butoxy-9-(2,5-dichlorobenzyl)-N-(2-morpholin-4-yl methyl)-9H-purin-6-amine</td>
<td>479 [MH$^+$] for C$<em>{22}$H$</em>{26}$Cl$_2$N$_6$O$_2$</td>
<td>0.89 (t, J=7 Hz, 3 H) 1.3 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.28 - 3.4 (m, 2 H) 3.5 - 3.75 (m, 6 H) 3.9 - 4.0 (m, 3 H) 4.17 (m, 2 H) 5.35 (s, 2 H) 7.25 - 7.33 (m, 1 H) 7.36 - 7.43 (m, 1 H) 7.5 (m, 1 H) 8.1 (s, 1 H)</td>
<td>1</td>
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<tr>
<td>158</td>
<td>2-butoxy-N-(2-morpholin-4-yl methyl)-9-[4-[(trifluoromethyl)benzyl]-9H-purin-6-amine</td>
<td>479 [MH$^+$] for C$<em>{23}$H$</em>{29}$F$_3$N$_6$O$_2$</td>
<td>0.89 (t, J=7 Hz, 3 H) 1.3 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.0 - 3.4 (m, 2 H) 3.55 - 4.0 (m, 9 H) 4.17 (m, 2 H) 5.35 (s, 2 H) 7.52 (d, J= 8.2 Hz, 2 H) 7.75 (d, J= 8.2 Hz, 1 H) 8.2 (s, 1 H)</td>
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<tr>
<td>159</td>
<td>2-butoxy-9-(2,6-dichlorobenzyl)-N-(2-morpholin-4-yl methyl)-9H-purin-6-amine</td>
<td>479 [MH$^+$] for C$<em>{22}$H$</em>{26}$Cl$_2$N$_6$O$_2$</td>
<td>0.89 (t, J=7 Hz, 3 H) 1.3 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.0 - 3.1 (m, 2 H) 3.28 - 3.4 (m, 2 H) 3.55 - 3.7 (m, 6 H) 3.9 - 4.0 (m, 3 H) 4.2 (m, 2 H) 5.35 (s, 2 H) 7.35 - 7.43 (m, 1 H) 7.7 (m, 2 H) 8.0 (s, 1 H)</td>
<td>1</td>
</tr>
<tr>
<td>160</td>
<td>2-butoxy-9-(2,4-difluorobenzyl)-N-(2-morpholin-4-yl methyl)-9H-purin-6-amine</td>
<td>445 [M-H$^-$] for C$<em>{22}$H$</em>{26}$F$_2$N$_6$O$_2$</td>
<td>0.9 (t, J=7 Hz, 3 H) 1.3 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.28 - 3.7 (m, 6 H) 3.9 - 4.0 (m, 7 H) 4.2 - 4.3 (m, 2 H) 5.35 (s, 2 H) 7.02 - 7.14 (m, 1 H) 7.2 - 7.35 (m, 1 H) 7.4 - 7.5 (m, 1 H) 8.1 (s, 1 H)</td>
<td>1</td>
</tr>
<tr>
<td>161</td>
<td>2-butoxy-9-(2-chlorobenzyl)-N-(2-morpholin-4-yl methyl)-9H-purin-6-amine</td>
<td>445 [MH$^+$] for C$<em>{22}$H$</em>{26}$ClN$_6$O$_2$</td>
<td>0.9 (t, J=7 Hz, 3 H) 1.3 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.0 - 3.1 (m, 2 H) 3.28 - 3.4 (m, 2 H) 3.5 - 4.0 (m, 9 H)</td>
<td>1</td>
</tr>
<tr>
<td>Ex</td>
<td>Name</td>
<td>MS (m/z)</td>
<td>$^1$H NMR (300MHz, DMSO-D6) $\delta$ ppm</td>
<td>Note</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------------------------------------</td>
<td>---------------</td>
<td>-----------------------------------------</td>
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<tr>
<td>162</td>
<td>2-butoxy-9-[2-chloro-5-((trifluoromethyl)benzyl)-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>513 [MH$^+$] for C$<em>{23}$H$</em>{26}$ClF$_3$N$_6$O$_5$</td>
<td>4.2 - 4.3 (m, 2 H) 5.35 (s, 2 H) 7.1 - 7.2 (m, 1 H) 7.3 - 7.4 (m, 2 H) 7.5 - 7.6 (m, 1 H) 8.1 (s, 1 H)</td>
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<tr>
<td>163</td>
<td>9-(4-bromo-2-fluorobenzyl)-2-butoxy-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>507 [MH$^+$] for C$<em>{22}$H$</em>{26}$BrF$_6$N$_6$O$_2$</td>
<td>0.89 (t, $J$=7.7 Hz, 3 H) 1.29 - 1.42 (m, 2 H) 1.57 - 1.68 (m, 2 H) 2.37 - 2.43 (m, 4 H) 3.25 - 3.4 (m, 4 H) 3.45 - 3.58 (m, $J$=4.1 Hz, 4 H) 4.18 (t, $J$=6.7 Hz, 2 H) 5.34 (s, 2 H) 7.23 (d, $J$=2.3 Hz, 1 H) 7.40 - 7.49 (m, 1 H) 7.50 - 7.58 (m, 1 H) 7.66 (s, 1 H) 8.01 (s, 1 H)</td>
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<td>164</td>
<td>2-butoxy-9-[2-fluoro-4-((trifluoromethyl)benzyl)-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>497 [MH$^+$] for C$<em>{23}$H$</em>{26}$F$_4$N$_6$O$_2$</td>
<td>0.91 (t, $J$=7.3 Hz, 3 H) 1.32 - 1.45 (m, 2 H) 1.60 - 1.71 (m, 2 H) 3.31 - 3.4 (m, $J$=8.3 Hz, 2 H) 3.61 - 3.67 (m, 2 H) 3.70 - 3.76 (m, 3 H) 3.88 - 4.04 (m, 2 H) 4.25 (t, $J$=6.5 Hz, 2 H) 5.31 (s, 2 H) 7.08 - 7.21 (m, 2 H) 7.31 - 7.44 (m, 1 H) 8.12 (bs, 1H) 8.16 (s, 1 H)</td>
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<tr>
<td>165</td>
<td>2-butoxy-9-(3-chloro-2-fluorobenzyl)-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>463 [MH$^+$] for C$<em>{22}$H$</em>{28}$ClF$_6$N$_6$O$_2$</td>
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<tr>
<td>166</td>
<td>2-butoxy-9-(4-ethylbenzyl)-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>439 [MH$^+$] for C$<em>{24}$H$</em>{34}$N$_6$O$_2$</td>
<td>0.92 (t, $J$=7.3 Hz, 3 H) 1.11 (t, $J$=7.6 Hz, 3 H) 1.22 - 1.30 (m, 2 H) 1.34 - 1.46 (m, 2 H) 1.61 - 1.74 (m, 2 H) 2.52 - 2.60 (m, 2 H) 3.11 (m, 2 H) 3.34 (m, 2 H) 3.48 - 3.63 (m, 2 H) 3.80 (s, 2 H) 3.94 (s, 2 H) 4.28 (t, $J$=6.6 Hz, 2 H) 5.27 (s, 2 H) 7.14 - 7.22 (m, 2 H) 7.22 - 7.31 (m, 2 H) 8.33 (s, 1 H)</td>
<td></td>
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<tr>
<td>167</td>
<td>2-butoxy-9-(2-fluoro-6-methylbenzyl)-N-(2-morpholin-4-yethyl)-9H-</td>
<td>443 [MH$^+$] for C$<em>{23}$H$</em>{31}$FN$_6$O$_2$</td>
<td>0.90 (t, $J$=7.3 Hz, 3 H) 1.31 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 2.35 (s, 3 H) 3.05 - 3.19 (m, 3 H) 3.26 - 3.42 (m, 2 H) 3.51 - 3.65 (m, 3 H) 3.69 - 3.85 (m, 4 H) 4.22 (t,</td>
<td></td>
</tr>
<tr>
<td>Ex</td>
<td>Name</td>
<td>MS (m/z)</td>
<td>$^1$H NMR (300MHz, DMSO-D6) δ ppm</td>
<td>Note</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------------------------------</td>
<td>------------------------------------------------------------</td>
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</tr>
<tr>
<td>168</td>
<td>2-butoxy-9-(4-fluoro-3-methylbenzyl)-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>443 [MH$^+$] for C$<em>{23}$H$</em>{31}$FN$_6$O$_2$</td>
<td>0.90 (t, $J$=7.3 Hz, 3 H) 1.33 - 1.45 (m, 2 H) 1.59 - 1.71 (m, 2 H) 3.04 - 3.19 (m, 2 H) 3.29 - 3.41 (m, 2 H) 3.51 - 3.64 (m, 2 H) 3.71 - 3.86 (m, 4 H) 3.89 - 4.04 (m, 2 H) 4.21 (t, $J$=6.6 Hz, 2 H) 5.30 (s, 2 H) 6.84 (dd, $J$=8.1, 2.4 Hz, 1 H) 7.02 (s, 1 H) 7.08 (d, $J$=7.7 Hz, 1 H) 7.13 - 7.26 (m, 3 H) 7.30 - 7.40 (m, 2 H) 8.25 (bs, 1 H) 8.31 (s, 1 H)</td>
<td></td>
</tr>
<tr>
<td>169</td>
<td>2-butoxy-9-[3-(2-fluorophenoxy)benzyl]-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>521 [MH$^+$] for C$<em>{23}$H$</em>{33}$FN$_6$O$_3$</td>
<td>0.90 (t, $J$=7.3 Hz, 3 H) 1.33 - 1.45 (m, 2 H) 1.59 - 1.71 (m, 2 H) 3.04 - 3.19 (m, 2 H) 3.29 - 3.41 (m, 2 H) 3.51 - 3.64 (m, 2 H) 3.71 - 3.86 (m, 4 H) 3.89 - 4.04 (m, 2 H) 4.21 (t, $J$=6.6 Hz, 2 H) 5.30 (s, 2 H) 6.84 (dd, $J$=8.1, 2.4 Hz, 1 H) 7.02 (s, 1 H) 7.08 (d, $J$=7.7 Hz, 1 H) 7.13 - 7.26 (m, 3 H) 7.30 - 7.40 (m, 2 H) 8.25 (bs, 1 H) 8.31 (s, 1 H)</td>
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</tr>
<tr>
<td>170</td>
<td>9-(1,3-benzodioxol-5-ylmethyl)-2-butoxy-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>455 [MH$^+$] for C$<em>{23}$H$</em>{30}$N$_6$O$_4$</td>
<td>0.92 (t, $J$=7.3 Hz, 3 H) 1.35 - 1.47 (m, 2 H) 1.60 - 1.75 (m, 2 H) 3.01 - 3.2 (m, 3 H) 3.3 - 3.4 (m, 2 H) 3.5 - 3.6 (m, 2 H) 3.75 - 3.9 (m, 4 H) 3.93 - 4.0 (m, 2 H) 4.29 (t, $J$=6.6 Hz, 2 H) 5.22 (s, 2 H) 5.98 (s, 2 H) 6.87 (s, 2 H) 7.00 (s, 1 H) 8.41 (s, 1 H)</td>
<td></td>
</tr>
<tr>
<td>171</td>
<td>2-butoxy-9-[3-chloro-2-fluoro-5-(trifluoromethyl)benzyl]-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>531 [MH$^+$] for C$<em>{23}$H$</em>{27}$ClF$_4$N$_6$O$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>172</td>
<td>2-butoxy-9-[3-(4-fluorophenoxy)benzyl]-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>521 [MH$^+$] for C$<em>{28}$H$</em>{33}$FN$_6$O$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>173</td>
<td>2-butoxy-9-[3-fluoro-2-(trifluoromethyl)benzyl]-N-(2-morpholin-4-yethyl)-9H-purin-6-amine</td>
<td>497 [MH$^+$] for C$<em>{23}$H$</em>{28}$F$_4$N$_6$O$_2$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 6 Footnotes

1. Reaction carried out at ambient temperature.
2. Purified by silica gel chromatography using 0-5% methanol in dichloromethane.
Example 177: 4-[[2-butoxy-9-(2-morpholin-4-ylethyl)-9H-purin-6-yl]amino]methyl]benzenesulfonamide

Scheme XXXVII

A solution of 4-[[2-chloro-9-(2-morpholin-4-ylethyl)-9H-purin-6-yl]amino]methyl]benzenesulfonamide (Intermediate 43) (0.730g, 1.62mmol) in n-butanol (10 mL) was treated with sodium hydroxide pellets (1.0g, 25mmol). The reaction was heated in a sealed tube at 80°C overnight. The reaction was concentrated at reduced pressure to afford a light yellow solid. The solid was dissolved in ethyl acetate, washed with water, dried over MgSO₄ and evaporated to obtain the product as a solid. Purification by reverse phase chromatography [5-95% acetonitrile/water/0.1% TFA] gave the product as a TFA salt (0.175g). 1H NMR (300MHz, DMSO-D6) δ ppm 0.9 (t, J=7 Hz, 3 H) 1.3 - 1.44 (m, 2 H) 1.57 - 1.70 (m, 2 H) 3.1 - 4.0 (m, 11 H) 4.15 - 4.25 (m, 2 H) 4.7 (s, 2 H) 7.3 (s, 2 H) 7.5 (d, J= 8.2 Hz, 2 H) 7.8 (d, J= 8.2 Hz, 2 H) 8.65 (bs, 1 H) 15 MS (ESP) m/z= 490 [MH+] for C₂₂H₃₂N₇O₄S
**Example 178**: 4-f{2-butoxy-6-2-morpholin-4-ylethyl)aminol-9 H -purin-9-yl}methyl)-3-
methoxybenzoic acid

Scheme XXXVIII

To a solution of methyl 4-((2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9 H -purin-9-
yl)methyl)-3-methoxybenzoate [Example 175] (97mg, 0.197mmol) in methanol (4mL) and
water (1mL) was added sodium hydroxide (1 pellet). The reaction was allowed to stir at rt
overnight. The mixture was evaporated at reduced pressure, partitioned between
dichloromethane and water. The aqueous layer was extracted with dichloromethane (2 X
5mL). The organic extracts were dried over MgSO4 and evaporated to obtain the title
compound as a solid. 1H NMR (300MHz, DMSO-D6) δ ppm 0.84 -0.96 (m, 3 H) 1.3 - 1.44
(m, 2 H) 1.57 - 1.70 (m, 2 H) 3.0 - 3.1 (m, 2 H) 3.25 - 3.37 (m, 2 H) 3.43 - 3.7 (m, 5 H) 3.74
- 3.95 (m, 6 H) 4.16 - 4.24 (m, 2 H) 5.29 (s, 2 H) 7.04 (d, J= 7.7 Hz , 1 H) 7.44 -7.55 (m, 2
H) 8.09-8.21 (m, 2 H) 10.6 (bs, 1 H)  MS (ESP) m/z= 485 [MH+] for C24H32N6O5
Example 179: 2-butoxy-N-[2-morpholin-4-ylethyl]-9-[2-(trifluoromethyl)benzyll-9 \( H \)-purin-6-amine

Scheme XXXIX

To a solution of 2-butoxy-N-(2-morpholin-4-ylethyl)-9 \( H \)-purin-6-amine (Intermediate 17) (96mg, 0.3mmol) in DMF (1mL) was added 2-trifluoromethylbenzyl bromide (87mg, 0.33mmol) and MP carbonate TM (500mg) the reaction was allowed to stir for 24h. The reaction was treated with thiophenol resin (-1mmol thiophenol) and filtered. Purification by reverse phase chromatography (5-95% acetonitrile/water 0.1% TFA) gave the title compound as a TFA salt. 1H NMR (300 MHz, DMSO-D6) \( \delta \) ppm 0.85 (t, \( J=7.3 \) Hz, 3 H) 1.24 - 1.37 (m, 2 H) 1.49 - 1.63 (m, 2 H) 2.41 (s, 5 H) 3.47 - 3.59 (m, 7 H) 4.13 (t, \( J=6.6 \) Hz, 2 H) 5.47 (s, 2 H) 6.88 (d, \( J=7.5 \) Hz, 1 H) 7.47 - 7.62 (m, 2 H) 7.70 (s, 1 H) 7.79 (d, \( J=7.5 \) Hz, 1 H) 7.99 (s, 1 H) MS (ESP) m/z= 479 [MH+] for \( C_{23}H_{29}F_3N_6O_2 \)

Table 7: The Examples in Table 7 were prepared as described for Example 179 using the appropriate alkylating agent and Intermediate 17 as starting material.

<table>
<thead>
<tr>
<th>EX.</th>
<th>Name</th>
<th>MS</th>
<th>NMR1H NMR (300 MHz, DMSO-D6) ( \delta ) ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>180</td>
<td>[4-(2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9( H )-purin-9-yl)methyl]phenylmethanol</td>
<td>441 [MH+] for ( C_{23}H_{32}N_6O_3 )</td>
<td>0.91 (t, ( J=7.3 ) Hz, 3 H) 1.31 - 1.45 (m, 2 H) 1.58 - 1.71 (m, 2 H) 2.40 (s, 5 H) 3.45 - 3.58 (m, 7 H) 4.21 (t, ( J=6.6 ) Hz, 2 H) 4.43 (s, 2 H) 5.22 (s, 2 H) 7.26 (s, 2 H) 7.59 (s, 1 H) 8.02 (s, 1 H)</td>
</tr>
<tr>
<td>181</td>
<td>2-butoxy-N-(2-morpholin-4-ylethyl)-9-[2,3,5,6-tetrafluoro-4-methylbenzyl]-9( H )-purin-6-amine</td>
<td>497 [MH+] for ( C_{23}H_{28}F_4N_6O_2 )</td>
<td>0.89 (t, ( J=7.3 ) Hz, 3 H) 1.27 - 1.41 (m, 2 H) 1.61 (s, 2 H) 2.16 - 2.27 (m, 3 H) 2.34 - 2.44 (m, 5 H) 3.45 - 3.56 (m, 7 H) 4.14 (t, ( J=6.8 ) Hz, 2 H) 5.40 (s, 2 H) 7.60 (s, 1 H) 8.02 (s, 1 H)</td>
</tr>
<tr>
<td>182</td>
<td>2-butoxy-9-(4-chloro-2-</td>
<td>490 [MH+] for</td>
<td>0.91 (t, ( J=7.3 ) Hz, 3 H) 1.31 - 1.43 (m,</td>
</tr>
<tr>
<td>EX.</td>
<td>Name</td>
<td>MS</td>
<td>NMR1H NMR (300 MHz, DMSO-D6) δ ppm</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------------------------------------</td>
<td>---------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>183</td>
<td>nitrobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>C_{22}H_{28}ClN_{7}O_{4}</td>
<td>2 H) 1.53 - 1.65 (m, 2 H) 3.02 - 3.17 (m, 2 H) 3.25 - 3.39 (m, 3 H) 3.57 - 3.73 (m, 5 H) 3.88 - 4.01 (m, 2 H) 4.06 (t, J=6.7 Hz, 2 H) 5.60 (s, 2 H) 7.64 - 7.74 (m, 2 H) 7.92 (dd, J=6.6, 2.8 Hz, 1 H) 8.01 (s, 1 H) 8.10 (bs, 1 H)</td>
</tr>
<tr>
<td>184</td>
<td>2-butoxy-9-(2-methyl-3-nitrobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>470 [MH+] for C_{23}H_{31}N_{7}O_{4}</td>
<td>0.83 (t, J=7.3 Hz, 3 H) 1.24 - 1.37 (m, 2 H) 1.49 - 1.63 (m, 2 H) 2.40 (s, 5 H) 3.46 - 3.59 (m, 6 H) 4.15 (t, J=6.6 Hz, 2 H) 5.58 (s, 2 H) 7.11 (d, J=8.5 Hz, 1 H) 7.59 - 7.74 (m, 3 H) 7.94 (dd, J=13.5, 8.4 Hz, 2 H) 8.06 (s, 1 H) 8.25 (d, J=8.5 Hz, 1 H)</td>
</tr>
<tr>
<td>185</td>
<td>9-[(1-bromo-2-naphthyl)methyl]-2-butoxy-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>539 [MH+] for C_{26}H_{31}BrN_{6}O_{2}</td>
<td>0.83 (t, J=7.3 Hz, 3 H) 1.24 - 1.37 (m, 2 H) 1.49 - 1.63 (m, 2 H) 2.40 (s, 5 H) 3.46 - 3.59 (m, 6 H) 4.15 (t, J=6.6 Hz, 2 H) 5.58 (s, 2 H) 7.11 (d, J=8.5 Hz, 1 H) 7.59 - 7.74 (m, 3 H) 7.94 (dd, J=13.5, 8.4 Hz, 2 H) 8.06 (s, 1 H) 8.25 (d, J=8.5 Hz, 1 H)</td>
</tr>
<tr>
<td>186</td>
<td>2-butoxy-9-[(6-fluoro-4H-1,3-benzodioxin-8-yl)methyl]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>487 [MH+] for C_{24}H_{31}FN_{6}O_{4}</td>
<td>0.83 - 0.92 (m, 3 H) 1.27 - 1.40 (m, 2 H) 1.53 - 1.64 (m, 2 H) 2.34 - 2.45 (m, 6 H) 3.47 - 3.58 (m, 7 H) 4.07 - 4.21 (m, 4 H) 5.58 (s, 2 H) 7.01 (d, J=8.5 Hz, 1 H) 7.76 (dd, J=8.4, 2.2 Hz, 1 H) 7.81 - 7.90 (m, 1 H) 7.96 (s, 1 H) 8.22 (d, J=2.3 Hz, 1 H)</td>
</tr>
<tr>
<td>187</td>
<td>N-[4-((2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-yl)methyl)phenyl]acetamide</td>
<td>468 [MH+] for C_{24}H_{33}N_{7}O_{3}</td>
<td>0.83 - 0.92 (m, 3 H) 1.27 - 1.35 (m, 2 H) 1.50 - 1.60 (m, 2 H) 2.35 (s, 6 H) 3.4 - 3.53 (m, 8 H) 4.07 - 4.16 (m, 2 H) 5.33 (s, 2 H) 7.15 (d, 1 H) 7.32 (t, 1 H) 7.6 (bs, ~1 H) 7.82 (d, 1 H) 7.96 (s, 1 H)</td>
</tr>
<tr>
<td>188</td>
<td>9-(4-bromobenzyl)-2-butoxy-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>489 [MH+] for C_{22}H_{29}BrN_{6}O_{2}</td>
<td>0.91 (t, J=7.3 Hz, 3 H) 1.32 - 1.45 (m, 2 H) 1.58 - 1.70 (m, 2 H) 3.04 - 3.20 (m, 2 H) 3.28 - 3.42 (m, 2 H) 3.50 - 3.65 (m, 4 H) 3.65 - 3.80 (m, 2 H) 3.89 - 4.04 (m, 2 H) 4.23 (t, J=6.6 Hz, 2 H) 5.27 (s, 2 H) 7.27 (d, J=8.5 Hz, 2 H)</td>
</tr>
<tr>
<td>EX.</td>
<td>Name</td>
<td>MS</td>
<td>NMR1H NMR (300 MHz, DMSO-D6) δ ppm</td>
</tr>
<tr>
<td>-----</td>
<td>--------------------------------------------------------</td>
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<td>-----------------------------------</td>
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<tr>
<td>188</td>
<td>2-butoxy-9-(3-chlorobenzyl)-N-(2-morpholin-4-ylthethyl)-9H-purin-6-amine</td>
<td>445 [MH+] for C_{22}H_{29}ClN_{6}O_{2}</td>
<td>H) 7.54 (d, J=8.1 Hz, 2 H) 8.14 (s, 1 H) 9.9 (bs, 1 H)</td>
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<tr>
<td>189</td>
<td>2-butoxy-N-(2-morpholin-4-ylthethyl)-9-(2,3,5,6-tetramethylbenzyl)-9H-purin-6-amine</td>
<td>467 [MH+] for C_{26}H_{38}N_{6}O_{2}</td>
<td>0.91 (t, J=7.3 Hz, 3 H) 1.32 - 1.46 (m, 2 H) 1.60 - 1.72 (m, 2 H) 3.12 (s, 2 H) 3.35 (m, 2H) 3.64 (m, 2H) 3.74 (m, 4 H) 3.96 (m, 2 H) 4.25 (t, J=6.5 Hz, 2 H) 5.30 (s, 2 H) 7.30 (d, J=2.8 Hz, 1 H) 7.32 - 7.40 (m, 2 H) 7.45 (s, 1 H) 8.11 (s, 1 H) 8.17 (s, 1 H)</td>
</tr>
<tr>
<td>190</td>
<td>2-butoxy-9-(2-fluoro-6-nitrobenzyl)-N-(2-morpholin-4-ylthethyl)-9H-purin-6-amine</td>
<td>474 [MH+] for C_{22}H_{28}FN_{7}O_{4}</td>
<td>0.83 - 0.92 (m, 3 H) 1.27 - 1.35 (m, 2 H) 1.50 - 1.60 (m, 2 H) 2.15 (s, 16 H) 3.4 - 3.53 (m, 8 H) 4.07 - 4.16 (m, 2 H) 5.2 (s, 2 H) 6.95 (s, 1 H) 8.05 (bs, 1 H)</td>
</tr>
<tr>
<td>191</td>
<td>2-butoxy-9-(5-methyl-2-nitrobenzyl)-N-(2-morpholin-4-ylthethyl)-9H-purin-6-amine</td>
<td>470 [MH+] for C_{23}H_{31}N_{7}O_{4}</td>
<td>0.91 (t, J=7.3 Hz, 3 H) 1.32 - 1.46 (m, 2 H) 1.60 - 1.72 (m, 2 H) 2.22 (s, 3 H) 3.05 - 3.2 (m, 2 H) 3.58 - 3.8 (m, 6 H) 3.9 - 4.07 (m, 4 H) 4.1 (t, J=6.5 Hz, 2 H) 5.6 (s, 2 H) 7.0 (s, 1 H) 7.33 (d, J=8.3 Hz, 1 H) 7.95 - 8.05 (m, 2 H) 8.10 (bs, 1 H)</td>
</tr>
<tr>
<td>192</td>
<td>9-(2-bromo-5-methoxybenzyl)-2-butoxy-N-(2-morpholin-4-ylthethyl)-9H-purin-6-amine</td>
<td>519 [MH+] for C_{23}H_{31}BrN_{6}O_{3}</td>
<td>0.91 (t, J=7.3 Hz, 3 H) 1.32 - 1.46 (m, 2 H) 1.60 - 1.72 (m, 2 H) 3.05 - 3.2 (m, 2 H) 3.58 - 3.8 (m, 9 H) 3.9 - 4.07 (m, 4 H) 4.2 (t, J=6.5 Hz, 2 H) 5.28 (s, 2 H) 6.6 (d, J=3.0 Hz, 1 H) 6.85 (dd, J=8.7, 3.0 Hz, 1H) 7.5 (d, J=8.7 Hz, 1 H) 8.05 (s, 1 H) 8.10 (bs, 1 H)</td>
</tr>
<tr>
<td>193</td>
<td>2-butoxy-9-(2,5-dimethoxybenzyl)-N-(2-morpholin-4-ylthethyl)-9H-purin-6-amine</td>
<td>471 [MH+] for C_{24}H_{34}N_{6}O_{4}</td>
<td>0.91 (t, J=7.4 Hz, 3 H) 1.32 - 1.45 (m, 2 H) 1.61 - 1.71 (m, 2 H) 3.04 - 3.19 (m, 2 H) 3.5 - 3.75 (m, 13 H) 3.9 - 4.07 (m, 3 H) 4.24 (t, J=6.6 Hz, 2 H) 5.19 (s, 2 H) 6.62 (d, J=2.8 Hz, 1 H) 6.81 - 6.88 (m, 1 H) 6.91 - 6.99 (m, 1 H) 8.00 (s, 1 H) 8.09 (bs, 1 H)</td>
</tr>
<tr>
<td>194</td>
<td>2-butoxy-9-(2,4-dichlorobenzyl)-N-(2-morpholin-4-ylthethyl)-9H-purin-6-amine</td>
<td>479 [MH+] for C_{22}H_{28}Cl_{2}N_{6}O_{2}</td>
<td>0.89 (t, J=7.3 Hz, 3 H) 1.29 - 1.42 (m, 2 H) 1.54 - 1.67 (m, 2 H) 3.05 - 3.20 (m, 3 H) 3.61 - 3.77 (m, 6 H) 3.89 - 4.05 (m, 3 H) 4.19 (t, J=6.5 Hz, 2 H)</td>
</tr>
<tr>
<td>EX.</td>
<td>Name</td>
<td>MS</td>
<td>NMR 1H NMR (300 MHz, DMSO-D6) δ ppm</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------------------------------------</td>
<td>----------</td>
<td>--------------------------------------------------------</td>
</tr>
<tr>
<td>195</td>
<td>2-butoxy-9-(3-methoxybenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>441 [MH+] for C_{23}H_{32}N_{6}O_{3}</td>
<td>0.91 (t, J=7.3 Hz, 3 H) 1.32 - 1.46 (m, 2 H) 1.60 - 1.74 (m, 2 H) 3.0 - 3.2 (m, 2 H) 3.5 - 3.75 (m, 10 H) 3.9 - 4.07 (m, 3 H) 4.25 (t, J=6.5 Hz, 2 H) 5.25 (s, 2 H) 6.82 - 6.95 (m, 3 H) 7.24 (t, J=7.9 Hz, 1H) 8.05 - 8.17 (m, 1 H) 8.5 (s, 1 H)</td>
</tr>
<tr>
<td>196</td>
<td>4-({2-butoxy-6-[2-morpholin-4-ylethyl]amino}-9H-purin-9-yl}methylphenyl acetate</td>
<td>469 [MH+] for C_{24}H_{32}N_{6}O_{4}</td>
<td>0.88 (t, J=7.3 Hz, 3 H) 1.3 - 1.4 (m, 2 H) 1.57 - 1.67 (m, 2 H) 2.2 (s, 3 H) 3.0 - 3.2 (m, 2 H) 3.5 - 4.0 (m, 10 H) 4.2 (t, J=6.5 Hz, 2 H) 5.20 (s, 2 H) 7.0 (d, J=8.5 Hz, 2H) 7.35 (d, J=8.5Hz, 2H) 8.05 (bs, 1 H) 8.13 (s, 1 H)</td>
</tr>
<tr>
<td>197</td>
<td>2-butoxy-9-(3-fluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>429 [MH+] for C_{22}H_{29}FN_{6}O_{2}</td>
<td>0.82 - 0.97 (m, 3 H) 1.30 - 1.45 (m, 2 H) 1.56 - 1.71 (m, 2 H) 3.09 - 3.19 (m, 2 H) 3.44 - 3.59 (m, 6 H) 4.14 - 4.27 (m, 2 H) 5.17 (s, 2 H) 7.17 - 7.31 (m, 2 H) 7.51 (m, 2 H) 8.00 (s, 1 H)</td>
</tr>
<tr>
<td>198</td>
<td>2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2-nitrobenzyl)-9H-purin-6-amine</td>
<td>456 [MH+] for C_{22}H_{29}N_{6}O_{4}</td>
<td>0.89 (t, J=7.3 Hz, 3 H) 1.30 - 1.44 (m, 2 H) 1.56 - 1.68 (m, 2 H) 3.13 (m, 2 H) 3.72 (m, 6 H) 3.96 (m, 4 H) 4.21 (t, J=6.5 Hz, 2 H) 5.36 (s, 2 H) 7.18 - 7.32 (m, 2 H) 7.51 (dd, J=8.8, 2.4 Hz, 1H) 8.06 - 8.20 (m, 2 H)</td>
</tr>
<tr>
<td>199</td>
<td>2-butoxy-9-(2-chloro-4-fluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>463 [MH+] for C_{22}H_{28}ClFN_{6}O_{2}</td>
<td>0.82 - 0.97 (m, 3 H) 1.30 - 1.45 (m, 2 H) 1.56 - 1.68 (m, 2 H) 3.13 (m, 2 H) 3.72 (m, 6 H) 3.96 (m, 4 H) 4.21 (t, J=6.5 Hz, 2 H) 5.36 (s, 2 H) 7.18 - 7.32 (m, 2 H) 7.51 (dd, J=8.8, 2.4 Hz, 1H) 8.06 - 8.20 (m, 2 H)</td>
</tr>
<tr>
<td>200</td>
<td>2-butoxy-9-(3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>425 [MH+] for C_{23}H_{27}N_{6}O_{2}</td>
<td>0.92 (t, J=7.3 Hz, 3 H) 1.33 - 1.47 (m, 2 H) 1.60 - 1.73 (m, 2 H) 2.25 (s, 3 H) 3.05 - 3.20 (m, 2 H) 3.55 - 3.70 (m, 4 H) 3.70 - 3.84 (m, 3 H) 3.88 - 4.04 (m, 2 H) 4.26 (t, J=6.5 Hz, 2 H) 5.24 (s, 3 H) 7.10 (t, J=6.9 Hz, 2 H) 7.19 (s, 1 H) 7.20 - 7.25 (m, 1 H) 8.10 (s, 1 H) 8.14 (s, 1 H)</td>
</tr>
<tr>
<td>201</td>
<td>2-butoxy-N-(2-morpholin-4-ylethyl)-9-{4-[(E)-2-phenylvinyl]benzyl}-9H-purin-6-amine</td>
<td>513 [MH+] for C_{30}H_{36}N_{6}O_{2}</td>
<td>0.92 (t, J=7.4 Hz, 3 H) 1.34 - 1.48 (m, 2 H) 1.60 - 1.74 (m, 2 H) 3.06 - 3.20 (m, 2 H) 3.55-3.75 (m, 6 H) 3.97 (m, 4 H) 4.20 - 4.30 (m, 2 H) 5.29 (s, 2 H) 7.17 - 7.31 (m, 3 H) 7.31 - 7.39 (m, 4 H) 7.57 (d, J=7.9 Hz, 4 H) 8.11 (s, 1 H) 8.16 (s, 1 H)</td>
</tr>
<tr>
<td>EX.</td>
<td>Name</td>
<td>MS</td>
<td>NMR1H NMR (300 MHz, DMSO-D6) δ ppm</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------------------------------------</td>
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<td>----------------------------------</td>
</tr>
<tr>
<td>202</td>
<td>2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,4,6-triisopropylbenzyl)-9H-purin-6-amine</td>
<td>537 [MH+] for C$<em>{31}$H$</em>{48}$N$_6$O$_2$</td>
<td>0.94 (t, J=7.3 Hz, 3 H) 1.08 (d, J=6.8 Hz, 12 H) 1.20 (d, J=6.8 Hz, 6 H) 1.43 (d, J=14.9, 7.4 Hz, 2 H) 1.64 - 1.76 (m, 2 H) 2.81 - 2.94 (m, 1 H) 3.09 - 3.25 (m, 4 H) 3.73 (bs, 10 H) 4.28 (t, J=6.4 Hz, 2 H) 5.26 (s, 2 H) 7.09 (s, 2 H) 7.35 (s, 1 H) 8.10 (s, 1 H)</td>
</tr>
<tr>
<td>203</td>
<td>ethyl 3-([2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9H-purin-9-yl]methyl)benzoate</td>
<td>483 [MH+] for C$<em>{25}$H$</em>{34}$N$_6$O$_4$</td>
<td>0.89 (t, J=7.3 Hz, 3 H) 1.28 (t, J=6.9 Hz, 3 H) 1.32 - 1.43 (m, 2 H) 1.56 - 1.69 (m, 2 H) 3.05 - 3.21 (m, 2 H) 3.66 - 3.77 (m, 6 H) 3.88 - 4.04 (m, 4 H) 4.19 - 4.25 (m, 2 H) 4.25 - 4.33 (m, 2 H) 5.38 (s, 2 H) 7.42 (d, J=8.1 Hz, 2 H) 7.88 - 7.98 (m, 2 H) 8.12 (s, 1 H) 8.16 (s, 1 H)</td>
</tr>
<tr>
<td>204</td>
<td>2-butoxy-9-(mesitylmethyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>453 [MH+] for C$<em>{25}$H$</em>{36}$N$_6$O$_2$</td>
<td>0.92 (t, J=7.4 Hz, 3 H) 1.37 - 1.44 (m, 2 H) 1.61 - 1.69 (m, 2 H) 2.20 (s, 3 H) 2.28 (s, 6 H) 3.70 (s, 8 H) 3.95 (s, 4 H) 4.20 (t, J=6.6 Hz, 2 H) 5.22 (s, 2 H) 6.87 (s, 2 H) 7.70 (s, 1 H) 8.09 (bs, 1 H)</td>
</tr>
<tr>
<td>205</td>
<td>2-butoxy-9-[5-chloro-2-(trifluoromethyl)benzyl]-N-(2-morpholin-4- ylethyl)-9H-purin-6-amine</td>
<td>513 [MH+] for C$<em>{23}$H$</em>{58}$ClF$_3$N$_6$O$_2$</td>
<td>0.87 (t, J=7.3 Hz, 3 H) 1.26 - 1.40 (m, 2 H) 1.53 - 1.65 (m, 2 H) 3.05 - 3.21 (m, 2 H) 3.28 - 3.43 (m, 3 H) 3.71 (bs, 4 H) 3.90 - 4.06 (m, 3 H) 4.16 (t, J=6.6 Hz, 2 H) 5.50 (s, 2 H) 7.20 (s, 1 H) 7.64 (d, J=8.5 Hz, 1 H) 7.84 (d, J=8.5 Hz, 1 H) 8.09 (s, 1 H) 8.17 (s, 1 H)</td>
</tr>
<tr>
<td>206</td>
<td>2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,5-trifluorobenzyl)-9H-purin-6-amine</td>
<td>465 [MH+] for C$<em>{22}$H$</em>{27}$F$_3$N$_6$O$_2$</td>
<td>0.90 (t, J=7.3 Hz, 3 H) 1.30 - 1.44 (m, 2 H) 1.57 - 1.69 (m, 2 H) 3.04 - 3.20 (m, 3 H) 3.60 - 3.76 (m, 5 H) 3.89 - 4.04 (m, 3 H) 4.22 (t, J=6.6 Hz, 2 H) 5.40 (s, 2 H) 7.01 - 7.13 (m, 1 H) 7.44 - 7.59 (m, 1 H) 8.13 (s, 2 H)</td>
</tr>
<tr>
<td>207</td>
<td>2-butoxy-9-(2,3-dimethoxybenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>471 [MH+] for C$<em>{24}$H$</em>{34}$N$_6$O$_4$</td>
<td>0.91 (t, J=7.3 Hz, 3 H) 1.32 - 1.45 (m, 2 H) 1.59 - 1.70 (m, 2 H) 3.13 (s, 2 H) 3.5 – 3.7 (m, 6 H) 3.76 (s, 3 H) 3.78 (s, 3 H) 3.84 - 4.00 (m, 4 H) 4.23 (t, J=6.6 Hz, 2 H) 5.26 (s, 2 H) 6.60 - 6.72 (m, 1 H) 6.96 - 7.02 (m, 2 H) 8.01 (s, 1 H) 8.08 (s, 1 H)</td>
</tr>
<tr>
<td>208</td>
<td>2-butoxy-9-(2-chloro-6-fluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>463 [MH+] for C$<em>{22}$H$</em>{28}$ClF$_3$N$_6$O$_2$</td>
<td>0.90 (t, J=7.3 Hz, 3 H) 1.30 - 1.43 (m, 2 H) 1.55 - 1.66 (m, 2 H) 3.04 - 3.17 (m, 4 H) 3.24 - 3.38 (m, J=4.5 Hz, 6 H) 3.86 - 4.01 (m, 2 H) 4.16 (t, J=6.6 Hz, 2 H) 5.42 (s, 2 H) 7.23 - 7.31 (m, 1 H) 7.32 - 7.38 (m, 1 H) 7.43 (dd, J=8.1, 1.1 Hz)</td>
</tr>
</tbody>
</table>


**Example 209:** 9-[2-fluoro-6-pent-2-yn-1-yl oxy)benzyl]-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yl oxy)-9H-purin-6-amine

Scheme XL

A solution of 2-chloro-9-(2,6-difluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine (Intermediate 44) (0.115g, 0.282mmol) in dioxane (0.7mL) was treated with 2-pentyn-1-ol (0.2mL, 0.198g, 2.35mmol) and sodium hydroxide (one pellet). The reaction was heated at 80°C for 60h. The reaction mixture was filtered and evaporated. The residue was purified by reverse phase chromatography ([35-95% CH₃CN/H₂O/0.1% TFA] to obtain the product as a solid TFA salt. (28mg) 1H NMR (300 MHz, DMSO-D6) δ ppm 1.05 (m, 6H) 2.15 - 2.28 (m, 4H) 3.03 - 3.18 (m, 2H) 3.26 - 3.40 (m, 2H) 3.55 - 3.63 (m, 2H) 3.65 - 3.74 (m, 4H) 3.92 - 4.07 (m, 2H) 4.84 (s, 2H) 4.92 (s, 2H) 5.24 (s, 2H) 6.83 - 6.96 (m, 2H) 7.26 - 7.41 (m, 1H) 7.96 (s, 1H) 8.11 (s, 1H) MS ESP M/z: 521 [M+H] for C_{28}H_{33}FN_{6}O_{3}

**Table 8:** Compounds in Table 8 were prepared as for Example 209 using the appropriate alcohol and the starting material as shown.

<table>
<thead>
<tr>
<th>EX</th>
<th>Name</th>
<th>MS</th>
<th>1H NMR (300 MHz, DMSO-D6) δ ppm</th>
<th>Start Mat.</th>
</tr>
</thead>
<tbody>
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<td>210</td>
<td>2-[(2E)-but-2-en-1-yl oxy]-9-{2-[(2E)-but-2-en-1-yl oxy]-6-fluorobenzyl]-N-(2-morpholin-4-ylethyl)-9H-</td>
<td>497 [M+H] for C_{26}H_{33}FN_{6}O_{3}</td>
<td>1.67 (d, J=6 Hz, 6H) 3.03 - 3.18 (m, 2H) 3.24 - 3.39 (m, 2H) 3.58 - 3.74 (m, 6H) 3.86 - 4.02 (m, 2H) 4.51 (d, J=6 Hz, 2H) 4.68 (d, J=6 Hz, 2H) 5.25 (s, 2H) 5.57 - 5.66 (m, 2H) 5.74 - 5.88 (m, 2H) 6.76 - 6.91 (m, 2H) 7.24 - 7.38 (m, 1H) 7.91 (s, 1H) 8.06 (s, 1H)</td>
<td>INT 44</td>
</tr>
<tr>
<td>EX.</td>
<td>Name</td>
<td>MS</td>
<td>1H NMR (300 MHz, DMSO-D6) δ ppm</td>
<td>Start Mat.</td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------</td>
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<td>--------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>211</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-(hex-2-yn-1-yl oxy)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>485 [M+H] for C_{25}H_{30}F_{2}N_{6}O_{2}</td>
<td>0.90 (t, J=7.35 Hz, 3 H) 1.35 - 1.50 (m, 2 H) 2.18 (s, 5 H) 3.03 - 3.18 (m, 2 H) 3.27 - 3.41 (m, 2 H) 3.50 - 3.64 (m, 2 H) 3.64 - 3.78 (m, 4 H) 3.90 - 4.04 (m, 2 H) 4.89 (s, 2 H) 5.35 (s, 2 H) 6.99 - 7.05 (m, 1H) 7.23 - 7.38 (m, 1H) 8.08 (s, 1H) 8.17 (s, 1H)</td>
<td>INT 20</td>
</tr>
<tr>
<td>212</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yl oxy)-9H-purin-6-amine</td>
<td>471 [M+H] for C_{24}H_{28}F_{2}N_{6}O_{2}</td>
<td>1.05 (t, J=7.54 Hz, 3H) 2.14 - 2.27 (m, 5 H) 3.03 - 3.18 (m, J=8.48 Hz, 2 H) 3.29 - 3.42 (m, 2H) 3.50 - 3.65 (m, 2H) 3.65 - 3.79 (m, 4H) 3.90 - 4.04 (m, 2H) 4.85 - 4.94 (m, 2H) 5.35 (s, 2H) 7.02 (t, J=9 Hz, 1H) 7.24 - 7.39 (m, 1H) 8.07 (s, 1H) 8.15 (s, 1H)</td>
<td>INT 20</td>
</tr>
<tr>
<td>213</td>
<td>2-(allyloxy)-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>445 [M+H] for C_{22}H_{26}F_{2}N_{6}O_{2}</td>
<td>2.17 (s, 3 H) 3.10 (s, 2 H) 3.26 - 3.40 (m, 2 H) 3.57 - 3.66 (m, 4 H) 3.68 - 3.74 (m, 2 H) 3.95 (s, 2 H) 4.74 (d, J=5.5 Hz, 2 H) 5.15 - 5.26 (m, 1 H) 5.28 - 5.40 (m, 3 H) 6.02 (ddd, J=17.5, 5.5, 5.0 Hz, 1 H) 7.02 (t, J=9 Hz, 1 H) 7.23 - 7.36 (m, 1 H) 8.07 (s, 1 H) 8.11 (s, 1 H)</td>
<td>INT 20</td>
</tr>
<tr>
<td>214</td>
<td>2-[(2E)-but-2-en-1-yloxy]-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>459 [M+H] for C_{23}H_{28}F_{2}N_{6}O_{2}</td>
<td>1.65 (d, J=6 Hz, 3 H) 2.17 (s, 3 H) 2.33 - 2.43 (m, 5 H) 3.43 - 3.57 (m, 6 H) 4.62 (d, J=6 Hz, 2 H) 5.31 (s, 2 H) 5.60 - 5.70 (m, 1 H) 5.71 - 5.81 (m, 1 H) 7.01 (t, J=9 Hz, 1 H) 7.25 - 7.38 (m, 1 H) 7.58 (s, 1 H) 7.95 (s, 1 H)</td>
<td>INT 20</td>
</tr>
<tr>
<td>215</td>
<td>9-(2,6-difluoro-3-methylbenzyl)-2-[(3-methylbut-2-en-1-yloxy)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine</td>
<td>473 [M+H] for C_{24}H_{30}F_{2}N_{6}O_{2}</td>
<td>1.70 (d, J=4 Hz, 3 H) 2.18 (s, 3 H) 2.33 - 2.43 (m, 5 H) 3.43 - 3.57 (m, 6 H) 4.70 (d, J=8 Hz, 2 H) 5.32 (s, 2 H) 5.42 (m, 1 H) 7.01 (t, J=9 Hz, 1 H) 7.25 - 7.38 (m, 1 H) 7.55 (bs, 1 H) 7.95 (s, 1 H)</td>
<td>INT 20</td>
</tr>
<tr>
<td>216</td>
<td>2-(but-2-yn-1-yloxy)-9-(2,6-difluoro-3-</td>
<td>457 [M+H] for C_{23}H_{28}F_{2}N_{6}O_{2}</td>
<td>1.78 (t, J=2 Hz, 3 H) 2.18 (s, 3 H) 2.32 - 2.44 (m, 5 H) 3.44 - 3.58 (m, 6 H) 4.83 (d, J=2 Hz, 2 H) 5.31 (s, 2 H) 6.96</td>
<td>INT 20</td>
</tr>
</tbody>
</table>
Example 217: ethyl 2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9H-purine-8-carboxylate

To a suspension of 2-butoxy-N^6-(3,4-dichlorobenzyl)-6-morpholin-4-ylpyrimidine-4,5-diamine (Intermediate 49) (approx. 1.7g, 4.0mmol) in N-methyl pyrrolidone (NMP) (6mL) at O°C was added ethyl oxalyl chloride (0.5mL, 4.4mmol). The reaction was allowed to warm to rt for 20min and then heated at 120°C overnight. The reaction was diluted with water and extracted with ethyl acetate. The organic extract was washed with water (4 times), dried over MgSO₄ and evaporated. Purification by reverse phase chromatography (50-80%
acetonitrile/water/0.1% TFA] gave the product as a TFA salt (0.135g).  

**Example 218:** 2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9·H-purine-8-carboxylic acid

To a solution of ethyl 2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9·H-purine-8-carboxylate [Example 226] (0.12g, 0.24mmol) in THF (20 mL) was added sodium hydroxide (1N, 2mL). The reaction was heated to 60°C overnight. The reaction mixture was neutralized with 1N HCl, partitioned between ethyl acetate and water. The aqueous layer was extracted with ethyl acetate (2X) and dichloromethane (2X). The organic extracts were combined dried over MgSO₄ and evaporated. The solid was triturated with methanol to obtain the title compound.  

**Example 219:** N-αH-benzimidazol-2-ylmethyl)-2-butoxy-9·q-morpholin-4·ylethyl)-9·H-purin-6-amine

1H NMR (300 MHz, DMSO-D6) δ ppm 0.89 (t, J=7.3 Hz, 3 H) 1.31 - 1.44 (m, 2 H) 1.59 - 1.70 (m, 2 H) 3.66 - 3.79 (m, 5 H) 4.17 - 4.31 (m, Hz, 3 H) 5.61 (s, 2 H) 7.12 (dd, J=8.4, 2.0 Hz, 1 H) 7.52 - 7.59 (m, 2 H) MS ESP M/z: 480 [M+H] for C₂₃H₂₇Cl₂N₅O₄
A solution of N-[(1H-benzimidazol-2-ylmethyl)-2-chloro-9-(2-morpholin-4-ylethyl)-9H-purin-6-amine (Intermediate 55) (1.5 g, 3.63 mmol) in n-butanol was treated with sodium hydroxide pellets (2.0 g, excess). The reaction was heated in a sealed tube at 80°C over night. The reaction was concentrated at reduced pressure to afford a light yellow solid. The solid was dissolved in ethylacetate, washed with water, dried over MgSO₄ and evaporated to obtain the product as a yellow foam.

¹H NMR (300 MHz, DMSO-D6) δ ppm 0.77 - 0.91 (m, 3 H) 1.24 - 1.38 (m, 2 H) 1.50 - 1.61 (m, 2 H) 2.30 - 2.40 (m, 4 H) 2.56 - 2.71 (m, 2 H) 3.24 - 3.36 (m, 3 H) 3.43 - 3.57 (m, 4 H) 4.16 (t, J=6.1 Hz, 2 H) 7.07 - 7.23 (m, 2 H) 7.52 (dd, J=7.3, 5.0 Hz, 2 H) 7.96 (s, 1 H) MS (ESP) m/z= 451 [MH⁺] for C₂₃H₃₀N₈O₂

Example 220: 9-[4-(aminomethyl)benzyl]-2-butoxy- N-(2-morpholin-4-ylethyl)-9H-purin-6-amine

Scheme XLIII
To a solution of 4-({2-butoxy-6-[(2-morpholin-4-ylethyl)amino]-9-purin-9-yl}methyl)benzonitrile (Example 83) (95mg, 0.218mmol) in THF (4 ml) was added a solution of lithium aluminum hydride (0.436 ml, 0.436mmol) at room temperature. The reaction was completed in 2 hrs. The reaction was quenched by slow addition of methanol. After removing THF and methanol, the residue was extracted with ethyl acetate and washed with water. The aqueous phase was evaporated to obtain the crude product. The product was purified by reverse phase HPLC (Acetonitrile/Water /TFA). The product (80mg, 84% yield) was obtained as an oil.

**Example 221: LGDH Coupled Enzyme Assay**

Compounds were tested for inhibition of glutamate racemase using a coupled enzyme assay as previously described (Lundqvist et al, "Exploitation of structural and regulatory diversity in glutamate racemases" Nature, 2007, in press). Assays were performed in 96-well polystyrene flat-bottom black plates (FLUOTRAC 200) in 102 µl reactions containing 2 µl compound dissolved in dimethylsulfoxide, 85 µl Enzyme Working Solution (final concentrations were 100 mM Tris pH 8.0, 0.03 % PEG 8000, 0.03 mg/mL bovine serum albumin, 15 LVmL L-glutamate dehydrogenase (LGDH), 5 mM dithiothreitol, 10 mM NAD+...
and either 80 nM *E. faecalis* Murl or 100 nM *E. faecium* Murl or 1 uM *S. aureus* Murl) and 15 µl 6.67 mM D-glutamate to initiate the reaction (final concentration was 1 mM).

The proteins of interest were prepared as follows: *E. faecalis* Murl and *S. aureus* Murl were cloned into pET28b expression vector to allow expression of N-terminal histidine tagged protein. Each vector was co-transformed with a groESL expression vector (to facilitate proper folding) into *E. coli* strain BL21(DE3). Cultures were grown in LB medium containing 10µg/ml tetracycline and 50µg/ml kanamycin to mid-log phase. Induction was carried out overnight at room temperature in the presence of 500uM IPTG and 1mM D/L Glutamate.

*E. faecium* Murl was cloned into a modified pET28b expression vector. This protein contains an N-terminal histidine tag and was expressed in *E. coli* strain BL21(DE3) as follows: the culture was grown to mid-log phase in LB medium containing 25µg/ml kanamycin, then induced with 400uM IPTG for 2 hours at 37°C.

**S. aureus murl cloned in pET28b** (Thrombin cleaving his tag)

15

ATGGGCAGCGACATCATCATCATCATACACAGCCGCTGGTGGCGCGCGGCGGAGCATAT
GAATACAAAAATATGTTGTAATAGCCTGTTGCGAGGTGTTGACATGCTAAGAATA
TGGTCATGTTGCGCGATGATTATATTAGGTGATATGGGCATGGTCCATATGGG
CCAAAGACAAAGCGCGAATTACATACAGCTACAGTTTACATGGGACTAAGCAGG
ACGACTGAAATACACATATTACAGTCATGAGGACAGGCTGGTCCGAG
TTGTGGCCCTGGTAGAAGAAATGAGATATGATTTCTGGTGGACTAAGGCA
CAGCGCAGATTTATCATGGGACTATGACATGGGACTAAGGCA

20

TGGATATACAAATGTCGTGATTCGTTGTAATACCTGAAGATCTGTTAGTTGAGATGCTGATAC
AAAAAGACCTTATCAATCTCAGTGATTGGCGTAAATTGAGGATGCTGACCAGTT
TTGTGGCCCTGGTAGAAGAAATGAGATATGATTTCTGGTGGACTAAGGCA
CAGCGCAGATTTATCATGGGACTATGACATGGGACTAAGGCA

25

CAAAAGACCTTATCAATCTCAGTGATTGGCGTAAATTGAGGATGCTGACCAGTT
TTGTGGCCCTGGTAGAAGAAATGAGATATGATTTCTGGTGGACTAAGGCA
CAGCGCAGATTTATCATGGGACTATGACATGGGACTAAGGCA

**S. aureus murl cloned in pET28b** (Thrombin cleaving his tag)

30

MGSSHHHHHHSSGLVPRGSWMNKPIGVIGSVDGSSGGLVTVAEKIMQPLNETNYLGDIRCP
YGPRPGQVKQYTVEIARKLMEFDIKMLVLACNTATAVALEYLQKTLISVIGIVIEPGAR
TAIMTRNQVNLVLQTEGTIKSEAYRTHKKRINHPHEVHGAVCPFGVPLVEQMRSDPTICTSVIHQTLKRNNSEDSTVGLCTHPPLYKPYIDFYGKKTIVSSGETAREVSALLTFSNEHASYTEHPDHRRFATGDTTHITNIIKEWLNLSNVNVERISVND

35

**E. faecalis murl cloned in pET28b** (Thrombin cleaving his tag)

40

ATGGGCAGCGACATCATCATCATCATACACAGCCGCTGGTGGCGCGCGGCGGAGCATAT
GAGCAATCAAGAGACATTGATTAATGATCTGGTGCTGGAGTATACGTTTAAAGG
AAGCGCTAAAGCAATTACCAAATGAACGATTAATTTATTTAGGAGATACAGCCCGTTGCCCA
TATGGTCCACGACCAGCCGGACAAAGTCGTTCACTTTACCTTGGGAAATGCGCAGATTITTTATT
GAAAAACGAATAAAAAATGCCTAATACCGATTAATACCGCGAGCTGCACTATTAGAGAA
AAATTTAGCTCCCTGGCAATTACCCATTTAGCTGATTATTTAGCTTGGGCCACACGGAC

5 GTTAAAGTCACAAAAAATAACAAAAATTTGCTGTCATAGGTACCTTAAAGGACAAATACAGCC
TTCTTATGGAAAAACGCCAATTTAAAGGATAGCAGCAAGATGTTAGTTTTAGCTTGGCC
CTAAATTTGTCCCATTGGGAAATATCAATATCGTTCTCTCCGAGCAAAAAATTTGTC
GAGAAGCACTTCAAAGACTCAAATGAAAAGAGTTCTTGTGAGGATAGTTTTAGTGTGAAGCC
TTACCGGATTGATTTACCGGATTTGAGGTATTGTTAGTTAGCTGAATACAGGC

10 CAGGGACCCCAGACGTGGCACTAGCAGTCCTTCCGATTTAGTACCAGCAGACCAATG
GTGCAGAAACACAAAATAAACAAGTTGGCATTATCGATACGATTGGTACGGTAAAAAG
TCAATCTTATGAAAAAGCAGCTGAAAAAGGAAAGTACCAGAATTGACTGTGACAAGTCTTGCTT
GTCCAAAATTTGTTGCTATGAGAAATGCAATACCATTATCCTAGTGGGCAGAAAAATTT
GTGGCAGAACATTAGCCTCTTTAACACATATAAAAACATCAGTAACTTTTACGGATTGCAC
CCATATTACCCATATTACCGGGGATTCTTAAAATGTAATGGGAAATGTGCAATGCTAGT
ATTCTTGACAGAAACATAGTTGAAATCTATGCTGTTAGATTATTTCAATCTGAGCATT

15 MGSSHHHHHSHHSLVPRGSMSQNAEGILSDSVGGLTVKLAKELQPNERLIYLDGTAR
CPYGRPAEQWQFTWEMADFLKLKRIKMLVI ACNTATAVALEE IKAALPI PWGVILPG
ARAAAVKVTNNKIGVIGTGLTIKSYEIAISKAPAIEVSLCPKFPVIESYNRS
VAKKIVETLQLQLKLDLTLIGCTHYPPLRVIPQNMGSHTVLDSAGETVEVSML
DYFDIAHTPEAPTQPHFYTTGSAKMFEEIASSWLGIELKAIQLQLGNNED

20 E. faecium murl cloned in modified pET28b vector (Factor Xa cleavable his tag)

ATGGGCAGCAGCCATCATCATCATTACCGACACACGAGGAGATGATACG
ATTGACAGATAATCGCCAATCCCTAGTCACTAGATGTTAGGTGCGGCGTTGTAGCTAA

25 AAGAAGCCTTCCCAAAATAACCGGAAATGAAAAATATTATTATTGAGGAGACACGACACGCTGC
CCATATGCGCCCTAGACCCCGCAGAAACAGTTAATTACATGTTACTTGGGAAATGACGAGATTATCT
GGTGGACAGGAAATCAGATGCTGAGTAGCCTGCAATACCCGCAAACGCGTGGTGTCTTATAG
AAAGAAATCAAGAGCGTTCTCTTCTATTCATCGATATCCTGAGTGATCTCCCGCTGACTAGCCG
GCAGTAAAAAACACAAAAAATAAACAAGTTGGCAGATTCGATATTGCTGACATGGTAAAAAG

30 TCAAGCTTATGAAAAAGCAGCTGAAAAAGGAAAGTACCAGAATTGACTGTGACAAGTCTTGCTT
GTCCAAAATTTGTTGCTATGAGAAATGCAATACCATTATCCTAGTGGGCAGAAAAATTT
GTGGCAGAACATTAGCCTCTTTAACACATATAAAAACATCAGTAACTTTTACGGATTGCAC
CCATATTACCCATATTACCGGGGATTCTTAAAATGTAATGGGAAATGTGCAATGCTAGT
ATTCTTGACAGAAACATAGTTGAAATCTATGCTGTTAGATTATTTCAATCTGAGCATT

35 TCAACGCGAAAAATGGCGGACATTTGACGTCTGTCACATCTAAAATGACAACTACGAGTCT
GAGAAATAGCTGGAAGACTGCGTGGGAAGTCGACACTTTAATATGAAACATATCAGAATGGGAA
GAAAAATAA

40 MGSSHHHHHSHSSTGIEGRMLDNRPIGRFIDGSGVGLTWKEALQLPQNYLENLFVGDAT
RCYPGRPAEQWQFTWEMADFLKLKRIKMLVI ACNTATAVALEE IKAALPI PWGVILPG
GTRAAVKTQNKQVGI TGTVSKSAKEYKELKEVKPFLTVSLACPKFVSWESNEYHS
SVAKKIVETLQLQLKLDLTLIGCTHYPPLRVIPQNMGSHTVLDSAGETVEVSML
LDYFNLSNSPQNRCTLQFYTGGSAKLFEEIAEDWLIGHLNVEHIELGGK
Purification of E. faecalis Murl and E. faecium Murl and S. aureus Murl was carried out as follows. The frozen cell paste was resuspended in 50 ml of Lysis Buffer [20 mM Tris/HCl, pH 7.5, 5 mM DL-Glutamate, 1 EDTA-free protease inhibitor cocktail tablet (Roche Molecular Biochemical)]. Cells were disrupted by French press at 18,000 psi twice at 4°C, and the crude extract was centrifuged at 20,000 rpm (45Ti rotor, Beckman) for 30 minutes at 4°C. The supernatant was loaded at a flow rate of 2.0 ml/min onto a 5 ml HiTrap Ni²⁺ chelating column (GE Healthcare Lifebioscines) pre-equilibrated with Buffer A (20 mM Tris/HCl, pH 7.5, 5 mM DL-Glu). The column was then washed with Buffer A, and the protein was eluted by a linear gradient from 0 to 0.5 M Imidazole in Buffer A. Fractions containing Murl were pooled, and solid (NH₄)₂SO₄ (0.4 g/ml) was added to precipitate all the proteins and mixed on ice for 1 hour. The sample was centrifuged at 25,000 rpm for 30 min at 4°C (45Ti rotor, Beckman); the pellet was then dissolved in 9 ml of Buffer A. The 5 ml sample was applied at a flow rate of 1.0 ml/min to a 320 ml Sephacryl S-200 (HR 26/60) (GE Healthcare Lifebioscines) pre-equilibrated with Buffer A. The fractions containing Murl were pooled and dialyzed against 1 L Storage buffer (10 mM Tris/HCl, pH 7.5, 0.1 mM EGTA, 150 mM NaCl, 1 mM TCEP, 5 mM DL-Glu, 50% Glycerol). The protein was characterized by SDS-PAGE analysis and analytical LC-MS and judged to be at 95% purity. The protein was stored at -20°C.

The assay reactions were incubated at room temperature for 60 minutes. Plates were read using a Tecan Ultra plate reader (excitation wavelength 340 nm, emission wavelength 465 nm). Data were reported as the difference between the fluorescence reads at 60 and 0 minutes. Compound potency was based on IC₅₀ measurements determined from reactions performed in the presence of different compound concentrations. Assay artifacts due to insoluble compounds under assay conditions were assessed using nephelometry to measure turbidity. The limit of compound solubility was defined as the maximum concentration before a detectable increase in turbidity was observed by nephelometry.

The compounds of the invention described herein have a measured IC₅₀ in this assay against at least one isozyme of Murl (e.g., E. faecalis Murl, E. faecium Murl or S. aureus Murl) of <400 µM or the compounds inhibit the glutamate racemase reaction by >20% at the limit of their solubility in the assay medium.

Representative IC₅₀ values for E. faecalis Murl, E. faecium Murl or S. aureus Murl inhibition by the compounds of the instant invention is indicated in Table 9 below.
Table 9

<table>
<thead>
<tr>
<th>Ex. #</th>
<th>IC₅₀ <em>E. faecalis</em> Murl</th>
<th><em>E. faecium</em> Murl</th>
<th><em>S. aureus</em> Murl</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>1.98 µM</td>
<td>2.62 µM</td>
<td>&gt;400 µM</td>
</tr>
<tr>
<td>81</td>
<td>1.98 µM</td>
<td>2.71 µM</td>
<td>&gt;400 µM</td>
</tr>
<tr>
<td>79</td>
<td>4.11 µM</td>
<td>5.03 µM</td>
<td>&gt;400 µM</td>
</tr>
</tbody>
</table>

All publications, patent applications, patents, and other documents cited herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting in any way.
What we claim:

1. A compound represented by formula (I):

\[
\begin{array}{c}
\text{N} \\
\text{N} \\
\text{X}_3 \\
\text{X}_4 \\
\text{R}_3 \\
\text{R}_4
\end{array}
\]

(I)

or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein:

- \( X_i \) is a divalent C\(_{1-6}\)alkyl, a divalent C\(_{1-6}\)alkenyl or a divalent C\(_{1-6}\)alkynyl,
- the divalent alkyl, alkenyl or alkynyl may be optionally substituted with one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, \( =O, =S, =S(O), =N- \), amino, C\(_{1-4}\)alkylamino, and C\(_{1-4}\)dialkylamino;
- \( X_2 \) is -O-, -S-, or -NR\(^a\), wherein R\(^a\) is hydrogen or a C\(_{1-6}\)alkyl;
- \( X_3 \) is CR\(_{10}\) or N;
- R\(_i\) is a C\(_{3-14}\)carbocycle, morpholinyl, quinolinyl, benzodioxinyl, benzodioxolyl, 1-H-pyrazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 2-oxo-2,3-dihydro-1,3-benzoazolyl, tetrahydro-1H-pyran, 1-benzothiophenyl, furanyl, thiazolyl, isoxazolyl, or oxetanyl, wherein the carbocycle, morpholinyl, quinolinyl, benzodioxinyl, benzodioxolyl, 1-H-pyrazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 2-oxo-2,3-dihydro-1,3-benzoazolyl, tetrahydro-1H-pyran, 1-benzothiophenyl, furanyl, thiazolyl, isoxazolyl, and oxetanyl are optionally substituted on one or more carbon atoms with one or more R\(_5\); and wherein each \( =N- \) of the quinolinyl, pyrazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, thiazolyl, and isoxazolyl, may be each independently optionally substituted with an oxo; and wherein the -NH- of morpholinyl, 1-H-pyrazolyl, and 2-oxo-2,3-dihydro-1,3-benzoazolyl may be optionally substituted with R\(_{17}\);

- R\(_2\) is a C\(_{1-6}\)alkyl, C\(_{1-6}\)alkenyl, C\(_{1-6}\)alkynyl, C\(_{3-14}\)carbocycle, heterocycle, C\(_3\)

CarbocycleC\(_{1-6}\)alkyl, or heterocycleC\(_{1-6}\)alkyl, wherein the alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl may be optionally substituted on one or more carbon atoms with one or more R\(_6\), and wherein if R\(_2\) is a heterocycle or a heterocyclealkyl comprising one or more -S-, \( =N- \) or both, each -S- may be independently optionally substituted with one or two oxo groups and each \( =N- \).
may be independently optionally substituted with one oxo group; and wherein if R₂ is a heterocycle or a heterocycle-alkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R₈:

R₃ and R₄ are each, independently, hydrogen, C₆₆-alkyl, C₆_6-alkenyl, C₂₂-
6-alkynyl, C₃₆-4-carbocycle, heterocycle, C₃₆-alicyclic, or heterocyclo-C₁.
₆-alkyl, wherein the alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocycle-alkyl, or heterocyclo-alkyl may be optionally substituted on one or more carbon atoms with one or more R₇, and wherein if R₃ or R₄ is a heterocycle or a heterocycle-alkyl comprising one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₃ or R₄ is a heterocycle or a heterocycle-alkyl that contains one or more -NH-, each -NH- may be independently optionally substituted with R₉; or R₃ and R₄ taken together with the nitrogen atom to which they are attached form a heterocycle which may be optionally substituted on one or more carbon atoms with one or more R₇, wherein if the heterocycle comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with R₉;

R₅, R₆ and R₇, for each occurrence, are independently selected from the group consisting of a halo, nitro, cyano, C₆₆-alkyl, C₆₆-alkenyl, C₆₆-alkynyl, C₃₆-4-carbocycle, heterocycle, C₃₆-carbocycle-C₄₆-alkyl, heterocycle-C₄₆-alkyl, C₆₆-haloalkyl, -ORn, -SR₁, -NR₂R₃, -C(O)R₁, -C(O)OR₁, -C(O)NR₂R₃, -NR₂C(O)R₁, -OC(O)R₁, -NR₂C(O)OR₁, -OC(O)NR₂R₃, -NR₂C(O)NR₂R₃, -NR₂C(NR₄)NR₂R₃, -S(O)(P)R₁, -NR₁S(O)(P)R₁, and -S(O)(P)NR₂R₃, wherein if R₅, R₆ or R₇ is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocycle-alkyl, or heterocyclo-alkyl, it may be optionally further substituted on one or more carbon atoms with one or more R₈; and wherein if R₅, R₆ or R₇ is a heterocycle or a heterocycle-alkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₅, R₆ or R₇ is a heterocycle or a heterocycle-alkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R₉;
Rs, R₉, or Ri₉, for each occurrence, are independently selected from the group consisting of C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₈ carbocycle, heterocycle, C₃₋₈ carbocycleCi-₆ alkyl, heterocycleCi-₆ alkyl, Ci-₆ haloalkyl, -C(O)Rn, -C(O)ORn, -C(O)NRi₂R₉, -S(O)pRₙ, and -S(O)ₚNRi₆Rₙ, wherein if R₈, R₉ or R₁₇ is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be optionally substituted on one or more carbon atoms with one or more Ri₆; and wherein if R₈, R₉ or R₁₇ is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₈, R₉ or R₁₇ is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R₁₆;

Rio is hydrogen, a C₁₋₆ alkyl, a heterocycleCi-₆ alkyl, -NRi₂R₉, -C(O)Rn, -C(O)ORn, -C(O)NRi₂R₁₃, -NRnC(O)Rn, -OC(O)Rn, -NRnC(O)ORn, -OC(O)NRi₂R₁₃, -NRnC(NRi₄)NRi₂R₁₃, -S(O)pRₙ, -NRnS(O)pRₙ, and -S(O)pNRi₂R₁₃;

Rₙ, for each occurrence, is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₈ carbocycle, heterocycle, C₃₋₈ carbocycleCi-₆ alkyl, heterocycleCi-₆ alkyl, wherein if Rₙ is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more Ri₅, and wherein if Rₙ is heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if Rₙ is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with R₁₆;

Ri₂ and Ri₃, for each occurrence, are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₈ carbocycle, heterocycle, C₃₋₈ carbocycleCi-₆ alkyl, heterocycleCi-₆ alkyl, wherein if Ri₂ or Ri₃ is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more Ri₅, and wherein if Ri₂ or Ri₃ is heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or more Ri₅.
substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R12 or Rn is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6; or R12 and Rn taken together with the nitrogen atom to which they are attached for a heterocycle, wherein the heterocycle may be optionally substituted on one or more carbon atoms with one or more Ri5, and wherein if the heterocycle comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6;

Ri5, for each occurrence, is independently selected from the group consisting of halo, nitro, cyano, Ci.6alkyl, C2-6alkenyl, C2-6alkynyl, C3.4carbocycle, heterocycle, Cs-ncarbocycleCi-oalkyl, heterocycleCi-6alkyl, Ci-6haloalkyl, -ORis, -SRis, -NR1gR20, -C(O)Ri8, -C(O)ORi8, -C(O)NRi8R20, -NRi8C(O)Ri8, -OC(O)Ri8, -NRi8C(O)ORi8, -OC(O)NRi8R20, -NRi8C(O)NRi8R20, -NRi8C(NRi4)NRi8R20, -S(O)pRi8, -NRi8S(O)pRi8, and -S(O)pNRi8R20;

Ri4 and R21, for each occurrence, are independently selected from the group consisting of hydrogen, a C1.6alkyl, nitro, cyano, amino, alkylamino, dialkylamino, or hydroxy;

Ri6, for each occurrence, is independently selected from the group consisting of C1.6alkyl, C2.6alkenyl, C2.6alkynyl, C3.4carbocycle, heterocycle, C3.14carbocycleC6alkyl, heterocycleCi-ealkyl, Ci.6haloalkyl, -C(O)Ri8, -C(O)ORi8, -C(O)NRi8R20, -S(O)pRi8, and -S(O)pNRi8R20;

Ri8, for each occurrence, is independently selected from the group consisting of hydrogen, C1.4alkyl, C2.6alkenyl, C2.6alkynyl, C3.4carbocycle, heterocycle, C3.14carbocycleC1.6alkyl, heterocycleC1.6alkyl;

Ri9 and R20, for each occurrence, are independently selected from the group consisting of hydrogen, C1.6alkyl, C2.6alkenyl, C2.6alkynyl, C3.4carbocycle, heterocycle, C3.14carbocycleC1.6alkyl, heterocycleC1.6alkyl; or Ri9 and R20 taken together with the nitrogen atom to which they are attached for a heterocycle; and p is 1 or 2,

provided that Ri is not an unsubstituted phenyl, unsubstituted biphenyl, an unsubstituted cyclopropyl, or 3-cyclopentyloxy-4-methoxyphenyl;
provided that when \( R_1 \) is 4-chlorophenyl, 4-fluorophenyl, cyclohexyl, or furanyl, \( R_2 \) is not unsubstituted naphthyl or unsubstituted cyclopentyl;

provided that when \( R_1 \) is morpholinyl, one of \( R_3 \) and \( R_4 \) are not 4-aminobenzyl or phenylethyl;

provided that when \( X_2 \) is -\( \text{NR} \)\( \text{a} \), \( R_2 \) is a \( C_{1-6} \text{alkyl} \) which is optionally substituted with on one or more carbon atom with one or more \( R_6 \), and \( R_1 \) is not 4-aminophenyl, 2-chlorophenyl, 4-methylphenyl, 3-(methoxycarbonylmethyl)-phenyl, 2-fluorophenyl, or 2,6-difluorophenyl;

provided that when -\( X_2 \)-\( R_2 \) is methylsulfanyl, \( R_1 \) is not 4-methylphenyl, 2-methoxyphenyl, or 2-fluorophenyl;

provided that when -\( X_2 \)-\( R_2 \) is an unsubstituted \( n \)-butyloxy, \( R_1 \) is not 3-(2-methoxy-2-oxoethyl)-phenyl, 3-cyanomethyl-phenyl, 3-chloromethyl-phenyl, 3-hydroxymethyl-phenyl, 4-benzoyloxyphenyl, 3-cyanomethyl-4-fluoro-phenyl, 3-chloromethyl-4-fluoro-phenyl, 3-hydroxymethyl-4-fluoro-phenyl, 3-methoxycarbonyl-4-fluoro-phenyl, 2-methoxy-5-cyanomethyl-phenyl, 2-methoxy-5-chloromethyl-phenyl, 2-methoxy-5-hydroxymethyl-phenyl, 2-methoxy-5-methoxycarbonyl-phenyl, 3,4-di-(methoxycarbonyl)-phenyl, 4-hydroxyphenyl, or 3-(1,1,2-trimethoxy-2-oxoethyl)-phenyl; and

provided that when -\( X \)-\( R_2 \) is an unsubstituted \( n \)-butyloxy and -\( \text{NR} \)\( \text{a} \)\( \text{R} \) is -\( \text{NH} \)\( \text{a} \), \( R_1 \) is not 3-methoxycarbonyl-phenyl or 4-acetoxyphenyl.

2. A compound represented by formula (II):

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R_3 N R_4
\( \text{N} \)
R_2 X_4
\( \text{N} \)
X_3
\( \text{N} \)
R_22
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or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein:

\( X_3 \) is \( \text{CR} \)\( \text{a} \) or \( \text{N} \);

\( X_4 \) is -\( \text{O} \)- or -\( \text{S} \)-;

\( R_2 \) is a \( C_{1-6} \text{alkyl} \), \( C_{6} \text{alkenyl} \), \( C_{6} \text{alkynyl} \), \( C_3 \text{i4carbocycle} \), \( \text{heterocycle} \), \( C_3 \text{i4carbocycle} C_{1-6} \text{alkyl} \), or \( \text{heterocycle} C_{1-6} \text{alkyl} \), wherein the alkyl, alkenyl, alkynyl,
carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl may be optionally substituted on one or more carbon atoms with one or more R₆, and wherein if R₂ is a heterocycle or a heterocyclealkyl comprising one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₂ is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with Rs;

R₃ and R₄ are each, independently, hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₅₋₁₀carbocycle, heterocycle, C₃₋₁₄carbocycleC₆₋₁₀alkyl, or heterocycloC₆₋₁₀alkenyl, wherein the alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl may be optionally substituted on one or more carbon atoms with one or more R₇, and wherein if R₃ or R₄ is a heterocycle or a heterocyclealkyl comprising one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R₃ or R₄ is a heterocycle or a heterocyclealkyl that contains one or more -NH-, each -NH- may be independently optionally substituted with R₉; or R₃ and R₄ taken together with the nitrogen atom to which they are attached form a heterocycle which may be optionally substituted on one or more carbon atoms with one or more R₇, wherein if the heterocycle comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with R₉;

R₂₂ is a C₃₋₆alkyl which is optionally substituted on one or more carbon atom

with one or more substituents selected from the group consisting of halo, nitro, cyano, -OR, -SR, -NR, -C(O)R, -C(O)OR, -C(O)NR, -OC(O)R, -OC(O)OR, -OC(O)NR, -NR, -C(NR)NR, -N=C=N-, -C≡N, -C=N-, -S-, -SO₂-, -SO₂R, -SO₂R, -C₆H₄, -R, and -SO₂R NR R;

R₅ and R₇, for each occurrence, are independently selected from the group consisting of a halo, nitro, cyano, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₁₀carbocycle, heterocycle, C₃₋₁₄carbocycleC₁₋₆alkyl, heterocycloC₁₋₆alkyl, C₁₋₆haloalkyl, -OR, -SR, -NR, -C(O)R, -C(O)OR, -C(O)NR, -OC(O)R, -OC(O)OR, -OC(O)NR, -NR, -C(NR)NR, -N=C=N-, -C≡N, -C=N-, -S-, -SO₂-, -SO₂R, -SO₂R, -C₆H₄, -R, and -SO₂R NR R.
S(O)pRn, -NRiiS(O)pRn, and -S(O)pNRi2Ri3, wherein if R6 or R7 is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be optionally further substituted on one or more carbon atoms with one or more Ri5; and wherein if R6 or R7 is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R6 or R7 is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6;  

Rs or R9, for each occurrence, are independently selected from the group consisting of C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-4 carbocycle, heterocycle, C3-4 carbocycleCi-6 alkyl, heterocycleCi-6 alkyl, Ci-6 haloalkyl, -C(O)Rn, -C(O)ORn, -C(O)NRi2Ri3, -S(O)pRn, and -S(O)pNRi2Ri3, wherein if R8 or R9 is alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be optionally substituted on one or more carbon atoms with one or more Ri5; and wherein if R8 or R9 is a heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if R8 or R9 is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6;  

Rio is hydrogen, a C1-6 alkyl, a heterocycleC1-6 alkyl, -NRi2Rn, -C(O)Rn, -C(O)ORn, -C(O)NRi2Ri3, -NRnC(O)Rn, -OC(O)Rn, -NRnC(O)ORn, -OC(O)NRi2Ri3, -NRnC(NRi4)NRi2Ri3, -S(O)pRn, -NRnS(O)pRn, and -S(O)pNRi2Ri3;  

Rn, for each occurrence, is independently selected from the group consisting of hydrogen, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-4 carbocycle, heterocycle, C3-4 carbocycleCi-6 alkyl, heterocycleCi-6 alkyl, wherein if Rn is an alkyl, alkenyl, alkynyl, carbocycle, heterocycle, carbocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more Ri5 and wherein if Rn is heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if Rn is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6;
Ri2 and Rn, for each occurrence, are independently selected from the group consisting of hydrogen, Ci_6 alkyl, C_2-6 alkenyl, C_2-6 alkynyl, C_3-14 carbocycle, heterocycle, C_3-14 carbocycleC_7 alkyl, heterocycleC_7 alkyl, wherein if Ri2 or Ri3 is an alkyl, alkenyl, alkynyl, or heterocyclealkyl, or heterocyclealkyl, it may be independently optionally substituted on one or more carbon atom with one or more Ri5, and wherein if Ri2 or Rn is heterocycle or a heterocyclealkyl that comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if Ri2 or Rn is a heterocycle or a heterocyclealkyl that comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6; or Ri2 and Rn taken together with the nitrogen atom to which they are attached for a heterocycle, wherein the heterocycle may be optionally substituted on one or more carbon atoms with one or more Ri5, and wherein if the heterocycle comprises one or more -S-, =N- or both, each -S- may be independently optionally substituted with one or two oxo groups and each =N- may be independently optionally substituted with one oxo group; and wherein if the heterocycle comprises one or more -NH-, each -NH- may be independently optionally substituted with Ri6;

Ri5, for each occurrence, is independently selected from the group consisting of halo, nitro, cyano, C_1-6 alkyl, C_2-6 alkenyl, C_2-6 alkynyl, C_3-14 carbocycle, heterocycle, C_3-14 carbocycleC_7 alkyl, heterocycleC_7 alkyl, C_1-6 haloalkyl, -OR_i, -SR_i, -NR19R20, -C(O)R_i, -C(O)OR_i, -C(O)NRi gR20, -NRi gC(O)NRi gR20, -OC(O)NRi gR20, -NRi gC(NR2_i)NRi gR20, -S(O)pRi g, and -S(O)pNRi gR20;

Ri4 and R_21, for each occurrence, are independently selected from the group consisting of hydrogen, a C_1-6 alkyl, nitro, cyano, amino, alkylamino, dialkylamino, or hydroxy;

R_16, for each occurrence, is independently selected from the group consisting of C_1-6 alkyl, C_2-6 alkenyl, C_2-6 alkynyl, C_3-14 carbocycle, heterocycle, C_3-14 carbocycleC_7 alkyl, heterocycleC_7 alkyl, C_1-6 haloalkyl, -C(O)R_i, -C(O)OR_i, -C(O)NRi gR20, -S(O)pRi g, and -S(O)pNRi gR20;

R_i8, for each occurrence, is independently selected from the group consisting of hydrogen, C_1-6 alkyl, C_2-6 alkenyl, C_2-6 alkynyl, C_3-14 carbocycle, heterocycle, C_3-14 carbocycleC_7 alkyl, heterocycleC_7 alkyl;
R₁₉ and R₂₀, for each occurrence, are independently selected from the group consisting of hydrogen, Cᵢ₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₄carbocycle, heterocycle, C₃₋₄carbocycleCi-₆alkyl, heterocycleCi-₆alkyl; or Rᵢ₉ and Rᵢ₂₀ taken together with the nitrogen atom to which they are attached for a heterocycle; and

p is 1 or 2,

provided that when both R₃ and R₄ are hydrogen, R₂ and R₂₂ are not both n-hexyl or both n-propyl, or R₂₂ is not n-propyl and R₂ is not methyl; and

provided that when R₂ is methyl, R₃ and R₄ taken together with the nitrogen atom to which they are attached are not a substituted or unsubstituted piperazino.

3. The compound of Claim 1, wherein Rᵢ is a C₃₋₄carbocycle which is optionally substituted on one or more carbon atoms with one or more independently selected R₅.

4. The compound of Claim 1 or 3, wherein Rᵢ is phenyl which is optionally substituted with one or more independently selected R₅.

5. The compound of Claim 1 or 3, wherein Rᵢ is morpholiny which is optionally substituted on one or more carbon atom with one or more independently selected R₅ and which is optionally substituted on the nitrogen atom with Rₙ.

6. The compound of Claim 1 or 3, wherein Rᵢ is benzodioxinyl or benzodioxolyl, which can be optionally substituted on one or more carbon atom with one or more independently selected R₅.

7. The compound of Claim 1 or 3, wherein Rᵢ is quinolinyl which is optionally substituted with one or more independently selected R₅ and which is optionally substituted on the nitrogen atom with an oxo.

8. The compound of any one of Claims 1 and 3 through 7, wherein R₅, for each occurrence, is independently selected from the group consisting of nitro, methoxy, methyl, fluoro, chloro, bromo, cyano, trifluoromethyl, acetyl, but-2-en-1-yloxy, methoxycarbonyl, methylsulfonyl, carbamoyl, pent-2-yn-1-yloxy, ethoxycarbonyl, carboxy, ethyl, carboxymethoxy, hydroxymethyl, acetoxy, amino, 2-carboxyphenyl,
The compound of Claim 1 or 5, wherein Rn, for each occurrence, is independently selected from the group consisting of C1-4 alkyl, benzyl, acetyl, C1-4 alkoxycarbonyl, carbamoyl, N-C1-4 alkylcarbamoyl, N,N-C1-4 dialkylcarbamoyl, C1-4 alkylsulfonyl.

10. The compound of Claim 2, wherein R2 is an unsubstituted C1-6 alkyl group.

11. The compound of Claim 2, wherein R2 is propyl, butyl, 2,3-dihydroxy-propyl, 3-cyanopropyl, 2-methyl-propyl, 3-phenoxy-2-hydroxy-propyl, 2-hydroxy-2-methyl-propyl, 2-hydroxy-3-methoxy-propyl, 4,4,4-trifluoro-butyl, 2-hydroxybutyl, 2-ethylbutyl, 4-cyanobutyl, or isopentyl.

12. The compound of any one of Claims 1 and 3 through 9, wherein Xi is -CH2-.

13. The compound of any one of Claims 1 and 3 through 11, wherein Xi is -C(O)CH2-, -CH2C(O)-, -C(O)-, -CH(OH)CH2-, or -CH2CH2-.

14. The compound of any one of Claims 1, 3 through 9, 12 and 13, wherein X2 is -O-.

15. The compound of any one of Claims 1, 3 through 9, 12 and 13, wherein X2 is -S-.

16. The compound of any one of Claims 1, 3 through 9, 12 and 13, wherein X2 is -NRa-.

17. The compound of Claim 2, 10 or 11, wherein X4 is -O-.

18. The compound of Claim 2, 10, or 11, wherein X4 is -S-.

19. The compound of any one of Claims 1 through 18, wherein R2 is C1-6 alkyl which is optionally substituted on one or more carbon atoms with one or more R6.
20. The compound of Claim 19, wherein R is a C<sub>1-6</sub> alkyl selected from the group consisting of methyl, ethyl, n-propyl, n-butyl, n-pentyl, isobutyl, isopentyl, and 2-methylbutyl, wherein the Cl-6alkyl may be optionally substituted on one or more carbon atom with one or more R<sub>α</sub>.

21. The compound of any one of Claims 1 through 15, 17 and 18, wherein R<sub>2</sub> is cyclopentyl, cyclohexyl, piperidinyl, decahydronaphthalenyl, phenyl, but-2-en-1-yl, pent-2-yn-1-yl, but-2-yn-1-yl, or phenyl.

22. The compound of Claim 19, 20, or 21 wherein R<sub>α</sub>, for each occurrence, is independently selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxy, methyl, 7N,7N-dimethylamino, acetamido, fluoro, hydroxy, phenyl, and methylsulfonyl.

23. The compound of any one of Claims 1 through 22, wherein R<sub>3</sub> and R<sub>4</sub> are hydrogen.

24. The compound of any one of Claims 1 through 22, wherein one of R<sub>3</sub> or R<sub>4</sub> is hydrogen and the other is methyl, n-butyl, morpholinoethyl, (furan-3-yl)-methyl, (5-methyl-furan-2-yl)-methyl, benzyl, 2,6-difluorobenzyl, cyclopropyl, 2-phenyl-cyclopropyl, or benzoimidazol-2-yl.

25. The compound of any one of Claims 1 through 22, wherein R<sub>3</sub> or R<sub>4</sub> are both methyl or R<sub>3</sub> and R<sub>4</sub> together with the nitrogen atom to which they are attached form morpholino.

26. The compound any one of Claims 1 through 25, wherein X<sub>3</sub> is CR<sub>10</sub>.

27. The compound of Claim 26, wherein R<sub>0</sub> is H.

28. The compound of Claim 26, wherein R<sub>0</sub> is selected from the group consisting of 2-piperizino-ethylamino, 2-(4-methyl-piperazino)-ethylamino, 2-morpholino-
ethylamino, 2-hydroxyethylamino, 2-(diethylamino)ethylamino, morpholino, piperazine, methyl, carboxy, and ethoxycarbonyl.

29. The compound of any one of Claims 1 through 25, wherein $X_3$ is N.

30. The compound of Claim 1, wherein the compound is selected from the group consisting of:

2-(butylthio)-9-(3-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[3-(trifluoromethyl)benzyl]-9H-purin-6-amine;
2-(butylthio)-9-(3-chlorobenzyl)-9H-purin-6-amine;
3-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]benzonitrile;
2-(butylthio)-9-(3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,4-dichlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-methoxy-5-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-chloro-4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,6-dichlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-chloro-5-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,6-difluorobenzyl)-9H-purin-6-amine;
methyl 3-[[6-amino-2-(butylthio)-9H-purin-9-yl]methyl]benzoate;
2-(butylthio)-9-(4-chloro-2-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[2-fluoro-6-(trifluoromethyl)benzyl]-9H-purin-6-amine;
2-(butylthio)-9-(3-methoxybenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-fluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[4-(methylsulfonyl)benzyl]-9H-purin-6-amine;
2-(butylthio)-9-(4-methoxy-3-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-[[4-chloro-2-(trifluoromethyl)quinolin-6-yl]methyl]-9H-purin-6-amine;
2-(butylthio)-9-(2-chloro-5-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,4-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(4,5-dimethoxy-2-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(5-chloro-2-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-chloro-2,6-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-dimethoxybenzyl)-9H-purin-6-amine;
2-(butylthio)-9-{2-[(phenylsulfonyl)methyl]benzyl}-9H-purin-6-amine;
2-(butylthio)-9-(4-fluoro-3-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(4-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,4-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,5-difluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-chlorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-chloro-4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-nitrobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3-chloro-4-fluorobenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-dimethylbenzyl)-9H-purin-6-amine;
2-{{[6-amino-2-(butylthio)-9H-purin-9-yl]methyl}benzonitrile;
4-{{[6-amino-2-(butylthio)-9H-purin-9-yl]methyl}benzonitrile;
9-(4-bromo-2-fluorobenzyl)-2-(butylthio)-9H-purin-6-amine;
2-(butylthio)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(2,5-dichlorobenzyl)-9H-purin-6-amine;
methyl 4-{{[6-amino-2-(butylthio)-9H-purin-9-yl]methyl}-3-methoxybenzoate;
2-(butylthio)-9-(3-fluoro-4-methylbenzyl)-9H-purin-6-amine;
2-(butylthio)-9-(3,5-dimethoxybenzyl)-9H-purin-6-amine;
9-(3-chloro-2,6-difluorobenzyl)-(2-morpholin-4-ylethyl)-2-(4,4,4-
trifluorobutoxy)-9H-purin-6-amine;
2-(butylthio)-9-(2,3-dichlorobenzyl)-9 \textit{H}-purin-6-amine;
2-(butylthio)-9-[5-(chloro-1-benzothien-3-yl)methyl]-9 \textit{H}-purin-6-amine;
2-(butyl)[9-(3-chloro-2,6-difluorobenzyl)-6-{(2-morpholin-4-ylethyl)amino}]-9 \textit{H}-purin-2-yl amino)ethanol;
2-butoxy-9-(2,3-dichlorobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-[4-(methylsulfonyl)benzyl]-7\textit{V}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(2-methoxy-5-nitrobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
3-({2-butoxy-6-{(2-morpholin-4-ylethyl)amino}]-9 \textit{H}-purin-9-yl}methylbenzonitrile;
9-(5-amino-2-methoxybenzyl)-2-butoxy- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
9-(2,6-difluorobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-2-phenoxy-9 \textit{H}-purin-6-amine;
5-(butylthio)-3-(3-chloro-2,6-difluorobenzyl)-3 \textit{H}[^{1,2,3}]{triazolo}[4,5-\textit{a}]pyrimidin-7-amine;
5-(butylthio)-3-(2,6-difluoro-3-methylbenzyl)-3 \textit{H}[^{1,2,3}]{triazolo}[4,5-\textit{a}]pyrimidin-7-amine;
5-(butylthio)-3-(2,6-difluorobenzyl)-3 \textit{H}[^{1,2,3}]{triazolo}[4,5-\textit{a}]pyrimidin-7-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzyl)- \textit{N}-(2-morpholin-4-ylethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzyl)- \textit{N}-(pyridin-3-ylmethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzyl)- \textit{N}-(3-furylmethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzyl)- \textit{N}-(furylmethyl)-9 \textit{H}-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzyl)- \textit{N}-(3-furylmethyl)-9 \textit{H}-purin-6-amine;
4-({2-butoxy-6-{(2-morpholin-4-ylethyl)amino}]-9 \textit{H}-purin-9-yl}methylbenzonitrile;
2-(butylthio)- \textit{N},9-bis(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-(cyclopropylmethoxy)-9-[3-(trifluoromethyl)benzyl]-9 \textit{H}-purin-6-amine;
2-(cyclopentylmethoxy)-9- [3-(trifluoromethyl)benzyl]-9 \textit{H}-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-(pentyloxy)-9 \textit{H}-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-[(3-methylcyclopentyl)oxy]-9 \textit{H}-purin-6-amine;
2-(benzyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9 \textit{H}-purin-6-amine;
2-(cyclobutylmethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(cyclopentyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
2-(1-cyclopropylethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-[(1-methylcyclopropyl)methoxy]-9H-purin-6-amine;
2-(cyclopropylmethoxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-methoxy-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-propoxy-9H-purin-6-amine;
2-(cyclohexyloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-isobutoxy-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-N₂,N²-dimethyl-9H-purine-2,6-diamine;
N-(2-[(6-amino-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-2-yl)oxy]ethyl)acetamide;
9-(2,6-difluoro-3-methylbenzyl)-2-[(4,4,5,5,5-pentafluoropentyl)oxy]-9H-purin-6-amine;
2-[[6-amino-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-2-yl](methyl)amino]ethanol;
9-(2,6-difluoro-3-methylbenzyl)-2-(4,4,4-trifluorobutoxy)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-(piperidin-4-yloxy)-9H-purin-6-amine;
2-(decahydro-naphthalen-2-yloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine / 2-(decahydronaphthalen-1-yloxy)-9-(2,6-difluoro-3-methylbenzyl)-9H-purin-6-amine;
N₂-buty1-9-(2,6-difluoro-3-methylbenzyl)-N⁵-(2-morpholin-4-ylethyl)-N₂-propyl-9H-purine-2,6-diamine;
N₂-buty1-9-(2,6-difluoro-3-methylbenzyl)-N⁵-(2-morpholin-4-ylethyl)-9H-purine-2,6-diamine;
2-butoxy-9-[[3-(trifluoromethyl)benzyl]-9H-purin-6-amine;
3-[(6-amino-2-butoxy-9H-purin-9-yl)methyl]benzoic acid;
2-butoxy-9-(2,6-difluorobenzyl)-9H-purin-6-amine;
2-butoxy-9-(2,6-difluorobenzyl)-N,N-dimethyl-9H-purin-6-amine;
N₂-buty1-9-(2,6-difluorobenzyl)-9H-purine-2,6-diamine;
2-butoxy-9-(2,6-difluorobenzyl)-N-methyl-9H-purin-6-amine;
2-butoxy-9-(2-butoxy-6-fluorobenzyl)-N-methyl-9H-purin-6-amine;
2-(cyclopropylmethoxy)-9-[2-(cyclopropylmethoxy)-6-fluorobenzyl]- N-methyl-9H-purin-6-amine;
9-(2,6-difluorobenzyl)-N-methyl-2-[2-(methylsulfonyl)ethoxy]-9 H-purin-6-amine;
9-(2,6-difluorobenzyl)-N-methyl-2-(2-methylbutoxy)-9 H-purin-6-amine;
2-(cyclobutylmethoxy)-9-(2,6-difluorobenzyl)- N-methyl-9 H-purin-6-amine;
9-(2,6-difluorobenzyl)-N-methyl-2-(pentyloxy)-9 H-purin-6-amine;
2-(cyclopentylxoy)-9-(2,6-difluorobenzyl)- N-methyl-9 H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)- N-ethyl-9H-purin-6-amine;
N-benzyl-2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-9 H-purin-6-amine;
N-benzyl-9-(2,6-difluoro-3-methylbenzyl)-2-(pentyloxy)-9 H-purin-6-amine;
2-butoxy-N-cyclopropyl-9-(2,6-difluoro-3-methylbenzyl)-9 H-purin-6-amine;
2-(butylthio)-9-[2-(6-difluorophenyl)acetyl]-9 H-purin-6-amine;
2-(butylthio)-9-(2,6-difluorobenzoyl)-9 H-purin-6-amine;
2-butoxy-9-(3-chloro-2,6-difluorobenzoyl)- N-(2-morpholin-4-ylethyl)-9 H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzoyl)\ -N-(2-morpholin-4-ylethyl)-9 H-purin-6-amine;
l-[6-amino-2-(butylthio)-9 H-purin-9-yl]-2-(2,6-difluorophenyl)ethanol;
3-\{(2-butoxy-6-{[2-morpholin-4-ylethyl]amino})-1-oxido-9 H-purin-9-yl\}methylbenzamide;
3-{(2-butoxy-6-{[2-morpholin-4-ylethyl]amino}]-9 H-purin-9-yl}methylbenzamide;
2-\{{[6-amino-2-(butylthio)-9 H-purin-9-yl}methyl]-4-nitrophenol;
4-{(2-butoxy-6-{[2-morpholin-4-ylethyl]amino}]-1-oxido-9 H-purin-9-yl}methylbenzamide;
4-{(2-butoxy-6-{[2-morpholin-4-ylethyl]amino}]-9 H-purin-9-yl}methylbenzamide;
l-[4-{(2-butoxy-6-{[2-morpholin-4-ylethyl]amino}]9H-purin-9-yl}methyl]phenyl\_etheranone;
2-butoxy-9-(2,6-difluorobenzyl)-8-methyl-9 H-purin-6-amine;
2-butoxy-9-(2,6-difluorobenzyl)- N\(^8\)-(2-morpholin-4-ylethyl)-9 H-purine-6,8-diamine;
2-butoxy-9-(2,6-difluorobenzyl)-8-(4-methylpiperazin-1-yl)-9 H-purin-6-amine;
2-butoxy-N\(^8\)-[2-(diethylamino)ethyl]-9-(2,6-difluorobenzyl)-9 H-purine-6,8-diamine;
2-\{[6-amino-2-butoxy-9-(2,6-difluorobenzyl)-9 H-purin-8-yl]amino\}ethanol;
2-butoxy-9-(2,6-difluorobenzyl)-8-morpholin-4-yl-9 H-purin-6-amine;
2-butoxy-9-(2,6-difluorobenzyl)-N\(^8\)-(2-(4-methylpiperazin-1-yl)ethyl)-9\(^H\)-purine-6,8-diamine;
2-butoxy-9-(2-fluoro-6-{[2-(4-methylpiperazin-1-yl)ethyl]amino}benzyl)-N\(^8\)-(2-(4-methylpiperazin-1-yl)ethyl)-9\(^H\)-purine-6,8-diamine;
2-butoxy-9-(2,6-difluorobenzyl)-N\(^8\)-(2-piperazin-1-ylethyl)-9\(^H\)-purine-6,8-diamine;
2-butoxy-N\(^8\)-(2-morpholin-4-ylethyl)-9-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-N\(^8\)-[(5-methyl-2-furyl)methyl]-9-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(2,3-difluorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-N\(^8\)-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetrafluorobenzyl)-9\(^H\)-purine-6-amine;
9-[3,5-bis(trifluoromethyl)benzyl]-2-butoxy-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-N\(^8\)-(2-morpholin-4-ylethyl)-9-(2,3,4,5-tetrafluorobenzyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(3,4-difluorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(2,5-dichlorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-7\(^H\)-(2-morpholin-4-ylethyl)-9-[4-(trifluoromethyl)benzyl]-9\(^H\)-purine-6-amine;
2-butoxy-9-(2,6-dichlorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(2,4-difluorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(2-chlorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-[2-chloro-5-(trifluoromethyl)benzyl]-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
9-(4-bromo-2-fluorobenzyl)-2-butoxy-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-[2-fluoro-4-(trifluoromethyl)benzyl]-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(3-chloro-2-fluorobenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(4-ethylbenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(2-fluoro-6-methylbenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-(4-fluoro-3-methylbenzyl)-N\(^8\)-(2-morpholin-4-ylethyl)-9\(^H\)-purine-6-amine;
2-butoxy-9-[3-(2-fluorophenoxy)benzyl]-7\text{H}-purin-6-amine;
9-(1,3-benzodioxol-5-ylmethyl)-2-butoxy-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
2-butoxy-9-[3-chloro-2-fluoro-5-(trifluoromethyl)benzyl]-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
2-butoxy-9-[3-(4-fluorophenoxy)benzyl]-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
2-butoxy-9-[3-fluoro-2-(trifluoromethyl)benzyl]-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
2-butoxy-9-(2,3-dichlorobenzyl)-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
methyl 4-({2-butoxy-6-[\text{2-butoxy-9-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-}

2-butoxy-7\text{H}-purin-6-amine;
[4-({2-butoxy-6-[\text{2-butoxy-9-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-}

2-butoxy-\textit{N}-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetrafluoro-4-methylbenzyl)-9\text{H}-purin-6-amine;
2-butoxy-9-(4-chloro-2-nitrobenzyl)-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
2-butoxy-9-(2-methyl-3-nitrobenzyl)-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
9-[(1-bromo-2-naphthyl)methyl]-2-butoxy-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
2-butoxy-9-[6-fluoro-4\text{H}-1,3-benzodioxin-8-yl]methyl]-\textit{N}-(2-morpholin-4-ylethyl)-9\text{H}-purin-6-amine;
\textit{N}-(4-[({2-butoxy-6-[\text{2-butoxy-9-(2-morpholin-4-ylethyl)amino]-9\text{H}-purin-9-}

2-butoxy-\textit{N}-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetrafluoro-4-methylbenzyl)-9\text{H}-purin-6-amine;
2-butoxy-9-(4-bromobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(3-chlorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,5,6-tetramethylbenzyl)-9H-purin-6-amine;
2-butoxy-9-(2-fluoro-6-nitrobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(5-methyl-2-nitrobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-(2-bromo-5-methoxybenzyl)-2-butoxy-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(2,5-dimethoxybenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(2,4-dichlorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(3-methoxybenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-{4-[(E)-2-phenylvinyl]benzyl}-9H-purin-6-amine;
2-butoxy-9-(2,4,6-triisopropylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(2,3,5-trifluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(2,3-dimethoxybenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-9-(2-chloro-6-fluorobenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-butoxy-7V-(2-morpholin-4-ylethyl)-9-{4-[[(E)-2-phenylvinyl]benzyl]}-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,4,6-triisopropylbenzyl)-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,5-trifluorobenzyl)-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,6-dimethoxybenzyl)-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,6-difluorobenzyl)-9H-purin-6-amine;
2-butoxy-N-(2-morpholin-4-ylethyl)-9-(2,3,5-trifluorobenzyl)-9H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yloxy)-9H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yloxy)-9H-purin-6-amine;
2-butoxy-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yloxy)-9H-purin-6-amine;
9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-2-(pent-2-yn-1-yloxy)-9H-purin-6-amine;
2-(allyloxy)-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-[(2E)-but-2-en-1-ylxyloxy]-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-(2,6-difluoro-3-methylbenzyl)-2-[(3-methylbut-2-en-1-yl)oxy]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
2-(but-2-yn-1-ylxyloxy)-9-(2,6-difluoro-3-methylbenzyl)-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
ethyl 2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9H-purine-8-carboxylate;
2-butoxy-9-(3,4-dichlorobenzyl)-6-morpholin-4-yl-9H-purine-8-carboxylic acid;
N-(1H-benzimidazol-2-ylmethyl)-2-butoxy-9-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-[4-(aminomethyl)benzyl]-2-butoxy-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine; and pharmaceutically acceptable salt, solvate, or prodrug thereof.

31. The compound of Claim 2, wherein the compound is selected from the group consisting of:
2-(butylthio)-9-(4,4,4-trifluorobutyl)-9H-purin-6-amine;
2-(butylthio)-9-(2-ethylbutyl)-9H-purin-6-amine;
2-(butylthio)-9-propyl-9H-purin-6-amine;
2-(butylthio)-9-(3-methylbutyl)-9H-purin-6-amine;
2-(butylthio)-9-isobutyl-9H-purin-6-amine;
4-[6-amino-2-(butylthio)-9H-purin-9-yl]butanenitrile;
5-[6-amino-2-(butylthio)-9H-purin-9-yl]pentanenitrile;
2-(benzyloxy)-9-butyl-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
9-butyl-N-(2-morpholin-4-ylethyl)-2-phenoxy-9H-purin-6-amine;
9-butyl-N-(2-morpholin-4-ylethyl)-2-(pyridin-2-ylxyloxy)-9H-purin-6-amine;
9-butyl-2-[(4-methylpyridin-2-yl)oxy]-N-(2-morpholin-4-ylethyl)-9H-purin-6-amine;
and pharmaceutically acceptable salt, solvate, or prodrug thereof.
32. A pharmaceutical composition which comprises a compound, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as claimed in any one of Claims 1 through 31, in association with a pharmaceutically-acceptable diluent or carrier.

33. A compound, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as claimed in any one of Claims 1 through 31, for use as a medicament.

34. The use of a compound, in free or salt form, as claimed in any one of Claims 1 through 31, in the manufacture of a medicament for use in the production of bacterial Murl inhibitory effect in a warm-blooded animal such as man.

35. The use of a compound, in free or salt form, as claimed in any one of Claims 1 through 31, in the manufacture of a medicament for use in the production of an anti-bacterial effect in a warm-blooded animal such as man.

36. The use of a compound, in free or salt form, as claimed in any one of Claims 1 through 31, in the manufacture of a medicament for use in the treatment or prophylaxis of bacterial infection, e.g., infection by Murl expressing bacteria, e.g., Gram positive bacterial infection, e.g., infection caused by Gram positive coci such as staphylococcal, streptococcal or enterococcal infections, for example, *E. faecalis* or *E. faecium* infection; for example in the treatment of pneumonia, septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial meningitis, or post-operative infection; for example in the treatment or prophylaxis of antibiotic resistant infection; in a warm-blooded animal, e.g., man.

37. A pharmaceutical composition which comprises a compound, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as claimed in any one of Claims 1 through 31, in association with a pharmaceutically-acceptable diluent or carrier for use in the production of a bacterial Murl inhibitory effect in a warm-blooded animal such as man.
38. A pharmaceutical composition which comprises a compound, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as claimed in any one of Claims 1 through 31, in association with a pharmaceutically-acceptable diluent or carrier for use in the production of an anti-bacterial effect in a warm-blooded animal such as man.

39. A pharmaceutical composition which comprises a compound, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as claimed in any one of Claims 1 through 31, in association with a pharmaceutically-acceptable diluent or carrier for use in the treatment or prophylaxis of bacterial infection, e.g., infection by Murl expressing bacteria, e.g., Gram positive bacterial infection, e.g., infection caused by Gram positive cocci such as staphylococcal, streptococcal or enterococcal infections, for example, *E. faecalis* or *E. faecium* infection; for example in the treatment of pneumonia, septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial meningitis, or post-operative infection; for example in the treatment or prophylaxis of antibiotic resistant infection; in a warm-blooded animal, e.g., man.

40. A method of treatment or prophylaxis of bacterial infection in a patient in need of such treatment or prophylaxis, comprising administering to the patient an effective amount of a compound, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as claimed in any one of Claims 1 through 31.

41. The method of Claim 40, wherein the infection is caused by Gram positive cocci.

42. The method of Claim 40 or 41, wherein the infection is *E. faecalis* or *E. faecium* infection.

43. The method of any of Claims 40 through 42, wherein the infection is resistant to penicillin or cephalosporin.

44. The method of any of Claims 40 through 43, wherein the infection is selected from pneumonia, septicemia, puerperal sepsis, endocarditis, toxic shock, osteomyelitis, enterocolitis, bacterial meningitis, and post-operative infection.
INTERNATIONAL SEARCH REPORT

PCT/GB2008/050812

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D473/16 C07D473/18 C07D473/24 C07D487/04 A61P31/00

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

B. RELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D

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 practical, search terms used)

EPO-Internal, BEILSTEIN Data, WPI Data, CHEMABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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see patent family annex

Further documents are listed in the continuation of Box C

Date of the actual completion of the international search 10 December 2008

Date of mailing of the international search report 22/01/2009

Name and mailing address of the ISA/Authorized officer

European Patent Office P B 5818 Patentlaan 2 NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040, Fax (+31-70) 340-3016

Sahagun Krause, H

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## INTERNATIONAL SEARCH REPORT

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