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PROSTAGLANDIN ENDOPEROXIDE H SYNTHASE BIOSYNTHESIS INHIBITORS

This application is a continuation-in-part application of U.S. Serial No. 09/261,872 filed March 3, 1999 now abandoned, which in turn is a continuation-in-part of U.S. Serial No. 09/179,605, filed October 27, 1998 now abandoned, which in turn is a continuation-in-part of U.S. Serial No. 09/129,570 filed August 5, 1998, now abandoned, which in turn is a continuation-in-part of U.S. Serial No. 09/137,457 filed August 20, 1998 now abandoned, which is a conversion of U. S. Provisional Patent Application 60/056,777 filed August 22, 1997

TECHNICAL FIELD

The present invention encompasses novel pyridazinone compounds useful in the treatment of cyclooxygenase-2 mediated diseases. More particularly, this invention concerns a method of inhibiting prostaglandin biosynthesis, particularly the induced prostaglandin endoperoxide H synthase (PGHS-2, cyclooxygenase-2, COX-2) protein.

BACKGROUND OF THE INVENTION

The prostaglandins are extremely potent substances which produce a wide variety of biological effects, often in the nanomolar to picomolar concentration range. The discovery of two forms of prostaglandin endoperoxide H synthase, isoenzymes PGHS-1 and PGHS-2, that catalyze the oxidation of arachidonic acid leading to prostaglandin biosynthesis has resulted in renewed research to delineate the role of these two isozymes in physiology and pathophysiology. These isozymes have been shown to have different gene regulation and represent distinctly different prostaglandin biosynthesis pathways. The PGHS-1 pathway is expressed constitutively in most cell types. It responds to produce prostaglandins that regulate acute events in vascular homeostasis and also has a role in maintaining normal stomach and renal function. The PGHS-2 pathway involves an induction mechanism which has been linked to inflammation. mitogenesis and ovulation phenomena.



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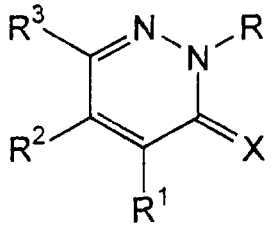
Prostaglandin inhibitors provide therapy for pain, fever, and inflammation, and are useful therapies, for example in the treatment of rheumatoid arthritis and osteoarthritis. The non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen and fenamates inhibit both isozymes. Inhibition of the constitutive enzyme PGHS-1 results in gastrointestinal side effects including ulcers and bleeding and incidence of renal problems with chronic therapy. Inhibitors of the induced isozyme PGHS-2 may provide anti-inflammatory activity without the side effects of PGHS-1 inhibitors.

The problem of side-effects associated with NSAID administration has never completely been solved in the past. Enteric coated tablets and co-administration with misoprostol, a prostaglandin derivative, have been tried in an attempt to minimize stomach toxicity. It would be advantageous to provide compounds which are selective inhibitors of the induced isozyme PGHS-2.

The present invention discloses novel compounds which are selective inhibitors of PGHS-2.

SUMMARY OF THE INVENTION

The present invention discloses pyridazinone compounds which are selective inhibitors of cyclooxygenase-2 (COX-2). The compounds of the present invention have the formula I:



I,

or a pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

X is selected from the group consisting of O, S, $-NR^4$, $-NOR^a$, and $-NNR^bR^c$;

R^4 is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclic, and heterocyclic alkyl;

R^a, R^b, and R^c are independently selected from the group consisting of alkyl, aryl, arylalkyl, cycloalkyl, and cycloalkylalkyl;

R is selected from the group consisting of alkenyl, alkoxy, alkoxyalkyl, alkoxyiminoalkoxy, alkyl, alkylcarbonylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, arylalkynyl, arylhaloalkyl, arylhydroxyalkyl, aryloxy, aryloxyhaloalkyl, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylidenealkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkynyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic oxy, hydroxyalkyl, hydroxyiminoalkoxy, $-(CH_2)_nC(O)R^5$, $-(CH_2)_nCH(OH)R^5$, $-(CH_2)_nC(NOR^d)R^5$, $-(CH_2)_nCH(NOR^d)R^5$, $-(CH_2)_nCH(NR^dR^e)R^5$, $-R^6R^7$, $-(CH_2)_nC{\equiv}CR^7$, $-(CH_2)_n[CH(CX'_3)]_m(CH_2)_pR^7$, $-(CH_2)_n(CX'_2)_m(CH_2)_pR^7$, and $-(CH_2)_n(CHX')_m(CH_2)_pR^7$;

R^5 is selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkenyl, haloalkyl, haloalkynyl, heterocyclic, and heterocyclic alkyl;

R^6 is selected from the group consisting of alkenylene, alkylene, halo-substituted alkenylene, and halo-substituted alkylene;

R^7 is selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkenyl, haloalkyl, heterocyclic, and heterocyclic alkyl;

R^d and R^e are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkyl, heterocyclic, and heterocyclic alkyl;

X' is halogen;

m is an integer from 0-5;

n is an integer from 0-10; and

p is an integer from 0-10; and

R^1, R^2, and R^3 are independently selected from the group consisting of hydrogen,

alkenyl, alkoxyalkyl, alkoxyiminoalkoxy, alkoxyiminoalkyl, alkyl, alkynyl, alkylcarbonylalkoxy, alkylcarbonylamino, alkylcarbonylaminoalkyl, aminoalkoxy, aminoalkylcarbonyloxyalkoxy aminocarbonylalkyl, aryl, arylalkenyl, arylalkyl, arylalkynyl, carboxyalkylcarbonyloxyalkoxy, cyano, cycloalkenyl, cycloalkyl, cycloalkylidenealkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halogen, heterocyclic, hydroxyalkoxy, hydroxyiminoalkoxy, hydroxyiminoalkyl, mercaptoalkoxy, nitro, phosphonatoalkoxy, Y, and W; provided that one of R^1, R^2, or R^3 must be W, and further provided that only one of R^1, R^2, or R^3 is W;

W is selected from the group consisting of



and

;

X^1 is selected from the group consisting of $S(O)_2$, $S(O)(NR^{10})$, $S(O)$, $Se(O)_2$, $P(O)(OR^{11})$, and $P(O)(NR^{12}R^{13})$;

X^2 is selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl and halogen;

R^9 is selected from the group consisting of alkenyl, alkoxy, alkyl, alkylamino, alkylcarbonylamino, alkynyl, amino, cycloalkenyl, cycloalkyl, dialkylamino, $-NHNH_2$, and $-NCHN(R^{10})R^{11}$;

R^{10}, R^{11}, R^{12}, and R^{13} are independently selected from the group consisting of hydrogen, alkyl, and cycloalkyl, or R^{12} and R^{13} can be taken together, with the nitrogen to which they are attached, to form a 3-6 membered ring containing 1 or 2 heteroatoms selected from the group consisting of O, S, and NR^7;

Y is selected from the group consisting of $-OR^{14}$, $-SR^{14}$, $-C(R^{16})(R^{17})R^{14}$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-N(R^{16})C(O)R^{14}$, $-NC(R^{16})R^{14}$, and $-N(R^{16})R^{14}$;

R^{14} is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl,alkylthioalkyl, alkynyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, heterocyclic alkyl, hydroxyalkyl, and $NR^{18}R^{19}$; and

R^{16}, R^{17}, R^{18}, and R^{19} are independently selected from the group consisting of hydrogen, alkenyl, alkoxy, alkyl, cycloalkenyl, cycloalkyl, aryl, arylalkyl, heterocyclic, and heterocyclic alkyl.

DETAILED DESCRIPTION OF THE INVENTION

All patents, patent applications, and literature references cited in the specification are hereby incorporated by reference in their entirety. In the case of inconsistencies, the present disclosure, including definitions, will prevail.

In one embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

X^1 is selected from $S(O)_2$, S(O), $Se(O)_2$, and $S(O)(NR^{10})$;

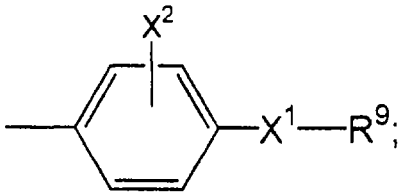
R^9 is selected from alkenyl, alkoxy, alkyl, alkylamino, alkylcarbonylamino, alkynyl, amino, cycloalkenyl, cycloalkyl, and dialkylamino; and

X, X^2, R, R^1, R^3, and R^{10} are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^1 is selected from $S(O)_2$, S(O), $Se(O)_2$, and $S(O)(NR^{10})$;

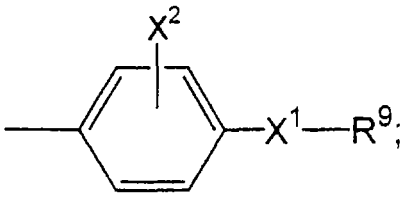
R^9 is selected from alkenyl, alkoxy, alkyl, alkylamino, alkylcarbonylamino, alkynyl, amino, cycloalkenyl, cycloalkyl, and dialkylamino; and

X, X^2, R, R^1, R^3, and R^{10} are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^2 is selected from hydrogen and halogen;

R is selected from hydrogen, alkenyl, alkyl, alkynyl, alkylcarbonylalkyl, alkylsulfonylalkyl, carboxyalkyl, cyanoalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkenyl, arylalkynyl, heterocyclic, heterocyclic alkyl, arylalkyl, -$(CH_2)_nC(O)R^5$,-$(CH_2)_nC{\equiv}CR^7$, and -$(CH_2)_n[CH(CX'_3)]_m(CH_2)_pR^7$;

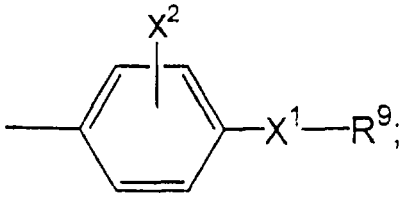
R^1 and R^3 are independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, aminocarbonylalkyl, aryl, cyano, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, halogen, nitro, and Y; and

X, X^1, X', R^5, R^7, R^9, n, m, p, and Y are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^2 is selected from hydrogen and halogen;

R is selected from hydrogen, alkenyl, alkyl, alkynyl, alkylcarbonylalkyl, alkylsulfonylalkyl, carboxyalkyl, cyanoalkyl, haloalkyl, hydroxyalkyl, cycloalkyl,

cycloalkylalkyl, aryl, arylalkenyl, arylalkynyl, heterocyclic, heterocyclic alkyl, arylalkyl, and $-(CH_2)_nC(O)R^5$;

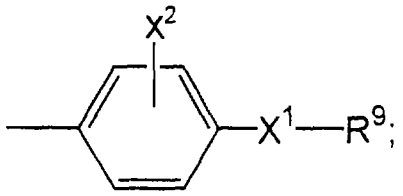
R^1 and R^3 are independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, aminocarbonylalkyl, aryl, cyano, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, halogen, heterocyclic, heterocyclic alkyl, nitro, and Y; and

X, X^1, R^5, R^9, n, and Y are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^2 is selected from hydrogen and halogen;

R is selected from hydrogen, alkyl, aryl, haloalkyl, heterocyclic, heterocyclic alkyl, and $-(CH_2)_nC(O)R^5$;

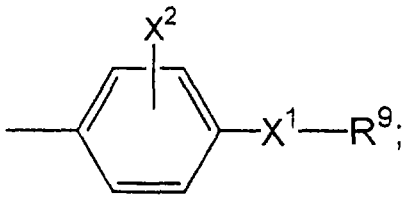
R^1 and R^3 are independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, aminocarbonylalkyl, aryl, cyano, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, halogen, heterocyclic, heterocyclic alkyl, nitro, and Y; and

X, X^1, R^5, R^9, n, and Y are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^2 is selected from hydrogen and halogen;

R is selected from alkyl, aryl, haloalkyl, heterocyclic, heterocyclic alkyl, and arylalkyl wherein the aryl portion is optionally substituted with 1, 2, 3, 4, or 5 substituents selected from halogen; and

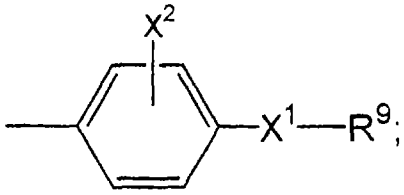
R^1 is selected from aryl, arylalkyl, heterocyclic, heterocyclic alkyl, hydroxyalkoxy, and Y; and

X, X^1, R^3, R^9, and Y are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^2 is selected hydrogen and halogen;

R is selected from the group consisting of alkyl, aryl, haloalkyl, heterocyclic, heterocyclic alkyl and arylalkyl wherein the aryl portion is optionally substituted with 1, 2, 3, 4, or 5 substituents selected from halogen;

R^1 is selected from the group consisting of aryl, arylalkyl, heterocyclic, heterocyclic alkyl, hydroxyalkoxy, and Y;

Y is $-OR^{14}$;

R^{14} is selected from the group consisting of alkenyl, alkyl, and aryl;

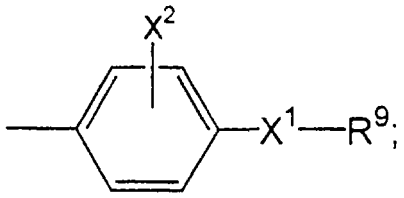
R^3 is hydrogen; and

X, X^1, and R^9 are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^1 is $S(O)_2$;

X^2 is selected from hydrogen and halogen;

R is selected from aryl, haloalkyl, heterocyclic, heterocyclic alkyl and arylalkyl wherein the aryl portion is optionally substituted with 1, 2, 3, 4, or 5 substituents selected from halogen;

R^1 is aryl optionally substituted with 1, 2, or 3 substituents independently selected from chlorine and fluorine;

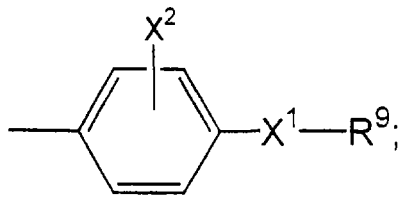
R^3 is hydrogen; and

X and R^9 are as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X is O;

X^1 is $S(O)_2$;

R^9 is selected from the group consisting of alkyl and amino.

X^2 is selected from hydrogen and halogen;

R is selected from alkenyl, alkyl, alkynyl, aryl, arylalkyl, and haloalkyl;

R^1 is selected from alkyl, aryl, arylalkyl, haloalkoxy, hydroxyalkoxy, and Y;

Y is $-OR^{14}$;

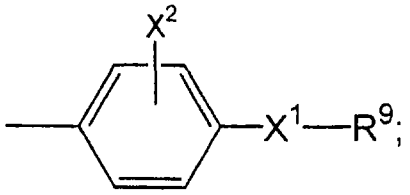
R^{14} is selected from alkenyl, alkyl, and aryl; and

R^3 is hydrogen.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X^1 is $S(O)_2$;

R^9 is selected from alkyl and amino;

X^2 is selected from hydrogen and fluorine;

R is selected from haloalkyl, aryl, and alkyl;

R^1 is selected from isobutyloxy, isopentyloxy, 1-(3-methyl-3-butenyl)oxy, 2-hydroxy-2-methyl-propyloxy, 3-hydroxy-3-methylbutoxy, neopentyloxy, isopentyl, aryloxy, 4-fluorophenoxy, and aryl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of chlorine and fluorine;

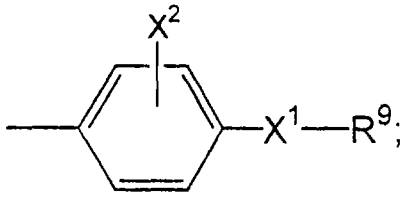
R^3 is hydrogen; and

X is as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X is O;

X^1 is selected from $S(O)_2$ and $S(O)(NR^{10})$;

R^9 is alkyl;

X^2 is selected from hydrogen and fluorine;

R is selected from alkenyl, alkyl, alkynyl, aryl, arylalkyl and haloalkyl;

R^1 is selected from alkyl, aryl, hydroxyalkoxy and Y;

Y is $-OR^{14}$;

R^{14} is selected from alkenyl, alkyl, and aryl;

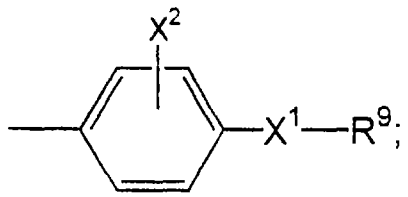
R^3 is hydrogen; and

R^{10} is as defined in formula I.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X is O;

X^1 is $S(O)_2$;

R^9 is amino;

X^2 is selected from hydrogen and fluorine;

R is selected from alkenyl, alkyl, alkynyl, aryl, arylalkyl, and haloalkyl;

R^1 is selected from alkyl, aryl, hydroxyalkoxy and Y;

Y is -OR^{14};

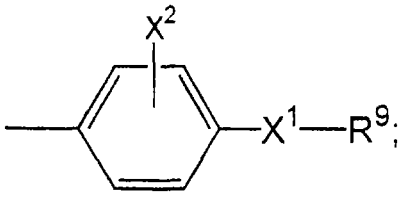
R^{14} is selected from alkenyl, alkyl, and aryl; and

R^3 is hydrogen.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X is O;

X^1 is SO_2;

R^9 is methyl;

X^2 is hydrogen;

R is selected from t-butyl, 3-chlorophenyl, 3,4-difluorophenyl, 4-fluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, and 2,2,2-trifluoroethyl;

R^1 is selected from isobutoxy, isopentyloxy, (3-methyl-3-butenyl)oxy, 2-hydroxy-2-methyl-propoxy, 3-hydroxy-3-methylbutoxy, neopentyloxy, isopentyl, 4-fluorophenyl, 4-chlorophenyl, 4-chloro-3-fluoro-phenyl, 4-fluorophenoxy and Y;

Y is -OR^{14};

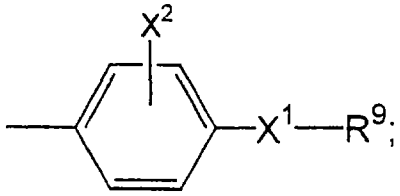
R^{14} is aryl; and

R^3 is hydrogen.

In another embodiment, compounds of the present invention have formula I wherein,

R^2 is W;

W is



X is O;

X^1 is $S(O)_2$;

R^9 is amino;

X^2 is hydrogen;

R is selected from t-butyl, 3-chlorophenyl, 3,4-difluorophenyl, 4-fluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, and 2,2,2-trifluoroethyl;

R^1 is selected consisting of isobutoxy, isopentyloxy, (3-methyl-3-butenyl)oxy, 2-hydroxy-2-methyl-propoxy, 3-hydroxy-3-methylbutoxy, neopentyloxy, isopentyl, 4-fluorophenyl, 4-chlorophenyl, 4-chloro-3-fluoro-phenyl, 4-fluorophenoxy, and Y;

Y is $-OR^{14}$;

R^{14} is aryl; and

R^3 is hydrogen.

Another embodiment of the present invention relates to pharmaceutical compositions comprising a therapeutically effective amount of a compound of formula I or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof in combination with a pharmaceutically acceptable carrier for inhibiting prostaglandin biosynthesis.

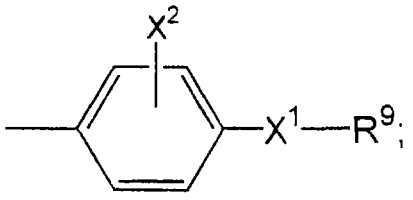
Another embodiment of the invention relates to a method of inhibiting prostaglandin biosynthesis comprising administering a therapeutically effective amount of a compound of formula I or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Another embodiment of the invention relates to a method of treating pain, fever, inflamation, rheumatoid arthritis, osteoarthritis, adhesions, and cancer comprising administering a therapeutically effective amount of a compound of formula I or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Another embodiment of the present invention relates to a method of preparing a compound of formula I wherein,

R^2 is W;

W is



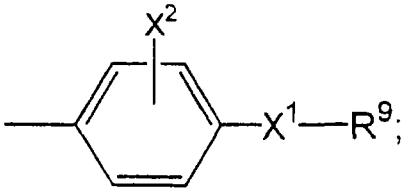
and

X, X^1, X^2, R, R^1, and R^3 are as defined in formula I; comprising the step of treating a compound of formula I wherein R is hydrogen with an alkylating agent.

Another embodiment of the present invention relates to a method of preparing a compound of formula I wherein,

R^2 is W;

W is



and

X, X^1, X^2, R, R^1, R^2, and R^3 are as defined in formula I;

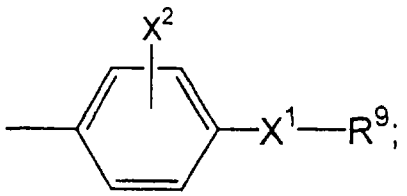
comprising the step of treating a compound of formula I wherein R is hydrogen with an alkylating agent, wherein the alkylating agent has the formula R^{99}-Q wherein Q is a leaving group and R^{99} is selected from the group consisting of methyl, ethyl, 1,1,1-trifluoroethyl, cyclopropylmethyl, 3-(2-methyl)propenyl, 4-(2-methyl)but-2-enyl, 1,1-dichloropropen-3-yl, 2,2-dimethyl-3-oxo-4-butyl, 2,3,3,4,4,4-hexafluorobuten-1-yl, propargyl, phenylpropargyl, phenyl, phenethyl, 1-phenylpropen-3-yl, benzyl, α-methyl-4-fluorobenzyl, 2,3,4,5,6-pentafluorobenzyl, 4-trifluomethoxyphenacyl, 4-fluorobenzyl, 4-fluorophenyl, 2-trifluoromethylbenzyl, 2,4-difluorobenzyl, 2,4-difluorophenacyl, 4-

trifluomethylphenacyl, phenacyl, 4-carboxyphenacyl, 4-chlorophenacyl, 4-cyanophenacyl, 4-diethylaminophenacyl, 3-thienylmethyl, 5-methylthien-2-ylmethyl, 5-chlorothien-2-ylmethyl, 2-benzo[b]thienylmethyl, 3-benzothienacyl, 5-chlorothiazol-2-ylmethyl, 5-methylthiazol-2-ylmethyl, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, quinolin-2-ylmethyl, and fluoroquinolin-2-ylmethyl.

Another embodiment of the present invention relates to a method of preparing a compound of formula I wherein,

R^2 is W;

W is



and

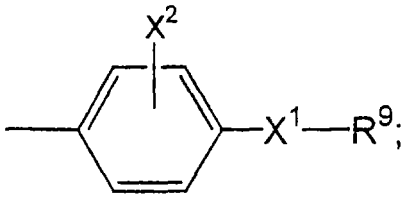
X, X^1, X^2, R, R^1, R^2, and R^3 are as defined in formula I:

comprising the step of treating a compound of formula I wherein R is hydrogen with an alkylating agent, wherein the alkylating agent has the formula R^{99}-Q wherein Q is a leaving group and R^{99} is selected from the group consisting of methyl, ethyl, 1,1,1-trifluoroethyl, cyclopropylmethyl, 3-(2-methyl)propenyl, 4-(2-methyl)but-2-enyl, 1,1-dichloropropen-3-yl, 2,3,3,4,4,4-hexafluorobuten-1-yl, propargyl, phenylpropargyl, phenyl, phenethyl, 1-phenylpropen-3-yl, benzyl, α-methyl-4-fluorobenzyl, 2,3,4,5,6-pentafluorobenzyl, 4-trifluomethoxyphenacyl, 4-fluorobenzyl, 4-fluorophenyl, 2,4-difluorobenzyl, 2,4-difluorophenacyl, 4-trifluomethylphenacyl, phenacyl, 4-carboxyphenacyl, 4-chlorophenacyl, 4-cyanophenacyl, 4-diethylaminophenacyl, 3-thienylmethyl, 5-methylthien-2-ylmethyl, 5-chlorothien-2-ylmethyl, 2-benzo[b]thienylmethyl, and 3-benzothienacyl.

Another embodiment of the present invention relates to a method of preparing a compound of formula I wherein,

R^2 is W;

W is



and

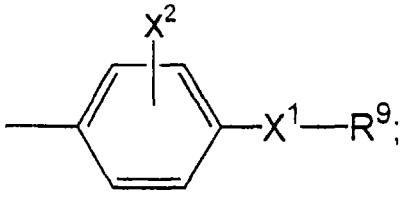
X, X^1, X^2, R, R^1, R^2, and R^3 are as defined in formula I;

comprising the step of treating a compound of formula I wherein R is hydrogen with an alkylating agent, wherein the alkylating agent has the formula R^{99}-Q wherein Q is a leaving group and R^{99} is selected from the group consisting of 1,1,1-trifluoroethyl, 3-(2-methyl)propenyl, 4-(2-methyl)but-2-enyl, 1,1-dichloropropen-3-yl, 2,3,3,4,4,4-hexafluorobuten-1-yl, propargyl, phenylpropargyl, phenyl, benzyl, α-methyl-4-fluorobenzyl, 2,3,4,5,6-pentafluorobenzyl, 4-fluorobenzyl, 4-fluorophenyl, 2,4-difluorobenzyl, 3-thienylmethyl, 5-methylthien-2-ylmethyl, 5-chlorothien-2-ylmethyl, and 2-benzo[b]thienylmethyl.

Another embodiment of the present invention relates to a method of preparing a compound of formula I wherein,

R^2 is W;

W is



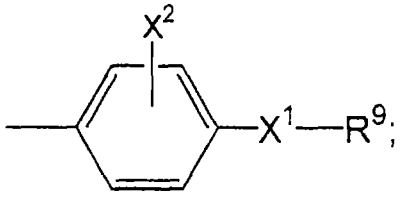
X, X^1, X^2, R, R^1, R^2, and R^3 are as defined in formula I;

comprising the step of treating a compound of formula I wherein R is hydrogen with an alkylating agent, wherein the alkylating agent has the formula R^{99}-Q wherein Q is a leaving group and R^{99} is selected from the group consisting of 1,1,1-trifluoroethyl, phenyl, benzyl, α-methyl-4-fluorobenzyl, 4-fluorobenzyl, 4-fluorophenyl, and 2,4-difluorobenzyl.

Another embodiment of the present invention relates to a method of preparing a compound of formula I wherein,

R^2 is W;

W is



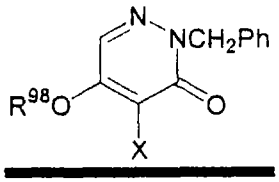
and

X, X^1, X^2, R, R^1, R^2, and R^3 are as defined in formula I;

comprising the step of treating a compound of formula I wherein R is hydrogen with an alkylating agent, wherein the alkylating agent has the formula R^{99}-Q wherein Q is a leaving group and R^{99} is selected from the group consisting of 1,1,1-trifluoroethyl, benzyl, and 4-fluorophenyl.

Another embodiment of the present invention relates to a method for regioselectively preparing a 4,5-disubstituted pyridazinone comprising the steps of

a) treating a compound of formula IV



IV,

wherein R^{98} is an alkyl or aryl group; and X is a leaving group;

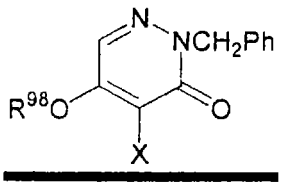
with a nucleophilic agent to displace the X group;

b) converting the -OR^{98} to a leaving group; and

c) treating the compound with a second nucleophilic agent to provide the 4,5-disubstituted pyridazinone.

Another embodiment of the present invention relates to a method for regioselectively preparing a 4,5-disubstituted pyridazinone comprising the steps of

a) treating a compound of formula IV



IV,

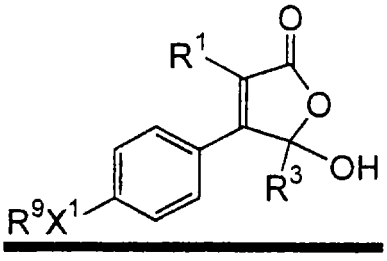
wherein R^{98} is an alkyl or aryl group; and X is a leaving group;

with a nucleophilic agent to displace the X group;

b) converting the $-OR^{98}$ to a leaving group; and

c) treating the compound with a second nucleophilic agent to provide the 4,5-disubstituted pyridazinone wherein the benzyl group is removed using a Lewis acid.

Another embodiment of the present invention relates to a method for regioselectively preparing a 4,5-disubstituted pyridazinone comprising the steps of treating a compound of formula V



V,

wherein

R^1 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, aminoalkoxy, alkylcarbonylalkoxy, aminocarbonylalkyl, aryl, arylalkenyl, arylalkyl, arylalkynyl, cyano, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl,

cycloalkylidenealkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halogen, heterocyclic, heterocyclic alkyl, hydroxyalkoxy, hydroxyalkylamino, hydroxyalkylthio, mercaptoalkoxy, nitro, and Y;

Y is selected from the group consisting of $-OR^{14}$, $-SR^{14}$, $-C(R^{16})(R^{17})R^{14}$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-N(R^{16})C(O)R^{14}$, $-NC(R^{16})R^{14}$, and $-N(R^{16})R^{14}$;

R^{14} is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkylthioalkyl, alkynyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, heterocyclic alkyl and $NR^{18}R^{19}$; and

R^{16}, R^{17}, R^{18}, and R^{19} are independently selected from the group consisting of hydrogen, alkenyl, alkoxy, alkyl, cycloalkenyl, cycloalkyl, aryl, arylalkyl, heterocyclic, and heterocyclic alkyl;

X^1 is selected from the group consisting of $S(O)_2$, $S(O)(NR^{10})$, $S(O)$, $Se(O)_2$, $P(O)(OR^{11})$, and $P(O)(NR^{12}R^{13})$;

R^9 is selected from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, amino, cycloalkenyl, cycloalkyl, dialkylamino, $-NHNH_2$, and $-NCHN(R^{10})R^{11}$; and

R^{10}, R^{11}, R^{12}, and R^{13} are independently selected from the group consisting of hydrogen, alkyl, and cycloalkyl, or R^{12} and R^{13} can be taken together, with the nitrogen to which they are attached, to form a 3-6 membered ring containing 1 or 2 heteroatoms selected from the group consisting of O, S, and NR^7;

R^7 is selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkenyl, haloalkyl, heterocyclic, and heterocyclic alkyl;

with a hydrazine having the formula $RNHNH_2$ wherein R is selected from the group consisting of alkenyl, alkoxy, alkoxyalkyl, alkyl, alkylcarbonylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, arylalkynyl, arylhaloalkyl, arylhydroxyalkyl, aryloxy, aryloxyhaloalkyl, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkynyl,

heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic oxy, hydroxyalkyl, -$(CH_2)_nC(O)R^5$, -$(CH_2)_nCH(OH)R^5$, -$(CH_2)_nC(NOR^d)R^5$, -$(CH_2)_nCH(NOR^d)R^5$, -$(CH_2)_nCH(NR^dR^e)R^5$, -R^6R^7,-$(CH_2)_nC{\equiv}CR^7$, -$(CH_2)_n[CH(CX'_3)]_m(CH_2)_nR^7$, -$(CH_2)_n(CX'_2)_m(CH_2)_nR^7$, and -$(CH_2)_n(CHX')_m(CH_2)_nR^7$;

R^5 is selected from the group consisting of alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkenyl, haloalkyl, haloalkynyl, heterocyclic, and heterocyclic alkyl;

R^6 is selected from the group consisting of alkenylene, alkylene, halo-substituted alkenylene, and halo-substituted alkylene,

R^7 is selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkenyl, haloalkyl, heterocyclic, and heterocyclic alkyl;

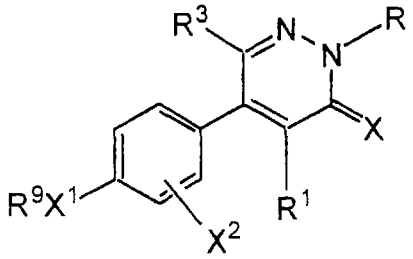
R^d and R^e are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkyl, heterocyclic, and heterocyclic alkyl;

X' is halogen;

n is an integer from 0-10;

m is an integer from 0-5;

to furnish the pyridazinone of formula III



III,

wherein X^1, R, R^1, R^3, and R^9 are as previously defined;

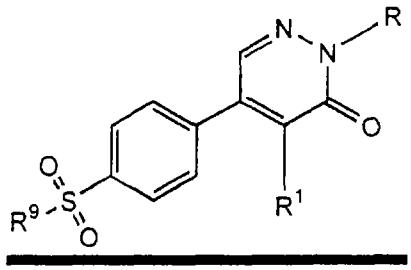
X is selected from the group consisting of O, S, -NR^4, -NOR^a, and -NNR^bR^c;

R^4 is selected from the group consisting of alkenyl, alkyl, aryl, arylalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclic, and heterocyclic alkyl;

R^a, R^b, and R^c are independently selected from the group consisting of alkyl, aryl, arylalkyl, cycloalkyl, and cycloalkylalkyl; and

X^2 is selected from the group consisting of hydrogen, alkenyl, alkyl, alkynyl and halogen.

A preferred embodiment of the present invention relates to a compound of formula VI



VI,

or a pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

R is selected from alkyl, aryl, arylalkyl, haloalkyl, and haloalkenyl;

R^1 is selected from alkoxy, aminoalkylcarbonyloxyalkoxy, carboxyalkylcarbonyloxyalkoxy, hydroxyalkyl, hydroxyalkoxy, and phosphonatoalkoxy,

R^9 is selected from alkyl, alkylcarbonylamino, and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is aryl;

R^1 is hydroxyalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is aryl;

R^1 is hydroxyalkoxy; and

R^9 is methyl.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is phenyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and haloalkyl;

R^1 is hydroxyalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is phenyl optionally substituted with 1 or 2 substituents independently selected from chlorine and fluorine;

R^1 is hydroxyalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is haloalkyl; and

R^1 is hydroxyalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is phenyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and haloalkyl;

R^1 is aminoalkylcarbonyloxyalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is phenyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently selected from halogen and haloalkyl;

R^1 is carboxyalkylcarbonyloxyalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is phenyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently selected from halogen and haloalkyl,

R^1 is phosphonatoalkoxy; and

R^9 is selected from alkyl and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is phenyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently selected from halogen and haloalkyl;

R^1 is hydroxyalkoxy; and

R^9 is alkylcarbonylamino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is selected from haloalky and phenyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and haloalkyl;

R^1 is alkoxy; and

R^9 is selected from the group consisting of alkyl, alkylcarbonylamino, and amino.

Another preferred embodiment of the present invention relates to a compound of formula VI wherein,

R is tert-butyl;

R^1 is selected from the group consisting of aminoalkylcarbonyloxyalkoxy, carboxyalkylcarbonyloxyalkoxy, hydroxyalkoxy, and phosphonatoalkoxy; and

R^9 is selected from the group consisting of alkyl, alkylcarbonylamino, and amino.

Another preferred embodiment of the present invention relates to 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone or a pharmaceutically acceptable salt, ester, or prodrug thereof.

Definitions of Terms

As used throughout this specification and the appended claims, the following terms have the following meanings:

The term "alkenyl," as used herein, refers to a straight or branched chain hydrocarbon containing from 2 to 10 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, 3-decenyl and the like.

The term "alkenylene," denotes a divalent group derived from a straight or branched chain hydrocarbon of from 2 to 10 carbon atoms containing at least one double bond. Representative examples of alkenylene include, but are not limited to, -CH=CH-, $-CH=CH_2CH_2-$, $-CH=C(CH_3)CH_2-$, and the like.

The term "alkoxy," as used herein, refers to an alkyl group, as defined herein,

appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, hexyloxy and the like.

The term "alkoxyalkoxy," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through another alkoxy group, as defined herein. Representative examples of alkoxyalkoxy include, but are not limited to, tert-butoxymethoxy, 2-ethoxyethoxy, 2-methoxyethoxy, methoxymethoxy, and the like.

The term "alkoxyalkoxyalkyl," as used herein, refers to an alkoxyalkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyalkoxyalkyl include, but are not limited to, tert-butoxymethoxymethyl, ethoxymethoxymethyl, (2-methoxyethoxy)methyl, 2-(2-methoxyethoxy)ethyl, and the like.

The term "alkoxyalkyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyalkyl include, but are not limited to, tert-butoxymethyl, 2-ethoxyethyl, 2-methoxyethyl, methoxymethyl, and the like.

The term "alkoxyalkylcarbonyl," as used herein, refers to an alkoxyalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkoxyalkylcarbonyl include, but are not limited to, tert-butoxymethylcarbonyl, 2-ethoxyethylcarbonyl, 2-methoxyethylcarbonyl, methoxymethylcarbonyl, and the like.

The term "alkoxycarbonyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkoxycarbonyl include, but are not limited to, methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl, and the like.

The term "alkoxycarbonylalkenyl," as used herein, refers to an alkoxycarbonyl group, as defined herein, appended to the parent molecular moiety through an alkenyl group, as defined herein. Representative examples of alkoxycarbonylalkenyl include, but are not limited to, 3-methoxycarbonyl-1-propenyl, 4-ethoxycarbonyl-2-butenyl, and the

like.

The term "alkoxycarbonylalkyl," as used herein, refers to an alkoxycarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxycarbonylalkyl include, but are not limited to, 3-methoxycarbonylpropyl, 4-ethoxycarbonylbutyl, 2-tert-butoxycarbonylethyl, and the like.

The term "alkoxycarbonylalkylthio," as used herein, refers to an alkoxycarbonylalkyl group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of alkoxycarbonylalkylthio include, but are not limited to, 3-methoxycarbonylpropylsulfanyl, 4-ethoxycarbonylbutylsulfanyl, and the like.

The term "alkoxyimino," refers to a $R_{85}ON=$ group wherein R_{85} is alkyl, as defined herein.

The term "alkoxyiminoalkoxy," as used herein, refers to an alkoxyimino group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of alkoxyiminoalkoxy include, but are not limited to, 2-(methoxyimino)ethoxy, 2-(ethoxyimino)-1-propoxy, 3-(isopropoxyimino)-1-butoxy, and the like.

The term "alkoxyiminoalkyl," as used herein, refers to an alkoxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyiminoalkyl include, but are not limited to, 2-(methoxyimino)ethyl, 2-(ethoxyimino)-1-propyl, 3-(isopropoxyimino)-1-butyl, and the like.

The term "alkyl," as used herein, refers to a straight or branched chain hydrocarbon containing from 1 to 10 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, n-decyl, and the like

The term "alkylamino," as used herein, refers to an alkyl group, as defined herein.

appended to the parent molecular moiety through an amino group, as defined herein. Representative examples of alkylamino include, but are not limited to, methylamino, ethylamino, propylamino, and the like.

The term "alkylaminosulfonyl," as used herein, refers to an alkylamino group, as defined herein, appended to the parent molecular moiety through a sulfonyl group, as defined herein. Representative examples of alkylaminosulfonyl include, but are not limited to, methylaminosulfonyl, ethylaminosulfonyl, propylaminosulfonyl, and the like.

The term "alkylcarbonyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkylcarbonyl include, but are not limited to, acetyl, 1-oxopropyl, 2,2-dimethyl-1-oxopropyl, 1-oxobutyl, 1-oxopentyl, and the like.

The term "alkylcarbonylalkoxy," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of alkylcarbonylalkoxy include, but are not limited to, 2-oxopropoxy, 3,3-dimethyl-2-oxopropoxy, 3-oxobutoxy, 3-oxobutoxy, 3-oxopentyloxy, and the like.

The term "alkylcarbonylalkyl," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylcarbonylalkyl include, but are not limited to, 2-oxopropyl, 3,3-dimethyl-2-oxopropyl, 3-oxobutyl, 3-oxopentyl, and the like.

The term "alkylcarbonylamino," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an amino group, as defined herein. Representative examples of alkylcarbonylamino include, but are not limited to, acetylamino, 1-oxopropylamino, 2,2-dimethyl-1-oxopropylamino, and the like.

The term "alkylcarbonylaminoalkyl," as used herein, refers to an alkylcarbonylamino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylcarbonylaminoalkyl include, but are not limited to, acetylaminomethyl, 2-(1-oxopropylamino)ethyl, and the like.

The term "alkylcarbonyloxy," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of alkylcarbonyloxy include, but are not limited to, acetyloxy, ethylcarbonyloxy, tert-butylcarbonyloxy, and the like.

The term "alkylene," denotes a divalent group derived from a straight or branched chain hydrocarbon of from 1 to 10 carbon atoms. Representative examples of alkylene include, but are not limited to, $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2CH(CH_3)CH_2-$, and the like.

The term "alkylimino," as used herein, refers to $R_{81}N=$ group, wherein R_{81} is alkyl, as defined herein.

The term "alkylsulfinyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a sulfinyl group, as defined herein. Representative examples of alkylsulfinyl include, but are not limited, methylsulfinyl, ethylsulfinyl, and the like.

The term "alkylsulfinylalkyl," as used herein, refers to an alkylsulfinyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylsulfinylalkyl include, but are not limited, methylsulfinylmethyl, ethylsulfinylmethyl, and the like

The term "alkylsulfonyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a sulfonyl group, as defined herein. Representative examples of alkylsulfonyl include, but are not limited, methylsulfonyl, ethylsulfonyl, and the like.

The term "alkylsulfonylalkyl," as used herein, refers to an alkylsulfonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylsulfonylalkyl include, but are not limited, methylsulfonylmethyl, 2-(ethylsulfonyl)ethyl, and the like.

The term "alkylsulfonylamino," as used herein, refers to an alkylsulfonyl group, as defined herein, appended to the parent molecular moiety through an amino group, as defined herein. Representative examples of alkylsulfonylamino include, but are not

limited, methylsulfonylamino, ethylsulfonylamino, and the like.

The term "alkylthio," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of alkylthio include, but are not limited, methylsulfanyl, ethylsulfanyl, tert-butylsulfanyl, hexylsulfanyl, and the like.

The term "alkylthioalkyl," as used herein, refers to an alkylthio group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylthioalkyl include, but are not limited, methylsulfanylmethyl, 2-(ethylsulfanyl)ethyl, and the like.

The term "alkylthioalkylcarbonyl," as used herein, refers to an alkylthioalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkylthioalkylcarbonyl include, but are not limited, methylsulfanylmethylcarbonyl, 2-(ethylsulfanyl)ethylcarbonyl, and the like.

The term "alkynyl," as used herein, refers to a straight or branched chain hydrocarbon group containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, 1-butynyl and the like.

The term "alkynylene," denotes a divalent group derived from a straight or branched chain hydrocarbon of from 2 to 10 carbon atoms containing at least one triple bond. Representative examples of alkynylene include, but are not limited to, -C≡C-, $-CH_2C\equiv C-$, $-CH(CH_3)CH_2C\equiv C-$, $-C\equiv CCH_2-$, $-C\equiv CCH(CH_3)CH_2-$, and the like.

The term "amino," as used herein, refers to a $-NH_2$ group.

The term "aminoalkoxy," as used herein, refers to an amino group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of aminoalkoxy include, but are not limited to, 2-aminomethoxy, 3-aminopropoxy, 4-amino-1-methylhexyloxy, and the like.

The term "aminoalkyl," as used herein, refers to an amino group, as defined herein,

appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of aminoalkyl include, but are not limited to, aminomethyl, 2-aminoethyl, 3-aminopropyl, 4-amino-1-methylhexyl, and the like.

The term "aminoalkylcarbonyl," as used herein, refers to an aminoalkyl group, as defined herein, appended to the parent molecular moiety through an carbonyl group, as defined herein. Representative examples of aminoalkylcarbonyl include, but are not limited to, 2-amino-1-oxoethyl (2-aminoacetyl), 3-amino-1-oxopropyl, and the like.

The term "aminoalkylcarbonyloxy," as used herein, refers to an aminoalkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of aminoalkylcarbonyloxy include, but are not limited to, 2-amino-1-oxoethyloxy (2-aminoacetoxy), 3-amino-1-oxopropyloxy, and the like.

The term "aminoalkylcarbonyloxyalkoxy," as used herein, refers to an aminoalkylcarbonyloxy group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of aminoalkylcarbonyloxyalkoxy include, but are not limited to, 2-(2-amino-1-oxoethyloxy)ethoxy, 4-(3-amino-1-oxopropyloxy)butoxy, 3-(3-amino-1-oxopropyloxy)-3-methyl-1-butoxy, 3-(2-amino-1-oxoethyloxy)-3-methyl-1-butoxy and the like.

The term "aminocarbonyl," as used herein, refers to a $H_2NC(O)$- group.

The term "aminocarbonylalkoxy," as used herein, refers to an aminocarbonyl group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of aminocarbonylalkoxy include, but are not limited to, 2-(aminocarbonyl)ethoxy, 3-(aminocarbonyl)propoxy, and the like.

The term "aminocarbonylalkyl," as used herein, refers to an aminocarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of aminocarbonylalkyl include, but are not limited to, 2-(aminocarbonyl)ethyl, 3-(aminocarbonyl)propyl, and the like.

The term "aminosulfonyl," as used herein, refers to $H_2NS(O)_2$- group.

The term "aryl," as used herein, refers to a monocyclic-ring system, or a bicyclic-

or a tricyclic- fused ring system wherein one or more of the fused rings are aromatic. Representative examples of aryl include, but are not limited to, azulenyl, indanyl, indenyl, naphthyl, phenyl, tetrahydronaphthyl, and the like.

The aryl groups of this invention can be substituted with 1, 2, or 3 substituents independently selected from alkenyl. alkenyloxy, alkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkenyl, alkoxycarbonylalkyl, alkoxycarbonylalkylthio, alkyl, alkylamino, alkylaminosulfonyl, alkylcarbonyl, alkylcarbonylalkyl. alkylcarbonylamino, alkylcarbonyloxy, alkylimino, alkylsulfinyl, alkylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkylsulfonylamino, alkylthio, alkylthioalkyl, alkylthioalkylcarbonyl, alkynyl, amino, aminocarbonyl, aminocarbonylalkoxy, aminosulfonyl, aryl, arylalkoxy, arylalkyl, aryloxy, arylcarbonyl, carboxy, carboxyalkenyl, carboxyalkoxy, carboxyalkyl, cyano, cyanoalkoxy, cyanoalkyl, cycloalkyl, dialkylamino, dialkylaminosulfonyl, ethylenedioxy, formyl, formylalkyl. halogen, haloalkoxy, haloalkyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic carbonyl, hydroxy, hydroxyalkoxy, hydroxyalkyl, methylenedioxy, mercapto, nitro, and sulfo. Representative examples of substituted aryl include, but are not limited to, 3-chlorophenyl, 3-fluorophenyl, 4-chlorophenyl, 4-fluorophenyl, 3,4-dichlorophenyl, 3-chloro-4-fluoro-phenyl, 3,4,-difluoorophenyl, 4-methylsulfonylphenyl, 4-aminosulfonylpheny,l and pentaflurophenyl.

The term "arylalkenyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an alkenyl group, as defined herein. Representative examples of arylalkenyl include, but are not limited to, 3-phenylpropen-2-yl, 3-phenylpropen-3-yl, 2-naphth-2-ylbuten-4-yl, and the like.

The term "arylalkoxy," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of arylalkoxy include, but are not limited to, 2-phenylethoxy, 3-naphth-2-ylpropoxy, 5-phenylpentyloxy. and the like.

The term "arylalkoxycarbonyl," as used herein, refers to an arylalkoxy group, as

defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of arylalkoxycarbonyl include, but are not limited to, benzyloxycarbonyl, naphth-2-ylmethoxycarbonyl, and the like.

The term "arylalkyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of arylalkyl include, but are not limited to, benzyl, 2-phenylethyl, 3-phenylpropyl, 2-naphth-2-ylethyl, and the like.

The term "arylalkylthio," as used herein, refers to an arylalkyl group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of arylalkylthio include, but are not limited to, 2-phenylethylsulfanyl, 3-naphth-2-ylpropylsulfanyl, 5-phenylpentylsulfanyland the like.

The term "arylalkynyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an alkynyl group, as defined herein. Representative examples of arylalkynyl include, but are not limited to, 3-phenylpropyn-2-yl, 3-phenylpropyn-3-yl, 2-naphth-2-ylbutyn-4-yl, and the like.

The term "arylcarbonyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of arylcarbonyl include, but are not limited to, benzoyl, naphthoyl, and the like.

The term "arylcarbonylalkyl," as used herein, refers to an arylcarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of arylcarbonylalkyl include, but are not limited to, 3-benzoylpropyl, 3-naphthoylpropyl, and the like.

The term "arylhaloalkyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through a haloalkyl group, as defined herein. Representative examples of arylhaloalkyl include, but are not limited to, 1,1-difluoro-3-phenylpropyl, 1,1-dibromo-3-phenylpropyl, 1,1-difluoro-2-naphth-2-ylethyl, and the like.

The term "arylhydroxyalkyl," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through a hydroxyalkyl group, as defined

herein. Representative examples of arylhydroxyalkyl include, but are not limited to, 1-hydroxy-3-phenylpropyl, 2-hydroxy-3-phenylpropyl, 1-hydroxy-2-naphth-2-ylethyl, and the like.

The term "aryloxy," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of aryloxy include, but are not limited to, phenoxy, naphthyloxy, 3-bromophenoxy, 4-chlorophenoxy, 4-methylphenoxy, 3,5-dimethoxyphenoxy, and the like.

The term "aryloxyalkyl," as used herein, refers to an aryloxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of aryloxyalkyl include, but are not limited to, 2-phenoxyethyl, 3-naphth-2-yloxypropyl, 3-bromophenoxymethyl, and the like.

The term "aryloxyhaloalkyl," as used herein, refers to an aryloxy group, as defined herein, appended to the parent molecular moiety through a haloalkyl group, as defined herein. Representative examples of aryloxyhaloalkyl include, but are not limited to, 1,1-difluoro-3-(naphth-2-yloxy)propyl, 1,1-difluoro-3-(4-bromophenoxy)butyl, and the like.

The term "aryloxyhydroxyalkyl," as used herein, refers to an aryloxy group, as defined herein, appended to the parent molecular moiety through a hydroxyalkyl group, as defined herein. Representative examples of aryloxyhydroxyalkyl include, but are not limited to, 1-hydroxy-3-(naphth-2-yloxy)propyl, 1-hydroxy-3-(4-bromophenoxy)butyl, and the like.

The term "arylthio," as used herein, refers to an aryl group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of arylthio include, but are not limited to, phenylsulfanyl, naphth-2-ylsulfanyl, 5-phenylhexylsulfanyl, and the like.

The term "arylthioalkyl," as used herein, refers to an arylthio group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein Representative examples of arylthioalkyl include, but are not limited to, phenylsulfanylmethyl, 2-naphth-2-ylsulfanylethyl, 5-phenylhexylsulfanylmethyl, and the

like.

The term "azido," as used herein, refers to a $-N_3$ group.

The term "carbonyl," as used herein, refers to a -C(O)- group.

The term "carboxy," as used herein, refers to a $-CO_2H$ group.

The term "carboxyalkenyl," as used herein, refers to a carboxy group, as defined herein, appended to the parent molecular moiety through an alkenyl group, as defined herein. Representative examples of carboxyalkenyl include, but are not limited to, 3-carboxy-1-propenyl, 4-carboxy-1-butenyl, and the like.

The term "carboxyalkoxy," as used herein, refers to a carboxy group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of carboxyalkoxy include, but are not limited to, 3-carboxypropoxy, 4-carboxybutoxy, and the like.

The term "carboxyalkyl," as used herein, refers to a carboxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. The alkyl portion of carboxyalkyl may contain 1 or 2 hydroxy groups, as defined herein. Representative examples of carboxyalkyl include, but are not limited to, carboxymethyl, 2-carboxyethyl, 1-hydroxy-3-carboxypropyl, 1,2-dihydroxy-3-carboxypropyl and the like.

The term "carboxyalkylcarbonyl," as used herein, refers to a carboxyalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of carboxyalkylcarbonyl include, but are not limited to, 2-carboxy-1-oxoethyl, 3-carboxy-2,3-dihydroxy-1-oxopropyl, 3-carboxy-1-oxopropyl, and the like.

The term "carboxyalkylcarbonyloxy," as used herein, refers to a carboxyalkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of carboxyalkylcarbonyloxy include, but are not limited to, 2-carboxy-1-oxoethoxy, 3-carboxy-2,3-dihydroxy-1-oxopropoxy, 3-carboxy-1-oxopropoxy, and the like.

The term "carboxyalkylcarbonyloxyalkoxy," as used herein, refers to a carboxyalkylcarbonyloxy group, as defined herein, appended to the parent molecular

moiety through an alkoxy group, as defined herein. Representative examples of carboxyalkylcarbonyloxyalkoxy include, but are not limited to, 2-(2-carboxy-1-oxoethoxy)ethoxy, 3-(3-carboxy-2,3-dihydroxy-1-oxopropoxy)-3-methylbutoxy, 3-(3-carboxy-1-oxopropoxy)-2-methyl-1-propoxy, and the like.

The term "cyano," as used herein, refers to a -CN group.

The term "cyanoalkoxy," as used herein, refers to a cyano group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of cyanoalkoxy include, but are not limited to, 2-cyanoethoxy, 3-cyanopropoxy, and the like.

The term "cyanoalkyl," as used herein, refers to a cyano group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of cyanoalkyl include, but are not limited to, cyanomethyl, 2-cyanoethyl, 3-cyanopropyl, and the like.

The term "cycloalkenyl," as used herein, refers to a cyclalkyl group, as defined herein, containing one double bond. Representative examples of cycloalkenyl include, but are not limited to, cyclopentenyl, cyclohexenyl, cycloheptenyl, and the like.

The cycloalkenyl groups of this invention can be substituted with 1, 2, or 3 substituents selected from alkoxy, alkoxyalkoxy, alkoxycarbonyl, alkyl, alkylamino, alkylimino, alkylthio, amino, aminocarbonyl, aryl, arylalkyl, carboxy, cyano, cycloalkyl, dialkylamino, formyl, halogen, haloalkyl, hydroxy, oxo, mercapto, and nitro.

The term "cycloalkenylalkyl," as used herein, refers to cycloalkenyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of cycloalkenylalkyl include, but are not limited to, cyclopentenylmethyl, cyclohexenylmethyl, and the like.

The term "cycloalkyl," as used herein, refers to a saturated cyclic hydrocarbon group containing from 3 to 8 carbons. Representative examples of cycloalkyl include, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl.

The cycloalkyl groups of this invention can be substituted with 1, 2, or 3 substituents selected from alkoxy, alkoxyalkoxy, alkoxycarbonyl, alkyl, alkylamino,

alkylimino, alkylthio, amino, aminocarbonyl, aryl, arylalkyl, carboxy, cyano, cycloalkyl, dialkylamino, formyl, halogen, haloalkyl, hydroxy, oxo, mercapto, and nitro.

The term "cycloalkylalkyl," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of cycloalkylalkyl include, but are not limited to, cyclopropylmethyl, 2-cyclobutylethyl, cyclopentylmethyl, cyclohexylmethyl, 4-cycloheptylbutyl, and the like.

The term "cycloalkylcarbonyl," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of cycloalkylcarbonyl include, but are not limited to, cyclopropylcarbonyl, 2-cyclobutylcarbonyl, cyclohexylcarbonyl, and the like.

The term "cycloalkylidene," as used herein, refers to cycloalkyl group, as defined herein, appended to the parent molecular moiety through a double bond. Representative examples of cycloalkylidene include, but are not limited to, cyclopropylidene, cyclohexylidene, and the like.

The term "cycloalkylidenealkyl," as used herein, refers to cycloalkylidene group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of cycloalkylidenealkyl include, but are not limited to, 2-cyclopropylideneethyl, 3-cyclohexylidenepropyl, and the like.

The term "dialkylamino," as used herein, refers to two independent alkyl groups, as defined herein, appended to the parent molecular moiety through an amino group. Representative examples of dialkylamino include, but are not limited to, diethylamino, dimethylamino, ethylmethylamino, and the like.

The term "dialkylaminosulfonyl," as used herein, refers to a dialkylamino group, as defined herein, appended to the parent molecular moiety through a sulfonyl group. Representative examples of dialkylaminosulfonyl include, but are not limited to, diethylaminosulfonyl, dimethylaminosulfonyl, ethylmethylaminosulfonyl, and the like.

The term "ethylenedioxy," as used herein, refers to a $-O(CH_2)_2O-$ group wherein the oxygen atoms of the ethylenedioxy group are attached to the parent molecular moiety

through one carbon atom forming a 5 membered ring or the oxygen atoms of the ethylenedioxy group are attached to the parent molecular moiety through two adjacent carbon atoms forming a six membered ring.

The term "formyl," as used herein, refers to a -C(O)H group.

The term "formylalkyl," as used herein, refers to a formyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of formylalkyl include, but are not limited to, formylmethyl, 2-formylethyl, and the like.

The term "halo" or "halogen," as used herein, refers to -Cl, -Br, -I or -F.

The term "haloalkenyl," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkenyl group, as defined herein. Representative examples of haloalkenyl include, but are not limited to, 2,3,3-trifluoropropen-3-yl, 2,2-difluoroethenyl, and the like.

The term "haloalkenyloxy," as used herein, refers to a haloalkenyl group, as defined herein, appended to the parent molecular moiety through an oxy group, as defined herein. Representative examples of haloalkenyloxy include, but are not limited to, 2,3,3-trifluoropropen-3-yloxy, 2,2-difluoroethenyloxy, and the like.

The term "haloalkoxy," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of haloalkoxy include, but are not limited to, chloromethoxy, 2-fluoroethoxy, trifluoromethoxy, pentafluoroethoxy, and the like.

The term "haloalkoxyhydroxyalkyl," as used herein, refers to a haloalkoxy group, as defined herein, appended to the parent molecular moiety through a hydroxyalkyl group, as defined herein. Representative examples of haloalkoxyhydroxyalkyl include, but are not limited to, 4-(trifluoromethoxy)-1-hydroxybutyl, 4-(difluoromethoxy)-1-hydroxybutyl, and the like.

The term "haloalkyl," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of haloalkyl include, but are not limited to, chloromethyl, 2-

fluoroethyl, trifluoromethyl, pentafluoroethyl, 2-chloro-3-fluoropentyl, and the like.

The term "haloalkynyl," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkynyl group, as defined herein. Representative examples of haloalkynyl include, but are not limited to, 4,4,4-trifluorobutyn-2-yl, 3,3-difluoropropy-1-nyl, and the like.

The term "heterocycle" or "heterocyclic," as used herein, refers to a monocyclic, bicyclic, or tricyclic ring system. Monocyclic ring systems are exemplified by any 3- or 4-membered ring containing a heteroatom independently selected from oxygen, nitrogen and sulfur; or a 5-, 6- or 7-membered ring containing one, two or three heteroatoms wherein the heteroatoms are independently selected from nitrogen, oxygen and sulfur. The 5-membered ring has from 0-2 double bonds and the 6- and 7-membered ring have from 0-3 double bonds. Representative examples of monocyclic ring systems include, but are not limited to, azetidinyl, azepinyl, aziridinyl, diazepinyl, 1,3-dioxolanyl, dioxanyl, dithianyl, furyl, imidazolyl, imidazolinyl, imidazolidinyl, isothiazolyl, isothiazolinyl, isothiazolidinyl, isoxazolyl, isoxazolinyl, isoxazolidinyl, morpholinyl, oxadiazolyl, oxadiazolinyl, oxadiazolidinyl, oxazolyl, oxazolinyl, oxazolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, pyridyl, pyrimidinyl, pyridazinyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothiophenyl, tetrazinyl, tetrazolyl, thiadiazolyl, thiadiazolinyl, thiadiazolidinyl, thiazolyl, thiazolinyl, thiazolidinyl, thiophenyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl, thiopyranyl, triazinyl, triazolyl, trithianyl, and the like. Bicyclic ring systems are exemplified by any of the above monocyclic ring systems fused to an aryl group as defined herein, a cycloalkyl group as defined herein, or another monocyclic ring system. Representative examples of bicyclic ring systems include but are not limited to, for example, benzimidazolyl, benzothiazolyl, benzothiophenyl, benzoxazolyl, benzofuranyl, benzopyranyl, benzothiopyranyl, benzodioxinyl, 1,3-benzodioxolyl, cinnolinyl, indazolyl, indolyl, indolinyl, indolizinyl, naphthyridinyl, isobenzofuranyl, isobenzothiophenyl, isoindolyl, isoindolinyl, isoquinolyl, phthalazinyl, pyranopyridyl, quinolyl, quinolizinyl, quinoxalinyl, quinazolinyl, tetrahydroisoquinolyl, tetrahydroquinolyl, thiopyranopyridyl, and the like.

Tricyclic rings systems are exemplified by any of the above bicyclic ring systems fused to an aryl group as defined herein, a cycloalkyl group as defined herein, or a monocyclic ring system. Representative examples of tricyclic ring systems include, but are not limited to, acridinyl, carbazolyl, carbolinyl, dibenzofuranyl, dibenzothiophenyl, naphthofuranyl, naphthothiophenyl, oxanthrenyl, phenazinyl, phenoxathiinyl, phenoxazinyl, phenothiazinyl, thianthrenyl, thioxanthenyl, xanthenyl, and the like.

The heterocyclic groups of this invention can be substituted with 1, 2,or 3 substituents independently selected from alkenyl, alkenyloxy, alkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, alkoxyalkyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkenyl, alkoxycarbonylalkyl, alkoxycarbonylalkylthio, alkyl, alkylamino, alkylaminosulfonyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonylamino, alkylcarbonyloxy, alkylimino, alkylsulfinyl, alkylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkylsulfonylamino, alkylthio, alkylthioalkyl, alkylthioalkylcarbonyl, alkynyl, amino, aminocarbonyl, aminocarbonylalkoxy, aminosulfonyl, aryl, arylalkoxy, arylalkyl, aryloxy, arylcarbonyl, carboxy, carboxyalkenyl, carboxyalkoxy, carboxyalkyl, cyano, cyanoalkoxy, cyanoalkyl, cycloalkyl, dialkylamino, dialkylaminosulfonyl, ethylenedioxy, formyl, formylalkyl, halogen, haloalkoxy, haloalkyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic carbonyl, hydroxy, hydroxyalkoxy, hydroxyalkyl, methylenedioxy, mercapto, nitro, and sulfo.

The term "heterocyclic alkoxy," as used herein, refers to a heterocyclic group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of heterocyclic alkoxy include, but are not limited to, 2-pyrid-3-ylethoxy, 3-quinolin-3-ylpropoxy, 5-pyrid-4-ylpentyloxy, and the like.

The term "heterocyclic alkyl," as used herein, refers to a heterocyclic, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of heterocyclic alkyl include, but are not limited to, pyrid-3-ylmethyl, 2-pyrimidin-2-ylpropyl, and the like.

The term "heterocyclic alkylthio," as used herein, refers to a heterocyclic alkyl

group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of heterocyclic alkylthio include, but are not limited to, 2-pyrid-3-ylethysulfanyl, 3-quinolin-3-ylpropysulfanyl, 5-pyrid-4-ylpentylsulfanyl, and the like.

The term "heterocyclic carbonyl," as used herein, refers to a heterocyclic, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of heterocyclic carbonyl include, but are not limited to, pyrid-3-ylcarbonyl, quinolin-3-ylcarbonyl, sulfanylphen-2-ylcarbonyl, and the like.

The term "heterocyclic oxy," as used herein, refers to a heterocyclic group, as defined herein, appended to the parent molecular moiety through an oxy moiety, as defined herein. Representative examples of heterocyclic oxy include, but are not limited to, pyrid-3-yloxy, quinolin-3-yloxy, and the like.

The term "heterocyclic oxyalkyl," as used herein, refers to a heterocyclic oxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of heterocyclic oxyalkyl include, but are not limited to, pyrid-3-yloxymethyl, 2-quinolin-3-yloxyethyl, and the like.

The term "heterocyclic thio," as used herein, refers to a heterocyclic group, as defined herein, appended to the parent molecular moiety through a thio moiety, as defined herein. Representative examples of heterocyclic thio include, but are not limited to, pyrid-3-ylsulfanyl, quinolin-3-ylsulfanyl, and the like.

The term "heterocyclic thioalkyl," as used herein, refers to a heterocyclic thio group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of heterocyclic thioalkyl include, but are not limited to, pyrid-3-ylsulfanylmethyl, 2-quinolin-3-ylsulfanylethyl, and the like.

The term "hydroxy," as used herein, refers to an -OH group.

The term "hydroxyalkoxy," as used herein, refers to 1 or 2 hydroxy groups, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of hydroxyalkoxy include, but are not limited to,

hydroxymethoxy, 2-hydroxyethoxy, 2-hydroxy-2-methylethoxy, 3-hydroxy-1-propoxy, 4-hydroxy-1-butoxy, 3-hydroxy-3-methyl-1-butoxy, 2,3-dihydroxy-1-propoxy, and the like.

The term "hydroxyalkyl," as used herein, refers to 1 or 2 hydroxy groups, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of hydroxyalkyl include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2-ethyl-4-hydroxyheptyl, 2,3-dihydroxypropyl, and the like.

The term "hydroxyimino," refers to a HON= group.

The term "hydroxyiminoalkoxy," as used herein, refers to a hydroxyimino group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of hydroxyiminoalkoxy include, but are not limited to, hydroxyiminomethoxy, 2-hydroxyiminoethoxy, 2-hydroxyiminopropoxy, and the like.

The term "hydroxyiminoalkyl," as used herein, refers to a hydroxyimino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of hydroxyiminoalkyl include, but are not limited to, hydroxyiminomethyl, 2-hydroxyiminoethyl, 2-hydroxyiminopropyl, and the like.

The term "imino," as used herein , refers to a HN= group.

The term "iminoalkoxy," as used herein, refers to an imino group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of iminoalkoxy include, but are not limited to, 2-iminoethoxy, 2-imino-1-propoxy, 3-imino-1-butoxy, and the like.

The term "iminoalkyl," as used herein, refers to an imino group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of iminoalkyl include, but are not limited to, 2-iminoethyl, 2-imino-1-propyl, 3-imino-1-butyl, and the like.

The term "mercapto," as used herein, refers to a -SH group.

The term "mercaptoalkoxy," as used herein, refers to a mercapto group, as defined

herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of mercaptoalkoxy include, but are not limited to, 2-mercaptoethoxy, 3-mercaptopropoxy, and the like.

The term "mercaptoalkyl," as used herein, refers to a mercapto group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of mercaptoalkyl include, but are not limited to, 2-mercaptoethyl, 3-mercaptopropyl, and the like.

The term "methylenedioxy," as used herein, refers to a $-OCH_2O-$ group wherein the oxygen atoms of the methylenedioxy are attached to the parent molecular moiety through two adjacent carbon atoms.

The term "nitro," as used herein, refers to a $-NO_2$ group.

The term "oxo," as used herein, refers to a =O moiety.

The term "oxy," as used herein, refers to a -O- moiety.

The term "phosphonato," as used herein , refers to a $(R_{84}O)_2P(O)O-$ group wherein R_{84} is selected from hydrogen and alkyl, as defined herein.

The term "phosphonatoalkoxy," refers to a phosphonato group, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative example of phosphonatoalkoxy include, but are not limited to, 3-hydroxypropyl dihydrogen phosphate, 3-hydroxy-1,1-dimethylpropyl dihydrogen phosphate, and the like.

The term "sulfinyl," as used herein, refers to a -S(O)- group.

The term "sulfo," as used herein, refers to a $-SO_3H$ group.

The term "sulfonyl," as used herein, refers to a $-S(O)_2-$ group.

The term "thio," as used herein, refers to a -S- moiety.

The compounds of the present invention can be used in the form of salts derived from inorganic or organic acids. These salts include but are not limited to the following: acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, cyclopentanepropionate, dodecylsulfate, ethanesulfonate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate,

fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxy-ethanesulfonate, lactate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, pamoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, p-toluenesulfonate and undecanoate. Also, the basic nitrogen-containing groups can be quaternized with such agents as loweralkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides, and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl, and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

Examples of acids which may be employed to form pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, sulphuric acid and phosphoric acid and such organic acids as oxalic acid, maleic acid, succinic acid and citric acid.

Basic addition salts can be prepared in situ during the final isolation and purification of the compounds of formula I, or separately by reacting a carboxylic acid function with a suitable base such as the hydroxide, carbonate or bicarbonate of a pharmaceutically acceptable metal cation or with ammonia, or an organic primary, secondary or tertiary amine. Such pharmaceutically acceptable salts include, but are not limited to, cations based on the alkali and alkaline earth metals, such as sodium, lithium, potassium, calcium, magnesium, aluminum salts and the like, as well as nontoxic ammonium, quaternary ammonium, and amine cations, including, but not limited to ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, ethylamine, and the like. Other representative organic amines useful for the formation of base addition salts include diethylamine, ethylenediamine, ethanolamine, diethanolamine, piperazine and the like.

The term "pharmaceutically acceptable ester" as used herein refers to esters which hydrolyze in vivo and include those that break down readily in the human body to leave the parent compound or a salt thereof. Suitable ester groups include, for example, those derived from pharmaceutically acceptable aliphatic carboxylic acids, particularly alkanoic,

alkenoic, cycloalkanoic and alkanedioic acids, in which each alkyl or alkenyl moiety advantageously has not more than 6 carbon atoms. Examples of particular esters includes formates, acetates, propionates, butyates, acrylates and ethylsuccinates.

The term "pharmaceutically acceptable prodrug" as used herein refers to those prodrugs of the compounds of the present invention which are, within the scope of sound medical judgement, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the invention. The term "prodrug" refers to compounds that are rapidly transformed in vivo to provide the parent compound having the above formula, for example by hydrolysis in blood. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A.C.S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference.

As used throughout this specification and the appended claims, the term metabolically cleavable group denotes a moiety which is readily cleaved in vivo from the compound bearing it, wherein said compound, after cleavage remains or becomes pharmacologically active. Metabolically cleavable groups form a class of groups reactive with the carboxyl group of the compounds of this invention are well known to practitioners of the art. They include, but are not limited to groups such as, for example, alkylcarbonyl, such as acetyl, propionyl, butyryl, and the like; unsubstituted and substituted arylcarbonyl, such as benzoyl and substituted benzoyl; alkoxycarbonyl, such as ethoxycarbonyl; trialkylsilyl, such as trimethyl- and triethysilyl; monoesters formed with dicarboxylic acids, such as succinyl, and the like. Because of the ease with which the metabolically cleavable groups of the compounds of this invention are cleaved in vivo, the compounds bearing such groups act as pro-drugs of other prostaglandin biosynthesis inhibitors The compounds bearing the metabolically cleavable groups have the advantage that they may exhibit improved bioavailability as a result of enhanced solubility and/or

rate of absorption conferred upon the parent compound by virtue of the presence of the metabolically cleavable group.

Asymmetric centers may exist in the compounds of the present invention. The present invention contemplates the various stereoisomers and mixtures thereof. Individual stereoisomers of compounds of the present invention are made by synthesis from starting materials containing the chiral centers or by preparation of mixtures of enantiomeric products followed by separation as, for example, by conversion to a mixture of diastereomers followed by separation by recrystallization or chromatographic techniques, or by direct separation of the optical enantiomers on chiral chromatographic columns. Starting compounds of particular stereochemistry are either commercially available or are made by the methods detailed below and resolved by techniques well known in the organic chemical arts.

The present invention discloses pyridazinone compounds which are cyclooxygenase (COX) inhibitors and are selective inhibitors of cyclooxygenase-2 (COX-2). COX-2 is the inducible isoform associated with inflammation, as opposed to the constitutive isoform, cyclooxygenase-1 (COX-1) which is an important "housekeeping" enzyme in many tissues, including the gastrointestinal (GI) tract and the kidneys.

Preferred compounds of the present invention include, but are not limited to,

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-methoxy-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-hydroxy-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-(trifluoromethylsulfonyloxy)-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-Phenyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Phenylpropargyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(2,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Methyl-2-propenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Methyl-2-butenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Trifluoromethylbenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Cyclopropylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Pyridylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Pyridylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Pyridylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(6-Fluoroquinolin-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Quinolin-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinethione

2-Benzyl-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,3-Dichloro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Phenyl-2-propenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Carboxyphenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Methylthiazol-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Chlorothiazol-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,3,4,4,4-Hexafluorobuten-1-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,4-Difluorophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Chlorothien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Methylthien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Diethylaminophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,4,5,6-Pentafluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Phenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Chlorophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Propargyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Cyanophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(α-Methyl-4-fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Phenethyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(3-chloro-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-chloro-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Trifluoromethoxyphenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Trifluoromethylphenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[2-(Benzo[b]thien-3-yl)-2-oxoethyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,3-Dimethyl-2-oxobutyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Thienylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Benzo[b]thienylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2,4-Bis(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

4-(4-Fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-6-methyl-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-6-methyl-3(2H)-pyridazinone;

2-Benzyl-4-(3,4-dichlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-n-propylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-chloro-3-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-chlorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2,4-Bis-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-chloro-3-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-chlorophenyl)-5-[4-(methylsulfinyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-chloro-3-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3,4-dichlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(2-propylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-cyclohexyloxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-cyclopentyloxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-propylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-morpholino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,3-Trifluoro-2-propen-1-yl)]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2,4-Bis(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-cyclopropylmethoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-propen-1-oxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluoro-α-methylbenzyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[4-(Methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2,5-Bis[4-(methylsulfonyl)phenyl]-4-(4-fluorophenyl)-3(2H)-pyridazinone;

2-(3-Methyl-2-thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Trifluoromethyl-4-nitrophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[3-(Methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[3-(Methylsulfonyl)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Chloro-2-thienyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(3-Trifluoromethylphenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[2-(Methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Nitro-2-thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Benzothienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(4-Fluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Bromophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,5-Difluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Nitrobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(4-Acetoxybenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Hydroxybenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Nitrobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4,4-Trifluoro-3-butenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Hexynyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,3-Dichloro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-Cyclohexyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Cyclopentyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Cyclobutyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Methyl-2-butenyl)-4-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Pentafluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Cyclohexenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3-Dihydro-1H-inden-2-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3-Dihydro-1H-inden-1-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-

3(2H)-pyridazinone;

2-(4-Tetrahydro-2H-pyran-4-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Methylcyclopentyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Adamantyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Methylcyclopentyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(1-Methylcyclopentyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluoro-3-vinylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(6-methyl-3-heptenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-cyclopropylidenepropyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(5-methyl-3-hexenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(5-methylhexyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-1-methyl-2E-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,3-Trifluoro-2-propen-1-yl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(1,1,2-Trifluoro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,3-Difluoro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(α-Methyl-3-fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(1-Cyclohexenylmethyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(α-Methyl-2,3,4-trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(α-Methyl-3,5-difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(α-Methyl-3,4-difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,4,6-Trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,4,5-Trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,4-Trifluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4,4,4-Trifluoro-3-methyl-2E-butenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Biphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Bromophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Nitrophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Phenoxyphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone,

2-(4-t-Butylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Chlorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Methylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Vinylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Formylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Nitrophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Bromophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Cyanophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Methyl-2-thienyl))-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Biphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,5-Dimethylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Trifluoromethylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[4-(1-Pyrroyl)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(5-Chloro-2-thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Methylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-ethyl-1-hexyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,5-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Furyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Fluoro-4-methoxyphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[4-(Aminosulfonyl)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,5-Dichlorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluoro-3-methylphenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Chloro-3-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone; :

2-(4-Chloro-2-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(1-Adamantyloxycarbonyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(2,2,2-Trifluoroethyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-fluorophenoxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-fluorophenoxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-phenoxymethyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(t-butylthiomethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-methylpropylthiomethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-propoxy)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Fluorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Bromophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,5-Difluorophenyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(2-methylpropoxy)-5-[3-fluoro-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone:

2-(3,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[3-methyl-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-fluorophenoxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(benzoyloxymethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-methylbutyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3,5-dichlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-ethoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-trifluoromethylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-nitrophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-vinylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[3-(trifluoromethyl)phenyl]-5-[4-

(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-fluoro-4-methoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-fluoro-4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3,5-difluoro-4-methoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(1-oxo-1,3-dihydro-2-benzofuran-5-yl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-propenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-buten-2-yl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(1-cyclohexenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-methylbutyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-benzyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-cyclohexyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-benzyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(phenylethynyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-cyclohexyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(3,4-Difluorophenyl)-4-benzyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-5-[4-(methylsulfonyl)phenyl]-4-vinyl-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-thienyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(1-propynyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-t-butyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-cyclohexyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-cyclohexyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-

(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-benzyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-fluoro-4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3,5-difluoro-4-methoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-methylbutyl)-5-[3-fluoro-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-fluorobenzyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(phenylethynyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3,4-difluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-methylbutyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-methylbutyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-methylbutyl)-5-[3-fluoro-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[4-Fluoro-3-(methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-[4-(trifluoromethylsulfonyl)phenyl]-3(2H)-pyridazinone; :

2-(2,2,2-Trifluoroethyl)-4-(2,2-dimethylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-methoxyphenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-fluoro-5-trifluoromethylphenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-cyanophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-pyridyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-n-propylphenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[4-(methylsulfonyl)phenoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-phenylphenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[2-(methylthio)ethoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(phenylmethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-furylmethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[2-(3,4-dimethoxyphenyl)ethoxy)]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[2-(4-morpholino)ethoxy)]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[2-(1-piperidinyl)ethoxy)]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone:

2-(2,2,2-Trifluoroethyl)-4-[4-(carboxamido)phenoxy)]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(1-indanyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[4-(acetamido)phenoxy)]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-methylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(1-methylcyclopropylmethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3,3-dimethylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-chlorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-bromophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(cyclopentylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(1H-1,2,4-triazole-3-ylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-phenylmethylthio-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(cyclohexylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-chloro-4-fluorophenylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2,2,2-trifluoroethylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(tert-butylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-acetamidophenylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-propylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-methylprop-1-ylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-amino-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-methoxypropylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(cyclopentylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(cyclobutylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3,4-dimethoxyphenethylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(cyclohexylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[2-(1-piperidinyl)ethylamino]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-tetrahydrofurfurylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(cyclopropylmethylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2,3-dihydro-1H-inden-1-ylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(1-piperidinyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-hydroxypropylamino)-5-[4-(methylsulfonyl)phenyl]-

3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[3-(1H-imidazol-1-yl)propylamino]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2R-hydroxylpropylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-cyanoethylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-cyanoanilino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-[3-methoxy-5-(trifluoromethyl)anilino]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-anilino-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2.5-dimethoxyphenylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-fluoroanilino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2.4-difluoroanilino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2.3.5-trifluoroanilino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(4-fluoroanilino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(3-thienyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(2-benzofuranyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(1-oxo-1,3-dihydro-2-benzofuran-5-yl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(5-chloro-2-thienyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(3-nitrophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-vinylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-trifluormethylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(2-methoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(3,4-dimethylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(3-fluoro-4-methoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(2-methoxypyrid-3-yl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(3-ethoxyphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-Benzyl-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-(2H)-pyridazinone;

2-(tert-Butyl)-4-(3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-methoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-hydroxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-Chlorophenyl)-4-(2-methylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(t-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(cyclohexyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2,2-dimethylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-octyn-1-yloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-[2-(dimethylamino)ethoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-[2-methyl-1-(1-methylethyl)propoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(phenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-[3-(dimethylamino)phenoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-methoxyphenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-methylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorophenoxy)-5-[3-fluoro-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2,2-dimethylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-[2-(isopropoxy)ethoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-methylpentyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-methyl-3-penten-1-yloxy)-5-[4-(methylsulfonyl)phenyl]-5-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-[3-(methoxy)butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(N-methylbenzylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone; :

2-(4-Fluorophenyl)-4-(1-piperidinyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(4-Fluorophenyl)-4-(1-pyrrolidinyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-methylphenylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-pyridylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(phenylmethylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-furylmethylthio)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-]2-(methylpropyl)thio]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(cyclopentyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-methylpropyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(cyclopentylmethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-cyclopentylethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-methylbutyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-benzyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-Chlorophenyl)-4-cyclohexyl-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-fluoro-4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(phenethyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-methylpropoxy)-5-[3-fluoro-4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(benzyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-methylpropoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-fluorobenzyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methylbutyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(Tetrahydro-2H-pyrano-2-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-(4-Fluorophenyl)phenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2,2-dimethylpropoxy)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-methylpropoxy)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorobenzyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-Benzyl-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-fluorophenoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-fluoro-4-methylphenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-fluoro-4-methylphenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorophenoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(aminosulfonyl)phenyl]-3(2h)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-methylbutyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(phenethyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-methylbutoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-methylpropoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methylbutyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-methylpropoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methylbutoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(t-Butyl)-4-(3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluoro-3-methylphenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-methylpropoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-methylbutyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-Chloro-4-fluorophenyl)-4-(3-methylbutyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2,2-dimethylpropoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-fluorophenoxy)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,3-Difluoro-2-propenyl)]-4-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-[2-(2-propoxy)ethoxy]-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-methyl-3-pentenyloxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-methylpropoxy)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-methylpentyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-methylpentyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-hydroxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-cyclopropylmethoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-cyclopropyl-1-ethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-cyclopropanemethoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-cyclopropane-1-ethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-methylpentyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-methylpentyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methyl-2-butenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-methyl-2-butenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-methyl-3-pentenyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methyl-3-butenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-methyl-3-pentenyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-methyl-3-butenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(1,5-hexadienyl-3-oxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(5-methyl-2-hexyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-ethyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-thioisopropyl-1-ethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-methylthio-1-hexyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-methyl-4-pentenyl-1-oxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-trifluoromethyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-ethoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-methyl-1-pentyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-methyl-2-pentyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-cyclopentyl-1-ethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-cyclopent-2-enyl-1-ethoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Hydroxy-2-phenylethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Methoxy-2-phenylethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2-Methoxyimino-2-phenylethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-methylpentyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-

3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2,2-dimethylpropoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-methylbutoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-methylpropoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,3-Trifluoropropenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-methoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,3,4,5,6-Pentafluorobenzyl)-4-(4-fluorophenyl)-5-[4-(dimethylamino)methylaminosulfonylphenyl]-3(2H)-pyridazinone;

2-(2,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(dimethylamino)methylaminosulfonylphenyl]-3(2H)-pyridazinone;

(4-Fluorophenyl)-5-[4-(methylselenonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(2-oxo-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-

pyridazinone;

2-(3,4-Difluorophenyl)-4-[2-(methoxyimino)-1-propoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3,4-Difluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3,4-Difluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3,4-Difluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3,4-Difluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-oxo-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-oxo-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-hydroxy-2-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone.

2-(3-Chloro-4-fluorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-

(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(4-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(4-Fluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(4-Fluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-Chlorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-Chlorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone,

(R)-2-(3-Chlorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

(R)-2-(3-Chlorophenyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone:

(S)-2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2-methyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-Fluorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(4-Fluorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(aminosulfonyl)-phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(amino-sulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chlorophenyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

N-[[4-[2-(3,4-Difluorophenyl)-4-(2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(3,4-Difluorophenyl)-4-(2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]-sulfonyl]acetamide, sodium salt;

N-[[4-[2-(4-Fluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-2H-pyridazin-3-on-5-

yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(4-Fluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide, sodium salt;

N-[[4-[2-(3,4-Difluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(3,4-Difluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide, sodium salt;

N-[[4-[2-(3-Chloro-4-fluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(3-Chloro-4-fluorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide, sodium salt,

N-[[4-[2-(3-Chlorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(3-Chlorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide, sodium salt;

N-[[4-[2-(2,2,2-Trifluoroethyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(2,2,2-Trifluoroethyl)-4-(2-hydroxy-2-methyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide, sodium salt,

N-[[4-[2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide;

N-[[4-[2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-2,2-dimethyl-1-propoxy)-2H-pyridazin-3-on-5-yl]phenyl]sulfonyl]acetamide, sodium salt;

2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(2,2,2-Trifluoroethyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Dichlorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone.

2-[(3-Trifluoromethyl)phenyl]-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Dichlorophenyl)-4-(2-hydroxy-2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R,S)-2-(4-Fluorophenyl)-4-(3-hydroxy-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-Chloro-4-fluorophenyl)-4-(3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Dichlorophenyl)-4-(2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Dichlorophenyl)-4-(3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3,4-Difluorophenyl)-4-(4-hydroxy-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[3-(Trifluoromethyl)phenyl]-4-(2-methyl-1-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-[3-(Trifluoromethyl)phenyl]-4-(3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-[3-(Trifluoromethyl)phenyl]-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

(R)-2-(3,4-Difluorophenyl)-4-(3-hydroxy-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3,4-Difluorophenyl)-4-(3-hydroxy-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3,4-Difluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-

(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(4-chlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-chlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

(S)-2-(3-bromophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-trifluoromethylphenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-chloro-4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-fluoro-4-chlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3,4-dichlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-trifluoromethyl-4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(S)-2-(3-bromo-4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3,4-Difluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(4-chlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

(R)-2-(3-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-chlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-bromophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-trifluoromethylphenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-chloro-4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-fluoro-4-chlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3,4-dichlorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-trifluoromethyl-4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

(R)-2-(3-bromo-4-fluorophenyl)-4-(2-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-chlorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chlorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-trifluoromethylphenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-chloro-4-fluorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluoro-4-chlorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3,4-dichlorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-trifluoromethyl-4-fluorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-bromo-4-fluorophenyl)-4-[(S)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-chlorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-fluorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chlorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-trifluoromethylphenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-chloro-4-fluorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-

(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluoro-4-chlorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3,4-dichlorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluoro-3-trifluoromethylphenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromo-4-fluorophenyl)-4-[(R)-2,3-dihydroxy-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-chlorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chlorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone.

2-(3-bromophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-trifluoromethylphenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chloro-4-fluorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluoro-4-chlorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-dichlorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone.

2-(4-fluoro-3-trifluoromethylphenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromo-4-fluorophenyl)-4-(4-hydroxy-4-methyl-1-pentyloxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3,4-Difluorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-chlorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-fluorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-chlorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-trifluoromethylphenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chloro-4-fluorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluoro-4-chlorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-dichlorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(4-fluoro-3-trifluoromethylphenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromo-4-fluorophenyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-Difluorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-

3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-fluorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(4-chlorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chlorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-bromophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-trifluoromethylphenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-chloro-4-fluorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-fluoro-4-chlorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3,4-dichlorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(3-trifluoromethyl-4-fluorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone,

2-(3-bromo-4-fluorophenyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

3-({2-(3,4-difluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-

pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate,

3-({2-(3-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-bromophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-trifluoromethylphenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-chloro-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-fluoro-4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3,4-dichlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-trifluoromethyl-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

3-({2-(3-bromo-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate;

2-(tert-Butyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(tert-Butyl)-4-[3-(2-aminoacetyloxy)-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone;

2-(tert-butyl)-4-[3-{[(2R,3R)-3-carboxy-2,3-dihydroxypropanoyl]oxy}-3-methylbutoxy]-3-methyl-1-butoxy]-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone; and

3-({2-(tert-butyl)-5-[4-(methylsulfonyl)phenyl]-3-oxo-2,3-dihydro-4-pyridazinyl}oxy)-1,1-dimethylpropyl dihydrogen phosphate; or pharmaceutically acceptable salts or prodrugs thereof.

Preparation of Compounds of the Invention

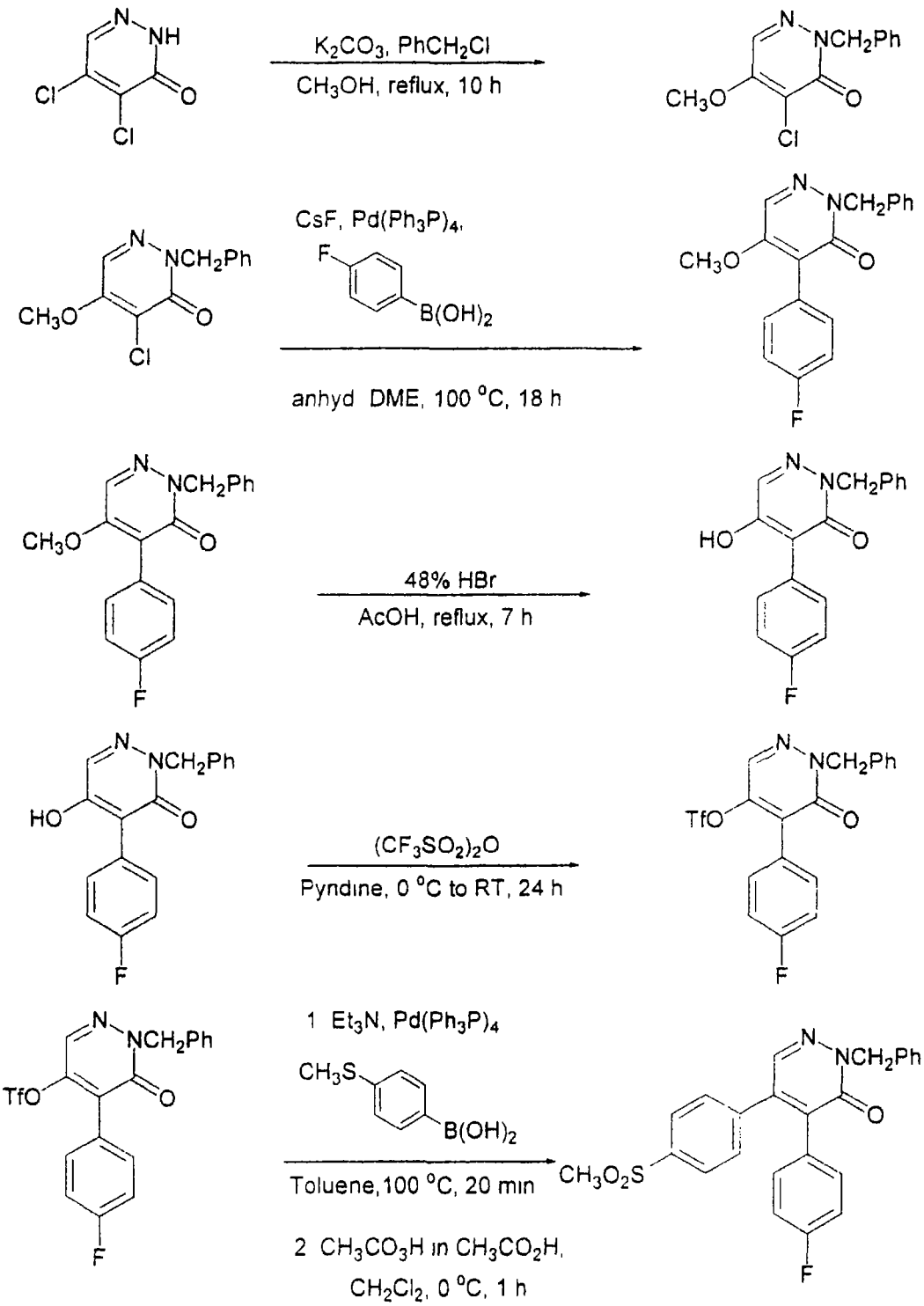
Abbreviations

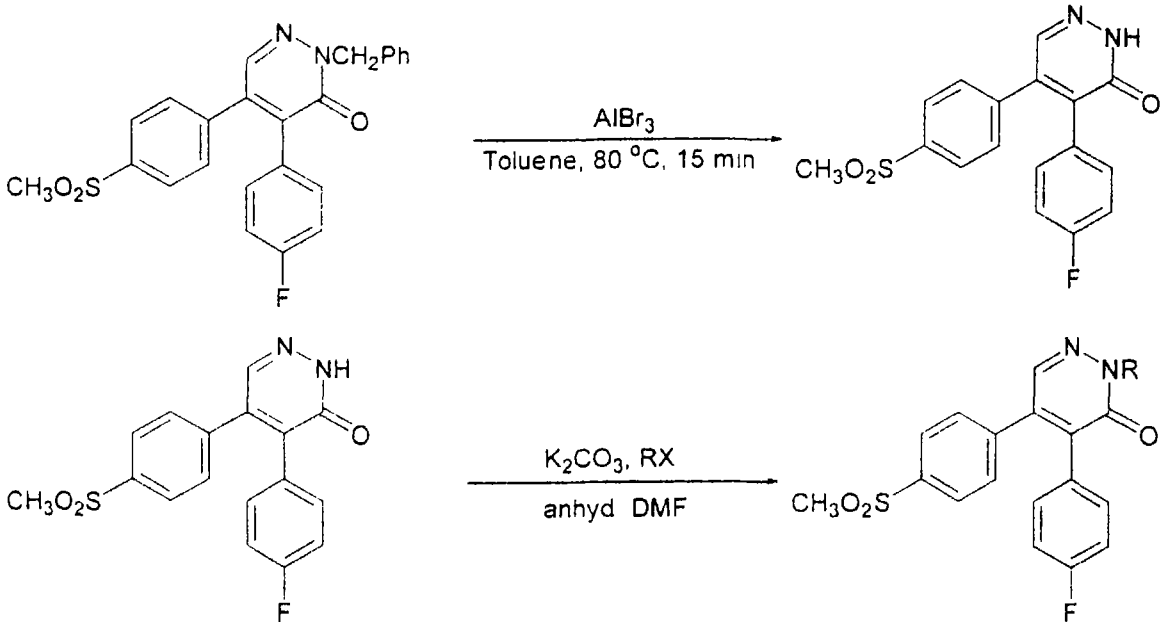
As used throughout this specification and the appended claims, the following abbreviations have been used:

ACD for acid citrate dextrose. CAP for carrageenan induced air pouch prostaglandin. CIP for rat carrageenan pleural inflammation model. COX-2 for cyclooxygenase-2, CPE for carrageenan induced paw edema in rats. DBAD for di-t-butylazodicarboxylate. DEAD for diethyl azodicarboxylate. DIAD for disopropylazodicarboxylate. DMAP for 4-(dimethylamino)pyridine. DME for 1,2-dimethoxyethane, DMF for N,N-dimethylformamide. DMSO for dimethyl sulfoxide, DMSO for dimethyl sulfoxide, EDTA for ethylenediaminetetraacetic acid, EIA for enzyme immunoassay, FAB for fast atom bombardment, GI for gastrointestinal. HMDS. lithium or Li HMDS for lithium 1,1,1,3,3,3-hexamethyldisilazide. HWPX for Human Whole Platelet Cyclooxygenase-1, MCPBA for meta-chloroperoxybenzoic acid. NSAIDs for non-steroidal anti-inflammatory drugs, PEG 400 for polyethyleneglycol. PGE_2 for prostaglandin E_2, PGHS for prostaglandin endoperoxide H synthase, RHUCX1 for recombinant human cyclooxygenase-1, RHUCX2 for recombinant human cyclooxygenase-2, r-hu Cox1 for recombinant human Cox-1, TEA for triethylamine. TFA for trifluoroacetic acid, and THF for tetrahydrofuran and WISH for human amnionic whole cell cyclooxygenase-2. The following examples illustrate the process of the invention, without limitation.

The compounds of the invention may be prepared by a variety of synthetic routes. Representative procedures are outlined in Schemes 1-10, below

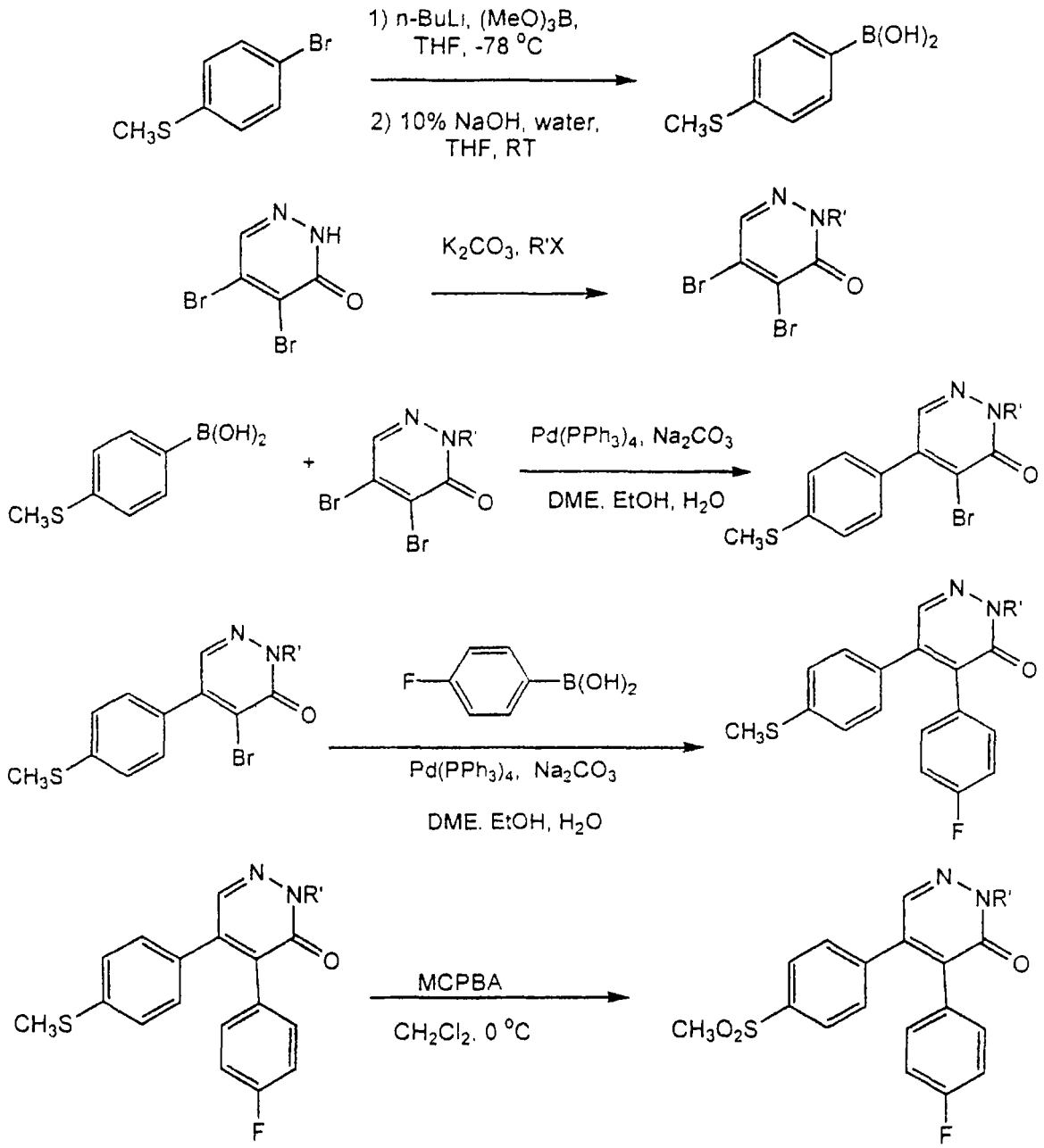
Scheme 1


K2CO3, PhCH2Cl
CH3OH, reflux, 10 h
CsF, Pd(Ph3P)4,
B(OH)2
anhyd DME, 100 °C, 18 h
48% HBr
AcOH, reflux, 7 h
(CF3SO2)2O
Pyridine, 0 °C to RT, 24 h
1 Et3N, Pd(Ph3P)4
Toluene, 100 °C, 20 min
2 CH3CO3H in CH3CO2H,
CH2Cl2, 0 °C, 1 h



A general route to the compounds of the invention having Formula III, where the aryl group at the 5-position on the pyridazinone ring is substituted with a sulfonyl group is described in Scheme 1. Dichloro-3(2H)-pyridazinone can be treated with benzyl chloride and potassium carbonate in methanol to provide 2-benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone. 2-Benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone can be treated with a boronic acid such as 4-fluorobenzeneboronic acid (shown) and a palladium catalyst and the methoxy group can be hydrolyzed with 48% hydrobromic acid to provide the 5-hydroxypyridazinone compound. The 5-hydroxypyridazinone product can be treated with triflic anhydride followed by substitution on the pyridazinone ring using 4-methylthiobenzeneboronic acid to provide the methyl thioether compound. The methyl thioether compound which can be treated with peracetic acid in acetic acid and methylene chloride to provide the methyl sulfone. The benzyl group can be removed using aluminum bromide or another suitable Lewis acid. The R group can be added using an appropriate alkylating agent and base.

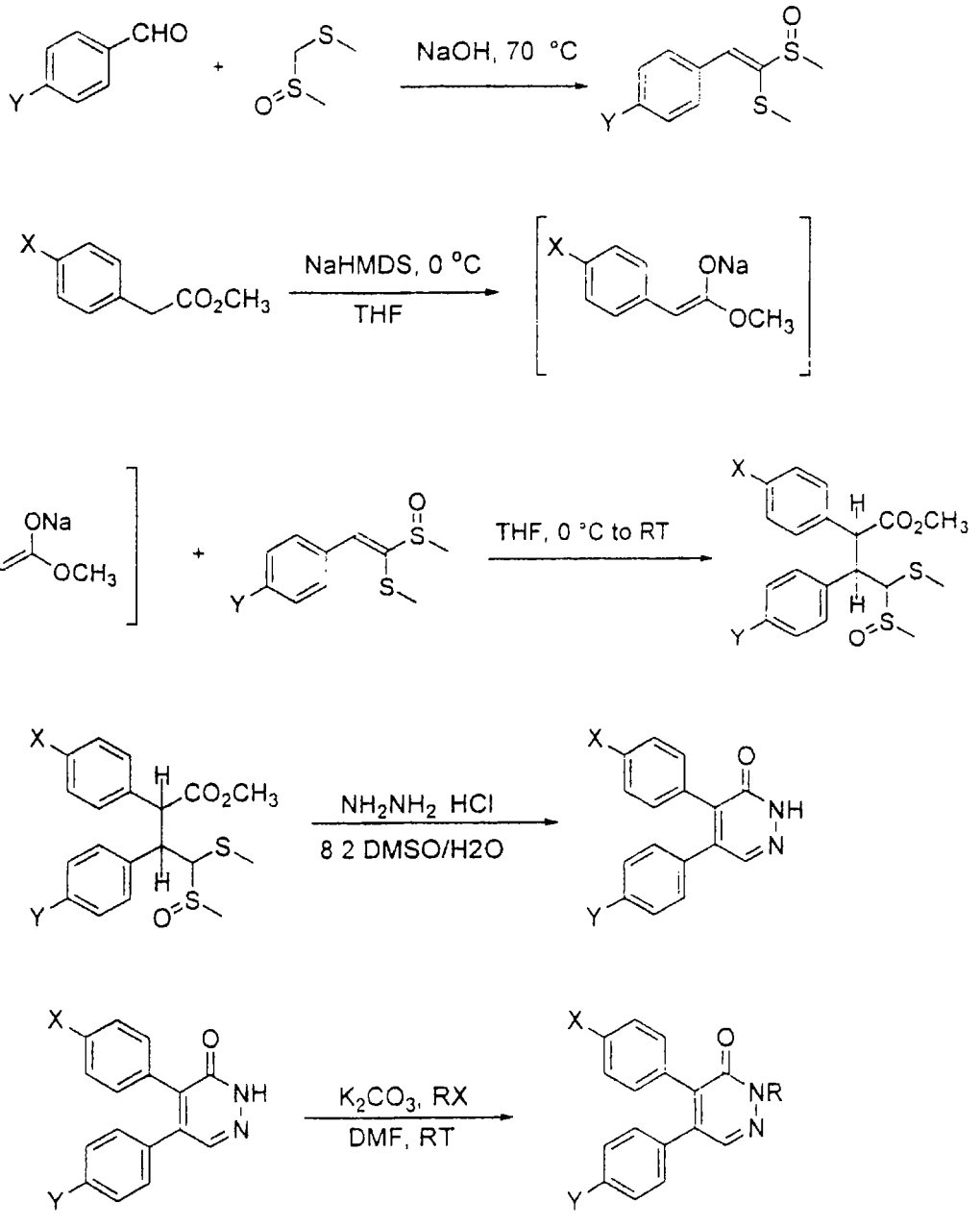
Scheme 2



An alternative route to the compounds of the present invention having Formula III is described in Scheme 2. 4-Bromothioanisole or another suitable thioether can be treated with a trialkoxyborate, such as trimethoxyborate or triisopropylborate to provide 4-(methylthio)benzeneboronic acid. The boronic acid can be treated with 2-benzyl-4,5-dibromo-3(2H)-pyridazinone using tetrakis(triphenylphosphine)palladium (0) in

dimethoxyethane and then coupled with a second boronic acid such as 4-fluorobenzeneboronic acid (shown) in the presence of a palladium catalyst to provide the thioether. The methyl thioether compound can be treated with meta-chloroperoxybenzoic acid (MCPBA) in methylene chloride to provide the methyl sulfone.

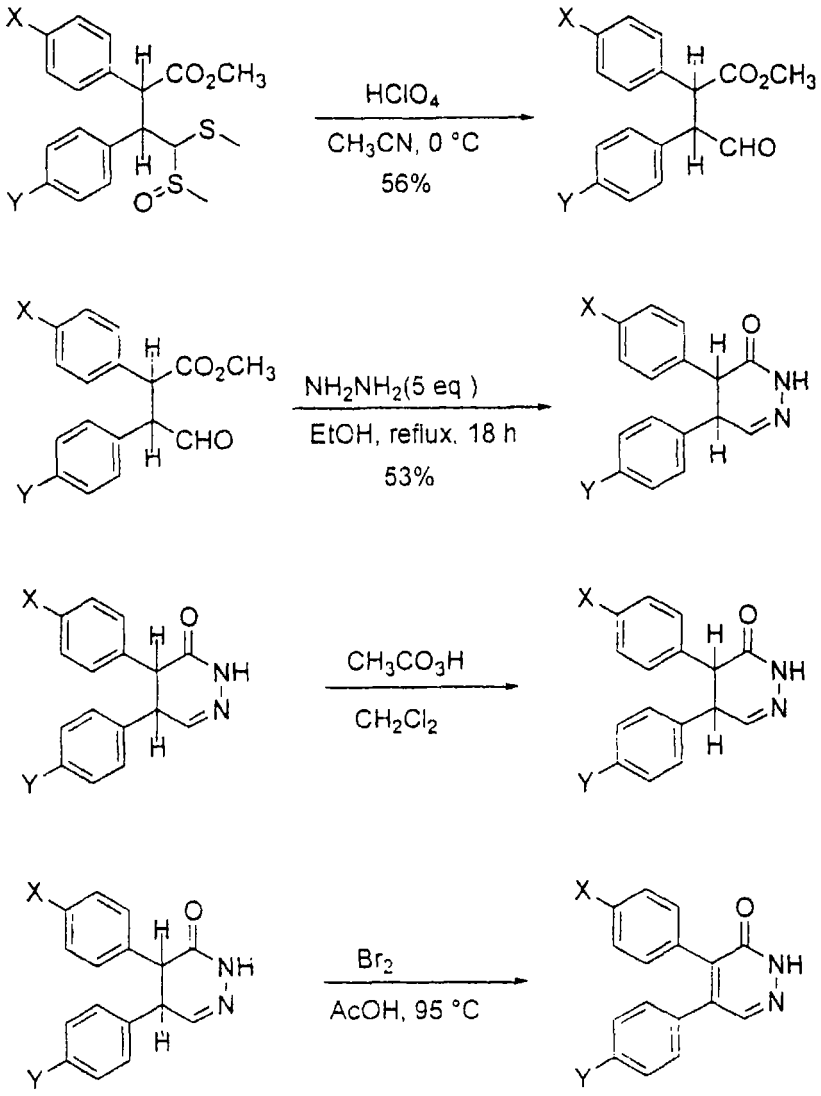
Scheme 3

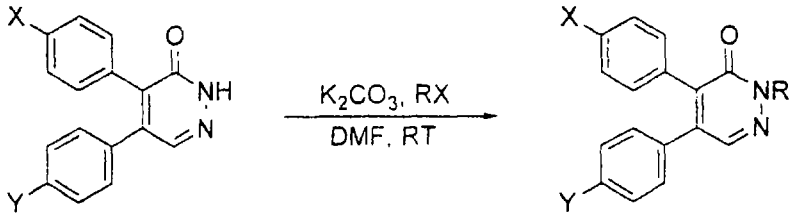


An alternative route to the compounds of the present invention having Formula III

is described in Scheme 3. (4-Thiomethylphenyl)dimethylthioketene acetal, mono-S-oxide can be prepared by reaction of 4-thiomethylbenzaldehyde (Y is CH_3S) with methyl(methylsulfinylmethyl)sulfide and sodium hydroxide. The thioketene acetal and methyl 4-fluorophenylacetate or suitable ester (X is fluorine) can be treated with a strong base such as sodium hexamethyldisilazide in THF to provide the butyrate ester. The dithioacetal ketene can be directly cyclized to the N-unsubstituted pyridazinone using hydrazine and a salt The pyridazinone can be then be alkylated using an appropriate alkylating agent and a base.

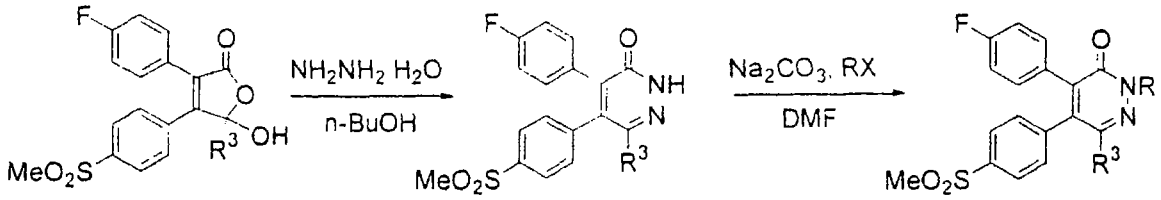
Scheme 4





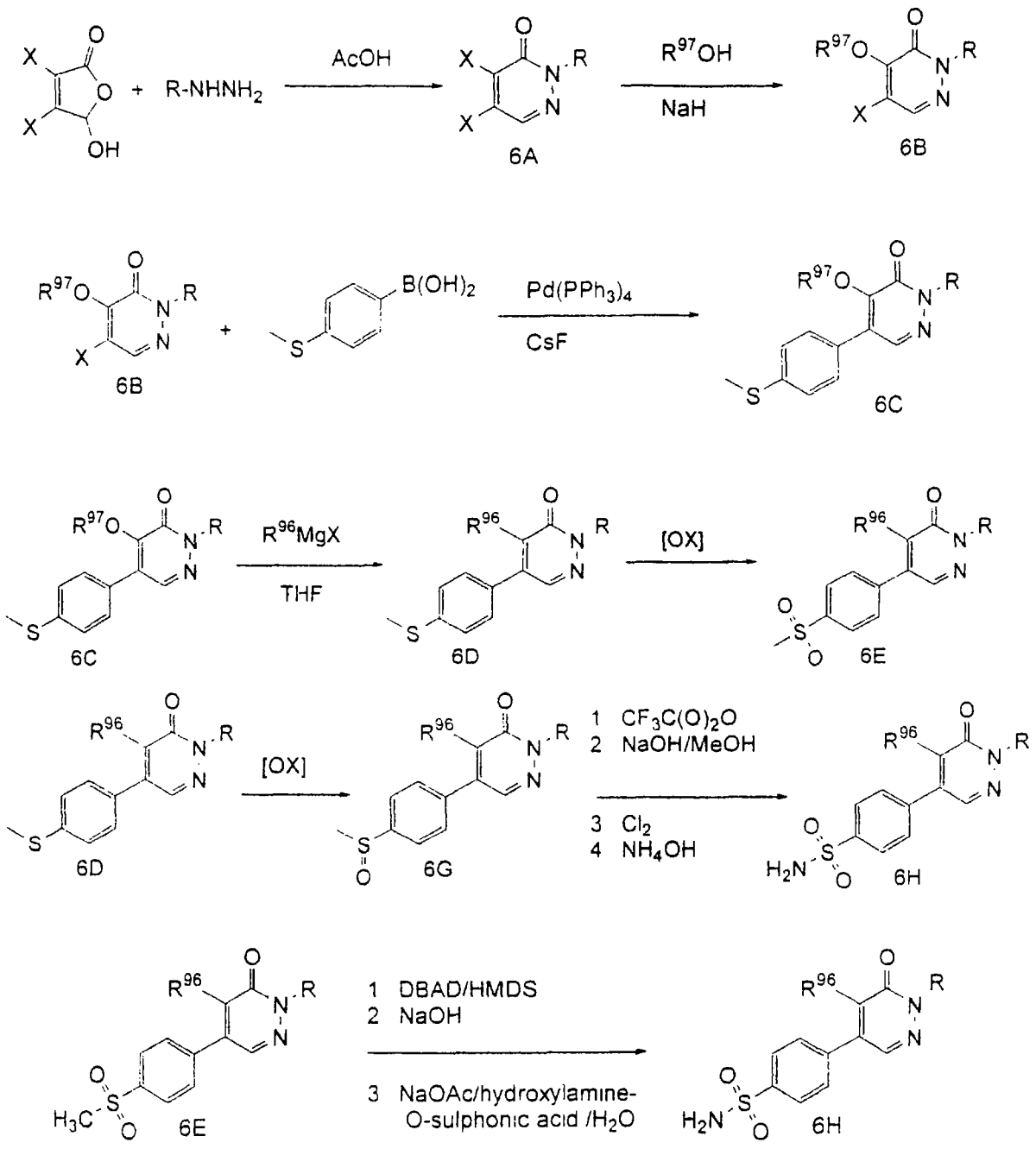
In an alternate route, shown in Scheme 4, the thioacetal ketene (X=F and Y=CH_3S) can be treated with perchloric acid to provide an ester-aldehyde as a mixture of diastereomers. The oxidation products can be treated with hydrazine and then oxidized with peroxyacetic acid to provide the sulfonyl dihydropyridazinone (Y=CH_3SO_2). The dihydropyridazinone can be dehydrogenated to form the pyridazinone by treatment with reagents such as bromine in acetic acid. The R group may be added via substitution using an appropriate alkylating agent and base.

Scheme 5



The preparation of the 5-hydroxy-2(5H)-furanones can be accomplished by the application of methodologies published in a variety of sources, including: J. Med. Chem., 1987, 30, 239-249 and WO 96/36623, hereby completely incorporated by reference. These 5-hydroxy-2(5H)-furanones can be converted to 6-substituted-4,5-diaryl-3(2H)pyridazinones as described in Scheme 5

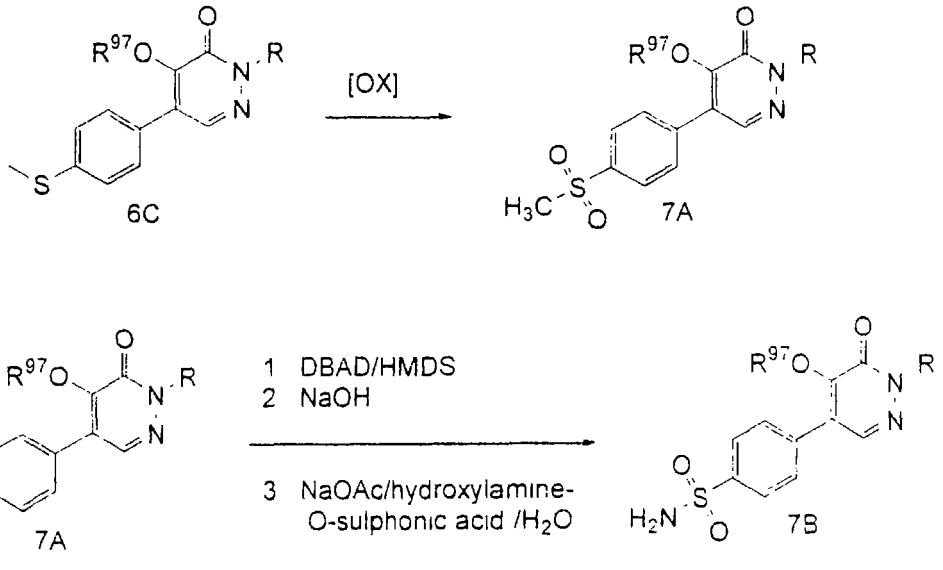
Scheme 6

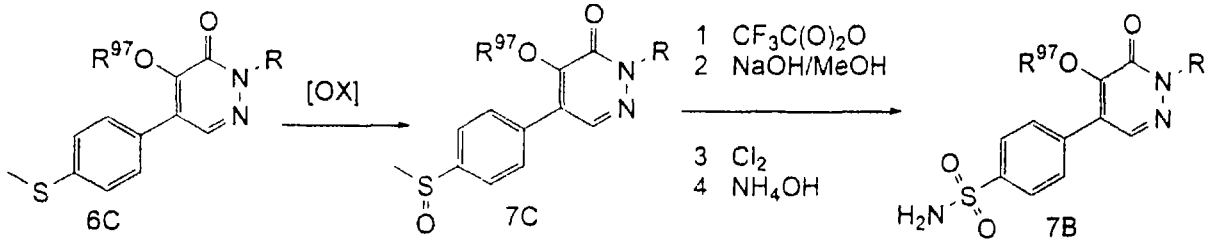


A general route to the compounds of the invention having Formula III, where the aryl group at the 5-position on the pyridazinone ring is substituted with a para-sulfonyl group is described in Scheme 6. A mucohalo acid, such as mucobromic or mucochloric acid, can be treated with an hydrazine having the desired R group to provide the dihalopyridazinone compound, 6A. The dihalo-compound can be treated with an alcohol

in the presence of a base, such as sodium or potassium hydride, to provide an alkoxide 6B where R^{97} is selected from alkyl, aryl, arylalkyl, heterocyclic, and heterocyclic alkyl. (If the alkoxy group is to be removed at a later time then methanol is the preferred alcohol.) The alkoxy-halide can be treated with methylthiophenylboronic acid to provide the alkoxy-pyridazinone 6C. The alkoxy group can be converted to a hydrocarbyl group by treatment with a Grignard reagent to provide thioether 6D where R^{96} is alkyl. The thioether 6D can be oxidized with an oxidizing agent, such as peracetic acid, meta-chloroperoxybenzoic acid and the like, to form the sulfinyl compound 6G, or the methylsulfone compound 6E. The methylsulfinyl compound, 6G, can be treated with trifluoroacetic anhydride and NaOH/MeOH followed by addition of chlorine gas and then ammonia hydroxide to provide the aminosulfonyl compound, 6H Alternatively, the methylsulfonyl compound, 6E, can be treated with a diazodicarboxylate, such as DBAD, DIAD, DEAD and the like, and a disilazane anion, such as lithium HMDS and the like, followed by treatment with sodium acetate and hydroxylamine-O-sulphonic acid in water to provide the aminosulfonyl compound, 6H.

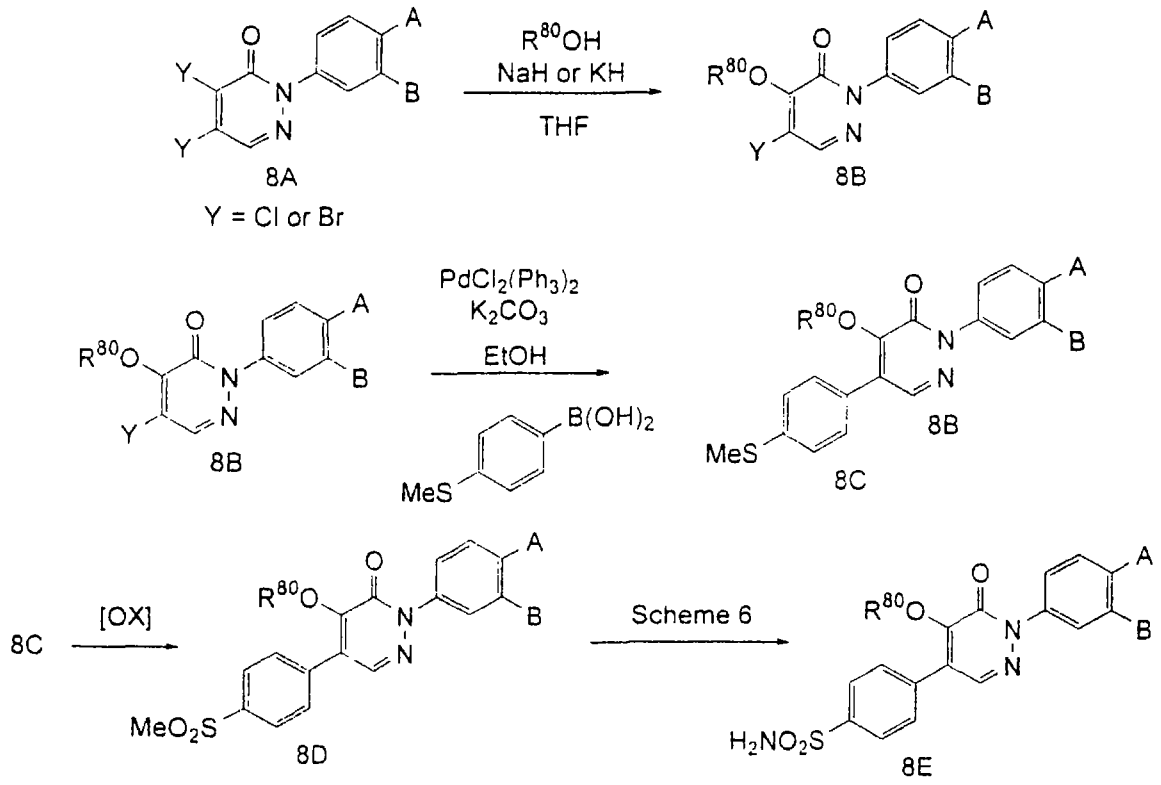
Scheme 7





Methylsulfonyl alkoxy pyridazinones and aminosulfonyl alkoxy pyridazinones can be prepared as described in Scheme 7 Alkoxy-pyridazinone, 6C, from Scheme 6, can be oxidized using peracetic acid to provide methyl sulfone, 7A Methyl sulfone alkoxy pyridazinone, 7A, can be treated as described in Scheme 6 to provide aminosulfonyl alkoxy pyridazinone, 7B. Alternatively, alkoxy-pyridazinone 6C, from Scheme 6, can be oxidized with one equivalent of meta-chloroperoxybenzoic acid or one equivalent of hydroxy(tosyloxy)iodobenzene to provide the methylsulfinyl alkoxy pyridazinone, 7C. Methylsulfinyl alkoxy pyridazinone, 7C, can be treated as described in Scheme 6 to provide aminosulfonyl alkoxy pyridazinone, 7B.

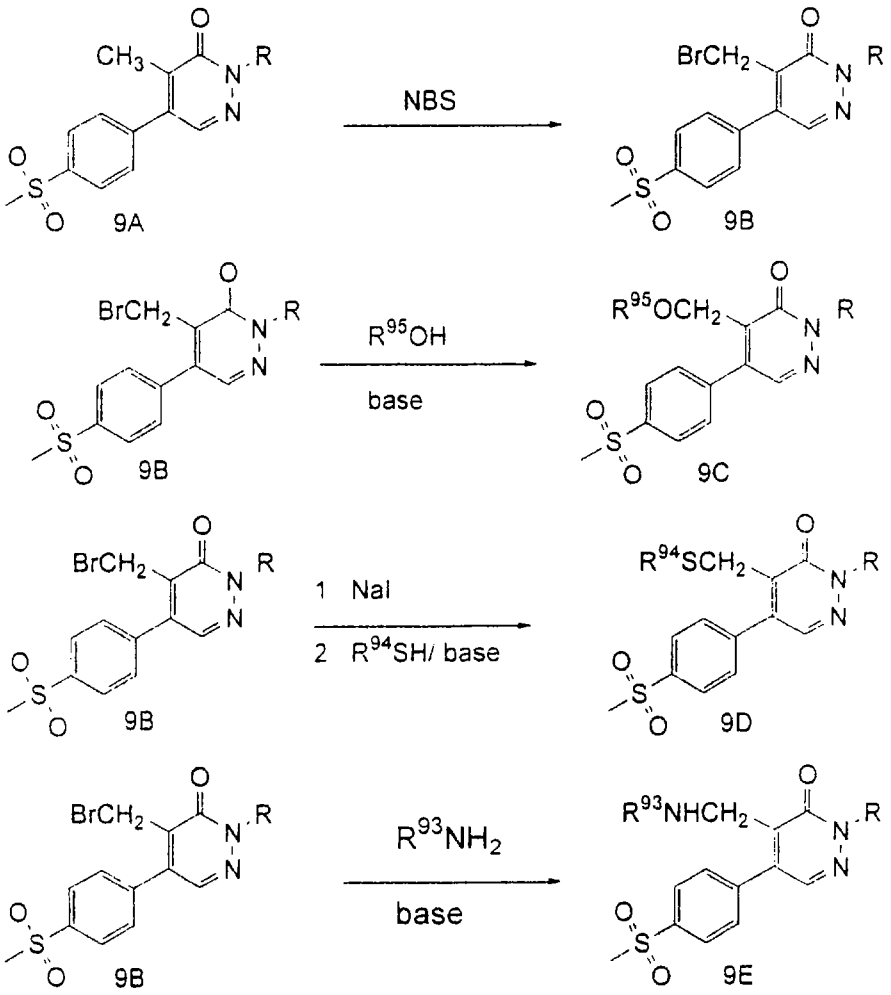
Scheme 8



Pyridazinones of general formula 8D and 8E, wherein R^{80} is hydroxyalkyl, and A and B are selected from alkenyl, alkyl, haloalkyl, and halogen, can be prepared as described in Scheme 8. Pyridazinones of general formula 8A can be treated with diols and a base such as sodium hydride or potassium hydride in THF to selectively provide 4-substituted pyridazinones of general formula 8B. 4-Substituted pyridazinones of general formula 8B can be treated with 4-(methylthio)phenylboronic acid, a base such as potassium carbonate, and a palladium catalyst such as dichlorobis(triphenylphosphine)palladium(II) in ethanol to provide methylthio compounds of general formula 8C. Methylthio compounds of general formula 8C can be oxidized with meta-chloroperoxybenzoic acid or peracetic acid to provide methylsulfones of general formula 8D. Methylsulfones of general formula 8D can be processed as described in Scheme 6 to provide aminosulfonyl compounds of general formula 8E. Alternatively, methylthio compounds of general formula 8C can be oxidized to the sulfoxide and then processed as described in Scheme 6 to provide aminosulfonyl compounds of general

formula 8E.

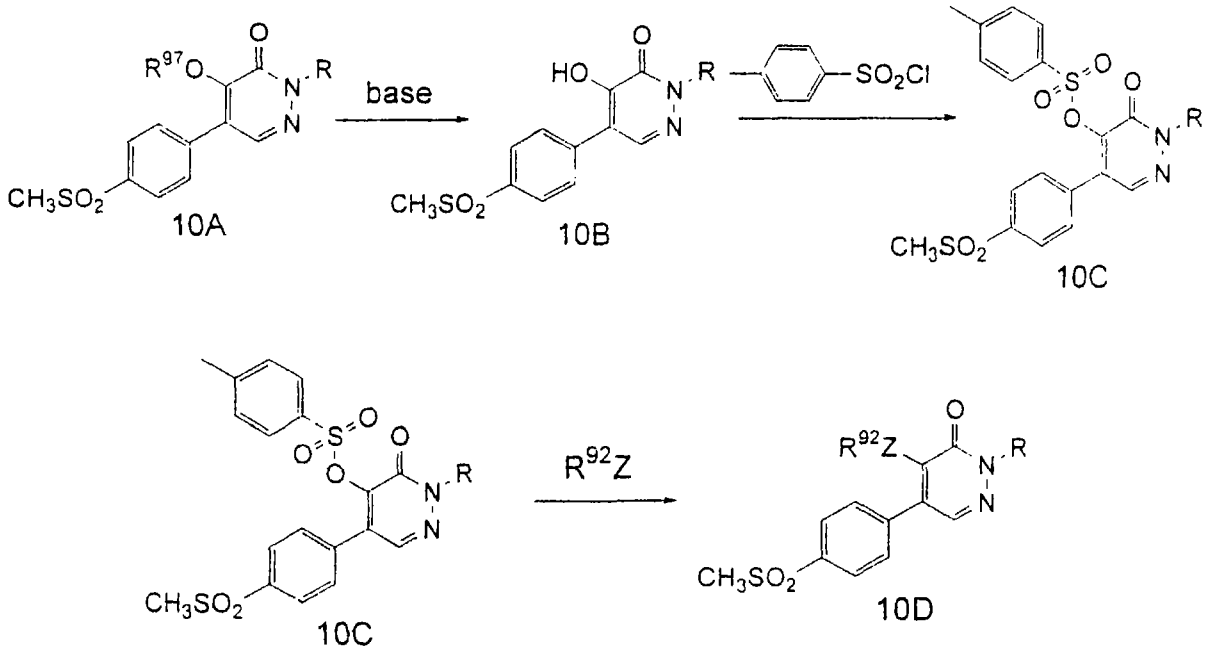
Scheme 9



Preparation of compounds of the invention having Formula III, where the group at the 4-position on the pyridazinone ring is a substituted alkyl or alkenyl group is described in Scheme 9. Pyridazinone 9A can be treated with a halogenating reagent, such as NBS and peroxide, to provide bromo compound 9B The bromo compound can be reacted with an alcohol and a weak base, such as sodium or potassium carbonate, to provide 4-alkyl-ether, 9C where R^{95} is alkyl. Alternatively, bromo compound 9B can be treated with a thio compound in the presence of a base, such as silver carbonate, to provide 4-alkyl-thioether, 9D where R^{94} is alkyl Alternatively, bromo compound 9B can be treated with an amine

and a weak base, such as sodium or potassium carbonate to provide 4-alkylaminoalkyl compound 9E where R^{91} is alkyl.

Scheme 10



A general route to the compounds of the present invention having Formula III, where the group at the 4-position on the pyridazinone ring can be readily substituted is illustrated in Scheme 10. Alkoxide, 10A, where R^{97} is methyl, can be treated with a base, such as sodium or potassium hydroxide, to provide 4-hydroxy-pyradizinone, 10B. The alcohol can be treated with p-toluenesulfonyl chloride to provide tosyloxy compound, 10C. The tosyloxy compound can be readily substituted with a compound $R^{92}Z$ that can undergo a S_NAr reaction. Examples of these compounds are alcohols, thiols, amines or hydrocarbyl anions.

Compounds of the present invention include, but are not intended to be limited to, the following Examples:

Example 1

4-(Methylthio)benzeneboronic acid

A stirred solution of 4-bromothioanisole (5 0 g, 0.0246 mol) in anhydrous tetrahydrofuran (THF) was chilled to -78 °C under a nitrogen atmosphere. A 2.5 M solution of n-butyl lithium (12 mL, 0.030 mol) in hexanes was added dropwise to the chilled solution. When the addition was complete, the reaction mixture was stirred at -78 °C for about 45 minutes. Trimethylborate (8 5 mL, 0.0748) was introduced via syringe. The reaction mixture was then allowed to warm to room temperature overnight. The room temperature solution was treated successively with 10% aqueous sodium hydroxide solution (50 mL) and water (33.5 mL) and stirred at room temperature for 1 hour The reaction mixture was lowered to about pH=4-5 using 10% aqueous citric acid and the THF was removed under reduced pressure. The aqueous residue was saturated with sodium chloride and extracted with ethyl acetate. The organic extract was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to provide a white solid which was washed with hexanes to provide the product as a white solid (yield: 1.5 g; 36%). mp 170 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2 47 (s, 3H), 7.20 (d, J=8 Hz, 2H), 7.71 (d, J=8 Hz, 2H), 7.96 (br s, 2H).

Example 2

2-Benzyl-4,5-dibromo-3(2H)-pyridazinone

Benzyl bromide (0.59 mL, 0.005 mol) was added to a stirred solution of 4,5-dibromo-3(2H)-pyridazinone (1.27 g, 0.005 mol) and potassium carbonate (0.76 g, 0.0055 mol) in 20 mL of anhydrous dimethylformamide (DMF). The solution was stirred overnight at room temperature, and partitioned between aqueous citric acid and ethyl acetate. The aqueous layer was extracted twice with ethyl acetate The combined organic extracts were washed with brine, dried over $MgSO_4$ and filtered The filtrate was concentrated under reduced pressure to provide a beige solid, which was purified by column chromatography (silica gel, 9·1 hexanes/ethyl acetate) The product was obtained as a white solid (yield: 1.32 g, 76.7%) mp 95-96 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.31 (s, 2H), 7.29-7.37 (m, 3H), 7.41-7 47 (m, 2H), 7 79 (s, 1H). MS (DCI/NH_3) m/z 345 $(M-H)^-$ IR (KBr) 1645 cm^{-1}

Example 3

2-Benzyl-4-bromo-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A solution of the boronic acid (0.318 g, 0 mol), from Example 1, the dibromopyridazinone (0.975 g, 0. mol), prepared according to the method of Example 2, and tetrakis(triphenylphosphine)palladium (0) (0.16 g, 0.0142 mol), in dimethoxyethane (30 mL) was prepared. A 2 M aqueous solution of sodium carbonate (2 83 mL, 0. mol) was added to the dimethoxyethane solution and the mixture was heated at reflux. After 16 hours, a chromatographic (TLC) check (9:1 hexanes/ethyl acetate) indicated that both starting materials were still present and a fresh aliquot of palladium catalyst was added. The reaction mixture was stirred at reflux for an additional 5 hours, allowed to cool to room temperature and stand over the weekend The volatile materials were removed under reduced pressure and the residue was partitioned between water and ethyl acetate. The aqueous layer was extracted with ethyl acetate The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered The filtrate was concentrated under reduced pressure to provide an oil which was purified by column chromatography (silica gel, 95:5 hexanes/ethyl acetate). Fractions containing the desired product were combined and concentrated under reduced pressure. This material was rechromatographed (95:5 hexanes/ethyl acetate) to furnish 0.200 g of a beige solid. The solid was crystallized from ether/hexanes to provide white crystals (yield: 110 mg, 15%) mp 115-118 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.53 (s, 3H), 5.40 (s, 2H), 7.30-7.42 (m, 7 H), 7.49-7.54 (m, 2H), 7.65 (s, 1H). MS (DCI/NH_3) m/z 387 $(M+H)^+$.

Example 4

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A solution of the product from Example 3, (0.100 g, 0. mol), 4-fluorobenzeneboronic acid (0.072 g, 0 mol), tetrakis(triphenylphosphine)palladium (0) (0.015 g, 0. mol), and a 2 M aqueous solution of sodium carbonate (0 64 mL, 0. mol) in 30 mL of dimethoxyethane (DME) was stirred at reflux for 16 hours A fresh aliquot of

palladium catalyst was added with an additional equivalent of the boronic acid. The reaction was maintained at reflux for 24 hours. The volatile materials were removed under reduced pressure and the residue was partitioned between water and ethyl acetate. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was adsorbed onto silica gel The silica gel/product was placed at the top of a column of silica gel and the product eluted with 93:7 hexanes/ethyl acetate. Fractions containing product were combined and concentrated under reduced pressure. The residue was purified further by a second column chromatography (silica gel, 95:5 hexanes/ethyl acetate) Fractions containing product were concentrated under reduced pressure to provide a viscous oil (yield: 0 028 g, 27%) ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 5.39 (s, 2H), 6.95 (t, J=9 Hz, 2H), 6.99 (d, J=9 Hz, 2H), 7.11 (d, J=9 Hz, 2H), 7.16-7.23 (m, 2H), 7.30-7.40 (m, 3H), 7.52-7 57 (m, 2H), 7.86 (s, 1H). MS (DCI/NH_3) m/z 403 $(M+H)^+$.

Example 5

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of meta-chloroperoxybenzoic acid (MPCBA) (0.039 g, 0 00013 mol) in dichloromethane (5 mL) was added dropwise to a stirred solution of the sulfide (0.027 g, 0. mol), from Example 4, in chilled (0 °C) dichloromethane (10 mL). After 5 minutes, TLC (1:1 hexanes/ethyl acetate) indicated that the starting sulfide had been consumed. The reaction was quenched with aqueous sodium sulfite. The organic layer was washed twice with aqueous sodium hydroxide and once with brine The dichloromethane solution was dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure The residue was purified by column chromatography (silica gel, 7:3 hexanes/ethyl acetate) to provide the desired sulfone product Further elution with 100% ethyl acetate removed the sulfoxide from the column The sulfoxide product was re-subjected to the MCA oxidant (0.04 g, 1 hour, 0 °C) and worked-up as described above. The residue obtained was combined with the sulfone from the first column and the mixture was purified by column chromatography (silica gel, 7:3 hexanes/ethyl acetate) Fractions containing

product were combined and concentrated under reduced pressure. The residue was crystallized from ether/hexanes to provide the product as white crystals (yield: 13 mg, 44.6%). mp 101-103 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 3H), 5.40 (s, 2H), 6.95 (t, J=9 Hz, 2H), 7.12-7.20 (m, 2H), 7.28-7.41 (m, 3H), 7.31 (d, J=9 Hz, 2H), 7.58-7.53 (m, 2H), 7.84 (s, 1H), 7.87 (d, J=9 Hz, 2H) MS (DCI/NH_3) m/z 435 $(M+H)^+$. MS (F. high res.) calculated: m/z 435.1179 $(M+H)^+$, found: m/z 435.1184 $(M+H)^+$.

Example 6

2-Benzyl-4-(4-fluorophenyl)-5-methoxy-3(2H)-pyridazinone

To a mixture of 2-benzyl-5-methoxy-4-bromo-3(2H)-pyridazinone, prepared according to the method of (S. Cho et al. described in J. Het. Chem., (1996),33, 1579-1582), (2.94 g; 10 mmol), 4-fluorobenzeneboronic acid (1.54 g; 11 mmol), and CsF (3.04 g; 22 mmol) in 25 mL of anhydrous DME, under N_2, was added $Pd(Ph_3P)_4$ (347 mg 0.3 mmol) After addition, the mixture was heated at reflux for at 100 °C, for 18 hours. The mixture was concentrated in vacuo and the residue partitioned between ethyl acetate and water. The acetate layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo The solid residue was suspended in ethyl ether-hexanes and filtered to provide a solid product (yield: 3.1 g; about 100%; > 95% purity). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 3H), 5.36 (s, 2H), 7.09 (t, J=9 Hz, 2H), 7.31 (m, 3H), 7.50 (m, 4H), 7.91 (s, 1H). MS (DCI/NH_3) m/z 311 $(M+H)^+$, 328 $(M+NH_4)^+$.

Example 7

2-Benzyl-4-(4-fluorophenyl)-5-hydroxy-3(2H)-pyridazinone

The product from Example 6 (1.24 g; 4 mmol) in 20 mL of acetic acid was treated with aqueous 48% HBr (25 mL). The mixture was heated at reflux for about 5 to about 8 hours (TLC analysis). The mixture was concentrated in vacuo. The product was dissolved in ethyl acetate, washed with 10% bicarbonate, brine and concentrated in vacuo The residue was treated with diethyl ether-hexanes (2:1) and the solid was filtered to provide an almost pure product (yield 1.16 g; 98%) ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.24 (2H),

7.21 (m, 2H), 7.30 (m, 5H), 7.55 (m, 2H), 7.85 (s, 1H), 11 31 (br s, 1H). MS (DCI/NH_3) m/z 296 $(M+H)^+$, 314 $(M+NH_4)^+$.

Example 8

2-Benzyl-4-(4-fluorophenyl)-5-(trifluoromethylsulfonyloxy)-3(2H)-pyridazinone

A solution of the product from Example 7, (89 mg, 0.3 mmol) in 2.5 mL of anhydrous pyridine under a N_2 atmosphere and maintained at 0 °C was treated with triflic anhydride (Tf_2O; 0.06 mL; 0.32 mmol) dropwise. The resulting mixture was stirred at 0 °C for 5 minutes and at room temperature for 16 hours. (The pyridine and Tf_2O should be pure for good results. Occasionally an additional amount of Tf_2O is necessary to force the reaction to completion.) The mixture was then poured to a cold solution of citric acid and extracted with ethyl acetate to obtain an almost pure product (yield. 127 mg, about 99%) ^1H NMR (300 MHz, DMSO-d_6) δ 5.34 (s, 2H), 7.35 (m, 7H), 7.60 (m, 2H), 8.48 (s, 1H). MS (DCI/NH_3) m/z 429 $(M+H)^+$, 446 $(M+NH_4)^+$.

Example 9

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A mixture of the product from Example 8 (154 mg, 0.36 mmol), 4-(methylthio)benzeneboronic acid (67 mg, 0.4 mmol), Et_3N (0.11 mmol, 0.8 mmol) and $Pd(Ph_3P)_4$ (30 mg, 0 025 mmol) in 15 mL of toluene was heated at reflux, about 100 °C for about 45 minutes The mixture was concentrated in vacuo and the residue purified by column chromatography (hexanes-ethyl acetate 3:1) to provide the title compound (yield: 98 mg, 68%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.47 (s, 3H), 5.38 (s, 2H), 6.98 (m, 4H), 7.12 (m, 2H), 7.20 (m, 2H), 7.35 (m, 3H), 7.54 (m, 2H), 7.86 (s, 1H) MS (DCI/NH_3) m/z 403 $(M+H)^+$, 420 $(M+NH_4)^+$.

Example 10

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

To a solution of the product from Example 9 (140 mg, 0.348 mmol), in 10 mL of CH_2Cl_2, at 0 °C was added peracetic acid (CH_3COOOH; 0.5 mL, 30%). The mixture was stirred at 0 °C for 90 minutes. The dichloromethane was then removed in vacuo. The residue was dissolved in ethyl acetate, washed with 10% $NaHCO_3$, and brine. The ethyl acetate was removed under reduced pressure. The residue was chromatographed (silica gel, CH_2Cl_2-diethyl ether 19:1) to provide the title compound (yield, 130 mg, 86%). ^1H NMR (300 MHz, $CDCl_3$) δ 3.04 (s, 3H), 5.40 (s, 2H), 6.95 (m, 2H), 7.16 (m, 2H), 7.33 (m, 5H), 7.55 (m, 2H), 7.86 (m, 3H). MS (DCI/NH_3) m/z 434 $(M+H)^+$, 452 $(M+NH_4)^+$.

Example 11

4-(4-Fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A mixture of the product from Example 10 (37 mg, 0.085 mmol) and $AlBr_3$ (70 mg, 0.26 mmol) in 10 mL of toluene was heated at reflux, about 80 °C for about 15 minutes and cooled to 0 °C. The cooled mixture was treated with 1N HCl and extracted with ethyl acetate. The acetate layer was washed with water, brine and concentrated in vacuo. Purification of the residue on silica gel column (ethyl acetate as an eluent) provided the title compound (yield: 22 mg, 76%) ^1H NMR (300 MHz, $CDCl_3$) δ 3.07 (s, 3H), 7.00 (t, J=9 Hz, 2H), 7.20 (m, 2H), 7.56 (d, J=9 Hz, 2H), 7.86 (s, 1H), 7.91 (d, J=9 Hz, 2H), 10.94 (br s, 1H). MS (DCI/NH_3) m/z 345 $(M+H)^+$, 362 $(M+NH_4)^+$.

Example 12

2-Phenyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 12A

2-Phenyl-4-chloro-5-methoxy-3(2H)-pyridazinone

The title compound was prepared according to the method of (S. Cho et al. described in J. Het. Chem., (1996), 33, 1579-1582), starting with the N-phenyl-dichloropyridazinone. A mixture of 2-phenyl-4,5-dichloro-3(2H)-pyridazinone (1 g, 4.1 mmol) and finely powdered, anhydrous K_2CO_3 (580 mg, 4.2 mmol) in 50 mL of methanol

was heated at reflux for 5 hours and concentrated in vacuo. The residue was partitioned between water and ethyl acetate. The acetate layer was washed with water, and brine to provide 2-phenyl-4-chloro-5-methoxy-3(2H)-pyridazinone (yield: 920 mg, 95%) ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.15 (s, 3H), 7.50 (m, 5H), 8.43 (s, 1H). MS (DCI/NH_3) m/z 237 $(M+H)^+$, 254 $(M+NH_4)^+$.

Example 12B

2-Phenyl-4-(4-fluorophenyl)-5-methoxy-3(2H)-pyridazinone

The 2-phenyl-4-chloro-5-methoxy-3(2H)-pyridazinone product was coupled with 4-fluorophenylboronic acid according to the method of Example 6 to provide 2-phenyl-4-(4-fluorophenyl)-5-methoxy-3(2H)-pyridazinone (yield: 1.1 g; 96%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00 (s, 3H), 7.10 (t, J=9 Hz, 2H), 7.45 (m, 3H), 7.60 (m, 4H), 8.06 (s, 1H). MS (DCI/NH_3) m/z 297 $(M+H)^+$.

Example 12C

2-Phenyl-4-(4-fluorophenyl)-5-hydroxy-3(2H)-pyridazinone

The 2-phenyl-4-(4-fluorophenyl)-5-methoxy-3(2H)-pyridazinone product was treated with 48% HBr according to the method of Example 7 to furnish 2-phenyl-4-(4-fluorophenyl)-5-hydroxy-3(2H)-pyridazinone (yield: 957 mg, 92%) MS (DCI/NH_3) m/z 283 $(M+H)^+$, 300 $(M+NH_4)^+$.

Example 12D

2-Phenyl-4-(4-fluorophenyl)-5-trifluoromethanesulfonyloxy-3(2H)-pyridazinone

The 2-phenyl-4-(4-fluorophenyl)-5-hydroxy-3(2H)-pyridazinone product was sulfonylated according to the method of Example 8 to furnish 2-phenyl-4-(4-fluorophenyl)-5-trifluoromethanesulfonyloxy-3(2H)-pyridazinone (yield, 1.35 g, 96%) MS (DCI/NH_3) m/z 415 $(M-H)^-$, 432 $(M+NH_4)^+$.

Example 12E

2-Phenyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The 2-phenyl-4-(4-fluorophenyl)-5-trifluoromethanesulfonyloxy-3(2H)-pyridazinone was coupled with 4-(methylthio)phenylboronic acid as in Example 9 to provide 2-phenyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (yield: 915 mg, 92%) which was immediately oxidized with peracetic acid as in Example 9 to provide the title compound after column chromatography (silica gel, 1:1 hexanes-ethyl acetate) and crystallization from diethyl ether-hexanes (yield: 288 mg, 69%). mp 219-220 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 7.15 (t, J=9 Hz, 2H), 7.30 (m, 2H), 7.46 (m, 1H), 7.56 (m, 4H), 7.64 (m, 2H), 7.90 (d, J=9 Hz, 2H), 8.24 (s, 1H). MS (DCI/NH_3) m/z 421 $(M+H)^+$, 438 $(M+NH_4)^+$.

Example 13

4-Fluorophenylacetic acid, methyl ester

A catalytic amount (0.5 mL) of concentrated sulfuric acid was added to a solution of 4-fluorophenylacetic acid (30.8 g, 0.20 mol) in 500 mL of methanol. The solution was stirred at reflux for 4 hours. The volatile materials were removed under reduced pressure to furnish a colorless oil which was dissolved in ether/ethyl acetate and washed with 2 N aqueous Na_2CO_3, brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to provide an oil which was dried overnight under high vacuum (yield, 33.6 g; 95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.59 (s, 2H), 3.65 (s, 3H), 7.01 (t, J=9 Hz, 2H), 7.20-7.28 (m, 2H). MS (DCI/NH_3) m/z 186 $(M+NH_4)^+$.

Example 14

[4-(Methylthio)phenyl]dimethylthioketene acetal, mono-S-oxide

A mixture of methyl(methylsulfinylmethyl)sulfide (50 g, 0.40 mol), and finely powdered sodium hydroxide (3.12 g, 0.078 mol) was stirred at 70 °C for 4 hours. 4-(Methylthio)benzaldehyde (27.4 mL, 0.195 mol) was then added in one lot and the reaction mixture was stirred at 70 °C for an additional 4 hours. The mixture was cooled to room temperature and partitioned between 10% aqueous citric acid and dichloromethane.

The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to provide a brown oil. The oil was purified by column chromatography (7:3 hexanes/ethyl acetate) to provide a solid The solid was crystallized from ether/hexanes (yield: 24.7 g; 72%). mp 52-53 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.53 (s, 3H), 2.77 (s, 3H), 7.17 (d, J=9 Hz, 2H), 7.57 (s, 1H), 7.86 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 259 $(M+H)^+$ and m/z 276 $(M+NH_4)^+$.

Example 15

2-(4-Fluorophenyl)-3-[4-(methylthio)phenyl]-4-methylthio-4-methylsulfinyl-n-butyric acid, methyl ester

A solution of the ester product from Example 13, (16.24 g, 0 0966 mol) in 50 mL of THF was added dropwise to a stirred solution of 1.0 M sodium hexamethyldisilazide in THF (96.6 mL, 0.0966 mol), maintained at 0 °C, under an atmosphere of dry nitrogen. After 30 minutes, a solution of the ketene thioacetal, prepared according to the method of Example 14 (20.8 g, 0 0805 mol), in 50 mL of THF, was added dropwise to the reaction mixture maintained at 0 °C After 4 hours, the reaction mixture was acidified with 10% aqueous citric acid. The aqueous layer was washed twice with ethyl acetate. The organic extracts were combined, washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to provide a brown oil which was purified by column chromatography (85 15 to 1 1 dichloromethane/ethyl acetate gradient). Several products having different Rf values and NMR spectra were isolated These compounds had identical mass spectra. The mixture of compounds was carried on in the following reactions (yield: 22.4 g; 65%). MS (DCI/NH_3) m/z 444 $(M-NH_4)^+$

Example 16

2-(4-Fluorophenyl)-3-[4-(methylthio)phenyl]-3-formyl-n-propanoic acid, methyl ester

The mixture of compounds from Example 17, (9 0 g, 0.021 mol) were dissolved in acetonitrile (80 mL) and cooled to 0 °C. Perchloric acid (60%: 1 06 g, 0.006 mol) was added to the stirred solution. The reaction mixture was stirred at 0 °C for 8 hours, and

quenched with 2 N aqueous Na_2CO_3. The acetonitrile was removed under reduced pressure and the resulting aqueous mixture was extracted with ethyl acetate. The organic solution was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a yellow oil which was purified by column chromatography (silica gel, 7:3 hexanes/ethyl acetate). Fractions containing the highest Rf diastereomers from the product mixture were concentrated in vacuo and the residue was crystallized from methanol to furnish the title aldehyde-ester compound as white crystals (yield. 0.27 g, 4.0%). mp =112-113 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.49 (s, 3H), 2.46 (s, 3H), 4.39 (s, 2H), 7.03 (t, J=9 Hz, 1H), 7.21 (d, J=9 Hz, 1H), 7.25 (d, J=9 Hz, 2H), 7.40-7.47 (m, 2H). MS (DCI/NH_3) m/z 333 $(M+H)^+$ and m/z 350 $(M+NH_4)^+$. Fractions containing lower Rf compounds from the product mixture were concentrated in vacuo and the residue was identified as the hydrate of the aldehyde-ester (yield: 2.6 g, 35.2%) ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 & 2.46 (2 s, 3H), 3.56 & 3.48 (2 s, 3H), 3.55 & 3.76 (2 dd, J=6 Hz, J=6 Hz, 1H), 3.98 & 4.26 (2 d, J=12 Hz, 1H), 5.41 & 5.47 (2 d, J=6 Hz, 1H), 6.96 & 7.00 (t, J=9 Hz, 2H), 7.11-7.26 (m, 6H). MS (DCI/NH_3) m/z 333 $(M-H)^-$ and m/z 350 $(M+NH_4)^+$.

The lowest Rf compound was identified as the hydroxy lactone formed when a hydroxy group from the hydrate displaces the methoxy group from the ester (yield: 1.1 g, 16.4%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 3.54-3.71 (m, 1H), 3.98-4.21 (m, 1H), 4.61 (br s, 1H), 5.85-6.01 (m, 1H), 6.98 (t, J=9 Hz, 2H), 7.12-7.27 (m, 6H). MS (DCI/NH_3) m/z 336 $(M+NH_4)^+$.

Example 17

4-(4-Fluorophenyl)-5-[4-(methylthio)phenyl]-4,5-dihydro-3(2H)-pyridazinone

The aldehyde-ester, hydrate, and hydroxy lactone from Example 16 (0.10 g, 3 mmol), were dissolved in 100 mL of ethanol. This solution was treated with hydrazine monohydrate (0.15 mL, 30 mmol) and the resulting solution was stirred at reflux in a Soxhelet apparatus containing molcular sieves. After 18 hours, the reaction mixture was cooled and the volatile materials removed under reduced pressure. The residue was partitioned between ethyl acetate and aqueous HCl. The aqueous layer was washed twice

with ethyl acetate. The combined organic extracts were washed twice with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (4:1 hexanes/ethyl acetate) to obtain the title compound (yield: 50 mg, 53%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.75 (d, J=12 Hz, 1H), 3.87 (d, J=12 Hz, 1H), 6.93-7.08 (m, 6H), 7.16 (d, J=9 Hz, 2H), 8.71 (s(br), 1H). MS (DCI/NH_3) m/z 315 $(M+H)^+$ and m/z 332 $(M+NH_4)^+$.

Example 18

4-(4-Fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-4,5-dihydro-3(2H)-pyridazinone

A solution of peracetic acid, 32% in acetic acid, (0.4 mL, 1.6 mmol) was added to a stirred solution of the sulfide from Example 17 (0.050 g, 0.16 mmol) in dichloromethane, and maintained at 0 °C. The reaction mixture was stirred for 5 hours at 0 °C then diluted with water. The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to provide an oil which solidified on trituration with ether (yield: 47 mg, 85%). ^1H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 3H), 3.77 (d, J=12 Hz, 1H), 4.05 (d, J=12 Hz, 1H), 6.95-7.08 (m, 4H), 7.28 (d, J=9 Hz, 2H), 7.90 (d, J=9 Hz, 2H), 8.75 (s, broad, 1H). MS (DCI/NH_3) m/z 364 $(M+NH_4)^+$.

Example 19

4-(4-Fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The dihydropyridazinone product from Example 18 (47 mg, 0.136 mmol) was dissolved in acetic acid (25 mL). Bromine (0.025 mL, 0.16 mmol) was added to the solution and the reaction mixture was stirred at 95 °C for 20 minutes. The reaction mixture was concentrated under reduced pressure. The residue was partitioned between ethyl acetate and water. The organic layer was washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to provide a solid which was eluted through a short pad of silica gel with ethyl acetate. The title compound was crystallized from ethyl acetate/hexanes (yield: 35 mg, 75%). mp 255-256 °C ^1H NMR (300 MHz, $CDCl_3$) δ 3.07 (s, 3H), 6.98 (t, J=9 Hz, 2H), 7.16-7.23 (m, 2H), 7.35 (d, J=9

Hz, 2H), 7.86 (s, 1H), 7.91 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 345 $(M+H)^+$ and m/z 362 $(M+NH_4)^+$.

Example 20

2-(4-Fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of the nitrogen-unsubstituted pyridazinone product from Example 19 (160 mg, 0.465 mmol), K_2CO_3 (193 mg, 1.4 mmol), 4-fluorobenzylbromide (0.09 mL, 0.7 mmol) and NaI (catalytic) in 10 mL of anhydrous N,N-dimethylformamide (DMF) was stirred at room temperature for 18 hours. The reaction mixture was quenched with 2N HCl, extracted with ethyl acetate (2 x 20 mL), washed with brine and water, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography (2:2:6 ethyl acetate/dichloromethane/pentanes). Crystallization from ether/pentanes provided white crystals (yield: 110 mg, 52%). mp 153-154 °C. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 5.36 (s, 2H), 6.96 (t, J=8.4 Hz, 2H), 7.04 (t, J=8.7 Hz, 2H), 7.16 (dd, J=9.1 Hz, J=5.4 Hz, 2H), 7.31 (d, J=8.5 Hz, 2H), 7.54 (dd, J=8.8 Hz, 5.5 Hz, 2H), 7.84 (s, 1H), 7.87 (d, J=8.8 Hz, 2H). MS (DCI/NH_3) m/z 453 $(M+H)^+$

Example 21

2-(Phenylpropargyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting phenylpropargyl bromide for 4-fluorobenzyl bromide mp 100-103 °C. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 5.26 (s, 2H), 6.97 (t, J=9 Hz, 2H), 7.20 (dd, J=9 Hz, J=6 Hz, 2H), 7.31 (m, 3H), 7.34 (d, J=9 Hz, 2H), 7.48 (m, 2H), 7.89 (d, J=9 Hz, 2H), 7.9 (s, 1H). MS (DCI/NH_3) m/z 459 $(M+H)^+$.

Example 22

2-(2,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2,4-difluorobenzyl bromide for 4-fluorobenzyl bromide. mp 179-182 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 5.45 (s, 2H), 6.87 (m, 2H), 6.96 (t, J=9 Hz, 2H), 7.17 (dd, J=9 Hz, J=6 Hz, 2H), 7.32 (d, J=9 Hz, 2H), 7.54 (m, 1H), 7.86 (s, 1H), 7.88 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 471 $(M+H)^+$.

Example 23

2-(Methyl-2-propenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 3-chloro-2-methylpropene for 4-fluorobenzyl bromide. mp 140-142 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.86 (s, 3H), 3.08 (s, 3H), 4.83 (s, 2H), 4.94 (t, J=1 Hz, 1H), 5.05 (t, J=1 Hz, 1H), 6.98 (t, J=9 Hz, 2H), 7.21 (dd, J=9 Hz, J=6 Hz, 2H), 7.37 (d, J=9 Hz, 2H), 7.89 (s, 1H), 7.91 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 399 $(M+H)^+$.

Example 24

2-(3-Methyl-2-butenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The desired compound was prepared according to the method of Example 20 substituting 4-bromo-2-methyl-2-butene for 4-fluorobenzyl bromide. mp 169-172 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.78 (s, 3H), 1.85 (s, 3H), 3.06 (s, 3H), 4.86 (d, J=7.5 Hz, 2H), 5.47 (t, J=7.5 Hz, 1H), 6.96 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, J=6 Hz, 2H), 7.33 (d, J=9 Hz, 2H), 7.84 (s, 1H), 7.88 (d, J=9 Hz, 2H) MS (DCI/NH_3) m/z 413 $(M+H)^+$.

Example 25

2-(2-Trifluoromethylbenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(trifluoromethyl)benzyl bromide for 4-fluorobenzyl bromide. mp 87-90 °C.

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^{1}H NMR ($CDCl_3$, 300 MHz) δ 3 07 (s, 3H), 5.66 (s, 2H), 6.97 (t, J=9 Hz, 2H), 7.21 (dd, J=9 Hz, J=6 Hz, 2H), 7.26 (d, J=7.7 Hz 1H), 7.37 (d, J=9 Hz, 2H), 7.42 (t J=7.7 Hz, 1H), 7.53 (t, J=7.7 Hz, 1H), 7.73 (d J=7.7 Hz, 1H), 7.9 (s, 1H), 7.91 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 503 $(M+H)^+$.

Example 26

2-(Cyclopropylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(bromomethyl)cyclopropane for 4-fluorobenzyl bromide. mp 118-121 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.45-0.52 (m, 2H), 0.54-0.63 (m, 2H), 1.40-1.52 (m, 1H), 3 07 (s, 3H), 4.07 (d, J=7 Hz, 2H), 6.97 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, J=6 Hz, 2H), 7.35 (d, J=9 Hz, 2H), 7.83 (s, 1H), 7.88 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 399 $(M-H)^-$ and m/z 416 $(M+NH_4)^+$.

Example 27

2-(2-Pyridylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(bromomethyl)pyridine for 4-fluorobenzyl bromide. mp 182-184 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.07 (s, 3H), 5.56 (s, 2H), 6.95 (m, 2H), 7.17 (m, 2H), 7 26 (m, 1H), 7.35 (m, 2H), 7.46 (m, 1H), 7.71 (m, 1H), 7.90 (m, 3H), 8.63 (m, 1H). MS (DCI/NH_3) m/z 436 $(M+H)^+$.

Example 28

2-(4-Pyridylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 4-(bromomethyl)pyridine for 4-fluorobenzyl bromide. mp 153-156 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.07 (s, 3H), 5 40 (s, 2H), 6 97 (m, 2H), 7.17 (m, 2H), 7 34 (m, 2H), 7 42 (m, 2H), 7 90 (m, 3H), 8 63 (m, 2H) MS (DCI/NH_3) m/z 436 $(M+H)^+$.

Example 29

2-(3-Pyridylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 3-(bromomethyl)pyridine for 4-fluorobenzyl bromide. mp 160-161 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.07 (s, 3H), 5.43 (s, 2H), 6.97 (m, 2H), 7.15 (m, 2H), 7.34 (m, 4H), 7.35 (m, 2H), 7.87 (m, 2H), 7.97 (s, 1H), 8.60 (m, 1H), 8.81 (m, 1H). MS (DCI/NH_3) m/z 436 $(M+H)^+$.

Example 30

2-(6-Fluoroquinolin-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(chloromethyl)-6-fluoroquinoline for 4-fluorobenzyl bromide. mp 116-119 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.07 (s, 3H), 5.73 (s, 2H), 6.96 (m, 2H), 7.18 (m, 2H), 7.34 (m, 4H), 7.35 (m, 2H), 7.46 (m, 2H), 7.58 (m, 3H), 7.90 (m, 3H), 8.12 (m, 2H) MS (DCI/NH_3) m/z 504 $(M+H)^+$.

Example 31

2-(Quinolin-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(chloromethyl)-quinoline for 4-fluorobenzyl bromide. mp 97-100 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 5.75 (s, 2H), 6.95 (m, 2H), 7.19 (m, 2H), 7.35 (m, 2H), 7.55 (m, 2H), 7.73 (m, 1H), 7.82 (m, 1H), 7.90 (m, 3H), 8.15 (m, 2H) MS (DCI/NH_3) m/z 386 $(M+H)^+$

Example 32

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinethione

A mixture of 2-benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone, prepared according to the method of Example 5, (109 mg, 0.25 mmol) and Lawesson's reagent (202 mg, 0.5 mmol) in 15 mL of toluene was stirred at reflux for 48 hours. The mixture was concentrated in vacuo and the residue was chromatographed (silica gel, ethyl acetate) to provide the title compound (yield: 100 mg, 88%). mp 88-90 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.04 (s, 3H), 6.05 (s, 2H), 6.96 (m, 2H), 7.08 (m, 2H), 7.26 (m, 2H), 7.37 (m, 3H), 7.61 (m, 2H), 7.84 (d, J=9 Hz, 2H), 8.13 (s, 1H) MS (DCI/NH_3) m/z 451 $(M+H)^+$.

Example 33

2-Benzyl-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

Example 33 was prepared using a similar procedure as that described in (M. De Vleeschauwer and J.V. Gauthier, Syn. Lett., (1997) 375).

Example 33A

2-Benzyl-4-(4-fluorophenyl)-5-[4-(methylsulfinyl)phenyl]-3(2H)-pyridazinone

A solution of 2-benzyl-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone, prepared according to the method of Example 4, (450 mg, 1.12 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a suspension of hydroxy(tosyloxy)iodobenzene (439 mg, 1.12 mmol) in CH_2Cl_2 (15 mL) and the mixture was stirred until a clear solution was obtained (about 1 hour). The reaction mixture was then washed with water and dried with $MgSO_4$. Removal of solvent in vacuo provided the corresponding sulfoxide (yield: 485 mg, about 100%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.72 (s, 3H), 5.40 (s, 2H), 6.90 (m, 2H), 7.15 (m, 3H), 7.33 (m, 3H), 7.57 (m, 3H), 7.71 (m, 1H), 7.86 (s, 1H). MS (DCI/NH_3) m/z 419 $(M+H)^+$, 436 $(M+NH_4)^+$.

Example 33B

2-benzyl-4-(4-fluorophenyl)-5-(acetoxymethylsulfonylphenyl)-3(2H)-pyridazinone

A suspension of the sulfoxide from Example 33A, (485 mg, 1.12 mmol) and AcONa (1 4 g) in 15 mL of Ac_2O was stirred at reflux for 2 hours and concentrated in vacuo. The residue was distilled twice with toluene, dissolved in 25 mL of CH_2Cl_2, cooled to 0 °C, and treated with CH_3CO_3H (1 mL). After 1 hour, the mixture was washed, successively, with saturated $NaHCO_3$ and brine The solvent was removed in vacuo. The residue was chromatographed (silica gel, 1:1 hexanes-ethyl acetate) to provide the desired product, 2-benzyl-4-(4-fluorophenyl)-5-(acetoxymethylsulfonylphenyl)-3(2H)-pyridazinone (yield 150 mg, 27%). MS (DCI/NH_3) m/z 493 $(M+H)^+$.

Example 33C

2-Benzyl-4-(4-fluorophenyl)-5-[4-(sodiumsulfinate)phenyl]-3(2H)-pyridazinone

To a solution of the acetoxymethylsulfone from Example 33B (150 mg, 0.305 mmol), in 10 mL of THF and 5 mL of methanol at 0 °C, was added 1 N NaOH (0.305 mL, 0.305 mmol) The mixture was stirred at 0 °C for 1 hour. The mixture was concentrated in vacuo, the residual water was removed via an EtOH/toluene azeotrope followed by a toluene azeotrope. The residue was dried under high vacuum for 48 hours to provide the sodium sulfinate (yield: 140 mg, 96%). MS (DCI/NH_3) m/z 443 $(M+H)^+$

Example 33D

2-Benzyl-4-(4-fluorophenyl)-5-[4-(chlorosulfonyl)phenyl]-3(2H)-pyridazinone

The sodium sulfinate (about 0.31 mmol) in CH_2Cl_2 (10 mL) was treated at 0 °C with $SOCl_2$ (0.033 mL, 0.4 mmol) for 2 hours. The mixture was washed with brine, dried with $MgSO_4$ and concentrated in vacuo to provide the crude sulfonyl chloride (yield, 145 mg, about 100%). MS (DCI/NH_3) m/z 455 $(M+H)^+$.

Example 33E

2-Benzyl-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The crude chloride prepared according to the method of Example 33D, in 10 mL of THF, was added to a solution of 50% NH_4OH, in 10 mL of THF, maintained at 0 °C. The

mixture was allowed to warm to room temperature over 3.5 hours. The THF was removed in vacuo and the product was extracted with ethyl acetate. The ethyl acetate was removed in vacuo and the residue was treated with diethyl ether-hexanes 2:1 to provide the sulfonamide (yield: 113 mg, 84%). mp 188-191 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.70 (dd, J=15 Hz, 2H), 5.36 (s, 2H), 7.13 (t, J=9 Hz, 2H), 7.22 (m, 2H), 7.40 (m, 7H), 7.73 (d, J=9 Hz, 2H), 8.11 (s, 1H) MS (DCI/NH_3) m/z 436 $(M+H)^+$.

Example 34

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-iodo-1,1,1-trifluoroethane for 4-fluorobenzyl bromide. mp 177-179 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 4.88 (q, J=9 Hz, 2H), 6.98 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, J=6 Hz, 2H), 7.35 (d, J=9 Hz, 2H), 7.89 (s, 1H), 7.91 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 427 $(M+H)^+$ and m/z 444 $(M+NH_4)^+$.

Example 35

2-(3,3-Dichloro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 1,1,3-trichloropropene for 4-fluorobenzyl bromide. mp 150-152 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 4.98 (d, J=7 Hz, 2H), 6.25 (t, J=7 Hz, 1H), 6.98 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, J=6 Hz, 2H), 7.33 (d, J=9 Hz, 2H), 7.85 (s, 1H), 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 453 $(M+H)^+$ and m/z 470 $(M+NH_4)^+$.

Example 36

2-(3-Phenyl-2-propenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting cinnamyl bromide for 4-fluorobenzyl bromide. mp 165-167 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 5.01 (d, J=7 Hz, 2H), 6.48 (dt, J=15 Hz, 7 Hz, 1H), 6.79 (d, J=15 Hz, 1H), 6 97 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, J=6 Hz, 2H), 7.25-7.44 (m, 5H), 7.37 (d, J=9 Hz, 2H), 7.86 (s, 1H), 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 461 $(M-H)^-$ and m/z 478 $(M+NH_4)^-$.

Example 37

2-(4-Carboxyphenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting methyl 4-(bromomethyl)benzoate for 4-fluorobenzyl bromide and hydrolysis of the resulting ester. mp 239-241 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.06 (s, 3H), 5.46 (s, 2H), 6.96 (t, J=9 Hz, 2H), 7.17 (dd, J=9 Hz, 6 Hz, 2H), 7.33 (d, J=9 Hz, 2H), 7.63 (d, J=9 Hz, 2H), 7.87 (s, 1H), 7 89 (d, J=9 Hz, 2H), 8.08 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 479 $(M-H)^-$ and m/z 496 $(M+NH_4)^+$.

Example 38

2-(5-Methylthiazol-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(bromomethyl)-5-methylthiazole for 4-fluorobenzyl bromide mp 114-116 °C. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 2.64 (s, 3H), 3.23 (s, 2H), 5.37 (s, 2H), 7.13 (m, 2H), 7.23 (m, 2H), 7.40 (s, 1H), 7.47 (d, J=8 Hz, 2H), 7.87 (d, J=8 Hz, 2H), 8 10 (s, 1H). MS (DCI/NH_3) m/z 356 $(M+H)^+$.

Example 39

2-(5-Chlorothiazol-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(bromomethyl)-5-chlorothiazole for 4-fluorobenzyl bromide. mp 185-186 °C. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 2.32 (s, 3H), 5 50 (s, 2H), 7.15 (m, 2H), 7.24 (m, 2H), 7.47 (m, 2H), 7.87 (m, 3H), 8.14 (s, 1H). MS (DCI/NH_3) m/z 476 $(M+H)^+$ and m/z 493 $(M+NH_4)^+$.

Example 40

2-(2,3,3,4,4,4-Hexafluorobuten-1-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2,2,3,3,4,4,4-heptafluoro-1-iodobutane for 4-fluorobenzyl bromide. Under the alkylation conditions, elimination of HF provided the unsaturated product. mp 167-169 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.07 (s, 3H), 7 00 (t, J=9 Hz, 2H), 7.17 (dd, J=9 Hz, 6 Hz, 2H), 7.33 (d, J=9 Hz, 2H), 7.68 (d, J=24 Hz, 1H), 7.93 (d, J=9 Hz, 2H), 8.01 (s, 1H). MS (DCI/NH_3) m/z 507 $(M+H)^+$ and m/z 524 $(M+NH_4)^+$.

Example 41

2-(2,4-Difluorophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-chloro-2',4'-difluoroacetophenone for 4-fluorobenzyl bromide. mp 191-192 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.08 (s, 3H), 5.57 (d, J=3 Hz, 2H), 6.94-7.07 (m, 2H), 6 96 (t, J=9 Hz, 2H), 7.39 (dd, J=9 Hz, 6 Hz, 2H), 7.91 (s, 1H), 7.91 (d, J=9 Hz, 2H), 8.03-8.12 (m, 1H). MS (DCI/NH_3) m/z 499 $(M+H)^+$ and m/z 516 $(M+NH_4)^+$

Example 42

2-(5-Chlorothien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(bromomethyl)-5-chlorothiophene for 4-fluorobenzyl bromide. mp 139-141 °C. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 3.23 (s, 3H), 5.43 (s, 2H), 7.03 (d, J=4 Hz, 1H), 7.09-7.29 (m, 5H), 7.47 (d, J=8 Hz, 2H), 7.87 (d, J=8 Hz, 3H), 8.13 (s, 1H). MS (DCI/NH_3) m/z 474 $(M+H)^+$ and m/z 492 $(M+NH_4)^+$.

Example 43

2-(5-Methylthien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-(bromomethyl)-5-methylthiophene for 4-fluorobenzyl bromide. mp 172-175 °C. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 3.22 (s, 3H), 5.49 (s, 2H), 7.03 (m, 1H), 7.14 (m, 2H), 7.23 (m, 3H), 7.48 (m, 3H), 7.86 (m, 2H), 8.11 (s, 1H). MS (DCI/NH_3) m/z 441 $(M+H)^+$ and m/z 458 $(M+NH_4)^+$

Example 44

2-(4-Diethylaminophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-chloro-4'-diethylaminoacetophenone for 4-fluorobenzyl bromide. mp 105-108 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 (t, J=7 Hz, 3H), 3.07 (s, 3H), 3.44 (q, J=7 Hz, 2H), 5.61 (s, 2H), 6.66 (d, J=9 Hz, 2H), 6.94 (t, J=9 Hz, 2H), 7.21 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.87-7.94 (m, 4H), 7.90 (s, 1H). MS (DCI/NH_3) m/z 534 $(M+H)^+$.

Example 45

2-(2,3,4,5,6-Pentafluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2,3,4,5,6-pentafluorobenzyl bromide for 4-fluorobenzyl bromide mp 115-116

°C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.06 (s, 3H), 5.50 (s, 2H), 6.96 (t, J=9 Hz, 2H), 7.17 (dd, J=9 Hz, 6 Hz, 2H), 7.33 (d, J=9 Hz, 2H), 7.82 (s, 1H), 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 525 $(M+H)^+$ and m/z 542 $(M+NH_4)^+$.

Example 46

2-(Phenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-bromoacetophenone for 4-fluorobenzyl bromide mp 228-230 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.07 (s, 3H), 5.68 (s, 2H), 6.95 (t, J=9 Hz, 2H), 7.20 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.53 (t, J=7 Hz, 2H), 7.65 (t, J=7 Hz, 1H), 7.90 (d, J=9 Hz, 2H), 7.91 (s, 1H), 8.04 (d, J=7 Hz, 2H). MS (DCI/NH_3) m/z 463 $(M+H)^+$ and m/z 480 $(M+NH_4)^+$.

Example 47

2-(4-Chlorophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-bromo-4'-chloroacetophenone for 4-fluorobenzyl bromide. mp 186-188 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.07 (s, 3H), 5.63 (s, 2H), 6.95 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.51 (d, J=9 Hz, 2H), 7.65 (t, J=7 Hz, 1H), 7.90 (d, J=9 Hz, 2H), 7.91 (s, 1H), 7.98 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 497 $(M+H)^+$ and m/z 514 $(M+NH_4)^+$.

Example 48

2-(Propargyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting propargyl bromide for 4-fluorobenzyl bromide. mp 196-198 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 2.42 (t, J=3 Hz, 1H), 3.06 (s, 3H), 5.04 (d, J=3 Hz, 2H), 6.97 (t, J=9

Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.34 (d, J=9 Hz, 2H), 7.90 (s, 1H), 7.91 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 383 $(M+H)^+$ and m/z 400 $(M+NH_4)^+$.

Example 49

2-(4-Cyanophenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-bromo-4'-cyanoacetophenone for 4-fluorobenzyl bromide. mp 188-189 °C. ^1H NMR ($CDCl_3$, 300 MHz) 3.08 (s, 3H), 5.64 (s, 2H), 6.96 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.84 (d, J=9 Hz, 2H), 7.91 (d, J=9 Hz, 2H), 7.93 (s, 1H), 8.14 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 488 $(M+H)^+$.

Example 50

2-(α-Methyl-4-fluorobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting α-methyl-4-fluorobenzyl bromide for 4-fluorobenzyl bromide. mp 162-164 °C ^1H NMR ($CDCl_3$, 300 MHz) 3.06 (s, 3H), 6.40 (t, J=9 Hz, 2H), 6.95 (t, J=9 Hz, 2H), 7.05 (t, J=9 Hz, 2H), 7.15 (dd, J=9 Hz and 6 Hz, 2H), 7.31 (d, J=9 Hz, 2H), 7.53 (dd, J=9 Hz and 6 Hz, 2H), 7.87 (d, J=9 Hz, 2H), 7.88 (s, 1H). MS (DCI/NH_3) m/z 467 $(M+H)^+$ and m/z 484 $(M+NH_4)^+$.

Example 51

2-Phenethyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting (2-bromoethyl)benzene for 4-fluorobenzyl bromide. mp 170-171 °C ^1H NMR ($CDCl_3$, 300 MHz) 3.07 (s, 3H), 3.20 (t, J=9 Hz, 2H), 4.28 (t, J=9 Hz, 2H), 6.98 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz and 6 Hz, 2H), 7.22-37 (m, 5 H), 7.34 (d, J=9 Hz, 2H), 7.83 (s, 1H), 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 449 $(M+H)^+$ and m/z 466 $(M+NH_4)^+$

Example 52

2-Benzyl-4-(3-chloro-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method described in Examples 6-10 substituting 3-chloro-4-fluorobenzeneboronic acid for 4-fluorobenzeneboronic acid in Example 6 mp 134-136 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.06 (s, 3H), 5.41 (s, 2H), 6.96-7.02 (m, 2H), 7.29-7.41 (m, 3H), 7.33 (d, J=9 Hz, 2H), 7.51-7.56 (m, 2H), 7.85 (s, 1H), 7.91 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 469 $(M+H)^+$ and m/z 486 $(M+NH_4)^+$.

Example 53

2-Benzyl-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method described in Examples 6-10 except substituting 4-chlorobenzeneboronic acid for 4-fluorobenzeneboronic acid in Example 6. mp 157-159 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.05 (s, 3H), 5.40 (s, 2H), 7.11 (d, J=9 Hz, 2H), 7.24 (d, J=9 Hz, 2H), 7.28-7.40 (m, 2H), 7.31 (d, J=9 Hz, 2H), 7.51-7.57 (m, 2H), 7.84 (s, 1H), 7.88 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 451 $(M+H)^+$ and m/z 468 $(M+NH_4)^+$.

Example 54

2-(2,2,2-Trifluoroethyl)-4-(3-chloro-4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by N-debenzylation of the product, prepared in Example 52 according to the method of Example 11, followed by alkylation with 2-iodo-1,1,1-trifluoroethane according to the method of Example 20 mp 165-166 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.07 (s, 3H), 4.89 (q, J=9 Hz, 2H), 7.00-7.06 (m, 2H), 7.31-7.35 (m, 1H), 7.37 (d, J=9 Hz, 2H), 7.90 (s, 1H), 7.94 (d, J=9 Hz, 2H) MS (DCI/NH_3) m/z 461 $(M+H)^+$ and m/z 478 $(M+NH_4)^+$.

Example 55

2-(4-Trifluoromethoxyphenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-bromo-4'-trifluoromethoxyacetophenone for 4-fluorobenzyl bromide. mp 160-161 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.08 (s, 3H), 5.65 (s, 2H), 6.96 (t, J=9 Hz, 2H), 7.20 (dd, J=9 Hz, 6 Hz, 2H), 7.37 (d, J=9 Hz, 2H), 7.91 (d, J=9 Hz, 2H), 7.93 (s, 1H), 8.11 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 547 $(M+H)^+$ and m/z 564 $(M+NH_4)^+$.

Example 56

2-(4-Trifluoromethylphenacyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 2-bromo-4'-trifluoromethylacetophenone for 4-fluorobenzyl bromide. mp 205-206 °C ^{1}H NMR ($CDCl_3$, 300 MHz) 3.07 (s, 3H), 5 66 (s, 2H), 6.96 (t, J=9 Hz, 2H), 7.20 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.80 (d, J=9 Hz, 2H), 7.91 (d, J=9 Hz, 2H), 7.92 (s, 1H), 8.15 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 531 $(M+H)^+$ and m/z 548 $(M+NH_4)^+$

Example 57

2-[2-(Benzo[b]thien-3-yl)-2-oxoethyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 3-chloroacetylbenzo[b]thiophene for 4-fluorobenzyl bromide mp 183-184 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3 08 (s, 3H), 5.68 (s, 2H), 6 96 (t, J=9 Hz, 2H), 7.21 (dd, J=9 Hz, 6 Hz, 2H), 7.39 (d, J=9 Hz, 2H), 7.42-7.54 (m, 2H), 7 91 (d, J=9 Hz, 2H), 7.91 (d, J=7 Hz, 1H), 7.94 (s, 1H), 8.53 (s 1H), 8.72 (d, J=7 Hz, 1H) MS (DCI/NH_3) m/z 519 $(M+H)^+$.

Example 58

2-(2,2,2-Trifluoroethyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by N-debenzylation of the product, prepared in Example 53 according to the method of Example 12, followed by alkylation with 2-iodo-1,1,1-trifluoroethane according to the method of Example 20 mp 55-57 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 3.07 (s, 3H), 4.88 (q, J=9 Hz, 2H), 7.13 (d, J=9 Hz, 2H), 7.26 (d, J=9 Hz, 2H), 7.36 (d, J=9 Hz, 2H), 7 89 (s, 1H), 7.92 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 443 $(M+H)^+$ and m/z 460 $(M+NH_4)^+$

Example 59

2-(3,3-Dimethyl-2-oxobutyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 1-bromopinacolone for 4-fluorobenzyl bromide. mp 168-170 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) 1 31 (s, 9H), 3 06 (s, 3H), 5.21 (s, 2H), 6.95 (t, J=9 Hz, 2H), 7.17 (dd, J=9 Hz, 6 Hz, 2H), 7.35 (d, J=7 Hz, 2H), 7.86 (s, 1H) 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 443 $(M+H)^+$ and m/z 460 $(M+NH_4)^+$

Example 60

2-(3-Thienylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 3-(chloromethyl)thiophene for 4-fluorobenzyl bromide. mp 169-172 °C. ^{1}H NMR (300 MHz, DMSO d_6) δ 3.22 (s, 3H), 5.36 (s, 2H), 7 18 (m, 5H), 7.51 (m, 4H), 7.88 (m, 2H), 8.08 (s, 1H). MS (DCI/NH_3) m/z 441 $(M-H)^-$ and m/z 458 $(M+NH_4)^+$.

Example 61

2-(2-Benzo[b]thienylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

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The title compound was prepared according to the method of Example 20 substituting 2-(chloromethyl)benzo[b]thiophene for 4-fluorobenzyl bromide. mp 93-96 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 3H), 5.64 (s, 2H), 6.97 (m, 2H), 7.18 (m, 2H), 7.33 (m, 5H), 7.78 (m, 2H), 7.86 (m, 3H). MS (DCI/NH_3) m/z 491 $(M+H)^+$ and m/z 508 $(M+NH_4)^+$.

Example 62

2,4-Bis(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A mixture of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (172 mg, 0 5 mmol), prepared according to the method of Example 10, Cu powder (32 mg), anhydrous K_2CO_3 (207 mg, 1.5 mmol) and 4-fluoroiodobenzene (0.12 mL, 1 mmol) was prepared in 20 mL of pyridine . The solution was stirred at reflux for 14 hours. The mixture was then cooled to room temperature and partitioned between water and ethyl acetate. The ethyl acetate layer was washed with 10% citric acid, water, brine and concentrated in vacuo Separation by column chromatography (silica gel, CH_2Cl_2-diethyl ether 15:1) provided 190 mg of crude product. Crystallization from CH_2Cl_2-diethyl ether-hexanes furnished the title compound (yield, 175 mg, 79.9%). mp 168-169 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.07 (s, 3H), 6.98 (t, J=9 Hz, 2H), 7.20 (m, 4H), 7.40 (d, J=9 Hz, 2H), 7.69 (m, 2H), 7.92 (d, J=9 Hz, 2H), 7.98 (s, 1H). MS (DCI/NH_3) m/z 439 $(M+H)^+$, 456 $(M+NH4)^+$. Anal. calc. for $C_{23}H_{16}F_2N_2O_3S.0.25\ H_2O$: C, 62.36; H, 3.75, N, 6.32 Found: C, 62.23; H, 3.55, N, 6 26.

Example 63

4-(4-Fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-6-methyl-3(2H)-pyridazinone

The 5-hydroxy-5-methyl-2(5H)-furanone prepared via above cited methods (454 mg, 1.25 mmol) was dissolved in n-butanol (10 mL) and treated with hydrazine hydrate (0.3 mL, 6.2 mmol) and stirred at reflux for 18 hours. On cooling, white crystals (224 mg, 50%) were obtained. mp 290 °C (dec) 1HNMR (300 MHz, d_6-DMSO) δ 1 99 (s, 3H), 3.10 (s, 3H), 7.05 (t, J=9 Hz, 2H), 7 15 (dd, J=6 Hz, J=9 Hz, 2H), 7.48 (d, J=9 Hz, 2H),

7.85 (d, J=9 Hz, 2H), 13.10 (br s, 1H). MS (DCI/NH_3) 376 $(M+NH_4)^+$. Anal. calc. for $C_{18}H_{15}N_2FSO_3$ 0.25 H_2O: C, 59.57, H, 4.30; N, 7.71. Found: C, 59.28; H, 4.39; N, 8.39

Example 64

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-6-methyl-3(2H)-pyridazinone

The product of Example 63 (100 mg, 0.28 mmol) was dissolved in anhydrous DMF (3 mL) and treated with 1,1,1-trifluoro-2-iodoethane (27.5 mL, 280 mmol) in presence of anhydrous sodium carbonate (130 mg, 1.2 mmol) at 50-60 oC for 2 hours. The reaction mixture was partitioned between water and ethyl acetate to provide the desired compound as an amorphous solid (60 mg, 48%). 1HNMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 3.10 (s, 3H), 4.85 (q, J=9 Hz, 2H), 6.90 (m, 2H), 7.10 (dd, J=6 Hz, J=9 Hz, 2H), 7.25 (m, 2H), 7.95 (d, J=9 Hz, 2H),. MS (DCI/NH_3) 458 $(M+NH_4)^+$ Anal. calc. for $C_{20}H_{16}N_2F_4SO_3$: C, 54.54, H, 3.66; N, 6.36. Found: C, 54.41; H, 3.56; N, 6.35.

Example 65

2-Benzyl-4-(3,4-dichlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by coupling 3,4-dichlorophenylboronic acid with 2-benzyl-4-bromo-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., (1996) 33, 1579-1582) according to the method of Example 6. This product was converted to the 5-hydroxy-derivative according to the method of Example 7. The 5-hydroxy compound was converted to the 5-trifluoromethylsufonyloxy-derivative according to the method of Example 8. Coupling of 4-(methylthio)phenylboronic acid to the triflate according to the method of Example 9 provided the 5-[4-(methylthio)phenyl]-intermediate which was oxidized according to the method of Example 10 to provide the final product (yield: 780 mg, 84%) mp 161-163 °C. ^1H NMR (300 MHz, DMSO-d_6) δ 3.22 (s, 3H), 5.35 (s, 2H), 7.08 (dd, J=9 Hz, 3 Hz, 1H), 7.32-7.44 (m, 5H), 7.47 (dd, J=9 Hz, 3 Hz, 3H), 7.48 (d, J=3 Hz, 1H), 7.90 (d, J=9 Hz, 2H), 8.13 (s, 1H) MS (DCI/NH_3) m/z 485 $(M+H)^+$ Anal. calc for $C_{24}H_{18}Cl_2N_2O_3S$ C, 59.38; H, 3.73; N, 5.77 Found: C, 59.28; H, 3.92; N, 5.42

Example 66

2-(2,2,2-Trifluoroethyl)-4-(4-n-propylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by coupling 4-(n-propyl)phenylboronic acid with 2-benzyl-4-bromo-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., 1996, 33, 1579-1582) according to the method of Example 6. This product was converted to the 5-hydroxy derivative according to the method of Example 7. This product was converted to the 5-trifluoromethylsufonyloxy-derivative according to the method of Example 8. Coupling of 4-(methylthio)phenylboronic acid to the triflate according to the method of Example 9 provided the 5-[4-(methylthio)phenyl]-intermediate which was oxidized according to the method of Example 10 to provide the final product (yield, 220 mg, 70%) mp 64-66 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J=7.5 Hz, 3H), 1.6 (h, J=7.5 Hz, 2H), 2.55 (q, J=7.5 Hz, 2H), 3.05 (s, 3H), 4.88 (q, J=9 Hz, 2H), 7.08 (s, 4H), 7.35 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 7.87 (s, 1H). MS (DCI/NH_3) m/z 451 $(M+H)^+$. Anal. calc. for $C_{22}H_{21}F_3N_2O_3S$. C, 58.65, H, 4.69; N, 6.21. Found: C, 58.71, H, 4.72; N, 6.20

Example 67

2-(2,2,2-Trifluoroethyl)-4-(4-chloro-3-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by first coupling 3-fluoro-4-chlorophenylboronic acid with 2-benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone according to the method of Example 6 The product was converted to the 5-hydroxy compound according to the method of Example 7. This 5-hydroxy compound was converted to the 5-trifluoromethylsufonyloxy-derivative according to the method of Example 8. Coupling of 4-(methylthio)phenylboronic acid to the triflate according to the method of Example 9 provided the 5-[4-(methylthio)phenyl]-intermediate which was oxidized according to the method of Example 10 to provide the final product (yield: 170 mg, 84%). mp 174-175 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.09 (s, 3H), 4.89 (q, J=9 Hz, 2H), 6.87 (dm, J=9 Hz, 1H),

7.09 (dd, J=9 Hz, 3 Hz, 1H), 7.30 (t, J=9 Hz, 1H), 7.39 (d, J=9 Hz, 2H), 7 91 (s, 1H), 7.95 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 461 $(M+H)^+$. Anal. calc. for $C_{19}H_{13}ClF_4N_2O_3S$: C, 49.52; H, 2.84, N, 6.07. Found: C, 49.66; H, 2.70; N, 5.96

Example 68

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

A solution of 2-(2,2,2-trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfinyl)phenyl]-3(2H)-pyridazinone (680 mg, 1.53 mmol) in trifluoroacetic anhydride (30 mL) was stirred at room temperature for 1 hour The excess solvent was evaporated in vacuo and the residue was treated with a deoxygenated 1N solution of methanol-NaOH (50 mL, 4:1) at 0 °C. The solution was stirred at room temperature for 2 hours and quenched with dilute HCl solution until acidic. The white suspension formed was concentrated in vacuo to evaporate the methanol. THF was added to the resulting suspension until a clear solution was obtained. Chlorine gas was slowly bubbled into the solution, maintained at 0 °C After 10 minutes, nitrogen gas was bubbled into the solution for a few minutes to displace residual chlorine. Ammonium hydroxide solution (30%, 5 to 10 mL), at 0 °C, was slowly added to the solution (to consume all starting sulfonyl chloride) and stirred at room temperature for 5 minutes The solution was partitioned between water and ethyl acetate. The organic layer was washed first with water, then brine, and dried over $MgSO_4$, and filtered The filtrate was concentrated in vacuo. The residue was purified by chromatography on silica gel (40:60 ethyl acetate/hexanes) to provide the title compound (yield: 500 mg, 75%). mp 193-195 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.82 (s, 2H), 4.88 (q, J=9 Hz, 2H), 6.98 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.30 (d, J=9 Hz, 2H), 7.88 (d, J=9 Hz, 2H), 7.90 (s, 1H). MS (DCI/NH_3) m/z 428 $(M+H)^+$. Anal. calc. for $C_{18}H_{13}F_4N_3O_3S$: C, 50.58, H, 3.06; N, 9.83. Found: C, 51.04; H, 3.26; N, 9 63.

Example 69

2-(2,2,2-Trifluoroethyl)-4-(4-chlorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound from Example 77 was converted to the sulfonamide product according to the method of Example 68 (yield: 540 mg, 70%). mp 154-156 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.86 (s, 2H), 4.87 (q, J=9 Hz, 2H), 7.14 (d, J=9 Hz, 2H), 7.29 (d, J=9 Hz, 2H), 7.31 (d, J=9 Hz, 2H), 7.89 (d, J=9 Hz, 2H), 8.00 (s, 1H). MS (DCI/NH_3) m/z 444 $(M+H)^+$. Anal. calc. for $C_{18}H_{13}ClF_3N_3O_3S$: C, 48.71; H, 2.95; N, 9.46. Found: C, 49.05; H, 3.01; N, 9.15.

Example 70

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide intermediate prepared in Example 83C was oxidized with one equivalent of meta-chloroperoxybenzoic acid to provide the methylsulfoxide which was converted to the sulfonamide final product according to the method of Example 68 (yield, 396 mg, 60%) mp 158-160 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (d, J=6 Hz, 6H), 4.83 (q, J=7.5 Hz, 2H), 4.86 (s, 2H), 5.46 (p, J=6 Hz, 1H), 7.72 (d, J=9 Hz, 2H), 7.82 (s, 1H), 8.03 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 392 $(M+H)^+$ Anal. calc. for $C_{15}H_{16}F_3N_3O_4S$: C, 46.03; H, 4.12; N, 10.73. Found C, 46.08, H, 4.22, N, 10.52.

Example 71

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenoxy)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide intermediate of Example 76 was oxidized with one equivalent of meta-chloroperoxybenzoic acid to provide the methylsulfoxide which was converted to the sulfonamide final product according to the method of Example 68 (yield: 180 mg, 37%). mp 150-152 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.71 (q, J=7.5 Hz, 2H), 4.72 (s, 2H), 6.88 (dd, J=9 Hz, 4.5 Hz, 2H), 7.0 (t, J=9 Hz, 2H), 7.73 (d, J=9 Hz, 2H), 7.98 (s, 1H), 8.05 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 444 $(M+H)^+$. Anal calc. for $C_{18}H_{13}F_4N_3O_4S$: C, 48.76, H, 2.95; N, 9.47 Found C, 48.49; H, 2.8; N, 8.95

Example 72

2,4-Bis-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

Example 72A

2-Fluorothioanisole

A deoxygenated solution of 2-fluorothiophenol (10 g, 78 mmol) in anhydrous DMF (10 mL) was treated with iodomethane (4.9 mL, 78 mmol) and potassium carbonate (10.8 g, 78 mmol). The reaction mixture was stirred at room temperature for 1 hour. A thin layer chromotography (100% hexanes) sample indicated that the reaction had not gone to completion, so an additional equivalent of base and iodomethane were added and the reaction mixture was stirred overnight at room temperature The reaction was acidified with 10% aqueous citric acid and extracted with hexanes (2 X 125 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to provide the desired compound as a pale yellow oil (yield: 6.68 g; 60%).

Example 72B

2-Fluorothioanisole

An alternative method for preparing 2-fluorothioanisole begins with a solution of 1,2-difluorobenzene (0.79 mL, 8 mmol) in anhydrous DMF (50 mL) was treated with sodium thiomethoxide (0.59 g, 8 mmol). The reaction mixture was stirred at room temperature for 6 hours, and partitioned between hexanes and water. The organic layer was washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to provide the desired compound (1.1 g, 100%) slightly contaminated with 1,2-bis(methylthio)benzene, a lower Rf material, which was removed by chromatography with 100% hexanes (0 9 g, 80%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 6.98-7.19 (m, 3H) 2.26 (dt, J=9 Hz, 3 Hz, 1H).

Example 72C

4-Bromo-2-fluorothioanisole

A solution of 2-fluorothioanisole (1.42 g, 10 mmol) and iron powder (0.03 g, 0.5 mmol) in dichloromethane (20 mL) was chilled to °C and treated dropwise with Bromine (0.5 mL, 10 mmol). Upon completion of the Bromine treatment, the reaction was sampled for TLC (100% hexanes). A new, higher Rf material was present but the reaction had not gone to completion so another equivalent of bromine was added along with a catalytic amount of aluminum chloride The reaction mixture was stirred overnight at room temperature. Aqueous sodium sulfite was added to the reaction mixture and the organic layer was isolated, dried over $MgSO_4$, and filtered The filtrate was filtered through a pad of silica gel to remove color then concentrated under reduced pressure to provide the product as a clear, colorless oil (yield. 1.3 g; 60%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.48 (s, 3H), 7.31 (t, J=9 Hz, 1H), 7.43 (dd, J=9 Hz, 3 Hz, 1H) 7.54 (dd, J=9 Hz, 3 Hz, 1H).

Example 72D

3-Fluoro-4-(methylthio)benzeneboronic acid

A solution of 4-bromo-2-fluorothioanisole (0.5 g, 22.6 mmol) in dry THF (20 mL) was chilled to -78 °C under a nitrogen atmosphere The reaction mixture was treated with 1.6 M n-butyllithium in hexanes (1.7 mL, 27.1 mmol), and the mixture was warmed to -40°C where it was maintained for 0.5 hours. The reaction mixture was then chilled to -78°C and three equivalents of triisopropyl borate (1.56 mL, 67.8 mmol) were added. The reaction mixture was allowed to warm to room temperature and stirred for 1 5 hours. At this point, 10% aqueous KOH (200 mL, 360 mmol) was added and the mixture was stirred overnight at room temperature. The reaction mixture was then poured into an ice/concentrated HCl mixture with stirring to yield a white precipitate. This solid was dried in a vacuum oven (65 °C, 29 in Hg) overnight to provide the title compound (yield: 0.22 g; 52.4%) ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.48 (s, 3H), 7.31 (t, J=9 Hz, 1H), 7.49 (dd, J=12 Hz, 1.5 Hz, 1H) 7.54 (dd, J=9 Hz, 1 5 Hz, 1H).

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Example 72E

2,4-Bis-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., 1996, 33, 1579-1582) was converted to the 5-hydroxy-analog according to the method of Example 7 and then to the 5-trifluoromethylsulfonyloxy-analog following the method of Example 8. Subsequent coupling to 3-fluoro-4-(methylthio)phenylboronic acid, according to the method of Example 9, provided 2-benzyl-4-chloro-5-[3-fluoro-4-(methylthio)phenyl]-3(2H)-pyridazinone. This intermediate was coupled in the 4-position with 4-fluorophenylboronic acid following the method of Example 6. This product was N-debenzylated according to the method of Example 11 and N-arylated with 4-fluoroiodobenzene according to the method of Example 62. The resulting sulfide was oxidized with one equivalent of meta-chloroperoxybenzoic acid to provide the methylsulfoxide which was converted to the sulfonamide final product according to the method of Example 68 (yield: 500 mg, 75%). mp 222-224 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (s, 2H), 7.01 (t, J=9 Hz, 2H), 7.06 (d, J=9 Hz, 2H), 7.10 (d, J=9 Hz, 2H), 7.18 (t, J=9 Hz, 2H), 7.69 (dd, J=9 Hz, 3 Hz, 2H), 7.88 (t, J=9 Hz, 1H), 7.95 (s, 1H). MS (DCI/NH_3) m/z 458 $(M+H)^+$. Anal. calc. for $C_{22}H_{14}F_3N_3O_3S$: C, 57.76; H, 3.08; N, 9.18 Found: C, 57.5, H, 3.15; N, 8.8

Example 73

2-(2,2,2-Trifluoroethyl)-4-(4-chloro-3-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide intermediate prepared in Example 67 was oxidized with one equivalent of meta-chloroperoxybenzoic acid, according to the method of Example 68 to provide the methyl sulfoxide. The methyl sulfoxide was converted to the sulfonamide product according to the method of Example 68 (yield: 1.5 g, 63%). mp 180-183 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.09 (q, J=9 Hz, 2H), 7.01 (dd, J=9 Hz, 3 Hz, 1H), 7.15 (dd, J=9 Hz, 3 Hz, 1H), 7.39 (dd, J=9 Hz, 3 Hz, 1H), 7.47 (dd, J=9 Hz, 3 Hz, 1H), 7.55 (t, J=9 Hz, 1H), 7.71 (t, J=9 Hz, 1H), 7.78 (s, 2H), 8.37 (s, 1H). MS (DCI/NH_3) m/z 480

(M+H)$^+$. Anal. calc. for $C_{18}H_{11}ClF_3N_3O_3S$. C, 45.05; H, 2.31; N, 8 75. Found: C, 46 19; H, 3.02; N, 7.43.

Example 74

2-Benzyl-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., 1996, 33, 1579-1582) was converted to the 5-hydroxy-analog according to the method of Example 7 and then to the 5-trifluoromethylsulfonyloxy-analog following the method of Example 8. Subsequent coupling to 4-(methylthio)phenylboronic acid according to the method of Example 9 provided 2-benzyl-4-chloro-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone This 4-chloro-intermediate thus prepared was treated with 2-propanol (20 mL, 261 mmol) and potassium t-butoxide (110 mg, 0.98 mmol) at reflux for 45 minutes furnished 2-benzyl-4-(2-propoxy)-5-[4-(methylthio)pentyl]-3(2H)-pyridazinone This methyl sulfide was oxidized according to the method of Example 10 to provide the title compound (yield: 180 mg, 80%) mp 109-111 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (d, J=6 Hz, 6H), 3.12 (s, 3H), 5.36 (s, 2H), 5 49 (h, J=6 Hz, 1H), 7.35 (m, 3H), 7.47 (dd, J=9 Hz, 3 Hz, 2H), 7.74 (d, J=9 Hz, 2H), 7.79 (s, 1H), 8.03 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 399 (M+H)$^+$ Anal. calc. for $C_{21}H_{22}N_2O_4S$: C, 63.29; H, 5.56; N, 7.03 Found: C, 63.17; H, 5 57; N, 6.95.

Example 75

2-Benzyl-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 74 substituting 4-fluorophenol in place of 2-propanol (yield: 180 mg, 99%) mp 188-190 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.12 (s, 3H), 5.26 (s, 2H), 6.86 (dd, J=9 Hz, 6 Hz, 2H), 6 99 (t, J=9 Hz, 2H), 7.34 (m, 3H), 7.46 (dd, J=9 Hz, 3 Hz, 2H), 7.72 (d, J=9 Hz, 2H), 7.92 (s, 1H), 8.02 (d, J=9 Hz, 2H) MS (DCI/NH_3) m/z 451 (M+H)$^+$. Anal. calc. for $C_{24}H_{19}FN_2O_4S$. C, 63.98, H, 4.25; N, 6.21 Found: C, 63.74; H, 4.2; N, 6.12

Example 76

2-(2,2,2-Trifluoroethyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 75 substituting 2-(2,2,2-trifluoroethyl)-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 2-benzyl-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (yield: 180 mg, 63%). mp 161-164 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.09 (s, 3H), 4.81 (q, J=9 Hz, 2H), 6 88 (dd, J=9 Hz, 4.5 Hz, 2H), 7.0 (t, J=9 Hz, 2H), 7.78 (d, J=9 Hz, 2H), 7.79 (s, 1H), 8 06 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 443 $(M+H)^+$. Anal. calc. for $C_{19}H_{14}F_4N_2O_4S$: C, 51.58; H, 3 18, N, 6.33. Found: C, 51.8; H, 3.3; N, 6.22.

Example 77

2-(2,2,2-Trifluoroethyl)-4-(4-chlorophenyl)-5-[4-(methylsulfinyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., 1996, 33, 1579-1582) was converted to the 5-hydroxy-analog according to the method of Example 7 and then to the 5-trifluoromethylsulfonyloxy-analog according to the method of Example 8. Subsequent coupling to 4-(methylthio)phenylboronic acid, according to the method of Example 9, provided 2-benzyl-4-chloro-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone. This intermediate was coupled with 4-chlorophenylboronic acid according to the method of Example 6. This product was N-debenzylated according to the method of Example 11 and N-alkylated with 2-iodo-1,1,1-trifluoroethane according to the method of Example 20 The resulting sulfide was oxidized to the corresponding sulfoxide with one equivalent of meta-chloroperoxybenzoic acid, according to the method of Example 5 to provide the title compound (yield: 130 mg, 70%). mp 154-155 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.74 (s, 3H), 4.88 (q, J=9 Hz, 2H), 7.14 (d, J=9 Hz, 2H), 7.26 (d, J=9 Hz, 2H), 7.31 (d, J=9 Hz, 2H), 7.61 (d, J=9 Hz, 2H), 7.82 (s, 1H). MS (DCI/NH_3) m/z 427 $(M+H)^+$ Anal. calc. for $C_{19}H_{14}ClF_3N_2O_2S$: C, 53 46; H, 3.3; N, 6.56. Found: C, 53.58; H, 3.34; N, 6.42

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Example 78

2-Benzyl-4-chloro-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by oxidizing 2-benzyl-4-chloro-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone, (prepared as an intermediate in Example 77) according to the method of Example 10 (yield: 180 mg, 83%). mp 166-167 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.12 (s, 3H), 5.41 (s, 2H), 7.37 (m, 3H), 7.53 (dd, J=9 Hz, 3 Hz, 2H), 7.68 (d, J=9 Hz, 2H), 7.74 (s, 1H), 8.08 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 375 $(M+H)^+$. Anal. calc. for $C_{18}H_{15}ClN_2O_3S$: C, 57.67; H, 4.03; N, 7.47. Found: C, 57.43; H, 4.06; N, 7.35.

Example 79

2-(2,2,2-Trifluoroethyl)-4-(4-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-bromo-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., 1996, 33, 1579-1582) was converted to the 5-hydroxy-analog according to the method of Example 7 and then to the 5-(trifluoromethyl)sulfonyloxy-analog according to the method of Example 8. Subsequent coupling to 4-(methylthio)phenylboronic acid, according to the method of Example 9, provided 2-benzyl-4-bromo-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone. This intermediate was coupled with 4-methylphenylboronic acid according to the method of Example 6. This product was N-debenzylated according to the method of Example 11 and N-alkylated with 2-iodo-1,1,1-trifluoroethane according to the method of Example 20. The resulting sulfide was oxidized to the title compound according to the method of Example 10 (yield: 210 mg, 98%). mp 154-156 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.07 (s, 3H), 4.89 (q, J=9 Hz, 2H), 7.08 (s, 4H), 7.37 (d, J=9 Hz, 2H), 7.88 (s, 1H), 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 423 $(M-H)^-$. Anal. calc. for $C_{20}H_{17}F_3N_2O_3S$: C, 56.86; H, 4.05; N, 6.63. Found: C, 56.59; H, 4.11; N, 6.53.

Example 80

2-(2,2,2-Trifluoroethyl)-4-(4-chloro-3-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-chloro-5-methoxy-3(2H)-pyridazinone (J. Het. Chem., 1996, 33, 1579-1582) was converted to the 5-hydroxy-analog according to the method of Example 7 and then to the 5-(trifluoromethyl)sulfonyloxy-analog according to the method of Example 8. Subsequent coupling to 4-(methylthio)phenylboronic acid, according to the method of Example 9, provided 2-benzyl-4-chloro-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone. This intermediate was coupled with 4-chloro-3-fluorophenylboronic acid according to the method of Example 6. This product was N-debenzylated according to the method of Example 11 and N-alkylated with 2-iodo-1,1,1-trifluoroethane according to the method of Example 20. The resulting sulfide was oxidized to the corresponding sulfoxide with one equivalent of meta-chloroperoxybenzoic acid to provide the methylsulfoxide which was converted to the sulfonamide final product according to the method of Example 68 (yield: 500 mg, 75%). mp 214-215 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (s, 2H), 4.88 (q, J=9 Hz, 2H), 6.88 (m, 1H), 7.09 (dd, J=9 Hz, 3 Hz, 1H), 7.31 (d, J=9 Hz, 1H), 7.32 (d, J=9 Hz, 2H), 7.90 (s, 1H), 7.92 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 462 $(M+H)^+$. Anal. calc. for $C_{18}H_{12}F_4ClN_3O_3S$: C, 46.81, H, 2.61; N, 9.09 Found: C, 46.79, H, 2.59, N, 8.86.

Example 81

2-(2,2,2-Trifluoroethyl)-4-(3,4-dichlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The product described in Example 65 was N-debenzylated according to the method of Example 11. The intermediate was N-alkylated according to the method of Example 20, substituting 2-iodo-1,1,1-trifluoroethane in place of 4-fluorobenzyl bromide to provide the title compound (yield: 165 mg, 55%). mp 197-198 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.09 (s, 3H), 4.88 (q, J=9 Hz, 2H), 6.98 (dd, J=9 Hz, 3 Hz, 1H), 7.37 (d, J=9 Hz, 4H), 7.91 (s, 1H), 7.95 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 477 $(M+H)^+$. Anal. calc. for $C_{19}H_{13}F_3Cl_2N_2O_3S$: C, 47.81; H, 2.74; N, 5.86. Found: C, 47.94; H, 2.87; N, 5.83.

Example 82

2-Benzyl-4-(2-propylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4,5-dibromo-3(2H)-pyridazinone (2 g, 6 mmol) was reacted with 2-aminopropane (2 mL, 23.5 mmol) and potassium t-butoxide (910 mg, 6.6 mmol) in toluene (40 mL) at reflux for 18 hours to provide the 4-(2-propylamino) derivative after column chromatography (silica gel, 92:8 hexanes/ethyl acetate). The intermediate was coupled in the 5-position with 4-(methylthio)phenylboronic acid according to the method of Example 6. The methyl sulfide was oxidized, according to the method of Example 10, to provide the title compound (yield: 120 mg, 48%). mp 146-147 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J=6 Hz, 6H), 3.11 (m, 1H), 3.13 (s, 3H), 5.34 (s, 2H), 5.59 (m, 1H), 7.33 (m, 3H), 7.42 (s, 1H), 7.48 (dd, J=9 Hz, 3 Hz, 2H), 7.56 (d, J=9 Hz, 2H), 8.00 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 399 $(M+H)^+$. Anal. calc. for $C_{21}H_{23}N_3O_3S$: C, 63.45, H, 5.83; N, 10.57. Found: C, 63.31; H, 5.87; N, 10.44.

Example 83

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 83A

2-(2,2,2-Trifluoroethyl)-4,5-dibromo-3(2H)-pyridazinone

A solution of mucobromic acid (10 g, 38.8 mmol) and trifluoroethyl hydrazine (70% in water, 4.88 mL, 38.8 mmol) in 100 mL of methanol was prepared and heated at reflux for 3 hours. The reaction mixture was concentrated in vacuo and partitioned between ethyl acetate and water. The ethyl acetate layer was dried over $MgSO_4$, filtered, passed through a silica gel pad, and concentrated in vacuo . The product was obtained as yellowish solid (yield: 8.8 g, 68%) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.78 (q, J=9 Hz, 2H), 7.87 (s, 1H). MS (DCI/NH_3) m/z 337 $(M+H)^+$

Example 83B

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-bromo-3(2H)-pyridazinone

A solution of 2-(2,2,2-trifluoroethyl)-4,5-dibromo-3(2H)-pyridazinone (2 g, 6 mmol), isopropyl alcohol (3 mL) and sodium hydride (60% dispersed in oil, 290 mg, 7.2 mmol) in toluene (40 mL) was heated at reflux for 5 hours. The reaction mixture was partitioned between ethyl acetate and water. The ethyl acetate layer was filtered, and concentrated in vacuo . The residue was purified by chromatography (95:5 hexanes/ethyl acetate) to provide the product as a greenish oil (yield: 1.22 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 (d, J=7.5 Hz, 6H), 5.48 (h, J=6 Hz, 1H), 7.87 (s, 1H). MS (DCI/NH_3) m/z 316 $(M+H)^+$

Example 83C

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A solution of 2-(2,2,2-trifluoroethyl)-4-(2-propoxy)-5-bromo-3(2H)-pyridazinone (1.2 g, 3.8 mmol), 4-(methylthio)phenylboronic acid (704 mg, 4.19 mmol), tetrakis(triphenylphosphine)palladium(0) (220 mg, 5% mmol) and cesium carbonate (2.72 g, 8.3 mmol) in 20 mL of ethylene glycol dimethyl ether was heated to reflux for 5 hours. The mixture was partitioned between ethyl acetate and water. The ethyl acetate layer was washed with water, brine, dried over $MgSO_4$ and concentrated in vacuo . The residue was purified by chromatography on silica gel (94:6 hexanes/ethyl acetate). The product was obtained as a greenish solid (yield: 1.1 g, 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, J=7.5 Hz, 6H), 2.55 (s, 3H), 4.83 (q, J=9 Hz, 2H), 5.28 (h, J=6 Hz, 1H), 7.32 (d, J=9 Hz, 2H), 7.52 (d, J=9 Hz, 2H), 7.85 (s, 1H). MS (DCI) m/z 359 $(M+H)^+$.

Example 83D

2-(2,2,2-Trifluoroethyl)-4-(2-propoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 10, substituting 2-(2,2,2-trifluoroethyl)-4-(2-propoxy)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (yield: 220 mg, 100%). mp 152-153 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.2 (d, J=6 Hz, 6H), 3.13 (s, 3H), 4.84 (q, J=9 Hz, 2H), 5.49 (p, J=6 Hz, 1H), 7.78 (d, J=9 Hz, 2H), 7.82

(s, 1H), 8.05 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 391 $(M+H)^+$. Anal. calc. for $C_{16}H_{17}F_3N_2O_4S$: C, 49.22; H, 4.38; N, 7.17. Found: C, 49.34; H, 4.25; N, 7.01.

Example 84

2-(2,2,2-Trifluoroethyl)-4-cyclohexyloxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 83, substituting cyclohexanol in place of 2-propanol (yield: 250 mg, 52%). mp 129-130 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.1-1.6 (m, 8H), 1.84 (m, 2H), 3.12 (s, 3H), 4.83 (q, J=9 Hz, 2H), 5.21 (h, J=4.5 Hz, 1H), 7.77 (s, 1H), 7.80 (d, J=9 Hz, 2H), 8.06 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 431 $(M+H)^+$ Anal. calc. for $C_{19}H_{21}F_3N_2O_4S$: C, 53.01; H, 4.91; N, 6.50. Found: C, 52.96, H, 4.84, N, 6.45.

Example 85

2-(2,2,2-Trifluoroethyl)-4-cyclopentyloxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 83, substituting cyclopentanol in place of 2-propanol (yield: 250 mg, 52%). mp 148-150 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.35-1.55 (m, 4H), 1.68-1.75 (m, 4H), 3.12 (s, 3H), 4.83 (q, J=9 Hz, 2H), 5.89 (h, J=4.5 Hz, 1H), 7.75 (d, J=9 Hz, 2H), 7.83 (s, 1H), 8.04 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 417 $(M+H)^+$. Anal. calc for $C_{18}H_{19}F_3N_2O_4S$. C, 51.91; H, 4.59; N, 6.72. Found: C, 52.04, H, 4.50; N, 6.65.

Example 86

2-(2,2,2-Trifluoroethyl)-4-(2-propylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 86A

2-(2,2,2-Trifluoroethyl)-4-(2-propylamino)-5-bromo-3(2H)-pyridazinone

The title compound was prepared according method of the Example 83B, substituting 2-propylamine in place of 2-propanol (yield: 70%). MS (DCI/NH_3) m/z 315 $(M+H)^+$.

Example 86B

2-(2,2,2-Trifluoroethyl)-4-(2-propylamino)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

The title compound was prepared according method of the Example 83C, substituting 2-(2,2,2-trifluoroethyl)-4-(2-propylamino)-5-bromo-3(2H)-pyridazinone in place of 2-(2,2,2-trifluoroethyl)-4-isopropoxy-5-bromo-3(2H)-pyridazinone (yield: 80%). MS (DCI/NH_3) m/z 358 $(M+H)^+$.

Example 86C

2-(2,2,2-Trifluoroethyl)-4-(2-propylamino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 10 , substituting 2-(2,2,2-Trifluoroethyl)-4-(2-propylamino)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (yield: 180 mg, 83%). mp 173-174 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, J=6 Hz, 6H), 3.13 (s, 3H), 4.81 (q, J=9 Hz, 2H), 5.97 (s, 1H), 7.45 (s, 1H), 7.59 (d, J=9 Hz, 2H), 8.03 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 340 $(M+H)^+$. Anal. calc. for $C_{16}H_{18}F_3N_3O_4S$: C, 49.35; H, 4.65; N, 10.79 Found: C, 49.29; H, 4.52; N, 10.65

Example 87

2-Benzyl-4-(4-morpholino)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4,5-dichloro-3(2H)-pyridazinone, prepared following the procedure in Example 2, was reacted with morpholine following the procedure of Example 86 to provide the 4-morpholino-derivative. The morpholino intermediate was coupled at the 5-position with 4-(methylthio)phenylboronic acid according to the method of Example 6. The resulting methyl sulfide was oxidized to the title compound according to the method

of Example 10 (yield: 150 mg, 69%). mp 158-160 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.06 (t, J=4 5 Hz, 3H), 3.12 (s, 3H), 3.69 (t, J=4.5 Hz, 3H), 5.33 (s, 2H), 7.35 (m, 3H), 7.5 (m, 4H), 7.58 (s, 1H), 8.05 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 426 $(M+H)^+$. Anal. calc. for $C_{22}H_{23}N_3O_4S$: C, 62.10; H, 5.44; N, 9.87. Found: C, 61.74; H, 5.47; N, 9.59.

Example 88

2-(2,3,3-Trifluoro-2-propen-1-yl)]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 88A

1-Methylsulfonyloxy-2,3,3-trifluoro-2-propene

2,3,3-Trifluoro-2-propen-1-ol was prepared as reported in (J. Org.Chem., (1989) 54, 5640-5642) The mesylate was obtained by reacting 2,3,3-trifluoro-2-propen-1-ol with mesyl chloride in diethyl ether. Standard workup provided the product, which was used without purification.

Example 88B

2-(2,3,3-Trifluoro-2-propen-1-yl)-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone.

4-(4-Fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone is prepared starting with the 2-benzyl-pyridazinone from Example 9 and debenzylating the compound according to the procedure of Example 11.

A mixture of 4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (250 mg, 0.8 mmol), Cs_2CO_3 (650 mg, 2 mmol), and 3-methylsufonyloxy-1,1,2-trifluoropropene (mesylate, 250 mg, 1.19 mmol) in ethyl acetate (30 mL) was stirred at 55 °C for 1.5 hours. The mixture was partitioned between ethyl acetate and water. The organic layer was washed with brine, dried with $MgSO_4$ and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel

eluted with 15% ethyl acetate/hexanes, to provide the methyl sulfide, 2-(2,3,3-trifluoro-2-propen-1-yl)-4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone as a greenish oil (yield: 175 mg, 53%).

Example 88C

2-(2,3,3-Trifluoro-2-propen-1-yl)]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The methyl sulfide, prepared above, was oxidized to the title compound according to the method of Example 10 (yield: 125 mg, 68%). mp 154-156 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.07 (s, 3H), 5.1 (ddd, J=21 Hz, 3 Hz, 1.5 Hz, 2H), 6 98 (t, J=9 Hz, 2H), 7.19 (dd, J=9 Hz, 6 Hz, 2H), 7.35 (d, J=9 Hz, 2H), 7.89 (s, 1H), 7.9 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 439 $(M+H)^+$. Anal. calc. for $C_{20}H_{14}F_4N_2O_3S$: C, 54.79; H, 3.21; N, 6.38. Found: C, 54.52; H, 3.15; N, 6.21.

Example 89

2,4-Bis(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 68 substituting 2,4-bis(4-fluorophenyl)-5-[4-(methylsulfinyl)phenyl]-3(2H)-pyridazinone in place of 2-(2,2,2-trifluoroethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfinyl)phenyl]-3(2H)-pyridazinone (yield: 118 mg, 43%). mp 213-216 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.15 (t, 2H), 7.27 (m, 2H), 7.4 (m, 6H), 7.7 (dd, 2H), 7.76 (d, J=9 Hz, 2H), 8.2 (s, 1H). MS (DCI/NH_3) m/z 440 $(M+H)^+$, 439.44 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{15}FN_2O_3S_2$: C, 60.13; H, 3.44; N, 9.56. Found: C, 59.94; H, 3.37; N, 9.46.

Example 90

2-(2,2,2-Trifluoroethyl)-4-cyclopropylmethoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 90A

2-(2,2,2-Trifluoroethyl)-4-methoxy-5-bromo-3(2H)-pyridazinone

The title compound was prepared according method of the Example 83B, substituting methanol in place of isopropanol (yield: 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.3 (s, 3H), 4.76 (q, J=9 Hz, 2H), 7.85 (s, 1H). MS (DCI/NH_3) m/z 288 $(M+H)^+$.

Example 90B

2-(2,2,2-Trifluoroethyl)-4-methoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

The title compound was prepared according method of the Example 83C, substituting 2-(2,2,2-trifluoroethyl)-4-methoxy-5-bromo-3(2H)-pyridazinone in place of 2-(2,2,2-trifluoroethyl)-4-(2-propoxy)-5-bromo-3(2H)-pyridazinone (yield: 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.54 (s, 3H), 4.11 (s, 3H), 4.82 (q, J=9 Hz, 2H), 7.33 (d, J=9 Hz, 2H), 7.48 (d, J=9 Hz, 2H), 7.84 (s, 1H). MS (DCI/NH_3) m/z 331 $(M+H)^+$.

Example 90C

2-(2,2,2-Trifluoroethyl)-4-hydroxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A solution of 2-(2,2,2-Trifluoroethyl)-4-methoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (2 g, 6.1 mmol) and hydrobromic acid (40% in water, 20 mL) in acetic acid (40 mL) was heated at reflux for 3 hours. The reaction mixture was cooled to room temperature and water (50 mL) was added. The crystals formed were filtered, washed with water and 5% ethyl acetate in hexanes, and dried to constant weight. The product was obtained as a white solid (yield: 1.75 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.54 (s, 3H), 4.82 (q, J=9 Hz, 2H), 7.47 (d, J=9 Hz, 2H), 7.65 (d, J=9 Hz, 2H), 7.73 (br s, 1H), 8.00 (s, 1H). MS (DCI) m/z 317 $(M+H)^+$.

Example 90D

2-(2,2,2-Trifluoroethyl)-4-cyclopropylmethoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone

A solution of 2-(2,2,2-trifluoroethyl)-4-hydroxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (150 mg, 0.47 mmol), cyclopropyl methanol (43 mL, 0.52 mmol) and

triphenylphosphine (124 mg, 0.47 mmol) in freshly distilled THF was prepared and added dropwise to diethyl azodicarboxylate (75 mL, 0.52 mmol) at 0 °C. The mixture was allowed to warm to room temperature, stirred for 5 hours and concentrated in vacuo. The residue was purified by chromatography on silica gel (95:5 hexanes/ethyl acetate) to provide the product as a colorless oil (yield: 140 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.22 (m, 2H), 0.48 (m, 2H), 1.6 (m, 1H), 2.53 (s, 3H). 4.26 (d, J=7.5 Hz, 2H), 4.72 (q, J=9 Hz, 2H), 7.32 (d, J=9 Hz, 2H), 7.55 (d, J=9 Hz, 2H). 7.87 (s, 1H). MS (DCI/NH_3) m/z 371 $(M+H)^+$.

Example 90E

2-(2,2,2-Trifluoroethyl)-4-cyclopropylmethoxy-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of example 10, substituting 2-(2,2,2-trifluoroethyl)-4-cyclopropylmethoxy-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-pyridazinone (yield: 130 mg, 85%). mp 133-135 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.22 (m, 2H), 0.5 (m, 2H), 1.07 (m, 1H), 3.12 (s, 3H). 4.4 (d, J=9 Hz. 2H), 4.83 (q, J=9 Hz, 2H), 7.79 (s, 1H), 7.83 (d, J=9 Hz, 2H), 8.07 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 403 $(M+H)^+$. Anal. calc. for $C_{17}H_{17}F_3N_2O_4S$: C, 50.74; H, 4.25; N. 6.96. Found: C, 50.56; H, 4.09; N, 6.88.

Example 91

2-(2,2,2-Trifluoroethyl)-4-(3-propen-1-oxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 90, substituting 2-propen-1-ol in place of cyclopropylmethanol (yield: 120 mg, 77%). mp 121-123 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.12 (s, 3H), 4.84 (q, J=12 Hz, 2H), 5.07 (d, J=6 Hz, 2H), 5.21 (dd, J=13.5 Hz, 1 Hz, 1H), 5.27 (dd, J=15 Hz. 1 Hz, 1H), 5.85 (m, 1H), 7.25 (d, J=9 Hz, 2H), 7.83 (s, 1H), 8.06 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 389 $(M+H)^+$.

Anal. calc. for $C_{16}H_{15}F_3N_2O_4S$. C, 49.48, H, 3.89; N, 7.21. Found: C, 49.24, H, 3.77; N, 7.16.

Example 92

2-(2,2,2-Trifluoroethyl)-4-(4-fluoro-α-methylbenzyloxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 90, substituting 4-fluoro-alpha-methylbenzyl alcohol in place of cyclopropylmethanol (yield: 155 mg, 76%). mp 133-135 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.57 (d, J=6 Hz, 3H), 3.13 (s, 3H), 4.75 (q, J=7.5 Hz, 1H), 4.87 (q, J=7.5 Hz, 1H), 6.34 (q, J=6 Hz, 1H), 6.83 (t, J=9 Hz, 2H), 6.98 (dd, J=9 Hz, 6 Hz, 2H), 7.59 (d, J=9 Hz), 7.70 (s, 1H), 8.03 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 471 $(M+H)^+$. Anal. calc. for $C_{21}H_{18}F_4N_2O_4S$: C, 53.61; H, 3.85; N, 5.95. Found: C, 53.54; H, 3.73; N, 5.86.

Example 93

2-[4-(Methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of the product from Example 11, 4-(4-Fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (344 mg, 1.0 mmol), 4-bromothioanisole (812 mg, 4.0 mmol), and copper (70 mg, 1.1 mmol) in 20 mL of pyridine was stirred at reflux under a nitrogen atmosphere for 18 hours. After cooling to room temperature, the reaction mixture was diluted with a mixture of water and ethyl acetate. The two layers were filtered through Celite®, and separated. The organic layer was washed with 10% aqueous citric acid, with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo and the residue purified by column chromatography (silica gel, 93:7 dichloromethane/ethyl acetate) to provide the title compound as a foam (yield: 380 mg, 81.5%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 3H), 3.05 (s, 3H), 6.98 (t, J=9 Hz, 2H), 7.22 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (dd, J=8 Hz, 2 Hz, 4H), 7.64 (d, J=9 Hz, 2H), 7.91 (d,

J=9 Hz, 2H), 7.98 (s, 1H). MS (DCI/NH_3) m/z 467 $(M+H)^+$. Anal. calc. for $C_{24}H_{19}FN_2O_3S_2.0.5\ H_2O$: C, 60.63; H, 4.21; N, 5.90. Found: C, 60.72; H, 3.96; N, 5.70.

Example 94

2,5-Bis[4-(methylsulfonyl)phenyl]-4-(4-fluorophenyl)-3(2H)-pyridazinone

The title compound was prepared by oxidizing the product of Example 93, according to the method of Example 10 (yield: 156 mg, 78%). ^1H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 3H), 3.12 (s, 3H), 7.02 (m, 2H), 7.24 (m, 2H), 7.42 (br d, J=9 Hz, 2H), 7.94 (dd, J=9 Hz, 2 Hz, 2H), 8.02 (dd, J=9 Hz, 2 Hz, 2H), 8.10 (m, 3H). MS (DCI/NH_3) m/z 499 $(M+H)^+$, 516 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{19}FN_2O_5S_2.0.5\ H_2O$: C, 56.80; H, 3.94; N, 5.53. Found: C, 56.50; H, 3.88; N, 5.38.

Example 95

2-(3-Methyl-2-thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 2-bromo-3-methylthiophene in place of 4-bromothioanisole (yield: 190 mg, 43%). mp 215-217 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 2.21 (s, 3H), 3.08 (s, 3H), 6.90 (d, J=9 Hz, 1H), 6.98 (t, J=9 Hz, 2H), 7.24 (dd, J=9 Hz, 6 Hz, 3H), 7.41 (d, J=9 Hz, 2H), 7.94 (d, J=9 Hz, 2H), 7.98 (s, 1H). MS (DCI/NH_3) m/z 441 $(M+H)^+$, 458 $(M+NH_4)^+$. Anal. calc. for $C_{22}H_{17}FN_2O_3S_2.0.5\ H_2O$: C, 58.80; H, 4.01; N, 6. 24. Found: C, 58.85; H, 3.78; N, 5.99.

Example 96

2-(2-Trifluoromethyl-4-nitrophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 2-bromo-5-nitrobenzotrifluoride in place of 4-bromothioanisole (yield. 390 mg, 73%) ^1H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 3H), 6.98 (t, J=9 Hz, 2H), 7.21 (dd, J=9 Hz, 6 Hz, 2H), 7.43 (d, J=9 Hz, 2H), 7.80 (d, J=9 Hz, 1H), 7.96 (d, J=9 Hz, 2H), 8.02 (s, 1H), 8.61 (dd, J=9

Hz, 3 Hz, 1H), 8.75 (d, J=3 Hz, 1H). MS (DCI/NH_3) m/z 534 $(M+H)^+$, 551 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{15}F_4N_3O_5S.0.75\ H_2O$: C, 52.70, H, 3 02; N. 7.69. Found. C, 52.42; H, 3.04; N, 6.82.

Example 97

2-[3-(Methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 3-bromothioanisole in place of 4-bromothioanisole (yield: 355 mg, 76%). mp 196 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 3H), 3.08 (s, 3H), 6.99 (t, J=9 Hz, 2H), 7.23 (dd, J=9 Hz, 6 Hz, 2H), 7.28-7.33 (m, 1H), 7.37-7.49 (m, 2H), 7.40 (d, J=9 Hz, 2H), 7.58 (m, 1H), 7.92 (d, J=9 Hz, 2H), 7.99 (m, 1H). MS (DCI/NH_3) m/z 467 $(M+H)^+$, 484 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{19}FN_2O_3S_2$: C, 61.80, H. 4.08; N, 6.01. Found. C, 61.56; H, 3.93; N, 5.86.

Example 98

2-[3-(Methylsulfonyl)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by oxidizing the product of Example 97, according to the method of Example 10 (yield: 98 mg, 65.6%). mp 141-142 °C. ^1H NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 3H), 3.35 (s, 3H), 7.18 (t, J=9 Hz, 2H), 7.32 (dd, J=9 Hz, 6 Hz, 2H), 7.52 (d, J=9 Hz, 2H), 7.83 (t, J=9 Hz, 1H), 7.95 (d, J=9 Hz, 2H), 8.05 (m, 1H), 8.25 (t, J=1.5 Hz, 1H), 8.33 (s, 1H). MS (DCI/NH_3) m/z 516 $(M+NH_4)^+$ Anal. calc. for $C_{24}H_{19}FN_2O_5S_2.H_2O$: C, 55.81; H, 4.07; N, 5.43 Found. C, 56.24; H, 4.29; N, 5.10.

Example 99

2-(4-Fluorophenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

4-(4-Chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone is prepared starting with the 2-benzylpyridazinone from Example 53 and debenzylating the compound according to the method of Example 11.

The title compound was prepared according to the method of Example 93, starting with 4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 1-fluoro-4-iodobenzene in place of 4-bromothioanisole (yield. 245 mg, 54%). mp 195-197 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 3H), 7.19 (m, 4H), 7.25 (m, 2H), 7.41 (d, J=9 Hz, 2H), 7.70 (m, 2H), 7.95 (d, J=9 Hz, 2H). 8.01 (s, 1H). MS (DCI/NH_3) m/z 455 $(M+H)^+$, 472 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{16}ClFN_2O_3S$: C, 60.78; H, 3.52; N, 6.17 Found: C, 60 81, H, 3.53; N, 5.93.

Example 100

2-(5-Chloro-2-thienyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 2-bromo-5-chlorothiophene in place of 4-bromothioanisole (yield: 150 mg. 45%). mp 249-251 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (s. 3H), 6.92 (d, J=9 Hz, 1H), 7.18 (d, J=9 Hz, 2H), 7.31 (d, J=9 Hz, 2H), 7.39 (d. J=9 Hz, 2H), 7.58 (d, J=6 Hz, 1H), 7.94 (d, J=9 Hz, 2 Hz, 2H), 8.04 (s, 1H). MS (DCI/NH_3) m/z 477 $(M+H)^+$, 494 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{14}Cl_2N_2O_3S_2.H_2O$: C, 50.9; H. 3.03; N, 5.60. Found: C, 50.5; H, 2.79; N. 5.26.

Example 101

2-(3-Trifluoromethylphenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , starting with 4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 4-(4-

fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 3-iodobenzotrifluoride in place of 4-bromothioanisole (yield: 210 mg, 59.5%). mp 103-105 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 3H), 7.18 (d, J=9 Hz, 2H), 7.28 (d, J=9 Hz, 2H), 7.41 (d, J=9 Hz, 2H), 7.65 (m, 2H), 7.95 (m, 3H), 8.04 (m, 2H). MS (DCI/NH_3) m/z 505 $(M+H)^+$, 525 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{16}ClF_3N_2O_3S$: C, 57.14; H, 3.17; N, 5.56. Found. C, 56.61; H, 3.28; N, 5.38.

Example 102

2-(3-Chloro-4-fluorophenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , starting with 4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (described in Example 99) in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 1-bromo-3-chloro-4-fluorobenzene in place of 4-bromothioanisole (yield: 330 mg, 58.8%). mp 205 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 3H), 7.17 (d, J=9 Hz, 2H), 7.23-7.31 (m, 1H), 7 28 (d, J=9 Hz, 2H), 7.41 (d, J=9 Hz, 2H), 7.65 (ddd, J=9 Hz, 3 Hz, 1.5 Hz, 1H), 7.85 (dd, J=9 Hz, 3 Hz, 1H), 7.93 (d, J=9 Hz, 2H), 8.01 (s, 1H). MS (DCI/NH_3) m/z 489 $(M+H)^+$, 508 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}Cl_2N_2O_3S$. C, 56.44; H, 3.17; N, 5.73. Found: C, 56.37; H, 3.19; N, 5.64.

Example 103

2-(3-Fluorophenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 1-fluoro-3-iodobenzene in place of 4-bromothioanisole (yield: 310 mg, 70.8%). mp 245-247 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 3H), 6.98 (t, J=9 Hz, 2H), 7.14 (m, 1H), 7.24 (dd, J=9 Hz, 6 Hz, 2H), 7.40 (m, 2H), 7.52 (m, 3H), 7.92 (d, J=9 Hz, 2H), 8.01 (s, 1H). MS (DCI/NH_3) m/z 439 $(M+H)^+$, 456 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}F_2N_2O_3S.0.25\ H_2O$: C, 62.34, H, 3.67; N, 6.38. Found: C, 62.33; H, 3.68; N, 6.22.

Example 104

2-[2-(Methylthio)phenyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 2-bromothioanisole in place of 4-bromothioanisole (yield: 280 mg. 60%). mp 206-208 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.49 (s, 3H), 3.08 (s, 3H), 6.95 (t, J=9 Hz, 2H), 7.25 (dd, J=9 Hz, 6 Hz, 2H), 7.29-7.51 (m, 4H), 7.43 (d, J=9 Hz, 2H), 7 92 (d, J=9 Hz, 3H), 8.01 (s, 1H), 7.98 (s, 1H). MS (DCI/NH_3) m/z 467 $(M+H)^+$, 484 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{19}FN_2O_3S_2.H_2O$: C, 59.50; H, 4.13; N, 5.79. Found: C, 59.62; H, 4.15; N, 5.52.

Example 105

2-(5-Nitro-2-thienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93, substituting 2-bromo-5-nitrothiophene in place of 4-bromothioanisole (yield: 330 mg, 70%). mp 252-253 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.06 (s, 3H), 7.05 (t, J=9 Hz, 2H), 7.25 (dd, J=9 Hz, 6 Hz, 2H), 7.40 (d, J=9 Hz, 2H), 7.71 (d, J=6 Hz, 1H), 7.95 (m, 3H), 8.14 (s, 1H). MS (DCI/NH_3) m/z 472 $(M+H)^+$, 489 $(M+NH_4)^+$ Anal. calc. for $C_{21}H_{14}FN_3O_5S_2.0.5\ H_2O$: C, 52.50; H, 3.02; N, 8.75. Found. C, 52.79; H, 3.18; N, 8.74.

Example 106

2-(3,4-Difluorophenyl)-4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , starting with 4-(4-chlorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 1-bromo-3,4-difluorobenzene in place of 4-bromothioanisole (yield: 310 mg, 65.7%). mp 187-188 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.09 (s, 3H), 7.18 (d, J=9 Hz, 2H), 7.29 (m, 3H), 7.41 (d, J=9 Hz, 2H), 7.52 (m, 1H), 7.65 (m, 1H), 7.92 (d, J=9 Hz, 2H), 8.01 (s, 1H).

MS (DCI/NH_3) m/z 473 $(M+H)^+$, 490 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}ClF_2N_2O_3S.0.5$ H_2O: C, 57.38; H, 3.33; N, 5.82. Found: C, 57.44; H, 3.38; N, 5.52.

Example 107

2-(3-Benzothienyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 3-bromobenzothiophene in place of 4-bromothioanisole (yield: 185 mg, 41%). mp 265-267 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.09 (s, 3H), 7.0 (t, J=9 Hz, 2H), 7.27 (dd, J=9 Hz, 6 Hz, 2H), 7.39-7.47 (m, 2H), 7.44 (d, J=9 Hz, 2H), 7.75-7.82 (m, 1H), 7.87-7.94 (m, 2H), 7.94 (d, J=9 Hz, 2H), 8.05 (s, 1H). MS (DCI/NH_3) m/z 477 $(M+H)^+$, 494 $(M+NH_4)^+$. Anal. calc. for $C_{25}H_{17}FN_2O_3S_2$: C, 63.03; H, 3.57; N, 5.88 Found: C, 62.89; H, 3.55; N, 5.71.

Example 108

2-(4-Fluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

Example 108A

4-(4-Fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared by treating 2-benzyl-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (Example 75) with $AlBr_3$ in toluene according to the procedure in Example 11 (yield: 1.8 g, 95%).

Example 108B

2-(4-Fluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , starting with 4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone and substituting 1-fluoro-4-iodobenzene in place of 4-bromothioanisole (yield: 60 mg, 53%). mp 83-85 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 3H), 6.89-7.03 (m, 4H), 7.15 (t, J=9 Hz, 2H), 7.65 (dd, J=9 Hz, 6 Hz, 2H), 7.83 (d, J=6 Hz, 2H), 8.07 (d, J=9 Hz, 2H), 8.08 (s, 1H). MS (DCI/NH_3) m/z 455 $(M+H)^+$, 472 $(M+NH_4)^+$.

Example 109

2-(3,4-Difluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 1-bromo-3,4-difluorobenzene in place of 4-bromothioanisole and 4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (Example 108A) in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (yield: 185 mg, 39%). mp 178-180 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.11 (s, 3H), 6.89-7.04 (m, 4H), 7.45-7.52 (m, 1H), 7.45-7.52 (m, 1H), 7.61 (dt, J=6 Hz, 3 Hz, 1H), 7.82 (d, J=9 Hz, 2H), 8.07 (d, J=9 Hz, 2H), 8.08 (s, 1H). MS (DCI/NH_3) m/z 473 $(M+H)^+$, 490 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}F_3N_2O_4S.0.5\ H_2O$: C, 57.38; H, 3.33; N, 5.83. Found: C, 57.17; H, 3.13; N, 5.62.

Example 110

2-(3-Bromophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 1,3-dibromobenzene in place of 4-bromothioanisole and 4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (Example 108A) in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (yield: 260 mg, 50.5%). mp 208-210 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.09 (s, 3H), 6.89-7.04 (m, 4H), 7.34 (t, J=9 Hz, 1H), 7.53 (br d, J=9 Hz, 1H), 7.64 (br d, J=9 Hz, 1H), 7.82 (d, J=9 Hz, 2H), 7.87 (t, J=1.5 Hz, 1H), 8.08 (d, J=9 Hz, 2H), 8.09 (s, 1H). MS (DCI/NH_3) m/z 517 $(M+H)^+$, 534 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{16}BrFN_2O_4S$. C, 53.7; H, 3.11, N, 5 45. Found: C, 53.46; H, 2.88; N, 5.18.

Example 111

2-(3,5-Difluorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 1-bromo-3,4-difluorobenzene in place of 4-bromothioanisole and 4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (Example 108A) in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (yield: 175 mg, 37%). mp 209-211 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 3H), 6.85 (tt, J=9 Hz, 3 Hz, 1H), 6.90-7.04 (m, 4H), 7.38 (dd, J=9 Hz, 3 Hz, 2H), 7.81 (d, J=9 Hz, 2H), 8.07 (d, J=9 Hz, 2H), 8.10 (s, 1H). MS (DCI/NH_3) m/z 473 $(M+H)^+$, 490 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{15}F_3N_2O_4S.H_2O$: C, 58.47; H, 3.18; N, 5.94. Found: C, 58.31; H, 3.15; N, 5.82.

Example 112

2-(3-Chlorophenyl)-4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to Example 93 , substituting 1-bromo-3-chlorobenzene in place of 4-bromothioanisole and 4-(4-fluorophenoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (Example 108A) in place of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (yield: 25 mg, 5.3%). mp 211-213 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.30 (s, 3H), 7.15 (d, J=9 Hz, 4H), 7.51-7.64 (m, 3H), 7.71-7.75 (m, 1H), 7.91 (d, J=9 Hz, 2H), 8.06 (d, J=9 Hz, 2H), 8.41 (s, 1H). MS (DCI/NH_3) m/z 471 $(M+H)^+$, 488 $(M+NH_4)^+$. Anal calc. for $C_{23}H_{16}ClFN_2O_4S.0.5$ H_2O: C, 57.62; H, 3.44; N, 5.85. Found: C, 57.62; H, 3.52; N, 5.48.

Example 113

2-(4-Nitrobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 4-nitrobenzyl bromide in place of 4-fluorobenzyl bromide (yield: 164 mg, 58.9%). mp 183-184 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 3H), 5.47 (s, 2H), 6.96 (t,

J=9 Hz, 2H), 7.16 (dd, J=9 Hz, 3 Hz, 2H), 7.32 (d, J=9 Hz, 2H), 7.70 (d, J=9 Hz, 2H), 7.87 (s, 1H), 7.88 (d, J=9 Hz, 2H), 8.22 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 480 $(M+H)^+$, m/z 497 $(M+NH_4)^+$. Anal. calc. for $C_{24}H_{18}FN_3O_5S$: C, 60.12; H, 3.78; N, 8.76. Found: C, 59.89; H, 3.83; N, 8.61.

Example 114

2-(4-Acetoxybenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 4-(chloromethyl)phenyl acetate in place of 4-fluorobenzyl bromide (yield: 220 mg, 76.9%). mp 172-174 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.05 (s, 3H), 5.38 (s, 2H), 6.95 (t, J=9 Hz, 2H), 7.06 (d, J=9 Hz, 2H), 7.16 (dd, J=9 Hz, 5 Hz, 2H), 7.31 (d, J=9 Hz, 2H), 7.60 (d, J=9 Hz, 2H), 7.81 (s, 1H), 7.87 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 510 $(M+NH_4)^+$. Anal. calc. for $C_{26}H_{21}FN_2O_5S$: C, 63.40; H, 4.30; N, 5.69. Found: C, 63.28; H, 4.41; N, 5.39.

Example 115

2-(4-Hydroxybenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of 2-(4-acetoxybenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (0.2 g, 4.06 mmol) (Example 114) in THF (20 mL) was treated with a solution of lithium hydroxide monohydrate (0.05 g, 1.22 mmol) in water (5 mL). Methanol (2 mL) was added to provide a homogeneous solution which was stirred at room temperature overnight. The reaction mixture was then acidified with 10% aqueous citric acid and extracted with ethyl acetate. The ethyl acetate layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated in vacuo to provide a white foam which was purified by column chromatography (silica gel, 65:35 hexanes/ethyl acetate). Product fractions were combined and concentrated in vacuo. The residue was crystallized from ethyl acetate/hexanes (yield: 195 mg, 70%). mp 225-226 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 3H), 4.86 (s, 1H), 5.33 (s, 2H), 6.80 (d, J=8.5 Hz, 2H), 6.95

(t, J=9 Hz, 2H), 7.15 (dd, J=9 Hz, 5 Hz, 2H), 7.30 (d, J=8.5 Hz, 2H), 7.46 (d, J=8.5 Hz, 2H), 7.83 (s, 1H), 7.87 (d, J=8.5 Hz, 2H). MS (DCI/NH_3) m/z 451 $(M+H)^+$. Anal. calc. for $C_{24}H_{19}FN_2O_4S$: C, 63.99; H, 4.25; N, 6.22. Found: C, 63.73, H, 4.16; N, 6.11.

Example 116

2-(3-Nitrobenzyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 3-nitrobenzyl bromide in place of 4-fluorobenzyl bromide (yield: 195 mg, 70%). mp 156-157 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 3H), 5.48 (s, 2H), 6.96 (t, J=9 Hz, 2H), 7.16 (dd, J=9 Hz, 5 Hz, 2H), 7.33 (d, J=8.5 Hz, 2H), 7.54 (t, J=7 Hz, 1H), 7.88 (s, 1H), 7.90 (d, J=8.5 Hz, 2H), 8.19 (br d, J=7 Hz, 1H), 8.37 (t, J=1.7 Hz, 1H). MS (DCI/NH_3) m/z 480 $(M+H)^+$, m/z 497 $(M+NH_4)^+$. Anal. calc for $C_{24}H_{18}FN_3O_5S$: C, 60.12; H, 3.78; N, 8.76. Found. C, 59.98; H, 3.73; N, 8.67.

Example 117

2-(3,4,4-Trifluoro-3-butenyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 4-bromo-1,1,2-trifluoro-1-butene in place of 4-fluorobenzyl bromide (yield, 38 mg, 14.5%). mp 131-132 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 2.92 (br d, J=21.7 Hz, 2H), 3.06 (s, 3H), 4.47 (t, J=6.6 Hz, 2H), 6.98 (t, J=9 Hz, 2H), 7.17 (dd, J=9 Hz, 5 Hz, 2H), 7.35 (d, J=8.5 Hz, 2H), 7.85 (s, 1H), 7.89 (d, J=8.5 Hz, 2H). MS (DCI/NH_3) m/z 453 $(M+H)^+$, m/z 470 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{16}F_4N_2O_3S$. C, 55.75; H, 3.56; N, 6.19. Found: C, 55.63; H, 3.62; N, 6.10.

Example 118

2-(2-Hexynyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 1-chloro-2-hexyne in place of 4-fluorobenzyl bromide (yield: 170 mg, 69%).

mp 79-80 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, J=7.5 Hz, 3H), 1.56 (h, J=7.5 Hz, 2H), 2.21 (m, 2H), 3.06 (s, 3H), 5.01 (t, J=3 Hz, 2H), 6.96 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, 6 Hz, 2H), 7.34 (d, J=9 Hz, 2H), 7.88 (s, 1H), 7.89 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 425 $(M+H)^+$. Anal. calc. for $C_{23}H_{21}FN_2O_3S$: C, 65.07; H, 4.98; N, 6.59. Found: C, 64.87; H, 4.90; N, 6.58.

Example 119

2-(3,3-Dichloro-2-propenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting 1,1,3-trichloropropene in place of 4-fluorobenzyl bromide (yield: 1.15 g, 68%). mp 184-185 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.39 (d, J=7.5 Hz, 2H), 6.43 (t, J=7.5 Hz, 1H), 7.14 (t, J=9 Hz, 2H), 7.23 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.43 (s, 2H), 7.73 (d, J=9 Hz, 2H), 8.11 (s, 1H). MS (DCI/NH_3) m/z 454 $(M+H)^+$. Anal. calc. for $C_{19}H_{14}Cl_2F_4N_3O_3S$: C, 50.23; H, 3.1; N, 9.24. Found. C, 50.28, H, 3.29, N, 9.19.

Example 120

2-Cyclohexyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20 substituting cyclohexyl bromide in place of 4-fluorobenzyl bromide (yield: 163 mg, 76%). mp 169-171 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.23 (m, 1H), 1.41 (m, 2H), 1.71 (m, 3H), 1.87 (m, 4H), 3.23 (s, 3H), 4.85 (m, 1H), 7.11 (m, 2H), 7.22 (m, 2H), 7.46 (d, J=9 Hz, 2H), 7.85 (d, J=9 Hz, 2H), 8.11 (s, 1H). MS (DCI/NH_3) m/z 427 $(M+H)^+$ and m/z 444 $(M+NH_4)^+$. Anal. calc. for $C_{23}H_{23}FN_2O_3S.0.5\ H_2O$: C, 63.43; H, 5.55; N, 6.43. Found: C, 63.25; H, 5.28; N, 6.28.

Example 121

2-Cyclopentyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting cyclopentyl bromide in place of 4-fluorobenzyl bromide (yield: 165 g, 80%). mp 191-193 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.67 (m, 2H), 1.85 (m, 4H), 2.05 (m, 2H), 3.23 (s, 3H), 5.36 (m, 1H), 7.12 (t, J=9 Hz, 2H), 7.22 (m, 2H), 7.45 (d, J=9 Hz, 2H), 7.85 (d, J=9 Hz, 2H), 8.13 (s, 1H). MS (DCI/NH_3) m/z 413 $(M+H)^+$ and m/z 430 $(M+NH_4)^+$. Anal. calc. for $C_{22}H_{21}FN_2O_3S.0.5\ H_2O$: C, 62.69; H, 5.26; N, 6.57. Found: C, 62.53; H, 4.93; N, 6.50

Example 122

2-Cyclobutyl-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 20, substituting cyclobutyl bromide in place of 4-fluorobenzyl bromide (yield: 270 g, 68%). mp 202-203 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.85 (m, 2H), 2.32 (m, 2H), 2.50 (m, 2H), 5.40 (quintet, J=7 Hz, 1H), 7.11 (t, J=9 Hz, 2H), 7.21 (m, 2H), 7.47 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 8.16 (s, 1H). MS (DCI/NH_3) m/z 399 $(M+H)^+$ and m/z 416 $(M+NH_4)^+$. Anal. calc. for $C_{21}H_{19}FN_2O_3S.0.75\ H_2O$: C, 61.22; H, 5.01; N, 6.80. Found: C, 61.19; H, 4.62; N, 6.73.

Example 123

2-(3-Methyl-2-butenyl)-4-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-(4-fluorophenyl)-5-[3-fluoro-4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone, prepared according to the method of Example 68, was N-debenzylated according to the method of Example 11. The intermediate was N-alkylated according to the method of Example 20, substituting 1-bromo-3-methyl-2-butene in place of 4-fluorobenzyl bromide, to provide the title compound (yield, 50 mg, 30%). mp 134-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 3H), 1.86 (s, 3H), 4.78 (s, 2H), 4.85 (d, J=7.5 Hz, 2H), 5.48 (t, J=6 Hz, 1H), 6 96 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, 6 Hz, 2H), 7.28 (d,

J=9 Hz, 2H), 7.83 (s, 1H), 7.85 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 414 $(M+H)^+$ Anal. calc. for $C_{21}H_{20}FN_3O_3S$: C, 61; H, 4.87; N, 10.16. Found: C, 60.98; H, 4.66; N, 9.95.

Example 124

2-(2,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

2-Benzyl-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone, prepared according to the method of Example 68, was N-debenzylated according to the method of Example 11. The intermediate was N-alkylated according to the method of Example 20, substituting 2,4-difluorobenzylbromide in place of 4-fluorobenzyl bromide to provide the title compound (yield: 65 mg, 24%). mp 236-238 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.78 (s, 2H), 5.43 (s, 2H), 6.88 (m, 2H), 6.97 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, 6 Hz, 2H), 7.38 (d, J=9 Hz, 2H), 7.55 (m, 1H), 7.85 (s, 1H), 7.86 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 472 $(M+H)^+$. Anal calc. for $C_{23}H_{16}F_3N_3O_3S$: C, 58.59; H, 3.42; N, 8.91 Found: C, 58.44; H, 3.47; N, 8.72.

Example 125

2-(Pentafluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 2,3,4,5,6-pentafluorobenzyl bromide in place of 1-bromo-3-methyl-2-butene (yield: 105 mg, 35%). mp 201-203 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 4.8 (s, 2H), 5.5 (s, 2H), 6.98 (t, J=9 Hz, 2H), 7.18 (dd, J=9 Hz, 6 Hz, 2H), 7.28 (d, J=9 Hz, 2H), 7.32 (s, 1H), 7.37 (d, J=9 Hz, 2H). MS (DCI/NH_3) m/z 526 $(M+H)^+$. Anal. calc. for $C_{23}H_{13}F_6N_3O_3S$: C, 52.57; H, 2.49; N, 7.99. Found: C, 52.66, H, 2.68; N, 7.8

Example 126

2-(3-Cyclohexenyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 3-bromocyclohexene in place of 1-bromo-3-methyl-2-butene (yield: 30 mg, 10%). mp 206-208 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75-1.85 (m, 3H), 2.1-2.3 (m, 3H), 4.8 (s, 2H), 5.75 (m, 2H), 6.1 (m, 1H), 6.97 (t, J=9 Hz, 2H), 7.20 (dd, J=9 Hz, 6 Hz, 2H), 7.28 (d, J=9 Hz, 2H), 7.86 (d, J=9 Hz, 2H), 7.90 (s, 1H). MS (DCI/NH_3) m/z 426 $(M+H)^+$. Anal. calc. for $C_{22}H_{20}FN_3O_3S$: C, 62.10; H, 4.73; N, 9.87. Found: C, 61.27; H, 4.75; N, 9.56.

Example 127

2-(3,4-Difluorobenzyl)-4-(4-fluorophenyl)-5-[4-(aminosulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 124, substituting 3,4-difluorobenzyl bromide in place of 1-bromo-3-methyl-2-butene and running the reaction in DMSO instead of DMF to prevent formation of byproducts (yield: 210 mg, 62%). mp 253-255 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.33 (s, 2H), 7.13 (t, J=9 Hz, 2H), 7.22 (dd, J=9 Hz, 6 Hz, 2H), 7.28 (m, 1H), 7.39 (d, J=9 Hz, 2H), 7.42 (s, 2H), 7.47 (m, 2H), 7.73 (d, J=9 Hz, 2H), 8.12 (s, 1H). MS (DCI/NH_3) m/z 472 $(M+H)^+$. Anal. calc. for $C_{23}H_{16}F_3N_3O_3S$: C, 58.59; H, 3.42; N, 8.91. Found: C, 58.05; H, 3.55; N, 8.49.

Example 128

2-(2,3-Dihydro-1H-inden-2-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

A solution of 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone (172 mg, 0.5 mmol), prepared in Example 11, 2-indanol (67 mg, 0.5 mmol) and Ph_3P (262 mg, 1 mmol) in toluene (20 mL) and ethyl acetate (5 mL) was prepared and added dropwise a solution of DIAD (0.2 mL, 1 mmol) in toluene (10 mL). The mixture was stirred at room temperature for 6 hours and concentrated in vacuo. The residue was chromatographed (silica gel, 19:1 CH_2Cl_2-ethyl acetate) to provide 200 mg of product

(contaminated with reduced DIAD). A second column chromatography (hexanes-ethyl acetate 1:1) furnished the title product (yield: 170 mg, 74%). mp 97-100 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.22 (s. 3H), 3.32 (m, 2H), 3.44 (dd, J=9 Hz and 15 Hz, 2H), 5.83 (m, 1H), 7.25 (m, 4H), 7.34 (m. 4H), 7.46 (d, J=9 Hz, 2H), 7.85 (d, J=9 Hz, 2H), 8.06 (s, 1H). MS (DCI/NH_3) m/z 461 $(M+H)^+$ and m/z 478 $(M+NH_4)^+$.

Example 129

2-(2,3-Dihydro-1H-inden-1-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 128 substituting 1-indanol in place of 2-indanol (yield: 110 mg, 48%). mp 128-130 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.40 (m, 1H), 2.60 (m, 1H), 3 00 (m, 1H), 3.22 (s+m, 4H), 6.60 (dd, J=9 Hz, 6 Hz, 1H), 7.16 (m, 4H), 7.27 (m, 4H), 7.47 (d, J=9 Hz, 2H), 7.85 (d, J=9 Hz, 2H), 8.02 (s, 1H). MS (DCI/NH_3) m/z 461 $(M+H)^+$ and m/z 478 $(M+NH_4)^+$.

Example 130

2-(4-Tetrahydro-2H-pyran-4-yl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone

The title compound was prepared according to the method of Example 128 substituting 4-tetrahydropyranol in place of 2-indanol (yield: 140 g, 65%). mp 230-231 °C ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.75 (m, 2H), 1.93 (m, 2H), 3.14 (s, 3H), 3.46 (m, 2H), 3 93 (m, 2H); 5.02 (m, 1H), 7.05 (t, J=9 Hz, 2H), 7.15 (m, 2H), 7.40 (d, J=9 Hz, 2H), 7.80 (d, J=9 Hz, 2H), 8.08 (s, 1H). MS (APCI-) m/z 428 (M-H)- and m/z 463 (M+Cl)- Anal. calc. for $C_{22}H_{21}FN_2O_4S.1.25\ H_2O$: C, 58.59; H, 5.25; N, 6.21. Found: C, 58.31; H, 4.75; N, 6.05.

Example 131

2-(2-Methylcyclopentyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone