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United States Patent [19]

Ewing et al.

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[54] **SUBSTITUTED (SULFINIC ACID, SULFONIC ACID, SULFONYLAMINO OR SULFINYLAMINO) N-[(AMINOMINOMETHYL)PHENYLALKYL]-AZAHETEROCYCLYLAMIDE COMPOUNDS**

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[*] Notice: This patent is subject to a terminal disclaimer.

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[22] Filed: **Nov. 21, 1997**

Related U.S. Application Data

[63] Continuation of application No. PCT/US96/09816, Jun. 7, 1996, which is a continuation-in-part of application No. 08/481,024, Jun. 7, 1995, Pat. No. 5,612,353.

[51] **Int. Cl.**[6] **C07D 401/02**; A61K 31/40; A61K 31/435

[52] **U.S. Cl.** **514/212**; 514/307; 514/309; 514/329; 514/343; 514/422; 514/426; 540/606; 546/141; 546/223; 546/281; 546/139; 546/276.4; 548/527; 548/557

[58] **Field of Search** 540/606; 546/141, 546/223, 281, 139, 276.4; 548/527, 557; 514/212, 307, 309, 343, 320, 422, 426

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,612,353	3/1997	Ewing et al. .
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Valerio et al, Synthesis, vol. 10, pp. 786–789, 1988.

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[57] **ABSTRACT**

The compounds of formula I exhibit useful pharmacological activity and accordingly are incorporated into pharmaceutical compositions and used in the treatment of patients suffering from certain medical disorders. More especially, they are inhibitors of the activity of Factor Xa. The present invention is directed to compounds of formula I, compositions containing compounds of formula I, and their use, which are for treating a patient suffering from, or subject to, physiological condition which can be ameliorated by the administration of an inhibitor of the activity of Factor Xa.

57 Claims, No Drawings

SUBSTITUTED (SULFINIC ACID, SULFONIC ACID, SULFONYLAMINO OR SULFINYLAMINO) N-[(AMINOMINOMETHYL)PHENYLALKYL]-AZAHETEROCYCLYLAMIDE COMPOUNDS

This application is a continuation of copending International Application No. PCT/US96109816, filed Jun. 7, 1996, which designates the United States, which, in turn, is a continuation-in-part application of U.S. patent application Ser. No. 08/481,024, filed Jun. 7, 1995, now U.S. Pat. No. 5,612,353.

FIELD OF THE INVENTION

The compounds of formula I exhibit useful pharmacological activity and accordingly are incorporated into pharmaceutical compositions and used in the treatment of patients suffering from certain medical disorders. More especially, they are Factor Xa inhibitors. The present invention is directed to compounds of formula I, compositions containing compounds of formula I, and their use, which are for treating a patient suffering from, or subject to, conditions which can be ameliorated by the administration of an inhibitor of Factor Xa.

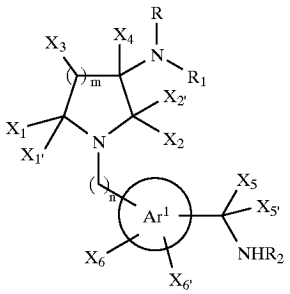
Factor Xa is the penultimate enzyme in the coagulation cascade. Both free factor Xa and factor Xa assembled in the prothrombinase complex (Factor Xa, Factor Va, calcium and phospholipid) are inhibited by compounds of formula I. Factor Xa inhibition is obtained by direct complex formation between the inhibitor and the enzyme and is therefore independent of the plasma co-factor antithrombin III. Effective factor Xa inhibition is achieved by administering the compounds either by oral administration, continuous intravenous infusion, bolus intravenous administration or any other parenteral route such that it achieves the desired effect of preventing the factor Xa induced formation of thrombin from prothrombin.

Anticoagulant therapy is indicated for the treatment and prophylaxis of a variety of thrombotic conditions of both the venous and arterial vasculature. In the arterial system, abnormal thrombus formation is primarily associated with arteries of the coronary, cerebral and peripheral vasculature. The diseases associated with thrombotic occlusion of these vessels principally include acute myocardial infarction (AMI), unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy and percutaneous transluminal coronary angioplasty (PTCA), transient ischemic attacks, stroke, intermittent claudication and bypass grafting of the coronary (CABG) or peripheral arteries. Chronic anticoagulant therapy may also be beneficial in preventing the vessel luminal narrowing (restenosis) that often occurs following PTCA and CABG, and in the maintenance of vascular access patency in long-term hemodialysis patients. With respect to the venous vasculature, pathologic thrombus formation frequently occurs in the veins of the lower extremities following abdominal, knee and hip surgery (deep vein thrombosis, DVT). DVT further predisposes the patient to a higher risk of pulmonary thromboembolism. A systemic, disseminated intravascular coagulopathy (DIC) commonly occurs in both vascular systems during septic shock, certain viral infections and cancer. This condition is characterized by a rapid consumption of coagulation factors and their plasma inhibitors resulting in the formation of life-threatening thrombin throughout the microvasculature of several organ systems. The indications discussed above include some, but not all, of the possible

clinical situations where anticoagulant therapy is warranted. Those experienced in this field are well aware of the circumstances requiring either acute or chronic prophylactic anticoagulant therapy.

SUMMARY OF THE INVENTION

This invention is directed to the pharmaceutical use of a compound of formula I below for treating a patient suffering from a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa, where formula I is as follows:



is phenyl or monocyclic heteroaryl;

R is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted heteroaralkyl or hydroxyalkyl;

R_1 is hydrogen, $R_3S(O)_p$— or $R_3R_4NS(O)_p$—;

R_2 is hydrogen, or when X_5 and $X_{5'}$ taken together are $=NR_5$, then R_2 is hydrogen, optionally substituted lower alkyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;

R_3 is optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted heteroaralkyl, optionally substituted aralkenyl or optionally substituted heteroaralkenyl, or R and R_3 taken together form a 5 to 7 membered ring; and

R_4 is optionally substituted alkyl, optionally substituted cycloalkyl or optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form an optionally substituted 4 to 7 membered heterocyclyl;

X_1 and $X_{1'}$ are independently selected from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl or hydroxyalkyl, or X_1 and $X_{1'}$ taken together form oxo;

X_2 and $X_{2'}$ are hydrogen, or taken together form oxo;

X_3 is hydrogen, hydroxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or X_3 and one of X_1 and $X_{1'}$ taken together form a 4 to 7 membered ring;

X_4 is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, or hydroxyalkyl;

X_5 and $X_{5'}$ are hydrogen or taken together are $=NR_5$;

R_5 is hydrogen, R_6O_2C—, R_6O—, cyano, R_6CO—, optionally substituted lower alkyl, nitro or $Y^{1'}Y^{2'}N$—;

$Y^{1'}$ and $Y^{2'}$ are independently hydrogen, alkyl, aralkyl or heteroaralkyl;

X_6 and $X_{6'}$ are independently hydrogen, R_7R_8N—, R_9O—, R_7R_8NCO—, $R_7R_8NSO_2$—, R_9CO—, halo, cyano or nitro;

R_6 is hydrogen, optionally substituted lower alkyl or optionally substituted aralkyl or optionally substituted heteroaralkyl;

R_7 and R_8 are independently hydrogen or optionally substituted lower alkyl, or one of R_7 and R_8 is hydrogen and the other of R_7 and R_8 is $R_{10}(O)CCH_2$— or lower acyl;

R_9 is hydrogen, optionally substituted lower alkyl, lower acyl or $R_{10}(O)CCH_2$—;

R_{10} is hydrogen, optionally substituted lower alkyl, alkoxy or hydroxy;

m is 0, 1, 2 or 3;

n is 1, 2 or 3; or

p is 1 or 2,

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

DETAILED DESCRIPTION OF THE INVENTION

As used above, and throughout the description of the invention, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

Definitions

"Patient" includes both human and other mammals.

"Alkyl" means an aliphatic hydrocarbon group which may be straight or branched having about 1 to about 20 carbon atoms in the chain. Preferred alkyl groups have 1 to about 12 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl are attached to a linear alkyl chain. "Lower alkyl" means about 1 to about 4 carbon atoms in the chain which may be straight or branched. The alkyl may be substituted with one or more "alkyl group substituents" which may be the same or different, and include halo, cycloalkyl, alkoxy, amino, acylamino, aroylamino, carboxy, alkoxycarbonyl, aralkyloxycarbonyl, heteroaralkyloxycarbonyl or $Y^{1'}Y^{2'}NCO$—, where $Y^{1'}$ and $Y^{2'}$ are independently hydrogen, alkyl, aralkyl or heteroaralkyl. Exemplary alkyl groups include methyl, trifluoromethyl, cyclopropylmethyl, cyclopentylmethyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-pentyl, 3-pentyl, methoxyethyl, carboxymethyl, methoxycarbonylethyl, benzyloxycarbonylmethyl, pyridylmethyloxycarbonylmethyl.

"Cycloalkyl" means a non-aromatic mono- or multicyclic ring system of about 3 to about 10 carbon atoms. Exemplary monocyclic cycloalkyl rings include cyclopentyl, fluorocyclopentyl, cyclohexyl and cycloheptyl. The cycloalkyl group is optionally partially unsaturated or optionally substituted by one or more halo, methylene (H_2C═), alkyl, fused ary or fused heteroaryl. Exemplary multicyclic cycloalkyl rings include 1-decalin, adamant-(1- or 2-)yl and norbornyl.

"Heterocyclyl" means a non-aromatic monocyclic or multicyclic ring system of about 3 to about 10 ring atoms. Preferred rings include about 5 to about 6 ring atoms wherein one of the ring atoms is oxygen, nitrogen or sulfur. The heterocyclyl is optionally partially unsaturated or optionally substituted by one or more alkyl, halo, aryl, heteroaryl, fused aryl or fused heteroaryl. Exemplary monocyclic rings include pyrrolidyl, piperidyl, tetrahydrofuranyl, tetrahydrothienyl and tetrahydrothiopyranyl. The thio or nitrogen moiety of the heterocyclyl may also be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide.

"Aryl" means aromatic carbocyclic radical containing about 6 to about 10 carbon atoms. Exemplary aryl include phenyl or naphthyl, or phenyl substituted or naphthyl substituted with one or more aryl group substituents which may be the same or different, where "aryl group substituent" includes hydrogen, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, acylamino, aroylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, fused cycloalkyl, fused heterocyclyl, arylazo, heteroarylazo, Y^1Y^2N—, Y^1Y^2NCO— or $Y^1Y^2NSO_2$—, where Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or Y^1, Y^2 and N taken together form a heterocyclyl. The aryl group substituents are as defined herein.

Preferred aryl groups are optionally substituted phenyl or optionally substituted naphthyl. Preferred aryl group substituents include hydrogen, alkyl, hydroxy, acyl, aryl aroyl, aryloxy, halo, nitro, alkoxy, cyano, alkoxycarbonyl, acylamino, alkylthio, $Y^{1'}Y^{2'}N$—, $Y^{1'}Y^{2'}NCO$— or $Y^{1'}Y^{2'}NSO_2$—, where $Y^{1'}$ and $Y^{2'}$ are independently hydrogen, alkyl, aralkyl or heteroaralkyl; preferred phenyl group substituents are aryloxy and aryl; and preferred naphthyl group substituents are nitro, alkoxy and amino.

"Heteroaryl" means about a 5- to about a 10- membered aromatic monocyclic or multicyclic hydrocarbon ring system in which one or more of the carbon atoms in the ring system is/are element(s) other than carbon, for example nitrogen, oxygen or sulfur. The "heteroaryl" may also be substituted by one or more of the above-mentioned "aryl group substituents". Exemplary heteroaryl groups include pyrazinyl, furanyl, thienyl, pyridyl, pyrimidinyl, isoxazolyl, isothiazolyl, oxazolyl, thiazolyl, pyrazolyl, furazanyl, pyrrolyl, imidazo[2,1-b]thiazolyl, benzofurazanyl, indolyl, azaindolyl, benzimiddazolyl, benzothienyl, quinolinyl, imidazolyl and isoquinolinyl. Preferred heteroaryl groups in the R substituent include benzothienyl, thienyl, imidazolyl, pyridyl and quinolinyl all of which may be optionally substituted. Where

is monocylic heteroaryl, then preferred heteroaryls include thienyl, pyridyl and furanyl.

"Aralkyl" means an aryl-alkyl- group in which the aryl and alkyl are as previously described. Preferred aralkyls contain a lower alkyl moiety. Exemplary aralkyl groups include benzyl, 2-phenethyl and naphthalenemethyl.

"Heteroaralkyl" means a heteroaryl-alkyl- group in which the heteroaryl and alkyl are as previously described. Preferred heteroaralkyls contain a lower alkyl moiety. Exemplary heteroaralkyl groups may contain thienyl, pyridyl, imidazolyl and pyrazinyl.

"Aralkenyl" means an aryl-alkenyl- group in which the aryl and alkenyl are as previously described. Preferred aralkenyls contain a lower alkenyl moiety. An exemplary aralkenyl group is 2-phenethenyl.

"Heteroaralkenyl" means a heteroaryl-alkenyl- group in which the heteroaryl and alkenyl are as previously

described. Preferred heteroaralkenyls contain a lower alkenyl moiety. Exemplary heteroaralkenyl groups may contain thienyl, pyridyl, imidazolyl and pyrazinyl.

"Hydroxyalkyl" means a HO-alkyl- group in which alkyl is as previously defined. Preferred hydroxyalkyls contain lower alkyl. Exemplary hydroxyalkyl groups include hydroxymethyl and 2-hydroxyethyl.

"Acyl" means an H—CO— or alkyl-CO— group in which the alkyl group is as previously described. Preferred acyls contain a lower alkyl. Exemplary acyl groups include formyl, acetyl, propanoyl, 2-methylpropanoyl, butanoyl and palmitoyl.

"Aroyl" means an aryl-CO— group in which the alkyl group is as previously described. Exemplary groups include benzoyl and 1- and 2-naphthoyl.

"Alkoxy" means an alkyl-O— group in which the alkyl group is as previously described. Exemplary alkoxy groups include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy and heptoxy.

"Aryloxy" means an aryl-O— group in which the aryl group is as previously described. Exemplary aryloxy groups include phenoxy and naphthoxy.

"Aralkyloxy" means an aralkyl-O— group in which the aralkyl groups is as previously described. Exemplary aralkyloxy groups include benzyloxy and 1- or 2-naphthalenemethoxy.

"Alkylthio" means an alkyl-S— group in which the alkyl group is as previously described. Exemplary alkylthio groups include methylthio, ethylthio, i-propylthio and heptylthio.

"Arylthio" means an aryl-S— group in which the aryl group is as previously described. Exemplary arylthio groups include phenylthio and naphthylthio.

"Aralkylthio" means an aralkyl-S— group in which the aralkyl group is as previously described. An exemplary aralkylthio group is benzylthio.

"Y^3Y^4N—" means a substituted or unsubstituted amino group, wherein Y^3 and Y^4 are as previously described. Exemplary groups include amino (H_2N—), methylamino, ethylmethylamino, dimethylamino and diethylamino.

"Alkoxycarbonyl" means an alkyl-O—CO— group. Exemplary alkoxycarbonyl groups include methoxy- and ethoxycarbonyl.

"Aryloxycarbonyl" means an aryl-O—CO— group. Exemplary aryloxycarbonyl groups include phenoxy- and naphthoxycarbonyl.

"Aralkoxycarbonyl" means an aralkyl-O—CO— group. An exemplary aralkoxycarbonyl group is benzyloxycarbonyl.

"Y^3Y^4NCO—" means a substituted or unsubstituted carbamoyl group, wherein Y^3 and Y^4 are as previously described. Exemplary groups are carbamoyl (H_2NCO—) and dimethylaminocarbamoyl (Me_2NCO—).

"$Y^3Y^4NSO_2$—" means a substituted or unsubstituted sulfamoyl group, wherein Y^3 and Y^4 are as previously described. Exemplary groups are aminosulfamoyl (H_2NSO_2—) and dimethylaminosulfamoyl (Me_2NSO_2—).

"Acylamino" is an acyl-NH— group wherein acyl is as defined herein.

"Aroylamino" is an aroyl-NH— group wherein aroyl is as defined herein.

"Alkylsulfonyl" means an alkyl-SO_2— group. Preferred groups are those in which the alkyl group is lower alkyl.

"Alkylsulfinyl" means an alkyl-SO— group. Preferred groups are those in which the alkyl group is lower alkyl.

"Arylsulfonyl" means an aryl-SO_2— group.

"Arylsulfinyl" means an aryl-SO— group.

"Halo" means fluoro, chloro, bromo, or iodo. Preferred are fluoro, chloro or bromo, and more preferred are fluoro or chloro.

Preferred Embodiments

A preferred embodiment of the invention is a method for treating a patient suffering from a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa by administering a therapeutically effective amount of a compound of formula I.

A preferred compound aspect of the invention is the compound of formula I wherein R_3 is optionally substituted phenyl, optionally substituted naphthyl, optionally substituted thienyl or optionally substituted benzothienyl.

Another preferred compound aspect of the invention is the compound of formula I wherein n is 1, and m is 1.

Another preferred compound aspect of the invention is the compound of formula I wherein X_2 and $X_{2'}$ taken together are oxo.

Another preferred compound aspect of the invention is the compound of formula I wherein X_1, $X_{1'}$, X_3 and X_4 are hydrogen.

Another preferred compound aspect of the invention is the compound of formula I wherein X_5 and $X_{5'}$ taken together are =NH.

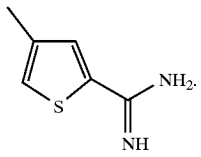
Another preferred compound aspect of the invention is the compound of formula I wherein X_5 and $X_{5'}$ taken together are $=NR_5$ wherein R_5 is R_6O_2C—.

Another preferred compound aspect of the invention is the compound of formula I wherein

is phenyl and the carbon substituted with X_5, $X_{5'}$ and HR_2N— is attached to the 3-position of the phenyl.

Another preferred compound aspect of the invention is the compound of formula I wherein

is of the formula



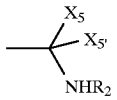
Another preferred compound aspect of the invention is the compound of formula I wherein R is hydrogen, methyl, aralkyl, heteroaralkyl, HO_2CCH_2—, $HOC(O)CH_2$—, $H_2NC(O)CH_2$—, (aralkyl)$HNC(O)CH_2$— or (heteroaralkyl)$HNC(O)CH_2$—.

Another preferred compound aspect of the invention is the compound of formula I wherein X_1 is hydrogen and $X_{1'}$ is carboxyalkyl, alkoxycarbonylalkyl or aryl, or X_1 and $X_{1'}$ taken together form oxo.

Another preferred compound aspect of the invention is the compound of formula I wherein R_1 is R_3SO_2—.

Another preferred compound aspect of the invention is the compound of formula I wherein R_1 is $R_3R_4NSO_2$—.

Another preferred compound aspect of the invention is the compound of claim **1** wherein one of X_6 and $X_{6'}$ is amino in a para position relative to the



moiety.

Species according to the invention are selected from the group consisting of:

Naphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

Dibenzofuran-2-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]-5-oxopyrrolidin-3-yl}amide trifluoroacetate;

Toluene-4-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

3,4-Dihydro-1H-isoquinoline-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

3'-Methoxy-biphenyl-4-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

Naphthalene-1-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

5-Pyrid-2-ylthiophene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

Biphenyl-4-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Ethoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

5-Chloro-6-methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

5-Chloro-6,7-dimethoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Aminonaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide bistrifluoroacetate;

Naphthalene-2-sulfonic acid {1-[4-(aminoiminomethyl) benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(3-aminomethylbenzyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;

Naphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]-2-oxopyrrolidin-3-(S)-yl}methyl amide trifluoroacetate;

Naphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]pyrrolidin-3-(S)-yl}amide bistrifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2,5-dioxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

Naphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl) benzyl]-2-oxopiperidin-3-yl}amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxo-azepan-3-(S)-yl}amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}methyl amide trifluoroacetate;

6-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

6-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}methyl amide trifluoroacetate;

2-[{1-[3-(Aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}-6-methoxynaphthalene-2-sulfonylamino]-N-phenethylacetamide trifluoroacetate;

9,10-Dioxo-8a,9, 10,10a-tetrahydroanthracene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

8-Chloro-7-methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)-benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[4-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

6,7-Dimethoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

Naphtho(2,3-d)-(1,3)dioxole-6-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Benzyloxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Hydroxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

6-Hydroxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

5-Chloro-3-methylbenzo[b]thiophene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

5-Chloro-3-methylbenzo[b]thiophene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}methyl amide trifluoroacetate;

7-Methylnaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

7-Ethylnaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide trifluoroacetate;

5-Chloro-6-aminonaphthalene-2-sulfonic acid {1-[3-aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide bistrifluoroacetate;

7-Methylaminonaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide bistrifluoroacetate;

2-Methyl-1,2,3,4-tetrahydroisoquinolinyl-7-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}amide bistrifluoroacetate;

1,2,3,4-Tetrahydroisoquinolinyl-7-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}methyl amide dihydrochloride;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}-(4-nitrobenzyl)amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}-(4-aminobenzyl)amide bistrifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl}(3-nitrobenzyl)amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3-(S)-yl)}(3-aminobenzyl)amide bistrifluoroacetate;

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Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

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Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

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API

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LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

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Sync your system to PACER to automate legal marketing.