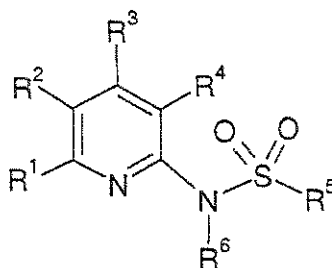


ALKYL-PYRIDINES AS 11-BETA INHIBITORS FOR DIABETES

The present invention is concerned with novel pyridine derivatives useful as 11b-HSD1 inhibitors (T2D).

The invention is concerned particularly with compounds of formula I



(I)

5

and pharmaceutically acceptable salts and esters thereof, wherein

R¹ is hydrogen, alkyl, cycloalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, aryl, heterocyclyl, alkylsulfonyl, alkylsulfanyl, alkylcarbonylalkyl, alkylcarbonyloxyalkyl, aminocarbonylalkyl, heterocyclylcarbonylalkyl, heterocyclylalkoxyalkyl, alkoxyalkylaminocarbonylalkyl, cycloalkylalkoxyalkyl, arylalkyloxyalkyl, aryloxyalkyl, haloalkyl, haloalkoxy or haloalkoxyalkyl;

10

R² is hydrogen, alkyl, cycloalkylalkoxyalkyl, alkoxyalkyl, arylalkoxyalkyl, haloalkoxyalkyl, piperidyl, pyrrolidyl, morpholinyl, thiomorpholinyl arylalkyl, arylalkoxy, aryloxy, heterocyclylalkoxy or heterocyclylalkyl;

15 R³ is hydrogen or alkyl;

R⁴ is hydrogen, alkyl or halogen;

R⁵ is phenyl, naphthyl, thiophenyl, pyridyl, quinolyl, piperidyl, morpholyl, thiomorpholyl or 1,2,3,4-tetrahydro-isoquinolyl optionally substituted with one or more substituents independently selected from alkyl, cycloalkyl, halogen, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkoxyalkoxy, cyano, nitro, 5 trifluoromethyl, trifluoromethoxy, trifluoromethylcarbonyl, aryl, arylalkyl, aryloxy, alkoxycarbonylalkoxy and alkylsulfonyl;

R⁶ is hydrogen or alkyl;

with the proviso that N-(6-(1,1-dimethylethyl)-2-pyridinyl)-4-methyl-benzenesulfonamide is excluded and in case R¹ is hydrogen or methyl then R² is not 10 hydrogen or methyl.

Glucocorticoids (cortisol in humans, corticosterone in mice and rats) are an important class of adrenocorticosteroids that regulate many metabolic and homeostatic processes and form a key component of the response to stress. Glucocorticoids act via intracellular glucocorticoid receptors and, in some tissues, mineralocorticoid receptors; 15 both being nuclear transcription factors. Glucocorticoid action on target tissues depends not only on circulating steroid concentrations and the cellular expression of receptors, but also on intracellular enzymes that critically determine to which extent glucocorticoids gain access to receptors in an active form. 11beta-hydroxysteroid dehydrogenases (11beta-HSD's) catalyze the interconversion of the principal active 11-hydroxy-glucocorticoid 20 (Cortisol in men) and their inactive 11-keto metabolites (cortisone in men).

The enzyme 11beta-hydroxysteroid dehydrogenase type 1 (11beta-HSD1) interconverts inactive into active glucocorticoids, thereby playing a major role in local modulation of cellular agonist concentration and thus activation of corticosteroid receptors in target tissues. In a recent study made by F. Hoffmann-La Roche differences in 25 gene expression in lean and obese men were analyzed using gene array technology in order to identify specific changes in gene expression that might be associated with insulin resistance or altered metabolism. This study revealed that the mRNA for 11beta-HSD1 is approximately two-fold up regulated in adipose tissue in obese individuals. Moreover, overexpressing 11beta-HSD1 in adipocytes of mice led to visceral obesity and to a 30 syndrome-X like phenotype (Masuzaki H. et al., Science. 2001 Dec 7; 294(5549):2166-70.). Taken together, these data very strongly support an important role of 11beta-HSD1 in the induction of obesity and the impairment of glucose homeostasis and lipid parameters.

Thus, selective inhibition of this enzyme could lower blood glucose levels in Type 2 diabetic patients, normalize elevated lipid parameters and/or reduce weight in obese subjects .

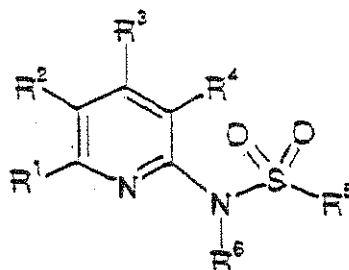
5 The first pharmacological indication that 11beta-HSD1 inhibition in men might have beneficial effects were obtained by using carbenoxolone, an anti-ulcer drug which inhibits both 11beta-HSD1 and the related enzyme 11beta-HSD2. Treatment with carbenoxolone led to an increase in insulin sensitivity indicating that that inhibition of 11beta-HSD1 may reduce cellular cortisol levels and therefore minimizing some of its deleterious effects. (Walker et al. 1995; J. Clin. Endocrinol. Metab. 80, 31155-3159).

10 11beta-HSD1 is expressed in many tissues including liver, adipose tissue, vascular smooth muscles, pancreas and brain. Its activity is dependent on NADP(H) and it has a relatively low affinity for its substrate (compared to 11beta-HSD2). 11 beta-HSD1 in tissue homogenates and when purified is bidirectional, exhibiting both 11beta-dehydrogenase and 11beta-reductase reactions, with greater stability of the dehydrogenase activity (P.M. Stewart and Z.S. Krozowski, Vitam. Horm. 57 (1999), pp. 249-324). However, when the
15 enzyme activity is tested in intact cells, the 11beta-reductase activity predominates, which regenerates active glucocorticoids from inert 11-keto forms. Such glucocorticoid regeneration will increase effective intracellular glucocorticoid levels and thereby amplifying glucocorticoid activity. It is this elevated cellular cortisol concentration that
20 might lead to increased hepatic glucose production, adipocyte differentiation and insulin resistance.

Inhibition of 11beta-HSD1 should not only reduce the typical Syndrome-X / Diabetes associated symptoms, but it should also be save and without major side effect. Studies with the unspecific inhibitor carbenoxolone highlight the importance of
25 developing specific 11beta-HSD1 inhibitors. The inhibition of the 11beta-HSD2 enzyme is badly tolerated and results in increased blood pressure. In contrast inhibition of 11beta-HSD1 should be well tolerated since 11beta-HSD1 knockout mice were found be healthy and to resist hyperglycemia provoked by obesity or stress (Kotelevtsev Y. et al., Proc Natl Acad Sci U S A. 1997 Dec 23; 94(26):14924-9). Similar upon starvation these mice had
30 attenuated activation of key hepatic enzymes that are involved in gluconeogenesis. In addition, these mice had improved lipid and lipoprotein profiles suggesting that inhibition of HSD1 might be highly efficacious and safe. Recent reports indicate that 11beta-HSD1 inhibitors might also be beneficial to reduce high blood pressure (Masuzaki H. et al., J Clin Invest. 2003 July;112(1):83-90; Rauz S. et al., QJM. 2003 July;96(7):481-90) to improve

cognition (Sandeep TC. et al., Proc Natl Acad Sci U S A. 2004 Apr. 27;101(17):6734-9) or to improve Alzheimer associated deficits. Taken together 11beta-HSD1 inhibition might be a save and efficacious approach to treat symptoms of diabetes, obesity and other diseases.

According to a first aspect, there is provided compounds of formula



(I)

5 wherein

R¹ is alkyl, cycloalkyl, hydroxalkyl, alkoxyalkyl, aryl, alkoxyalkylaminocarbonylalkyl, cycloalkylalkoxyalkyl, arylalkyloxyalkyl or trifluoroalkoxyalkyl;

R² is hydrogen, alkyl, cycloalkylalkoxyalkyl, alkoxyalkyl, arylalkoxyalkyl, haloalkoxyalkyl, piperidyl, pyrrolidyl, morpholinyl, thiomorpholinyl, arylalkyl, arylalkoxy, aryloxy, heterocyclylalkoxy or heterocyclylalkyl;

15 R³ is hydrogen or alkyl;

R⁴ is hydrogen, alkyl or halogen;

20 R⁵ is phenyl, naphthyl, thiophenyl, pyridyl, quinolyl, piperidyl, morpholyl, thiomorpholyl or 1,2,3,4-tetrahydro-isoquinolinyl optionally substituted with one or more substituents independently selected from alkyl, cycloalkyl, halogen, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkoxyalkoxy, cyano, nitro, trifluoromethyl, trifluoromethoxy, trifluoromethylcarbonyl, aryl, arylalkyl, aryloxy, alkoxycarbonylalkoxy and alkylsulfonyl;

R⁶ is hydrogen or alkyl;

wherein aryl is phenyl or naphthyl optionally substituted with one to three, substituents independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl,

wherein hydroxyalkyl is hydroxymethyl;

and pharmaceutically acceptable salts and esters thereof;

with the proviso that

N-(6-(1,1-dimethylethyl)-2-pyridinyl)-4-methyl-benzenesulfonamide,

3-Chloro-N-(6-ethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide,

N-(6-ethyl-pyridin-2-yl)-4-trifluoromethyl-benzenesulfonamide,

N-(6-ethyl-pyridin-2-yl)-4-isopropyl-benzenesulfonamide,

3-Chloro-N-(6-hydroxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide,

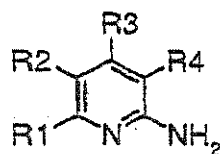
6-(4-Trifluoromethyl-phenyl)-pyridine-3-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide, and

2-[6-3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide

are excluded and in case R¹ is hydrogen or methyl then R² is not hydrogen or methyl.

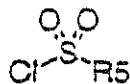
According to a second aspect, there is provided a process for the preparation of a compound as defined above comprising

a) reaction of a compound according to formula

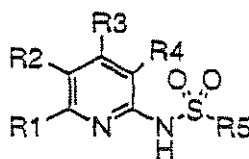


II

15 in the presence of a compound according to formula



in order to obtain a compound of the formula

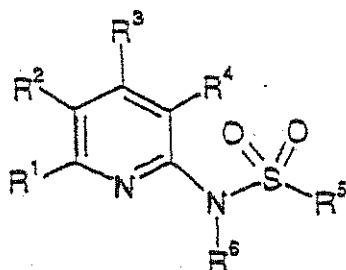


Ia

4b

and optionally

b) further reaction in the presence of a compound of the formula R^6-X in order to obtain a compound of the formula



(I)

wherein R^1 to R^6 are defined as in claim 1 and X is Cl, Br or I.

According to a third aspect, there is provided compounds as defined above for use as therapeutically active substance.

According to a fourth aspect, there is provided compounds as defined above for the preparation of medicaments for the prophylaxis and therapy of illnesses which are caused by disorders associated with the enzyme 11 beta-hydroxysteroid dehydrogenase 1.

According to a fifth aspect, there is provided a pharmaceutical composition comprising a compound as defined above and a therapeutically inert carrier.

According to a sixth aspect, there is provided the use of a compound as defined above for the preparation of medicaments for the treatment and prophylaxis of diabetes, obesity, eating disorders, dyslipidemiae and hypertension.

According to a seventh aspect, there is provided the use of a compound as defined above for the preparation of medicaments for the treatment and prophylaxis of diabetes Type II.

According to an eighth aspect, there is provided a compound as defined above, when manufactured according to a process of the second aspect.

The compounds of formula I and their pharmaceutically acceptable salts and esters are novel and have valuable pharmacological properties. In particular they are 11b-HSD1 inhibitors (T2D) and they display selectivity against the related 11beta-HSD2 enzyme. Therefore the compounds which are specific 11beta-HSD1 inhibitors (T2D) represent an approach to e.g. lower blood glucose levels and normalize lipid parameters in Type 2 diabetic patients by modulating the local concentration of the active glucocorticoid cortisol in target tissue (liver, adipose tissue).

The compounds of the present invention can be used in the prophylaxis and/or treatment of metabolic disorders, obesity, dyslipidemiae, hypertension and/or diabetes, particularly diabetes Type II.

The compounds of this invention can further be used in the prophylaxis and/or treatment of high ocular eye pressure, cognition, Alzheimer and/or neurodegeneration.

Objects of the present invention are the compounds of formula I and their aforementioned salts and esters per se and their use as therapeutically active substances, a process for the manufacture of the said compounds, intermediates, pharmaceutical compositions, medicaments containing the said compounds, their pharmaceutically acceptable salts and esters, the use of the said compounds, esters and salts for the prophylaxis and/or therapy of illnesses, especially in the treatment or prophylaxis of eating disorders, obesity, dyslipidemiae, hypertension and/or diabetes, particularly diabetes Type II, and the use of the said compounds, salts and esters for the production of medicaments for the treatment or prophylaxis of metabolic disorders, obesity, dyslipidemiae, hypertension and/or diabetes, particularly diabetes Type II.

The compounds of the present invention can further be combined with PPAR (alpha, gamma, delta) agonists, DHEA (dehydroepiandrosterone), DPPIV inhibitors, insulin and/or lipase inhibitors, particularly orlistat.

In the present description the term "alkyl", alone or in combination, signifies a straight-chain or branched-chain alkyl group with 1 to 8 carbon atoms, preferably a straight or branched-chain alkyl group with 1 to 6 carbon atoms and particularly preferred

a straight or branched-chain alkyl group with 1 to 4 carbon atoms. Examples of straight-chain and branched C₁-C₈ alkyl groups are methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert.-butyl, the isomeric pentyls, the isomeric hexyls, the isomeric heptyls and the isomeric octyls, preferably methyl and ethyl and most preferred methyl.

5 The term "cycloalkyl", alone or in combination, signifies a cycloalkyl ring with 3 to 8 carbon atoms and preferably a cycloalkyl ring with 3 to 6 carbon atoms. Examples of C₃-C₈ cycloalkyl are cyclopropyl, methyl-cyclopropyl, dimethylcyclopropyl, cyclobutyl, methyl-cyclobutyl, cyclopentyl, methyl-cyclopentyl, cyclohexyl, methyl-cyclohexyl, dimethyl-cyclohexyl, cycloheptyl and cyclooctyl, preferably cyclopropyl.

10 The term "alkoxy", alone or in combination, signifies a group of the formula alkyl-O- in which the term "alkyl" has the previously given significance, such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec. butoxy and tert.butoxy, preferably methoxy and ethoxy and most preferred methoxy.

15 The term "hydroxyalkyl", alone or in combination, signifies an alkyl group as defined before, wherein one or more hydrogen atoms, preferably one hydrogen atom is replaced by a hydroxy group. Examples of hydroxyalkyl are hydroxymethyl and hydroxyethyl.

20 The term "aryl", alone or in combination, signifies a phenyl or naphthyl group, preferably a phenyl group which optionally carries one or more substituents, preferably one to three, each independently selected from halogen, trifluoromethyl, trifluoromethoxy, amino, alkyl, alkoxy, alkylcarbonyl, cyano, carbamoyl, alkoxycarbamoyl, methylenedioxy, carboxy, alkoxycarbonyl, aminocarbonyl, alkyaminocarbonyl, dialkylaminocarbonyl, hydroxy, nitro, alkyl-SO₂-, amino-SO₂-, cycloalkyl and the like. Preferred is phenyl or naphthyl, particularly phenyl optionally substituted with one to three, preferably one or
25 two substituents independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl. Particularly preferred is phenyl.

 The term "aryloxy", alone or in combination, signifies a aryl-O- group in which the term "aryl" has the previously given significance.

30 The term "heterocyclyl", alone or in combination signifies a saturated, partially unsaturated or aromatic 5- to 10-membered heterocycle which contains one or more hetero atoms selected from nitrogen, oxygen and sulphur. If desired, it can be substituted

on one or more carbon atoms e.g. by halogen, alkyl, alkoxy, oxo etc. and/or on a secondary nitrogen atom (i.e. -NH-) by alkyl, cycloalkyl, aralkoxycarbonyl, alkanoyl, phenyl or phenylalkyl or on a tertiary nitrogen atom (i.e. =N-) by oxido, with halogen, alkyl, cycloalkyl and alkoxy being preferred. Examples of such heterocyclyl groups are

5 pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrazoyl, imidazolyl (e.g. imidazol-4-yl and 1-benzyloxycarbonyl-imidazol-4-yl), pyrazoyl, pyridyl, pyrazinyl, pyrimidinyl, hexahydro-pyrimidinyl, furyl, thienyl, thiazolyl, oxazolyl, indolyl (e.g. 2-indolyl), quinolyl (e.g. 2-quinolyl, 3-quinolyl and 1-oxido-2-quinolyl), isoquinolyl (e.g. 1-isoquinolyl and 3-isoquinolyl), tetrahydroquinolyl (e.g. 1,2,3,4-tetrahydro-2-quinolyl),

10 1,2,3,4-tetrahydroisoquinolyl (e.g. 1,2,3,4-tetrahydro-1-oxo-isoquinolyl) and quinoxalinyl. Preferred examples are thiophenyl, quinolyl, piperidyl, morpholyl, thiomorpholyl, oxazolyl, pyridinyl, pyrimidinyl, pyrazolyl, imidazolyl, pyrrolidinyl and thiazolyl. Particularly preferred examples are piperidyl, morpholyl, thiomorpholyl, pyridinyl and pyrrolidinyl.

15 The term "amino", alone or in combination, signifies a primary, secondary or tertiary amino group bonded via the nitrogen atom, with the secondary amino group carrying an alkyl or cycloalkyl substituent and the tertiary amino group carrying two similar or different alkyl or cycloalkyl substituents or the two nitrogen substituents together forming a ring, such as, for example, -NH₂, methylamino, ethylamino,

20 dimethylamino, diethylamino, methyl-ethylamino, pyrrolidin-1-yl or piperidino etc., preferably primary amino, dimethylamino and diethylamino and particularly dimethylamino.

The term "halogen", alone or in combination, signifies fluorine, chlorine, bromine or iodine and preferably fluorine, chlorine or bromine.

25 The term "haloalkyl", alone or in combination, signifies an alkyl group as defined before, wherein one or more, preferably one to five hydrogen atoms are replaced by halogen, preferably fluoro. Examples of such haloalkyl groups are difluoromethyl, trifluoromethyl and pentafluoroethyl. Preferred is trifluoromethyl.

The term "haloalkoxy", alone or in combination, signifies an alkoxy group as defined

30 before, wherein one or more, preferably one to five hydrogen atoms are replaced by halogen, preferably fluoro. Examples of such haloalkoxy groups are difluoromethoxy, trifluoromethoxy, monofluoroethoxy and pentafluoroethoxy. Preferred is trifluoromethoxy and monofluoroethoxy.

The term "hydroxyalkyl", alone or in combination, signifies an alkyl group as defined before, wherein one or more hydrogen atoms, preferably one hydrogen atom is replaced by a hydroxy group. Examples of hydroxyalkyl are hydroxymethyl and hydroxyethyl.

5 The term "carbonyl", alone or in combination, signifies the -C(O)- group.

The term "oxy", alone or in combination, signifies the -O- group.

The term "nitro", alone or in combination signifies the -NO_2 group.

The term "cyano", alone or in combination signifies the group -CN .

The term "pharmaceutically acceptable salts" refers to those salts which retain the
10 biological effectiveness and properties of the free bases or free acids, which are not biologically or otherwise undesirable. The salts are formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, preferably hydrochloric acid, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric
15 acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, N-acetylcystein and the like. In addition these salts may be prepared from addition of an inorganic base or an organic base to the free acid. Salts derived from an inorganic base include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium salts and the
20 like. Salts derived from organic bases include, but are not limited to salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, lysine, arginine, N-ethylpiperidine, piperidine, polyamine resins and the like. The compound of
25 formula I can also be present in the form of zwitterions. Particularly preferred pharmaceutically acceptable salts of compounds of formula I are the hydrochloride salts.

The compounds of formula I can also be solvated, e.g. hydrated. The solvation can be effected in the course of the manufacturing process or can take place e.g. as a consequence of hygroscopic properties of an initially anhydrous compound of formula I
30 (hydration). The term pharmaceutically acceptable salts also includes physiologically acceptable solvates.

"Pharmaceutically acceptable esters" means that compounds of general formula (I) may be derivatised at functional groups to provide derivatives which are capable of conversion back to the parent compounds in vivo. Examples of such compounds include physiologically acceptable and metabolically labile ester derivatives, such as

5 methoxymethyl esters, methylthiomethyl esters and pivaloyloxymethyl esters. Additionally, any physiologically acceptable equivalents of the compounds of general formula (I), similar to the metabolically labile esters, which are capable of producing the parent compounds of general formula (I) in vivo, are within the scope of this invention.

The compounds of formula I can contain several asymmetric centers and can be

10 present in the form of optically pure enantiomers, mixtures of enantiomers such as, for example, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates or mixtures of diastereoisomeric racemates.

Preferred are the compounds of formula I and pharmaceutically acceptable salts thereof, particularly the compounds of formula I.

15 Preferred are the compounds of formula I, wherein R^5 is phenyl, naphthyl, thiophenyl, pyridyl, quinolyl, piperidyl, morpholyl, thiomorpholyl or 1,2,3,4-tetrahydro-isoquinolinyll optionally substituted with one or more substituents, preferably one to three substituents, independently selected from alkyl, cycloalkyl, halogen, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkoxyalkoxy, cyano, nitro, trifluoromethyl, trifluoromethoxy,

20 trifluoromethylcarbonyl, aryl, arylalkyl, aryloxy, alkoxycarbonylalkoxy and alkyl-SO₂-.

Particularly preferred are those compounds of formula I, wherein R^5 is phenyl, naphthyl, thiophenyl, pyridyl, quinolyl, piperidyl, morpholyl, thiomorpholyl or 1,2,3,4-tetrahydro-isoquinolinyll optionally substituted with one or two substituents independently selected from alkyl, cycloalkyl, halogen, hydroxy, hydroxyalkyl, alkoxy,

25 alkoxyalkyl, hydroxyalkoxy, alkoxyalkoxy, cyano, nitro, trifluoromethyl, trifluoromethoxy, trifluoromethylcarbonyl, aryl, arylalkyl, aryloxy, alkoxycarbonylalkoxy and alkyl-SO₂-.

Further preferred are compounds according to formula I, wherein R^5 is phenyl, naphthyl, piperidyl or 1,2,3,4-tetrahydro-isoquinolinyll optionally substituted with one to three substituents independently selected from alkyl, halogen, alkoxy, nitro,

30 trifluoromethyl, trifluoromethoxy, trifluoromethylcarbonyl, aryl, aryloxy and alkyl-SO₂-.

Particularly preferred are compounds of formula I, wherein R⁵ is phenyl or naphthyl optionally substituted with one to three substituents independently selected from alkyl, halogen, trifluoromethyl, trifluoromethoxy and aryl.

Also preferred are compounds according to formula I, wherein R⁶ is hydrogen.

5 Preferred are compounds of formula I, wherein R¹ is hydrogen, alkyl, cycloalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, aryl, heterocyclyl, alkylsulfonyl, alkylsulfanyl, alkylcarbonylalkyl, alkylcarbonyloxyalkyl, aminocarbonylalkyl, heterocyclylcarbonylalkyl, heterocyclylalkoxyalkyl such as e.g. pyridylmethoxymethyl, alkoxyalkyl, alkoxyalkylaminocarbonylalkyl, cycloalkylalkoxyalkyl, arylalkoxyalkyl, aryloxyalkyl, haloalkyl, haloalkoxy or haloalkoxyalkyl.

Further preferred are compounds of formula I, wherein R¹ is alkyl, cycloalkyl, hydroxyalkyl, alkoxyalkyl, aryl, alkoxyalkylaminocarbonylalkyl, cycloalkylalkoxyalkyl, arylalkoxyalkyl or trifluoroalkoxyalkyl.

Another preferred embodiment of the present invention are compounds of formula
15 I, wherein R¹ is hydrogen.

Preferred are the compounds of formula I, wherein R² is hydrogen, alkyl, cycloalkylalkoxyalkyl, alkoxyalkyl, arylalkoxyalkyl, haloalkoxyalkyl such as e.g. fluoroethoxymethyl or trifluoroethoxymethyl, piperidyl, pyrrolidyl, morpholinyl, thiomorpholinyl arylalkyl, arylalkoxy, aryloxy, heterocyclylalkoxy or heterocyclylalkyl;

20 Further preferred are compounds of formula I, wherein R² is hydrogen, cycloalkylalkoxyalkyl, alkoxyalkyl, piperidyl, pyrrolidyl, morpholinyl, thiomorpholinyl, arylalkyl or aryloxy.

Also preferred are compounds according to formula I, wherein R³ is hydrogen.

Further preferred are compounds according to formula I, wherein R⁴ is hydrogen or
25 halogen.

Particularly preferred are those compounds of formula I, wherein R⁴ is hydrogen.

Examples of preferred compounds of formula (I) are:

- 3-Chloro-N-(6-ethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
Biphenyl-4-sulfonic acid (6-ethyl-pyridin-2-yl)-amide;
Biphenyl-4-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
3-Chloro-2-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
5 Naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
3,4-Dichloro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
2,5-Difluoro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
2,4-Dichloro-6-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
5-Chloro-naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
10 3,4-Dimethoxy-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
4,5-Dichloro-2-fluoro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
2,4-Dichloro-5-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
Piperidine-1-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
3-Chloro-N-(6-isopropyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
15 2,5-Difluoro-N-(6-isopropyl-pyridin-2-yl)-benzenesulfonamide;
N-(6-Isopropyl-pyridin-2-yl)-4-(4-trifluoromethyl-phenoxy)-benzenesulfonamide;
2,4-Dichloro-N-(6-isopropyl-pyridin-2-yl)-5-methyl-benzenesulfonamide;
N-(6-Isopropyl-pyridin-2-yl)-4-methanesulfonyl-benzenesulfonamide;
N-(6-Isopropyl-pyridin-2-yl)-4-trifluoromethoxy-benzenesulfonamide;
20 2-(2,2,2-Trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline-7-sulfonic acid (6-isopropyl-pyridin-2-yl)-amide;
N-(6-Isopropyl-pyridin-2-yl)-3-(4-trifluoromethyl-phenoxy)-benzenesulfonamide;
Naphthalene-2-sulfonic acid (6-isopropyl-pyridin-2-yl)-amide;

- N-(6-Isopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide;
3-Chloro-N-[6-(2-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
Biphenyl-4-sulfonic acid [6-(2-chloro-phenyl)-pyridin-2-yl]-amide;
5 3-Chloro-N-[6-(2,4-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-N-[6-(3-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-N-[6-(2,3-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-N-[6-(2,5-dichloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
N-[6-(2,5-Dichloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide;
10 3-Chloro-N-[6-(3-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
N-[6-(3-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide;
3-Chloro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
5-Fluoro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
15 5-Fluoro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-2,5-difluoro-benzenesulfonamide;
N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-2-trifluoromethyl-benzenesulfonamide;
3-Chloro-N-[6-(2-methoxy-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
20 5-Fluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
N-[2,3']Bipyridinyl-6-yl-3-chloro-2-methyl-benzenesulfonamide;
2,5-Difluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;

- 2,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 3,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-N-(6-methoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 5 Biphenyl-4-sulfonic acid (6-methoxy-pyridin-2-yl)-amide;
- 5-Fluoro-N-(6-methoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Naphthalene-2-sulfonic acid (6-methoxy-pyridin-2-yl)-amide;
- 3-Chloro-N-(6-ethoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Biphenyl-4-sulfonic acid (6-ethoxy-pyridin-2-yl)-amide;
- 10 Naphthalene-2-sulfonic acid (6-ethoxy-pyridin-2-yl)-amide;
- 3-Chloro-N-(6-ethylsulfanyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Biphenyl-4-sulfonic acid (6-ethylsulfanyl-pyridin-2-yl)-amide;
- Naphthalene-2-sulfonic acid (6-ethylsulfanyl-pyridin-2-yl)-amide;
- Naphthalene-2-sulfonic acid (6-ethanesulfonyl-pyridin-2-yl)-amide;
- 15 3-Chloro-2-methyl-N-[6-(2-oxo-pentyl)-pyridin-2-yl]-benzenesulfonamide;
- 2-[6-(Biphenyl-4-sulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide;
- Biphenyl-4-sulfonic acid [6-(2-morpholin-4-yl-2-oxo-ethyl)-pyridin-2-yl]-amide;
- [6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester;
- [6-(5-Fluoro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester;
- 20 N,N-Diethyl-2-[6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetamide;
- 4-Fluoro-biphenyl-4-sulfonic acid [6-(2-morpholin-4-yl-2-oxo-ethyl)-pyridin-2-yl]-amide;
- 2-[6-(4-Fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-N-(2-methoxy-ethyl)-acetamide;

- 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide;
- 2-[6-(3,4-Dichloro-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide
- 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide;
- 5 2-[6-(3,4-Dichloro-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide;
- 3-Chloro-N-(6-hydroxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 2,5-Difluoro-N-(6-methoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 10 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
- N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide;
- 5-Fluoro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 2,5-Difluoro-N-(6-hydroxymethyl-pyridin-2-yl)-benzenesulfonamide;
- Acetic acid 6-(2,5-difluoro-benzenesulfonylamino)-pyridin-2-ylmethyl ester;
- 15 Naphthalene-2-sulfonic acid (6-hydroxymethyl-pyridin-2-yl)-amide;
- 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
- N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-4-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 20 2,5-Difluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 5-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- Piperidine-1-sulfonic acid (6-methoxymethyl-pyridin-2-yl)-amide;
- Piperidine-1-sulfonic acid (6-cyclopropylmethoxymethyl-pyridin-2-yl)-amide

- 3-Chloro-4-methyl-N-[6-(4-trifluoromethyl-phenoxy)methyl]-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-2-methyl-N-[6-(4-trifluoromethyl-phenoxy)methyl]-pyridin-2-yl]-benzenesulfonamide;
- 5 2,5-Difluoro-N-[6-(4-trifluoromethyl-phenoxy)methyl]-pyridin-2-yl]-benzenesulfonamide;
- 5-Fluoro-2-methyl-N-[6-(4-trifluoromethyl-phenoxy)methyl]-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 10 3,4-Dichloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- N-(5-Cyclopropyl-methoxymethyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide
- 15 4-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-3-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide;
- Piperidine-1-sulfonic acid (5-cyclopropyl-methoxymethyl-pyridin-2-yl)-amide;
- 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 20 N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide;
- N-(5-Methoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 25 3-Chloro-N-(5-methoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;

- N-[5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethylbenzenesulfonamide;
- 3-Chloro-N-[5-(4-fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-2-methylbenzenesulfonamide;
- 5 N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethylbenzenesulfonamide;
- 3-Chloro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide;
- 5-Fluoro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide;
- 10 3-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Naphthalene-1-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide;
- 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2,5-dimethyl-benzenesulfonamide;
- 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-3-methyl-benzenesulfonamide;
- 15 N-(6-Cyclopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(6-cyclopropyl-pyridin-2-yl)-5-methylbenzenesulfonamide;
- Naphthalene-2-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide;
- N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3,5-bis-trifluoromethyl-benzenesulfonamide;
- 20 4-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 4-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 4-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2,5-dimethyl-
- 25 benzenesulfonamide;

- 3-Trifluoromethyl-N-[6-(4-trifluoromethyl-phenoxy)methyl]-pyridin-2-yl]-benzenesulfonamide;
- N-[5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 5 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 10 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 15 2,4-Difluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 2,4-Difluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 20 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 25 4-Fluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;

- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethoxy-benzenesulfonamide;
- 5 N-(6-Methoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(6-methoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Trifluoromethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 10 2,4-Dichloro-6-methyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- N-[6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-6-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-
- 15 benzenesulfonamide;
- 3-Chloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-
- 20 benzenesulfonamide;
- 2,4-Dichloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 2,4-Dichloro-5-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 25 2-Chloro-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-5-trifluoromethyl-benzenesulfonamide;

- 2,4-Dichloro-N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-[6-(3-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 5 N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-[5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 10 2,4-Dichloro-5-methyl-N-[5-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide;
- 15 3-Chloro-2-methyl-N-(5-pyrrolidin-1-yl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-morpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- N-(5-Benzyl-pyridin-2-yl)-3-chloro-2-methyl-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-phenethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(6-methyl-5-phenethyl-pyridin-2-yl)-benzenesulfonamide;
- 20 3-Chloro-2-methyl-N-(5-thiomorpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-[5-[2-(4-chloro-phenyl)-ethyl]-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 3-Chloro-N-[5-[2-(4-methoxy-phenyl)-ethyl]-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 25 3-Chloro-N-[5-[2-(3-fluoro-phenyl)-ethyl]-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 3-Chloro-2-methyl-N-[5-[2-(2-trifluoromethyl-phenyl)-ethyl]-pyridin-2-yl]-benzenesulfonamide

- 3-Chloro-N-{5-[2-(4-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-benzenesulfonamide;
3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;
3-Chloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
5 2,4-Dichloro-6-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;
2,4-Dichloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
2,4-Dichloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
3-Chloro-2-methyl-N-[5-(2-quinolin-2-yl-ethyl)-pyridin-2-yl]-benzenesulfonamide;
2,4-Dichloro-6-methyl-N-[5-(2-quinolin-2-yl-ethyl)-pyridin-2-yl]-benzenesulfonamide;
10 and
3-Chloro-2-methyl-N-[5-(2-pyridin-2-yl-ethyl)-pyridin-2-yl]-benzenesulfonamide.

Examples of particularly preferred compounds of formula (I) are:

- 3-Chloro-N-(6-ethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
15 Biphenyl-4-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
3-Chloro-2-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
2,4-Dichloro-6-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
5-Chloro-naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
3-Chloro-N-(6-isopropyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
20 N-(6-Isopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
3-Chloro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
2,5-Difluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;

- 2,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide;
- 3-Chloro-N-(6-hydroxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 5 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3,4-Dichloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 10 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(5-methoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethylbenzenesulfonamide;
- 15 3-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Naphthalene-1-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide;
- 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2,5-dimethyl-benzenesulfonamide;
- N-(6-Cyclopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 20 4-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-4-fluoro-3-trifluoromethyl-
- 25 benzenesulfonamide;

- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 5 2,4-Dichloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethoxy-
- 10 benzenesulfonamide;
- N-(6-Methoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 3-Trifluoromethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-6-methyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-
- 15 benzenesulfonamide;
- 2,4-Dichloro-6-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 20 2,4-Dichloro-N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-
- 25 benzenesulfonamide;
- 3-Chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-pyrrolidin-1-yl-pyridin-2-yl)-benzenesulfonamide;

- 3-Chloro-2-methyl-N-(5-morpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
N-(5-Benzyl-pyridin-2-yl)-3-chloro-2-methyl-benzenesulfonamide;
3-Chloro-2-methyl-N-(6-methyl-5-phenethyl-pyridin-2-yl)-benzenesulfonamide;
3-Chloro-2-methyl-N-(5-thiomorpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- 5 2,4-Dichloro-N-{5-[2-(4-chloro-phenyl)-ethyl]-pyridin-2-yl}-6-methyl-benzenesulfonamide;
- 3-Chloro-N-{5-[2-(3-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-benzenesulfonamide;
3-Chloro-N-{5-[2-(4-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-benzenesulfonamide;
3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;
- 10 3-Chloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
3-Chloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
2,4-Dichloro-6-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;
2,4-Dichloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-6-methyl-benzenesulfonamide; and
2,4-Dichloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-6-methyl-benzenesulfonamide.

15

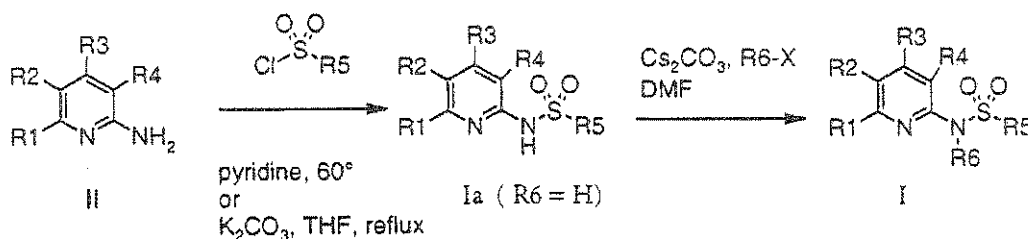
Processes for the manufacture of compounds of formula I are an object of the invention.

The preparation of compounds of formula I of the present invention may be carried out in sequential or convergent synthetic routes. Syntheses of the invention are shown in the following Schemes. The skills required for carrying out the reaction and purification of the resulting products are known to those persons skilled in the art. The substituents and indices used in the following description of the processes have the significance given above unless indicated to the contrary.

In general, compounds of type I are readily accessible by sulfonylation of appropriately substituted 2-amino-pyridines of formula II with sulfonyl chlorides under various conditions that are known to persons skilled in the art. Examples of such conditions are – as indicated in Scheme 1 below – e.g. pyridine at elevated temperatures or

THF under reflux conditions in the presence of a base such as potassium carbonate, sodium carbonate, sodium hydride, triethyl amine or the like.

Scheme 1:



X means Cl, Br or I

- 5 Optionally, compounds of formula Ia with R⁶ is H obtained in this way can be further substituted at the sulfonamide nitrogen by treatment with a base such as sodium hydride, cesium carbonate, potassium carbonate or the like in a solvent such as DMF or THF or similar followed by alkylation of the resulting anion with an alkyl halide such as methyl iodide, ethyl bromide, benzyl bromide or the like in order to introduce the desired R⁶ substituent.
- 10

Appropriately substituted 2-amino-pyridines of formula II are either commercially available, are known in the literature or can be made in analogy to literature procedures from known starting materials. General approaches that have been used for the synthesis of various aminopyridines of general formula II in the course of this invention are outlined below.

15

2-Aminopyridines of formula IIb with R¹ is alkyl, cycloalkyl, aryl or heterocyclyl can be made according to scheme 2 from compounds of formula III via metal-catalysed (Pd or Ni) cross-coupling reaction with corresponding organometallic reagent such as heterocyclyl-, alkyl-, cycloalkyl or aryl-boron, -zinc or -tin reagents using Suzuki-, Stille- or Negishi-type coupling reactions (for literature: Suzuki, Chem. Rev., 1995, 95, 2475; Stille, Angew. Chem. IEE, 1986, 25, 508; Negishi, Acc. Chem. Res., 1982, 15, 340). The corresponding organometallic reagents used are either commercially available, known in the literature or were prepared according to standard procedures known in the art.

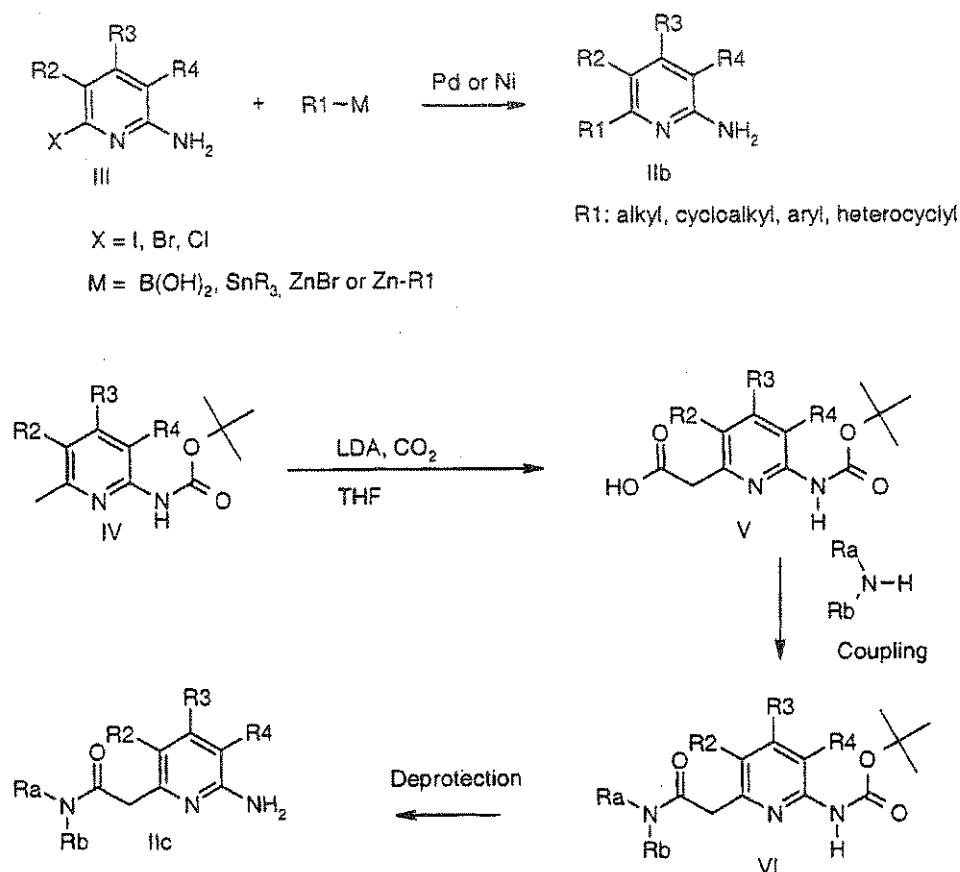
20

Compounds of formula IIc with R¹= aminocarbonylmethyl can be prepared according to scheme 2 from compounds IV, selective lithiation with for example lithium diisopropylamide (LDA) in THF, addition of CO₂ (dry ice) to give compounds of formula V. Subsequent coupling with appropriate amines in the presence of a coupling reagent such as benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate

25

(BOP) in acetonitrile gives compounds of formula VI, which are then de-protected with trifluoro-acetic acid in a solvent such as methylene chloride to give compounds of formula IIc.

Scheme 2



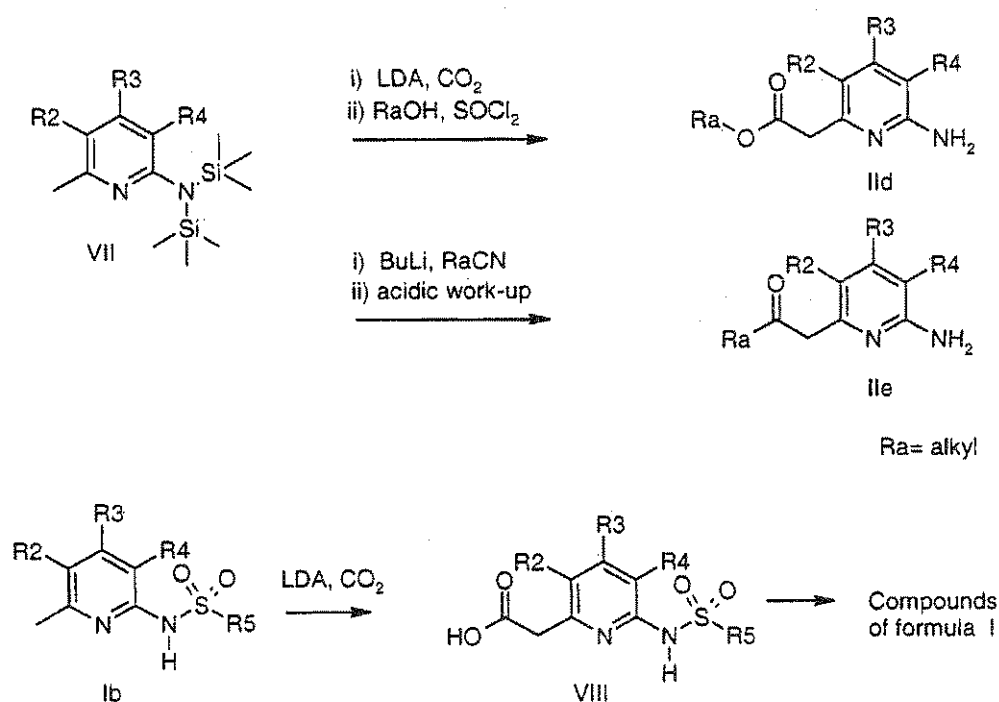
5 (Ra)(Rb)N- means amino as defined before

Compounds of formula IIc with R1 = alkoxy carbonylmethyl can be prepared according to scheme 3 from protected 2-amino-6-methyl pyridines of formula VII by selective lithiation with for example with LDA, subsequent addition of CO₂ followed by standard esterification reactions, for example with an alcohol as solvent in the presence of thionyl chloride or with an alcohol in a suitable solvent in the presence of acid, or by applying a coupling reagent as discussed above, under simultaneous removal of the trimethylsilyl protecting groups when acidic reaction conditions are applied, to give compounds of formula IIc.

10

Compounds of formula IIe with R1 is alkylcarbonylmethyl can be obtained from VII via lithiation with N-butyllithium (BuLi), subsequent reaction with an appropriate alkyl nitrile and an acidic work-up to yield IIe. Alternatively, compounds of formula IIc-d can be prepared from compounds of formula VIII, obtained from Ib via lithiation with LDA and CO₂ addition, by standard esterification or amide formation reactions known in the art. Next higher homologues of above described amines of formula II, such as aminocarbonyl ethyl as R1 and the like, can be prepared from intermediates described in schemes 2,3 via homologation reactions known in the art, e.g. via Arndt-Eistert synthesis starting with compounds of formula V to give analogues with aminocarbonyl ethyl as R1.

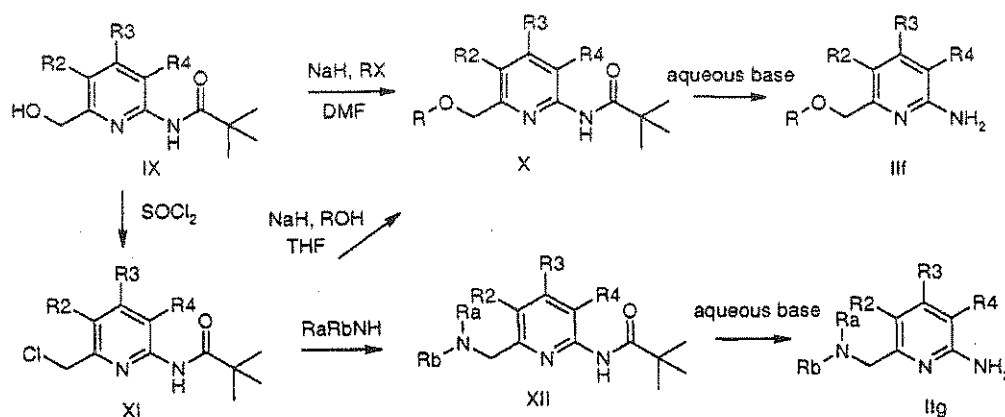
10 Scheme 3



Compounds of formula IIc with R1 is alkoxymethyl, heterocyclalkoxymethyl, cycloalkylalkoxyalkyl, arylalkoxymethyl, aryloxyethyl, haloalkoxymethyl and the like can be prepared according to scheme 4 starting from compounds of formula IX. Accordingly, de-protonation of IX with NaH in THF and subsequent reaction with an alkyl, arylalkyl or heterocyclalkyl halide and the like gives rise to compound of formula X. Upon hydrolysis with a base such as aqueous 3N NaOH at elevated temperature compounds of formula IIc are obtained. The aryloxyethyl analogues are prepared from X via Mitsunobu reaction. Alternatively, intermediates of formula X can be obtained from XI via reaction with an appropriate alcohol ROH in the presence of a base such as NaH and in THF as solvent.

- Compounds of formula XI are obtained from IX via reaction with thionyl chloride.
- Compounds of formula IIg with R1= aminomethyl and the like can be prepared from XI upon reaction with an appropriate amine in acetone as solvent, in the presence of KHCO_3 as base and with catalytic amounts of potassium iodide, to give XII that can subsequently
- 5 be deprotected to give IIg. Intermediates of scheme 4 can also be converted to the next higher homologues as mentioned above and as known to persons skilled in the art.

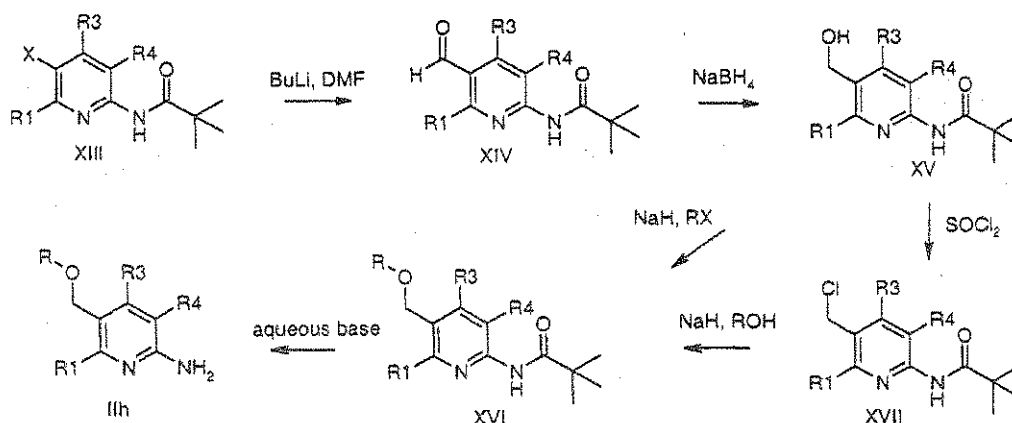
Scheme 4



R means e.g. alkyl, haloalkyl, heterocyclylalkyl or arylalkyl
 (Ra)(Rb)N- means amino as defined before

- Compounds of formula IIh with R2 is cycloalkyloxymethyl, alkoxymethyl, arylalkoxyxymethyl, haloalkoxyxymethyl can be prepared according to scheme 5 from
- 10 compounds of formula XIII via halogen lithium exchange with BuLi, reaction with DMF to give XIV, followed by NaBH_4 reduction to yield XV. Functionalization reactions are then carried out in analogy to the reaction sequences discussed above, either via reacting
- 15 XV with appropriate alkyl halogenids in the presence of NaH to give compounds of formula XVI, or from XVII via reaction with ROH and with NaH. XVII can be obtained from XV via treatment with thionyl chloride. Again, all intermediates can be used as already discussed above to make the next higher homologues.

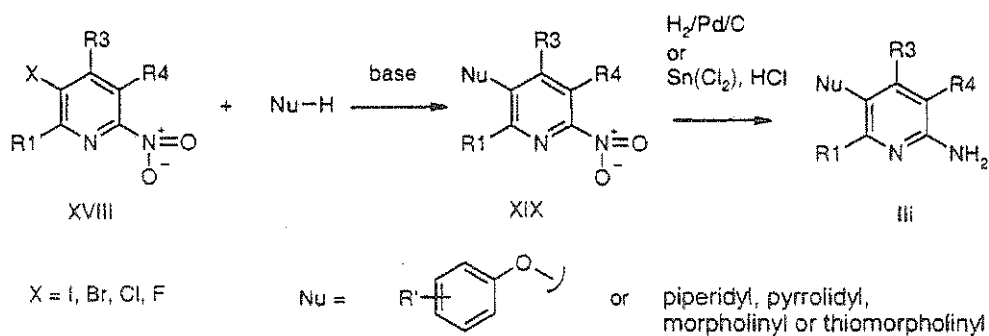
Scheme 5



R means e.g. alkyl, haloalkyl, cycloalkylalkyl or arylalkyl
 X means Cl, Br or I

- 2-Aminopyridines of type IIi in which R₂ is represented by a nucleophile Nu that is defined as outlined in Scheme 6 – e.g. a phenol or an amine – can be made in the following way: An appropriately substituted 5-halo-2-nitropyridine of formula XVIII is treated with
- 5 an appropriate nucleophile – e.g. a phenol or an amine or the like – in the presence of a base such as sodium hydride, potassium carbonate or the like in a suitable solvent such as DMF, DMSO, THF or similar at temperatures ranging from 0 °C to 200 °C to give nitropyridine XIX. The nitro group present in compound XIX can be reduced using standard reduction conditions such as catalytic hydrogenation in the presence of a suitable catalyst such as Pd,
- 10 Pt or the like or alternative conditions such as Sn(II)Cl₂ in the presence of an acid such as HCl, HBr or the like to give the desired 2-aminopyridines IIi that can be treated in subsequent reaction steps as outlined in Scheme 1 to give sulfonamides of formula Ia and/or I.

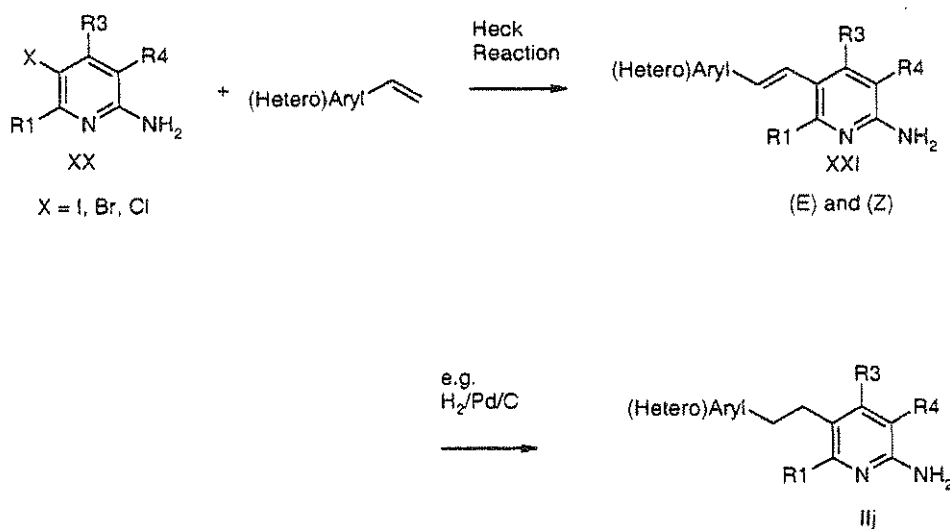
Scheme 6:



R' means e.g. halogen, alkyl, amino or haloalkyl

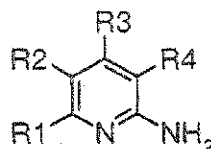
- 2-Aminopyridines of type IIj in which R2 is represented by a (hetero)aryl-ethyl side chain as shown in Scheme 7 are made in the following way: An appropriately substituted 2-amino-5-halo-pyridine of formula XX is subjected to a Heck-type reaction in the presence of an appropriately substituted styrene or vinyl-(hetero)aromate under conditions that are known in the literature (see e.g. Heck et al., J. Am. Chem. Soc. 1968, 90, 5518) to furnish intermediate XXI. The double bond that is present in this material can optionally be reduced using conditions such as catalytic hydrogenation with various catalysts such as Pd, Pt or the like to give the desired 2-aminopyridines IIj that can be used in subsequent reaction steps as outlined in Scheme 1 to give compounds of formula Ia and/or I.

Scheme 7:



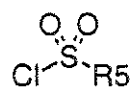
Preferred is the process for the preparation of a compound according to formula I comprising

a) reaction of a compound according to formula

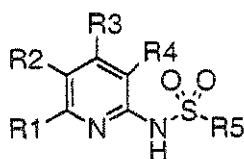


II

5 in the presence of a compound according to formula



in order to obtain a compound of the formula

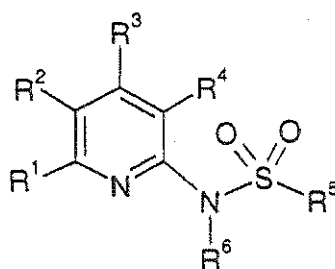


Ia

;

and optionally

10 b) further reaction in the presence of a compound of the formula R⁶-X in order to obtain a compound of the formula



(I)

;

wherein R¹ to R⁶ are defined as before and X is Cl, Br or I. Particularly preferred is the above reaction a) in the presence of pyridine or THF and particularly in the presence of a base such as e.g. potassium carbonate, sodium carbonate, sodium hydride or triethyl amine. Particularly preferred is the above reaction b) in the presence of sodium hydride, cesium carbonate, potassium carbonate particularly in DMF or THF. Preferred examples of compounds according to formula R⁶-X are methyl iodide and ethyl bromide.

Preferred intermediates are:

- 6-Isopropyl-pyridin-2-ylamine;
- 10 6-(2-Chloro-phenyl)-pyridin-2-ylamine;
- 6-(2,4-Difluoro-phenyl)-pyridin-2-ylamine;
- 6-(3-Fluoro-phenyl)-pyridin-2-ylamine;
- 6-(2,3-Difluoro-phenyl)-pyridin-2-ylamine;
- 6-(2,5-Dichloro-phenyl)-pyridin-2-ylamine;
- 15 6-(3-Chloro-phenyl)-pyridin-2-ylamine;
- 6-(2-Fluoro-phenyl)-pyridin-2-ylamine;
- 6-(2-Trifluoromethyl-phenyl)-pyridin-2-ylamine;
- 6-(2-Methoxy-phenyl)-pyridin-2-ylamine;
- 6-(4-Fluoro-2-methyl-phenyl)-pyridin-2-ylamine;
- 20 [2,3']Bipyridinyl-6-ylamine;
- 6-Ethylsulfanyl-pyridin-2-ylamine;
- 1-(6-Amino-pyridin-2-yl)-pentan-2-one;
- (6-Amino-pyridin-2-yl)-acetic acid methyl ester;
- 2-(6-Amino-pyridin-2-yl)-N,N-diethyl-acetamide;
- 25 2-(6-Amino-3-methyl-pyridin-2-yl)-N,N-diethyl-acetamide;
- 6-Cyclopropylmethoxymethyl-pyridin-2-ylamine;
- 6-(4-Fluoro-benzyloxymethyl)-pyridin-2-ylamine;
- 6-(4-Trifluoromethyl-phenoxy-methyl)-pyridin-2-ylamine;
- 5-Cyclopropylmethoxymethyl-pyridin-2-ylamine;
- 30 5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine;
- 5-Methoxymethyl-6-methyl-pyridin-2-ylamine;
- 5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-ylamine;
- 5-Ethoxymethyl-6-methyl-pyridin-2-ylamine;

- 6-[(Methyl-propyl-amino)-methyl]-pyridin-2-ylamine;
6-Cyclopropyl-pyridin-2-ylamine;
5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-ylamine;
6-(3-Fluoro-benzyloxymethyl)-pyridin-2-ylamine;
5 6-(3,3,3-Trifluoro-propoxymethyl)-pyridin-2-ylamine;
6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine;
6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-ylamine;
6-(3-Chloro-benzyloxymethyl)-pyridin-2-ylamine;
6-(4-Chloro-benzyloxymethyl)-pyridin-2-ylamine;
10 5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine;
3,4,5,6-Tetrahydro-2H-[1,3']bipyridinyl-6'-ylamine;
6-Methyl-5-phenethyl-pyridin-2-ylamine and
5-Phenoxy-pyridin-2-ylamine.

- 15 The compounds of formula I described above for use as therapeutically active substance are a further object of the invention.

- Also an object of the present invention are compounds as described above for the preparation of medicaments for the prophylaxis and therapy of illnesses which are caused by disorders associated with the enzyme 11beta-hydroxysteroid dehydrogenase 1
20 (11bHSD1).

Likewise an object of the invention are pharmaceutical compositions comprising a compound of the formula I as described above and a therapeutically inert carrier.

- A further preferred embodiment of the present invention is the use of a compound of the formula I as described above for the preparation of medicaments for the treatment
25 and prophylaxis of diabetes, obesity, eating disorders, dyslipidemiae and hypertension.

Particularly preferred is the use of a compound according to formula I as described above for the preparation of medicaments for the treatment and prophylaxis of diabetes Type II.

- A further object of the present invention comprises a compound according to
30 formula I as described above, when manufactured according to any one of the described processes.

Also an object of the invention is a method for the treatment and prophylaxis of diabetes, obesity, eating disorders, dyslipidemiae and hypertension, which method comprises administering an effective amount of a compound of formula I as described above.

- 5 Particularly preferred is a method for the treatment and prophylaxis of diabetes Type II, which method comprises administering an effective amount of a compound according to formula I as described above.

Assay Procedures

- 10 Transient expression and partial Purification:

The cDNA encoding the human 11beta-HSD1 protein was cloned into the expression vector pcDNA3 (Stratagene). This construct (for details see Alex Odermatt et al.; J Biol Chem., 1999, Vol. 274, Issue 40, 28762-28770) was used to transiently express the protein in HEK293 cells (ATCC number: CRL-1573, described in Graham, F.L., Smiley, J., Russell, 15 W.C., Nairn, R.; (1977)) using lipofectamine. 48h after transfection cells were washed twice with ice-cold PBS (Phosphate buffered Saline). To 1 volume of cell suspension in PBS 2 volumes of ice-cold lysis buffer (50mM Tris; pH7.5; 1mM EDTA; 100mM NaCl) were added. The cells were lysed by Potter-homogenization (20 strokes). The resulting homogenate was sonicated with a tip sonicator (10% output; 2 x 30 sec.) and cleared by a 20 low speed centrifugation (10min x 9000g; 4°C). The microsomal fraction was collected by a high speed centrifugation (60 min x 110'000g). The resulting pellet was resuspended in storage buffer (20mM Tris pH 7.5; 1 mM EDTA; 10% Glycerol) and the centrifugation was repeated. The resulting pellet containing the microsomal fraction was again taken up into storage buffer and aliquots were kept frozen in liquid Nitrogen until use.

25

Generation of stable cell lines expressing 11beta-HSD1:

The same construct used for transient expression of human 11beta-HSD1 was also used to establish cell lines stably expressing the protein. Briefly, (HEK293) cells were transfected with 11beta-HSD1 construct using the lipofectamine reagent (Gibco BRL) according to 30 the manufacturer's instruction. Two days after transfection, geneticin selection (0.8

mg/ml) was initiated and several stable clones were isolated. One clone was further used for pharmacological characterization.

Microsome Assay

- 5 Microsomes isolated from HEK293 cells transiently expressing human 11beta-HSD1 (for details see above) were incubated in assay buffer (100 mM NaCl; 1mM EDTA; 1mM EGTA; 1mM MgCl₂; 250 mM Sucrose; 20 mM Tris pH 7.4; Cortisone 50-200nM and NADPH 1mM) together with different concentrations of test substances. After 60 min. of incubation at 37°C the assay was stopped by heating to 80°C (5 min.) and by addition of
10 the inhibitor Carbenoxolone (1 uM). The amount of Cortisol produced in this assay was determined using a commercially available, ELISA-based Cortisol-detection kit (Distributed by Assay Design, Inc.). Inhibitors were characterized by there IC₅₀ values, e.g. the concentration at which the production of cortisol was 50% reduced.

- In this test preferred compounds as described above have IC₅₀ values below 1000 nM;
15 more preferred compounds have IC₅₀ values below 100 nM. Most preferred compounds have IC₅₀ values below 10nM.

Cellular Assay

- To measure the effect of inhibitors in intact cells HEK293 cells stably expressing human
20 11beta-HSD1 (see above) were cultivated in 96 well plates in DMEM. First inhibitors and 60 min later Cortisone was added to the cells. After 60 min of incubation at 37°C in a 5% CO₂ atmosphere part of the medium was removed and the conversion from Cortisone to Cortisol was measured using a commercially available ELISA kit (Distributed by Assay Design, Inc.).

25

Results obtained in the microsome assay using representative compounds of the invention as the test compounds are shown in the following table:

<u>Compound</u>	<i>h</i> 11-beta-HSD 1 IC ₅₀ (nM)
Example 105	16
Example 186	5

Compounds as described above have IC₅₀ values below 1000 nM; preferred compounds have IC₅₀ values below 100 nM. More preferred compounds have IC₅₀ values below 10 nM. These results have been obtained by using the foregoing test.

5

The compounds of formula I and their pharmaceutically acceptable salts and esters can be used as medicaments (e.g. in the form of pharmaceutical preparations). The pharmaceutical preparations can be administered internally, such as orally (e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatin capsules, solutions, emulsions or suspensions), nasally (e.g. in the form of nasal sprays) or rectally (e.g. in the form of suppositories). However, the administration can also be effected parentally, such as intramuscularly or intravenously (e.g. in the form of injection solutions).

The compounds of formula I and their pharmaceutically acceptable salts and esters can be processed with pharmaceutically inert, inorganic or organic adjuvants for the production of tablets, coated tablets, dragées and hard gelatin capsules. Lactose, corn starch or derivatives thereof, talc, stearic acid or its salts etc. can be used, for example, as such adjuvants for tablets, dragées and hard gelatin capsules.

Suitable adjuvants for soft gelatin capsules, are, for example, vegetable oils, waxes, fats, semi-solid substances and liquid polyols, etc.

Suitable adjuvants for the production of solutions and syrups are, for example, water, polyols, saccharose, invert sugar, glucose, etc.

Suitable adjuvants for injection solutions are, for example, water, alcohols, polyols, glycerol, vegetable oils, etc.

Suitable adjuvants for suppositories are, for example, natural or hardened oils, waxes, fats, semi-solid or liquid polyols, etc.

Moreover, the pharmaceutical preparations can contain preservatives, solubilizers, viscosity-increasing substances, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. They can also contain still other therapeutically valuable substances.

In accordance with the invention the compounds of formula I and their pharmaceutically acceptable salts can be used for the prophylaxis and treatment of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity. The dosage can vary in wide limits and will, of course, be fitted to the individual requirements in each particular case. In general, in the case of oral administration a daily dosage of about 0.1 mg to 20 mg per kg body weight, preferably about 0.5 mg to 4 mg per kg body weight (e.g. about 300 mg per person), divided into preferably 1-3 individual doses, which can consist, for example, of the same amounts, should be appropriate. It will, however, be clear that the upper limit given above can be exceeded when this is shown to be indicated.

The invention is illustrated hereinafter by Examples, which have no limiting character. Examples 1 to 5, 8, 11 to 14, 16 and 17 are included for preparation purpose and are not covered by claim 1.

20

Examples

Example 1: Naphthalene-2-sulfonic acid (6-methyl-pyridin-2-yl)-amide

6-Methyl-pyridin-2-ylamine (1 g) and 2-naphthalenesulfonyl chloride (2.3 g) were dissolved in pyridine (5 mL) and the resulting mixture was allowed to stir at RT for 12 hours. After concentration in vacuo the residue was taken up in EtOAc, the solution washed with 1 N aqueous HCl, saturated brine then dried over sodium sulphate and concentrated in vacuo. The residue was purified by flash chromatography (heptane/EtOAc 5:1) to give the desired product naphthalene-2-sulfonic acid (6-methyl-pyridin-2-yl)-amide as a white foam (2.18 g). MS (ESI⁺): 297.2 ([M-H]⁺).

30

Example 2: N-(6-Methyl-pyridin-2-yl)-4-nitro-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine with 4-nitro-benzenesulfonyl chloride as a yellow solid. MS (ESI⁺): 292.0 ([M-H]⁺).

5

Example 3: N-[4-(6-Methyl-pyridin-2-yl)sulfamoyl]-phenyl]-acetamide

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine and 4-acetamido-benzenesulfonyl chloride as a white solid. MS (ESI⁺): 304.0 ([M-H]⁺).

10 **Example 4: 3-Chloro-2-methyl-N-(6-methyl-pyridin-2-yl)-benzenesulfonamide**

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine (0.108 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.259 g) as an off-white crystalline solid (0.24 g). MS (ESI⁺): 295.1 ([M-H]⁺).

15 **Example 5: Biphenyl-4-sulfonic acid (6-methyl-pyridin-2-yl)-amide**

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine (0.108g) and biphenyl-4-sulfonyl chloride (0.278 g) as an off-white crystalline solid (0.157 g). MS (ESI⁺): 323.2 ([M-H]⁺).

20 **Example 6: 3-Chloro-N-(6-ethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide**

This material was obtained in analogy to example 1 from 6-ethyl-pyridin-2-ylamine (0.25 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.5 g) as a white solid (0.13 g). MS (ESI⁺): 309.1 ([M-H]⁺).

25 **Example 7: Biphenyl-4-sulfonic acid (6-ethyl-pyridin-2-yl)-amide**

This material was obtained in analogy to example 1 from 6-ethyl-pyridin-2-ylamine (0.25 g) and biphenyl-4-sulfonyl chloride (0.57 g) as a white foam (0.156 g). MS (ESI⁺): 337.1 ([M-H]⁺)

5 **Example 8: 5-Fluoro-2-methyl-N-(6-methyl-pyridin-2-yl)-benzenesulfonamide**

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine (0.2 g) and biphenyl-4-sulfonyl chloride (0.42 g) as a yellow solid (0.132 g). MS (ESI⁺): 278.9 ([M-H]⁺).

10 **Example 9: Biphenyl-4-sulfonic acid (6-propyl-pyridin-2-yl)-amide**

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.2 g) and biphenyl-4-sulfonyl chloride (0.408 g) as an off-white solid (0.132 g). MS (ESI⁺): 351.2 ([M-H]⁺).

15 **Example 10: 3-Chloro-2-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide**

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.2 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.386 g) as a white solid (0.34 g). MS (ESI⁺): 323.2 ([M-H]⁺).

20 **Example 11: 3-Chloro-N-(4,6-dimethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide**

This material was obtained in analogy to example 1 from 4,6-dimethyl-pyridin-2-ylamine and 3-chloro-2-methyl-benzenesulfonyl chloride as a light yellow solid. MS (ESI⁺): 309.1 ([M-H]⁺).

25 **Example 12: Biphenyl-4-sulfonic acid (4,6-dimethyl-pyridin-2-yl)-amide**

This material was obtained in analogy to example 1 from 4,6-dimethyl-pyridin-2-ylamine and biphenyl-4-sulfonyl chloride as a white amorphous solid. MS (ESI⁺): 337.0 ([M-H]⁺).

Example 13: N-(3-Bromo-6-methyl-pyridin-2-yl)-3-chloro-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 3-bromo-6-methyl-pyridin-2-ylamine (0.2 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.265 g) as an off-white solid (0.351 g). MS (ESI⁺): 372.9 ([M-H]⁺).

Example 14: Biphenyl-4-sulfonic acid (3-bromo-6-methyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 3-bromo-6-methyl-pyridin-2-ylamine (0.2 g) and biphenyl-4-sulfonyl chloride (0.297 g) as a white foam (0.307 g). MS (ESI⁺): 401.2 ([M-H]⁺).

Example 15: Naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.2 g) and naphthalene-2-sulfonyl chloride (0.366 g) as a white foam (0.392 g). MS (ESI⁺): 325.2 ([M-H]⁺).

Example 16: 4'-Chloro-biphenyl-4-sulfonic acid (6-methyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine (0.22 g) and 4'-chloro-biphenyl-4-sulfonyl chloride (0.622 g) as a white solid (0.074 g). MS (ESI⁺): 357.2 ([M-H]⁺).

Example 17: 4'-Fluoro-biphenyl-4-sulfonic acid (6-methyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-methyl-pyridin-2-ylamine (0.4 g) and 4'-fluoro-biphenyl-4-sulfonyl chloride (1 g) as a white foam (0.779 g). MS (ESI⁺): 341.1 ([M-H]⁺).

Example 18: 3,4-Dichloro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.15 g) and 3,4-dichloro-benzenesulfonyl chloride (0.27 g) as a white solid (0.199 g). MS (ESI⁺): 342.9 ([M-H]⁺).

5

Example 19: 2,5-Difluoro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.1 g) and 2,5-difluoro-benzenesulfonyl chloride (0.17 g) as a white solid (0.114 g). MS (ESI⁺): 311.0 ([M-H]⁺).

10

Example 20: 2,4-Dichloro-6-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.1 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.191 g) as a light brown oil. (0.039 g). MS (ESI⁺): 357.1 ([M-H]⁺).

15

Example 21: 5-Chloro-naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.1 g) and 5-chloro-naphthalene-2-sulfonyl chloride (0.191 g) as white solid. (0.047 g). MS (ESI⁺): 359.0 ([M-H]⁺).

20

Example 22: 3,4-Dimethoxy-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.1 g) and 3,4-dimethoxy-benzenesulfonyl chloride (0.174 g) as a colorless oil. (0.043 g). MS (ESI⁺): 335.2 ([M-H]⁺).

25

Example 23: 4,5-Dichloro-2-fluoro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.1 g) and 4,5-dichloro-2-fluoro-benzenesulfonyl chloride (0.213 g) as a colorless oil. (0.176 g). MS (ESI): 363.1 (MH⁺).

5 Example 24: 2,4-Dichloro-5-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-propyl-pyridin-2-ylamine (0.1 g) and 2,4-dichloro-5-methyl-benzenesulfonyl chloride (0.194 g) as a light yellow amorphous solid. (0.194 g). MS (ESI⁺): 357.1 ([M-H]⁺).

10 Example 25: Piperidine-1-sulfonic acid (6-propyl-pyridin-2-yl)-amide

A solution of 6-propyl-pyridin-2-ylamine (0.2 g) and piperidine-1-sulfonyl chloride (0.296 g, Bull. Soc. Chim. Fr.; 1936, 2143) in pyridine (7 mL) was heated to reflux for 15 h. After concentration of the reaction mixture in vacuo the residue was taken up in EtOAc, which was then washed with 1N aqueous HCl, saturated brine, dried over sodium sulphate and
15 concentrated in vacuo. The residue was applied to a silica gel column with EtOAc/toluene (9:1 to 1:1) as eluent. Combination of the purified fractions and concentration in vacuo gave the desired piperidine-1-sulfonic acid (6-propyl-pyridin-2-yl)-amide (0.133 g) as a colorless amorphous solid. MS (ESI⁺): 282.0 ([M-H]⁺).

20 Example 26: 3-Chloro-N-(6-isopropyl-pyridin-2-yl)-4-methyl-benzenesulfonamide

Step A): 6-Isopropyl-pyridin-2-ylamine

2-Amino-6-bromopyridine (2 g) was dissolved in dioxane (50 mL), and at 0° C under an argon atmosphere 1,3-bis(diphenylphosphino)propane nickel (II) chloride (0.627 g) was added followed by diisopropyl zinc (23.12 mL of a 1M solution in toluene, via syringe over
25 30 minutes). The mixture was allowed to reflux for 15 h, poored into 2-propanol, which was then concentrated in vacuo. The residue was partitioned between AcOEt and saturated aqueous NH₄Cl solution, the layers were separated and the organic layer dried over Na₂SO₄, filtered and evaporated. The residue was purified by flash chromatography (methylene chloride/methanol 95:5) to give 6-isopropyl-pyridin-2-ylamine as ligh brown
30 oil (0.48 g). MS (EI): 136.1 (M⁺).

Step B] 3-Chloro-N-(6-isopropyl-pyridin-2-yl)-4-methyl-benzenesulfonamide

This compound was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.1 g), and 3-chloro-4-methyl-benzenesulfonyl chloride (0.182 g) as a white solid
5 (30 mg). MS (ESI⁺): 324.1 ([M-H]⁺).

Example 27: 2,5-Difluoro-N-(6-isopropyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.1 g) and 2,5-difluoro-benzenesulfonyl chloride (0.172 g) as a colorless foam. (20 mg).
10 MS (ESI⁺): 311.1 ([M-H]⁺).

Example 28: N-(6-Isopropyl-pyridin-2-yl)-4-(4-trifluoromethyl-phenoxy)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.1 g) and 4-(4-trifluoromethyl-phenoxy)-benzenesulfonyl chloride (0.272 g) as an
15 amorphous colorless solid (31 mg). MS (ESI⁺): 435.1 ([M-H]⁺).

Example 29: 2,4-Dichloro-N-(6-isopropyl-pyridin-2-yl)-5-methyl-benzenesulfonamide

20 This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.1 g) and 2,4-dichloro-5-methyl-benzenesulfonyl chloride (0.194 g) as an amorphous light yellow solid (35 mg). MS (ESI⁺): 357.2 ([M-H]⁺).

Example 30: N-(6-isopropyl-pyridin-2-yl)-4-methanesulfonyl-benzenesulfonamide

25 This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.1 g) and 4-methylsulfonyl-benzenesulfonyl chloride (0.206 g) as a white foam (46.8 mg). MS (ESI⁺): 353.1 ([M-H]⁺).

Example 31: N-(6-Isopropyl-pyridin-2-yl)-4-trifluoromethoxy-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.1 g) and 4-(trifluoromethoxy)-benzenesulfonyl chloride (0.21 g) as an amorphous
5 colorless solid (40 mg). MS (ESI⁺): 359.0 ([M-H]⁺).

Example 32: 2-(2,2,2-Trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline-7-sulfonic acid (6-isopropyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine
10 (0.08 g) and 2-(2,2,2-trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline-7-sulfonyl chloride (0.212 g) as a white foam (35.2 mg). MS (ESI⁺): 426.2 ([M-H]⁺).

Example 33: N-(6-Isopropyl-pyridin-2-yl)-3-(4-trifluoromethyl-phenoxy)-benzenesulfonamide

15 This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.08 g) and 3-(4-trifluoromethyl-phenoxy)-benzenesulfonyl chloride (0.218 g) as an amorphous light yellow solid (37 mg). MS (ESI⁺): 435.1 ([M-H]⁺).

Example 34: Naphthalene-2-sulfonic acid (6-isopropyl-pyridin-2-yl)-amide

20 This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.07 g) and naphthalene-2-sulfonyl chloride (0.128 g) as an amorphous light yellow solid (51 mg). MS (ESI⁺): 325.2 ([M-H]⁺).

Example 35: N-(6-Isopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

25 This material was obtained in analogy to example 1 from 6-isopropyl-pyridin-2-ylamine (0.06 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.119 g) as an amorphous colorless solid (38.3 mg). MS (ESI⁺): 343.0 ([M-H]⁺).

Example 36: N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide

Step A]: 6-(2-Chloro-phenyl)-pyridin-2-ylamine

- 5 2-Amino-6-bromopyridine (1 g) and 2-chlorophenylboronic acid (1.039 g) were dissolved in toluene/ethanol (30 mL/3 mL) and at RT under an argon atmosphere treated with 2N aqueous sodium carbonate solution (6.13 mL). The mixture was stirred for 30 minutes at RT then treated with tetrakis(triphenylphosphine) palladium(0), 0.267 g, and heated to reflux for 24 h. The mixture was then cooled to RT and partitioned between AcOEt and
10 water, the layers were separated and the organic layer dried over Na₂SO₄, filtered and evaporated. The residue was purified by flash chromatography (heptane/AcOEt 4:1) to give 6-(2-chloro-phenyl)-pyridin-2-ylamine as white solid (0.632 g). MS (EI): 204 (M⁺).

Step B]: N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide

- 15 This compound was obtained in analogy to example 1 from 6-(2-chloro-phenyl)-pyridin-2-ylamine (0.1 g), and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.112 g) as a white solid (89.3 mg). MS (ESI⁺): 375.2 ([M-H]⁺).

Example 37: 3-Chloro-N-[6-(2-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide
20

This material was obtained in analogy to example 1 from 6-(2-chloro-phenyl)-pyridin-2-ylamine (0.1 g) and 3-(chloro)-2-methyl-benzenesulfonyl chloride (0.12 g) as an off-white foam (129 mg). MS (ESI⁺): 390.9 ([M-H]⁺).

25 Example 38: Biphenyl-4-sulfonic acid [6-(2-chloro-phenyl)-pyridin-2-yl]-amide

This material was obtained in analogy to example 1 from 6-(2-chloro-phenyl)-pyridin-2-ylamine (0.1 g) and biphenyl-4-sulfonyl chloride (0.136 g) as a white foam (126 mg). MS (ESI⁺): 419.0 ([M-H]⁺).

Example 39: 3-Chloro-N-[6-(2,4-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

Step A]: 6-(2,4-Difluoro-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-
5 bromopyridine (1 g) and 2,4-difluorophenylboronic acid (1.05 g) as a yellow solid (1.26 g).
MS (ESI): 207.2 (MH⁺).

Step B]: 3-Chloro-N-[6-(2,4-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

10 This material was obtained in analogy to example 1 from 6-(2,4-difluoro-phenyl)-pyridin-
2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.12 g) as a white
solid (0.132 g). MS (ESI⁺): 392.9 ([M-H]⁺).

Example 40 3-Chloro-N-[6-(3-fluoro-phenyl)-pyridin-2-yl]-2-methyl-
15 benzenesulfonamide

Step A]: 6-(3-Fluoro-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-
bromopyridine (0.75 g) and 3-fluorophenylboronic acid (0.7 g) as a yellow oil (0.81 g). MS
(ESI): 189.3 (MH⁺).

20

Step B]: 3-Chloro-N-[6-(3-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(3-fluoro-phenyl)-pyridin-2-
ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.132 g) as a white solid
(0.144 g). MS (ESI⁺): 375.1 ([M-H]⁺).

25

Example 41 3-Chloro-N-[6-(2,3-difluoro-phenyl)-pyridin-2-yl]-2-methyl-
benzenesulfonamide

Step A]: 6-(2,3-Difluoro-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.75 g) and 2,3-difluorophenylboronic acid (0.787 g) as a yellow solid (0.84 g). MS (ESI): 207.2 (MH⁺).

5

Step B]: 3-Chloro-N-[6-(2,3-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2,3-difluoro-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.12 g) as a white
10 solid (0.115 g). MS (ESI⁺): 392.9 ([M-H]⁺).

Example 42 3-Chloro-N-[6-(2,5-dichloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

Step A]: 6-(2,5-Dichloro-phenyl)-pyridin-2-ylamine

15 This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.75 g) and 2,5-dichlorophenylboronic acid (0.951 g) as an off-white solid (0.87 g). MS (ESI): 239.1 (MH⁺).

20 Step B]: 3-Chloro-N-[6-(2,5-dichloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2,5-dichloro-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.104 g) as a white solid (0.094 g). MS (ESI⁺): 425.0 ([M-H]⁺).

25 **Example 43:** N-[6-(2,5-Dichloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2,5-dichloro-phenyl)-pyridin-2-ylamine (0.1 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.096 g) as a white solid (142 mg). MS (ESI⁺): 409.0 ([M-H]⁺).

5 **Example 44 3-Chloro-N-[6-(3-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide**

Step A]: 6-(3-Chloro-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.75 g) and 3-chlorophenylboronic acid (0.75 g) as an off-white solid
10 (0.87 g). MS (ESI⁺): 205.1 (MH⁺).

Step B]: 3-Chloro-N-[6-(3-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(3-chloro-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.12 g) as a white solid
15 (0.132 g). MS (ESI⁺): 391.0 ([M-H]⁺).

Example 45: N-[6-(3-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(3-chloro-phenyl)-pyridin-2-ylamine (0.1 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.112 g) as a white solid
20 (172 mg). MS (ESI⁺): 375.2 ([M-H]⁺).

Example 46 3-Chloro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

25 Step A]: 6-(2-Fluoro-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.75 g) and 2-fluorophenylboronic acid (0.7 g) as an off-white solid (0.789 g). MS (ESI⁺): 189.2 (MH⁺).

Step B]: 3-Chloro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-fluoro-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.132 g) as a light-yellow solid (0.135 g). MS (ESI⁺): 375.2 ([M-H]⁺).

Example 47: 5-Fluoro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-fluoro-phenyl)-pyridin-2-ylamine (0.1 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.12 g) as an off-white solid (0.19 g). MS (ESI⁺): 359.0 ([M-H]⁺).

Example 48 3-Chloro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide

Step A]: 6-(2-Trifluoromethyl-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.7 g) and 2-(trifluoromethyl)phenylboronic acid (0.884 g) as a yellow solid (0.35 g). MS (ESI⁺): 239.2 (MH⁺).

Step B]: 3-Chloro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.086 g) as a white solid (0.08 g). MS (ESI⁺): 425.1 ([M-H]⁺).

Example 49: 5-Fluoro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine (0.1 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.088 g) as an amorphous light brown solid (0.139 g). MS (ESI⁺): 409.1 ([M-H]⁺).

5 **Example 50:** N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-2,5-difluoro-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-chloro-phenyl)-pyridin-2-ylamine (0.08 g) and 2,5-difluoro-benzenesulfonyl chloride (0.09 g) as a white foam (0.127 g). MS (ESI⁺): 379.0 ([M-H]⁺).

10

Example 51: N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-2-trifluoromethyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-chloro-phenyl)-pyridin-2-ylamine (0.08 g) and 2-(trifluoromethyl)-benzenesulfonyl chloride (0.105 g) as an
15 amorphous light yellow solid (0.167 g). MS (ESI⁺): 411.0 ([M-H]⁺).

Example 52 3-Chloro-N-[6-(2-methoxy-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

Step A]: 6-(2-Methoxy-phenyl)-pyridin-2-ylamine

20 This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.75 g) and 2-methoxyphenylboronic acid (0.758 g) as a crystalline yellow solid (0.76 g). MS (ESI): 201.1 (MH⁺).

Step B]: 3-Chloro-N-[6-(2-methoxy-phenyl)-pyridin-2-yl]-2-methyl-
25 benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(2-methoxy-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.102 g) as a colorless oil (0.091 g). MS (ESI⁺): 387.1 ([M-H]⁺).

Example 53 3-Chloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

Step A]: 6-(4-Fluoro-2-methyl-phenyl)-pyridin-2-ylamine

This material was obtained in analogy to example 36 step A] from 2-Amino-6-bromopyridine (0.75 g) and 4-fluoro-2-methyl-phenylboronic acid (0.767 g) as a yellow solid (0.828 g). MS (ESI): 203.1 (MH⁺).

Step B]: 3-Chloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

10 This material was obtained in analogy to example 1 from 6-(4-fluoro-2-methyl-phenyl)-pyridin-2-ylamine (0.1 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.101 g) as a white solid (0.097 g). MS (ESI⁺): 389.0 ([M-H]⁺).

Example 54: 5-Fluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(4-fluoro-2-methyl-phenyl)-pyridin-2-ylamine (0.1 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.103 g) as an colorless oil (0.101 g). MS (ESI⁺): 373.1 ([M-H]⁺).

Example 55 N-[2,3']Bipyridinyl-6-yl-3-chloro-2-methyl-benzenesulfonamide

Step A]: [2,3']Bipyridinyl-6-ylamine

This material was obtained via a Stille type coupling from 2-Amino-6-bromopyridine (0.75 g), 3-tributylstannanyl-pyridine (4.787 g), tetrakis(triphenylphosphine) palladium(0), 0.55 g, in DMF (5 mL) as solvent, by heating the mixture under argon at 100°C for 16 h, subsequent work-up as described in example 36 step A], and isolation of [2,3']bipyridinyl-6-ylamine by flash chromatography (heptane/AcOEt 1:4 then methylene chloride/methanol 95:5) as an amorphous yellow solid (0.179 g). MS (ESI): 172.1 (MH⁺).

Step B]: N-[2,3']Bipyridinyl-6-yl-3-chloro-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from [2,3']Bipyridinyl-6-ylamine (0.07 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.101 g) as a yellow solid (5.5 mg).

MS (ESI⁺): 358.0 ([M-H]⁺).

5

Example 56: 2,5-Difluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(4-fluoro-2-methyl-phenyl)-pyridin-2-ylamine (0.1 g) and 2,5-difluoro-benzenesulfonyl chloride (0.105 g) as an

10 orange solid (0.052 g). MS (ESI⁺): 377.2 ([M-H]⁺).

Example 57: 2,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-(4-fluoro-2-methyl-phenyl)-

15 pyridin-2-ylamine (0.1 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.128 g) as a white solid (0.118 g). MS (ESI⁺): 422.9 ([M-H]⁺).

Example 58: 3,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide

20 This material was obtained in analogy to example 1 from 6-(4-fluoro-2-methyl-phenyl)-pyridin-2-ylamine (0.1 g) and 3,4-dichloro-benzenesulfonyl chloride (0.121 g) as a white solid (0.182 g). MS (ESI⁺): 409.0 ([M-H]⁺).

Example 59: 3-Chloro-N-(6-methoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide

25 This material was obtained in analogy to example 1 from 6-methoxy-pyridin-2-ylamine (0.25 g, Bernstein, J. Amer. Chem Soc., 69, 1947, 1147) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.495 g) as a purple crystalline solid (0.38 g). MS (ESI⁺): 311.0 ([M-H]⁺).

Example 60: Biphenyl-4-sulfonic acid (6-methoxy-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-methoxy-pyridin-2-ylamine (0.25 g) and biphenyl-4-sulfonyl chloride (0.5 g) as a white solid (0.41 g). MS (ESI⁺): 339.0 ([M-H]⁺).

5

Example 61: 5-Fluoro-N-(6-methoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxy-pyridin-2-ylamine (0.25 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.45 g) as a red crystalline solid (0.38 g). MS (ESI⁺): 295.1 ([M-H]⁺).

10

Example 62: Naphthalene-2-sulfonic acid (6-methoxy-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-methoxy-pyridin-2-ylamine (0.25 g) and naphthalene-2-sulfonyl chloride (0.49 g) as a light red waxy solid (0.5 g). MS (ESI⁺): 312.9 ([M-H]⁺).

15

Example 63: 3-Chloro-N-(6-ethoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-ethoxy-pyridin-2-ylamine (0.4 g, Bijlsma, Recl. Trav. Chim. Pays-Bas, 75, 1956, 1187) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.7 g) as a light brown crystalline solid (0.6 g). MS (ESI⁺): 325.1 ([M-H]⁺).

20

Example 64: Biphenyl-4-sulfonic acid (6-ethoxy-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-ethoxy-pyridin-2-ylamine (0.4 g) and biphenyl-4-sulfonyl chloride (0.74 g) as a light brown viscous oil (1 g). MS (ESI⁺): 353.1 ([M-H]⁺).

25

Example 65: Naphthalene-2-sulfonic acid (6-ethoxy-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-ethoxy-pyridin-2-ylamine (0.4 g) and naphthalene-2-sulfonyl chloride (0.7 g) as a light brown crystalline solid (0.7 g). MS (ESI⁺): 327.2 ([M-H]⁺).

5 **Example 66: 3-Chloro-N-(6-ethylsulfanyl-pyridin-2-yl)-2-methyl-benzenesulfonamide**

Step A]: 6-Ethylsulfanyl-pyridin-2-ylamine

2-Amino-6-bromopyridine (0.88 g) and sodium ethanethiolate (0.46 g) were dissolved in DMF (10 mL) stirred at RT for 20 h and subsequently at 60°C for further 20 h to complete
10 the reaction according to HPLC analysis. The mixture was concentrated in vacuo, partitioned between AcOEt and water, the layers were separated and the organic layer dried over Na₂SO₄, filtered and evaporated to give to give 6-ethylsulfanyl-pyridin-2-ylamine as brown oil (1.6 g) that was used directly in the next reaction step.

15 **Step B]: N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide**

This compound was obtained in analogy to example 1 from 6-ethylsulfanyl-pyridin-2-ylamine (0.44 g), and 3-chloro-2-methyl-benzenesulfonyl chloride (0.7 g) as a light brown viscous oil (0.7 g). MS (ESI⁺): 341.1 ([M-H]⁺).

20 **Example 67: Biphenyl-4-sulfonic acid (6-ethylsulfanyl-pyridin-2-yl)-amide**

This material was obtained in analogy to example 1 from 6-ethylsulfanyl-pyridin-2-ylamine (0.44 g) and biphenyl-4-sulfonyl chloride (0.78 g) as a light brown viscous oil (0.53 g). MS (ESI⁺): 369.0 ([M-H]⁺).

25 **Example 68: Naphthalene-2-sulfonic acid (6-ethylsulfanyl-pyridin-2-yl)-amide**

This material was obtained in analogy to example 1 from 6-ethylsulfanyl-pyridin-2-ylamine (0.44 g) and naphthalene-2-sulfonyl chloride (0.7 g) as a light brown viscous oil (1 g). MS (ESI⁺): 342.9 ([M-H]⁺).

Example 69: Naphthalene-2-sulfonic acid (6-ethanesulfonyl-pyridin-2-yl)-amide

A solution of naphthalene-2-sulfonic acid (6-ethylsulfonyl-pyridin-2-yl)-amide (0.15 g, product of example 68) in CH_2Cl_2 (20 mL) was treated dropwise at RT with 3-chloroperoxybenzoic acid (0.15 g) in 5 mL CH_2Cl_2) and stirred for 2 h at RT. The reaction mixture was washed with diluted aqueous Na_2CO_3 and water, then dried over Na_2SO_4 , filtered and evaporated. The residue was purified by flash chromatography (toluene/EtOAc 1:1) to give naphthalene-2-sulfonic acid (6-ethanesulfonyl-pyridin-2-yl)-amide as a white foam (60 mg). MS (ESI⁺): 375.2 ([M-H]⁺).

Example 70: 3-Chloro-2-methyl-N-[6-(2-oxo-pentyl)-pyridin-2-yl]-benzenesulfonamide**Step A]: 1-(6-Amino-pyridin-2-yl)-pentan-2-one**

1,1,1,3,3,3-Hexamethyl-2-(6-methyl-pyridin-2-yl)-disilazane (1 g, Engelhardt, J. Chem. Soc. Chem. Commun., 1990, 89) under an argon atmosphere in THF (20 mL) was cooled to -20°C and treated dropwise at -20°C with 4.95 mL of a 1.6 M solution of N-butyllithium in hexane over a period of 1 h. The solution was stirred 1 h at -20°C, N-butyronitrile (0.301 g) was added and the mixture was allowed to warm to RT. It was then treated with 1.25 N HCL in methanol (6.34 mL) and stirred for 30 minutes at RT. The mixture was poured into water (pH 1) and extracted with AcOEt that was discarded, the water layer was brought to pH 8 with solid KHCO_3 and extracted twice with AcOEt. The layers were separated, the organic layer dried over Na_2SO_4 , filtered and evaporated to give 1-(6-Amino-pyridin-2-yl)-pentan-2-one as viscous yellow oil (0.34 g) that was used without further purification in the next step. MS (EI): 179.2 (M⁺).

Step B]: 3-Chloro-2-methyl-N-[6-(2-oxo-pentyl)-pyridin-2-yl]-benzenesulfonamide

1-(6-Amino-pyridin-2-yl)-pentan-2-one (0.15 g) in CH_2Cl_2 (5 mL) was treated at RT with 4-dimethylaminopyridine (0.103 g), 3-chloro-2-methyl-benzenesulfonyl chloride (0.208 g) and stirred at RT for 16 h. The mixture was partitioned between cold diluted aqueous HCl and AcOEt, the layers were separated, and the organic layer twice extracted with AcOEt. The combined organic layers were dried over Na_2SO_4 , filtered and evaporated. From the residue was isolated by flash chromatography (heptane/EtOAc 1:1) the vinyl sulfonate 3-chloro-2-methyl-benzenesulfonic acid 1-[1-[6-(3-chloro-2-methyl-

benzenesulfonylamino)-pyridin-2-yl]-meth-(Z)-ylidene]-butyl ester (23 mg) as an amorphous off-white solid (27 mg). MS (ESI⁺): 552.8 ([M-H]⁺).

This material was hydrolysed to the desired product as following: 20 mg of above material in methanol (3 mL) was treated with 0.035 mL 2N NaOH in methanol and heated to reflux
5 for 1,5 h. The mixture was partitioned between water and AcOEt and the aqueous layer adjusted to pH 7. The layers were separated, the organic layer dried over Na₂SO₄, filtered and evaporated to give 3-chloro-2-methyl-N-[6-(2-oxo-pentyl)-pyridin-2-yl]-benzenesulfonamide (12 mg) as an amoprphous light yellow solid. MS (ESI⁺): 365.0 ([M-H]⁺).

10

Example 71: 2-[6-(Biphenyl-4-sulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide

Step A): [6-(Biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid

Biphenyl-4-sulfonic acid (6-methyl-pyridin-2-yl)-amide (0.5 g, product of example 5) under an argon atmosphere in THF (5 mL) was cooled to -20°C and treated dropwise at -
15 20°C with 1.54 mL of a 2 M solution of lithium diisopropylamide in THF/heptane/ethylbenzene (Fluka). The solution was stirred 1 h at -20°C, cooled to -70°C and then treated with an access of dry ice. The mixture was allowed to warm to RT (1 h), partitioned between diluted aqueous HCl and AcOEt. The layers were separated, the aqueous layer extracted twice with AcOEt, the combined organic layers dried over Na₂SO₄,
20 filtered and evaporated to give [6-(biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid as light yellow gum (0.779 g) that was used without further purificatiation in the next step.

Step B): 2-[6-(Biphenyl-4-sulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide

[6-(Biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid (0.35 g) in acetonitrile (5 mL)
25 was treated at RT with N,N-ethyldiisopropylamine (0.16 mL), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP, 0.252 g) then diethylamine (0.05 mL), and the mixture was stirred at RT for 16 h. It was then partitioned between cold diluted aqueous HCl and AcOEt, the layers were separated, the organic layer dried over Na₂SO₄, filtered and evaporated. The residue was purified by flash
30 chromatography (heptane/EtOAc 1:1) to give 2-[6-(biphenyl-4-sulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide as a yellow solid (0.168 g). MS (ESI⁺): 422.2 ([M-H]⁺).

Example 72: Biphenyl-4-sulfonic acid [6-(2-morpholin-4-yl-2-oxo-ethyl)-pyridin-2-yl]-amide

This material was obtained in analogy to example 71 Step B] from [6-(biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid (0.16 g), BOP (0.23 g), N,N-ethyl-diisopropylamine (0.15 mL) and morpholine (0.042 g) as a light brown solid (67 mg). MS (ESI⁺): 436.2 ([M-H]⁺).

Example 73: [6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester

Step A]: (6-Amino-pyridin-2-yl)-acetic acid methyl ester

1,1,1,3,3,3-Hexamethyl-2-(6-methyl-pyridin-2-yl)-disilazane (1.7 g) under an argon atmosphere in THF (20 mL) was cooled to -20°C and treated dropwise at -20°C with 6.73 mL of a 2 M solution of lithium diisopropylamide in THF/heptane/ethylbenzene (Fluka). The solution was stirred 1 h at -20°C, cooled to -70°C and then treated with an excess of dry ice. The mixture was allowed to warm to 0°C and then quenched with trifluoroacetic acid (0.57 mL) and concentrated in vacuo. The residue was taken up in MeOH and added dropwise to a solution of thionyl chloride (9.77 mL) in MeOH (30 mL) at 0°C. The reaction mixture was then heated to reflux for 24 h, cooled to RT and concentrated in vacuo. The residue was partitioned between aqueous diluted NaHCO₃ and AcOEt, the layers were separated, the organic layer dried over Na₂SO₄, filtered, evaporated and the residue purified by flash chromatography (heptane/AcOEt 1:1) to give (6-amino-pyridin-2-yl)-acetic acid methyl ester as a crystalline off-white solid (0.429 g). MS (EI): 166.0 (M⁺).

Step B]: [6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester

This material was obtained in analogy to example 1 from (6-amino-pyridin-2-yl)-acetic acid methyl ester (0.15 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.223 g) as a light brown gum (14 mg). MS (ESI⁺): 353.1 ([M-H]⁺).

Example 74: [6-(5-Fluoro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester

This material was obtained in analogy to example 1 from (6-amino-pyridin-2-yl)-acetic acid methyl ester (0.15 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.207 g) as a
5 light brown gum (20 mg). MS (ESI⁺): 337.0 ([M-H]⁺).

Example 75: N,N-Diethyl-2-[6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetamide

Step A]: [6-(4'-Fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid

10 This material was obtained in analogy to example 71 step A] from 4'-fluoro-biphenyl-4-sulfonic acid (6-methyl-pyridin-2-yl)-amide (0.5 g, product of example 17), 1.46 mL of a 2 M lithium diisopropylamide solution in THF/heptane/ethylbenzene, and dry ice to give [6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid as a gum (0.69 g) that was used without further purification in the next step.

15

Step B]: N,N-Diethyl-2-[6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetamide

This material was obtained in analogy to example 71 step B] from [6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid (0.2 g), BOP (0.137 g), N,N-ethyl-diisopropylamine (0.09 mL), and diethylamine (0.03 mL) as an off-white foam (0.107
20 g). MS (ESI⁺): 440.2 ([M-H]⁺).

Example 76: 4'-Fluoro-biphenyl-4-sulfonic acid [6-(2-morpholin-4-yl-2-oxo-ethyl)-pyridin-2-yl]-amide

This material was obtained in analogy to example 71 step B] from [6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid (0.2 g), BOP (0.137 g), N,N-ethyl-diisopropylamine (0.067 mL), and morpholine (0.02 mL) as an off-white solid (0.114
25 g). MS (ESI⁺): 454.2 ([M-H]⁺).

Example 77: 2-[6-(4'-Fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-N-(2-methoxy-ethyl)-acetamide

This material was obtained in analogy to example 71 step B] from [6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetic acid (0.1 g), BOP (0.069 g), N,N-ethyl-diisopropylamine (0.04 mL), and 2-methoxyethylamine (0.01 mL) as an amorphous light brown solid (0.0475g). MS (ESI⁺): 444.2 ([M-H]⁺).

Example 78: 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide

10 Step A]: (6-tert-Butoxycarbonylamino-pyridin-2-yl)-acetic acid

(6-Methyl-pyridin-2-yl)-carbamic acid tert-butyl ester (1.04 g, Pitts, J. Med. Chem., 43, 2000, 27) under an argon atmosphere in THF (40 mL) was cooled to -20°C and treated dropwise at -20°C with 5.5 mL of a 2 M solution of lithium diisopropylamide in THF/heptane/ethylbenzene (Fluka). The solution was stirred 1 h at -20°C, cooled to -70°C and then treated with an excess of dry ice. The mixture was allowed to warm to 10°C and partitioned between aqueous 1N HCl and AcOEt, the layers were separated, the organic layer dried over Na₂SO₄, filtered, evaporated and the residue was purified by flash chromatography (MeOH/CH₂Cl₂ 0-15%). The obtained material was triturated with ether, the crystalline solid obtained was filtered off by suction and dried in vacuo to give 15 (6-tert-butoxycarbonylamino-pyridin-2-yl)-acetic acid as an off-white solid (0.3 g). MS (ESI⁺): 251.1 ([M-H]⁺).

Step B]: (6-Diethylcarbamoylmethyl-pyridin-2-yl)-carbamic acid tert-butyl ester

This material was obtained in analogy to example 71 step B] from (6-tert-butoxycarbonylamino-pyridin-2-yl)-acetic acid (0.298 g), BOP (0.575 g), N,N-ethyl-diisopropylamine (0.42 mL), and diethylamine (0.14 mL) as a yellow gum (0.202 g). MS (ESI⁺): 308.3 (MH⁺).

Step C]: 2-(6-Amino-pyridin-2-yl)-N,N-diethyl-acetamide

(6-Diethylcarbamoylmethyl-pyridin-2-yl)-carbamic acid tert-butyl ester (0.2 g) in CH_2Cl_2 (10 mL) was treated at RT with trifluoro-acetic acid (0.5 mL) and the solution was stirred for 1.5 h until the reaction was complete according to tlc analysis. The mixture was allowed to warm to 10°C and partitioned between aqueous diluted KHCO_3 and AcOEt, the
5 layers were separated, the organic layer dried over Na_2SO_4 , filtered, evaporated to give 2-(6-amino-pyridin-2-yl)-N,N-diethyl-acetamide (148 mg) as a light yellow solid that was directly used in the next step.

Step D]: 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-
10 acetamide

This material was obtained in analogy to example 1 from 2-(6-amino-pyridin-2-yl)-N,N-diethyl-acetamide (0.07 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.084 g) as a light yellow foam (41 mg). MS (ESI⁺): 394.0 ([M-H]⁺).

15 Example 79: 2-[6-(3,4-Dichloro-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide

This material was obtained in analogy to example 1 from 2-(6-amino-pyridin-2-yl)-N,N-diethyl-acetamide (0.07 g, product of example 78 step C)) and 3,4-dichloro-benzenesulfonyl chloride (0.091 g) as an amorphous yellow solid (41 mg). MS (ESI⁺): 414.1
20 ([M-H]⁺).

Example 80: 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide

Step A]: (3-Bromo-6-tert-butoxycarbonylamino-pyridin-2-yl)-acetic acid

25 This material was obtained in analogy to example 78 step A) from (5-bromo-6-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester, 4.3 g - prepared from 6-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester, example 78 step A) via bromination with NBS/AIBN, using a procedure described by Manabu, Chem. Lett. 1995, 614 - 2M lithium diisopropylamide solution (16.5 mL) and an excess of dry ice as a crystalline solid (2.6 g) that was used
30 directly without further purification in the next reaction step.

Step B]: (5-Bromo-6-diethylcarbamoylmethyl-pyridin-2-yl)-carbamic acid tert-butyl ester

This material was obtained in analogy to example 78 step B] from (3-bromo-6-tert-butoxycarbonylamino-pyridin-2-yl)-acetic acid (0.662 g), BOP (0.974 g), N,N-ethyl-diisopropylamine (0.78 mL), and diethylamine (0.23 mL) as a light brown solid (0.67 g). MS (ESI): 386.3. (MH⁺).

Step C]: (6-Diethylcarbamoylmethyl-5-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester

(5-Bromo-6-diethylcarbamoylmethyl-pyridin-2-yl)-carbamic acid tert-butyl ester (0.116 g in dioxane (5 mL) was treated successively at RT with potassium carbonate (0.124 g), tetrakis(triphenylphosphine) palladium(0), 35 mg, and trimethylboroxine (38 mg) and then heated to reflux for 22 h. The mixture was cooled to RT, filtered and the filter cake washed with AcOEt. The filtrate was concentrated in vacuo, the residue purified by flash chromatography (heptane/AcOEt 1:1 to 1:4) to give (6-diethylcarbamoylmethyl-5-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester (37 mg) as a colorless gum. MS (ESI): 322.4 (MH⁺).

Step D]: 2-(6-Amino-3-methyl-pyridin-2-yl)-N,N-diethyl-acetamide

This material was obtained in analogy to example 78 step C] from (6-diethylcarbamoylmethyl-5-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester (0.193 g) and trifluoro-acetic acid (0.69 mL) in CH₂Cl₂ (8 mL) as a yellow gum (0.148 g). MS (ESI): 222.2 (MH⁺).

Step E]: 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide

This material was obtained in analogy to example 1 from 2-(6-amino-3-methyl-pyridin-2-yl)-N,N-diethyl-acetamide (0.066 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.074 g) as an off-white foam (33 mg). MS (ESI): 408.1 ([M-H]⁺).

Example 81: 2-[6-(3,4-Dichloro-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide

This material was obtained in analogy to example 1 from 2-(6-amino-3-methyl-pyridin-2-yl)-N,N-diethyl-acetamide (0.066 g) and 3,4-dichloro-benzenesulfonyl chloride (0.081 g) as an off-white foam (55 mg). MS (ESI⁺): 428.1 ([M-H]⁺).

Example 82: 3-Chloro-N-(6-hydroxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

10 This material was obtained in analogy to example 1 from (6-amino-pyridin-2-yl)-methanol (0.095 g, Asensio, Tetrahedron, 49, 1993, 703) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.172 g) as a white solid (0.115 g). MS (ESI⁺): 311.0 ([M-H]⁺).

Example 83: 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.096 g, Shawcross, J. Heterocycl. Chem., 30, 1993, 563) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.172 g) as an off-white gum (0.158 g). MS (ESI⁺): 325.1 ([M-H]⁺)

20

Example 84: 2,5-Difluoro-N-(6-methoxymethyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.096 g) and 2,4-difluoro-benzenesulfonyl chloride (0.162 g) as an off-white gum (0.156 g). MS (ESI⁺): 312.9 ([M-H]⁺)

25

Example 85: 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-4-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.096 g) and 3-chloro-4-methyl-benzenesulfonyl chloride (0.172 g) as an off-white gum (0.169 g). MS (ESI⁺): 325.1 ([M-H]⁺)

5

Example 86: N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,5-difluorobenzenesulfonamide

Step A]: N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide

10 N-(6-Hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (1.04 g, Papadopoulou, J. Heterocycl. Chem., 32, 1995, 675) in DMF (25 mL) was treated with sodium hydride (0.64 g, 60% suspension in oil), the mixture was then stirred for 1 h at RT, bromomethyl cyclopropane (0.688 g) was added dropwise and stirring was continued for further 1.75 h. The reaction mixture was partitioned between 2 M aqueous KHCO₃ and AcOEt, the layers were separated, the aqueous layer extracted twice with AcOEt. The combined organic
15 layers were washed with saturated aqueous NaCl and water, dried over Na₂SO₄, filtered and evaporated. The residue was purified by flash chromatography (heptane/AcOEt 100% to 50%) to N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.884 g) as a yellow oil. MS (ESI): 263.2 (MH⁺).

20 Step B]: 6-Cyclopropylmethoxymethyl-pyridin-2-ylamine

N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.884 g) in ethanol (50 mL) was treated at RT with 3M aqueous NaOH (5.62 mL) and then heated at 100 °C for 20 h. The mixture was cooled to RT, partitioned between water and AcOEt. The layers were separated, the organic layer dried over magnesium sulphate, filtered and
25 evaporated in vacuo to give 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.566 g) as a light brown liquid. MS (ESI): 179.1 (MH⁺).

Step C]: N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,5-difluorobenzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089g) and 2, 5-difluoro-benzenesulfonyl chloride (0.122 g) as an light brown gum (0.175 g). MS (ESI⁺): 353.1 ([M-H]⁺)

5 Example 87: 5-Fluoro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.096 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.159 g) as an light yellow gum (0.16 g). MS (ESI⁺): 309.1 ([M-H]⁺)

10

Example 88: 2,5-Difluoro-N-(6-hydroxymethyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from (6-amino-pyridin-2-yl)-methanol (0.1 g) and 2,5-difluoro-benzenesulfonyl chloride (0.17 g) as an light brown amorphous solid MS (ESI⁺): 299.1 ([M-H]⁺)

15

Example 89: Acetic acid 6-(2,5-difluoro-benzenesulfonylamino)-pyridin-2-ylmethyl ester

This material was obtained as a second product in the preparation of example 88 (during work-up with AcOEt in the presence of acid) as a red amorphous solid (17 mg). MS (ESI⁺): 341.0 ([M-H]⁺)

20

Example 90: Naphthalene-2-sulfonic acid (6-hydroxymethyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from (6-amino-pyridin-2-yl)-methanol (0.042 g) and naphthalene-2-sulfonyl chloride (0.084 g) as an off-white foam (32 mg g). MS (ESI⁺): 312.9 ([M-H]⁺)

25

Example 91: 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-4-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and 3-chloro-4-methyl-benzenesulfonyl chloride (0.124 g) as a light-yellow gum (0.136 g). MS (ESI⁺): 364.9 ([M-H]⁺)

5 **Example 92: N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide**

This material was obtained in analogy to example 1 from 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.15 g) as an off-white gum (0.14 g). MS (ESI⁺): 349.2 ([M-H]⁺)

10

Example 93: 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-4-methyl-benzenesulfonamide

Step A]: N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide

15 This material was prepared in analogy to example 86 step A] from N-(6-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl- (0.625 g) and 4-fluorobenzyl bromide as a yellow oil (0.83 g). MS (ESI): 317.1 (MH⁺).

Step B]: 6-(4-Fluoro-benzyloxymethyl)-pyridin-2-ylamine

20 This material was prepared in analogy to example 86 step B] from N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide (0.825 g) and 3M aqueous NaOH (4.35 mL) as a yellow oil (0.596 g). MS (ESI): 233.1 (MH⁺).

Step C]: 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-4-methyl-benzenesulfonamide

25 This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 3-chloro-4-methyl-benzenesulfonyl chloride (0.062 g) as a light yellow gum (0.09 g). MS (ESI⁺): 419.0. ([M-H]⁺)

Example 94: 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.062 g) as a light yellow gum (0.087 g). MS (ESI⁺): 419.0. ([M-H]⁺)

5 **Example 95:** 2,5-Difluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 2,5-difluoro-benzenesulfonyl chloride (0.058 g) as a light yellow gum (0.075 g). MS (ESI⁺): 407.2 ([M-H]⁺)

10

Example 96: 5-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.057 g) as
15 a light yellow gum (0.0476 g). MS (ESI⁺): 403.2 ([M-H]⁺)

Example 97: Piperidine-1-sulfonic acid (6-methoxymethyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.096 g) and piperidine-1-sulfonyl chloride (0.153 g) as a light yellow gum
20 (0.024 g). MS (ESI⁺): 284.0 ([M-H]⁺)

Example 98: Piperidine-1-sulfonic acid (6-cyclopropylmethoxymethyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and piperidine-1-sulfonyl chloride (0.11 g) as a light yellow
25 gum (0.054 g). MS (ESI⁺): 324.2 ([M-H]⁺)

Example 99: 3-Chloro-4-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide

Step A]: 2,2-Dimethyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-propionamide

- 5 N-(6-Hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.625 g), triphenylphosphine (0.786 g) and 4-trifluoromethyl-phenol (0.486 g) in toluene was treated at RT under an argon atmosphere with diisopropyl azodicarboxylate (0.67 g). The mixture was stirred for 2 h, partitioned between ice water and AcOEt, the layers were separated, the aqueous layer twice extracted with AcOEt. The combined organic layers were washed with
10 water and saturated aqueous NaCl, dried over MgSO_4 , filtered and evaporated. The residue was purified by flash chromatography (heptane/AcOEt 100 to 85%) to give 2,2-dimethyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-propionamide (0.98 g) as a yellow oil. MS (ESI): 353.2 (MH^+).

- 15 Step B]: 6-(4-Trifluoromethyl-phenoxy-methyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from 2,2-Dimethyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-propionamide (0.99 g) and 3M aqueous NaOH (4.68 mL) as an off-white crystalline solid (0.647 g). MS (ESI): 269.3 (MH^+).

- 20 Step C]: 3-Chloro-4-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-ylamine (0.08 g) and 3-chloro-4-methyl-benzenesulfonyl chloride (0.074 g) as an off-white solid (0.105 g). MS (ESI): 455.2 ($[\text{M-H}]^-$).

25

Example 100: 3-Chloro-2-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide

- This material was prepared in analogy to example 1 from 6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-ylamine (0.08 g) and 3-chloro-2-methyl-benzenesulfonyl
30 chloride (0.074 g) as an off-white solid (0.113 g). MS (ESI): 455.2 ($[\text{M-H}]^-$).

Example 101: 2,5-Difluoro-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide

5 This material was prepared in analogy to example 1 from 6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-ylamine (0.08 g) and 2,5-difluoro-benzenesulfonyl chloride (0.07 g) as a light yellow solid (0.086 g). MS (ESI⁺): 443.0 ([M-H]⁺)

Example 102: 5-Fluoro-2-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide

10 This material was prepared in analogy to example 1 from 6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-ylamine (0.08 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.07 g) as a light yellow solid (0.1 g). MS (ESI⁺): 439.1 ([M-H]⁺)

15 Example 103: 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.09 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.13g) as an off-white gum (0.135 g). MS (ESI⁺): 365.0 ([M-H]⁺)

20 Example 104: 3,4-Dichloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.09 g) and 3,4-dichloro-benzenesulfonyl chloride (0.143g) as an off-white gum (0.143 g). MS (ESI⁺): 385.0 ([M-H]⁺)

25

Example 105: 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 4-fluoro-benzenesulfonyl chloride (0.054 g) as a light yellow gum (0.08 g). MS (ESI⁺): 389.1 ([M-H]⁺)

5 **Example 106:** N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.067 g) as a light yellow gum (0.08g). MS (ESI⁺): 439.1 ([M-H]⁺)

10

Example 107: 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

Step A]: N-(5-Formyl-pyridin-2-yl)-2,2-dimethyl-propionamide

A solution of N-(5-Bromo-pyridin-2-yl)-2,2-dimethyl-propionamide (8.7 g, Kelly,
15 Tetrahedron Lett., 32, 1991, 4263) in THF (200 mL) was cooled to -70°C under an argon atmosphere and treated dropwise over 30 minutes with n-butyllithium (45.78 mL, 1.6 M in hexane, Acros). The mixture was stirred 1 h at -70°C and then treated dropwise (over 10 minutes, at -70°C) with a mixture of N,N-dimethylformamide (5.25 mL) in THF (5 mL), and stirring was continued for further 30 minutes. The reaction mixture was then poured
20 into 2M aqueous KHCO₃ (1.2 L), tert-butyl methyl ether (1.2 L) was added, and after stirring for 20 minutes, the layers were separated, the organic layer extracted twice with tert-butyl methyl ether (total volume 0.3 L). The combined organic layers were dried over sodium sulphate, filtered and evaporated in vacuo to give N-(5-formyl-pyridin-2-yl)-2,2-dimethyl-propionamide (7 g) as an yellow oil that was used directly in the next step.

25

Step B]: N-(5-Hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide

N-(5-formyl-pyridin-2-yl)-2,2-dimethyl-propionamide (6.96 g) under an argon atmosphere in MeOH (120 mL) was cooled to 0°C and then treated portionwise with sodium borohydride (1.289 g). The cooling bath was removed, stirring was continued for
30 30 minutes and the reaction mixture was partitioned between half-saturated aqueous NH₄Cl and AcOEt. The layers were separated, the organic layer dried over sodium

sulphate, filtered and concentrated in vacuo. The residue was purified by flash chromatography (heptane/AcOEt 1:1 to 1:2) to give N-(5-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (3.4 g) as a crystalline white solid. MS (ESI): 209.2 (MH⁺).

5 Step C]: N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide

This material was prepared in analogy to example 86 step A] from N-(5-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (1.04 g) and bromomethyl cyclopropane (0.813 g) as a light yellow oil (0.87 g). MS (ESI): 263.1. (MH⁺).

10 Step D]: 5-Cyclopropylmethoxymethyl-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.87 g) and 3M aqueous NaOH (5.54 mL) as a yellow solid (0.527 g). MS (ESI): 179.1 (MH⁺).

15 Step E]: 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.142 g) as a light yellow gum (0.152 g). MS (ESI⁺): 365.0 ([M-H]⁺)

20

Example 108: 4 N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and 2,5-difluoro-benzenesulfonyl chloride (0.117 g) as an off-
25 white solid (0.119 g). MS (ESI⁺): 353.1 ([M-H]⁺)

Example 109: 4-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-3-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and 3-chloro-4-methyl-benzenesulfonyl chloride (0.124 g) as an off-white solid (0.128 g). MS (ESI⁺): 365.0 ([M-H]⁺)

5 **Example 110: 4 N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide**

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride (0.115 g) as an off-white solid (0.119 g). MS (ESI⁺): 349.3 ([M-H]⁺)

10

Example 111: Piperidine-1-sulfonic acid (5-cyclopropylmethoxymethyl-pyridin-2-yl)-amide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.089 g) and piperidine-1-sulfonyl chloride (0.142 g) as a light yellow
15 gum (0.027 g). MS (ESI⁺): 324.2 ([M-H]⁺)

Example 112: 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

Step A): N-(5-Formyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide

- 20 This material was prepared in analogy to example 107 step A) from N-(5-bromo-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide, 7.05 g - obtained via standard acylation of 5-bromo-6-methyl-pyridin-2-ylamine with 2,2-dimethyl-propionyl chloride in CH₂Cl₂, with triethylamine as base, as viscous brown oil, MS (ESI): 271.2 (MH⁺) - butyllithium (34.94 mL, 1.6 M in hexane, Agros) and N,N-dimethylformamide (4 mL) as an
25 amorphous light brown solid (5.7 g). MS (EI): 220.1 (M⁺)

Step B): N-(5-Hydroxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide

This material was prepared in analogy to to example 107 step B] from N-(5-formyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (5.9 g) and sodium borohydride (1.037 g) as a light yellow solid (1.41 g). MS (ESI): 223.2 (MH⁺).

- 5 Step C]: N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide

This material was prepared in analogy to example 86 step A] from N-(5-Hydroxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.445 g) and bromomethyl cyclopropane (0.275 g) as a light yellow oil (0.357g). MS (ESI): 277.2 (MH⁺).

10

- Step D]: 5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.357 g) and 3M aqueous NaOH (2.68 mL) as a dark red oil (0.163 g). MS (EI): 192.2 (M⁺).

15

- Step E]: 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.053 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.058 g) as a light brown solid (0.046 g). MS (ESI⁺): 379.1 ([M-H]⁺)

20

- Example 113: N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.053 g) and 2,5-difluoro-benzenesulfonyl chloride (0.059 g) as a light yellow solid (0.063 g). MS (ESI⁺): 367.0 ([M-H]⁺)

25

Example 114: N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.053 g) and 5-fluoro-2-methyl-benzenesulfonyl chloride
5 (0.058 g) as a light yellow solid (0.063 g). MS (ESI⁺): 363.3 ([M-H]⁺)

Example 115: N-(5-Methoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

Step A]: N-(5-Methoxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide

10 This material was prepared in analogy to example 86 step A] from N-(5-hydroxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.6 g, product of example 112 step B]) and iodomethane (0.421 g) as a white solid (0.4 g). MS (ESI): 237.2 (MH⁺).

Step B]: 5-Methoxymethyl-6-methyl-pyridin-2-ylamine

15 This material was prepared in analogy to example 86 step B] from N-(5-methoxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.4 g) and 3M aqueous NaOH (2.68 mL) as a crystalline orange solid (0.174 g). MS (EI): 152.2 (M⁺).

20 Step C]: N-(5-Methoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-methoxymethyl-6-methyl-pyridin-2-ylamine (0.058 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.103 g) as a light yellow gum (0.1 g). MS (ESI⁺): 359.0 ([M-H]⁺)

25 Example 116: 3-Chloro-N-(5-methoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-methoxymethyl-6-methyl-pyridin-2-ylamine (0.058 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.094 g) as an off-white foam (0.093 g). MS (ESI⁺): 339.0 ([M-H]⁺)

- 5 Example 117: N-[5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

Step A): N-[5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-2,2-dimethyl-propionamide

- 10 This material was prepared in analogy to example 86 step A] from N-(5-hydroxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.6 g, product of example 112 step B]) and 4-fluorobenzyl bromide (0.56 g) as an orange solid (0.8 g). MS (ESI⁺): 231.3 (MH⁺).

Step B): 5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-ylamine

- 15 This material was prepared in analogy to example 86 step B] from N-[5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-2,2-dimethyl-propionamide (0.78 g) and 3M aqueous NaOH (3.93 mL) as an amorphous orange solid (0.58 g). MS (ESI⁺): 247.2 (MH⁺).

- 20 Step C): N-[5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-(4-fluoro-benzyloxymethyl)-6-methyl-pyridin-2-ylamine (0.08 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.087 g) as an amorphous orange solid (0.1 g). MS (ESI⁺): 453.2 ([M-H]⁺)

- 25 Example 118: 3-Chloro-N-[5-(4-fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-(4-fluoro-benzyloxymethyl)-6-methyl-pyridin-2-ylamine (0.08 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.08 g) as an amorphous light yellow solid (0.067 g). MS (ESI⁺): 433.1 ([M-H]⁺)

Example 119: N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

Step A]: N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide

- 5 This material was prepared in analogy to example 86 step A] from N-(5-hydroxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.445 g, product of example 112 step B]) and iodoethane (0.34 g) as a light yellow oil (0.32 g). MS (ESI): 251.2 (MH⁺).

Step B]: 5-Ethoxymethyl-6-methyl-pyridin-2-ylamine

- 10 This material was prepared in analogy to example 86 step B] from N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.32 g) and 3M aqueous NaOH (2.62 mL) as a yellow oil (0.28 g) that was used directly in the next step.

Step C]: N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-

- 15 benzenesulfonamide

This material was prepared in analogy to example 1 from 5-Ethoxymethyl-6-methyl-pyridin-2-ylamine (0.066 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.108 g) as a light yellow solid (0.115 g). MS (ESI⁻): 373.1 ([M-H]⁻)

- 20 Example 120: 3-Chloro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide

Step A]: N-(6-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide

N-(6-Hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (2.03 g) in CH₂Cl₂ (75 mL) was treated at RT with thionyl chloride (1.785 mL) and then heated to reflux for 1.5 h.

- 25 The reaction mixture was cooled to RT and partitioned between water and AcOEt, the layers were separated, the organic layer dried over MgSO₄, filtered and evaporated to give N-(6-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.66 g) as a brown liquid. MS (ESI): 227.2 (MH⁺).

Step B]: 2,2-Dimethyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-propionamide

5 N-(6-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.66 g), methyl-propyl-amine (0.33 mL), KHCO_3 (0.32 g) and a catalytic amount of potassium iodide in acetone (10 mL) were heated to reflux for 6 h. The reaction mixture was cooled to RT and partitioned between water and AcOEt, the layers were separated, the organic layer dried over MgSO_4 , filtered and evaporated to give 2,2-dimethyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-propionamide (0.75 g) as a brown oil. MS (ESI): 264.3 (MH^+).

10

Step C]: 6-[(Methyl-propyl-amino)-methyl]-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from 2,2-dimethyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-propionamide (0.755 g) and 3M aqueous NaOH (5.73 mL) as a brown liquid (0.53 g). MS (ESI): 180.2 (MH^+).

15

Step D]: 3-Chloro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-[(methyl-propyl-amino)-methyl]-pyridin-2-ylamine (0.072 g) and 3-chloro-2-methyl-benzenesulfonyl chloride
20 (0.09 g), obtained as sodium salt, as a brown gum (0.06 g). MS (ESI⁺): 366.1 ($[\text{M}-\text{H}]^+$)

Example 121: 5-Fluoro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-[(methyl-propyl-amino)-methyl]-pyridin-2-ylamine (0.072 g) and 2-methyl-5-fluoro-benzenesulfonyl chloride
25 (0.09 g), obtained as sodium salt, as a brown gum (0.058 g). MS (ESI⁺): 350.3 ($[\text{M}-\text{H}]^+$)

Example 122: 3-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-ethoxymethyl-6-methyl-pyridin-2-ylamine (0.066 g) and 3-chloro-2-methyl-benzenesulfonyl chloride (0.099 g) as an off-white solid (0.08 g). MS (ESI⁺): 351.3 ([M-H]⁺)

5 Example 123: 3-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

Step A]: 6-Cyclopropyl-pyridin-2-ylamine

To a sealable vial under nitrogen was added 2-amino-6-bromo-pyridine (1.6 g), cyclopropyl boronic acid (1.03 g) (prepared according to Wallace et al. *Tetrahedron Lett.* 10 2002, 43, 6987-6990), potassium phosphate (6.87 g), tricyclohexylphosphine (0.260 g) followed by water (2 mL) and toluene (40 mL). Pd(OAc)₂ (0.104 g) was then added and the vial was sealed and heated at 100° C over 16 hours. The reaction was then allowed to cool to ambient temperature and diluted with water and ethyl acetate. The phases were separated and the aqueous phase was extracted with more ethyl acetate (3x). The 15 combined phases were washed with brine and dried over sodium sulfate. Filtration and evaporation of the volatiles afforded a crude residue which was purified via ISCO Combiflash chromatography using ethyl acetate/heptane as the eluent to give the desired 6-cyclopropyl-pyridin-2-ylamine as yellow solid (0.450 g).

20 Step B]: 3-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine (0.08 g) and 3-chloro-2-methylbenzenesulfonylchloride (0.134 g) as a colorless amorphous solid. (0.075 g). MS (ESI⁺): 323.1 ([M+H]⁺).

25 Example 124: Naphthalene-1-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide

This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine (0.1 g) and naphthalene-1-sulfonylchloride (0.169 g) as a light yellow amorphous gum. (0.03 g). MS (ESI⁺): 325.3 ([M+H]⁺).

Example 125: 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2,5-dimethyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine (0.1 g) and 4-chloro-2,5-dimethylbenzenesulfonylchloride (0.180 g) as an off-white
5 amorphous solid (0.023 g). MS (ESI⁺): 337.1 ([M+H]⁺).

Example 126: 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-3-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine
10 (0.1 g) and 3-chloro-4-methylbenzenesulfonylchloride (0.168 g) as waxy yellow solid (0.039 g). MS (ESI⁺): 323.3 ([M+H]⁺).

Example 127: N-(6-Cyclopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine
15 (0.1 g) and 3-(trifluoromethyl)benzenesulfonylchloride (0.182 g) as a light yellow gum (0.060 g). MS (ESI⁺): 343.1 ([M+H]⁺).

Example 128: 2,4-Dichloro-N-(6-cyclopropyl-pyridin-2-yl)-5-methyl-benzenesulfonamide

20 This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine (0.1 g) and 2,4-dichloro-5-methylbenzenesulfonylchloride (0.193 g) as a light yellow gum (0.047 g). MS (ESI⁺): 357.1 ([M+H]⁺).

Example 129: Naphthalene-2-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide

25 This material was obtained in analogy to example 1 from 6-cyclopropyl-pyridin-2-ylamine (0.1 g) and naphthalene-2-sulfonylchloride (0.169 g) as a light yellow gum (0.150 g). MS (ESI⁺): 325.3 ([M+H]⁺).

Example 130: N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.051 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.077 g) as
5 a crystalline white solid (0.062 g). MS (ESI⁺): 385.0 ([M-H]⁺)

Example 131: N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3,5-bis-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-ethoxymethyl-6-methyl-pyridin-2-ylamine (0.07 g) and 3,5-di(trifluoromethyl)-benzenesulfonyl chloride (0.145 g)
10 as an off-white solid (0.032 g). MS (ESI⁺): 441.1 ([M-H]⁺)

Example 132: 4-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

15 This material was prepared in analogy to example 1 from 5-ethoxymethyl-6-methyl-pyridin-2-ylamine (0.07 g) and 4-chloro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.129 g) as a yellow gum (0.068 g). MS (ESI⁺): 407.2 ([M-H]⁺)

Example 133: 4-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide
20

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 4-chloro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.077 g) as a light yellow gum (0.084 g). MS (ESI⁺): 472.8 ([M-H]⁺)

Example 134: 4-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2,5-dimethyl-benzenesulfonamide
25

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.058 g) and 4-chloro-2,5-dimethyl-benzenesulfonyl chloride (0.066 g) as a light yellow gum (0.089 g). MS (ESI⁺): 433.2 ([M-H]⁺)

Example 135: 3-Trifluoromethyl-N-[6-(4-trifluoromethyl-phenoxyethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-trifluoromethyl-phenoxyethyl)-pyridin-2-ylamine (0.08 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.081 g) as a light yellow gum (0.114 g). MS (ESI⁺): 475.0 ([M-H]⁺).

Example 136: N-[5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

10 Step A]: N-[5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-yl]-2,2-dimethyl-propionamide

This material was prepared in analogy to example 86 step A] from N-(5-hydroxymethyl-6-methyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.556 g, product of example 112 step B]) and 1-bromo-2-fluoro-ethane (0.475 g) as a light yellow gum (0.115 g). MS (ESI⁺): 269.3 (MH⁺).

Step B]: 5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from N-[5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-yl]-2,2-dimethyl-propionamide (0.165 g) and 3M aqueous NaOH (1.23 mL) as an gum (0.174 g) that was used directly in the next step.

Step C]: N-[5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-(2-fluoro-ethoxymethyl)-6-methyl-pyridin-2-ylamine (0.05 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.073 g) as a light yellow gum (39 mg g). MS (ESI⁺): 391.2 ([M-H]⁺)

Example 137: 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.06 g) and 3-chloro-benzenesulfonyl chloride (0.078 g) as an
5 amorphous off-white solid (0.059 g). MS (ESI⁺): 351.1 ([M-H]⁺)

Example 138: 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.06 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.096 g)
10 as an off-white solid (0.069 g). MS (ESI⁺): 399.1 ([M-H]⁺)

Example 139: 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide

15 This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-pyridin-2-ylamine (0.06 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.097 g) as a crystalline white solid (0.066 g). MS (ESI⁺): 403.2 ([M-H]⁺)

Example 140: 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-benzenesulfonamide
20

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.06 g) and 3-chloro-6-methyl-benzenesulfonyl chloride (0.072 g) as a light yellow solid (0.07 g). MS (ESI⁺): 364.9 ([M-H]⁺)

Example 141: 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-6-methyl-benzenesulfonamide
25

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.06 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.089 g) as an amorphous light yellow solid (0.058 g). MS (ESI⁺): 413.1 ([M-H]⁺)

Example 142: 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-6-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.06 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.084 g) as a light yellow solid. MS (ESI): 401.4 ($[MH]^+$)

Example 143: 2,4-Difluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

10 Step A): N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide

This material was prepared in analogy to example 86 step A) from N-(6-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.73 g) and 3-fluorobenzyl bromide as a yellow solid (0.66 g). MS (ESI): 317.1 (MH^+).

15 Step B): 6-(3-Fluoro-benzyloxymethyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B) from N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide (0.663 g) and 3M aqueous NaOH (4.19 mL) as a brown liquid (0.596 g). MS (ESI): 233.2 (MH^+).

20 Step C): 2,4-Difluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.06 g) and 2,4-difluoro-benzenesulfonyl chloride (0.06 g) as a yellow solid (0.07 g). MS (ESI): 407.2 ($[M-H]^+$).

25

Example 144: 3-Chloro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.06 g) and 3-chloro-benzenesulfonyl chloride (0.06 g) as a yellow gum (0.07 g). MS (ESI⁺): 405.1 ([M-H]⁺).

5 **Example 145:** 2,4-Dichloro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.06 g) and 2,4-dichloro-6methyl-benzenesulfonyl chloride (0.074 g) as a yellow solid (0.12 g). MS (ESI⁺): 453.1 ([M-H]⁺).

10

Example 146: 2,4-Difluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.07 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.07 g)
15 as a light yellow solid (0.104 g). MS (ESI⁺): 407.2 ([M-H]⁺).

Example 147: 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.07 g) and 3-chloro-benzenesulfonyl chloride (0.07 g) as a light yellow
20 gum (0.059 g). MS (ESI⁺): 405.2 ([M-H]⁺).

Example 148: 2,4-Dichloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide

25 This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.07 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.086 g) as a light yellow solid (0.11 g). MS (ESI⁺): 453.1 ([M-H]⁺).

Example 149: N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-ylamine (0.06 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.12 g) as a light yellow solid (0.12g). MS (ESI⁺): 417.0 ([M-H]⁺)

Example 150: 4-Fluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.06 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.075 g) as a light yellow solid (0.1 g). MS (ESI⁺): 457.2 ([M-H]⁺).

Example 151: 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.07 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.087 g) as a light yellow gum (0.11 g). MS (ESI⁺): 457.2 ([M-H]⁺).

Example 152: N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethoxy-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-fluoro-benzyloxymethyl)-pyridin-2-ylamine (0.07 g) and 3-(trifluoromethoxy)-benzenesulfonyl chloride (0.086 g) as a light yellow gum (0.097 g). MS (ESI⁺): 455.2 ([M-H]⁺).

Example 153: N-(6-Methoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.076 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.148 g) as a light yellow gum (0.13 g). MS (ESI⁺): 345.1. ([M-H]⁺)

Example 154: 2,4-Dichloro-N-(6-methoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.076 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.157 g) as an off-white solid (0.138 g). MS (ESI⁺): 358.9. ([M-H]⁺)

Example 155: 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-benzenesulfonamide

This material was obtained in analogy to example 1 from 6-methoxymethyl-pyridin-2-ylamine (0.076 g) and 3-chloro-benzenesulfonyl chloride (0.128 g) as a light yellow gum (0.147 g). MS (ESI⁺): 311.0 ([M-H]⁺)

Example 156: 3-Trifluoromethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide

Step A]: 2,2-Dimethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-propionamide

3,3,3-Trifluoro-propan-1-ol (0.214 g) in THF (8 mL) was treated under an argon atmosphere with sodium hydride (0.1 g, 60% suspension in oil) and stirred for 1 h at RT. N-(6-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide, 0.142 g, product of example 120 step A], was added and the mixture was heated at 85°C for 2.5 h. The reaction mixture was cooled, partitioned between ice water and AcOEt, the layers were separated, the organic layer dried over Na₂SO₄, filtered and evaporated to give 2,2-dimethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-propionamide (0.21 g) as a light brown oil. MS (ESI): 305.3 (MH⁺).

25

Step B]: 6-(3,3,3-Trifluoro-propoxymethyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from 2,2-dimethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-propionamide (0.2 g) and 3M aqueous NaOH (1.31 mL) as a brown oil (0.159 g). MS (ESI): 221.2 (MH⁺).

Step C]: 3-Trifluoromethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3,3,3-Trifluoro-propoxymethyl)-pyridin-2-ylamine (0.075 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.092 g) as a light yellow gum (0.048 g). MS (ESI⁺): 427.1 ([M-H]⁺).

Example 157: 2,4-Dichloro-6-methyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide

10 This material was prepared in analogy to example 1 from 6-(3,3,3-Trifluoro-propoxymethyl)-pyridin-2-ylamine (0.075 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.097 g) as a light yellow gum (0.08 g). MS (ESI⁺): 441.1 ([M-H]⁺).

Example 158: N-[6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

Step A]: 2,2-Dimethyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-propionamide

This material was obtained in analogy to example 156 step A from N-(6-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide, 0.567 g, product of example 120 step A], and 2,2,2-trifluoro-ethanol as a brown liquid (0.726 g) that was used directly in the next step.

20

Step B]: 6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from 2,2-Dimethyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-propionamide (0.726 g) and 3M aqueous NaOH (5 mL) as a brown liquid (0.4 g). MS (EI): 206.1 (M⁺).

25

Step C]: N-[6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.104 g) as a light yellow gum (0.066 g). MS (ESI⁺): 413.1 ([M-H]⁺).

- 5 Example 159: 2,4-Dichloro-6-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.11 g) as a light yellow solid (0.1 g). MS (ESI⁺): 427.1 ([M-H]⁺).

10

- Example 160: 3-Chloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide

Step A]: N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide

- 15 This material was obtained in analogy to example 156 step A from N-(6-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide, 0.567 g, product of example 120 step A], and 2-cyclopropyl-ethanol (0.51 g) as a light yellow oil (0.51 g). MS (ESI⁺): 277.2 ([MH]⁺).

Step B]: 6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-ylamine

- 20 This material was prepared in analogy to example 86 step B] from N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide (0.51 g) and 3M aqueous NaOH (3.7 mL) as a light yellow oil (0.39 g) that was used directly in the next step.

Step C]: 3-Chloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide

- 25 This material was prepared in analogy to example 1 from 6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 3-chloro-benzenesulfonyl chloride (0.095 g) as a light yellow gum (0.096 g). MS (ESI⁺): 365.0 ([M-H]⁺).

Example 161: N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.11 g) as a
5 light yellow gum (0.106 g). MS (ESI⁺): 399.2 ([M-H]⁺).

Example 162: N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.12
10 g) as a light yellow gum (0.08 g). MS (ESI⁺): 417.0 ([M-H]⁺).

Example 163: 2,4-Dichloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.117 g)
15 as a light yellow gum (0.088 g). MS (ESI⁺): 413.1 ([M-H]⁺).

Example 164: 2,4-Dichloro-5-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide
20

This material was prepared in analogy to example 1 from 6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 2,4-dichloro-5-methyl-benzenesulfonyl chloride (0.11 g) as a light yellow gum (0.095 g). MS (ESI⁺): 427.1 ([M-H]⁺).

Example 165: 2-Chloro-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-5-trifluoromethyl-benzenesulfonamide
25

This material was prepared in analogy to example 1 from 6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine (0.08 g) and 2-chloro-5-(trifluoromethyl)-

benzenesulfonyl chloride (0.119 g) as a light yellow solid (0.123 g). MS (ESI⁻): 447.0 ([M-H]⁻).

Example 166: 2,4-Dichloro-N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-
5 benzenesulfonamide

Step A]: N-[6-(3-Chloro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide

This material was prepared in analogy to example 86 step A] from N-(6-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.73 g) and 3-chlorobenzyl bromide as a yellow oil (0.75 g). MS (ESI): 332.2 (MH⁺).

10

Step B]: 6-(3-Chloro-benzyloxymethyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide (0.75 g) and 3M aqueous NaOH (4.51 mL) as a brown liquid (0.56 g). MS (ESI): 249.1 (MH⁺).

15

Step C]: 2,4-Dichloro-N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3-chloro-benzyloxymethyl)-pyridin-2-ylamine (0.08 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.092g)
20 as a light yellow gum (0.039 g). MS (ESI⁻): 469.0 ([M-H]⁻).

Example 167: N-[6-(3-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(3-chloro-benzyloxymethyl)-pyridin-2-ylamine (0.08 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride
25 (0.092g) as a light yellow gum (0.088 g). MS (ESI⁻): 472.8 ([M-H]⁻).

Example 168: N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide

Step A]: N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide

This material was prepared in analogy to example 86 step A] from N-(6-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.73 g) and 4-chlorobenzyl bromide as a yellow oil (0.868 g). MS (ESI): 332.2 (MH⁺).

Step B]: 6-(4-Chloro-benzyloxymethyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from N-[6-(4-chloro-benzyloxymethyl)-pyridin-2-yl]-2,2-dimethyl-propionamide (0.868 g) and 3M aqueous NaOH (5.22 mL) as a light yellow liquid (0.63 g). MS (ESI): 249.1 (MH⁺).

Step C]: N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-chloro-benzyloxymethyl)-pyridin-2-ylamine (0.08 g) and 4-fluoro-3-(trifluoromethyl)-benzenesulfonyl chloride (0.092g) as a light yellow gum (0.039 g). MS (ESI⁺): 472.8 ([M-H]⁺).

Example 169: 2,4-Dichloro-N-[6-(4-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 6-(4-chloro-benzyloxymethyl)-pyridin-2-ylamine (0.08 g) and 2,4-dichloro-6-methyl-benzenesulfonyl chloride (0.092 g) as an off-white solid (0.082 g). MS (ESI⁺): 469.0 ([M-H]⁺).

Example 170: N-[5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

Step A]: N-(5-Chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide

This material was obtained in analogy to example 120 step A], from N-(5-hydroxymethyl-pyridin-2-yl)-2,2-dimethyl-propionamide, 1.25 g, product of example 107 step B], and thionyl chloride (0.65 mL) as a brown solid (0.87 g). MS (ESI): 227.2 (MH⁺).

- 5 Step B]: 2,2-Dimethyl-N-[5-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-propionamide

This material was obtained in analogy to example 156 step A] from N-(5-chloromethyl-pyridin-2-yl)-2,2-dimethyl-propionamide (0.43 g) and 2,2,2-trifluoro-ethanol (0.41 mL) as a brown liquid (0.56 g) that was used directly in the next step.

- 10 Step C]: 5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine

This material was prepared in analogy to example 86 step B] from 2,2-dimethyl-N-[5-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-propionamide (0.56 g) and 3M aqueous NaOH (3.87 mL) as a crystalline white solid (0.123 g). MS (ESI): 207.1 (MH⁺).

- 15 Step D]: N-[5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide

This material was prepared in analogy to example 1 from 5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine (0.06 g) and 3-(trifluoromethyl)-benzenesulfonyl chloride (0.078 g) as an off-white solid (0.056 g). MS (ESI⁺): 413.1 ([M-H]⁺).

20

Example 171: 2,4-Dichloro-5-methyl-N-[5-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide

- This material was prepared in analogy to example 1 from 5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-ylamine (0.06 g) and 2,4-dichloro-6-methyl-benzenesulfonyl
25 chloride (0.083 g) as an off-white solid (0.072 g). MS (ESI⁺): 427.1 ([M-H]⁺).

Example 172: 3-Chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide

Step A]: 6'-Nitro-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl

5-Bromo-2-nitropyridine (3.0 g), tetrabutylammonium iodide (0.273 g), potassium carbonate (2.24 g) and piperidine (1.6 mL) were dissolved in DMSO (25 mL) and heated at 80 °C for 12 hours. The mixture was diluted with ethyl acetate, filtered and the filtrate
5 was concentrated in vacuo. To the residue was added water (75 mL) and the precipitate was isolated by filtration. The solid was evaporated three times from toluene to remove residual water and the product was further dried in vacuo to give 6'-nitro-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl (2.87 g) as a yellow powder. MS (EI): 207.2 (M⁺).

Step B]: 3,4,5,6-Tetrahydro-2H-[1,3']bipyridinyl-6'-ylamine

10 To 6'-Nitro-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl (0.25 g) in THF (8 mL) was added iron (0.539 mg) and water (2.5 mL). Then acetic acid (0.35 mL) was added dropwise and the mixture was allowed to stir at 45 °C for 12 hours. TLC analysis confirmed complete consumption of the starting material. The suspension was filtered through celite and the filter cake was washed well with ethyl acetate. The filtrate was concentrated in vacuo prior
15 to addition of 2N NaOH. The aqueous layer was saturated with NaCl and extracted with ethyl acetate. The organic phase was washed with brine, dried over Na₂SO₄ and evaporated to give a residue that was purified by flash chromatography on silica gel (gradient of MeOH in DCM containing 0.5% NH₄OH). 3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-ylamine was obtained as a black oil (0.196 g). MS (ESI): 178.1 (MH⁺).

20 Step C]: 3-Chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide

3,4,5,6-Tetrahydro-2H-[1,3']bipyridinyl-6'-ylamine (0.19 g) and 3-chloro-2-methylbenzenesulfonyl chloride (0.24 g) were dissolved in pyridine (4 mL) and heated at 50 °C over night. The mixture was concentrated in vacuo, taken up in ethyl acetate and
25 extracted with 1M Cu(II)SO₄ solution. The organic layer was washed once again with Cu(II)SO₄ solution, dried over Na₂SO₄ and evaporated in vacuo. The product was purified by flash chromatography on silica gel (gradient of ethyl acetate in heptane) to give 3-chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide (0.1 g) as a light brown foam. MS (ESI⁺): 364.0 ([M-H]⁺).

30

Example 173: 3-Chloro-2-methyl-N-(5-pyrrolidin-1-yl-pyridin-2-yl)-benzenesulfonamide

3-Chloro-2-methyl-N-(5-pyrrolidin-1-yl-pyridin-2-yl)-benzenesulfonamide was obtained in analogy to example 172, steps A] to C] from 5-bromo-2-nitropyridine, pyrrolidine and 3-chloro-2-methylbenzenesulfonyl chloride as a yellow foam. MS (ESI⁺): 350.2 ([M-H]⁺).

5 Example 174: 3-Chloro-2-methyl-N-(5-morpholin-4-yl-pyridin-2-yl)-
benzenesulfonamide

3-Chloro-2-methyl-N-(5-morpholin-4-yl-pyridin-2-yl)-benzenesulfonamide was obtained in analogy to example 172, steps A] to C] from 5-bromo-2-nitropyridine, morpholine and 3-chloro-2-methylbenzenesulfonyl chloride as a light yellow powder. MS (ESI⁺): 366.0
10 ([M-H]⁺).

Example 175: N-(5-Benzyl-pyridin-2-yl)-3-chloro-2-methyl-
benzenesulfonamide

N-(5-Benzyl-pyridin-2-yl)-3-chloro-2-methyl-benzenesulfonamide was made in analogy
15 to example 172, step C] from known 5-benzyl-pyridin-2-ylamine (made according to Kelly
et al., J. Am. Chem. Soc. 112 (22), 1990, 8024-8034) and 3-chloro-2-
methylbenzenesulfonyl chloride and was obtained as a white powder. MS (ESI⁺): 371.1
([M-H]⁺).

20 Example 176: 3-Chloro-2-methyl-N-(5-phenethyl-pyridin-2-yl)-
benzenesulfonamide

Step A]: 5-Phenethyl-pyridin-2-ylamine

5-Phenethyl-pyridin-2-ylamine which has been described in the literature (Kaminski et al.,
J. Med. Chem. 28 (7), 1985, 876-892) was made from known 5-styryl-pyridin-2-ylamine
25 (Bumagin et al., J. Organomet. Chem. 486 (1-2), 1995, 259-262) by catalytic
hydrogenation: 5-Styryl-pyridin-2-ylamine (0.3 g) was dissolved in ethanol (6 mL) and 5%
Pd on charcoal (38 mg) was added. A hydrogen atmosphere was introduced by repeated
evacuation / hydrogen introduction and the suspension was allowed to stir at RT for 2
hours. The mixture was filtered through celite and the filter cake was washed well with
30 ethanol. The filtrate was evaporated to give 5-phenethyl-pyridin-2-ylamine as a colorless
solid (100 mg) that was not further purified. MS (ESI): 199.1 (MH⁺).

Step B]: 3-Chloro-2-methyl-N-(5-phenethyl-pyridin-2-yl)-benzenesulfonamide

3-Chloro-2-methyl-N-(5-phenethyl-pyridin-2-yl)-benzenesulfonamide was made in analogy to example 172, step C] from 5-phenethyl-pyridin-2-ylamine (117 mg) and 3-chloro-2-methylbenzenesulfonyl chloride (133 mg) to give the desired product as a white powder (129 mg). MS (ESI⁺): 385.0 ([M-H]⁺)

Example 177: 3-Chloro-2-methyl-N-(6-methyl-5-phenethyl-pyridin-2-yl)-benzenesulfonamide

Step A]: 6-Methyl-5-styryl-pyridin-2-ylamine

10 5-Bromo-6-methyl-pyridin-2-ylamine (0.5 g), styrene (0.28 g) and potassium formate (0.68 g) were dissolved in DMF (5 mL). Tetrabutylammonium chloride (0.74 g) and palladium(II)acetate (30 mg) were added and the mixture was stirred under argon at 60 °C for 18 hours; a black suspension was obtained. The mixture was poured into saturated NaHCO₃ solution (75 mL) and extracted with ethyl acetate. The organic layers were
15 washed with brine, dried over Na₂SO₄ and evaporated. The residue was purified by flash chromatography (silica gel, gradient of ethyl acetate in heptane) to give 6-methyl-5-styryl-pyridin-2-ylamine (144 mg) as a 7:3 mixture of (E) and (Z) isomers as a white foam. MS (ESI): 211.3 (MH⁺). This material was contaminated with trace amounts of 6-methyl-5-phenethyl-pyridin-2-ylamine according to MS analysis.

20 Step B] 6-Methyl-5-phenethyl-pyridin-2-ylamine

6-Methyl-5-styryl-pyridin-2-ylamine (141 mg) was hydrogenated in analogy to example 176, step A] to give 6-methyl-5-phenethyl-pyridin-2-ylamine (139 mg) as light brown foam. MS (ESI): 213.3 (MH⁺).

Step C] 3-Chloro-2-methyl-N-(6-methyl-5-phenethyl-pyridin-2-yl)-
25 benzenesulfonamide

This material was obtained from 6-methyl-5-phenethyl-pyridin-2-ylamine (134 mg) and 3-chloro-2-methylbenzenesulfonyl chloride (142 mg) in analogy to example 172, step C] as white foam (166 mg). MS (ESI⁺): 399.1 ([M-H]⁺).

Example 178: 3-Chloro-2-methyl-N-(5-thiomorpholin-4-yl-pyridin-2-yl)-benzenesulfonamide

3-Chloro-2-methyl-N-(5-thiomorpholin-4-yl-pyridin-2-yl)-benzenesulfonamide was obtained in low yield in analogy to example 172, steps A] to C] from 5-bromo-2-nitropyridine, thiomorpholine and 3-chloro-2-methylbenzenesulfonyl chloride as a reddish, viscous oil. MS (ESI⁺): 382.1 ([M-H]⁺).

Example 179: 2,4-Dichloro-N-{5-[2-(4-chloro-phenyl)-ethyl]-pyridin-2-yl}-6-methyl-benzenesulfonamide

10 This material was obtained in analogy to example 177, steps A] to C] from 5-iodo-pyridin-2-ylamine, 1-chloro-4-vinyl-benzene and 2,4-dichloro-6-methylbenzenesulfonyl chloride as a light yellow powder. MS (ESI⁺): 353.1 ([M-H]⁺).

Example 180: 3-Chloro-N-{5-[2-(4-methoxy-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 177, steps A] to C] from 5-iodo-pyridin-2-ylamine, 1-methoxy-4-vinyl-benzene and 3-chloro-2-methylbenzenesulfonyl chloride as a light yellow foam. MS (ESI⁺): 415.3 ([M-H]⁺).

20 Example 181: 3-Chloro-N-{5-[2-(3-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 177, steps A] to C] from 5-iodo-pyridin-2-ylamine, 1-fluoro-3-vinyl-benzene and 3-chloro-2-methylbenzenesulfonyl chloride as a light yellow foam. MS (ESI⁺): 403.4 ([M-H]⁺).

25

Example 182: 3-Chloro-2-methyl-N-{5-[2-(2-trifluoromethyl-phenyl)-ethyl]-pyridin-2-yl} benzenesulfonamide

This material was obtained in analogy to example 177, steps A] to C] from 5-iodo-pyridin-2-ylamine, 1-trifluoromethyl-2-vinyl-benzene and 3-chloro-2-methylbenzenesulfonyl chloride as a white foam. MS (ESI⁺): 453.3 ([M-H]⁺).

- 5 Example 183: 3-Chloro-N-{5-[2-(4-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-benzenesulfonamide

This material was obtained in analogy to example 177, steps A] to C] from 5-iodo-pyridin-2-ylamine, 1-fluoro-4-vinyl-benzene and 3-chloro-2-methylbenzenesulfonyl chloride as a light yellow foam. MS (ESI⁺): 403.4 ([M-H]⁺).

10

- Example 184: 3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide

Step A] 2-Nitro-5-phenoxy-pyridine

- Phenol (306 mg) was dissolved in dry DMF (5 mL) and subsequently, sodium hydride
15 (60% in mineral oil, 130 mg) was added which resulted in strong hydrogen gas evolution. The mixture was then allowed to stir at RT for 30 minutes. Subsequently, 5-bromo-2-nitro-pyridine (600 mg) was added und the resulting mixture was stirred at 60 °C for 12 hours. The reaction mixture was poured into ice water and the aqueous phase was saturated with NaCl and extracted with ethyl acetate. The organic layer was separated,
20 washed with brine, dried over Na₂SO₄ and evaporated. The residue was purified by flash chromatography (silica gel, gradient of ethyl acetate in heptane) to give 2-nitro-5-phenoxy-pyridine as a light yellow foam (267 mg). MS (EI): 216.1 (M⁺).

Step B] 5-Phenoxy-pyridin-2-ylamine

- 2-Nitro-5-phenoxy-pyridine (262 mg) was dissolved in dry ethanol (12 mL) and 10%
25 palladium on charcoal (90 mg) was added. A hydrogen atmosphere was introduced by repeated evacuation / hydrogen introduction. The mixture was then allowed to stir for 18 hours. The catalyst was removed by filtration through celite and the filtrate was concentrated in vacuo to give 5-phenoxy-pyridin-2-ylamine (217 mg) as a yellow foam. This material was used without further purification. MS (EI): 186.1 (M⁺).

- 30 Step C] 3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide

5-Phenoxy-pyridin-2-ylamine (100 mg) was treated with 3-chloro-2-methylbenzenesulfonyl chloride (122 mg) in the presence of pyridine (3 mL) as described in example 172, step C] to give 3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide (37 mg) as a white foam. MS (ESI): 375.1 (MH⁺).

5

Example 185: 3-Chloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-2-methylbenzenesulfonamide

This material was obtained in analogy to example 184, steps A] to C] from 2-chlorophenol, 5-bromo-2-nitro-pyridine and 3-chloro-2-methylbenzenesulfonyl chloride as a
10 white foam. MS (ESI⁺): 407.1 ([M-H]⁺).

Example 186: 3-Chloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-2-methylbenzenesulfonamide benzenesulfonamide

This material was obtained in analogy to example 184, steps A] to C] from 4-fluorophenol, 5-bromo-2-nitro-pyridine and 3-chloro-2-methylbenzenesulfonyl chloride as a
15 white solid. MS (ESI): 392.9 (MH⁺).

Example 187: 2,4-Dichloro-6-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide

20 This material was obtained in analogy to example 184, steps A] to C] from phenol, 5-bromo-2-nitro-pyridine and 2,4-dichloro-6-methylbenzenesulfonyl chloride as a light brown solid. MS (ESI⁺): 407.1 ([M-H]⁺).

Example 188: 2,4-Dichloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-6-methylbenzenesulfonamide
25

This material was obtained in analogy to example 184, steps A] to C] from 2-chlorophenol, 5-bromo-2-nitro-pyridine and 2,4-dichloro-6-methylbenzenesulfonyl chloride as a light yellow foam. MS (ESI⁺): 441.0 ([M-H]⁺).

Example 189: 2,4-Dichloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-6-methylbenzenesulfonamide

This material was obtained in analogy to example 184, steps A) to C) from 4-fluorophenol, 5-bromo-2-nitro-pyridine and 2,4-dichloro-6-methylbenzenesulfonyl chloride as
5 a light brown solid. MS (ESI⁺): 425.0 ([M-H]⁺).

Example 190: 3-Chloro-2-methyl-N-[5-(2-quinolin-2-yl-ethyl)-pyridin-2-yl]benzenesulfonamide

This material was obtained in analogy to example 177, steps A) to C) from 5-iodo-pyridin-
10 2-ylamine, 2-vinyl-quinoline and 3-chloro-2-methylbenzenesulfonyl chloride as a light yellow foam. MS (ESI⁺): 436.2 ([M-H]⁺).

Example 191: 2,4-Dichloro-6-methyl-N-[5-(2-quinolin-2-yl-ethyl)-pyridin-2-yl]-benzenesulfonamide

15 This material was obtained in analogy to example 177, steps A) to C) from 5-iodo-pyridin-2-ylamine, 2-vinyl-quinoline and 2,4-dichloro -6-methylbenzenesulfonyl chloride as a light yellow foam. MS (ESI⁺): 470.0 ([M-H]⁺).

Example 192: 3-Chloro-2-methyl-N-[5-(2-pyridin-2-yl-ethyl)-pyridin-2-yl]benzenesulfonamide
20

This material was obtained in analogy to example 177, steps A) to C) from 5-iodo-pyridin-2-ylamine, 2-vinyl-pyridine and 3-chloro-2-methylbenzenesulfonyl chloride as a white powder. MS (ESI⁺): 386.0 ([M-H]⁺).

25

Example A

A compound of formula I can be used in a manner known per se as the active ingredient for the production of tablets of the following composition:

Per tablet

	Active ingredient	200 mg
	Microcrystalline cellulose	155 mg
	Corn starch	25 mg
	Talc	25 mg
5	Hydroxypropylmethylcellulose	<u>20 mg</u>
		425 mg

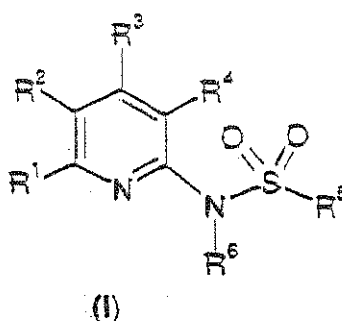
Example B

A compound of formula I can be used in a manner known per se as the active
10 ingredient for the production of capsules of the following composition:

	<u>Per capsule</u>
Active ingredient	100.0 mg
Corn starch	20.0 mg
Lactose	95.0 mg
15 Talc	4.5 mg
Magnesium stearate	<u>0.5 mg</u>
	220.0 mg

CLAIMS

1. Compounds of formula



5 wherein

R¹ is alkyl, cycloalkyl, hydroxalkyl, alkoxyalkyl, aryl, alkoxyalkylaminocarbonylalkyl, cycloalkylalkoxyalkyl, arylalkyloxyalkyl or trifluoroalkoxyalkyl;

R² is hydrogen, alkyl, cycloalkylalkoxyalkyl, alkoxyalkyl, arylalkoxyalkyl, haloalkoxyalkyl, piperidyl, pyrrolidyl, morpholinyl, thiomorpholinyl arylalkyl, arylalkoxy, aryloxy, heterocyclylalkoxy or heterocyclylalkyl;

15 R³ is hydrogen or alkyl;

R⁴ is hydrogen, alkyl or halogen;

20 R⁵ is phenyl, naphthyl, thiophenyl, pyridyl, quinolyl, piperidyl, morpholyl, thiomorpholyl or 1,2,3,4-tetrahydro-isoquinoliny optionally substituted with one or more substituents independently selected from alkyl, cycloalkyl, halogen, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkoxyalkoxy, cyano, nitro, trifluoromethyl, trifluoromethoxy, trifluoromethylcarbonyl, aryl, arylalkyl, aryloxy, alkoxyalkoxyalkoxy and alkylsulfonyl;

R⁶ is hydrogen or alkyl;

wherein aryl is phenyl or naphthyl optionally substituted with one to three, substituents independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl,

wherein hydroxyalkyl is hydroxymethyl;

and pharmaceutically acceptable salts and esters thereof;

with the proviso that

N-(6-(1,1-dimethylethyl)-2-pyridinyl)-4-methyl-benzenesulfonamide,

3-Chloro-N-(6-ethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide,

N-(6-ethyl-pyridin-2-yl)-4-trifluoromethyl-benzenesulfonamide,

N-(6-ethyl-pyridin-2-yl)-4-isopropyl-benzenesulfonamide,

3-Chloro-N-(6-hydroxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide,

6-(4-Trifluoromethyl-phenyl)-pyridine-3-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide, and

2-[6-3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide

are excluded and in case R^1 is hydrogen or methyl then R^2 is not hydrogen or methyl.

2. Compounds according to claim 1, wherein R^5 is phenyl, naphthyl, piperidyl or 1,2,3,4-tetrahydro-isoquinolinyl optionally substituted with one to three substituents independently selected from alkyl, halogen, alkoxy, nitro, trifluoromethyl, trifluoromethoxy, trifluoromethylcarbonyl, aryl, aryloxy and alkylsulfonyl.
3. Compounds according to claim 1 or 2, wherein R^5 is phenyl or naphthyl optionally substituted with one to three substituents independently selected from alkyl, halogen, trifluoromethyl, trifluoromethoxy and aryl.
4. Compounds according to any one of claims 1 to 3, wherein R^6 is hydrogen.
5. Compounds according to any one of claims 1 to 4, wherein R^1 is hydrogen.
6. Compounds according to any one of claims 1 to 5, wherein R^2 is hydrogen, cycloalkylalkoxyalkyl, alkoxyalkyl, piperidyl, pyrrolidyl, morpholinyl, thiomorpholinyl, arylalkyl or aryloxy.
7. Compounds according to any one of claims 1 to 6, wherein R^3 is hydrogen.
8. Compounds according to any one of claims 1 to 7, wherein R^4 is hydrogen or halogen.

9. Compounds according to any one of claims 1 to 8, wherein R⁴ is hydrogen.

10. Compounds according to any one of claims 1 to 9, selected from the group consisting of:

Biphenyl-4-sulfonic acid (6-ethyl-pyridin-2-yl)-amide;

Biphenyl-4-sulfonic acid (6-propyl-pyridin-2-yl)-amide;

3-Chloro-2-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

Naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide,

3,4-Dichloro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

2,5-Difluoro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

2,4-Dichloro-6-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

5-Chloro-naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide,

3,4-Dimethoxy-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

4,5-Dichloro-2-fluoro-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

2,4-Dichloro-5-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide,

Piperidine-1-sulfonic acid (6-propyl-pyridin-2-yl)-amide,

3-Chloro-N-(6-isopropyl-pyridin-2-yl)-4-methyl-benzenesulfonamide,

2,5-Difluoro-N-(6-isopropyl-pyridin-2-yl)-benzenesulfonamide,

N-(6-Isopropyl-pyridin-2-yl)-4-(4-trifluoromethyl-phenoxy)-benzenesulfonamide,

2,4-Dichloro-N-(6-isopropyl-pyridin-2-yl)-5-methyl-benzenesulfonamide,

N-(6-Isopropyl-pyridin-2-yl)-4-methanesulfonyl-benzenesulfonamide,

N-(6-Isopropyl-pyridin-2-yl)-4-trifluoromethoxy-benzenesulfonamide,

2-(2,2,2-Trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline-7-sulfonic acid (6-isopropyl-pyridin-2-yl)-amide,

N-(6-Isopropyl-pyridin-2-yl)-3-(4-trifluoromethyl-phenoxy)-benzenesulfonamide,

Naphthalene-2-sulfonic acid (6-isopropyl-pyridin-2-yl)-amide,

N-(6-Isopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide,

N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide, and

3-Chloro-N-[6-(2-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide.

- Biphenyl-4-sulfonic acid [6-(2-chloro-phenyl)-pyridin-2-yl]-amide;
- 3-Chloro-N-[6-(2,4-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(3-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(2,3-difluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 5 3-Chloro-N-[6-(2,5-dichloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- N-[6-(2,5-Dichloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(3-chloro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- N-[6-(3-Chloro-phenyl)-pyridin-2-yl]-5-fluoro-2-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 10 5-Fluoro-N-[6-(2-fluoro-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 3-Chloro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
- 5-Fluoro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
- 15 N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-2,5-difluoro-benzenesulfonamide;
- N-[6-(2-Chloro-phenyl)-pyridin-2-yl]-2-trifluoromethyl-benzenesulfonamide;
- 3-Chloro-N-[6-(2-methoxy-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 20 5-Fluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- N-[2,3']Bipyridinyl-6-yl-3-chloro-2-methyl-benzenesulfonamide;
- 2,5-Difluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 25

- 3,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-N-(6-methoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Biphenyl-4-sulfonic acid (6-methoxy-pyridin-2-yl)-amide;
- 5-Fluoro-N-(6-methoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 5 Naphthalene-2-sulfonic acid (6-methoxy-pyridin-2-yl)-amide;
- 3-Chloro-N-(6-ethoxy-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Biphenyl-4-sulfonic acid (6-ethoxy-pyridin-2-yl)-amide;
- Naphthalene-2-sulfonic acid (6-ethoxy-pyridin-2-yl)-amide;
- 3-Chloro-N-(6-ethylsulfanyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 10 Biphenyl-4-sulfonic acid (6-ethylsulfanyl-pyridin-2-yl)-amide;
- Naphthalene-2-sulfonic acid (6-ethylsulfanyl-pyridin-2-yl)-amide;
- Naphthalene-2-sulfonic acid (6-ethanesulfonyl-pyridin-2-yl)-amide;
- 3-Chloro-2-methyl-N-[6-(2-oxo-pentyl)-pyridin-2-yl]-benzenesulfonamide;
- 2-[6-(Biphenyl-4-sulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide;
- 15 Biphenyl-4-sulfonic acid [6-(2-morpholin-4-yl-2-oxo-ethyl)-pyridin-2-yl]-amide;
- [6-(3-Chloro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester;
- [6-(5-Fluoro-2-methyl-benzenesulfonylamino)-pyridin-2-yl]-acetic acid methyl ester;
- 20 N,N-Diethyl-2-[6-(4'-fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-acetamide;
- 4-Fluoro-biphenyl-4-sulfonic acid [6-(2-morpholin-4-yl-2-oxo-ethyl)-pyridin-2-yl]-amide;
- 2-[6-(4-Fluoro-biphenyl-4-sulfonylamino)-pyridin-2-yl]-N-(2-methoxy-ethyl)-acetamide;

- 2-[6-(3,4-Dichloro-benzenesulfonylamino)-pyridin-2-yl]-N,N-diethyl-acetamide
- 5 2-[6-(3-Chloro-2-methyl-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide;
- 2-[6-(3,4-Dichloro-benzenesulfonylamino)-3-methyl-pyridin-2-yl]-N,N-diethyl-acetamide;
- 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 10 2,5-Difluoro-N-(6-methoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
- N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide;
- 5-Fluoro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 2,5-Difluoro-N-(6-hydroxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 15 Acetic acid 6-(2,5-difluoro-benzenesulfonylamino)-pyridin-2-ylmethyl ester;
- Naphthalene-2-sulfonic acid (6-hydroxymethyl-pyridin-2-yl)-amide;
- 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
- N-(6-Cyclopropylmethoxymethyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide;
- 20 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-4-methyl-benzenesulfonamide;
- 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- 25 2,5-Difluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;

- 5-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2-methyl-benzenesulfonamide;
- Piperidine-1-sulfonic acid (6-methoxymethyl-pyridin-2-yl)-amide;
- Piperidine-1-sulfonic acid (6-cyclopropylmethoxymethyl-pyridin-2-yl)-amide
- 5 3-Chloro-4-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-2-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide;
- 10 2,5-Difluoro-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide;
- 5-Fluoro-2-methyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 15 3,4-Dichloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 20 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- N-(5-Cyclopropyl-methoxymethyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide
- 4-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-3-methyl-benzenesulfonamide;
- 25 N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide;
- Piperidine-1-sulfonic acid (5-cyclopropyl-methoxymethyl-pyridin-2-yl)-amide;

- 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2,5-difluoro-benzenesulfonamide;
- 5 N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-5-fluoro-2-methyl-benzenesulfonamide;
- N-(5-Methoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 10 3-Chloro-N-(5-methoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- N-[5-(4-Fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethylbenzenesulfonamide;
- 3-Chloro-N-[5-(4-fluoro-benzyloxymethyl)-6-methyl-pyridin-2-yl]-2-methylbenzenesulfonamide;
- 15 N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethylbenzenesulfonamide;
- 3-Chloro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide;
- 5-Fluoro-2-methyl-N-{6-[(methyl-propyl-amino)-methyl]-pyridin-2-yl}-benzenesulfonamide;
- 20 3-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Naphthalene-1-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide;
- 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2,5-dimethyl-benzenesulfonamide;
- 25 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-3-methyl-benzenesulfonamide;
- N-(6-Cyclopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(6-cyclopropyl-pyridin-2-yl)-5-methylbenzenesulfonamide;

- Naphthalene-2-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide;
- N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 5 N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3,5-bis-trifluoromethyl-benzenesulfonamide;
- 4-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 4-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 10 4-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-2,5-dimethyl-benzenesulfonamide;
- 3-Trifluoromethyl-N-[6-(4-trifluoromethyl-phenoxy-methyl)-pyridin-2-yl]-benzenesulfonamide;
- 15 N-[5-(2-Fluoro-ethoxymethyl)-6-methyl-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- 20 N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- 25 N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Difluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;

- 3-Chloro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 2,4-Difluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 5 3-Chloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 10 4-Fluoro-N-[6-(3-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethoxy-benzenesulfonamide;
- 15 N-(6-Methoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(6-methoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Trifluoromethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 20 2,4-Dichloro-6-methyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- N-[6-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 25 2,4-Dichloro-6-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;

- N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- N-[6-(2-Cyclopropyl-ethoxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 5 2,4-Dichloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 2,4-Dichloro-5-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 10 2-Chloro-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-5-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-[6-(3-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 15 N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 20 N-[5-(2,2,2-Trifluoro-ethoxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-5-methyl-N-[5-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide;
- 25 3-Chloro-2-methyl-N-(5-pyrrolidin-1-yl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-morpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- N-(5-Benzyl-pyridin-2-yl)-3-chloro-2-methyl-benzenesulfonamide;

- 3-Chloro-2-methyl-N-(5-phenethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(6-methyl-5-phenethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-thiomorpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-{5-[2-(4-chloro-phenyl)-ethyl]-pyridin-2-yl}-6-methyl-
5 benzenesulfonamide;
- 3-Chloro-N-{5-[2-(4-methoxy-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-
benzenesulfonamide;
- 3-Chloro-N-{5-[2-(3-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-
benzenesulfonamide;
- 10 3-Chloro-2-methyl-N-{5-[2-(2-trifluoromethyl-phenyl)-ethyl]-pyridin-2-yl}-
benzenesulfonamide
- 3-Chloro-N-{5-[2-(4-fluoro-phenyl)-ethyl]-pyridin-2-yl}-2-methyl-
benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;
- 15 3-Chloro-N-{5-(2-chloro-phenoxy)-pyridin-2-yl}-2-methyl-benzenesulfonamide;
- 3-Chloro-N-{5-(4-fluoro-phenoxy)-pyridin-2-yl}-2-methyl-benzenesulfonamide;
- 2,4-Dichloro-6-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-6-methyl-
benzenesulfonamide;
- 20 2,4-Dichloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-6-methyl-
benzenesulfonamide;
- 3-Chloro-2-methyl-N-[5-(2-quinolin-2-yl-ethyl)-pyridin-2-yl]-
benzenesulfonamide;
- 2,4-Dichloro-6-methyl-N-[5-(2-quinolin-2-yl-ethyl)-pyridin-2-yl]-
25 benzenesulfonamide; and
- 3-Chloro-2-methyl-N-[5-(2-pyridin-2-yl-ethyl)-pyridin-2-yl]-benzenesulfonamide.

11. Compounds according to any one of claims 1 to 10 selected from
 - Biphenyl-4-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
 - 3-Chloro-2-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
 - 5 2,4-Dichloro-6-methyl-N-(6-propyl-pyridin-2-yl)-benzenesulfonamide;
 - 5-Chloro-naphthalene-2-sulfonic acid (6-propyl-pyridin-2-yl)-amide;
 - 3-Chloro-N-(6-isopropyl-pyridin-2-yl)-4-methyl-benzenesulfonamide;
 - N-(6-Isopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
 - 3-Chloro-2-methyl-N-[6-(2-trifluoromethyl-phenyl)-pyridin-2-yl]-
 - 10 benzenesulfonamide;
 - 2,5-Difluoro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-benzenesulfonamide;
 - 2,4-Dichloro-N-[6-(4-fluoro-2-methyl-phenyl)-pyridin-2-yl]-6-methyl-
 - benzenesulfonamide;
 - 3-Chloro-N-(6-methoxymethyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
 - 3-Chloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-
 - benzenesulfonamide;
 - 20 3,4-Dichloro-N-(6-cyclopropylmethoxymethyl-pyridin-2-yl)-benzenesulfonamide;
 - 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-benzenesulfonamide;
 - N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-
 - benzenesulfonamide;
 - 3-Chloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-2-methyl-
 - 25 benzenesulfonamide;

- 3-Chloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 3-Chloro-N-(5-methoxymethyl-6-methyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- 5 N-(5-Ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethylbenzenesulfonamide;
- 3-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2-methyl-benzenesulfonamide;
- Naphthalene-1-sulfonic acid (6-cyclopropyl-pyridin-2-yl)-amide;
- 4-Chloro-N-(6-cyclopropyl-pyridin-2-yl)-2,5-dimethyl-benzenesulfonamide;
- N-(6-Cyclopropyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 10 N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 4-Chloro-N-(5-ethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- 15 N-(5-Cyclopropylmethoxymethyl-pyridin-2-yl)-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-(5-cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-6-methyl-benzenesulfonamide;
- 20 N-(5-Cyclopropylmethoxymethyl-6-methyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 4-Fluoro-N-[6-(4-fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethyl-benzenesulfonamide;
- 25 N-[6-(4-Fluoro-benzyloxymethyl)-pyridin-2-yl]-3-trifluoromethoxy-benzenesulfonamide;

- N-(6-Methoxymethyl-pyridin-2-yl)-3-trifluoromethyl-benzenesulfonamide;
- 3-Trifluoromethyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-6-methyl-N-[6-(3,3,3-trifluoro-propoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 5 2,4-Dichloro-6-methyl-N-[6-(2,2,2-trifluoro-ethoxymethyl)-pyridin-2-yl]-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(2-cyclopropyl-ethoxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 10 2,4-Dichloro-N-[6-(3-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- N-[6-(4-Chloro-benzyloxymethyl)-pyridin-2-yl]-4-fluoro-3-trifluoromethyl-benzenesulfonamide;
- 2,4-Dichloro-N-[6-(4-chloro-benzyloxymethyl)-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 15 3-Chloro-2-methyl-N-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-pyrrolidin-1-yl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-morpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- 20 N-(5-Benzyl-pyridin-2-yl)-3-chloro-2-methyl-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(6-methyl-5-phenethyl-pyridin-2-yl)-benzenesulfonamide;
- 3-Chloro-2-methyl-N-(5-thiomorpholin-4-yl-pyridin-2-yl)-benzenesulfonamide;
- 2,4-Dichloro-N-[5-[2-(4-chloro-phenyl)-ethyl]-pyridin-2-yl]-6-methyl-benzenesulfonamide;
- 25 3-Chloro-N-[5-[2-(3-fluoro-phenyl)-ethyl]-pyridin-2-yl]-2-methyl-benzenesulfonamide;

3-Chloro-N-[5-[2-(4-fluoro-phenyl)-ethyl]-pyridin-2-yl]-2-methyl-benzenesulfonamide;

3-Chloro-2-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;

3-Chloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-2-methyl-benzenesulfonamide;

5 3-Chloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-2-methyl-benzenesulfonamide;

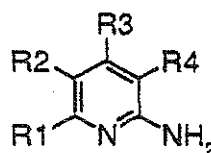
2,4-Dichloro-6-methyl-N-(5-phenoxy-pyridin-2-yl)-benzenesulfonamide;

2,4-Dichloro-N-[5-(2-chloro-phenoxy)-pyridin-2-yl]-6-methyl-benzenesulfonamide; and

10 2,4-Dichloro-N-[5-(4-fluoro-phenoxy)-pyridin-2-yl]-6-methyl-benzenesulfonamide.

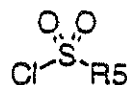
12. A process for the preparation of a compound according to any one of claims 1 to 11 comprising

a) reaction of a compound according to formula

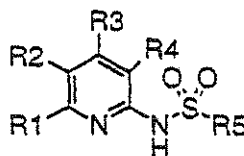


II

15 in the presence of a compound according to formula



in order to obtain a compound of the formula

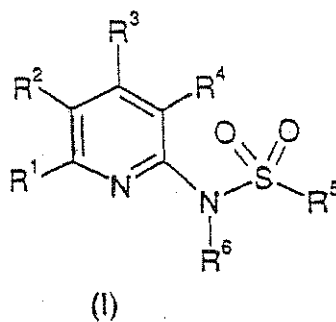


Ia

;

and optionally

b) further reaction in the presence of a compound of the formula R^6-X in order to obtain a compound of the formula



- 5 wherein R^1 to R^6 are defined as in claim 1 and X is Cl, Br or I.
13. Compounds according to any one of claims 1 to 11 for use as therapeutically active substance.
14. Compounds according to any one of claims 1 to 11 for the preparation of medicaments for the prophylaxis and therapy of illnesses which are caused by disorders associated with the enzyme 11beta-hydroxysteroid dehydrogenase 1.
- 10 15. A pharmaceutical composition comprising a compound in accordance with any one of claims 1 to 11 and a therapeutically inert carrier.
16. The use of a compound according to any one of claims 1 to 11 for the preparation of medicaments for the treatment and prophylaxis of diabetes, obesity, eating disorders, dyslipidemiae and hypertension.
- 15 17. The use of a compound according to any one of claims 1 to 11 for the preparation of medicaments for the treatment and prophylaxis of diabetes Type II.
18. A compound according to any one of claims 1 to 11, when manufactured according to a process of claim 12.