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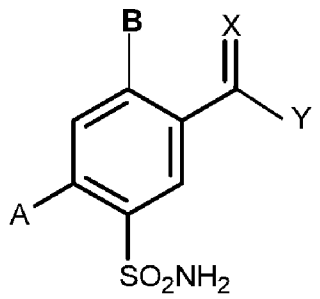
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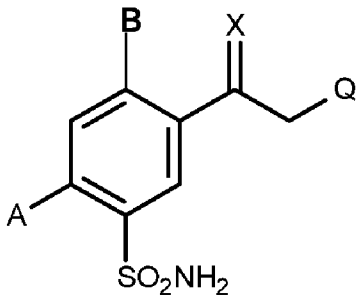
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[Continued on next page]

(54) Title: SELECTIVE INHIBITORS OF CARBONIC ANHYDRASE



(I)



(II)

(57) Abstract: Invention is related to novel compounds – benzenesulfonamides of general formulas (I) and (II). The compounds can be used in biomedicine as active ingredients in pharmaceutical formulations, because they inhibit enzymes which participate in disease progression. Acknowledgements: This research was funded by the European Social Fund under the Global Grant measure (no. VP1-3.1.-SMM-07-K-02-009).

WO 2017/017505 A1

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SELECTIVE INHIBITORS OF CARBONIC ANHYDRASE

Field of the Invention

This invention describes novel aromatic sulfonamide derivatives, potentially useful in biomedicine as active ingredients of pharmaceutical preparations because of their ability to selectively inhibit enzymes participating in disease progression. The enzymes in this description of the invention include different metal (mostly zinc) ion-possessing proteins, such as carbonic anhydrases, matrix metalloproteinases and histone deacetylases.

Background of the Invention

Carbonic anhydrases (CAs) are enzymes which catalyze reversible reaction of carbon dioxide hydration into bicarbonate and protons. CAs participate in essential physiological processes related to respiration, CO_2/bicarbonate transport between lungs and metabolizing tissues, pH and CO_2 homeostasis, electrolyte secretion in many tissues/organs, etc. There are 15 carbonic anhydrase isozymes (isoforms) genomically identified in humans – 12 contain zinc atom and are catalytically active while the remaining 3 (VIII, X and XI) are inactive and are called CA-related proteins. The 12 active isoforms have different cellular localization – 5 of them are cytosolic (I, II, III, VII and XIII), 4 – membrane bound (IV, IX, XII and XIV), 2 mitochondrial (VA and VB) and 1 – secreted (VI). The major class of CA inhibitors is aromatic compounds possessing sulfonamide group. Sulfonamide-class CA inhibitors are widely used as therapeutic agents for treatment of various diseases, since CA isozymes are widely distributed in cells, tissues and organs where they are responsible for essential physiological functions.

Another protein class is matrix and other metalloproteinases (MMPs), proteolytic enzymes, which are characterized by increased expression during various steps of cancer progression or histone deacetylases (HDACs), gene expression modifying enzymes. Sulfonamide inhibitors have a potencial to be applied for the inhibition of MMPs or HDACs when they contain zinc in the active site.

Regulation of CA catalytic activity through inhibition or activation proposes a therapeutic perspective. There are several diseases with the characteristic dis-balance of the inter-conversion between carbonic dioxide and bicarbonate resulting in pH alteration, disturbance of ion transport, fluid secretion, etc. CA inhibitors have been used as antiglaucoma agents, for treatment of diseases such as retinal and cerebral edema (inhibitors of CA I) (Gao, B.B. et al. (2007), *Nat. Med.* 13, 181), altitude sickness (inhibitors of CA II) (Basnyat, B. et al. (2003), *High Alt. Med. Biol.* 4, 45), epilepsy (inhibitors of CA II, CA VII, CA XIV) (Hen, N. et al. (2011), *J. Med. Chem.* 54, 3977). Several novel inhibitors of CA VA, CA VB, CA XII and CA IX are undergoing clinical investigation as anti-obesity and antitumor drugs or diagnostic tools (De Simone, G. et al. (2008), *Curr. Pharm. Des.* 14, 655; Guler, O. O. et al. (2010), *Curr. Med. Chem.* 17, 1516). CA inhibitors suppress the growth of leukemia, melanoma, lung, ovarian, colon, kidney, prostate, breast, and CNS cancer cells (Supuran, C. T. et al. (2000), *Eur. J. Med. Chem.* 35, 867; Guler, O.O. et al. (2010), *Curr. Med. Chem.* 17, 1516; De

Simone, G. et al. (2010), *Biochim. Biophys. Acta*, 1804, 404; Battke, C. et al. (2011), *Cancer Immunol. Immunother.* 60, 649). The use of CA IX-specific inhibitor set for detection and treatment of pre-cancer and neoplastic state (WO 2004048544). There are also reports about CA XIII involvement in the sperm mobility processes (likely together with CA XIV). Inhibition of these two CAs may be used as contraceptive agents (Lehtonen, I. et al. (2004), *J. Biol. Chem.* 279, 2791). It was established that CA inhibitors are useful diuretics for the treatment of patients who suffer from edema and heart deficiency. Inhibition of the CA II activity could be useful for the diminishment of bone resorption. It was shown in prokaryotes that CAs are essential for respiration, carbon dioxide transport and photosynthesis. Therefore it was hypothesized that CA inhibitors could be used as antibiotics. Ethoxzolamide was even used for the treatment of meningitis. It was noticed that CA inhibitors possess an antimallarial activity. (Merlin, C. et al. (2003), *J. Bacteriol.* 185, 6415; Pastorekova, S. et al. (2004), *J. Enzyme Inhib. Med. Chem.* 19, 199; WO 2005107470).

Two membrane-associated CA IX and CA XII are related to cancer development. The CA IX and CA XII are predominantly expressed in tumor cells and show a limited expression in normal tissues and are promising targets to develop anticancer drugs.

It has been shown that CA inhibitors suppress the growth of lung, renal, prostate, colon, breast, ovarian, CNS, leukemia and melanoma cancer cells (Supuran, C. T. et al, (2000*), Eur. J. Med. Chem.* 35, 867; Parkkila, S. et al.(2000), *Proc. Natl. Acad. Sci. USA.* 95, 2220; Pastorekova, S. et al. (2015), *Sem. Cancer Biol.* 31, 52; Ilie, M. I. et al. (2011), *Int. J. Cancer.* 128, 1614; Watson, P. H. et al. (2003), *Br. J. Cancer.* 88, 1065).

A number of membrane-impermeant aromatic sulfonamide derivatives bearing a pyridinium residue have been presented (WO2004048544) that specifically bind to the membrane-bound CA IX. A class of strong CA IX inhibitors bearing fluorescent tails as medicaments and diagnostic tools were disclosed in WO2006137092. Nitro-derivatives of aromatic sulfonamides as CA inhibitors having pharmacological activity were described for cancer treatment in WO2008071421. In WO2008124703, cell impermeable radioactively labeled aromatic sulfonamides having high affinity for CA IX, as positron emission tomography imaging agents were presented. Aromatic sulfonamide-based metal chelate complexes for diagnostic imaging were disclosed in WO2009089383 as CA IX inhibitors. Aromatic sulfamate and sulfamide derivatives have been proposed in WO2011098610 as inhibitors which are specific for CA IX and/or CA XII. Coumarin and thiocoumarin derivatives as specific inhibitors for CA IX and CA XII over CA I and II were disclosed in WO2012070024. A number of aromatic sulfonamide, sulfamate and sulfamide comprising a nitroimidazole moiety were presented as CA IX inhibitors for chemotherapy and radiotherapy in WO2012087115. Tetraline sulfonamide derivatives as selective inhibitors for CA IX and XII over CA I and II were described in WO2012175654. Derivatives of boron-containing clusters have been proposed in WO2013060307 as specific inhibitors as CA IX. Aromatic sulfonamide-based metal complexes of poly(carboxyl)amine were described in WO2013103813 as radiolabeled ligands that specifically bind to the CA IX. In

WO2015025283, heterocycle or phosphinate having sulfonamide, sulfamate or sulfamide groups and substituted with a nitroimidazole moiety are disclosed as CA IX inhibitors.

There is a need for new selective inhibitors for CA IX and CA XII for use in pharmaceutical applications including cancer imaging, diagnosis and therapy (treatment).

The CA VA and VB are located in the mitochondria. These isozymes are involved in various physiological processes including insulin secretion, lipogenesis, gluconeogenesis, and ureagenesis. Several studies have provided evidence that inhibition of CA VA and VB can reduce lipogenesis (Lynch, C. J. et al. (1995), *Biochem. J.* 310, 197; Hazen, S.A. et al.(1996), *FASEB J.* 10, 481).

There are no patents for the specific inhibitors of CA V (both CA VA and CA VB). There is a need for new selective inhibitors for CA VA and VB for use in pharmaceutical applications.

CA XIV is one of the last discovered human CA isoforms. CA XIV has been observed on neuronal membranes and axons in the mouse and human brain (Parkkila, S et al. (2001), *Proc. Natl. Acad. Sci. USA*. 98, 1918). There are no patents for the specific inhibitors of CA XIV. However, CA XIV is involved in different physiological processes and its expression has been described in human brain, heart, skeletal muscle, kidney, and liver, making this isoform a putative target for medical applications. Intra/extracellular acid–base balance changes have importance in regulating neuronal excitability and pH regulation is principally done by CA (Shah, G. N. et al.(2005), *Proc. Natl. Acad. Sci. USA*. 102, 16771). CA inhibitors are known to exhibit anticonvulsant properties and some of these inhibitors are clinically used to treat epilepsy (Thiry, A. et al. (2007), *Curr. Top. Med. Chem.* 7, 855). There is a need for new selective inhibitors for CA XIV for use in pharmaceutical applications.

Among above mentioned aromatic sulfonamide with CA inhibitory properties their design is created by *tail and/or ring approaches* (Supuran, C.T. et al. (2003), *Med. Res. Rev.*, 23, 146). However, prior inventors are mainly focusing by designing selective inhibitors bearing only one tail-group.

To date the idea to use two tails to obtain better selectivity has not been realized. Aromatic sulfonamides with two tails have been explored as CA inhibitors in only one work (Vernier, W. F. et al. (2010), *Bioorg. Med. Chem.* 18, 3307).

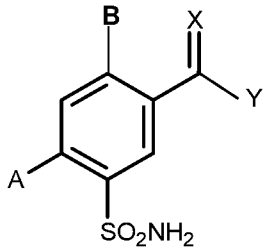
2-chloro-benzenesulfonamides containing two tails were described as diuretics in US3567746, US2910488, US3291824, DE2031067 and NL6607737; as diuretics containing (2-furylmethyl)amino group in US4563467, US2005059655, and WO2006055542; as compounds comprising (2-furylmethyl)amino group (WO2010085352), or not comprising (2-furylmethyl)amino group (WO2012018635) for the treatment and/or prophylaxis of conditions that involve the $Na^+K^+Cl^-$ co-transporter or $GABA_A$ receptor; as aquaporin modulators in WO2008052190; Several analogs of furosemide are mentioned in patents as inhibitor of the adenosine A1 receptor in US6649600; for the treatment or prophylaxis of CCR5-related diseases and disorders in WO2004054974. Therapeutic amines conjugated to arylsulfonamides (analogs of furosemide) with an *in vivo* cleavable chemical linker for the treatment of psychiatric, neurologic and metabolic disorders are disclosed in WO2007079470.

In this invention we focus on CA IX and CA XII selective inhibitors (over CA I and CA II) and inhibitors that are selective towards CA VA and CA XIV. In order to achieve those goals, the inhibitors bear two tails. The compounds of such type based on the selective inhibition of tumor-associated CA IX or CA XII may be particularly preferred specific inhibitors that could be used in new anticancer therapies and in the diagnostic/prognostic methods of this invention.

Despite the fact that a large number of different sulfonamides have been synthesized to date, the available pharmaceutical agents created on the basis of these sulfonamides have a number of problems, primarily – the non-selective inhibition of all CAs throughout the human body. This results in various unexpected side effects and toxicity. Especially toxic are systemic inhibitors. They cause electrolyte disbalance, drowsiness, head-ache, depression, apathy, malaise, irritability, nervousness, fatigue, gut irritability, anorexia, nausea, thirst, obstruction, muscle weakness, tremor, hyper- and hypoglycemia, kidney pain, disuria, bone marrow depression, metabolic acidosis and other. Therefore, the creation of isoform-specific or organ-selective sulfonamide inhibitors is still an important task. Our synthesized CA IX, CA XII, CA VA and CA XIV – selective inhibitors could be developed into drugs that would be useful in the treatment of above mentioned diseases.

Summary of the Invention

This invention describes new compounds with general structural formula (I)



(I)

where

A is F, Cl, Br, I, NO_2, OH, SH, NH_2, $NHCH_3$, $N(CH_3)_2$, $NHNH_2$, CN, SCH_3, $S(O)CH_3$, SO_2CH_3, CH_3, $COCH_3$, $C(O)NH_2$, C(O)OH, OCH_3, OCF_3, OCF_2H, $OCFH_2$, CF_3, CF_2H, CFH_2, $Si(CH_3)_3$, $B(OH)_3$,

B is OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $NHNHR^1$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, $S(O)_2NHR^1$, $S(O)_2N(R^1)_2$, $NHS(O)_2R^1$, $NR^1S(O)_2R^1$, $NH(SO)_2NHR^1$, $NHS(O)_2N(R^1)_2$, $NR^1S(O)_2NHR^1$, $NR^1S(O)_2N(R^1)_2$, $C(O)NHSO_2R^1$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$,

B is Cl, when X is O and Y is $O(CH_2)_2OCH_3$, $NH(CH_2)_3OH$, $NH(CH_2)_3OC(O)CH_3$, $NH(CH_2)_3C(O)OH$, $NH(CH_2)_3C(O)OCH_3$, $N(CH_2CH_2)_2O$, NH-cyclohexyl, $NHCH_2Ph$,

B is Br, when X is O and Y is OCH_3, $NH(CH_2)_2OH$, $NH(CH_2)_3CH_3$,

X is O, S, NH, NR^1,

Y is OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHNOR^1$, $C(O)NHSO_2R^1$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$,

R^1 is R^2, R^3, R^4, R^5, R^6, R^7,

R^2 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^3 is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^4 is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^5 is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

R^5 is R^8, OH, OR^8, SH, SR^8, $S(O)R^8$, SO_2R^8, $C(O)R^8$, $C(O)OR^8$, $OC(O)R^8$, NHR^8, $N(R^8)_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHC(O)OR^8$, $NR^8C(O)OR^8$, $NHC(O)NH_2$, $NHC(O)NHR^8$, $NHC(O)N(R^8)_2$, $NR^8C(O)NHR^8$, $NR^8C(O)N(R^8)_2$, SO_2NHR^8, $SO_2N(R^8)_2$, $NHSO_2R^8$, $NR^8SO_2R^8$, $NHSO_2NHR^8$, $NHSO_2N(R^8)_2$, $NR^8SO_2NHR^8$, $NR^8SO_2N(R^8)_2$, $C(O)NHNOH$, $C(O)NHNOR^8$, $C(O)NHSO_2R^8$, $C(NH)NH_2$, $C(NH)NHR^8$, $C(NH)N(R^8)_2$, $NHSO_2NHR^8$, $NHSO_2N(CH_3)R^8$, $N(CH_3)SO_2N(CH_3)R^8$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, $C(O)OH$, $C(O)NH_2$,

R^8 is R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14},

R^9 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{10} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{11} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{12} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{13} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{14} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^6 is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

R^6 is R^{15}, OH, OR^{15}, SH, SR^{15}, $S(O)R^{15}$, SO_2R^{15}, $C(O)R^{15}$, $C(O)OR^{15}$, $OC(O)R^{15}$, NHR^{15}, $N(R^{15})_2$, $C(O)NHR^{15}$, $C(O)N(R^{15})_2$, $NHC(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NHC(O)OR^{15}$, $NR^{15}C(O)OR^{15}$, $NHC(O)NH_2$, $NHC(O)NHR^{15}$, $NHC(O)N(R^{15})_2$, $NR^{15}C(O)NHR^{15}$, $NR^{15}C(O)N(R^{15})_2$, SO_2NHR^{15}, $SO_2N(R^{15})_2$, $NHSO_2R^{15}$, $NR^{15}SO_2R^{15}$, $NHSO_2NHR^{15}$, $NHSO_2N(R^{15})_2$, $NR^{15}SO_2NHR^{15}$, $NR^{15}SO_2N(R^{15})_2$, C(O)NHNOH, $C(O)NHNOR^{15}$, $C(O)NHSO_2R^{15}$, $C(NH)NH_2$, $C(NH)NHR^{15}$, $C(NH)N(R^{15})_2$, $NHSO_2NHR^{15}$, $NHSO_2N(CH_3)R^{15}$, $N(CH_3)SO_2N(CH_3)R^{15}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{15} is R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21},

R^{16} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{17} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{18} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{19} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{20} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{21} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^7 is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

R^7 is R^{22}, OH, OR^{22}, SH, SR^{22}, $S(O)R^{22}$, SO_2R^{22}, $C(O)R^{22}$, $C(O)OR^{22}$, $OC(O)R^{22}$, NHR^{22}, $N(R^{22})_2$, $C(O)NHR^{22}$, $C(O)N(R^{22})_2$, $NHC(O)R^{22}$, $NR^{22}C(O)R^{22}$, $NHC(O)OR^{22}$, $NR^{22}C(O)OR^{22}$, $NHC(O)NH_2$, $NHC(O)NHR^{22}$, $NHC(O)N(R^{22})_2$, $NR^{22}C(O)NHR^{22}$, $NR^{22}C(O)N(R^{22})_2$, SO_2NHR^{22}, $SO_2N(R^{22})_2$, $NHSO_2R^{22}$, $NR^{22}SO_2R^{22}$, $NHSO_2NHR^{22}$, $NHSO_2N(R^{22})_2$, $NR^{22}SO_2NHR^{22}$, $NR^{22}SO_2N(R^{22})_2$, C(O)NHNOH, $C(O)NHNOR^{22}$, $C(O)NHSO_2R^{22}$, $C(NH)NH_2$, $C(NH)NHR^{22}$, $C(NH)N(R^{22})_2$, $NHSO_2NHR^{22}$, $NHSO_2N(CH_3)R^{22}$, $N(CH_3)SO_2N(CH_3)R^{22}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{22} is R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28},

R^{23} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{24} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{25} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{26} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{27} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{28} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

with the proviso that B is not $(CH_2)_nH$, $(CH_2)_nCl$, $O(CH_2)_nH$, $NH(CH_2)_nH$, $N((CH_2)_nH)_2$ (n=1-4),

with the proviso that B is not (2-furanylmethyl)amino, acetylsulfanyl, acetoxy, acetamido,

with the proviso that when A is Cl and B is benzylamino then Y is not methoxy, 4-sulfamoylbenzylamino, ethylamino, methoxyamino, isopropoxyamino,

with the proviso that when A is Cl and Y is methoxy then B is not tosyloxy, 2-hydroxypropanamido, pyrrole-1-carbonylamino, (2-pyrrol-2-yl-ethylamino), 2-chloroacetamido,

with the proviso that when A is Cl and Y is ethoxy then B is not ethoxycarbonilamino, 4-isopropylcarbamoylamino,

with the proviso that when A is Cl and Y is 2-tolylamino then B is not 2-(dimethylamino)ethylamino, benzylamino, 2-hydroxyethylamino,

with the proviso that when A is Cl and Y is 2-(4-sulfamoylphenyl)ethylamino then B is not butylamino, cyclohexylamino.

The compounds according to formula I described herein exclude these compounds:

4-chloro-*N*-methoxy-5-sulfamoyl-2-(2-thienylmethylamino)benzamide;

methyl 4-amino-2-(4-tolylsulfonyloxy)-5-sulfamoyl-benzoate;

ethyl 2-(benzylamino)-4-fluoro-5-sulfamoyl-benzoate;

4-(benzylamino)-2-chloro-5-[4-[2-[(2R,4R,6S)-2-isopropyl-2,6-dimethyl-4-(2-methylbenzimidazol-1-yl)-1-piperidyl]ethyl]-4-phenyl-piperidine-1-carbonyl]benzenesulfonamide;

ethyl 2-[[(5S)-5-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]-(2,2,2-trichloroethoxycarbonyl)amino]propanoyl]amino]-6-ethoxy-6-oxo-hexyl]amino]-4-chloro-5-sulfamoyl-benzoate;

(2R)-2-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]amino]propanoyl]amino]-6-(5-chloro-2-ethoxycarbonyl-4-sulfamoyl-anilino)hexanoic acid;

ethyl 2-[[(5R)-5-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]amino]propanoyl]amino]-6-ethoxy-6-oxo-hexyl]amino]-4-chloro-5-sulfamoyl-benzoate;

ethyl 2-[[(5R)-5-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]amino]propanoyl]amino]-6-tert-butoxy-6-oxo-hexyl]amino]-4-chloro-5-sulfamoyl-benzoate.

Examples of the invented compouds of formula I are selected compounds from the group comprising:

2,4-dichloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4**),

methyl 4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **7**),

2,4-dichloro-5-(morpholine-4-carbonyl)benzenesulfonamide (compound **8**),

2,4-dichloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **9**),

N-benzyl-2,4-dichloro-5-sulfamoyl-benzamide (compound **10**),

2,4-dibromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **11**),

2,4-dibromo-*N*-butyl-5-sulfamoyl-benzamide (compound **12**),

3-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]propyl acetate (compound **13**),

2-methoxyethyl 2,4-dichloro-5-sulfamoyl-benzoate (compound **15**),

methyl 2,4-dibromo-5-sulfamoyl-benzoate (compound **16**),

2-benzylsulfinyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **44**),

2-(benzenesulfinyl)-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **45**),

4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoic acid (compound **46**),

4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoic acid (compound **47**),

4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoic acid (compound **48**),

4-chloro-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **3a**),

4-chloro-*N*-(3-hydroxypropyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **4a**),
N-butyl-4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **5a**),
4-chloro-*N*-(2-methoxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **6a**),
2-chloro-5-(morpholine-4-carbonyl)-4-phenylsulfanyl-benzenesulfonamide (compound **8a**),
4-chloro-*N*-cyclohexyl-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **9a**),
N-benzyl-4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **10a**),
4-bromo-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **11a**),
4-bromo-*N*-butyl-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **12a**),
3-[(4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoyl)amino]propyl acetate (compound **13a**),
methyl 4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoate (compound **14a**),
2-methoxyethyl 4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoate (compound **15a**),
methyl 4-bromo-2-phenylsulfanyl-5-sulfamoyl-benzoate (compound **16a**),
2-(benzenesulfonyl)-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **33a**),
2-(benzenesulfonyl)-4-chloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **34a**),
2-(benzenesulfonyl)-*N*-butyl-4-chloro-5-sulfamoyl-benzamide (compound **35a**),
2-(benzenesulfonyl)-4-chloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **36a**),
2-(benzenesulfonyl)-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **38a**),
2-(benzenesulfonyl)-*N*-benzyl-4-chloro-5-sulfamoyl-benzamide (compound **39a**),
2-(benzenesulfonyl)-4-bromo-*N*-butyl-5-sulfamoyl-benzamide (compound **41a**),
methyl 2-(benzenesulfonyl)-4-chloro-5-sulfamoyl-benzoate (compound **42a**),
methyl 2-(benzenesulfonyl)-4-bromo-5-sulfamoyl-benzoate (compound **43a**),
4-chloro-2-cyclohexylsulfanyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3b**),
4-chloro-2-cyclohexylsulfanyl-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4b**),
N-butyl-4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **5b**),
4-chloro-2-cyclohexylsulfanyl-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6b**),
methyl 4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoate (compound **7b**),
4-chloro-*N*-cyclohexyl-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **9b**),
N-benzyl-4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **10b**),
4-bromo-2-cyclohexylsulfanyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **11b**),
4-bromo-*N*-butyl-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **12b**),
methyl 4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoate (compound **14b**),
methyl 4-bromo-2-cyclohexylsulfanyl-5-sulfamoyl-benzoate (compound **16b**),
4-chloro-2-cyclohexylsulfonyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **33b**),
4-chloro-2-cyclohexylsulfonyl-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **34b**),
N-butyl-4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **35b**),
4-chloro-2-cyclohexylsulfonyl-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **36b**),

methyl 4-[(4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzoyl)amino]butanoate (compound **37b**),

4-chloro-*N*-cyclohexyl-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **38b**),

N-benzyl-4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **39b**),

4-bromo-2-cyclohexylsulfonyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **40b**),

4-bromo-*N*-butyl-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **41b**)

methyl 4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzoate (compound **42b**),

methyl 4-bromo-2-cyclohexylsulfonyl-5-sulfamoyl-benzoate (compound **43b**),

2-benzylsulfanyl-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3c**),

2-benzylsulfanyl-*N*-butyl-4-chloro-5-sulfamoyl-benzamide (compound **5c**),

methyl 4-[(2-benzylsulfanyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **7c**),

2-benzylsulfanyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **9c**),

2-benzylsulfanyl-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **11c**),

2-benzylsulfanyl-4-bromo-*N*-butyl-5-sulfamoyl-benzamide (compound **12c**),

methyl 2-benzylsulfanyl-4-chloro-5-sulfamoyl-benzoate (compound **14c**),

2-benzylsulfonyl-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **33c**),

methyl 4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **37c**),

2-benzylsulfonyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **38c**),

2-benzylsulfonyl-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **40c**),

methyl 2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoate (compound **42c**),

N-butyl-4-chloro-2-phenethylsulfanyl-5-sulfamoyl-benzamide (compound **5d**),

4-bromo-*N*-(2-hydroxyethyl)-2-phenethylsulfanyl-5-sulfamoyl-benzamide (compound **11d**),

4-bromo-*N*-butyl-2-phenethylsulfanyl-5-sulfamoyl-benzamide (compound **12d**),

methyl 4-chloro-2-phenethylsulfanyl-5-sulfamoyl-benzoate (compound **14d**),

4-chloro-*N*-cyclohexyl-2-(2-hydroxyethylsulfanyl)-5-sulfamoyl-benzamide (compound **9e**),

4-bromo-*N*-butyl-2-(2-hydroxyethylsulfanyl)-5-sulfamoyl-benzamide (compound **12e**),

4-chloro-*N*-cyclohexyl-2-(2-hydroxyethylsulfonyl)-5-sulfamoyl-benzamide (compound **38e**),

4-chloro-2-(cyclohexylamino)-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3f**),

4-chloro-2-(cyclohexylamino)-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4f**),

N-butyl-4-chloro-2-(cyclohexylamino)-5-sulfamoyl-benzamide (compound **5f**),

4-chloro-2-(cyclohexylamino)-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6f**),

4-bromo-*N*-butyl-2-(cyclohexylamino)-5-sulfamoyl-benzamide (compound **12f**),

methyl 4-chloro-2-(cyclohexylamino)-5-sulfamoyl-benzoate (compound **14f**),

2-(benzylamino)-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3g**),

2-(benzylamino)-4-chloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4g**),

2-(benzylamino)-*N*-butyl-4-chloro-5-sulfamoyl-benzamide (compound **5g**),

2-(benzylamino)-4-chloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6g**),

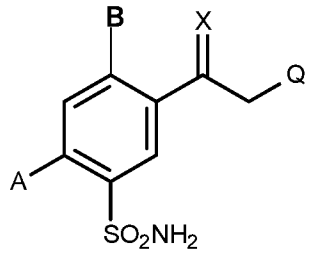
N-benzyl-2-(benzylamino)-4-chloro-5-sulfamoyl-benzamide (compound **10g**),

2-(benzylamino)-4-bromo-*N*-butyl-5-sulfamoyl-benzamide (compound **12g**),

methyl 2-(benzylamino)-4-chloro-5-sulfamoyl-benzoate (compound **14g**),

N-butyl-4-chloro-2-(cyclooctylamino)-5-sulfamoyl-benzamide (compound **5h**).

This invention also describes new compounds with general structural formula (II)



(II)

where

A is F, Cl, Br, I, NO_2, OH, SH, NH_2, NH_2NH_2, CN, SCH_3, $S(O)CH_3$, SO_2CH_3, CH_3, $COCH_3$, $C(O)NH_2$, C(O)OH, OCH_3, OCF_3, OCF_2H, $OCFH_2$, CF_3, CF_2H, CFH_2, $Si(CH_3)_3$, $B(OH)_3$,

B is H, R^1, OH, OR^1, SH, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $NHNH_2$, $NHNHR^1$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, C(O)NHNOH, $C(O)NHNOR^1$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

X is O, S, NH, NR^1,

Q is R^1, OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, CN, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^1 is R^2, R^3, R^4, R^5, R^6, R^7,

R^2 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^3 is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^4 is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^5 is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

R^5 is R^8, OH, OR^8, SH, SR^8, $S(O)R^8$, SO_2R^8, $C(O)R^8$, $C(O)OR^8$, $OC(O)R^8$, NHR^8, $N(R^8)_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHC(O)OR^8$, $NR^8C(O)OR^8$, $NHC(O)NH_2$, $NHC(O)NHR^8$, $NHC(O)N(R^8)_2$, $NR^8C(O)NHR^8$, $NR^8C(O)N(R^8)_2$, SO_2NHR^8, $SO_2N(R^8)_2$, $NHSO_2R^8$, $NR^8SO_2R^8$, $NHSO_2NHR^8$, $NHSO_2N(R^8)_2$, $NR^8SO_2NHR^8$, $NR^8SO_2N(R^8)_2$, C(O)NHNOH, $C(O)NHNOR^8$, $C(O)NHSO_2R^8$, $C(NH)NH_2$, $C(NH)NHR^8$, $C(NH)N(R^8)_2$, $NHSO_2NHR^8$, $NHSO_2N(CH_3)R^8$, $N(CH_3)SO_2N(CH_3)R^8$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^8 is R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14},

R^9 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{10} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{11} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{12} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{13} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{14} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^6 is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

R^6 is R^{15}, OH, OR^{15}, SH, SR^{15}, $S(O)R^{15}$, SO_2R^{15}, $C(O)R^{15}$, $C(O)OR^{15}$, $OC(O)R^{15}$, NHR^{15}, $N(R^{15})_2$, $C(O)NHR^{15}$, $C(O)N(R^{15})_2$, $NHC(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NHC(O)OR^{15}$, $NR^{15}C(O)OR^{15}$, $NHC(O)NH_2$, $NHC(O)NHR^{15}$, $NHC(O)N(R^{15})_2$, $NR^{15}C(O)NHR^{15}$, $NR^{15}C(O)N(R^{15})_2$, SO_2NHR^{15}, $SO_2N(R^{15})_2$, $NHSO_2R^{15}$, $NR^{15}SO_2R^{15}$, $NHSO_2NHR^{15}$, $NHSO_2N(R^{15})_2$, $NR^{15}SO_2NHR^{15}$, $NR^{15}SO_2N(R^{15})_2$, C(O)NHNOH, $C(O)NHNOR^{15}$, $C(O)NHSO_2R^{15}$, $C(NH)NH_2$, $C(NH)NHR^{15}$, $C(NH)N(R^{15})_2$, $NHSO_2NHR^{15}$, $NHSO_2N(CH_3)R^{15}$, $N(CH_3)SO_2N(CH_3)R^{15}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{15} is R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21},

R^{16} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{17} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{18} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{19} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{20} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{21} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^7 is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

R^7 is R^{22}, OH, OR^{22}, SH, SR^{22}, $S(O)R^{22}$, SO_2R^{22}, $C(O)R^{22}$, $C(O)OR^{22}$, $OC(O)R^{22}$, NHR^{22}, $N(R^{22})_2$, $C(O)NHR^{22}$, $C(O)N(R^{22})_2$, $NHC(O)R^{22}$, $NR^{22}C(O)R^{22}$, $NHC(O)OR^{22}$, $NR^{22}C(O)OR^{22}$, $NHC(O)NH_2$, $NHC(O)NHR^{22}$, $NHC(O)N(R^{22})_2$, $NR^{22}C(O)NHR^{22}$, $NR^{22}C(O)N(R^{22})_2$, SO_2NHR^{22}, $SO_2N(R^{22})_2$, $NHSO_2R^{22}$, $NR^{22}SO_2R^{22}$, $NHSO_2NHR^{22}$, $NHSO_2N(R^{22})_2$, $NR^{22}SO_2NHR^{22}$, $NR^{22}SO_2N(R^{22})_2$, C(O)NHNOH, $C(O)NHNOR^{22}$, $C(O)NHSO_2R^{22}$, $C(NH)NH_2$, $C(NH)NHR^{22}$, $C(NH)N(R^{22})_2$, $NHSO_2NHR^{22}$, $NHSO_2N(CH_3)R^{22}$, $N(CH_3)SO_2N(CH_3)R^{22}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{22} is R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28},

R^{23} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{24} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{25} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{26} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

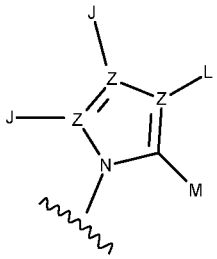
R^{27} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{28} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I.

In the particular embodiment of this invention are the compounds according to formula II, wherein Q is:



where

Z is independently C or N,

J is H when Z is C, or J is absent when Z is N,

L and M is each independently H, R^1, OH, OR^1, SH, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $NHNH_2$, $NHNHR^1$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, C(O)NHNOH, $C(O)NHNOR^1$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$

or the groups L and M together form aryl, heteroaryl, cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl ring, each of which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane and each of rings is unsubstituted or substituted by one or more identical or different groups selected from

R^1, OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^1 is defined as in the Summary of Invention for a compound of formula II.

with the proviso that when B is H then Q is not CH_2COOR^1, CH_2CONHR^1 or $CH_2CON(CH_3)R^1$,

with the proviso that when B is H then Q is not $(CH_2)_nH$, $(CH_2)_nNHR^1$, $(CH_2)_nN(R^1)_2$, $(CH_2)_nCl$ (n=2-4),

with the proviso that when B is H then Q is not benzylamino or *N*-substituted-benzylamino, methyl, phenylsulfanyl, acetylsulfanyl.

The compounds according to formula II described herein exclude these compounds:

5-(3-benzyl-4-methyl-pentanoyl)-2-hydroxy-benzenesulfonamide;

5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(2-methylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-methylsulfanylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-ethylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-isopropylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-[2-(hydroxymethyl)benzimidazol-1-yl]acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-propylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-isobutylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

5-[2-(2-butylbenzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

5-[2-(2-benzylbenzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-[2-(morpholinomethyl)benzimidazol-1-yl]acetyl]benzenesulfonamide;

2-chloro-5-(2-pyrimidin-2-ylsulfanylacetyl)benzenesulfonamide;

2-chloro-5-[2-(5-ethylpyrimidin-2-yl)sulfanylacetyl]benzenesulfonamide;

2-chloro-5-[2-(5-propylpyrimidin-2-yl)sulfanylacetyl]benzenesulfonamide;

5-[2-(5-butylpyrimidin-2-yl)sulfanylacetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(4,6-dimethylpyrimidin-2-yl)sulfanylacetyl]benzenesulfonamide;

2-chloro-5-[2-[(4-methyl-6-oxo-1H-pyrimidin-2-yl)sulfanyl]acetyl]benzenesulfonamide;

2-chloro-5-[2-[(6-oxo-4-propyl-1H-pyrimidin-2-yl)sulfanyl]acetyl]benzenesulfonamide;

5-[2-[(4-tert-butyl-6-oxo-1H-pyrimidin-2-yl)sulfanyl]acetyl]-2-chloro-benzenesulfonamide;

ethyl 2-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]sulfanyl-6-oxo-1H-pyrimidine-5-carboxylate;

5-[2-[(5-benzyl-4-methyl-6-oxo-1H-pyrimidin-2-yl)sulfanyl]acetyl]-2-chloro-benzenesulfonamide;

5-[2-(1H-benzimidazol-2-ylsulfanyl)acetyl]-2-chloro-benzenesulfonamide;

5-[2-[(5-bromo-1H-benzimidazol-2-yl)sulfanyl]acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(1H-imidazo[4,5-c]quinolin-2-ylsulfanyl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(6,7-dihydro-1H-[1,4]dioxino[2,3-f]benzimidazol-2-ylsulfanyl)acetyl]benzenesulfonamide;

5-[2-[[5-(1H-benzimidazol-2-yl)-1H-pyrazol-3-yl]oxy]acetyl]-2-chloro-benzenesulfonamide;

2-hydroxy-5-[2-[(2-methyl-1-phenyl-propyl)amino]acetyl]benzenesulfonamide;

2,4-dichloro-5-[3-[2-(3,4-diethoxyphenyl)thiazol-4-yl]propanoyl]benzenesulfonamide.

Examples of the invented compouds formula II are selected compounds from the group comprising:

2-chloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide (compound **20**),

2-chloro-5-[2-(5-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide and 2-chloro-5-[2-(6-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide (compounds mixture **21**),

2-chloro-5-(2-imidazol-1-ylacetyl)benzenesulfonamide (compound **22**),

2-chloro-5-[2-(2-ethylimidazol-1-yl)acetyl]benzenesulfonamide (compound **23**),

ethyl 1-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]imidazole-4-carboxylate and ethyl 3-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]imidazole-4-carboxylate (compounds mixture **24**),

2-chloro-5-[2-(2-phenylimidazol-1-yl)acetyl]benzenesulfonamide (compound **25**),

2-chloro-5-[2-(4,5-diphenylimidazol-1-yl)acetyl]benzenesulfonamide (compound **26**),

2-chloro-5-(2-indolin-1-ylacetyl)benzenesulfonamide (compound **27**),

2-chloro-5-[2-(3,4-dihydro-2H-quinolin-1-yl)acetyl]benzenesulfonamide (compound **28**),

5-[2-(benzimidazol-1-yl)acetyl]-2,4-dichloro-benzenesulfonamide (compound **29**),

2,4-dichloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide (compound **30**),

2,4-dichloro-5-[2-(5-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide and 2,4-dichloro-5-[2-(6-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide (compounds mixture **31**),

2,4-dichloro-5-(2-imidazol-1-ylacetyl)benzenesulfonamide (compound **32**),

5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-4-phenethylsulfanyl-benzenesulfonamide (compound **29d**),

2-chloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]-4-phenylsulfanyl-benzenesulfonamide (compound **30a**).

The objects of the invention are also radiolabeled compounds according to general formulas I and II, wherein the radionuclide is selected from the group consisting of ^{11}C, ^{18}F, ^{13}N and ^{15}O.

The objects of the invention are also compounds according to general formulas I and II, including single stereoisomers and mixtures of stereoisomers.

The objects of the invention are also the non-toxic, pharmaceutically acceptable salts of the compounds of general formulas (I) and (II). They include all salts which retain activity comparable to

original compounds and do not attain any harmful and undesirable effects. Such salts are obtained from compounds with general formulas (I) and (II), may be obtained, for example, by mixing their solution with pharmacologically acceptable acids or bases.

Among the pharmaceutically acceptable acids there may be mentioned, without implying any limitation, hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, acetic acid, trifluoroacetic acid, lactic acid, pyruvic acid, malonic acid, succinic acid, glutaric acid, fumaric acid, tartaric acid, maleic acid, citric acid, ascorbic acid, oxalic acid, methanesulfonic acid, benzenesulfonic acid, camphoric acid and other.

Among the pharmaceutically acceptable bases there may be mentioned, without implying any limitation, sodium hydroxide, potassium hydroxide, triethylamine and *tert*-butylamine.

All above listed compounds exhibit CA inhibitor properties and selectivity to one or several CA isoforms.

Detailed Description of the Invention

Abreviations used in the text

Ac – acetyl,

Bn – benzyl,

CA – carbonic anhydrase,

Cy – cyclohexyl,

DMSO – dimethyl sulfoxide,

Et – ethyl,

Et_3N – triethylamine,

HRMS – high-resolution mass spectrometry,

ITC – isothermal titration calorimetry,

K_d – dissociation constant,

Me – methyl,

NMR – nuclear magnetic resonance,

Ph – phenyl,

Pr – propyl,

THF – tertahydrofuran,

TLC – thin layer chromatography

FTSA – fluorescent thermal shift assay.

Materials and Methods

The starting materials used are products that are known or that are prepared according to known operating procedures. The melting points of the compounds were determined in open capillaries on a Thermo Scientific 9100 Series apparatus without further correction. ^1H and ^{13}C NMR spectra were recorded on a Bruker spectrometer (400 and 100 MHz, respectively) in DMSO-d_6 using

residual DMSO signals (2.52 ppm and 40.21 ppm for ^{1}H and ^{13}C NMR spectra, respectively) as the internal standard. TLC was performed with silica gel 60 F254 aluminum plates (Merck) and visualized with UV light. Column chromatography was performed using silica gel 60 (0.040-0.063 mm, Merck). High-resolution mass spectra (HRMS) were recorded on a Dual-ESI Q-TOF 6520 mass spectrometer (Agilent Technologies). The purity of target compounds was controled using an HPLC system with UV detection. Compound names were generated with Accelrys Draw 4.0, Accelrys Inc.

Brief description of the Drawings

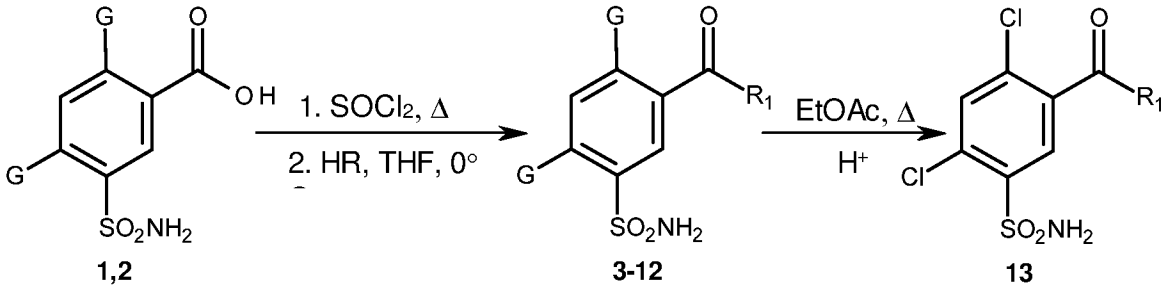
Figure 1. FTSA data of compounds **19** and **31** binding to CA VA. Top panel shows raw data of **19** binding to CA VA. Panel on the bottom shows the dependence of the protein melting temperatures on ligands concentrations. The curves in this panel show the simulation according to the model.

Figure 2. Compound **13a** binding to CA IX observed by ITC at pH 7.0, 37°C. Panel on the top shows raw data, panel on the bottom shows integrated ITC curve. Experiment was performed in sodium phosphate buffer at pH 7.0, 37 °C.

Figure 3. ITC data of compound **13a** binding to CA I, II, IX and XII. Experiments were performed in phosphate buffer at pH 7.0, 37 °C.

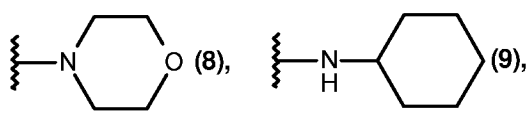
New compounds of the invention are obtained according to general synthesis schemes A-G.

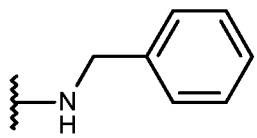
Scheme A. Synthesis of 2,4-dihalogeno-*N*-substituted-5-sulfamoylbenzamides (compounds **3-13**). The desired acid chlorides were obtained by heating the required acids **1, 2** and $SOCl_2$ at reflux. Amides **3-12** were prepared by amidation of acid chlorides with appropriate nucleophile in THF. Ester **13** was prepared by refluxing amide **4** with EtOAc in the presence of H_2SO_4.



G: Cl (**1**, **3-10**), Br (**2, 11, 12**)

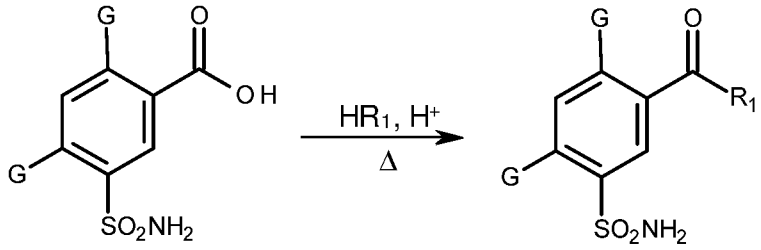
R_1: $NH(CH_2)_2OH$ (**3, 11**), $NH(CH_2)_3OH$ (**4**), $NH(CH_2)_3CH_3$ (**5, 12**), $NH(CH_2)_2OCH_3$ (**6**), $NH(CH_2)_3CO_2CH_3$ (**7**),





$NH(CH_2)_3OAc$ (**13**).

Scheme B. Synthesis of substituted 2,4-dihalogeno-5-sulfamoylbenzoates (compounds **14-16**). Sulfonamides **14-16** were obtained from **1, 2** by refluxing with appropriate alcohol in the presence of H_2SO_4.

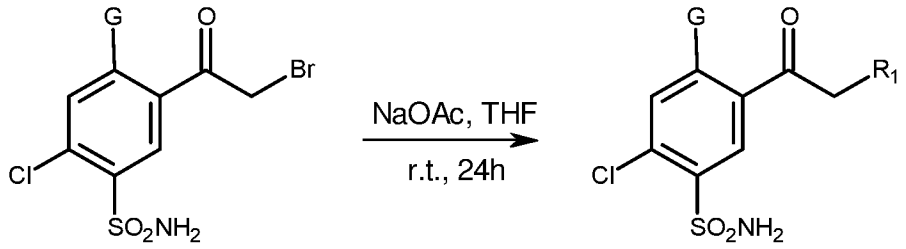


1, 2 **14-16**

G: Cl (**1, 14, 15**), Br (**2, 16**)

R_1: OCH_3 (**14, 16**), $O(CH_2)_2OCH_3$ (**15**).

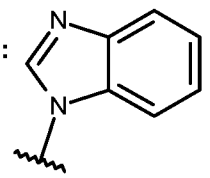
Scheme C. Synthesis of *N*-alkylated heterocycles (compounds **19-32**). *N*-alkylation of some heterocycles with 5-(bromoacetyl)-2-chlorobenzenesulfonamide (**17**) and 5-(bromoacetyl)-2,4-dichlorobenzenesulfonamide (**18**) to give *N*-substituted heterocycle derivatives **19-32** was carried out in the presence of NaOAc in THF at room temperature (excess of nucleophile was used in several cases instead of mentioned base).



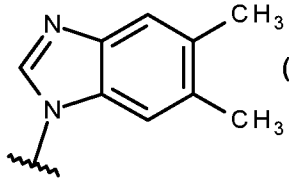
17, 18 **19-32**

G: H (**17**, **19-28**), Cl (**18**, **29-32**)

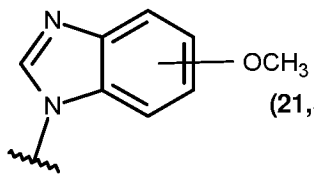
R1:



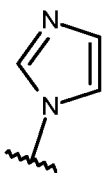
(19, 29),



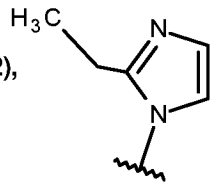
(20, 30),



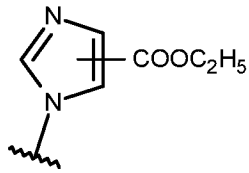
(21,31),



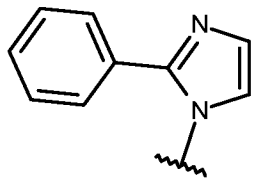
(22, 32),



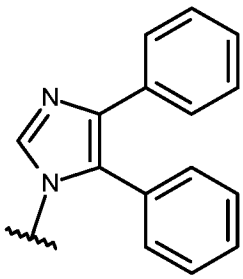
(23),



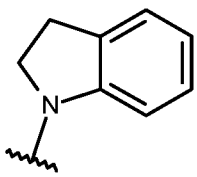
(24),



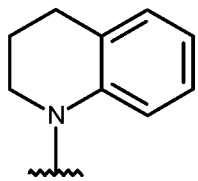
(25),



(26),

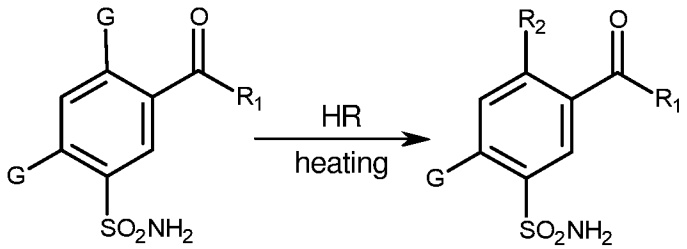


(27),



(28).

Scheme D. Synthesis of 2-halogeno-4,5-disubstitutedbenzenesulfonamides (compounds **3-16(a-h), 29d, 30a**). Sulfonamides **3-16(a-h), 29d, 30a** were obtained from compounds **3-16, 29, 30** by using appropriate nucleophile in methanol or DMSO in the presence of Et_3N, K_2CO_3, or Cs_2CO_3 (excess of nucleophile was used in several cases instead of mentioned bases and solvents).

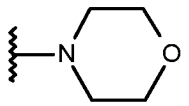


3-16, 29, 30

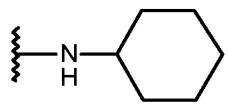
3(a-c, f, g), 4(a, b, f, g), 5(a-d, f-h), 6(a, b, f, g), 7(b, c), 8a, 9(a-c, e), 10(a, b, g), 11(a-d), 12(a-g), 13a, 14(a-d, f, g), 15a, 16(a, b), 29d, 30a.

G: Cl (**3-11, 14-15**), Br (**12, 13, 16**).

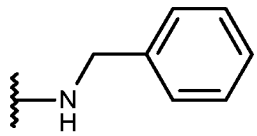
R_1: $NH(CH_2)_2OH$ (**3, 11**), $NH(CH_2)_3OH$ (**4**), $NH(CH_2)_3CH_3$ (**5, 12**), $NH(CH_2)_2OCH_3$ (**6**), $NH(CH_2)_3CO_2CH_3$ (**7**),



(8),

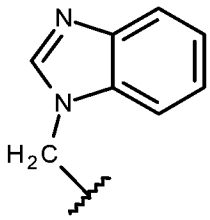


(9),

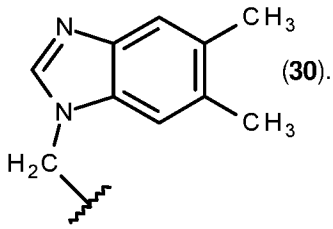


(10), $NH(CH_2)_3OCOCH_3$ (**13**),

OCH_3 (**14, 16**), $O(CH_2)_2OCH_3$ (**15**),

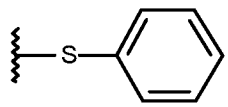


(29),

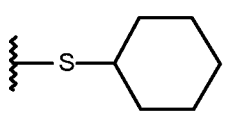


(30).

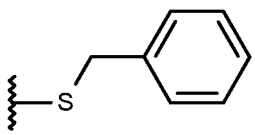
R_2:



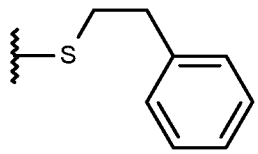
(a),



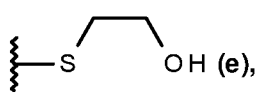
(b),



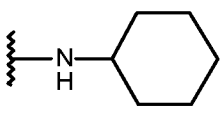
(c),



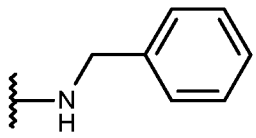
(d),



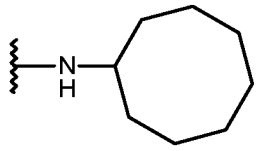
(e),



(f),



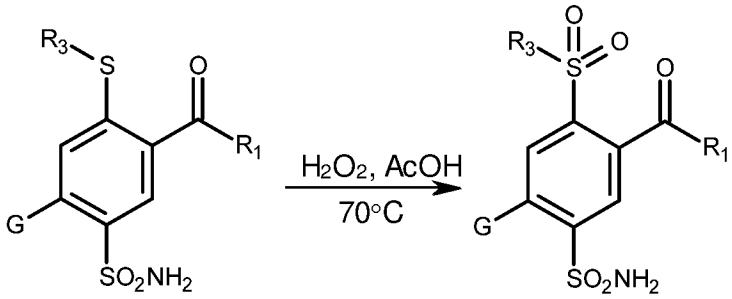
(g),



(h).

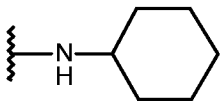
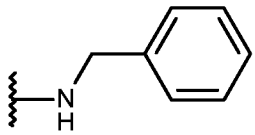
Scheme E. Synthesis of 2-halogeno-4-substitutedsulfonyl-5-substitutedbenzenesulfonamides (compounds **33-43(a-e)**). The compounds **33-43(a-e)** were prepared by oxidation of 2-halogeno-4-substitutedsulfanyl-5-substitutedbenzenesulfonamides **3-16(a-e)** with $AcOH/H_2O_2$.

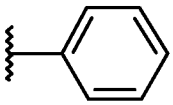
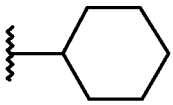
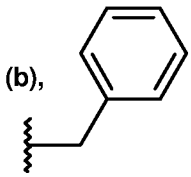
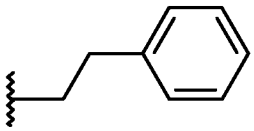
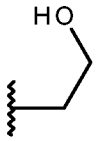
3(a-c), 4(a, b), 5(a, b), 6(a, b), 7(b, c), 9(a-c, e), 10(a, b), 11(b, c), 12(a, b), 14(a-c), 16(a, b).



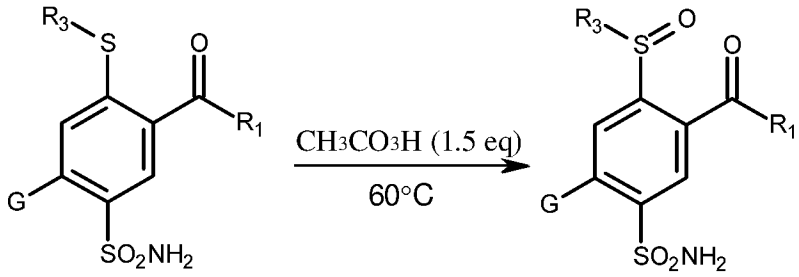
33(a-c), 34(a, b), 35(a, b), 36(a, b), 37(b, c), 38(a-c, e), 39(a, b), 40(b, c), 41(a, b), 42(a-c), 43(a, b).

G: Cl (**3-7, 9, 10, 14, 33-39, 42**), Br (**11, 12, 16, 40, 41, 43**).

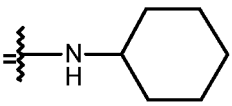
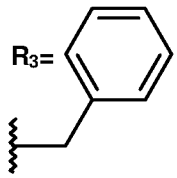
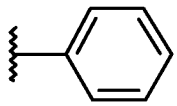
R_1: $NH(CH_2)_2OH$ (**3, 11, 33, 40**), $NH(CH_2)_3OH$ (**4, 34**), $NH(CH_2)_3CH_3$ (**5, 12, 35, 41**), $NH(CH_2)_2OCH_3$ (**6, 36**), $NH(CH_2)_3CO_2CH_3$ (**7, 37**),  (**9, 38**),  (**10, 39**), OCH_3 (**14, 16, 42, 43**).

R_3:  **(a),**  **(b),**  **(c),**  **(d),**  **(e).**

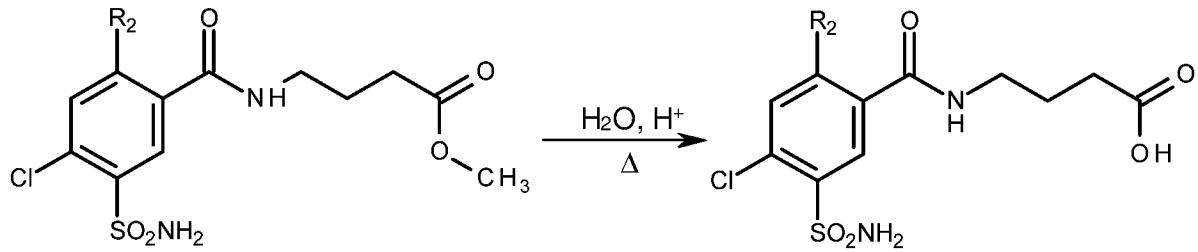
Scheme F. Synthesis of 2-halogeno-4-substitutedsulfinyl-5-substitutedbenzenesulfonamides (compounds **44**, **45**). The compounds **44**, **45** were prepared by oxidation of sulfanyl derivatives (compounds **9c**, **11a**) with peracetic acid.



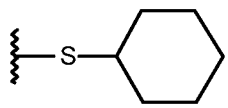
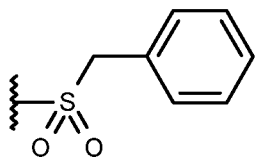
9c, 11a **44, 45**

44: G=Cl, R1=  , **R3=**  ; **45: G=Br, R1=** $NH(CH_2)_2OH$, **R3=**  .

Scheme G. Synthesis of 4-[(2,4-disubstituted-5-sulfamoyl-benzoyl)amino]butanoic acids (compounds **46-48**). Sulfonamides **46-48** were obtained from **7, 7b, 37c** by refluxing with diluted alcohol in the presence of H_2SO_4.



7, 7b, 37c **46-48**

R1: Cl (**7, 46**),  (**7b, 47**),  (**37, 48**).

Embodiments of the Invention

Represented below are specific examples of invention compounds' synthesis. These examples are presented only for illustrative purpose of the invention; they do not limit the scope of the invention.

Example 1. Preparation of 2,4-dichloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3**), 2,4-dichloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4**), *N*-butyl-2,4-dichloro-5-sulfamoyl-benzamide (compound **5**), 2,4-dichloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6**), methyl 4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **7**), 2,4-dichloro-5-(morpholine-4-carbonyl)benzenesulfonamide (compound **8**), 2,4-dichloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **9**), *N*-benzyl-2,4-dichloro-5-sulfamoyl-benzamide (compound **10**), 2,4-dibromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **11**), 2,4-dibromo-*N*-butyl-5-sulfamoyl-benzamide (compound **12**).

The mixture of appropriate 2,4-dichloro-5-sulfamoylbenzoic acid (compound **1**) or 2,4-dibromo-5-sulfamoylbenzoic acid (compound **2**) (10.0 mmol), $SOCl_2$ (2-3 eq), and 1 drop DMF in toluene (5 ml) was refluxed for 4 h. Excess $SOCl_2$ and toluene were removed by distillation under reduced pressure, and the crude acid chloride was used directly in the next step.

The solution of 2,4-dihalogeno-*N*-substituted-5-sulfamoylbenzoyl chloride in THF (30 ml) was added dropwise to a solution of appropriate amine (30.0 mmol) in THF (20 ml) at 0°C and allowed stirring for 1h (for compound **7** used methyl 4-aminobutanoate hydrochloride (1.3 eq), Et_3N (2 eq)). The mixture was warmed to room temperature and stirred for another 1-2 h. THF was removed under reduced pressure. Water was added to the residue and product was extracted with EtOAc. The organic layer was washed with 5% HCl(aq), dried over anhydrous $MgSO_4$, filtered and concentrated.

The compound **3.** Recrystallization was accomplished from EtOAc. Yield: 1.69 g, 54%, mp 182-183°C.

^{1}H NMR δ ppm: 3.31 (2H, q, J = 6.0 Hz, NH$\underline{CH_2}$), 3.51 (2H, t, J = 6.0 Hz, $\underline{CH_2}$OH), 4.77 (1H, br s, OH), 7.81 (2H, s, SO_2NH_2), 7.93 (1H, s, C_3-H), 7.95 (1H, s, C_6-H), 8.67 (1H, t, J = 5.6 Hz, NH).

^{13}C NMR δ ppm: 42.5, 60.0, 129.3, 132.1, 132.5, 134.5, 136.4, 140.3, 165.0.

HRMS calcd. for $C_9H_{10}Cl_2N_2O_4S$ [$(M+H)^+$]: 312.9811, found: 312.9814.

The compound **4.** Recrystallization was accomplished from H_2O. Yield: 1.96 g, 60%, mp 153-155°C.

^{1}H NMR δ ppm: 1.67 (2H, quint, J = 6.4 Hz, CH_2), 3.30 (2H, q, J = 6.4 Hz, NH$\underline{CH_2}$), 3.48 (2H, t, J = 6.4 Hz, $\underline{CH_2}$OH), 4.49 (1H, br s, OH), 7.83 (2H, s, SO_2NH_2), 7.92 (1H, s, C_3-H), 7.94 (1H, s, C_6-H), 8.65 (1H, t, J = 5.6 Hz, NH).

^{13}C NMR δ ppm: 32.6, 36.9, 58.9, 129.2, 132.1, 132.5, 134.4, 136.4, 140.4, 164.9.

HRMS calcd. for $C_{10}H_{12}Cl_2N_2O_4S$ [$(M+H)^+$]: 326.9968, found: 326.9971.

The compound **5.** Recrystallization was accomplished from toluene:MeOH (5:1). Yield: 3.03 g, 93%, mp 184-186°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2 Hz, CH_3), 1.36 (2H, sext, *J* = 7.2 Hz, CH_2), 1.50 (2H, quint, *J* = 7.2 Hz, CH_2), 3.24 (2H, q, *J* = 6.8 Hz, $NHCH_2$), 7.81 (2H, s, SO_2NH_2), 7.90 (1H, s, C_3-H), 7.94 (1H, s, C_6-H), 8.62 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 31.4, 39.2, 129.1, 132.1, 132.5, 134.4, 136.5, 140.4, 164.8.

HRMS calcd. for $C_{11}H_{14}Cl_2N_2O_3S$ [$(M+H)^+$]: 325.0175, found: 325.0174.

The compound **6.** Recrystallization was accomplished from toluene:MeOH (5:1). Yield: 2.13 g, 65%, mp 137-139°C.

^{1}H NMR δ ppm: 3.29 (3H, s, CH_3), 3.38-3.43 (2H, m, $NHCH_2$), 3.45-3.48 (2H, m, OCH_2), 7.80 (2H, s, SO_2NH_2), 7.91 (1H, s, C_3-H), 7.93 (1H, s, C_6-H), 8.74 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 39.4, 58.4, 70.7, 129.2, 132.2, 132.5, 134.5, 136.3, 140.3, 165.1.

HRMS calcd. for $C_{10}H_{12}Cl_2N_2O_4S$[$(M+H)^+$]: 326.9968, found: 326.9967.

The compound **7.** The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.80. Yield: 2.03 g, 55%, mp 138-140°C.

^{1}H NMR δ ppm: 1.77 (2H, quint, *J* = 7.2 Hz, CH_2), 2.41 (2H, t, *J* = 7.6 Hz, $COCH_2$), 3.27 (2H, q, *J* = 6.8 Hz, $NHCH_2$), 3.61 (3H, m, CH_3), 7.82 (2H, s, SO_2NH_2), 7.92 (1H, s, C_3-H), 7.95 (1H, s, C_6-H), 8.69 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 24.7, 31.1, 38.9, 51.8, 129.2, 132.2, 132.5, 134.4, 136.3, 140.4, 165.0, 173.5.

HRMS calcd. for $C_{12}H_{14}Cl_2N_2O_5S$[$(M+H)^+$]: 369.0073, found: 369.0074.

The compound **8.** Recrystallization was accomplished from EtOAc. Yield: 2.34 g, 69%, mp 235-236°C.

^{1}H NMR δ ppm: 3.17-3.20 (2H, m, CH_2), 3.54-3.57 (2H, m, CH_2), 3.58-3.74 (4H, m, $2CH_2$), 7.82 (2H, s, SO_2NH_2), 7.93 (1H, s, C_3-H), 7.98 (1H, s, C_6-H).

^{13}C NMR δ ppm: 42.2, 47.1, 66.3, 66.6, 128.6, 132.2, 132.5, 133.8, 134.9, 141.0, 164.3.

HRMS calcd. for $C_{11}H_{12}Cl_2N_2O_4S$[$(M+H)^+$]: 338.9968, found: 338.9966.

The compound **9.** Recrystallization was accomplished from H_2O:MeOH (1:1) and then from toluene:MeOH (5:1). Yield: 2.21 g, 63%, mp 214-215°C.

^{1}H NMR δ ppm: 1.17-1.34 (5H, m, Cy-H), 1.57-1.59 (1H, m, Cy-H), 1.71 (2H, br s, Cy-H), 1.84-1.86 (2H, m, Cy-H), 3.73 (1H, br s, Cy-H), 7.82 (2H, s, SO_2NH_2), 7.88 (1H, s, C_3-H), 7.93 (1H, s, C_6-H), 8.56 (1H, d, *J* = 7.2 Hz, NH).

^{13}C NMR δ ppm: 24.9, 25.6, 32.5, 48.8, 129.0, 132.0, 132.4, 134.5, 136.7, 140.3, 164.0.

HRMS calcd. for $C_{13}H_{16}Cl_2N_2O_3S$[$(M+H)^+$]: 351.0331, found: 351.0335.

The compound **10.** Recrystallization was accomplished from H_2O:MeOH (1:1) and then from toluene:MeOH (5:1). Yield: 3.05 g, 85%, mp 179-181°C.

^{1}H NMR δ ppm: 4.49 (2H, d, *J* = 6.0 Hz, CH_2), 7.26-7.33 (1H, m, Ph-H), 7.35-7.40 (4H, m, Ph-H),

7.84 (2H, s, SO_2NH_2), 7.96 (1H, s, C_3-H), 7.97 (1H, s, C_6-H), 9.21 (1H, t, *J* = 6.0 Hz, NH).

^{13}C NMR δ ppm: 43.1, 127.5, 127.8, 128.9, 129.3, 132.3, 132.6, 134.5, 136.1, 139.2, 140.4, 165.0.

HRMS calcd. for $C_{14}H_{12}Cl_2N_2O_3S[(M+H)^+]$: 359.0018, found: 359.0017.

The compound **11.** Recrystallization was accomplished from MeOH. Yield: 1.41 g, 35%, mp 196-198°C.

^{1}H NMR δ ppm: 3.30 (2H, q, *J* = 6.0 Hz, NH$\underline{CH_2}$), 3.51 (2H, br s, $\underline{CH_2}$OH), 4.77 (1H, s, OH), 7.74 (2H, s, SO_2NH_2), 7.91 (1H, s, C_6-H), 8.19 (1H, s, C_3-H), 8.64 (1H, t, *J* = 6.0 Hz, NH).

^{13}C NMR δ ppm: 42.5, 59.9, 120.4, 123.6, 129.0, 138.5, 139.1, 142.5, 166.2.

HRMS calcd. for $C_9H_{10}Br_2N_2O_4S[(M+H)^+]$: 402.8780 (100%), found: 402.8782 (100%).

The compound **12.** Recrystallization was accomplished from MeOH:H_2O (1:1). Yield: 1.33 g, 31%, mp 218-220°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2 Hz, CH_3), 1.36 (2H, sext, *J* = 7.2 Hz, CH_2), 1.50 (2H, quint, *J* = 7.2 Hz, CH_2), 3.23 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 7.79 (2H, s, SO_2NH_2), 7.86 (1H, s, C_6-H), 8.20 (1H, s, C_3-H), 8.61 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 31.4, 39.2, 120.3, 123.5, 128.8, 138.5, 139.3, 142.6, 165.9.

HRMS calcd. for $C_{12}H_{16}Br_2N_2O_3S[(M+H)^+]$: 428.9301 (100%), found: 428.9297 (100%).

Example 2. Preparation of 3-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]propyl acetate (compound **13**).

2,4-dichloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4**) (327 mg, 1.00 mmol) was refluxed in EtOAc (7 mL) with 3 drops of concentrated H_2SO_4 for 2 hours. The reaction mixture was concentrated under reduced pressure and the resultant precipitate was washed with H_2O. Yield: 288 mg, 78%, mp 149-151°C.

^{1}H NMR δ ppm: 1.83 (2H, quint, *J* = 6.4 Hz, CH_2), 2.02 (3H, s, CH_3), 3.30 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 4.08 (2H, t, *J* = 6.4 Hz, $\underline{CH_2}$O), 7.81 (2H, s, SO_2NH_2), 7.93 (1H, s, C_3-H), 7.95 (1H, s, C_6-H), 8.71 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 21.2, 28.5, 36.5, 62.1, 129.1, 132.2, 132.5, 134.4, 136.1, 140.2, 164.9, 170.9.

HRMS calcd. for $C_{12}H_{14}Cl_2N_2O_5S[(M+H)^+]$: 369.0073, found: 369.0071.

Example 3. Preparation of methyl 2,4-dichloro-5-sulfamoyl-benzoate (compound **14**), 2-methoxyethyl 2,4-dichloro-5-sulfamoyl-benzoate (compound **15**), and methyl 2,4-dibromo-5-sulfamoyl-benzoate (compound **16**).

The mixture of appropriate 2,4-dichloro-5-sulfamoylbenzoic acid (compound **1**) or 2,4-dibromo-5-sulfamoylbenzoic acid (compound **2**) (10.0 mmol) was refluxed in methanol (100 mL) with concentrated H_2SO_4 (1 mL) for 16 hours (for compounds **14** and **16**), or was heated at 120 °C in 2-methoxyethanol (30 mL) with concentrated H_2SO_4 (1 mL) for 20 hours (for compound **15**). The reaction mixture was concentrated under reduced pressure.

The compound **14.** Recrystallization was accomplished from MeOH. Yield: 2.70 g, 95%, mp 202°C.

^{1}H NMR δ ppm: 3.91 (3H, s, CH_3), 7.87 (2H, s, SO_2NH_2), 8.04 (1H, s, C_3-H), 8.40 (1H, s, C_6-H).

^{13}C NMR δ ppm: 53.5, 128.8, 131.7, 134.0, 135.0, 136.8, 140.5, 164.1.

HRMS calcd. for $C_8H_7Cl_2NO_4S$ [$(M+H)^+$]: 283.9546, found: 283.9546.

The compound **15.** Recrystallization was accomplished from toluene:EtOAc (6:1). Yield: 0.985 g, 30%, mp 112-113°C.

^{1}H NMR δ ppm: 3.31 (3H, s, CH_3), 3.66 (2H, t, J = 4.8 Hz, $\underline{CH_2}OCH_3$), 4.45 (2H, t, J = 4.8 Hz, $CO_2\underline{CH_2}$), 7.89 (2H, s, SO_2NH_2), 8.04 (1H, s, C_3-H), 8.39 (1H, s, C_6-H).

^{13}C NMR δ ppm: 58.6, 65.4, 70.0, 128.9, 131.6, 134.0, 135.0, 136.8, 140.6, 163.6.

HRMS calcd. for $C_{10}H_{11}Cl_2NO_5S$ [$(M+H)^+$]: 327.9808, found: 327.9811.

The compound **16**. Recrystallization was accomplished from MeOH. Yield: 2.35 g, 63%, mp 201-203°C. ^{1}H NMR δ ppm: 3.90 (3H, s, CH_3), 7.84 (2H, s, SO_2NH_2), 8.33 (1H, s, C_6-H), 8.35 (1H, s, C_3-H). ^{13}C NMR δ ppm: 53.6, 123.6, 125.2, 131.3, 131.6, 140.2, 142.8, 164.9.

HRMS calcd. for $C_8H_7Br_2NO_4S$[$(M+H)^+$]: 373.8515 (100%), found: 373.8514 (100%).

Example 4. Preparation of 5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide (compound **19**), 2-chloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide (compound **20**), 2-chloro-5-[2-(5-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide and 2-chloro-5-[2-(6-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide (compounds mixture **21**), 2-chloro-5-(2-imidazol-1-ylacetyl)benzenesulfonamide (compound **22**), 2-chloro-5-[2-(2-ethylimidazol-1-yl)acetyl]benzenesulfonamide (compound **23**), ethyl 1-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]imidazole-4-carboxylate and ethyl 3-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]imidazole-4-carboxylate (compounds mixture **24**), 2-chloro-5-[2-(2-phenylimidazol-1-yl)acetyl]benzenesulfonamide (compound **25**), 2-chloro-5-[2-(4,5-diphenylimidazol-1-yl)acetyl]benzenesulfonamide (compound **26**), 5-[2-(benzimidazol-1-yl)acetyl]-2,4-dichloro-

benzenesulfonamide (compound **29**), 2,4-dichloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide (compound **30**), 2,4-dichloro-5-[2-(5-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide and 2,4-dichloro-5-[2-(6-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide (compounds mixture **31**), 2,4-dichloro-5-(2-imidazol-1-ylacetyl)benzenesulfonamide (compound **32**).

A mixture of the appropriate benzimidazole or imidazole (0.750 mmol), appropriate compound **17** or **18** (0.500 mmol) and NaOAc (49.2 mg, 0.600 mmol) in THF (3 ml) was stirred at room temperature for 24 h. The reaction mixture was poured into H_2O. The precipitate was filtered off, washed with H_2O and then with Et_2O.

The compound **19** was synthesized as described previously (Čapkauskaitė, E. et al. (2010), *Bioorg. Med. Chem.* 18, 7357).

The compound **20.** The product was purified by flash chromatography over silica gel with EtOAc then EtOAc:MeOH (2:1), R_f = 0.80. Yield: 77.5 mg, 41%, mp 247-249 °C.

^{1}H NMR δ ppm: 2.29 (3H, s, CH_3), 2.31 (3H, s, CH_3), 6.01 (2H, s, CH_2CO), 7.33 (1H, s, $C_{7'}$-H), 7.45 (1H, s, $C_{4'}$-H), 7.89 (2H, s, SO_2NH_2), 7.95 (2H, d, *J* = 8.4 Hz, C_3-H), 8.03 (1H, s, $C_{2'}$-H), 8.35 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz, C_4-H), 8.55 (1H, d, *J* = 2.0 Hz, C_6-H).

^{13}C NMR δ ppm: 20.3, 20.5, 51.3, 111.1, 119.8, 128.6, 130.3, 131.4, 132.8, 133.2, 133.6, 133.8, 136.2, 142.1, 142.2, 144.4, 192.7.

HRMS calcd. for $C_{17}H_{16}ClN_3O_3S[(M+H)^+]$: 378.0674, found: 378.0679.

The compounds mixture **21.** The product was purified by flash chromatography over silica gel with EtOAc then EtOAc:MeOH (2:1), R_f = 0.79. Yield: 45.6 mg, 24%.

^{1}H NMR δ ppm: (1:0.9) 3.75 (3H, s, CH_3, compound A), 3.80 (2.7H, s, CH_3, compound B), 6.03 (2H, s, CH_2CO, A), 6.04 (1.8H, s, CH_2CO, B), 6.83 (1H, dd, *J* = 8.8 Hz, *J* = 2.4 Hz, $C_{5'(6')}$-H, A), 6.87 (0.9H, dd, *J* = 8.8 Hz, *J* = 2.4 Hz, $C_{5'(6')}$-H, B), 7.20 (1H, d, *J* = 2.4 Hz, $C_{7'(4')}$-H, A), 7.22 (0.9H, d, *J* = 2.0 Hz, $C_{7'(4')}$-H, B), 7.45 (0.9H, d, *J* = 8.8 Hz, $C_{4'(7')}$-H, B), 7.55 (1H, d, *J* = 8.8 Hz, $C_{4'(7')}$-H, A), 7.87 (1.8H, s, SO_2NH_2, B), 7.88 (2H, s, SO_2NH_2, A), 7.95 (0.9H, d, *J* = 8.4 Hz, C_3-H, B), 7.96 (1H, d, *J* = 8.0 Hz, C_3-H, A), 8.03 (1H, s, $C_{2'}$-H, A), 8.10 (0.9H, s, $C_{2'}$-H, B), 8.32-8.36 (1.9H, m, C_4-H, A, B), 8.55 (1H, d, *J* = 2.0 Hz, C_6-H, A), 8.56 (0.9H, d, *J* = 2.4 Hz, C_6-H, B).

HRMS calcd. for $C_{16}H_{14}ClN_3O_4S[(M+H)^+]$: 380.0466, found: 380.0462.

The compound **22.** The product was purified by chromatography on a column of silica gel with EtOAc:MeOH (2:1), R_f = 0.52. Yield: 80.9 mg, 54%, mp 228-230°C.

^{1}H NMR δ ppm: 5.78 (2H, s, CH_2CO), 6.94 (1H, s, $C_{4'}$-H), 7.13 (1H, s, $C_{5'}$-H), 7.60 (1H, s, $C_{2'}$-H), 7.87 (2H, s, SO_2NH_2), 7.91 (1H, d, *J* = 8.0 Hz, C_3-H), 8.26 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz, C_4-H), 8.50 (1H, d, *J* = 2.0 Hz, C_6-H).

^{13}C NMR δ ppm: 53.2, 121.3, 128.4 (2C), 132.8, 133.0, 133.8, 136.1, 138.8, 142.2, 192.8.

HRMS calcd. for $C_{11}H_{10}ClN_3O_3S[(M+H)^+]$: 300.0204, found: 300.0200.

The compound **23.** The product was purified by flash chromatography over silica gel with EtOAc then EtOAc:MeOH (2:1), R_f = 0.70. Yield: 52.5 mg, 32%, mp 223-225°C.

^{1}H NMR δ ppm: 1.14 (3H, d, *J* = 7.2 Hz, CH_3), 2.48-2.53 (2H, m, CH_2, superposed with DMSO), 5.74 (2H, s, CH_2CO), 6.81 (1H, d, *J* = 1.2 Hz, $C_{4'}$-H), 7.00 (1H, d, *J* = 1.2 Hz, $C_{5'}$-H), 7.86 (2H, s, SO_2NH_2), 7.92 (2H, d, *J* = 8.0 Hz, C_3-H), 8.29 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz, C_4-H), 8.52 (1H, d, *J* = 2.0 Hz, C_6-H).

^{13}C NMR δ ppm: 12.5, 19.5, 52.4, 121.4, 126.4, 128.5, 132.7, 133.2, 133.7, 136.2, 142.2, 149.8, 192.9.

HRMS calcd. for $C_{13}H_{14}ClN_3O_3S[(M+H)^+]$: 328.0517, found: 328.0518.

The compounds mixture **24.** The product was purified by flash chromatography over silica gel with EtOAc then EtOAc:MeOH (2:1), R_f = 0.80. Yield: 55.8 mg, 30%.

^{1}H NMR δ ppm: (1:0.8) 1.17 (2.4H, t, *J* = 7.2 Hz, CH_3, compound A), 1.28 (3H, t, *J* = 7.2 Hz, CH_3), compound B), 4.14 (1.6H, q, *J* = 7.2 Hz, $\underline{CH_2}CH_3$, A), 4.24 (3H, q, *J* = 7.2 Hz, $\underline{CH_2}CH_3$, B), 5.85 (2H, s, CH_2CO, B), 5.99 (1.6H, s, CH_2CO, A), 7.74 (1H, s, $C_{5'(4')}$-H, B), 7.75 (0.8H, s, $C_{2'}$-H, A), 7.88 (4.4H, s, SO_2NH_2, A and B, $C_{5'(4')}$-H, A), 7.93 (2H, d, *J* = 8.4 Hz, C_4-H, B), 7.93 (1.6H, d, *J* = 8.0 Hz, C_4-H, A), 7.99 (1H, s, $C_{2'}$-H, B), 8.25 (1H, dd, *J* = 8.4 Hz, *J* = 2.4 Hz, C_3-H, B), 8.31 (0.8H, dd, *J* = 8.4 Hz, *J* = 2.4 Hz, C_3-H, A), 8.51 (1H, d, *J* = 2.4 Hz, C_6-H, B), 8.52 (0.8H, d, *J* = 2.0 Hz, C_6-H, A).

HRMS calcd. for $C_{14}H_{14}ClN_3O_5S[(M+H)^+]$: 372.0415, found: 372.0410.

The compound **25.** The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.39. Yield: 54.5 mg, 29%, mp 131-132°C.

^{1}H NMR δ ppm: 5.87 (2H, s, CH_2CO), 7.07 (1H, d, *J* = 0.8 Hz, $C_{4'}$-H), 7.28 (1H, d, *J* = 1.2 Hz, $C_{5'}$-H), 7.37-7.44 (3H, m, Ph-H), 7.45-7.51 (2H, m, Ph-H), 7.85 (2H, s, SO_2NH_2), 7.89 (2H, d, *J* = 8.4 Hz, C_3-H), 8.26 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz, C_4-H), 8.48 (1H, d, *J* = 2.0 Hz, C_6-H).

^{13}C NMR δ ppm: 54.0, 123.9, 128.2, 128.4(2C), 129.0, 129.1, 131.1, 132.8, 133.2, 133.4, 136.5, 142.2, 147.7, 192.8.

HRMS calcd. for $C_{17}H_{14}ClN_3O_3S[(M+H)^+]$: 376.0517, found: 376.0522.

The compound **26.** The product was washed with 2M HCl(aq), dried and then recrystallization was accomplished from toluene:MeOH (1:1). Yield: 90.4 mg, 40%, mp 111-112°C.

^{1}H NMR δ ppm: 5.96 (2H, s, CH_2CO), 7.37-7.53 (10H, m, Ph-H), 7.87 (2H, d, *J* = 8.4 Hz, C_3-H), 7.89 (2H, s, SO_2NH_2), 8.17 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz, C_4-H), 8.43 (1H, d, *J* = 2.0 Hz, C_6-H), 8.36 (1H, s, $C_{2'}$-H).

^{13}C NMR δ ppm: 53.6, 126.0, 127.6, 127.7, 128.6, 129.4, 129.6, 129.9, 130.2, 130.5, 131.0, 131.3, 132.6, 132.9, 133.2, 137.0, 137.4, 142.3, 190.9.

HRMS calcd. for $C_{23}H_{18}ClN_3O_3S$[(M+H)$^+$]: 452.0830, found: 452.0836.

The compound **29.** Recrystallization was accomplished from MeOH:H_2O (2:1), (twice). Yield: 127 mg, 66%, mp 245-250°C (dec).

^{1}H NMR δ ppm: 5.95 (2H, s, CH_2), 7.20-7.32 (2H, m, $C_{5',6'}$-H), 7.56 (1H, dd, *J* = 6.8 Hz, *J* = 1.6 Hz, $C_{7'}$-H), 7.70 (1H, dd, *J* = 6.8 Hz, *J* = 1.6 Hz, $C_{4'}$-H), 7.92 (2H, s, SO_2NH_2), 8.11 (1H, s, C_3-H), 8.23 (1H, s,$C_{2'}$-H), 8.53 (1H, s, C_6-H).

^{13}C NMR δ ppm: 53.7, 111.1, 119.8, 122.2, 123.0, 130.3, 133.7, 134.8 (2C), 134.9, 135.3, 140.7, 143.4, 145.2, 194.6.

HRMS calcd. for $C_{15}H_{11}Cl_2N_3O_3S$[(M+H)$^+$]: 383.9971, found: 383.9973.

The compound **30.** Recrystallization was accomplished from MeOH:H_2O (2:1), (twice). Yield: 132 mg, 64%, mp 248-251°C.

^{1}H NMR δ ppm: 2.31 (3H, s, CH_3), 2.32 (3H, s, CH_3), 5.86 (2H, s, CH_2CO), 7.31 (1H, s, $C_{7'}$-H), 7.45 (1H, s, $C_{4'}$-H), 7.91 (2H, s, SO_2NH_2), 8.05 (1H, s, $C_{2'}$-H), 8.10 (1H, s, C_3-H), 8.51 (1H, s, C_6-H).

^{13}C NMR δ ppm: 20.3, 20.6, 53.6, 111.0, 119.9, 130.3, 130.4, 131.5, 133.4, 133.7, 134.7, 134.9, 135.3, 140.7, 142.1, 144.3, 194.7.

HRMS calcd. for $C_{17}H_{15}Cl_2N_3O_3S$[(M+H)$^+$]: 412.0284, found: 412.0279.

The compounds mixture **31.** Recrystallization was accomplished from MeOH:H_2O (1:1), (twice).Yield: 58.0 mg, 28%.

^{1}H NMR δ ppm: (1:0.8) 3.77 (3H, s, CH_3, compound A), 3.80 (2.4H, s, CH_3, compound B), 5.91 (3.6H, s, CH_2CO, A and B), 6.86 (1H, dd, *J* = 8.8 Hz, *J* = 2.4 Hz, $C_{5'(6')}$-H, A), 6.91 (0.8H, dd *J* = 8.8 Hz, *J* = 2.4 Hz, $C_{5'(6')}$-H, B), 7.16 (1H, d, *J* = 2.4 Hz, $C_{7'(4')}$-H, A), 7.22 (0.8H, d, *J* = 2.0 Hz, $C_{7'(4')}$-H, B), 7.46 (0.8H, d, *J* = 8.8 Hz, $C_{4'(7')}$-H, B), 7.57 (1H, d, *J* = 8.8 Hz, $C_{4'(7')}$-H, A), 7.92 (1.6H, s, SO_2NH_2, B), 7.93 (2H, s, SO_2NH_2, A), 8.11 (1.8H, s, C_3-H, A and B), 8.12 (1H, s, $C_{2'}$-H, A), 8.19 (0.8H, s, $C_{2'}$-H, B), 8.51 (0.8H, s, C_6-H, B), 8.53 (1H, s, C_6-H, A).

HRMS calcd. for $C_{16}H_{13}Cl_2N_3O_4S$ [(M+H)$^+$]: 414.0077, found: 414.0076.

The compound **32.** Recrystallization was accomplished from MeOH:EtOAc (1:1). Yield: 26.7 mg, 16%, mp 208-210°C.

^{1}H NMR δ ppm: 5.62 (2H, s, CH_2CO), 6.93 (1H, s, $C_{4'}$-H), 7.15 (1H, s, $C_{5'}$-H), 7.63 (1H, s, $C_{2'}$-H), 7.88 (2H, s, SO_2NH_2), 8.07 (1H, s, C_3-H), 8.43 (1H, s, C_6-H).

^{13}C NMR δ ppm: 55.4, 121.1, 128.5, 130.2, 133.6, 134.7, 135.0, 135.1, 138.7, 140.6, 194.9.

HRMS calcd. for $C_{11}H_9Cl_2N_3O_3S$[(M+H)$^+$]: 333.9814, found: 333.9818.

Example 5. Preparation of 2-chloro-5-(2-indolin-1-ylacetyl)benzenesulfonamide **(27)** and 2-chloro-5-[2-(3,4-dihydro-*2H*-quinolin-1-yl)acetyl]benzenesulfonamide **(28)**.

A mixture of the appropriate amine (1.30 mmol) and 5-(2-bromoacetyl)-2-chlorobenzene-1-sulfonamide **1** (200 mg, 0.640 mmol) in THF (4 ml) was stirred at room temperature for 48 h. The resulting mixture was filtered and the filtrate was evaporated under reduced pressure.

The compound **27.** Recrystallization was accomplished from 2-PrOH:H_2O (5:1). Yield: 114 mg, 51%, mp 195-198°C.

^{1}H NMR δ ppm: 2.96 (2H, t, *J* = 8.4 Hz, CH_2), 3.47 (2H, t, *J* = 8.4 Hz, CH_2), 4.76 (2H, s, CH_2CO), 6.48 (1H, d, *J* = 8.0 Hz, $C_{7'}$-H), 6.58 (1H, t, *J* = 7.6 Hz, $C_{5'}$-H), 6.95 (1H, t, *J* = 7,6 Hz, $C_{6'}$-H), 7.05 (1H, d, *J* = 7.2 Hz, $C_{4'}$-H), 7.80 (2H, s, SO_2NH_2), 7.85 (1H, d, *J* = 8.4 Hz, C_3-H), 8.24 (1H, dd, *J* = 8.0 Hz, *J* = 2.0 Hz, C_4-H), 8.50 (1H, d, *J* = 2.0 Hz, C_6-H).

^{13}C NMR δ ppm: 28.6, 53.4, 55.2, 107.0, 117.7, 124.7, 127.5, 128.4, 129.6, 132.6, 133.1, 134.6, 135.7, 142.0, 152.3, 195.6.

HRMS calcd. for $C_{16}H_{15}ClN_2O_3S$ [$(M+H)^+$]: 351.0565, found: 351.0569.

The compound **28.** Recrystallization was accomplished from 2-PrOH:H_2O (5:1). Yield: 195 mg, 84%, mp 210-213°C.

^{1}H NMR δ ppm: 1.91 (2H, quint, *J* = 6.4 Hz, CH_2), 2.74 (2H, t, *J* = 6.4 Hz, CH_2), 3.34 (2H, t, *J* = 5.6 Hz, CH_2), 4.93 (2H, s, CH_2CO), 6.34 (1H, d, *J* = 7.6 Hz, $C_{8'}$-H), 6.48 (1H, td, *J* = 7.2 Hz, *J* = 1.2 Hz, $C_{6'}$-H), 6.85 (1H, td, *J* = 7,6 Hz, *J* = 1.6 Hz, $C_{7'}$-H), 6.90 (1H, dd, *J* = 7.2 Hz, *J* = 1.2 Hz, $C_{5'}$-H), 7.80 (2H, s, SO_2NH_2), 7.87 (2H, d, *J* = 8.4 Hz, C_3-H), 8.26 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz, C_4-H), 8.48 (1H, d, *J* = 2.0 Hz, C_6-H).

^{13}C NMR δ ppm: 22.3, 28.0, 50.1, 57.7, 110.8, 116.2, 122.3, 127.2, 128.3, 129.3, 132.6, 132.9, 134.5, 135.8, 142.0, 145.6, 196.3.

HRMS calcd. for $C_{17}H_{17}ClN_2O_3S$ [$(M+H)^+$]: 365.0721, found: 365.0718.

Example 6. Preparation of 4-chloro-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **3a**), 4-chloro-*N*-(3-hydroxypropyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **4a**), *N*-butyl-4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **5a**), 4-chloro-*N*-(2-methoxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **6a**), 4-chloro-*N*-cyclohexyl-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **9a**), *N*-benzyl-4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **10a**), 4-bromo-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **11a**), 4-bromo-*N*-butyl-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **12a**), 3-[(4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoyl)amino]propyl acetate (compound **13a**), methyl 4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoate (compound **14a**), 2-methoxyethyl 4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoate

(compound **15a**), methyl 4-bromo-2-phenylsulfanyl-5-sulfamoyl-benzoate (compound **16a**), 2-chloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]-4-phenylsulfanyl-benzenesulfonamide (compound **30a**).

The mixture of appropriate 2,4-dihalogeno-*N*-substituted-5-sulfamoylbenzamides (compounds **3-6, 9-13**) or appropriate substituted 2,4-dihalogeno-5-sulfamoylbenzoate (compounds **14-16**) (1.00 mmol), or 2,4-dichloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide (compound **30**), MeOH (5 mL), thiophenol (121 mg, 1.10 mmol) and Et_3N (121 mg, 1.20 mmol) was refluxed for 2-6 h. MeOH was evaporated under reduced pressure and the resultant precipitate was washed with H_2O.

The compound **3a.** The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.34. Yield: 255 mg, 66%, mp 192-193°C.

^{1}H NMR δ ppm: 3.32-3.36 (2H, m, NHC<u>H</u>$_2$), 3.55 (2H, q, *J* = 6.0 Hz, C<u>H</u>$_2$OH), 4.79 (1H, t, *J* = 5.6 Hz, OH), 6.80 (1H, s, C_3-H), 7.53-7.57 (5H, m, Ph-H), 7.63 (2H, s, SO_2NH_2), 8.05 (1H, s, C_6-H), 8.74 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 42.6, 60.0, 128.8, 129.4, 130.4, 130.8, 131.5, 132.3, 133.4, 135.2, 137.8, 144.9, 166.1.

HRMS calcd. for $C_{15}H_{15}ClN_2O_4S_2$ [(M+H)$^+$]: 387.0235, found: 387.0233.

The compound **4a.** Recrystallization was accomplished from toluene:2-PrOH (8:1). Yield: 257 mg, 64%, mp 146-148°C.

^{1}H NMR δ ppm: 1.71 (2H, quint, *J* = 6.4 Hz, CH_2), 3.30-3.35 (2H, m, NHC<u>H</u>$_2$), 3.51 (2H, q, *J* = 6.0 Hz, C<u>H</u>$_2$OH), 4.50 (1H, t, *J* = 5.2 Hz, OH), 6.81 (1H, s, C_3-H), 7.54-7.57 (5H, m, Ph-H), 7.64 (2H, s, SO_2NH_2), 8.00 (1H, s, C_6-H), 8.73 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 32.7, 37.0, 59.0, 128.6, 129.5, 130.4, 130.8, 131.4, 132.2, 133.8, 135.2, 137.9, 144.6, 166.0.

HRMS calcd. for $C_{16}H_{17}ClN_2O_4S_2$ [(M+H)$^+$]: 401.0391, found: 401.0386.

The compound **5a.** Recrystallization was accomplished from toluene. Yield: 168 mg, 42%, mp 184-186°C.

^{1}H NMR δ ppm: 0.92 (3H, t, *J* = 7.0 Hz, CH_3), 1.38 (2H, sext, *J* = 7.6 Hz, CH_2), 1.53 (2H, quint, *J* = 6.8 Hz, CH_2), 3.26 (2H, q, *J* = 6.4 Hz, NHC<u>H</u>$_2$), 6.82 (1H, s, C_3-H), 7.55 (5H, s, Ph-H), 7.64 (2H, s, SO_2NH_2), 7.99 (1H, s, C_6-H), 8.72 (1H, br s, NH).

^{13}C NMR δ ppm: 14.2, 20.1, 31.5, 39.3, 128.6, 129.6, 130.3, 130.8, 131.5, 132.2, 133.9, 135.1, 137.9, 144.4, 165.9.

HRMS calcd. for $C_{17}H_{19}ClN_2O_3S_2$ [(M+H)$^+$]: 399.0598, found: 399.0596.

The compound **6a.** Recrystallization was accomplished from toluene:2-PrOH (8:1). Yield: 249 mg, 62%, mp 170-172°C.

^{1}H NMR δ ppm: 3.30 (3H, s, CH_3), 3.43 (2H, q, *J* = 5.2 Hz, NH$\underline{CH_2}$), 3.49 (2H, t, *J* = 5.2 Hz, OCH_2), 6.81 (1H, s, C_3-H), 7.54-7.57 (5H, m, Ph-H), 7.63 (2H, s, SO_2NH_2), 8.01 (1H, s, C_6-H), 8.84 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 39.5, 58.4, 70.7, 128.8, 129.5, 130.4, 130.8, 131.5, 132.4, 133.4, 135.2, 137.8, 144.8, 166.1.

HRMS calcd. for $C_{16}H_{17}ClN_2O_4S_2$ [(M+H)$^+$]: 401.0391, found: 401.0390.

The compound **9a.** Recrystallization was accomplished from toluene:2-PrOH (8:1). Yield: 344 mg, 81%, mp 236-238°C.

^{1}H NMR δ ppm: 1.14-1.19 (1H, m, Cy-H), 1.26-1.37 (4H, m, Cy-H), 1.58-1.61 (1H, m, Cy-H), 1.73-1.75 (2H, m, Cy-H), 1.85-1.87 (2H, m, Cy-H), 3.75 (1H, br s, Cy-H), 6.82 (1H, s, C_3-H), 7.53-7.58 (5H, m, Ph-H), 7.65 (2H, s, SO_2NH_2), 7.95 (1H, s, C_6-H),8.62 (1H, d, *J* = 8.0 Hz, NH).

^{13}C NMR δ ppm: 25.1, 25.7, 32.7, 48.9, 128.6, 129.6, 130.3, 130.8, 131.5, 132.1, 134.4, 135.0, 138.0, 144.1, 165.1.

HRMS calcd. for $C_{19}H_{21}ClN_2O_3S_2$ [(M+H)$^+$]: 425.0755, found: 425.0752.

The compound **10a.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (3:1), R_f = 0.35. Yield: 377 mg, 87%, mp 208-211°C.

^{1}H NMR δ ppm: 4.49 (2H, d, *J* = 6.0 Hz, CH_2), 6.82 (1H, s, C_3-H), 7.25-7.30 (1H, m, Ph-H), 7.37-7.40 (4H, m, Ph-H), 7.54-7.60 (5H, m, Ph-H), 7.66 (2H, s, SO_2NH_2), 8.07 (1H, s, C_6-H), 9.34 (1H, t, *J* = 6.0 Hz, NH_2).

^{13}C NMR δ ppm: 43.2, 127.4, 127.8, 128.7, 128.8, 129.6, 130.4, 130.9, 131.5, 132.5, 133.2, 135.2, 137.9, 139.4, 144.9, 166.0.

HRMS calcd. for $C_{20}H_{17}ClN_2O_3S_2$ [(M+H)$^+$]: 433.0442, found: 433.0443.

The compound **11a**. The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.34. Yield: 362 mg, 84%, mp 191-193°C.

^{1}H NMR δ ppm: 3.32 (2H, q, *J* = 6.0 Hz, NH$\underline{CH_2}$), 3.54 (2H, q, *J* = 5.6 Hz, $\underline{CH_2}$OH), 4.80 (1H, t, *J* = 5.2 Hz, OH), 6.79 (1H, s, C_3-H), 7.55 (5H, br s, Ph-H), 7.61 (2H, s, SO_2NH_2), 8.05 (1H, s, C_6-H), 8.74 (1H, br s, NH).

^{13}C NMR δ ppm: 42.6, 60.0, 121.0, 128.8, 130.4, 130.8, 131.5, 132.9, 134.0, 135.2, 139.5, 144.5, 166.2.

HRMS calcd. for $C_{15}H_{15}BrN_2O_4S_2$[(M+H)$^+$]: 432.9709 (100%), found: 432.9713 (100%).

The compound **12a**. Recrystallization was accomplished from toluene. Yield: 244 mg, 55%, mp 184-186°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2, Hz, CH_3), 1.37 (2H, sext, *J* = 7.6 Hz, CH_2), 1.52 (2H, quint, *J* = 7.2 Hz, CH_2), 3.25 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 6.99 (1H, s, C_3-H), 7.53-7.58 (5H, m, Ph-H), 7.62 (2H, s, SO_2NH_2), 7.99 (1H, s, C_6-H), 8.72 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.2, 20.1, 31.5, 39.3, 120.8, 128.6, 130.3, 130.8, 131.5, 133.1, 134.6, 135.1, 139.7, 144.1, 166.0.

HRMS calcd. for $C_{17}H_{19}BrN_2O_3S_2$[(M+H)$^+$]: 445.0073 (100%), found: 445.0071 (100%).

The compound **13a.** Recrystallization was accomplished from toluene:2-PrOH (8:1). Yield: 173 mg, 39%, mp 168-171°C.

^{1}H NMR δ ppm: 1.86 (2H, quint, *J* = 6.4 Hz, CH_2), 2.03 (3H, s, CH_3), 3.32-3.36 (2H, m, NH$\underline{CH_2}$), 4.10 (2H, t, *J* = 6.4 Hz, $\underline{CH_2}$O), 6.82 (1H, s, C_3-H), 7.55-7.56 (5H, m, Ph-H), 7.64 (2H, s, SO_2NH_2), 8.01 (1H, s, C_6-H), 8.81 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 21.2, 28.6, 36.7, 62.3, 128.6, 129.6, 130.4, 130.8, 131.4, 132.3, 133.6, 135.2, 138.0, 144.6, 166.0, 170.9.

HRMS calcd. for $C_{18}H_{19}ClN_2O_5S_2$[(M+H)$^+$]: 443.0497, found: 443.0495.

The compound **14a.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (10:1), R_f = 0.32. Yield: 161 mg, 45%, mp 223-226°C.

^{1}H NMR δ ppm: 3.94 (3H, s, CH_3), 6.68 (1H, s, C_3-H), 7.62-7.67 (5H, m, Ph-H), 7.71 (2H, s, SO_2NH_2), 8.50 (1H, s, C_6-H).

^{13}C NMR δ ppm: 53.3, 124.3, 128.7, 130.1, 131.2 (2C), 131.8, 135.2, 136.2, 137.5, 149.6, 164.8.

HRMS calcd. for $C_{14}H_{12}ClNO_4S_2$ [(M+H)$^+$]: 357.9969, found: 357.9970.

The compound **15a.** Recrystallization was accomplished from toluene (twice). Yield: 149 mg, 37%, mp 161-163°C.

^{1}H NMR δ ppm: 3.33 (3H, s, CH_3), 3.70 (2H, t, *J* = 4.8 Hz, $\underline{CH_2}OCH_3$), 4.48 (2H, t, *J* = 4.8 Hz, $CO_2\underline{CH_2}$), 6.69 (1H, s, C_3-H), 7.60-7.67 (5H, m, Ph-H), 7.75 (2H, s, SO_2NH_2), 8.52 (1H, s, C_6-H).

^{13}C NMR δ ppm: 58.6, 65.1, 70.1, 124.3, 128.7, 130.1, 131.1 (2C), 131.8, 135.3, 136.2, 137.5, 149.7, 164.3.

HRMS calcd. for $C_{16}H_{16}ClNO_5S_2$ [(M+H)$^+$]: 402.0231, found: 402.0234.

The compound **16a.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (15:1), R_f = 0.20, then recrystallization was accomplished from toluene. Yield: 145 mg, 36%, mp 202-204°C.

^{1}H NMR δ ppm: 3.93 (3H, s, CH_3), 6.89 (1H, s, C_3-H), 7.58-7.63 (5H, m, Ph-H), 7.71 (2H, s, SO_2NH_2), 8.52 (1H, s, C_6-H).

^{13}C NMR δ ppm: 25.6, 25.7, 32.4, 44.5, 53.2, 125.1, 127.5, 131.0, 133.6, 140.1, 142.5 165.0.

HRMS calcd. for $C_{14}H_{12}BrNO_4S_2$[$(M+H)^+$]: 403.9443 (100%), found: 403.9437 (100%).

The compound **30a.** Recrystallization was accomplished from acetone:MeOH (1:1). Yield: 146 mg, 30%, mp 229-231°C.

^{1}H NMR δ ppm: 2.30 (3H, s, CH_3), 2.32 (3H, s, CH_3), 6.01 (2H, s, CH_2CO), 6.78 (1H, s, C_3-H), 7.36 (1H, s, $C_{7'}$-H), 7.46 (1H, s, $C_{4'}$-H), 7.60 (5H, br s, Ph-H), 7.81 (2H, s, SO_2NH_2), 8.04 (1H, s, $C_{2'}$-H), 8.72 (1H, s, C_6-H).

^{13}C NMR δ ppm: 20.3, 20.6, 51.8, 111.2, 119.8, 129.1, 129.2, 130.3, 130.6, 131.0, 131.1, 131.3, 131.4, 133.7, 135.3, 135.8, 137.5, 142.3, 144.5, 149.0, 193.2.

HRMS calcd. for $C_{23}H_{20}ClN_3O_3S_2$ [$(M+H)^+$]: 486.0707, found: 486.0701.

Example 7. Preparation of 2-chloro-5-(morpholine-4-carbonyl)-4-phenylsulfanyl-benzenesulfonamide (campound **8a**). The mixture of 2,4-dichloro-5-(morpholine-4-carbonyl)benzenesulfonamide (compound **8**) (339 mg, 1.00 mmol), DMSO (2 mL), cyclohexanethiol (128 mg, 1.10 mmol) and Cs_2CO_3 (652 mg, 2.00 mmol) was heated at 120 °C temperature for 8 h. The mixture was cooled to room temperature and brine was added. The product was extracted with EtOAc (3x7 mL). The organic layer was washed with H_2O, dried over anhydrous $MgSO_4$, filtered and concentrated.

Recrystallization was accomplished from toluene:2-PrOH (8:1). Yield: 103 mg, 25%, mp 152-154°C.

^{1}H NMR δ ppm: 3.17 (2H, br s, CH_2), 3.54 (2H, br s, CH_2), 3.62-3,69 (4H, m, $2CH_2$), 6.83 (1H, s, C_3-H), 7.56-7.58 (3H, m, Ph-H), 7.62-7.64 (2H, m, Ph-H), 7.75 (2H, s, SO_2NH_2), 7.86 (1H, s, C_6-H).

^{13}C NMR δ ppm: 42.2, 47.2, 66.3, 66.6, 128.1, 129.0, 130.6, 130.9, 131.0, 132.7, 133.3, 135.5, 140.1, 140.6, 164.6.

HRMS calcd. for $C_{17}H_{17}ClN_2O_4S_2$ [$(M+H)^+$]: 413.0391, found: 413.0393.

Example 8. Preparation of methyl 4-chloro-2-cyclohexylsulfanyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3b**), 4-chloro-2-cyclohexylsulfanyl-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4b**), *N*-butyl-4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **5b**), 4-chloro-2-cyclohexylsulfanyl-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6b**), methyl 4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoate (compound **7b**), 4-chloro-*N*-cyclohexyl-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **9b**), *N*-benzyl-4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **10b**), 4-bromo-2-cyclohexylsulfanyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **11b**), 4-bromo-*N*-butyl-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide (compound **12b**), methyl 4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoate (compound **14b**), methyl 4-bromo-2-cyclohexylsulfanyl-5-sulfamoyl-benzoate (compound **16b**).

The mixture of appropriate 2,4-dihalogeno-*N*-substituted-5-sulfamoylbenzamides (compounds **3-7, 9-12**) or methyl 2,4-dihalogeno-5-sulfamoylbenzoate (compounds **14**, **16**) (1.00 mmol), DMSO (2 mL), cyclohexanethiol (128 mg, 1.10 mmol) and K_2CO_3 (553 mg, 4.00 mmol) was heated at 60 °C temperature for 2-4 h. The mixture was cooled to room temperature and brine was added. The product was extracted with EtOAc (3x7 mL). The organic layer was washed with H_2O, dried over anhydrous $MgSO_4$, filtered and concentrated.

The compound **3b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (1:2), R_f = 0.23. Yield: 307 mg, 78%, mp 136-140°C.

^{1}H NMR δ ppm: 1.23-1.45 (5H, m, Cy-H), 1.58-1.61 (1H, m, Cy-H), 1.69-1.72 (2H, m, Cy-H), 1.90-1.93 (2H, m, Cy-H), 3.29 (2H, q, *J* = 6.0 Hz, NHCH_2), 3.49-3.58 (3H, m, CH_2OH, Cy-H), 4.73 (1H, t, *J* = 5.6 Hz, OH), 7.62 (1H, s, C_3-H), 7.63 (2H, s, SO_2NH_2), 7.86 (1H, s, C_6-H), 8.50 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 25.6, 25.7, 32.8, 42.5, 44.2, 60.1, 128.4, 130.4, 131.8, 136.4, 137.6, 141.6, 166.5.

HRMS calcd. for $C_{15}H_{21}ClN_2O_4S_2$[(M+H)$^+$]: 393.0704, found: 393.0707.

The compound **4b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (1:2), R_f = 0.23. Yield: 366 mg, 90%, mp 157-159°C.

^{1}H NMR δ ppm: 1.24-1.47 (5H, m, Cy-H), 1.58-1.61 (1H, m, Cy-H), 1.63-1.72 (4H, m, Cy-H, CH_2), 1.90-1.93 (2H, m, Cy-H), 3.27 (2H, q, *J* = 6.4 Hz, NHCH_2), 3.49 (2H, q, *J* = 6.0 Hz, CH_2OH), 3.52-3.58 (1H, m, Cy-H), 4.47 (1H, t, *J* = 5.2 Hz, OH), 7.63 (1H, s, C_3-H), 7.64 (2H, s, SO_2NH_2), 7.81 (1H, s, C_6-H), 8.49 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 25.6, 25.7, 32.7, 32.8, 36.9, 44.3, 59.0, 128.2, 130.6, 131.7, 136.7, 137.7, 141.4, 166.4.

HRMS calcd. for $C_{16}H_{23}ClN_2O_4S_2$[(M+H)$^+$]: 407.0861, found407.0856.

The compound **5b.** The product was purified by chromatography on a column of silica gel with :$CHCl_3$:EtOAc (3:1), R_f = 0.35.Yield: 340 mg, 84%, mp 153-154°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2 Hz, CH_3), 1.24-1.41 (7H, m, Cy-H, CH_2), 1.49 (2H, quint, *J* = 6.8 Hz, CH_2), 1.57 (1H, br s, Cy-H), 1.69 (2H, br s, Cy-H), 1.90-1.93 (2H, m, Cy-H), 3.22 (2H, q, *J* = 6.0 Hz, NHCH_2), 3.55 (1H, br s, Cy-H), 7.64 (3H, s, C_3-H, SO_2NH_2), 7.80 (1H, s, C_6-H), 8.48 (1H, br s, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 25.5, 25.7, 31.5, 32.7, 39.1, 44.2, 128.2, 130.6, 131.7, 136.9, 137.8, 141.3, 166.3.

HRMS calcd. for $C_{17}H_{25}ClN_2O_3S_2$[(M+H)$^+$]: 405.1068, found: 405.1064.

The compound **6b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (1:1), R_f = 0.30. Yield: 285 mg, 70%, mp 130-133°C.

^{1}H NMR δ ppm: 1.24-1.42 (5H, m, Cy-H), 1.58-1.61 (1H, m, Cy-H), 1.69-1.71 (2H, m, Cy-H), 1.91-1.93 (2H, m, Cy-H), 3.29 (3H, m, CH_3), 3.36-3.39 (2H, m, $NHCH_2$), 3.44-3.46 (2H, m, OCH_2), 3.55 (1H, br s, Cy-H), 7.64 (3H, s, C_3-H, SO_2NH_2), 7.83 (1H, s, C_6-H), 8.61 (1H, br s, NH).

^{13}C NMR δ ppm: 25.6, 25.7, 32.8, 39.4, 44.2, 58.4, 70.8, 128.4, 130.6, 131.8, 136.4, 137.7, 141.5, 166.5.

HRMS calcd. for $C_{16}H_{23}ClN_2O_4S_2[(M+H)^+]$: 407.0861, found: 407.0862.

The compound **7b.** Yield: 418 mg, 93%, mp 165-167°C.

^{1}H NMR δ ppm: 1.15-1.44 (5H, m, Cy-H), 1.57-1.60 (1H, m, Cy-H), 1.68-1.73 (2H, m, Cy-H), 1.77 (2H, quint, *J* = 7.2 Hz, CH_2), 1.89-1.92 (2H, m, Cy-H), 2.43 (2H, t, *J* = 7.2 Hz, $COCH_2$), 3.24 (2H, q, *J* = 6.4 Hz, $NHCH_2$), 3.53-3.58 (1H, m, Cy-H), 3.61 (3H, s, CH_3), 7.65 (3H, s, C_3-H, SO_2NH_2), 7.81 (1H, s, C_6-H), 8.55 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 24.8, 25.5, 25.7, 31.1, 32.7, 38.7, 40.6, 51.8, 128.1, 130.8, 131.7, 136.9, 137.9, 141.2, 166.5, 173.6.

HRMS calcd. for $C_{18}H_{25}ClN_2O_5S_2[(M+H)^+]$: 449.0966, found: 449.0962.

The compound **9b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (5:1), R_f = 0.20. Yield: 410 mg, 95%, mp 92-94°C.

^{1}H NMR δ ppm: 1.10-1.38 (10H, m, Cy-H), 1.57-1.60 (2H, m, Cy-H), 1.69-1.73 (4H, m, Cy-H), 1.82-1.84 (2H, m, Cy-H), 1.90-1.92 (2H, m, Cy-H), 3.51-3.57 (1H, m, Cy-H), 3.67-3.75 (1H, m, Cy-H), 7.63 (1H, s, C_3-H), 7.64 (2H, s, SO_2NH_2), 7.77 (1H, s, C_6-H), 8.40 (1H, d, *J* = 7.6 Hz, NH).

^{13}C NMR δ ppm: 25.0, 25.6 (2C), 25.7, 32.6, 32.8, 40.4, 48.7, 128.2, 130.8, 131.5, 137.2, 137.8, 141.1, 165.5.

HRMS calcd. for $C_{19}H_{27}ClN_2O_3S_2[(M+H)^+]$: 431.1224, found: 431.1227.

The compound **10b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (3:1), R_f = 0.24. Yield: 378 mg, 86%, mp 160-162°C.

^{1}H NMR δ ppm: 1.21-1.43 (5H, m, Cy-H), 1.56-1.59 (1H, m, Cy-H), 1.68-1.71 (2H, m, Cy-H), 1.89-1.92 (2H, m, Cy-H), 3.54-3.60 (1H, m, Cy-H), 4.45 (2H, d, *J* = 6.0 Hz, CH_2), 7.25-7.29 (1H, m, Ph-H), 7.33-7.40 (4H, m, Ph-H), 7.67 (3H, s, C_3-H, SO_2NH_2), 7.87 (1H, s, C_6-H), 9.09 (1H, t, *J* = 6.0 Hz, NH_2).

^{13}C NMR δ ppm: 25.4, 25.7, 32.7, 43.0, 44.3, 127.4, 127.8, 128.3, 128.7, 130.8, 131.9, 136.5, 137.8, 139.5, 141.5, 166.5.

HRMS calcd. for $C_{20}H_{23}ClN_2O_3S_2[(M+H)^+]$: 439.0911, found: 439.0914.

The compound und **11b**. The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.46. Yield: 367 mg, 84%, mp 118-120°C.

^{1}H NMR δ ppm: 1.23-1.44 (5H, m, Cy-H), 1.57-1.60 (1H, m, Cy-H), 1.69-1.72 (2H, m, Cy-H), 1,89-1,92 (2H, m, Cy-H), 3.29 (2H, q, *J* = 6.4 Hz, NHC<u>H</u>$_2$), 3.48-3.56 (3H, m, HOC<u>H</u>$_2$, Cy-H), 4.72 (1H, t, *J* = 5.6 Hz, OH), 7.60 (2H, s, SO_2NH_2), 7.77 (1H, s, C_3-H), 7.88 (1H, s, C_6-H), 8.48 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 25.6, 25.7, 32.8, 42.4, 44.4, 60.1, 120.3, 128.4, 134.1, 137.2, 139.5, 141.2, 166.6.

HRMS calcd. for $C_{15}H_{21}BrN_2O_4S_2$ [(M+H)$^+$]: 439.0178 (100%), found: 439.0177 (100%).

The compound **12b**. The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (4:1), R_f = 0.31. Yield: 166 mg, 37%, mp 127-129°C.

^{1}H NMR δ ppm: 0.90 (3H, t, *J* = 7.2, Hz, CH_3), 1.21-1.40 (7H, m, CH_3C<u>H</u>$_2$, Cy-H), 1.43-1.52 (2H, m, CH_3CH_2C<u>H</u>$_2$), 1.57-1.60 (1H, m, Cy-H), 1.68-1.72 (2H, m, Cy-H), 1.89-1.92 (2H, m, Cy-H), 3.20 (2H, q, *J* = 6.4 Hz, NHC<u>H</u>$_2$), 3.52-3.57 (1H, m, Cy-H), 7.62 (2H, s, SO_2NH_2), 7.78 (1H, s, C_3-H), 7.82 (1H, s, C_6-H), 8.48 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 25.5, 25.7, 31.5, 32.7, 39.1, 44.4, 120.1, 128.2, 134.2, 137.7, 139.7, 140.9, 166.4.

HRMS calcd. for $C_{17}H_{25}BrN_2O_3S_2$[(M+H)$^+$]: 451.0542 (100%), found: 451.0546 (100%).

The compound **14b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (10:1), R_f = 0.40. Yield: 131 mg, 36%, mp 112-114°C.

^{1}H NMR δ ppm: 1.21-1.30 (2H, m, Cy-H), 1.38-1.50 (4H, m, Cy-H), 1.60-1.63 (1H, m, Cy-H), 1.70-1.76 (3H, m, Cy-H), 3.71-3.79 (1H, m, Cy-H), 3.88 (3H, s, CH_3), 7.65 (2H, s, SO_2NH_2), 7,71 (1H, s, C_3-H), 8.33 (1H, s, C_6-H).

^{13}C NMR δ ppm: 25.6, 25.7, 32.4, 40.6, 53.2, 125.1, 130.2, 131.5, 136.4, 140.2, 142.9, 164.4.

HRMS calcd. for $C_{14}H_{18}ClNO_4S_2$[(M+H)$^+$]: 364.0439, found: 364.0440.

The compound **16b**. The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (15:1), R_f = 0.29. Yield: 180 mg, 44%, mp 123–125°C.

^{1}H NMR δ ppm: 1.24-1.31 (1H, m, Cy-H), 1.38-1.50 (4H, m, Cy-H), 1.60-1.63 (1H, m, Cy-H), 1.70-1.75 (2H, m, Cy-H), 1.95-1.97 (2H, m, Cy-H), 3.69-3.74 (1H, m, Cy-H), 3.88 (3H, s, CH_3), 7.54 (2H, s, SO_2NH_2), 7.85 (1H, s, C_6-H), 8.27 (1H, s, C_3-H).

^{13}C NMR δ ppm: 25.6, 25.7, 32.4, 44.5, 53.2, 125.1, 127.5, 131.0, 133.6, 140.1, 142.5, 165.0.

HRMS calcd. for $C_{14}H_{18}BrNO_4S_2$[(M+H)$^+$]: 409.9913 (100%), found: 409.9915 (100%).

Example 9. Preparation of methyl 4-[(2-benzylsulfanyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **7c**), methyl 2-benzylsulfanyl-4-chloro-5-sulfamoyl-benzoate (compound **14c**), methyl 4-chloro-2-phenethylsulfanyl-5-sulfamoyl-benzoate (compound **14d**).

The mixture of appropriate methyl 4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **7**) or methyl 2,4-dichloro-5-sulfamoyl-benzoate (compound **14**) (1.00 mmol), DMSO (2 mL), appropriate phenylmethanethiol or 2-phenylethanethiol (1.10 mmol) and Et_3N (121 mg, 1.20 mmol) was heated at 50 °C temperature for 6-12 h. The progress of reaction was monitored by TLC. The mixture was cooled to room temperature and brine was added. The product was extracted with EtOAc (3x7 mL). The organic layer was washed with H_2O, dried over anhydrous $MgSO_4$, filtered and concentrated.

The compound **7c.** The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (1:1), R_f = 0.42, and then recrystallization was accomplished from H_2O:MeOH (5:1) . Yield: 306 mg, 67%, mp 115-118°C.

^{1}H NMR δ ppm: 1.75 (2H, quint, *J* = 7.2 Hz, CH_2), 2.38 (2H, t, *J* = 7.6 Hz, $COCH_2$), 3.22 (2H, q, *J* = 6.8 Hz, $NHCH_2$), 3.59 (3H, s, CH_3), 4.37 (2H, s, CH_2Ph), 7.25-7.36 (3H, m, Ph-H), 7.40-7.43 (2H, m, Ph-H), 7.62 (2H, s, SO_2NH_2), 7.64 (1H, s, C_3-H), 7.86 (1H, s, C_6-H), 8.64 (1H, t, *J* = 6.0 Hz, NH).

^{13}C NMR δ ppm: 24.7, 31.1, 36.2, 38.8, 51.8, 127.9, 128.1, 128.8, 129.0, 129.5, 132.2, 134.2, 136.6, 137.2, 143.4, 166.2, 173.5.

HRMS calcd. for $C_{19}H_{21}ClN_2O_5S_2$ [$(M+H)^+$]: 457.0653, found: 457.0652.

The compound **14c.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (4:1), R_f = 0.48. Yield: 119 mg, 32%, mp 125-126°C.

^{1}H NMR δ ppm: 3.84 (3H, s, CH_3), 4.50 (2H, s, CH_2), 7.27-7.38 (3H, m, Ph-H), 7.50-7.52 (2H, m, Ph-H), 7.64 (2H, s, SO_2NH_2), 7.69 (1H, s, C_3-H), 8.31 (1H, s, C_6-H).

^{13}C NMR δ ppm: 36.3, 53.2, 124.9, 128.0, 129.1, 129.2, 129.8, 131.3, 135.8, 136.4, 139.1, 143.7, 164.3.

HRMS calcd. for $C_{15}H_{14}ClNO_4S_2$ [$(M+H)^+$]: 372.0126, found: 372.0125.

The compound **14d.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (5:1), R_f = 0.67. Yield: 96.5 mg, 25%, mp 111-112°C.

^{1}H NMR δ ppm: 2.97 (2H, t, *J* = 7.6 Hz, CH_2Ph), 3.46 (2H, t, *J* = 7.6 Hz, CH_2S), 3.88 (3H, s, CH_3),

7.23 (1H, br s, Ph-H), 7.29-7.33 (4H, m, Ph-H), 7.59 (2H, s, SO_2NH_2), 7.65 (1H, s, C_3-H), 8.31 (1H, s, C_6-H).

^{13}C NMR δ ppm: 33.3, 34.1, 53.2, 124.8, 126.9, 128.9, 129.1, 129.2, 131.2, 136.5, 139.4, 140.0, 143.9, 164.4.

HRMS calcd. for $C_{16}H_{16}ClNO_4S_2$ [(M+H)$^+$]: 386.0282, found: 386.0282.

Example 10. Preparation of 2-benzylsulfanyl-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3c**), 2-benzylsulfanyl-*N*-butyl-4-chloro-5-sulfamoyl-benzamide (compound **5c**), *N*-butyl-4-chloro-2-phenethylsulfanyl-5-sulfamoyl-benzamide (compound **5d**), 2-benzylsulfanyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **9c**), 4-chloro-*N*-cyclohexyl-2-(2-hydroxyethylsulfanyl)-5-sulfamoyl-benzamide (compound **9e**), 2-benzylsulfanyl-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **11c**), 4-bromo-*N*-(2-hydroxyethyl)-2-phenethylsulfanyl-5-sulfamoyl-benzamide (compound **11d**), 2-benzylsulfanyl-4-bromo-*N*-butyl-5-sulfamoyl-benzamide (compound **12c**), 4-bromo-*N*-butyl-2-phenethylsulfanyl-5-sulfamoyl-benzamide (compound **12d**), 4-bromo-*N*-butyl-2-(2-hydroxyethylsulfanyl)-5-sulfamoyl-benzamide (compound **12e**).

The mixture of appropriate 2,4-dihalogeno-*N*-substituted-5-sulfamoylbenzamides (compounds **3**, **5**, **9, 11,** and **12**) (1.00 mmol), DMSO (2 mL), appropriate phenylmethanethiol, 2-phenylethanethiol, or 2-mercaptoethanol (1.10 mmol) and Et_3N (121 mg, 1.20 mmol) was heated at 50-70 °C temperature for 6-12 h. The progress of reaction was monitored by TLC. The mixture was cooled to room temperature and brine was added. The product was extracted with EtOAc (3x7 mL). The organic layer was washed with H_2O, dried over anhydrous $MgSO_4$, filtered and concentrated.

The compound **3c.** Recrystallization was accomplished from H_2O:MeOH (5:1) and then from toluene:MeOH (5:1). Yield: 241 mg, 60%, mp 193-195°C.

^{1}H NMR δ ppm: 3.28 (2H, q, *J* = 6.0 Hz, NH$\underline{CH_2}$), 3.50 (2H, q, *J* = 6.0 Hz, $\underline{CH_2}$OH), 4.35 (2H, s, $\underline{CH_2}$Ph), 4.73 (1H, t, *J* = 5.6 Hz, OH), 7.26-7.44 (5H, m, Ph-H), 7.59 (2H, s, SO_2NH_2), 7,62 (1H, s, C_3-H), 7,92 (1H, s, C_6-H), 8.56 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 36.2, 42.5, 60.0, 127.9, 128.3, 128.7, 129.0, 129.5, 132.2, 133.9, 136.6, 137.0, 134.8, 166.3.

HRMS calcd. for $C_{16}H_{17}ClN_2O_4S_2$ [(M+H)$^+$]: 401.0391, found: 401.0393.

The compound **5c.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (3:1), R_f = 0.40. Yield: 153 mg, 37%, mp 148-150°C.

^{1}H NMR δ ppm: 0.89 (3H, t, *J* = 7.2 Hz, CH_3), 1.33 (2H, sext, *J* = 7.2 Hz, CH_2), 1.48 (2H, quint, *J* = 7.2 Hz, CH_2), 3.20 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 4.36 (2H, s, $\underline{CH_2}$Ph), 7.25-7.36 (3H, m, Ph-H), 7.41-7.43 (2H, m, Ph-H), 7.61 (2H, s, SO_2NH_2), 7,63 (1H, s, C_3-H), 7.85 (1H, s, C_6-H), 8.56 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 31.4, 36.2, 39.2, 127.8, 128.1, 128.8, 129.0, 129.5, 132.1, 134.4, 136.6, 137.2, 143.4, 166.1.

HRMS calcd. for $C_{18}H_{21}ClN_2O_3S_2$ [(M+H)$^+$]: 413.0755, found: 413.0757.

The compound **5d.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (3:1), R_f = 0.45. Yield: 265 mg, 62%, mp 87-88°C.

^{1}H NMR δ ppm: 0.90 (3H, t, *J* = 7.2 Hz, CH_3), 1.34 (2H, sext, *J* = 7.2 Hz, CH_2), 1.48 (2H, quint, *J* = 7.2 Hz, CH_2), 2.89 (2H, t, *J* = 7.6 Hz, $\underline{CH_2}$Ph), 3.20 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 3.32-3.35 (2H, m, CH_2S), 7.21-7.25 (1H, m, Ph-H), 7.28-7.33 (4H, m, Ph-H), 7.60 (1H, s, C_3-H), 7.62 (2H, s, SO_2NH_2), 7.83 (1H, s, C_6-H), 8.53 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.1, 31.5, 33.2, 34.3, 39.2, 126.9, 128.1, 128.7, 128.8, 129.1, 132.1, 135.1, 137.2, 140.1, 143.2, 166.2.

HRMS calcd. for $C_{19}H_{23}ClN_2O_3S_2$ [(M+H)$^+$]: 427.0911, found: 427.0907.

The compound **9c.** Recrystallization was accomplished from H_2O:MeOH (5:1) and then from toluene:MeOH (5:1). Yield: 329 mg, 75%, mp 194-196°C.

^{1}H NMR δ ppm: 1.07-1.13 (1H, m, Cy-H), 1.22-1.33 (4H, m, Cy-H), 1.56-1.59 (1H, m, Cy-H), 1.66-1.72 (2H, m, Cy-H), 1.79-1.85 (2H, m, Cy-H), 3.63-3.72 (1H, m, Cy-H), 4.36 (2H, s, $\underline{CH_2}$Ph), 7.25-7.31 (1H, m, Ph-H), 7.33-7.36 (2H, m, Ph-H), 7.41-7.43 (2H, m, Ph-H), 7.61 (2H, s, SO_2NH_2), 7.62 (1H, s, C_3-H), 7.81 (1H, s, C_6-H), 8.47 (1H, d, *J* = 7.6 Hz, NH).

^{13}C NMR δ ppm: 25.1, 25.6, 32.6, 36.2, 48.8, 127.9, 128.1, 128.8, 128.9, 129.0, 129.5, 129.9, 131.9, 136.7, 143.2, 165.3.

HRMS calcd. for $C_{20}H_{23}ClN_2O_3S_2$ [(M+H)$^+$]: 439.0911, found: 439.0911.

The compound **9e.** The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (1:1), R_f = 0.18, and then recrystallization was accomplished from H_2O:MeOH (5:1) . Yield: 185 mg, 47%, mp 180-181°C.

^{1}H NMR δ ppm: 1.09-1.18 (1H, m, Cy-H), 1.20-1.35 (4H, m, Cy-H), 1.57-1.60 (1H, m, Cy-H), 1.70-1.74 (2H, m, Cy-H), 1.82-1.84 (2H, m, Cy-H), 3.13 (2H, t, *J* = 6.4 Hz, SCH_2), 3.61 (2H, q, *J* = 6.0 Hz, $\underline{CH_2}$OH), 3.66-3.74 (1H, m, Cy-H), 5.05 (1H, t, *J* = 5.6 Hz, OH), 7.61 (1H, s, C_3-H), 7.62 (2H, s, SO_2NH_2), 7.78 (1H, s, C_6-H), 8.44 (1H, d, *J* = 7.6 Hz, NH).

^{13}C NMR δ ppm: 25.1, 25.7, 32.6, 35.1, 48.7, 59.9, 128.1, 128.7, 131.9, 135.5, 137.2, 143.2, 165.5.

HRMS calcd. for $C_{15}H_{21}ClN_2O_4S_2$ [(M+H)$^+$]: 393.0704, found: 393.0706.

The compound **11c**. The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.50. Yield: 352 mg, 79%, mp 147-149°C.

^{1}H NMR δ ppm: 3.28 (2H, q, *J* = 6.0 Hz, NH$\underline{CH_2}$), 3.50 (2H, q, *J* = 6.4 Hz, HO$\underline{CH_2}$), 4.35 (2H, s, S$\underline{CH_2}$), 4.74 (1H, t, *J* = 5.2 Hz, OH), 7.26-7,45 (5H, m, Ph-H), 7.56 (2H, s, SO_2NH_2), 7.77 (1H, s, C_3-H), 7.94 (1H, s, C_6-H), 8.55 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 36.2, 42.5, 60.0, 120.9, 127.9, 128.3, 129.0, 129.5, 132.2, 134.6, 136.6, 138.9, 143.4, 166.4.

HRMS calcd. for $C_{16}H_{17}BrN_2O_4S_2[(M+H)^+]$: 446.9865 (100%), found: 446.9870 (100%).

The compound **11d**. The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.42. Yield: 193 mg, 42%, mp 154-156°C.

^{1}H NMR δ ppm: 2.89 (2H, t, *J* = 7.6 Hz, $SCH_2\underline{CH_2}$), 3.26-3,32 (4H, m, $NH\underline{CH_2}$, $S\underline{CH_2}$), 3.50 (2H, q, *J* = 6.0 Hz, $HO\underline{CH_2}$), 4.74 (1H, t, *J* = 5.2 Hz, OH), 7.21-7.34 (5H, m, Ph-H), 7.58 (2H, s, SO_2NH_2), 7.74 (1H, s, C_3-H), 7.92 (1H, s, C_6-H), 8.53 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 33.3, 34.3, 42.5, 60.1, 120.9, 126.9, 128.3, 128.9, 129.0, 132.1, 135.3, 138.9, 140.2, 143.1, 166.5.

HRMS calcd. for $C_{17}H_{19}BrN_2O_4S_2[(M+H)^+]$: 461.0022 (100%), found: 461.0016 (100%).

The compound **12c**. The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (4:1), R_f = 0.24. Yield: 165 mg, 36%, mp 155-157°C.

^{1}H NMR δ ppm: 0.89 (3H, t, *J* = 7.2, Hz, CH_3), 1.34 (2H, sext, *J* = 7.2 Hz, $CH_3\underline{CH_2}$), 1.48 (2H, quint, *J* = 6.8 Hz, $CH_3CH_2\underline{CH_2}$), 3.20 (2H, q, *J* = 6.8 Hz, $NH\underline{CH_2}$), 4.36 (2H, s, $S\underline{CH_2}$), 7.25-7.43 (5H, m, Ph-H), 7.57 (2H, s, SO_2NH_2), 7.78 (1H, s, C_3-H), 7.87 (1H, s, C_6-H), 8.54 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 31.4, 36.2, 39.2, 120.7, 127.8, 128.1, 129.0, 129.5, 132.3, 135.1 136.7, 139.0, 143.0, 166.2.

HRMS calcd. for $C_{18}H_{21}BrN_2O_3S_2[(M+H)^+]$: 459.0230 (100%), found: 459.0231 (100%).

The compound **12d**. The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc(4:1), R_f = 0.28. Yield: 259 mg, 55%, mp 157-159°C.

^{1}H NMR δ ppm0.91 (3H, t, *J* = 7.2, Hz, CH_3), 1.35 (2H, sext, *J* = 7.2 Hz, $CH_3\underline{CH_2}$), 1.49 (2H, quint, *J* = 6.8 Hz, $CH_3CH_2\underline{CH_2}$), 2.90 (2H, t, *J* = 7.2 Hz, $SCH_2\underline{CH_2}$), 3.21 (2H, q, *J* = 6.4 Hz, $NH\underline{CH_2}$), 3.33 (2H, t, *J* = 7.6 Hz, $S\underline{CH_2}$), 7.21-7.33 (5H, m, Ph-H), 7.53 (2H, s, SO_2NH_2), 7.74 (1H, s, C_3-H), 7.87 (1H, s, C_6-H), 8.44 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 31.5, 33.3, 34.4, 39.2, 120.7, 126.9, 128.2, 128.8, 129.0, 132.1 135.9, 139.0 140.1, 142.8, 166.3.

HRMS calcd. for $C_{19}H_{23}BrN_2O_3S_2[(M+H)^+]$: 473.0386 (100%), found: 473.0385 (100%).

The compound **12e**. The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (3:1), R_f = 0.32. Yield: 144 mg, 35%, mp 153-155°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2, Hz, CH_3), 1.35 (2H, sext, *J* = 7.2 Hz, $CH_3\underline{CH_2}$), 1.49 (2H, quint, *J* = 7.2 Hz, $CH_3CH_2\underline{CH_2}$), 3.13 (2H, t, *J* = 6.4 Hz, $S\underline{CH_2}$), 3.21 (2H, q, *J* = 6.8 Hz, $NH\underline{CH_2}$),

3.61 (2H, q, *J* = 6.0 Hz, $SCH_2\underline{CH_2}$), 5.05 (1H, t, *J* = 5.6 Hz, OH), 7.58 (2H, s, SO_2NH_2), 7.77 (1H, s, C_3-H), 7.84 (1H, s, C_6-H), 8.51 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 18.9, 24.8, 36.2, 39.8, 43.9, 64.7, 125.4, 132.9, 136.8, 140.6, 143.7, 147.8, 171.1.

HRMS calcd. for $C_{13}H_{19}BrN_2O_4S_2$[(M+H)$^+$]: 413.0022 (100%), found: 413.0018 (100%).

Example 11. Preparation of 5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-4-phenethylsulfanyl-benzenesulfonamide (compound **29d**).

The mixture of 5-[2-(benzimidazol-1-yl)acetyl]-2,4-dichloro-benzenesulfonamide (compound **29**) (65.0 mg, 0.168 mmol), DMSO (1 mL), 2-phenylethanethiol (24.0 mg, 0.168 mmol) and Et_3N (17.6 mg, 0.175 mmol) was stirred at room temperature for 24 h. The brine was added to the mixture and product was extracted with EtOAc (3x5 mL). The organic layer was washed with H_2O, dried over anhydrous $MgSO_4$, filtered and concentrated.

Recrystallization was accomplished from EtOAc:MeOH (5:1). Yield: 25.0 mg, 31%, mp 205-207°C.

^{1}H NMR δ ppm: 2.92 (2H, t, *J* = 7.2 Hz, $\underline{CH_2}$Ph), 3.33-3.40 (2H, m, CH_2S), 6.00 (2H, s, CH_2CO), 7.19-7.32 (7H, m, Ph-H, $C_{5',6'}$-H), 7.50 (1H, dd, *J* = 6.0 Hz, *J* = 2.8 Hz, $C_{7'}$-H), 7.69 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, $C_{4'}$-H), 7.72 (1H, s, C_3-H), 7.83 (2H, s, SO_2NH_2), 8.15 (1H, s, $C_{2'}$-H), 8.66 (1H, s, C_6-H).

^{13}C NMR δ ppm: 33.0, 33.7, 52.0, 111.1, 119.8, 122.0, 122.8, 126.9, 128.8, 128.9, 129.0, 129.1, 130.1, 135.1, 135.4, 136.8, 140.0, 143.6, 145.3, 147.7, 193.3.

HRMS calcd. for $C_{23}H_{20}ClN_3O_3S_2$ [(M+H)$^+$]: 486.0707, found: 486.0709.

Example 12. Preparation of 4-chloro-2-(cyclohexylamino)-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3f**), 2-(benzylamino)-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **3g**), 4-chloro-2-(cyclohexylamino)-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4f**), 2-(benzylamino)-4-chloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **4g**), *N*-butyl-4-chloro-2-(cyclohexylamino)-5-sulfamoyl-benzamide (compound **5f**), 2-(benzylamino)-*N*-butyl-4-chloro-5-sulfamoyl-benzamide (compound **5g**), *N*-butyl-4-chloro-2-(cyclooctylamino)-5-sulfamoyl-benzamide (compound **5h**), 4-chloro-2-(cyclohexylamino)-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6f**), 2-(benzylamino)-4-chloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **6g**), *N*-benzyl-2-(benzylamino)-4-chloro-5-sulfamoyl-benzamide (compound **10g**), methyl 4-chloro-2-(cyclohexylamino)-5-sulfamoyl-benzoate (compound **14f**), methyl 2-(benzylamino)-4-chloro-5-sulfamoyl-benzoate (compound **14g**).

The mixture of appropriate 2,4-dichloro-*N*-substituted-5-sulfamoylbenzamides (compounds **3-6, 10**) or methyl 2,4-dichloro-5-sulfamoyl-benzoate (compound **14**) (1.00 mmol), and appropriate amine (6 mmol) was heated at 120 °C for 3-4 h (for amides **3-6, 10**) or at 60 °C for 3 h (for ester **14**). The mixture was cooled to room temperature and 2N HCl(aq) (2 mL) was added. The resultant precipitate was washed with H_2O.

The compound **3f.** The product was purified by chromatography on a column of silica gel with EtOAc, R_f = 0.65 and then recrystallization was accomplished from toluene:2-PrOH (5:1). Yield: 90.2 mg, 24%, mp 210-212°C.

^{1}H NMR δ ppm: 1.20-1.30 (3H, m, Cy-H), 1.38-1.46 (2H, m, Cy-H), 1.55-1.58 (1H, m, Cy-H), 1.64-1.68 (2H, m, Cy-H), 1.86-1.89 (2H, m, Cy-H), 3.29 (2H, q, *J* = 6.0 Hz, NHCH$_2$), 3.48-3.54 (3H, m, CH$_2$OH, Cy-H), 4.72 (1H, t, *J* = 5.6 Hz, OH), 6.86 (1H, s, C$_3$-H), 7.17 (2H, s, SO$_2$NH$_2$), 8.11 (1H, s, C$_6$-H), 8.51 (1H, d, *J* = 8.0 Hz, CyNH), 8.56 (1H, t, *J* = 5.6 Hz, CONH).

^{13}C NMR δ ppm: 24.3, 25.7, 32.4, 40.6, 49.9, 60.0, 112.4, 113.1, 125.8, 130.7, 135.0, 151.3, 168.4.

HRMS calcd. for $C_{15}H_{22}ClN_3O_4S$ [(M+H)$^+$]: 376.1092, found: 376.1092.

The compound **3g.** Recrystallization was accomplished three times from toluene:2-PrOH (8:1). Yield: 61.4 mg, 16%, mp 225-228°C.

^{1}H NMR δ ppm: 3.31 (2H, q, *J* = 6.0 Hz, NHCH$_2$), 3.51 (2H, t, *J* = 6.0 Hz, CH$_2$OH), 4.49 (2H, d, *J* = 5.6 Hz, NHCH$_2$Ph), 4.73 (1H, br s, OH), 6.76 (1H, s, C$_3$-H), 7.19 (2H, s, SO$_2$NH$_2$), 7.25-7.39 (5H, m, Ph-H), 8.12 (1H, s, C$_6$-H), 8.62 (1H, t, *J* = 5.6 Hz, NHBn), 8.75 (1H, t, *J* = 5.6 Hz, CONH).

^{13}C NMR δ ppm: 42.4, 46.2, 60.0, 113.4, 113.5, 126.6, 127.5, 127.6, 129.1, 130.4, 134.7, 138.9, 151.9, 168.2.

HRMS calcd. for $C_{16}H_{18}ClN_3O_4S$ [(M+H)$^+$]: 384.0779, found: 384.0781.

The compound **4f.** Recrystallization was accomplished from: toluene:2-PrOH (1:1). Yield: 179 mg, 46%, mp 192-194°C.

^{1}H NMR δ ppm: 1.20-1.30 (3H, m, Cy-H), 1.37-1.49 (2H, m, Cy-H), 1.56-1.58 (1H, m, Cy-H), 1.63-1.68 (4H, m, Cy-H, CH$_2$), 1.87-1.89 (2H, m, Cy-H), 3.27 (2H, q, *J* = 6.4 Hz, NHCH$_2$), 3.46 (2H, t, *J* = 6.4 Hz, CH$_2$OH), 3.51 (1H, br s, Cy-H), 4.41 (1H, br s, OH), 6.85 (1H, s, C$_3$-H), 7.17 (2H, s, SO$_2$NH$_2$), 8.09 (1H, s, C$_6$-H), 8.49 (1H, d, *J* = 7.6 Hz, CyNH), 8.61 (1H, t, *J* = 5.2 Hz, CONH).

^{13}C NMR δ ppm: 24.3, 25.7, 32.4, 32.7, 39.4, 49.9, 59.1, 112.5, 113.1, 125.8, 130.6, 135.0, 151.3, 168.3.

HRMS calcd. for $C_{16}H_{24}ClN_3O_4S$ [(M+H)$^+$]: 390.1249, found: 390.1252.

The compound **4g.** The product was purified by chromatography on a column of silica gel with EtOAc:CHCl$_3$ (2:1), R_f = 0.25. Yield: 171 mg, 43%, mp 179-182°C.

^{1}H NMR δ ppm: 1.68 (2H, quint, *J* = 6.8 Hz, CH$_2$), 3.29 (2H, q, *J* = 6.4 Hz, NHCH$_2$), 3.45-3.49 (2H, m, CH$_2$OH), 4.48 (3H, d, *J* = 6.0 Hz, NHCH$_2$Ph, OH), 6.76 (1H, s, C$_3$-H), 7.20 (2H, s, SO$_2$NH$_2$), 7.26-7.39 (5H, m, Ph-H), 8.10 (1H, s, C$_6$-H), 8.68 (1H, t, *J* = 5.6 Hz, NHBn), 8.74 (1H, t, *J* = 5.6 Hz, CONH).

^{13}C NMR δ ppm: 32.7, 39.6, 46.2, 59.1, 113.4, 113.7, 126.6, 127.5, 127.6, 129.1, 130.3, 134.7, 138.9, 151.9, 168.0.

HRMS calcd. for $C_{17}H_{20}ClN_3O_4S$ [(M+H)$^+$]: 398.0936, found: 398.0936.

The compound **5f.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (5:1), R_f = 0,33. Yield: 167 mg, 43%, mp 182-184°C.

^{1}H NMR δ ppm: 0.90 (3H, t, *J* = 7.2 Hz, CH_3), 1.20-1.58 (10H, m, Cy-H, CH_2CH_2), 1.64-1.67 (2H, m, Cy-H), 1.87-1.89 (2H, m, Cy-H), 3.21 (2H, q, *J* = 6.4 Hz, NHCH$_2$), 3.50 (1H, br s, Cy-H), 6.85 (1H, s, C_3-H), 7.17 (2H, s, SO_2NH_2), 8.09 (1H, s, C_6-H), 8.47 (1H, d, *J* = 7.6 Hz, CyNH), 8.62 (1H, t, *J* = 5.2 Hz, CONH).

^{13}C NMR δ ppm: 14.2, 20.1, 24.2, 25.7, 31.5, 32.4, 39.4, 49.9, 112.7, 113.0, 125.8, 130.6, 134.9, 151.3, 168.2.

HRMS calcd. for $C_{17}H_{26}ClN_3O_3S$ [(M+H)$^+$]: 388.1456, found: 388.1456.

The compound **5g.** Recrystallization was accomplished from toluene:2-PrOH (8:1). Yield: 91.1 mg, 23%, mp 204-206°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2 Hz, CH_3), 1.33 (2H, sext, *J* = 7.2 Hz, CH_2), 1.50 (2H, quint, *J* = 7.2 Hz, CH_2), 3.23 (2H, q, *J* = 6.8 Hz, CONHCH$_2$), 4.48 (2H, d, *J* = 5.6 Hz, NHCH$_2$Ph), 6.76 (1H, s, C_3-H), 7.19 (2H, s, SO_2NH_2), 7.25-7.39 (5H, m, Ph-H), 8.10 (1H, s, C_6-H), 8.68 (1H, t, *J* = 5.6 Hz, NHBn), 8.72 (1H, t, *J* = 6.0 Hz, CONH).

^{13}C NMR δ ppm: 14.2, 20.1, 31.5, 39.1, 46.2, 113.4, 113.8, 126.6, 127.5, 127.6, 129.1, 130.3, 134.6, 138.9, 151.9, 167.9.

HRMS calcd. for $C_{18}H_{22}ClN_3O_3S$ [(M+H)$^+$]: 396.1143, found: 396.1145.

The compound **5h.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (5:1), R_f = 0.35. Yield: 112 mg, 27%, mp 172-174°C.

^{1}H NMR δ ppm: 0.90 (3H, t, *J* = 7.2 Hz, CH_3), 1.32 (2H, sext, *J* = 7.2 Hz, CH_2), 1.45-1.65 (14H, m, Cy-H, CH_2), 1.78-1.83 (2H, m, Cy-H), 3.19-3.23 (2H, m, NHCH$_2$), 3.66 (1H, br s, Cy-H), 6.75 (1H, s, C_3-H), 7.17 (2H, s, SO_2NH_2), 8.10 (1H, s, C_6-H), 8.52 (1H, d, *J* = 7.6 Hz, CyNH), 8.62 (1H, br s, CONH).

^{13}C NMR δ ppm: 14.2, 20.1, 23.4, 25.4, 27.3, 31.4, 31.5, 39.1, 51.4, 112.8, 113.3, 125.8, 130.6, 134.9, 151.1, 168.2.

HRMS calcd. for $C_{19}H_{30}ClN_3O_3S$ [(M+H)$^+$]: 416.1769, found: 416.1770.

The compound **6f.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (3:1), R_f = 0.21. Yield: 129 mg, 33%, mp 214-216°C.

^{1}H NMR δ ppm: 1.16-1.30 (3H, m, Cy-H), 1.37-1.47 (2H, m, Cy-H), 1.55-1.58 (1H, m, Cy-H), 1.64-1.68 (2H, m, Cy-H), 1.86-1.92 (2H, m, Cy-H), 3.27 (3H, m, CH_3), 3.35-3.40 (2H, m,

NHCH$_2$), 3.43-3.46 (2H, m, OCH$_2$), 3.47-3.60 (1H, m, Cy-H), 6.87 (1H, s, C$_3$-H), 7.19 (2H, s, SO$_2$NH$_2$), 8.11 (1H, s, C$_6$-H), 8.50 (1H, d, *J* = 8.0 Hz, CyNH),8.68 (1H, t, *J* = 5.6 Hz, CONH).

^{13}C NMR δ ppm: 24.3, 25.7, 32.4, 39.2, 49.9, 58.4, 70.7, 112.2, 113.1, 125.8, 130.7, 135.1, 151.3, 168.4.

HRMS calcd. for $C_{16}H_{24}ClN_3O_4S$ [(M+H)$^+$]: 390.1249, found: 390.1247.

The compound **6g.** The product was purified by chromatography on a column of silica gel with CHCl$_3$:EtOAc (1:1), R$_f$ = 0.25. Yield: 163 mg, 41%, mp 194-197°C.

^{1}H NMR δ ppm: 3.28 (3H, s, CH$_3$), 3.38-3.42 (2H, m, CONHCH$_2$), 3.45-3.47 (2H, m, OCH$_2$), 4.49 (2H, d, *J* = 5.6 Hz, NHCH$_2$Ph), 6.77 (1H, s, C$_3$-H), 7.21 (2H, s, SO$_2$NH$_2$), 7.25-7.39 (5H, m, Ph-H), 8.12 (1H, s, C$_6$-H), 8.75 (2H, br s, BnNH, CONH).

^{13}C NMR δ ppm: 39.2, 46.2, 58.4, 70.7, 113.3, 113.4, 126.6, 127.5, 127.6, 129.1, 130.4, 134.8, 138.8, 151.9, 168.2.

HRMS calcd. for $C_{17}H_{20}ClN_3O_4S$ [(M+H)$^+$]: 398.0936, found: 398.0932.

The compound **10g.** The product was purified by chromatography on a column of silica gel with CHCl$_3$:EtOAc (10:1), R$_f$ = 0.13. Yield: 116 mg, 27%, mp 213-216°C.

^{1}H NMR δ ppm: 4.45 (2H, d, *J* = 6.0 Hz, CONHCH$_2$), 4.50 (2H, d, *J* = 6.0 Hz, NHCH$_2$), 6.80 (1H, s, C$_3$-H),

7.22 (2H, s, SO$_2$NH$_2$), 7.26-7.39 (10H, m, Ph-H), 8.22 (1H, s, C$_6$-H), 8.82 (1H, t, *J* = 6.0 Hz, BnNH), 9.30 (1H, t, *J* = 6.0 Hz, CONH$_2$).

^{13}C NMR δ ppm: 42.9, 46.2, 113.1, 113.6, 126.6, 127.3, 127.5, 127.6, 127.7, 128.8, 129.1, 130.4, 134.9, 138.8, 139.9, 152.1, 168.1.

HRMS calcd. for $C_{21}H_{20}ClN_3O_3S$ [(M+H)$^+$]: 430.0987, found: 430.0987.

The compound **14f.** The product was purified by chromatography on a column of silica gel with CHCl$_3$:EtOAc (10:1), R$_f$ = 0.30. Yield: 38.2 mg, 11%, mp 184-186°C.

^{1}H NMR δ ppm: 1.25-1.33 (3H, m, Cy-H), 1.40-1.48 (2H, m, Cy-H), 1.56-1.59 (1H, m, Cy-H), 1.65-1.69 (2H, m, Cy-H), 1.90-1.92 (2H, m, Cy-H), 3.60-3.66 (1H, m, Cy-H), 3.84 (3H, s, CH$_3$), 7.02 (1H, s, C$_3$-H), 7.34 (2H, s, SO$_2$NH$_2$), 8.18 (1H, d, *J* = 8.0 Hz, NH), 8.40 (1H, s, C$_6$-H).

^{13}C NMR δ ppm: 24.2, 25.6, 32.4, 50.0, 52.6, 106.7, 114.0, 126.6, 133.6, 137.3, 152.0, 167.7.

HRMS calcd. for $C_{14}H_{19}ClN_2O_4S$ [(M+H)$^+$]: 347.0827, found: 347.0828.

The compound **14g.** The product was purified by chromatography on a column of silica gel with CHCl$_3$:EtOAc (10:1), R$_f$ = 0.29. Yield: 42.6 mg, 12%, mp 178-180°C.

^{1}H NMR δ ppm: 3.86 (3H, s, CH$_3$), 4.59 (2H, d, *J* = 6.0 Hz, CH$_2$), 6.88 (1H, s, C$_3$-H), 7.26-7.39 (7H, m, Ph-H, SO$_2$NH$_2$), 8.41 (1H, s, C$_6$-H), 8.59 (1H, t, *J* = 6.0 Hz, NH).

^{13}C NMR δ ppm: 46.2, 52.6, 107.7, 114.4, 127.2, 127.5, 127.7, 129.2, 133.4, 137.0, 138.5, 152.7, 167.3.

HRMS calcd. for $C_{15}H_{15}ClN_2O_4S$ [(M+H)$^+$]: 355.0514, found: 355.0513.

Example 13. Preparation of 4-bromo-N-butyl-2-(cyclohexylamino)-5-sulfamoyl-benzamide (compound **12f**), 2-(benzylamino)-4-bromo-N-butyl-5-sulfamoyl-benzamide (compound **12g**).

The mixture of 2,4-dibromo-N-butyl-5-sulfamoyl-benzamide (compounds **16**) (1.00 mmol), appropriate amine (2.50 mmol), and 1,4-dioxane was refluxed for 7 days. The solvent was removed under reduced pressure and 2N HCl(aq) (2 mL) was added. The resultant precipitate was washed with H_2O.

The compound **12f**. The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (5:1), R_f = 0.30. Yield: 151 mg, 35%, mp 203-205°C.

^{1}H NMR δ ppm: 0.90 (3H, t, *J* = 7.2, Hz, CH_3), 1.16-1.57 (10H, m, $CH_3\underline{CH_2}$, $CH_3CH_2\underline{CH_2}$, Cy-H), 1.64-1.67 (2H, m, Cy-H), 1.86-1.88 (2H, m, Cy-H), 3.20 (2H, q, *J* = 6.8 Hz, $NH\underline{CH_2}$), 3.49-3.51 (1H, m, Cy-H), 7.02 (1H, s, C_3-H), 7.13 (2H, s, SO_2NH_2), 8.11 (1H, s, C_6-H), 8.41 (1H, d, *J* = 7.6 Hz, $\underline{NH}$Cy), 8.61 (1H, t, *J* = 5.6 Hz, $\underline{NH}CH_2$).

^{13}C NMR δ ppm: 14.2, 20.1, 24.2, 25.7, 31.5, 32.4, 39.1, 49.8, 113.1, 116.6, 123.8, 127.4, 130.6, 151.0, 168.3.

HRMS calcd. for $C_{17}H_{26}BrN_3O_3S$[(M+H)$^+$]: 434.0932 (100%), found: 434.0933 (100%).

The compound **12g**. The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (5:1), R_f = 0.34. Yield: 176 mg, 40%, mp 207-209°C.

^{1}H NMR δ ppm: 0.90 (3H, t, *J* = 7.2, Hz, CH_3), 1.32 (2H, sext, *J* = 7.2 Hz, $CH_3\underline{CH_2}$), 1.50 (2H, quint, *J* = 7.2 Hz, $CH_3CH_2\underline{CH_2}$), 3.21 (2H, q, *J* = 6.8 Hz, $NH\underline{CH_2}CH_2$), 4.48 (2H, d, *J* = 5.6 Hz, $NH\underline{CH_2}Ph$), 6.95 (1H, s, C_3-H), 7.15 (2H, s, SO_2NH_2), 7.26-7.39 (5H, m, Ph-H), 8.11 (1H, s, C_6-H), 8.64-8.66 (2H, m, $\underline{NH}CH_2Ph$, $\underline{NH}CH_2$).

^{13}C NMR δ ppm: 14.2, 20.1, 31.5, 39.1, 46.2, 114.2, 117.0, 123.5, 127.5, 127.6, 128.2, 129.1, 130.3, 138.9, 151.6, 168.0.

HRMS calcd. for $C_{18}H_{22}BrN_3O_3S$[(M+H)$^+$]: 442.0619 (100%), found: 442.0623 (100%).

Example 14. Preparation of 2-(benzenesulfonyl)-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **33a**), 4-chloro-2-cyclohexylsulfonyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **33b**), 2-benzylsulfonyl-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **33c**), 2-(benzenesulfonyl)-4-chloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **34a**), 4-chloro-2-cyclohexylsulfonyl-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide (compound **34b**), 4-bromo-2-cyclohexylsulfonyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide

(compound **40b**), 2-benzylsulfonyl-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **40c**).

The 30% H_2O_2(aq) (1.50 mmol, 0.148 mL) was added to a solution of appropriate 2-halogeno-4-substitutedsulfanyl-5-substitutedbenzenesulfonamide (compounds **3(a-c), 4(a, b), 11(b, c)**) (0.500 mmol) in AcOH (1.77 mL) at 70°C and allowed stirring for 2-3h. The solvent was removed under reduced pressure, then methanol (2 mL), H_2O (1 mL) and concentrated HCl (aq) (1mL) was added and solution was refluxed for 3 hours. The solvents were removed at a reduced pressure and the resultant precipitate was washed with H_2O.

The compound **33a.** Yield: 182 mg, 87%, mp 168-170°C.

^{1}H NMR δ ppm: 3.31-3.36 (2H, m, NHC$\underline{H_2}$), 3.57 (2H, t, *J* = 6.0 Hz, C$\underline{H_2}$OH), 4.62 (1H, br s, OH), 7.64 (2H, t, *J* = 7.2 Hz, $C_{3',5'}$-H), 7.74 (1H, t, *J* = 7.6 Hz, $C_{4'}$-H), 7.94 (1H, s, C_3-H), 7.96 (2H, s, SO_2NH_2), 8.11 (2H, d, *J* = 7.6 Hz, $C_{2',6'}$-H), 8.35 (1H, s, C_6-H), 8.73 (1H, br s, NH).

^{13}C NMR δ ppm: 42.7, 59.9, 129.0, 129.8 (2C), 132.1, 132.7, 134.8, 136.9, 140.4, 142.1, 145.4, 165.9.

HRMS calcd. for $C_{15}H_{15}ClN_2O_6S_2$ [(M+H)$^+$]: 419.0133, found: 419.0135.

The compound **33b.** Yield: 170 mg, 80%, mp 246-248°C.

^{1}H NMR δ ppm: 1.17-1.24 (3H, m, Cy-H), 1.38-1.46 (2H, m, Cy-H), 1.64 (1H, br s, Cy-H), 1.80-1.83 (4H, m, Cy-H), 3.31 (2H, q, *J* = 5.6 Hz, NHC$\underline{H_2}$), 3.52 (2H, t, *J* = 6.0 Hz, C$\underline{H_2}$OH), 3.80 (1H, t, *J* = 12.0 Hz, Cy-H), 4.69 (1H, br s, OH), 7.99 (2H, s, SO_2NH_2), 8.00 (1H, s, C_3-H), 8.06 (1H, s, C_6-H), 8.83 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 24.9 (2C), 25.2, 42.6, 59.8, 63.0, 130.1, 131.8, 133.5, 137.6, 139.4, 145.4, 166.2.

HRMS calcd. for $C_{15}H_{21}ClN_2O_6S_2$ [(M+H)$^+$]: 425.0602, found: 425.0600.

The compound **33c.** Yield: 165 mg, 76%, mp 118-120°C.

^{1}H NMR δ ppm: 3.37 (2H, s, NHC$\underline{H_2}$, superposed with H_2O), 3.56 (2H, br s, C$\underline{H_2}$OH), 4.78 (1H, br s, OH), 4.98 (2H, br s, C$\underline{H_2}$Ph), 7.24 (2H, br s, Ph-H), 7.34 (3H, br s, Ph-H), 7.59 (1H, s, C_3-H), 8.00 (2H, s, SO_2NH_2), 8.07 (1H, s, C_6-H), 8.95 (1H, br s, NH).

^{13}C NMR δ ppm: 42.7, 59.9, 62.2, 128.2, 129.0, 129.3, 129.7, 131.5 (2C), 133.3, 137.2, 140.1, 145.5, 166.5.

HRMS calcd. for $C_{16}H_{17}ClN_2O_6S_2$ [(M+H)$^+$]: 433.0289, found: 433.0293.

The compound **34a.** Yield: 188 mg, 87%, mp 142-144°C.

^{1}H NMR δ ppm: 1.72 (2H, quint, *J* = 6.8 Hz, CH_2), 3.31 (2H, q, *J* = 6.8 Hz, NHC$\underline{H_2}$), 3.52 (2H, t, *J* = 6.0 Hz, C$\underline{H_2}$OH), 4.50 (1H, br s, OH), 7.64 (2H, t, *J* = 7.6 Hz, $C_{3',5'}$-H), 7.74 (1H, t, *J* = 7.2

Hz, $C_{4'}$-H), 7.89 (1H, s, C_3-H), 7.97 (2H, s, SO_2NH_2), 8.11 (2H, d, *J* = 7.6 Hz, $C_{2',6'}$-H), 8.35 (1H, s, C_6-H), 8.69 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 32.4, 37.1, 58.9, 129.0, 129.7, 129.8, 132.1, 132.7, 134.8, 136.9, 140.4, 142.1, 145.4, 165.7.

HRMS calcd. for $C_{16}H_{17}ClN_2O_6S_2$ [(M+H)$^+$]: 433.0289, found: 433.0288.

The compound **34b.** Yield: 189 mg, 86%, mp 153-155°C.

^{1}H NMR δ ppm: 1.14-1.24 (3H, m, Cy-H), 1.38-1.46 (2H, m, Cy-H), 1.64-1.71 (3H, m, Cy-H, CH_2), 1.81-1.83 (4H, m, Cy-H), 3.29 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 3.49 (2H, t, *J* = 6.4 Hz, $\underline{CH_2}$OH), 3.79 (1H, t, *J* = 11.6 Hz, Cy-H), 4.47 (1H, br s, OH), 8.00 (2H, s, $C_{3,6}$-H), 8.01 (2H, s, SO_2NH_2), 8.90 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 24.9 (2C), 25.2, 32.4, 37.1, 58.9, 63.1, 130.0, 131.8, 133.6, 137.7, 139.4, 145.5, 166.0.

HRMS calcd. for $C_{16}H_{23}ClN_2O_6S_2$ [(M+H)$^+$]: 439.0759, found: 439.0760.

The compound **40b**. Yield: 178 mg, 76%, mp 235-237°C.

^{1}H NMR δ ppm: 1.16-1.24 (3H, m, Cy-H), 1.37-1.45 (2H, m, Cy-H), 1.60-1.65 (1H, m, Cy-H), 1.80-1.82 (4H, m, Cy-H), 3.30 (2H, q, *J* = 6.0 Hz, NH$\underline{CH_2}$), 3.52 (2H, q, *J* = 5.6 Hz, HO$\underline{CH_2}$), 3.75-3.81 (1H, m, Cy-H), 4.70 (1H, t, *J* = 5.2 Hz, OH), 7.94 (2H, s, SO_2NH_2), 8.07 (1H, s, C_6-H), 8.13 (1H, s, C_3-H), 8.81 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 24.8, 24.9, 25.2, 42.6, 59.8, 63.0, 120.1, 130.0, 136.8, 138.1, 139.0, 147.3, 166.3.

HRMS calcd. for $C_{15}H_{21}BrN_2O_6S_2$[(M+H)$^+$]: 471.0077 (100%), found: 471.0081 (100%).

The compound **40c**. Yield: 168 mg, 78%, mp 139-141°C.

^{1}H NMR δ ppm: 3.36-3.42 (2H, m, NH$\underline{CH_2}$), 3.56-3.59 (2H, m, HO$\underline{CH_2}$), 4.77 (1H, br. s, OH), 4.98 (2H, s, S$\underline{CH_2}$), 7.23-7.36 (5H, m, Ph-H), 7.75 (1H, s, C_6-H), 7.96 (2H, s, SO_2NH_2), 8.09 (1H, s, C_3-H), 8.94 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 42.7, 59.9, 62.2, 119.9, 128.2, 129.0, 129.2, 129.7, 131.5, 136.7, 137.7, 139.7, 147.3, 166.6.

HRMS calcd. for $C_{16}H_{17}BrN_2O_6S_2$[(M+H)$^+$]: 478.9764 (100%), found: 478.9769 (100%).

Example 15. Preparation of 2-(benzenesulfonyl)-*N*-butyl-4-chloro-5-sulfamoyl-benzamide (compound **35a**), *N*-butyl-4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **35b**), 2-(benzenesulfonyl)-4-chloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **36a**), 4-chloro-2-cyclohexylsulfonyl-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide (compound **36b**), methyl 4-[(4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzoyl)amino]butanoate (compound **37b**), methyl 4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **37c**), 2-(benzenesulfonyl)-

4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **38a**), 4-chloro-*N*-cyclohexyl-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **38b**), 2-benzylsulfonyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **38c**), 4-chloro-*N*-cyclohexyl-2-(2-hydroxyethylsulfonyl)-5-sulfamoyl-benzamide (compound **38e**), 2-(benzenesulfonyl)-*N*-benzyl-4-chloro-5-sulfamoyl-benzamide (compound **39a**), *N*-benzyl-4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **39b**), 2-(benzenesulfonyl)-4-bromo-*N*-butyl-5-sulfamoyl-benzamide (compound **41a**), 4-bromo-*N*-butyl-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide (compound **41b**), methyl 2-(benzenesulfonyl)-4-chloro-5-sulfamoyl-benzoate (compound **42a**), methyl 4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzoate (compound **42b**), methyl 2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoate (compound **42c**), methyl 2-(benzenesulfonyl)-4-bromo-5-sulfamoyl-benzoate (compound **43a**), methyl 4-bromo-2-cyclohexylsulfonyl-5-sulfamoyl-benzoate (compound **43b**).

The 30% H_2O_2(aq) (1.50 mmol, 0.148 mL) was added to a solution of appropriate benzenesulfonamide (compounds **5(a, b), 6(a, b), 7(b, c), 9(a-c, e), 10(a, b), 12(a, b), 14(a-c), 16(a, b)**) (0.500 mmol) in AcOH (1.77 mL) at 70°C and allowed stirring for 2-3h. The solvent was removed under reduced pressure and the resultant precipitate was washed with H_2O.

The compound **35a.** Yield: 198 mg, 92%, mp 182-184°C.

^{1}H NMR δ ppm: 0.93 (3H, t, *J* = 7.2 Hz, CH_3), 1.39 (2H, sext, *J* = 7.2 Hz, CH_2), 1.54 (2H, quint, *J* = 7.2 Hz, CH_2), 3.26 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 7.65 (2H, t, *J* = 7.2 Hz, $C_{3',5'}$-H), 7.74 (1H, t, *J* = 7.2 Hz, $C_{4'}$-H), 7.89 (1H, s, C_3-H), 7.98 (2H, s, SO_2NH_2), 8.11 (2H, d, *J* = 7.6 Hz, $C_{2',6'}$-H), 8.35 (1H, s, C_6-H), 8.69 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.2, 20.1, 31.2, 39.5, 129.0, 129.7, 129.8, 132.1, 132.7, 134.7, 137.0, 140.4, 142.1, 145.4, 165.6.

HRMS calcd. for $C_{17}H_{19}ClN_2O_5S_2$ [(M+H)$^+$]: 431.0497, found: 431.0494.

The compound **35b.** Yield: 175 mg, 80%, mp 213-214°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.6 Hz, CH_3), 1.14-1.24 (3H, m, Cy-H), 1.32-1.54 (6H, m, Cy-H, $(CH_2)_2$), 1.64 (1H, br s, Cy-H), 1.80-1.83 (4H, m, Cy-H), 3.24 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 3.80 (1H, t, *J* = 12.0 Hz, Cy-H), 8.00 (4H, s, SO_2NH_2, $C_{3,6}$-H), 8.81 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 24.9 (2C), 25.2, 31.2, 39.4, 63.0, 130.0, 131.7, 133.6, 137.7, 139.4, 145.5, 165.9.

HRMS calcd. for $C_{17}H_{25}ClN_2O_5S_2$ [(M+H)$^+$]: 437.0966, found: 437.0966.

The compound **36a.** Yield: 186 mg, 86%, mp 208-211°C.

^{1}H NMR δ ppm: 3.31 (3H, s, CH_3), 3.42 (2H, q, *J* = 5.2 Hz, NH$\underline{CH_2}$), 3.51 (2H, t, *J* = 5.6 Hz, OCH_2), 7.65 (2H, t, *J* = 7.6 Hz, $C_{3',5'}$-H), 7.74 (1H, t, *J* = 7.2 Hz, $C_{4'}$-H), 7.89 (1H, s, C_3-H), 7.96 (2H, s, SO_2NH_2), 8.12 (2H, d, *J* = 7.6 Hz, $C_{2',6'}$-H), 8.34 (1H, s, C_6-H), 8.82 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 39.7, 58.5, 70.6, 129.0, 129.8, 129.9, 132.1, 132.7, 134.7, 136.7, 140.4, 142.1, 145.4, 165.9.

HRMS calcd. for $C_{16}H_{17}ClN_2O_6S_2$[(M+H)$^+$]: 433.0289, found: 433.0293.

The compound **36b.** Yield: 178 mg, 81%, mp 207-209°C.

^{1}H NMR δ ppm: 1.13-1.24 (3H, m, Cy-H), 1.38-1.46 (2H, m, Cy-H), 1.64 (1H, br s, Cy-H), 1.81-1.83 (4H, m, Cy-H), 3.29 (3H, s, CH_3), 3.40 (2H, q, *J* = 5.2 Hz, NH$\underline{CH_2}$), 3.47 (2H, t, *J* = 5.2 Hz, OCH_2), 3.78 (1H, t, *J* = 12.0 Hz, Cy-H), 8.00 (2H, s, $C_{3,6}$-H), 8.01 (2H, s, SO_2NH_2), 8.93 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 24.9 (2C), 25.2, 39.6, 58.4, 63.1, 70.6, 130.1, 131.8, 133.6, 137.5, 139.4, 145.4, 166.2.

HRMS calcd. for $C_{16}H_{23}ClN_2O_6S_2$ [(M+H)$^+$]: 439.0759, found: 439.0757.

The compound **37b.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (1:1), R_f = 0.41. Yield: 123 mg, 51%, mp 150-152°C.

^{1}H NMR δ ppm: 1.10-1.24 (3H, m, Cy-H), 1.38-1.46 (2H, m, Cy-H), 1.63 (1H, br s, Cy-H), 1.73-1.82 (6H, m, Cy-H, CH_2), 2.41 (2H, t, *J* = 7.2 Hz, $COCH_2$), 3.27 (2H, q, *J* = 6.4 Hz, NH$\underline{CH_2}$), 3.61 (3H, s, CH_3), 3.78 (1H, m, Cy-H), 8.00 (3H, s, C_3-H, SO_2NH_2), 8.02 (1H, s, C_6-H), 8.86 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 24.5, 24.9 (2C), 25.2, 31.0, 39.0, 51.7, 63.1, 129.9, 131.8, 133.6, 137.6, 139.4, 145.5, 166.1, 173.6.

HRMS calcd. for $C_{18}H_{25}ClN_2O_7S_2$ [(M+H)$^+$]: 481.0864, found: 481.0867.

The compound **37c.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (1:1), R_f = 0.48. Yield: 215 mg, 88%, mp 108-110°C.

^{1}H NMR δ ppm: 1.82 (2H, quint, *J* = 7.2 Hz, CH_2), 2.47 (2H, t, *J* = 7.6 Hz, $COCH_2$), 3.31-3.35 (2H, m, NH$\underline{CH_2}$, superposed with H_2O), 3.62 (3H, s, CH_3), 4.99 (2H, s, $\underline{CH_2}$Ph), 7.24-7.26 (2H, m, Ph-H), 7.32-7.39 (3H, m, Ph-H), 7.61 (1H, s, C_3-H), 8.02 (2H, s, SO_2NH_2), 8.04 (1H, s, C_6-H), 8.98 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 24.5, 31.1, 39.1, 51.8, 62.1, 128.2, 129.0, 129.3, 129.6, 131.5, 131.6, 133.3, 137.2, 140.1, 145.6, 166.4, 173.6.

HRMS calcd. for $C_{19}H_{21}ClN_2O_7S_2$ [(M+H)$^+$]: 489.0551, found: 489.0553.

The compound **38a.** Recrystallization was accomplished from MeOH. Yield: 128 mg 56%, mp 259-261°C.

^{1}H NMR δ ppm: 1.13-1.22 (1H, m, Cy-H), 1.23-1.39 (4H, m, Cy-H), 1.58-1.61 (1H, m, Cy-H), 1.73-1.76 (2H, m, Cy-H), 1.91-1.94 (2H, m, Cy-H), 3.71-3.78 (1H, m, Cy-H),7.64 (2H, t, *J* = 8.0

Hz, $C_{3',5'}$-H), 7.73 (1H, t, *J* = 7.6 Hz, $C_{4'}$-H), 7.86 (1H, s, C_3-H), 7.96 (2H, s, SO_2NH_2), 8.11 (2H, d, *J* = 7.2 Hz, $C_{2',6'}$-H), 8.33 (1H, s, C_6-H), 8.61 (1H, d, *J* = 7.6 Hz, NH).

^{13}C NMR δ ppm: 24.9, 25.7, 32.3, 48.9, 129.0, 129.7, 129.8, 131.9, 132.7, 134.7, 137.1, 140.5, 142.0, 145.4, 164.9.

HRMS calcd. for $C_{19}H_{21}ClN_2O_5S_2$[(M+H)$^+$]: 457.0653, found: 457.0656.

The compound **38b.** Yield: 201 mg, 87%, mp 264-266°C.

^{1}H NMR δ ppm: 1.11-1.46 (10H, m, Cy-H), 1.56-1.64 (2H, m, Cy-H), 1.71-1.74 (2H, m, Cy-H), 1.80-1.92 (6H, m, Cy-H), 3.68-3.80 (2H, m, Cy-H), 7.97 (1H, s, C_3-H), 7.99 (1H, s, C_6-H), 8.00 (2H, s, SO_2NH_2),

8.71 (1H, d, *J* = 7.6 Hz, NH).

^{13}C NMR δ ppm: 24.9 (3C), 25.2, 25.7, 32.3, 48.8, 63.0, 130.0, 131.6, 133.5, 137.8, 139.3, 145.4, 165.1.

HRMS calcd. for $C_{19}H_{27}ClN_2O_5S_2$ [(M+H)$^+$]: 463.1123, found: 463.1123.

The compound **38c.** Yield: 186 mg, 79%, mp 248-251°C.

^{1}H NMR δ ppm: 1.12-1.40 (5H, m, Cy-H), 1.58-1.61 (1H, m, Cy-H), 1.73-1.76 (2H, m, Cy-H), 1.91-1.93 (2H, m, Cy-H), 3.74-3.83 (1H, m, Cy-H), 4.98 (2H, s, $\underline{CH_2}$Ph), 7.23-7.25 (2H, m, Ph-H), 7.31-7.37 (3H, m, Ph-H), 7.57 (1H, s, C_3-H), 7.99 (1H, s, C_6-H), 8.02 (2H, s, SO_2NH_2), 8.83 (1H, d, *J* = 8.0 Hz, NH).

^{13}C NMR δ ppm: 24.9, 25.7, 32.3, 49.0, 62.2, 128.3, 129.0, 129.2, 129.6, 131.4, 131.5, 133.2, 137.4, 140.0, 145.5, 165.4.

HRMS calcd. for $C_{20}H_{23}ClN_2O_5S_2$ [(M+H)$^+$]: 471.0810, found: 471.0810.

The compound **38e.** Yield: 95.6 mg, 45%, mp 257-260°C.

^{1}H NMR δ ppm: 1.13-1.35 (5H, m, Cy-H), 1.56-1.59 (1H, m, Cy-H), 1.70-1.73 (2H, m, Cy-H), 1.85-1.88 (2H, m, Cy-H), 3.66-3.80 (5H, m, SCH_2, $\underline{CH_2}$OH, Cy-H), 5.03 (1H, t, *J* = 4.8 Hz, OH), 7.94 (1H, s, C_3-H), 8.00 (2H, s, SO_2NH_2), 8.05 (1H, s, C_6-H), 8.71 (1H, d, *J* = 7.6 Hz, NH).

^{13}C NMR δ ppm: 24.9, 25.6, 32.3, 48.9, 55.4, 59.4, 129.5, 131.5, 133.2, 137.1, 142.0, 145.2, 165.4.

HRMS calcd. for $C_{15}H_{21}ClN_2O_6S_2$ [(M+H)$^+$]: 425.0602, found: 425.0603.

The compound **39a.** Yield: 212 mg, 91%, mp 250-253°C.

^{1}H NMR δ ppm: 4.51 (2H, d, *J* = 5.6 Hz, CH_2), 7.29 (1H, t, *J* = 7.2 Hz, $C_{4''}$-H), 7.38 (2H, t, *J* = 7.2 Hz, $C_{3'',5''}$-H), 7.43 (2H, d, *J* = 7.2 Hz, $C_{2'',6''}$-H), 7.63 (2H, t, *J* = 7.6 Hz, $C_{3',5'}$-H), 7.73 (1H, t, *J* = 7.6 Hz, $C_{4'}$-H), 7.94 (1H, s, C_3-H), 7.98 (2H, s, SO_2NH_2), 8.11 (2H, d, *J* = 7.6 Hz, $C_{2',6'}$-H), 8.38 (1H, s, C_6-H), 9.22 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 43.4, 127.5, 128.1, 128.8, 129.0, 129.8 (2C), 132.3, 132.8, 134.8, 136.6, 139.0, 140.4, 142.2, 145.5, 165.8.

HRMS calcd. for $C_{20}H_{17}ClN_2O_5S_2$ [(M+H)$^+$]: 465.0340, found: 465.0338.

The compound **39b.** Recrystallization was accomplished from 1-BuOH:toluene (8:1). Yield: 113 mg, 48%, mp 270-272°C.

^{1}H NMR δ ppm: 1.17 (3H, br s, Cy-H), 1.42-1.45 (2H, m, Cy-H), 1.62 (1H, br s, Cy-H), 1.81 (4H, br s, Cy-H), 3.80 (1H, t, *J* = 11.2 Hz, Cy-H), 4.49 (2H, d, *J* = 4.8 Hz, CH_2), 7.28-7.39 (5H, m, Ph-H), 8.01 (2H, s, SO_2NH_2), 8.03 (1H, s, C_3-H,), 8.07 (1H, s, C_6-H), 9.35 (1H, br s, NH).

^{13}C NMR δ ppm: 24.8 (2C), 25.2, 43.3, 63.1, 127.5, 127.9, 128.8, 130.1, 132.0, 133.7, 137.3, 139.0, 139.5, 145.5, 166.0

HRMS calcd. for $C_{20}H_{23}ClN_2O_5S_2$ [(M+H)$^+$]: 471.0810, found: 471.0811.

The compound **41a**. Yield: 155 mg, 65%, mp 212-214°C.

^{1}H NMR δ ppm: 0.93 (3H, t, *J* = 7.2 Hz, CH_3), 1.39 (2H, sext, *J* = 7.2 Hz, $CH_3\underline{CH_2}$), 1.53 (2H, quint, *J* = 7.2 Hz, $CH_3CH_2\underline{CH_2}$), 3.25 (2H, q, *J* = 6.8 Hz, $NH\underline{CH_2}$), 7.62-7.75 (3H, m, Ph-H), 7.90 (1H, s, C_6-H), 7.93 (2H, s, SO_2NH_2), 8.08-8.10 (2H, m, Ph-H), 8.45 (1H, s, C_3-H), 8.66 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.2, 20.0, 31.1, 39.5, 120.3, 128.9, 129.7, 129.8, 134.7, 135.9, 137.5, 140.4, 141.7, 147.3, 165.7.

HRMS calcd. for $C_{17}H_{19}BrN_2O_5S_2$[(M+H)$^+$]: 476.9971 (100%), found: 476.9972 (100%).

The compound **41b**. Yield: 205 mg, 85%, mp 222-224°C.

^{1}H NMR δ ppm: 0.91 (3H, t, *J* = 7.2, Hz, CH_3), 1.16-1,24 (3H, m, Cy-H), 1.32-1.53 (2H, m, $CH_3\underline{CH_2}$, 2H, m, $CH_3CH_2\underline{CH_2}$ ir 2H, m, Cy-H), 1.63 (1H, m, Cy-H), 1.80-1.82 (4H, m, Cy-H), 3.23 (2H, q, *J* = 6.8 Hz, $NH\underline{CH_2}$), 3.75-3.81 (1H, m, Cy-H), 7.96 (2H, s, SO_2NH_2), 8.02 (1H, s, C_3-H), 8.14 (1H, s, C_6-H), 8.78 (1H, t, *J* = 5.6 Hz, NH).

^{13}C NMR δ ppm: 14.1, 20.0, 24.8, 24.9, 25.2, 31.2, 39.4, 63.0, 120.0, 130.0, 136.8, 138.2, 139.0, 147.3, 166.0.

HRMS calcd. for $C_{17}H_{25}BrN_2O_5S_2$[(M+H)$^+$]: 483.0441 (100%), found: 483.0435 (100%).

The compound **42a.** The product was purified by chromatography on a column of silica gel with $CHCl_3$:EtOAc (4:1), R_f = 0.33. Yield: 158 mg, 81%, mp 166-168°C.

^{1}H NMR δ ppm: 3.86 (3H, s, CH_3), 7.68 (2H, t, *J* = 7.6 Hz, $C_{3',5'}$-H), 7.68 (1H, t, *J* = 7.6 Hz, $C_{4'}$-H), 8.03 (2H, s, SO_2NH_2), 8.07 (2H, d, *J* = 7.6 Hz, $C_{2',6'}$-H), 8.23 (1H, s, C_3-H), 8.51 (1H, s, C_6-H).

^{13}C NMR δ ppm: 53.8, 128.5, 130.1, 130.3, 131.7, 133.5, 134.2, 134.9, 140.0, 142.3, 146.0, 165.7.

HRMS calcd. for $C_{14}H_{12}ClNO_6S_2$ [(M+H)$^+$]: 389.9867, found: 389.9869.

The compound **42b.** Yield: 164 mg, 83%, mp 184-187°C.

^{1}H NMR δ ppm: 1.16-1.20 (3H, m, Cy-H), 1.42-1.50 (2H, m, Cy-H), 1.63 (1H, br s, Cy-H), 1.81-1.87 (4H, m, Cy-H), 3.89-3.92 (1H, m, Cy-H), 3.96 (3H, s, CH_3), 7.48 (2H, s, SO_2NH_2), 8.11 (1H, s, C_3-H), 8.57 (1H, s, C_6-H).

^{13}C NMR δ ppm: 24.9 (2C), 25.1, 53.9, 62.2, 133.3, 135.1, 135.5, 136.7, 138.6, 142.1, 163.9.

HRMS calcd. for $C_{14}H_{18}ClNO_6S_2$ [$(M+H)^+$]: 396.0337, found: 396.0336.

The compound **42c.** Recrystallization was accomplished from MeOH. Yield: 123 mg, 61%, mp 154-156°C.

^{1}H NMR δ ppm: 3.95 (3H, s, CH_3), 5.04 (2H, s, CH_2), 7.24-7.26 (2H, m, Ph-H), 7.33-7.40 (3H, m, Ph-H), 7.58 (2H, s, SO_2NH_2), 7.77 (1H, s, C_3-H), 8.57 (1H, s, C_6-H).

^{13}C NMR δ ppm: 53.9, 60.9, 127.5, 129.1, 129.5, 131.7, 132.9, 135.0, 135.4, 136.3, 139.2, 142.0, 163.8.

HRMS calcd. for $C_{15}H_{14}ClNO_6S_2$ [$(M+H)^+$]: 404.0024, found: 404.0023.

The compound **43a**. Yield: 189 mg, 87%, mp 191-193°C.

^{1}H NMR δ ppm: 3.86 (3H, s, CH_3), 7.67-7.79 (3H, m, Ph-H), 7.98 (2H, s, SO_2NH_2), 8.04-8.07 (2H, m, Ph-H), 8.22 (1H, s, C_6-H), 8.62 (1H, s, C_3-H).

^{13}C NMR δ ppm: 53.8, 122.7, 128.5, 130.1, 130.2, 132.2, 134.9, 136.7, 140.0, 141.9, 147.8, 165.8.

HRMS calcd. for $C_{14}H_{12}BrNO_6S_2$[$(M+H)^+$]: 435.9342 (100%), found: 435.9345 (100%).

The compound **43b**. Yield: 172 mg, 78%, mp 217-219°C.

^{1}H NMR δ ppm: 1.16-1.24 (3H, m, Cy-H), 1.42-1.50 (2H, m, Cy-H), 1.57-1.63 (1H, m, Cy-H), 1.79-1.86 (4H, m, Cy-H), 3.89-3.92 (1H, m, Cy-H), 3.95 (3H, s, CH_3), 7.47 (2H, s, SO_2NH_2), 8.25 (1H, s, C_3-H), 8.50 (1H, s, C_6-H).

^{13}C NMR δ ppm: 21.5, 24.9, 25.1, 53.9, 62.2, 125.3, 132.8, 137.7, 138.1, 138.4, 142.6, 164.6.

HRMS calcd. for $C_{14}H_{18}BrNO_6S_2$[$(M+H)^+$]: 441.9811 (100%), found: 441.9806 (100%).

Example 16. Preparation of 2-benzylsulfinyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **44**) and 2-(benzenesulfinyl)-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide (compound **45**).

The ~38% AcOOH (0.748 mmol) solution in AcOH (0.130 mL) was added dropwise to a solution of 2-benzylsulfanyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide (compound **9c**) or 4-bromo-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide (compound **11a)** (219 mg, 0.500 mmol) in AcOH (2 mL) at 50-60°C and allows stirring for 2-3h. The progress of reaction was

monitored by TLC. The solvent was removed under reduced pressure and the resultant precipitate was filtered, washed with H_2O.

The compound **44.** The product was purified by chromatography on a column of silica gel with EtOAc:$CHCl_3$ (1:1), R_f = 0.35. Yield: 150 mg, 66%, mp 240-243°C.

^{1}H NMR δ ppm: 1.11-1.39 (5H, m, Cy-H), 1.61-1.64 (1H, m, Cy-H), 1.76 (2H, br s, Cy-H), 1.83-1.92 (2H, m, Cy-H), 3.76-3.85 (1H, m, Cy-H), 4.05 (1H_A, d, *J* = 12.4 Hz, $\underline{CH_2}$Ph), 4.51 (1H_B, d, *J* = 12.4 Hz, $\underline{CH_2}$Ph), 7.06-7.09 (2H, m, Ph-H), 7.28-7.32 (3H, m, Ph-H), 7.57 (1H, s, C_3-H), 7.81 (2H, s, SO_2NH_2), 8.40 (1H, s, C_6-H), 9.05 (1H, d, *J* = 8.0 Hz, NH).

^{13}C NMR δ ppm: 25.3, 25.6, 32.7, 49.3, 62.2, 128.2, 128.4, 128.5, 128.6, 130.9, 131.2, 131.5, 133.9, 142.7, 151.2, 163.8.

HRMS calcd. for $C_{20}H_{23}ClN_2O_4S_2$ [$(M+H)^+$]: 455.0861, found: 455.0856.

The compound **45.** Yield: 127 mg, 57%, mp 138-142°C (dec).

^{1}H NMR δ ppm: 3.28 (2H, q, *J* = 5.6 Hz, NH$\underline{CH_2}$), 3.45 (2H, br s, $\underline{CH_2}$OH), 4.78 (1H, s, OH), 7.48-7.49 (3H, m, $C_{3',4',5'}$-H), 7.71 - 7.73 (2H, m, $C_{2',6'}$-H), 7.77 (2H, s, SO_2NH_2), 8.34 (1H, s, C_3-H), 8.38 (1H, s, C_6-H), 9.03 (1H, t, *J* = 5.2 Hz, NH).

^{13}C NMR δ ppm: 42.8, 59.8, 123.0, 126.2, 129.1, 129.7, 130.5, 131.6, 132.5, 144.6, 146.4, 152.0, 164.5.

HRMS calcd. for $C_{15}H_{15}BrN_2O_5S_2$[$(M+H)^+$]: 448.9658 (100%), found: 448.9663 (100%).

Example 17. Preparation of 4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoic acid (compound **46**), 4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoic acid (compound **47**), and 4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoic acid (compound **48**).

Apropriate methyl 4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **7**), methyl 4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoate (compound **7b**), or methyl 4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate (compound **37c**) (0.501 mmol) was refluxed in methanol (2 mL), H_2O (1 mL), and concentrated HCl (aq) (1mL) solution for 12-24 hours. The progress of reaction was monitored by TLC. The reaction mixture was concentrated under reduced pressure.

The compound **46.** Recrystallization was accomplished from NaOAc (20.6 mg, 0.251 mmol) solution in H_2O. Yield: 107 mg, 60%, mp 136-139°C.

^{1}H NMR δ ppm: 1.74 (2H, quint, *J* = 7.2 Hz, CH_2), 2.31 (2H, t, *J* = 7.2 Hz, $COCH_2$), 3.27 (2H, q, *J* = 6.8 Hz, NH$\underline{CH_2}$), 7.82 (2H, s, SO_2NH_2), 7.92 (1H, s, C_3-H), 7.95 (1H, s, C_6-H), 8.69 (1H, t, *J* = 5.6 Hz, NH), 12.11 (1H, br s, CO_2H).

^{13}C NMR δ ppm: 24.8, 31.4, 39.0, 129.1, 132.2, 132.5, 134.4, 136.4, 140.4, 164.9, 174.6.

HRMS calcd. for $C_{11}H_{12}Cl_2N_2O_5S$ [(M+H)$^+$]: 354.9917, found: 354.9918.

The compound **47**. Recrystallization was accomplished from NaOAc (20.6 mg, 0.251 mmol) solution in H_2O. Yield: 142 mg, 65%, mp 163-165°C.

^{1}H NMR δ ppm: 1.18-1.45 (5H, m, Cy-H), 1.57-1.60 (1H, m, Cy-H), 1.69-1.71 (2H, m, Cy-H), 1.73 (2H, quint, *J* = 7.2 Hz, CH_2), 1.90-1.92 (2H, m, Cy-H), 2.32 (2H, t, *J* = 7.2 Hz, $COCH_2$), 3.23 (2H, q, *J* = 6.4 Hz, $NHCH_2$), 3.53-3.58 (1H, m, Cy-H), 7.64 (1H, s, C_3-H), 7.66 (2H, br s, SO_2NH_2), 7.82 (1H, s, C_6-H), 8.56 (1H, t, *J* = 5.6 Hz, NH), 12.17 (1H, br s, CO_2H).

^{13}C NMR δ ppm: 24.9, 25.5, 25.7, 31.6, 32.7, 38.9, 44.3, 128.2, 130.7, 131.7, 136.9, 137.8, 141.2, 166.4, 174.7.

HRMS calcd. for $C_{17}H_{23}ClN_2O_5S_2$[(M+H)$^+$]: 435.0810, found: 435.0809.

The compound **48.** Recrystallization was accomplished from NaOAc (20.6 mg, 0.251 mmol) solution in H_2O. Yield: 164 mg, 69%, mp 252-254°C.

^{1}H NMR δ ppm: 1.79 (2H, quint, *J* = 7.2 Hz, CH_2), 2.37 (2H, t, *J* = 7.2 Hz, $COCH_2$), 3.30-3.35 (2H, m, $NHCH_2$, superposed with H_2O), 4.99 (2H, s, CH_2Ph), 7.24-7.26 (2H, m, Ph-H), 7.32-7.39 (3H, m, Ph-H), 7.61 (1H, s, C_3-H), 8.03 (2H, s, SO_2NH_2), 8.04 (1H, s, C_6-H), 8.98 (1H, t, *J* = 6.0 Hz, NH), 12.10 (1H, s, OH).

^{13}C NMR δ ppm: 24.6, 31.4, 39.2, 62.1, 128.2, 129.0, 129.2, 129.6, 131.5 (2C), 133.3, 137.2, 140.1, 145.6, 166.3, 174.7.

HRMS calcd. for $C_{18}H_{19}ClN_2O_7S_2$ [(M+H)$^+$]: 475.0395, found: 475.0394.

The measurements of compound binding to proteins and inhibition of enzymes

Carbonic anhydrases (CA) catalyse reversible carbon dioxide conversion to bicarbonate ion and maintain pH of the cell surroundings (Krebs, J. F. and Fierke, C. A. (1993), *J. Biol. Chem.* 268, 948). Dysfunctional expression of this enzyme in the cells causes diseases such as glaucoma, edema, epilepsy, cancer, etc. Thus, CA inhibitors are clinically used for treatment and new compounds are being synthesized. The most successful design of inhibitors is tail modification of already known sulfonamide drugs.

Example 18. Determination of the observed binding constants by the fluorescent thermal shift assay (FTSA) and isothermal titration calorimetry (ITC).

To determine the binding affinity of newly synthesized compounds to CA, the fluorescent thermal shift assay (FTSA) and isothermal titration calorimetry (ITC) were used. These methods complement each other. It is known that bound ligands stabilize the protein. FTSA is based on the protein melting temperature (T_m) shift between protein with and without bound ligand. FTSA shows dissociation constant (K_d) with no limitation – tight and weak binding can be determined. However, ITC is not appropriate to observe millimolar (weak) or subnanomolar (very tight) binding, but the heat evolved upon binding can be measured.

The X-ray crystallographic structures of several compounds demonstrated that the sulfonamide-bearing compounds bound to the active center of CAs with a stoichiometry of 1:1 (Čapkauskaitė, E. et al. (2010), *Bioorg. Med. Chem.* 18, 7357).

Table 1 shows the dissociation constants of several selected CA VA-selective compounds for all twelve catalyticaly active human CAs. Data was obtained by FTSA and Figure 1 shows representative binding curves. FTSA experiments were performed as previously described by Čapkauskaitė et al. (Čapkauskaitė, E. et al. (2012), *Eur. J. Med. Chem.* 51, 259) and fit and analysed as described by Kazlauskas et al. (Kazlauskas, E. et al. (2012), *PLoS ONE*, 7, e36899).

The data in the Table 1 show that compound with general structural formula II bind CA XIV isozyme with nanomolar affinity (K_ds of selected compounds presented in the table are in the range of 20 – 300 nM), but exhibiting especially strong binding to CA VA (subnanomolar affinity from 0.3 to 6.0 nM).

Selected selective inhibitors of CA XIV are shown in table 2. FTSA results show that these compounds bind to CA XIV with subnanomolar affinity (K_ds of selected compounds are in the range of 0.03 – 6.7 nM). Affinities are more than 10 times higher between CA XIV and other CA isoforms. Compounds in the table show nanomolar affinity to CA II, CA VII, IX and XII. Binding to CA I, IV, VA, VB, VI and XIII is weaker. The last row of the table shows ITC data of compound 3 binding to several CA isoforms. ITC measurements were performed as previously described by Čapkauskaitė et al. (Čapkauskaitė, E. et al. (2012), *Eur. J. Med. Chem.* 51, 259). Due to laborious nature of ITC measurements, only few compounds were tested by ITC and demonstrated that there is relatively good agreement between TSA and ITC data.

Compounds listed in Table 3 are strong inhibitors for cancer-related CAs (CA IX and CA XII). Table shows the dissociation constants observed for CA I, II, IX and XII. CA I and II are the most abundant isoforms in human body, thus it is very importantto to avoid inhibition of these CAs. All compounds that are selective to cancer CAs have low affinity to CA I (from 83 to 33000 nM). Compounds, that have longer tail or ring at the end of the tail in *meta* position, show higher affinity to CA II compared to compounds that have shorter tail moiety and do not have ring in this position.

ITC raw and integrated data of **13a** binding to CA IX are shown in Figure 2. Figure 3 shows integrated ITC curves of **13a** binding to CA I, II, IX and XII. The binding of **13a** to CA I shows the case of a very weak binding and the curve can not be fit precisely.

Table 1. Dissociation constants (nM) of selected CA VA-selective compounds binding to 12 human recombinant CA isoforms as determined by FTSA at 37 °C and pH 7.0.

	CA I	**CA II**	**CA III**	**CA IV**	**CA VA**	**CA VB**	**CA VI**	**CA VII**	**CA IX**	**CA XII**	**CA XIII**	**CA XIV**
19	11000	1600	>200000	600	0.3	3300	700	1000	800	3100	800	50

20	7100	600	80000	3300	0.8	500	2000	1700	600	3100	800	50
29	5000	300	17000	1100	2.0	1000	1400	100	400	3300	700	20
30	7700	500	22000	2900	5.0	2500	4000	700	1100	4000	1100	300
31	7700	500	40000	1400	6.0	700	1800	300	400	2800	600	40

Table 2. Dissociation constants (nM) of selected CA XIV-selective compounds binding to twelve human recombinant CA isoforms as determined by FTSA and ITC (the last row) at 37 °C, pH 7.0.

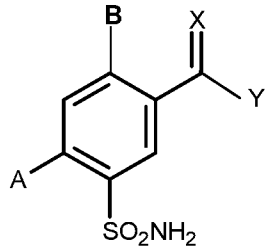
	CA I	**CA II**	**CA III**	**CA IV**	**CA VA**	**CA VB**	**CA VI**	**CA VII**	**CA IX**	**CA XII**	**CA XIII**	**CA XIV**
3	100000	83	8300	400	5000	400	630	10	170	125	560	6.7
3c	2100	13	50000	33	500	150	1600	3.3	15	10	91	0.7
6a	5000	8.3	10000	1.4	4500	40	670	2.5	1.7	2.5	140	0.1
7c	3200	7.7	>200000	11	670	43	1700	4.3	45	7.1	180	0.3
33b	1400	3.3	25000	33	330	10	1300	4.0	3.1	20	25	0.2
42a	140	0.9	3300	25	770	13	56	0.5	3.3	22	5.6	0.03
3 (by ITC)	n/d	39.4	n/d	n/d	n/d	n/d	n/d	n/d	n/d	79.9	218	n/d

Table 3. Dissociation constants (nM) of selected compounds binding to four human recombinant CA isoforms as determined by FTSA at 37 °C, pH 7.0.

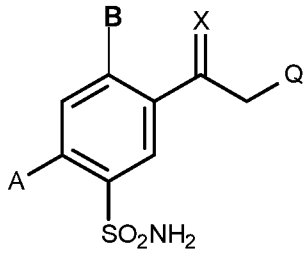
	CA I	**CA II**	**CA IX**	**CA XII**
3a	10000	31	4.0	6.3
3b	1000	10	1.3	2.0
3f	14000	420	20	4.0
3g	1100	8.3	1.4	2.0
4a	6700	5.0	0.3	0.8
4b	1300	3.7	0.7	1.0
4f	33000	170	8.3	660
5a	1100	4.5	1.3	1.0
5b	400	2.5	0.8	0.5
7b	2000	10	2.0	1.3
9b	560	50	3.3	33
10b	83	1.4	1.1	1.0
11a	3100	50	13	2.0
12a	830	10	2.5	0.8
13a	10000	25	5.0	10
14a	10000	36	2.5	6.7
14b	17000	250	0.3	33

14c	6900	110	2.9	22
14d	13000	170	13	53
38b	2000	22	2.0	33
47	3300	13	2.2	0.4

Newly synthesized compounds of general formulas (I) and (II)



(I)

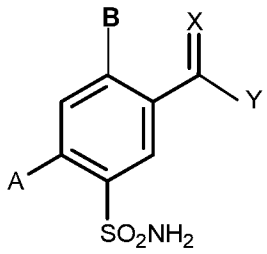


(II)

exhibit significant affinity and selectivity, often better than the existing compounds, promising to help in solving the issue of non-specific binding of clinically used inhibitors.

Claims

1. A compound of general formula (I):



(I)

where

A is F, Cl, Br, I, NO_2, OH, SH, NH_2, $NHCH_3$, $N(CH_3)_2$, $NHNH_2$, CN, SCH_3, $S(O)CH_3$, SO_2CH_3, CH_3, $COCH_3$, $C(O)NH_2$, C(O)OH, OCH_3, OCF_3, OCF_2H, $OCFH_2$, CF_3, CF_2H, CFH_2, $Si(CH_3)_3$, $B(OH)_3$,

B is OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $NHNHR^1$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, $S(O)_2NHR^1$, $S(O)_2N(R^1)_2$, $NHS(O)_2R^1$, $NR^1S(O)_2R^1$, $NH(SO)_2NHR^1$, $NHS(O)_2N(R^1)_2$, $NR^1S(O)_2NHR^1$, $NR^1S(O)_2N(R^1)_2$, $C(O)NHSO_2R^1$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$,

B is Cl, when X is O and Y is $O(CH_2)_2OCH_3$, $NH(CH_2)_3OH$, $NH(CH_2)_3OC(O)CH_3$, $NH(CH_2)_3C(O)OH$, $NH(CH_2)_3C(O)OCH_3$, $N(CH_2CH_2)_2O$, NH-cyclohexyl, $NHCH_2Ph$,

B is Br, when X is O and Y is OCH_3, $NH(CH_2)_2OH$, $NH(CH_2)_3CH_3$,

X is O, S, NH, NR^1,

Y is OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHNOR^1$, $C(O)NHSO_2R^1$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$,

R^1 is R^2, R^3, R^4, R^5, R^6, R^7,

R^2 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^3 is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^4 is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^5 is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

R^5 is R^8, OH, OR^8, SH, SR^8, $S(O)R^8$, SO_2R^8, $C(O)R^8$, $C(O)OR^8$, $OC(O)R^8$, NHR^8, $N(R^8)_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHC(O)OR^8$, $NR^8C(O)OR^8$, $NHC(O)NH_2$,

$NHC(O)NHR^8$, $NHC(O)N(R^8)_2$, $NR^8C(O)NHR^8$, $NR^8C(O)N(R^8)_2$, SO_2NHR^8, $SO_2N(R^8)_2$, $NHSO_2R^8$, $NR^8SO_2R^8$, $NHSO_2NHR^8$, $NHSO_2N(R^8)_2$, $NR^8SO_2NHR^8$, $NR^8SO_2N(R^8)_2$, C(O)NHNOH, $C(O)NHNOR^8$, $C(O)NHSO_2R^8$, $C(NH)NH_2$, $C(NH)NHR^8$, $C(NH)N(R^8)_2$, $NHSO_2NHR^8$, $NHSO_2N(CH_3)R^8$, $N(CH_3)SO_2N(CH_3)R^8$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^8 is R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14},

R^9 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{10} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{11} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{12} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{13} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{14} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^6 is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

R^6 is R^{15}, OH, OR^{15}, SH, SR^{15}, $S(O)R^{15}$, SO_2R^{15}, $C(O)R^{15}$, $C(O)OR^{15}$, $OC(O)R^{15}$, NHR^{15}, $N(R^{15})_2$, $C(O)NHR^{15}$, $C(O)N(R^{15})_2$, $NHC(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NHC(O)OR^{15}$, $NR^{15}C(O)OR^{15}$, $NHC(O)NH_2$, $NHC(O)NHR^{15}$, $NHC(O)N(R^{15})_2$, $NR^{15}C(O)NHR^{15}$, $NR^{15}C(O)N(R^{15})_2$, SO_2NHR^{15}, $SO_2N(R^{15})_2$, $NHSO_2R^{15}$, $NR^{15}SO_2R^{15}$, $NHSO_2NHR^{15}$, $NHSO_2N(R^{15})_2$, $NR^{15}SO_2NHR^{15}$, $NR^{15}SO_2N(R^{15})_2$, C(O)NHNOH, $C(O)NHNOR^{15}$, $C(O)NHSO_2R^{15}$, $C(NH)NH_2$, $C(NH)NHR^{15}$, $C(NH)N(R^{15})_2$, $NHSO_2NHR^{15}$, $NHSO_2N(CH_3)R^{15}$, $N(CH_3)SO_2N(CH_3)R^{15}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{15} is R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21},

R^{16} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{17} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{18} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{19} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{20} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{21} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^7 is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

R^7 is R^{22}, OH, OR^{22}, SH, SR^{22}, $S(O)R^{22}$, SO_2R^{22}, $C(O)R^{22}$, $C(O)OR^{22}$, $OC(O)R^{22}$, NHR^{22}, $N(R^{22})_2$, $C(O)NHR^{22}$, $C(O)N(R^{22})_2$, $NHC(O)R^{22}$, $NR^{22}C(O)R^{22}$, $NHC(O)OR^{22}$, $NR^{22}C(O)OR^{22}$, $NHC(O)NH_2$, $NHC(O)NHR^{22}$, $NHC(O)N(R^{22})_2$, $NR^{22}C(O)NHR^{22}$, $NR^{22}C(O)N(R^{22})_2$, SO_2NHR^{22}, $SO_2N(R^{22})_2$, $NHSO_2R^{22}$, $NR^{22}SO_2R^{22}$, $NHSO_2NHR^{22}$, $NHSO_2N(R^{22})_2$, $NR^{22}SO_2NHR^{22}$, $NR^{22}SO_2N(R^{22})_2$, C(O)NHNOH, $C(O)NHNOR^{22}$, $C(O)NHSO_2R^{22}$, $C(NH)NH_2$, $C(NH)NHR^{22}$, $C(NH)N(R^{22})_2$, $NHSO_2NHR^{22}$, $NHSO_2N(CH_3)R^{22}$, $N(CH_3)SO_2N(CH_3)R^{22}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{22} is R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28},

R^{23} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{24} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{25} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{26} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{27} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{28} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

and/or pharmaceutically acceptable salts thereof,

and/or single stereoisomer or mixtures of stereoisomers thereof,

with the proviso that B is not $(CH_2)_nH$, $(CH_2)_nCl$, $O(CH_2)_nH$, $NH(CH_2)_nH$, $N((CH_2)_nH)_2$ (n=1-4),

with the proviso that B is not (2-furanylmethyl)amino, acetylsulfanyl, acetoxy, acetamido,

with the proviso that when A is Cl and B is benzylamino then Y is not methoxy, 4-sulfamoylbenzylamino, ethylamino, methoxyamino, isopropoxyamino,

with the proviso that when A is Cl and Y is methoxy then B is not tosyloxy, 2-hydroxypropanamido, pyrrole-1-carbonylamino, (2-pyrrol-2-yl-ethylamino), 2-chloroacetamido,

with the proviso that when A is Cl and Y is ethoxy then B is not ethoxycarbonilamino, 4-isopropylcarbamoylamino;

with the proviso that when A is Cl and Y is 2-tolylamino then B is not 2-(dimethylamino)ethylamino, benzylamino, 2-hydroxyethylamino,

with the proviso that when A is Cl and Y is 2-(4-sulfamoylphenyl)ethylamino then B is not butylamino, cyclohexylamino,

with the proviso that compounds according to formula I exclude these compounds:

4-chloro-*N*-methoxy-5-sulfamoyl-2-(2-thienylmethylamino)benzamide;

methyl 4-amino-2-(4-tolylsulfonyloxy)-5-sulfamoyl-benzoate;

ethyl 2-(benzylamino)-4-fluoro-5-sulfamoyl-benzoate;

4-(benzylamino)-2-chloro-5-[4-[2-[(2R,4R,6S)-2-isopropyl-2,6-dimethyl-4-(2-methylbenzimidazol-1-yl)-1-piperidyl]ethyl]-4-phenyl-piperidine-1-carbonyl]benzenesulfonamide;

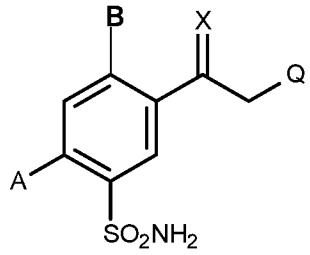
ethyl 2-[[(5S)-5-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]-(2,2,2-trichloroethoxycarbonyl)amino]propanoyl]amino]-6-ethoxy-6-oxo-hexyl]amino]-4-chloro-5-sulfamoyl-benzoate;

(2R)-2-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]amino]propanoyl]amino]-6-(5-chloro-2-ethoxycarbonyl-4-sulfamoyl-anilino)hexanoic acid;

ethyl 2-[[(5R)-5-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]amino]propanoyl]amino]-6-ethoxy-6-oxo-hexyl]amino]-4-chloro-5-sulfamoyl-benzoate;

ethyl 2-[[(5R)-5-[benzyl-[(2S)-2-[[(1S)-1-ethoxycarbonyl-3-phenyl-propyl]amino]propanoyl]amino]-6-tert-butoxy-6-oxo-hexyl]amino]-4-chloro-5-sulfamoyl-benzoate.

2. A compound of general formula (II):



(II)

where

A is F, Cl, Br, I, NO_2, OH, SH, NH_2, NH_2NH_2, CN, SCH_3, $S(O)CH_3$,$S(O)_2CH_3$, CH_3, $COCH_3$, $C(O)NH_2$, C(O)OH, OCH_3, OCF_3, OCF_2H, $OCFH_2$, CF_3, CF_2H,CFH_2, $Si(CH_3)_3$, $B(OH)_3$,

B is H, R^1, OH, OR^1, SH, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $NHNH_2$, $NHNHR^1$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHNOH$, $C(O)NHNOR^1$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

X is O, S, NH, NR^1,

Q is R^1, OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, CN, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^1 is R^2, R^3, R^4, R^5, R^6, R^7,

R^2 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^3 is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^4 is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^5 is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

R^5 is R^8, OH, OR^8, SH, SR^8, $S(O)R^8$, SO_2R^8, $C(O)R^8$, $C(O)OR^8$, $OC(O)R^8$, NHR^8, $N(R^8)_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHC(O)OR^8$, $NR^8C(O)OR^8$, $NHC(O)NH_2$, $NHC(O)NHR^8$, $NHC(O)N(R^8)_2$, $NR^8C(O)NHR^8$, $NR^8C(O)N(R^8)_2$, SO_2NHR^8, $SO_2N(R^8)_2$, $NHSO_2R^8$, $NR^8SO_2R^8$, $NHSO_2NHR^8$, $NHSO_2N(R^8)_2$, $NR^8SO_2NHR^8$, $NR^8SO_2N(R^8)_2$, C(O)NHNOH, $C(O)NHNOR^8$, $C(O)NHSO_2R^8$, $C(NH)NH_2$, $C(NH)NHR^8$, $C(NH)N(R^8)_2$, $NHSO_2NHR^8$, $NHSO_2N(CH_3)R^8$, $N(CH_3)SO_2N(CH_3)R^8$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^8 is R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14},

R^9 is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{10} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{11} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{12} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{13} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{14} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^6 is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

R^6 is R^{15}, OH, OR^{15}, SH, SR^{15}, $S(O)R^{15}$, SO_2R^{15}, $C(O)R^{15}$, $C(O)OR^{15}$, $OC(O)R^{15}$, NHR^{15}, $N(R^{15})_2$, $C(O)NHR^{15}$, $C(O)N(R^{15})_2$, $NHC(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NHC(O)OR^{15}$, $NR^{15}C(O)OR^{15}$, $NHC(O)NH_2$, $NHC(O)NHR^{15}$, $NHC(O)N(R^{15})_2$, $NR^{15}C(O)NHR^{15}$, $NR^{15}C(O)N(R^{15})_2$, SO_2NHR^{15}, $SO_2N(R^{15})_2$, $NHSO_2R^{15}$, $NR^{15}SO_2R^{15}$, $NHSO_2NHR^{15}$, $NHSO_2N(R^{15})_2$, $NR^{15}SO_2NHR^{15}$, $NR^{15}SO_2N(R^{15})_2$, C(O)NHNOH, $C(O)NHNOR^{15}$, $C(O)NHSO_2R^{15}$, $C(NH)NH_2$, $C(NH)NHR^{15}$, $C(NH)N(R^{15})_2$, $NHSO_2NHR^{15}$, $NHSO_2N(CH_3)R^{15}$, $N(CH_3)SO_2N(CH_3)R^{15}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^{15} is R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21},

R^{16} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{17} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{18} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{19} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{20} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{21} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^7 is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

R^7 is R^{22}, OH, OR^{22}, SH, SR^{22}, $S(O)R^{22}$, SO_2R^{22}, $C(O)R^{22}$, $C(O)OR^{22}$, $OC(O)R^{22}$, NHR^{22}, $N(R^{22})_2$, $C(O)NHR^{22}$, $C(O)N(R^{22})_2$, $NHC(O)R^{22}$, $NR^{22}C(O)R^{22}$, $NHC(O)OR^{22}$, $NR^{22}C(O)OR^{22}$, $NHC(O)NH_2$, $NHC(O)NHR^{22}$, $NHC(O)N(R^{22})_2$, $NR^{22}C(O)NHR^{22}$, $NR^{22}C(O)N(R^{22})_2$, SO_2NHR^{22}, $SO_2N(R^{22})_2$, $NHSO_2R^{22}$, $NR^{22}SO_2R^{22}$, $NHSO_2NHR^{22}$, $NHSO_2N(R^{22})_2$, $NR^{22}SO_2NHR^{22}$, $NR^{22}SO_2N(R^{22})_2$, C(O)NHNOH, $C(O)NHNOR^{22}$, $C(O)NHSO_2R^{22}$, $C(NH)NH_2$, $C(NH)NHR^{22}$, $C(NH)N(R^{22})_2$, $NHSO_2NHR^{22}$, $NHSO_2N(CH_3)R^{22}$, $N(CH_3)SO_2N(CH_3)R^{22}$, F, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$

R^{22} is R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28},

R^{23} is phenyl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{24} is heteroaryl, which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane,

R^{25} is cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl, each of which is unfused or fused with benzene, heteroarene,

R^{26} is alkyl, alkenyl or alkynyl each of which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{27} is phenyl which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

R^{28} is heteroaryl, which is unsubstituted or substituted by one or more identical or different groups selected from

NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SMe, $C(O)NH_2$, C(O)NHOH, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)H, C(O)OH, $C(O)OCH_3$, $C(O)OC_2H_5$, OH, OCH_3, OC_2H_5, CH_3, C_2H_5, $CH(CH_3)_2$, CN, N_3, NO_2, F, Cl, Br, I,

and/or pharmaceutically acceptable salts thereof,

and/or single stereoisomer or mixtures of stereoisomers thereof,

with the proviso that when B is H then Q is not CH_2COOR^1, CH_2CONHR^1 or $CH_2CON(CH_3)R^1$,

with the proviso that when B is H then Q is not $(CH_2)_nH$, $(CH_2)_nNHR^1$, $(CH_2)_nN(R^1)_2$, $(CH_2)_nCl$ (n=2-4),

with the proviso that when B is H then Q is not benzylamino or N-substituted-benzylamino, methyl, phenylsulfanyl, acetylsulfanyl,

wiht the proviso that compounds according to formula II exclude these compounds:

5-(3-benzyl-4-methyl-pentanoyl)-2-hydroxy-benzenesulfonamide;

5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(2-methylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-methylsulfanylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-ethylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-isopropylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-[2-(hydroxymethyl)benzimidazol-1-yl]acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-propylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-isobutylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

5-[2-(2-butylbenzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

5-[2-(2-benzylbenzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-[2-(morpholinomethyl)benzimidazol-1-yl]acetyl]benzenesulfonamide;

2-chloro-5-(2-pyrimidin-2-ylsulfanylacetyl)benzenesulfonamide;

2-chloro-5-[2-(5-ethylpyrimidin-2-yl)sulfanylacetyl]benzenesulfonamide;

2-chloro-5-[2-(5-propylpyrimidin-2-yl)sulfanylacetyl]benzenesulfonamide;

5-[2-(5-butylpyrimidin-2-yl)sulfanylacetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(4,6-dimethylpyrimidin-2-yl)sulfanylacetyl]benzenesulfonamide;

2-chloro-5-[2-[(4-methyl-6-oxo-1H-pyrimidin-2-yl)sulfanyl]acetyl]benzenesulfonamide;

2-chloro-5-[2-[(6-oxo-4-propyl-1H-pyrimidin-2-yl)sulfanyl]acetyl]benzenesulfonamide;

5-[2-[(4-tert-butyl-6-oxo-1H-pyrimidin-2-yl)sulfanyl]acetyl]-2-chloro-benzenesulfonamide;

ethyl 2-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]sulfanyl-6-oxo-1H-pyrimidine-5-carboxylate;

5-[2-[(5-benzyl-4-methyl-6-oxo-1H-pyrimidin-2-yl)sulfanyl]acetyl]-2-chloro-benzenesulfonamide;

5-[2-(1H-benzimidazol-2-ylsulfanyl)acetyl]-2-chloro-benzenesulfonamide;

5-[2-[(5-bromo-1H-benzimidazol-2-yl)sulfanyl]acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(1H-imidazo[4,5-c]quinolin-2-ylsulfanyl)acetyl]benzenesulfonamide;

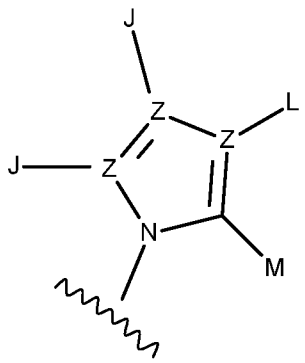
2-chloro-5-[2-(6,7-dihydro-1H-[1,4]dioxino[2,3-f]benzimidazol-2-ylsulfanyl)acetyl]benzenesulfonamide;

5-[2-[[5-(1H-benzimidazol-2-yl)-1H-pyrazol-3-yl]oxy]acetyl]-2-chloro-benzenesulfonamide;

2-hydroxy-5-[2-[(2-methyl-1-phenyl-propyl)amino]acetyl]benzenesulfonamide;

2,4-dichloro-5-[3-[2-(3,4-diethoxyphenyl)thiazol-4-yl]propanoyl]benzenesulfonamide.

3. A compound of claim 2, having the general formula II, wherein Q is



where

Z is independently C or N;

J is H when Z is C, or J is absent when Z is N;

L and M is each independently H, R^1, OH, OR^1, SH, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $NHNH_2$, $NHNHR^1$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, C(O)NHNOH, $C(O)NHNOR^1$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$

or the groups L and M together form aryl, heteroaryl, cycloalkyl, cycloalkenyl, cycloalkynyl, heterocycloalkyl, heterocycloalkenyl or heterocycloalkynyl a ring, each of which is unfused or fused with benzene, heteroarene, cycloalkane or heterocycloalkane and each of rings is unsubstituted or substituted by one or more identical or different groups selected from

R^1, OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NR^1C(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NR^1SO_2R^1$, $NHSO_2NHR^1$, $NHSO_2N(R^1)_2$, $NR^1SO_2NHR^1$, $NR^1SO_2N(R^1)_2$, $C(O)NHSO_2R^1$, $C(NH)NH_2$, $C(NH)NHR^1$, $C(NH)N(R^1)_2$, $NHSO_2NHR^1$, $NHSO_2N(CH_3)R^1$, $N(CH_3)SO_2N(CH_3)R^1$, Cl, Br, I, CN, NO_2, N_3, C(O)H, CHNOH, $CH(NOCH_3)$, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, C(O)OH, $C(O)NH_2$,

R^1 is defined as in the claim 2 for a compound of formula II,

and/or pharmaceutically acceptable salts thereof,

and/or single stereoisomer or mixtures of stereoisomers thereof,

with the proviso that compounds according to formula II exclude these compounds:

5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-(2-methylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-methylsulfanylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-ethylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-isopropylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-[2-(hydroxymethyl)benzimidazol-1-yl]acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-propylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

2-chloro-5-[2-(2-isobutylbenzimidazol-1-yl)acetyl]benzenesulfonamide;

5-[2-(2-butylbenzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

5-[2-(2-benzylbenzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide;

2-chloro-5-[2-[2-(morpholinomethyl)benzimidazol-1-yl]acetyl]benzenesulfonamide.

4. The compound of claim 1, wherein the compound is:

2,4-dichloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide,

methyl 4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoate,

2,4-dichloro-5-(morpholine-4-carbonyl)benzenesulfonamide,

2,4-dichloro-*N*-cyclohexyl-5-sulfamoyl-benzamide,

N-benzyl-2,4-dichloro-5-sulfamoyl-benzamide,

2,4-dibromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

2,4-dibromo-*N*-butyl-5-sulfamoyl-benzamide,

3-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]propyl acetate,

2-methoxyethyl 2,4-dichloro-5-sulfamoyl-benzoate,

methyl 2,4-dibromo-5-sulfamoyl-benzoate,

2-benzylsulfinyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide,

2-(benzenesulfinyl)-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

4-[(2,4-dichloro-5-sulfamoyl-benzoyl)amino]butanoic acid,

4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoic acid,

4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoic acid,

4-chloro-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide,

4-chloro-*N*-(3-hydroxypropyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide,

N-butyl-4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzamide,

4-chloro-*N*-(2-methoxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide,

2-chloro-5-(morpholine-4-carbonyl)-4-phenylsulfanyl-benzenesulfonamide,

4-chloro-*N*-cyclohexyl-2-phenylsulfanyl-5-sulfamoyl-benzamide,

N-benzyl-4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzamide,

4-bromo-*N*-(2-hydroxyethyl)-2-phenylsulfanyl-5-sulfamoyl-benzamide,

4-bromo-*N*-butyl-2-phenylsulfanyl-5-sulfamoyl-benzamide,

3-[(4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoyl)amino]propyl acetate,

methyl 4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoate,

2-methoxyethyl 4-chloro-2-phenylsulfanyl-5-sulfamoyl-benzoate,

methyl 4-bromo-2-phenylsulfanyl-5-sulfamoyl-benzoate,

2-(benzenesulfonyl)-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

2-(benzenesulfonyl)-4-chloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide,

2-(benzenesulfonyl)-*N*-butyl-4-chloro-5-sulfamoyl-benzamide,

2-(benzenesulfonyl)-4-chloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide,

2-(benzenesulfonyl)-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide,

2-(benzenesulfonyl)-*N*-benzyl-4-chloro-5-sulfamoyl-benzamide,

2-(benzenesulfonyl)-4-bromo-*N*-butyl-5-sulfamoyl-benzamide,

methyl 2-(benzenesulfonyl)-4-chloro-5-sulfamoyl-benzoate,

methyl 2-(benzenesulfonyl)-4-bromo-5-sulfamoyl-benzoate,

4-chloro-2-cyclohexylsulfanyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

4-chloro-2-cyclohexylsulfanyl-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide,

N-butyl-4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide,

4-chloro-2-cyclohexylsulfanyl-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide,

methyl 4-[(4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoyl)amino]butanoate,

4-chloro-*N*-cyclohexyl-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide,

N-benzyl-4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide,

4-bromo-2-cyclohexylsulfanyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

4-bromo-*N*-butyl-2-cyclohexylsulfanyl-5-sulfamoyl-benzamide,

methyl 4-chloro-2-cyclohexylsulfanyl-5-sulfamoyl-benzoate,

methyl 4-bromo-2-cyclohexylsulfanyl-5-sulfamoyl-benzoate,

4-chloro-2-cyclohexylsulfonyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

4-chloro-2-cyclohexylsulfonyl-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide,

N-butyl-4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide,

4-chloro-2-cyclohexylsulfonyl-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide,

methyl 4-[(4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzoyl)amino]butanoate,

4-chloro-*N*-cyclohexyl-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide,

N-benzyl-4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide,

4-bromo-2-cyclohexylsulfonyl-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

4-bromo-*N*-butyl-2-cyclohexylsulfonyl-5-sulfamoyl-benzamide,

methyl 4-chloro-2-cyclohexylsulfonyl-5-sulfamoyl-benzoate,

methyl 4-bromo-2-cyclohexylsulfonyl-5-sulfamoyl-benzoate,

2-benzylsulfanyl-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

2-benzylsulfanyl-*N*-butyl-4-chloro-5-sulfamoyl-benzamide,

methyl 4-[(2-benzylsulfanyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate,

2-benzylsulfanyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide,

2-benzylsulfanyl-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

2-benzylsulfanyl-4-bromo-*N*-butyl-5-sulfamoyl-benzamide,

methyl 2-benzylsulfanyl-4-chloro-5-sulfamoyl-benzoate,

2-benzylsulfonyl-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

methyl 4-[(2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoyl)amino]butanoate,

2-benzylsulfonyl-4-chloro-*N*-cyclohexyl-5-sulfamoyl-benzamide,

2-benzylsulfonyl-4-bromo-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

methyl 2-benzylsulfonyl-4-chloro-5-sulfamoyl-benzoate,

N-butyl-4-chloro-2-phenethylsulfanyl-5-sulfamoyl-benzamide,

4-bromo-*N*-(2-hydroxyethyl)-2-phenethylsulfanyl-5-sulfamoyl-benzamide,

4-bromo-*N*-butyl-2-phenethylsulfanyl-5-sulfamoyl-benzamide,

methyl 4-chloro-2-phenethylsulfanyl-5-sulfamoyl-benzoate,

4-chloro-*N*-cyclohexyl-2-(2-hydroxyethylsulfanyl)-5-sulfamoyl-benzamide,

4-bromo-*N*-butyl-2-(2-hydroxyethylsulfanyl)-5-sulfamoyl-benzamide,

4-chloro-*N*-cyclohexyl-2-(2-hydroxyethylsulfonyl)-5-sulfamoyl-benzamide,

4-chloro-2-(cyclohexylamino)-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

4-chloro-2-(cyclohexylamino)-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide,

N-butyl-4-chloro-2-(cyclohexylamino)-5-sulfamoyl-benzamide,

4-chloro-2-(cyclohexylamino)-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide,

4-bromo-*N*-butyl-2-(cyclohexylamino)-5-sulfamoyl-benzamide,

methyl 4-chloro-2-(cyclohexylamino)-5-sulfamoyl-benzoate,

2-(benzylamino)-4-chloro-*N*-(2-hydroxyethyl)-5-sulfamoyl-benzamide,

2-(benzylamino)-4-chloro-*N*-(3-hydroxypropyl)-5-sulfamoyl-benzamide,

2-(benzylamino)-*N*-butyl-4-chloro-5-sulfamoyl-benzamide,

2-(benzylamino)-4-chloro-*N*-(2-methoxyethyl)-5-sulfamoyl-benzamide,

N-benzyl-2-(benzylamino)-4-chloro-5-sulfamoyl-benzamide,

2-(benzylamino)-4-bromo-*N*-butyl-5-sulfamoyl-benzamide,

methyl 2-(benzylamino)-4-chloro-5-sulfamoyl-benzoate,

N-butyl-4-chloro-2-(cyclooctylamino)-5-sulfamoyl-benzamide.

5. The compound of claims 2 and 3, wherein the compound is:

2-chloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide,

2-chloro-5-[2-(5-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide and 2-chloro-5-[2-(6-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide,

2-chloro-5-(2-imidazol-1-ylacetyl)benzenesulfonamide,

2-chloro-5-[2-(2-ethylimidazol-1-yl)acetyl]benzenesulfonamide,

ethyl 1-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]imidazole-4-carboxylate and ethyl 3-[2-(4-chloro-3-sulfamoyl-phenyl)-2-oxo-ethyl]imidazole-4-carboxylate,

2-chloro-5-[2-(2-phenylimidazol-1-yl)acetyl]benzenesulfonamide,

2-chloro-5-[2-(4,5-diphenylimidazol-1-yl)acetyl]benzenesulfonamide,

2-chloro-5-(2-indolin-1-ylacetyl)benzenesulfonamide,

2-chloro-5-[2-(3,4-dihydro-2H-quinolin-1-yl)acetyl]benzenesulfonamide,

5-[2-(benzimidazol-1-yl)acetyl]-2,4-dichloro-benzenesulfonamide,

2,4-dichloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]benzenesulfonamide,

2,4-dichloro-5-[2-(5-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide and 2,4-dichloro-5-[2-(6-methoxybenzimidazol-1-yl)acetyl]benzenesulfonamide,

2,4-dichloro-5-(2-imidazol-1-ylacetyl)benzenesulfonamide,

5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-4-phenethylsulfanyl-benzenesulfonamide,

2-chloro-5-[2-(5,6-dimethylbenzimidazol-1-yl)acetyl]-4-phenylsulfanyl-benzenesulfonamide

6. The compound of claims 1-5 containing radionuclide, wherein the radionuclide is selected from the group consisting of ^{11}C, ^{18}F, ^{13}N and ^{15}O.

7. A pharmaceutical composition comprising a compound according to claims 1 to 6 and a pharmaceutically acceptable diluents, excipient or carrier.

8. Composition for use in control of conditions where inhibition of carbonic anhydrase is necessary, **characterized in that** it comprises effective amount of sulfonamide according to any one of claims 1 to 6.

9. Composition according to claim 8 for use in a method of treatment of disorders mediated by carbonic anhydrase isoforms selected from intraocular hypertension (glaucoma), epilepsy, altitude

sickness, headaches, migraine, neurological disorders, obesity and cancer, including signs and/or symptoms related to said deseases.

10. Composition according to claim 8 for use in a method for the detection, imaging, diagnosis and monitoring of disorders when they are related to CA expression.

11. Compound of any of claims 1-6 for use in a method of treatment or prophylaxis of numerous cancers, especially large solid hypoxic tumors where CA IX and CA XII isoforms are found to be overexpressed.

12. Compound of any of claims 1-6 for use in a method of treatment or prophylaxis of numerous brain-related illnesses such as schizophrenia, epilepsy, elevated intracranial pressure and other, where CA XIV isoform is found to be overexpressed.

13. Compound of any of claims 2, 3, 5, and 6 for use in a method of treatment or prophylaxis of obesity and potentially other metabolic diseases, where inhibition of CA VA isoform is beneficial or/and CA VA isoform is found to be overexpressed.

14. Compound 5-[2-(benzimidazol-1-yl)acetyl]-2-chloro-benzenesulfonamide (compound **19**) for use in a method of treatment or prophylaxis of obesity and potentially other metabolic diseases, where inhibition of CA VA isoform is beneficial or/and CA VA isoform is found to be overexpressed.

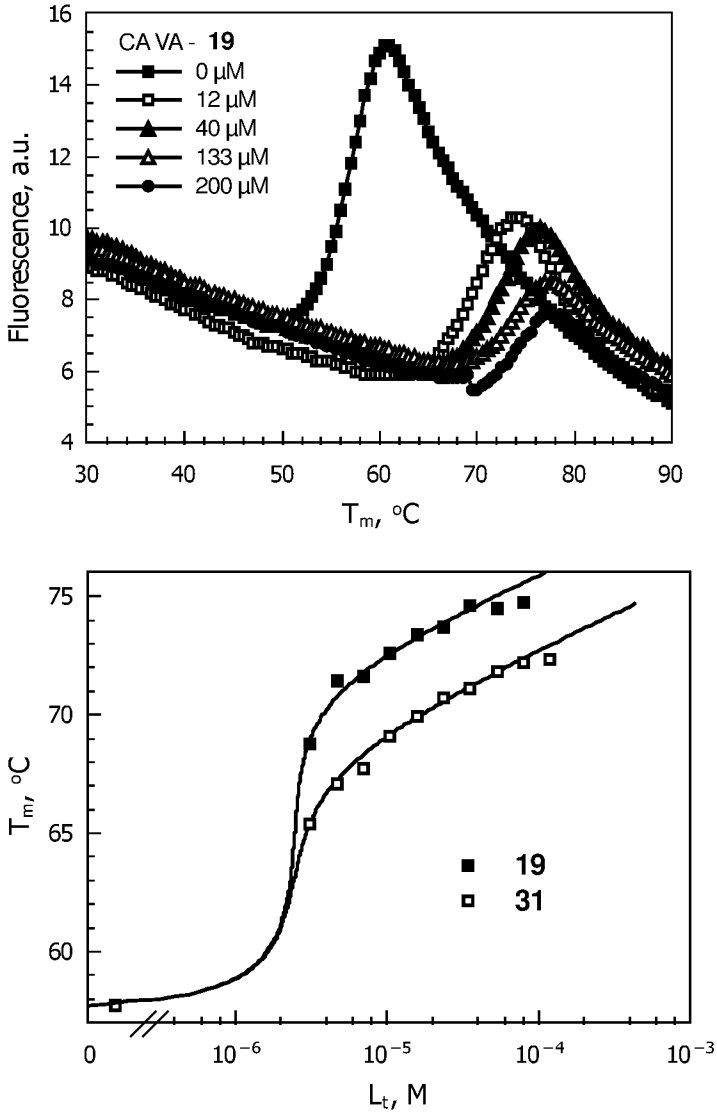

CA VA - 19
0 µM
12 µM
40 µM
133 µM
200 µM
Fluorescence, a.u.
16
14
12
10
8
6
4
30
40
50
60
70
80
90
T_m, °C
75
70
65
60
T_m, °C
19
31
0
10^{-6}
10^{-5}
10^{-4}
10^{-3}
L_t, M

Fig. 1.

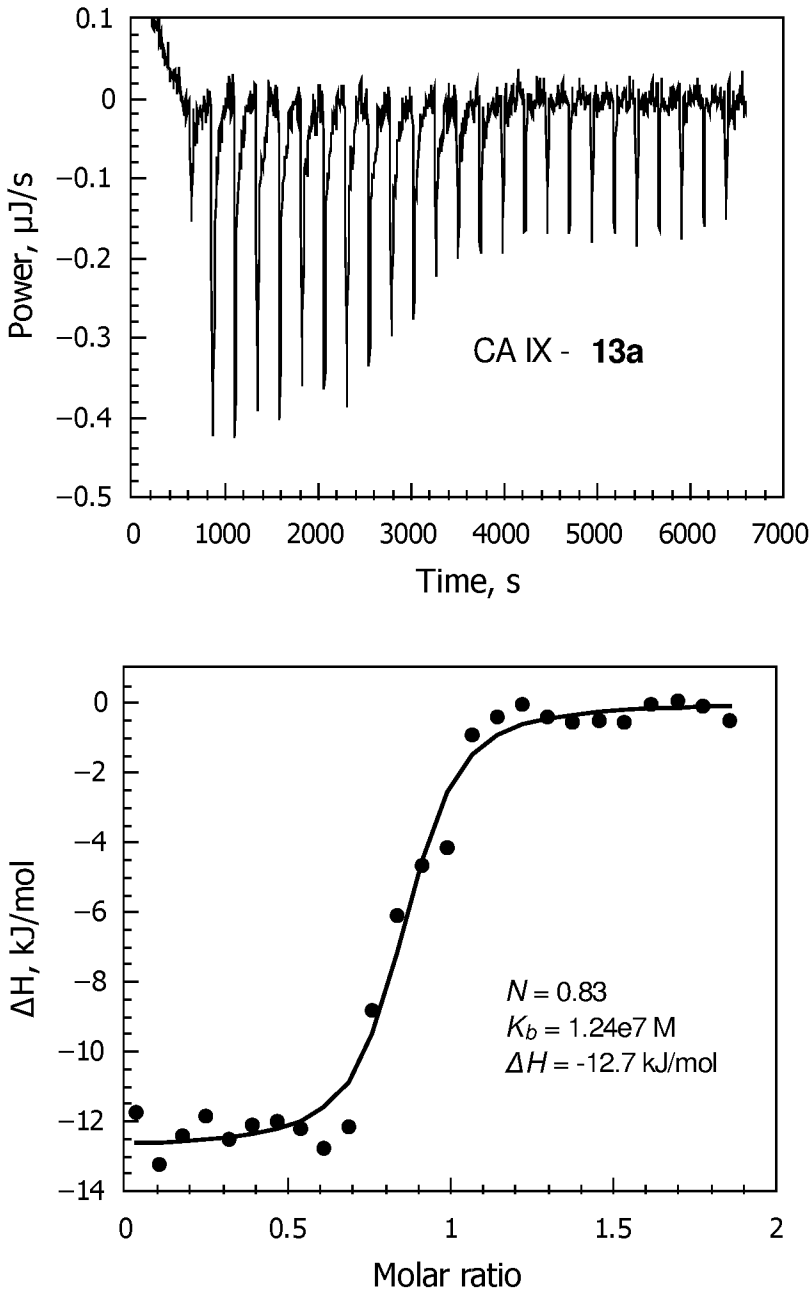

0.1
0
−0.1
−0.2
−0.3
−0.4
−0.5
Power, μJ/s
CA IX - 13a
0
1000
2000
3000
4000
5000
6000
7000
Time, s
0
−2
−4
−6
−8
−10
−12
−14
ΔH, kJ/mol
N = 0.83
Kb = 1.24e7 M
ΔH = -12.7 kJ/mol
0
0.5
1
1.5
2
Molar ratio

Fig. 2.

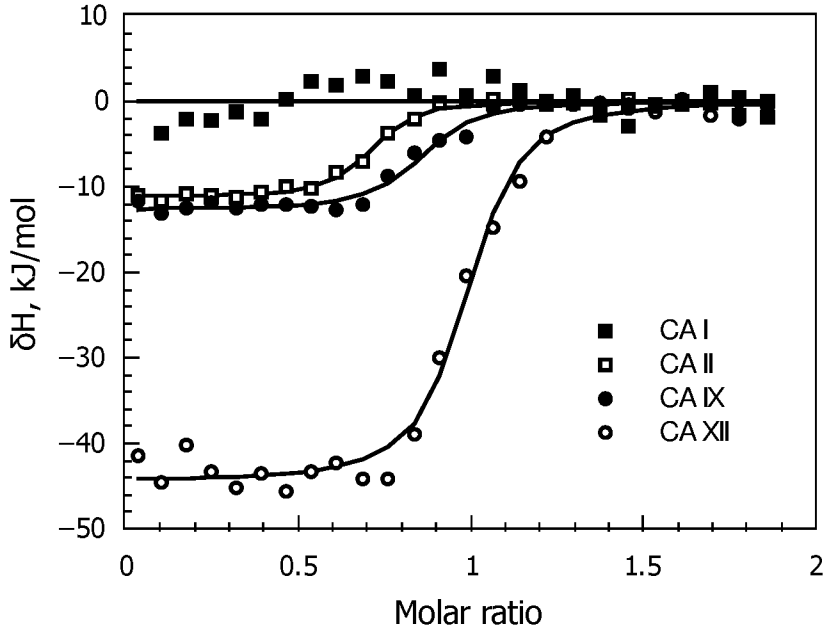

10
0
−10
−20
−30
−40
−50
δH, kJ/mol
0
0.5
1
1.5
2
Molar ratio
CA I
CA II
CA IX
CA XII

Fig. 3.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2015/056626

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D215/08 C07D233/58 C07C311/16 C07D235/08 C07D265/30
C07D209/08 A61K31/10 A61K31/4184 A61K31/4172 A61P43/00
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D C07C

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 December 2015	20/01/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Goss, Ilaria

2

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

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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2

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International application No
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