(51) International Patent Classification 5:
C07C 259/06, A61K 31/16
C07C 275/64, C07D 215/12, 215/18
C07D 311/60, 311/58
A61K 31/17, 31/35, 31/47

(11) International Publication Number: WO 91/16298
(43) International Publication Date: 31 October 1991 (31.10.91)

(21) International Application Number: PCT/US91/02674
(22) International Filing Date: 18 April 1991 (18.04.91)

(30) Priority data:
105046/90 20 April 1990 (20.04.90) JP

(71) Applicant (for all designated States except US): PFIZER INC [US/US]; Eastern Point Road, Groton, CT 06340 (US).

(72) Inventors: and

(74) Agents: LUMB, J., Trevor et al.; Pfizer Inc, Eastern Point Road, Groton, CT 06340 (US).

(81) Designated States: AT (European patent), AU, BE (European patent), BR, CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FI, FR (European patent), GB (European patent), GR (European patent), HU, IT (European patent), KR, LU (European patent), NL (European patent), NO, PL, SE (European patent), SU, US.

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: ANTIINFLAMMATORY HYDROXAMIC ACIDS AND N-HYDROXYUREAS

(57) Abstract

Compounds having structure (I) wherein X is nitrogen, oxygen, sulfur or a bond and Z is oxygen or sulfur have been synthesized. These compounds are lipoxynase inhibitors and are useful as the active agent in pharmaceutical compositions for treating inflammatory conditions in humans and other mammals for which lipoxynase activity has been implicated.
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ANTIINFLAMMATORY HYDROXAMIC ACIDS AND N-HYDROXYUREAS

Background of the Invention

This invention relates to novel hydroxamic acid and N-hydroxyurea derivatives and their use. The compounds of the present invention inhibit the action of lipoxygenase enzyme and are useful in the treatment of inflammatory diseases or conditions in general, for example, allergies and cardiovascular diseases in mammals, including humans. This invention also relates to pharmaceutical compositions comprising such compounds, methods of producing such compounds and methods of using such compounds and compositions in the treatment of the aforementioned diseases and conditions.

Arachidonic acid is known to be the biological precursor of several groups of endogenous metabolites, prostaglandins including prostacyclins, thromboxanes and leukotrienes. The first step of arachidonic acid metabolism is the release of esterified arachidonic acid and related unsaturated fatty acids from membrane phospholipids via the action of phospholipase. Free fatty acids are then metabolized either by cyclooxygenase to produce the prostaglandins and thromboxanes or by lipoxygenase to generate hydroperoxy fatty acids which may be further converted to leukotrienes. Leukotrienes have been implicated in the pathophysiology of inflammatory diseases, including rheumatoid arthritis, gout, asthma, ischemia reperfusion injury, psoriasis and inflammatory bowel disease. Any drug that inhibits lipoxygenase is expected to
provide significant new therapy for both acute and chronic inflammatory conditions.

Recently, several review articles on lipoxygenase inhibitors have been reported. See, for example, H. Masamune and L. S. Melvin, Sr., in Annual Reports in Medicinal Chemistry, 24, 71-80 (Academic Press, 1989) and B. J. Fitzsimmons and J. Rokach in Leukotrienes and Lipoxygenases, 427-502 (Elsevier, 1989).


The present inventors have worked to prepare compounds capable of inhibiting the action of lipoxygenase and, after extensive research, have succeeded in synthesizing a series of compounds as disclosed in detail herein.

Summary of the Invention

The present invention provides for the preparation and use of novel hydroxamic acids and N-hydroxyurea derivatives of the formula:

\[
R^4 \text{O} \quad \text{Z} \\
\quad \text{N} \quad \text{R^1} \\
\quad \text{(A)} \quad \text{m} \\
\quad \text{Y_n} \quad \text{X} \\
\]

Formula I

where \( R^1 \) is hydrogen, C1 to C4 alkyl, C2 to C4 alkenyl, alkylthioalkyl, alkoxyalkyl or \(-\text{NR}^2\text{R}^3\);

\( R^2 \) and \( R^3 \) are each independently hydrogen, C1 to C4 alkyl, hydroxyl, aryl or substituted aryl wherein the substituent or substituents are selected from the group
consisting of halo, nitro, cyano, C1 to C12 alkyl, C1 to C12 alkoxy, C1 to C12 halosubstituted alkyl, C1 to C12 hydroxysubstituted alkyl, C1 to C12 alkoxy carbonyl, aminocarbonyl, C1 to C12 alkylaminocarbonyl, C1 to C12 dialkylaminocarbonyl and C1 to C12 alkylsulfonyle, with the proviso that R² and R³ are not both hydroxyl;

R⁴ is hydrogen, a pharmaceutically acceptable cation, aroyl or C1 to C12 alkanoyl;
X is a chemical bond, oxygen, sulfur or NR⁵;

R⁵ is hydrogen, C1 to C6 alkyl, C3 to C6 alkenyl, C1 to C6 alkanoyl, aryl, arylalkyl or aroyl;
m is 0 or 1;
n is 1 to 3;
A is C1 to C6 alkylene, C2 to C6 alkenylene or C2 to C6 alkylidene;
each Y is independently hydrogen, halogen, hydroxy, cyano, C1 to C12 alkyl, halosubstituted alkyl, hydroxysubstituted alkyl, C2 to C12 alkenyl, C1 to C12 alkoxy, C3 to C12 alkenyloxy, C3 to C8 cycloalkyl, C1 to C8 thioalkyl, C1 to C12 alkoxy carbonyl, C1 to C12 arylalkoxy carbonyl, aminocarbonyl, C1 to C12 alkylaminocarbonyl, C1 to C12 dialkylaminocarbonyl, C1 to C12 arylalkylamino, C1 to C12 arylalkylaminocarbonyl, alkoxyalkyl, aryl, aryloxy, aroyl, C1 to C12 arylalkyl, C2 to C12 arylalkenyl, C1 to C12 arylalkoxy or C1 to C12 arylthioalkoxy wherein said aryl, aryloxy, aroyl, arylalkyl, aryalkenyl, arylalkoxy and arylthioalkoxy may be optionally substituted with a substituent or substituents selected from the group consisting of halo, nitro, cyano, C1 to C12 alkyl, halosubstituted alkyl and C1 to C12 alkoxy; and

Z is oxygen or sulfur.

The substituent(s) Y and the linking group A may be attached at any available position on either ring.
Detailed Description of the Invention

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

The term "aryl" as used herein means any substituted and unsubstituted carbocyclic and heterocyclic aromatic groups such as phenyl, naphthyl, pyridyl, furyl and pyrimidinyl. The substituents may be halo, nitro, cyano, C1 to C12 alkyl, C1 to C12 alkoxy, C3 to C12 alkenyloxy, C1 to C12 halosubstituted alkyl, C1 to C12 alkoxy carbonyl, aminocarbonyl, C1 to C12 alkylaminocarbonyl, C1 to C12 halosubstituted alkoxy, C1 to C12 dialkylaminocarbonyl and C1 to C12 alkylsulfonyl.

The term "cycloalkyl" as used herein means a cyclic group of 3 to 8 carbons, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

The term "alkyl" means optionally a straight or branched chain.

The term "aroyl" as used herein means benzoyl, naphthoyl and their derivatives substituted with hydroxy, halo, nitro, cyano, C1 to C12 alkyl, alkoxy, hydroxysubstituted alkyl and halosubstituted alkyl.

The term "pharmaceutically acceptable cation" as used herein means non-toxic cations, including those of alkali and alkaline earth metals such as sodium, lithium, potassium, calcium and magnesium, and organic cations based on ammoniums and amines.

Some of the compounds of Formula I may form acid addition salts. The pharmaceutically acceptable acid addition salts are those formed from acids which form non-toxic acid addition salts, for example, the hydrochloride, hydrobromide, sulfate or bisulfate, phosphate or acid...
phosphate, acetate, citrate, fumarate, gluconate, lactate, maleate, succinate, tartrate, methanesulfonate, benzenesulfonate, toluenesulfonate and formate salts.

This invention includes pharmaceutical compositions for treatment of inflammatory diseases, allergies and cardiovascular diseases in mammals which comprise a pharmaceutically acceptable carrier or diluent and a compound of Formula I or a pharmaceutically acceptable salt thereof.

This invention also includes pharmaceutical compositions for inhibiting the action of lipoxygenase enzyme in a mammal which comprise a pharmaceutically acceptable carrier and a compound of Formula I or a pharmaceutically acceptable salt thereof.

This invention further includes processes for synthesizing the compounds of Formula I.

This invention still further includes methods of using the novel compounds and compositions in the treatment of conditions and diseases for which lipoxygenase activity has been implicated, for example, inflammatory conditions and diseases.

The compounds of Formula I may be prepared by a number of synthetic methods. In Formulae II, III, IV and V below, Q is

![Chemical structure]

and X, Y, m and n are as defined previously. Although, in reaction Schemes 1 and 2 below, R' is methyl and NH₂, respectively, and Z is oxygen, compounds of Formula I
wherein R¹ and Z are as defined previously may be prepared in an analogous manner.

In one embodiment, compounds of Formula IV are prepared according to the reaction steps outlined in Scheme 1, below.

![Scheme 1](image)

In step 1, the diacetyl compound (III) is prepared by standard methods known in the art. For example, the hydroxylamine (II) is reacted with acetyl chloride or acetic anhydride in a reaction-inert solvent in the presence of a suitable base. Preferred bases are triethylamine and pyridine. Suitable reaction-inert solvents include methylene chloride, chloroform, tetrahydrofuran, benzene and toluene. The reaction is usually carried out in a temperature range of from 0°C to ambient temperature. Reaction times of from 30 minutes to a few hours are common. The product can be isolated and purified by conventional procedures, for example, recrystallization or chromatography.

Step 2 involves selective hydrolysis of the diacetyl compound (III) with an appropriate base. The bases suitably employed in this reaction include ammonia, ammonium hydroxide, sodium hydroxide, potassium hydroxide and lithium hydroxide, preferably in methanol, ethanol, isopropyl alcohol or water, though binary solvent systems such as alcohol-water, tetrahydrofuran-water and the like may be employed. Reaction temperatures are usually in the range of from -10°C to ambient temperature and the reaction is
usually complete from within a few minutes to several hours. The product, having the structure shown in Formula IV, is isolated by standard methods and purification can be achieved by conventional means, for example recrystallization and chromatography.

In another embodiment, compounds of Formula V are prepared as illustrated in reaction Scheme 2, below.

\[
\text{SCHEME 2} \\
\begin{align*}
\text{OH} \\
\text{O}-(\text{A})_n^{\text{NH}} & \xrightarrow{\text{}\text{}\text{O}} \text{O}-(\text{A})_n^{\text{N}} \\
\text{NH}_2 & \quad \text{NH}_2
\end{align*}
\]

Formula II \quad Formula V

In this step the hydroxylamine (II) is treated with trimethylsilyl isocyanate in a reaction-inert solvent, usually at ambient through to reflux temperature. Suitable solvents which do not react with the reactants and/or products include, for example, tetrahydrofuran, dioxane, methylene chloride and benzene. An alternative procedure employs treatment of the hydroxylamine (II) with gaseous hydrogen chloride in a reaction-inert solvent such as benzene or toluene and then subsequent treatment with phosgene. Reaction temperatures are usually in the range of ambient temperature to the boiling point of the solvent. The intermediate carbamoyl chloride is not isolated but is subjected to (e.g. in situ) reaction with aqueous ammonia. The product thus obtained, having the structure shown in Formula V, is isolated by standard methods and purification can be achieved by conventional means, such as recrystallization and chromatography.

The aforementioned hydroxylamine (II) is easily prepared by standard synthetic procedures from readily
available carbonyl compounds, e.g. ketones or aldehydes, or from alcohols or halogen compounds. For example, a suitable carbonyl compound is converted to its oxime and then reduced to the requisite hydroxylamine (II) with a suitable reducing agent (for example, see R. F. Borch, et al., J. Am. Chem. Soc., 93, 2897 (1971)). Preferred reducing agents include sodium cyanoborohydride and borane complexes such as boron-pyridine, boron-triethylamine and boron-dimethylsulfide. Triethylsilane in trifluoroacetic acid may also be employed.

Alternatively, the hydroxylamine (II) can be prepared by treating the corresponding alcohol with N,O-bis(tert-butoxyl-carbonyl)hydroxylamine under Mitsunobu-type reaction conditions followed by acid catalyzed hydrolysis of the N,O-protected intermediate product (See JP 1045344). It is also noteworthy that the N,O-diacyetyl compound (III) can be prepared employing N,O-diacyetyl hydroxylamine in place of N,O-bis(tert-butoxyl-carbonyl)hydroxylamine, thus providing a convenient route to the product of Formula IV.

The aforementioned hydroxylamine (II) may also be prepared from a suitable halide compound by reaction with O-protected hydroxylamine and subsequent deprotection (see W. P. Jackson, et al., J. Med. Chem., 31, 499 (1988)). Preferred O-protected hydroxylamines include O-tetrahydropyranyl-, O-trimethylsilyl- and O-benzylhydroxylamine.

The hydroxylamine of Formula II thus obtained by the above representative procedures is isolated by standard methods and purification can be achieved by conventional means, such as recrystallization and chromatography.

The pharmaceutically acceptable salts of the novel compounds of the present invention are readily prepared by contacting said compounds with a stoichiometric amount of an appropriate mineral or organic acid in either aqueous
solution or in a suitable organic solvent. The salt may then be obtained by precipitation or by evaporation of the solvent.

The compounds of this invention inhibit the activity of the lipoxygenase enzyme. This inhibition has been demonstrated by an assay using rat peritoneal cavity resident cells which determines the effect of said compounds on the metabolism of arachidonic acid.

In this test some preferred compounds indicate low IC₅₀ values, in the range of 0.1 to 30 μM, with respect to lipoxygenase inhibition. As used herein, IC₅₀ refers to the concentration of the compound tested necessary to effect a 50% inhibition of lipoxygenase.

The ability of the compounds of the present invention to inhibit lipoxygenase enzyme makes them useful for controlling the symptoms induced by the endogenous metabolites arising from arachidonic acid in mammalian subjects. The compounds are therefore valuable in the prevention and treatment of such conditions and disease states in which the accumulation of arachidonic acid metabolites is a causative factor. Examples of such disease states include allergic bronchial asthma, skin disorders, rheumatoid arthritis, osteoarthritis and thrombosis.

Thus, the compounds of Formula I and their pharmaceutically acceptable salts are of particular use in the treatment or alleviation of inflammatory diseases, allergies, cardiovascular diseases in human subjects as well in the inhibition of the lipoxygenase enzyme.

For treatment of the various conditions described above, the compounds of Formula I and their pharmaceutically acceptable salts can be administered to a human subject either alone or, preferably, in combination with
pharmaceutically acceptable carriers or diluents in a pharmaceutical composition, according to standard pharmaceutical practice. A compound can be administered by a variety of conventional routes of administration including orally, parenterally and by inhalation. When the compounds are administered orally, the dose range will be generally from about 0.1 to 20 mg/kg body weight of the subject to be treated, per day, preferably from about 0.1 to 1.0 mg/kg/day in single or divided doses. If parenteral administration is desired, then an effective dose will be generally from about 0.1 to 1.0 mg/kg body weight of the subject to be treated, per day. In some instances it may be necessary to use dosages outside these limits, since the dosage will necessarily vary according to the age, weight and response of the individual patient as well as the severity of the patient's symptoms and the potency of the particular compound being administered.

For oral administration, the compounds of Formula I and their pharmaceutically acceptable salts can be administered, for example, in the form of tablets, powders, lozenges, syrups or capsules, or as an aqueous solution or suspension. In the case of tablets for oral use, carriers which are commonly used include lactose and corn starch. In addition, lubricating agents, such as magnesium stearate, are commonly added. In the case of capsules, useful diluents are lactose and dried corn starch. When aqueous suspensions are required for oral use, the active ingredient is combined with emulsifying and suspending agents. If desired, certain sweetening and/or flavoring agents can be added. For intramuscular, intraperitoneal, subcutaneous and intravenous use, sterile injectable solutions of the active ingredient are usually prepared, and the pH of the solutions should be suitably adjusted and buffered. For intravenous use, the total concentration of solute should be controlled to make the preparation isotonic.
The present invention is illustrated by the following examples. However, it should be understood that the invention is not limited to the specific details of these examples. Proton nuclear magnetic resonance spectra (NMR) were measured at 270 MHz unless otherwise indicated, for solutions in perdeuterodimethyl sulfoxide (DMSO-\text{d}_6) and peak positions are expressed in parts per million (ppm) downfield from tetramethysilane. The peak shapes are denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; br, broad.

**EXAMPLES**

**Example 1**  
N-(Hydroxy)-N-(inden-1-yl)urea

1-Indanone (4.00 g, 30.3 mmol) and hydroxylamine hydrochloride (5.26 g, 75.7 mmol) were dissolved in a mixture of methanol (40 ml) and pyridine (10 ml) and stirred for 3 hours at ambient temperature. The reaction mixture was concentrated in vacuo and the resultant residue was diluted with 1 N HCl (100 ml) and extracted three times with methylene chloride. The organic layer was dried over MgSO$_4$ and concentrated in vacuo to provide 4.13 g (93% yield) of the desired 1-indanone oxime as white needles.

The oxime (4.08 g, 27.7 mmol) prepared in the above step was dissolved in acetic acid (50 ml) and sodium cyanoborohydride (9.40 g, 63 mmol) was added portionwise over 1 hour. After reaction was complete, the reaction mixture was poured carefully into ice cold aqueous Na$_2$CO$_3$ such that the pH was adjusted to 9. The mixture was extracted with methylene chloride, dried over MgSO$_4$ and concentrated in vacuo to afford 3.6 g of 1-indane hydroxylamine (87% yield) as a tan powder.

The hydroxylamine (1.26 g, 8.4 mmol) prepared in the above step was stirred for 1 hour with trimethylsilyl isocyanate (1.65 g, 16.8 mmol) in tetrahydrofuran. The reaction mixture was concentrated in vacuo and the residue
recrystallized from ethyl acetate to give 0.78 g (48% yield) of the product as a fine white powder.

m.p.: 158.7 - 159.4°C
IR (KBr): 3465, 3190, 1667, 1654, 1573, 759, 741 cm⁻¹
NMR (CDCl₃)δ: 7.34-7.21 (m, 4H), 5.92 (dd, J=5.8 and 8.1 Hz, 1H), 5.3 (br., s, 2H), 5.16 (s, 1H), 3.07-3.02 (m, 1H), 2.95-2.83 (m, 1H), 2.46-2.35 (m, 1H), 2.26-2.13 (m, 1H)

Example 2  N-Hydroxy-N-(inden-1-yl)acetamide

1-Indane hydroxylamine (2.33 g, 15.6 mmol), prepared as in Example 1, and triethylamine (3.48 g, 34.3 mmol) were dissolved in methylene chloride (40 ml), cooled to 0°C and acetyl chloride (2.33 ml, 32.8 mmol) was added. The mixture was stirred for thirty minutes and poured into 1 N HCl. The organic layer was separated, dried over MgSO₄ and concentrated in vacuo to afford 3.58 g (98% yield) of N-acetoxy-N-(inden-1-yl)acetamide.

The acetamide (3.56 g, 15.3 mmol) was dissolved in a mixture of methanol (20 ml) and ammonia water (10 ml) at ambient temperature. After thirty minutes the mixture was concentrated in vacuo and the residue partitioned between water and methylene chloride. The organic phase was dried over MgSO₄ and concentrated in vacuo. The resultant residue was recrystallized from benzene to afford 2.06 g (70% yield) of the product as a fine white powder.

m.p.: 137.9 - 139.5°C
IR (KBr): 3090, 2925, 1615 (br.), 757 cm⁻¹
NMR (DMSO-d₆)δ: 9.46 (s, 1H), 7.22-7.12 (m, 4H), 5.96 (br., t, J=8 Hz, 1H), 3.05-2.90 (m, 1H), 2.85-2.70 (m, 1H), 2.25-2.05 (m, 2H), 2.06 (s, 3H)

Example 3  N-Hydroxy-N-[2-(2,3-dihydro-1H-inden-1-ylidene)ethyl]acetamide

Diethyl azodicarboxylate (3.94 g) in dry toluene (10 ml) was added to a stirred solution of 2-(2,3-dihydro-1H-
-13-

inden-1-ylidene) ethanol (2.41 g), N,O-diacetyldihydroxylamine (1.85 g) and triphenylphosphine (5.94 g) in dry toluene (60 ml) at -78 °C under nitrogen atmosphere. The mixture was stirred at ambient temperature under nitrogen atmosphere for 30 minutes. The mixture was filtered and the residue was washed thoroughly with ethylacetate and hexane (1:1). The combined filtrate and washings were concentrated under reduced pressure. Chromatography on silica gel eluted with hexane-ethyl acetate (3:1) to give N-acetoxy-N-[2-(2,3-dihydro-1H-inden-1-ylidene) ethyl]acetamide (1.34 g). The diacetate was dissolved in methanol (10 ml), concentrated NH₄OH was added, the mixture was stirred at ambient temperature for 1 hour and concentrated under reduced pressure. The resulting pale yellow oil was extracted with ethyl acetate and washed with brine. The solution was dried over MgSO₄ and concentrated to give a pale yellow oil. Chromatography on silica gel eluted with hexane-ethyl acetate (1:1) followed by crystallization from isopropyl ether afforded the desired compound, a white solid (0.46 g).

20 m.p.: 96.0 - 96.6 °C
IR (KBr) ν: 1650, 1610
NMR (270 MHz, CDCl₃) δ: 8.30 and 6.40 (br. s, 1H),
7.44-7.51 (m, 1H), 7.16-7.31 (m, 3H),
6.08-6.18 (m, 1H), 4.40 (d, 2H, J=6.2 Hz),
3.00-3.09 (m, 2H), 2.78-2.87 (m, 2H), 2.16 (s, 3H)

Example 4 N-Hydroxy-N-[1-(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl)ethyl]urea

To a mixture of 1-benzyl-1,2,3,4-tetrahydroquinolin-6-ylenethan-1-ol (2.82 g, 10.6 mmol), BocNH-OBoc (2.48 g, 11.1 mmol) and triphenylphosphine (3.62 g, 13.8 mmol) in toluene (20 ml) was added diethyl azodicarboxylate (2.40 g, 13.8 mmol) at -78 °C under nitrogen atmosphere. The mixture was stirred at -78 °C to ambient temperature for 30 minutes. The mixture was concentrated in vacuo to give a reddish brown oil (11.87 g). Chromatography on silica gel eluted with hexane-ethyl acetate (15:1) to afford N,O-dibutoxycarbonyl-
N-[1-(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl)ethyl] hydroxylamine (2.57 g, 53.8% yield).

NMR (CDCl₃) δ: 7.17-7.35 (m, 5H), 6.91-7.05 (m, 2H), 6.43 (d, J=8.1 Hz, 1H), 5.24 (q, J=6.8 Hz, 1H), 4.45 (s, 2H), 3.34 (t, J=5.5 Hz, 2H), 2.79 (t, J=5.9 Hz, 2H), 1.92-2.05 (m, 2H), 1.21-1.63 (m, 21H)

To a solution of N,O-dibutoxycarbonyl-N-[1-(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl)ethyl]hydroxylamine (2.57 g, 5.70 mmol) in CH₂Cl₂ (30 ml) was added trifluoroacetic acid (9 ml) at ambient temperature. The mixture was stirred at ambient temperature for 1 hour, concentrated in vacuo to afford a viscous oil which was extracted with ethyl acetate and washed with water and brine. The solution was dried over MgSO₄ and concentrated to give a yellow oil (1.38 g). Without purification, the crude product was dissolved in tetrahydrofuran (5 ml) and treated with 90% trimethylsilyl isocyanate (1.1 ml, 7.33 mmol) for 1 hour at ambient temperature. Water (1 ml) was added to the mixture which was then concentrated in vacuo. The residue was dissolved in ethyl acetate and the insoluble material was removed by filtration. The filtrate was concentrated in vacuo and crystallized from isopropyl ether-ethyl acetate to give a white solid. Recrystallization from ethyl acetate-isopropyl ether (4:1) afforded the title compound as a white solid (0.223 g, 12% yield).

m.p.: 127.8 - 128.2°C (dec.)
IR (KBr): 3500, 3460, 1645
NMR (DMSO) δ: 8.84 (s, 1H), 7.18-7.37 (m, 5H), 6.87 (s, 1H), 6.84 (d, J=8.8 Hz, 1H), 6.36 (d, J=8.8 Hz, 1H), 6.15 (s, 2H), 5.11 (q, J=7.0 Hz, 1H), 4.45 (s, 2H), 3.20-3.56* (2H), 2.70 (t, J=6.2 Hz, 2H), 1.80-1.97 (m, 2H), 1.30 (d, J=7.0 Hz, 3H)

* This peak was hidden by H₂O in DMSO-d₆.

By analogous methods, the following were prepared.
Example 5  
N-Hydroxy-N-(inden-2-yl)acetamide

\[
\begin{align*}
\text{HO} \\
\text{N} \quad \text{CH}_3 \\
\text{O}
\end{align*}
\]

m.p.: 138.8 - 140.2 °C

IR:

(KBr): 2805, 1580 (br.), 736 cm\(^{-1}\)

NMR:

(CDCl\(_3\)) \(\delta\): 8.45 (br. s, 1H), 7.26 - 7.16 (m, 4H), 4.85 (br., 1H), 3.40 (br., 2H), 3.17 - 3.08 (m, 2H), 2.19 (s, 3H)

Example 6  
N-Hydroxy-N-(inden-2-yl)urea

\[
\begin{align*}
\text{HO} \\
\text{N} \quad \text{NH}_2 \\
\text{O}
\end{align*}
\]

m.p.: 153.4 - 154.5 °C

IR:

(KBr): 3195, 1627, 740 cm\(^{-1}\)

NMR:

(DMSO-\(_d_6\)) \(\delta\): 9.13 (s, 1H), 7.18 - 7.08 (m, 4H), 6.37 (br.s, 2H), 5.01 (quint., J=8Hz, 1H), 3.05 - 2.85 (m, 4H)
Example 7

N-Hydroxy-N-(2-phenyl-3,4-dihydro-2H-benzopyran-6-yl)methylacetamide

\[
\begin{align*}
\text{m.p.:} & \quad 119.5 - 121.0 \degree C \\
\text{IR:} \quad (\text{KBr, cm}^{-1}) & \quad 3430, 1611, 1584, 1490 \\
\text{NMR:} \quad (270\text{MHz, CDCl}_3) & \\
\delta & \quad 7.26-7.45 \ (m, 5H) \\
& \quad 7.03 \ (br s, 2H) \\
& \quad 6.90 \ (d, 1H, J= 8Hz) \\
& \quad 5.06 \ (dd, 1H, J= 3, 10Hz) \\
& \quad 4.73 \ (s, 2H) \\
& \quad 2.93-3.06 \ (m, 1H) \\
& \quad 2.74-2.86 \ (m, 1H) \\
& \quad 2.03-2.30 \ (m, 2H) \\
& \quad 2.20 \ (s, 3H)
\end{align*}
\]

Example 8

N-Hydroxy-N-[2-(inden-1-yl)ethyl]acetamide

\[
\begin{align*}
\text{m.p.:} & \quad \text{oil} \\
\text{IR:} \quad (\text{film, cm}^{-1}) & \quad \nu 3160, 1610 \\
\text{NMR:} \quad (270\text{MHz, CDCl}_3) & \delta 8.30-8.55 \ (br s, 1H), 7.10-7.28 \ (m, 4H), 3.73 \ (t, 2H, J=7.3 Hz), \\
& \quad 3.13-3.27 \ (m, 1H), 2.79-3.03 \ (m, 2H), 2.25-2.40 \ (m, 2H), 2.10 \ (s, 3H), \\
& \quad 1.90-1.63 \ (m, 2H)
\end{align*}
\]
Example 9

N-Hydroxy-N-(3,4-dihydro-2H-1-benzopyran-3-yl)acetamide

\[ \text{HO} \]
\[ \text{N} - \text{CH}_3 \]
\[ \text{O} \]

m. p.: 163.6 - 163.9 °C

IR:

(KBr): 2840, 1618, 1583, 751 cm\(^{-1}\)

NMR:

(270 MHz, DMSO-\(d_6\)) \(\delta: 9.78(s, 1H), 7.12-7.04(m, 2H), 6.86(dt, J = 1 \text{ and } 8 \text{ Hz, } 1H), 6.78(d, J = 8 \text{ Hz, } 1H), 4.68(br. s, 2H), 4.17-4.11(m, 1H), 3.92(t, J = 10 \text{ Hz, } 1H), 3.08(dd, J = 11 \text{ and } 16 \text{ Hz, } 1H), 2.80(dd, J = 4 \text{ and } 16 \text{ Hz, } 1H), 2.04(s, 3H)\)

Example 10

N-Hydroxy-N-(5-methoxyindan-1-yl)acetamide

\[ \text{CH}_3O \]
\[ \text{HO} \]
\[ \text{N} - \text{CH}_3 \]
\[ \text{O} \]

m. p.: 153.5 - 154.3 °C

IR:

(KBr): 3300, 1604, 1589, 1577 cm\(^{-1}\)

NMR:

(270 MHz, DMSO-\(d_6\)) \(\delta: 9.39(s, 1H), 7.01(d, J = 8 \text{ Hz, } 1H), 6.80(d, J = 2 \text{ Hz, } 1H), 6.73(dd, J = 2 \text{ and } 8 \text{ Hz, } 1H), 5.89(br. s, 1H), 3.72(t, 3H), 3.0 - 2.89(m, 1H), 2.79 - 2.73(m, 1H), 2.24 - 2.0(m, 2H), 2.0(s, 3H)\)
Example 11

N-Hydroxy-N-(5-methoxyindan-1-yl)urea

\[
\begin{align*}
\text{m. p.:} & \quad 159.3 - 159.7 ^\circ C \\
\text{IR:} & \quad (\text{KBr}): 3460, 3200, 1654, 1570 \text{ cm}^{-1}
\end{align*}
\]

\[
\begin{align*}
\text{NMR:} & \quad (270 \text{ MHz, DMSO-}d_6) \delta : 8.89(s, 1H), 7.05(d, J = 8 \text{ Hz, } 1H), 6.76(d, J = 2 \text{ Hz, } 1H), \\
& \quad 6.71(dd, J = 2 \text{ and } 8 \text{ Hz, } 1H), 6.35(t, 2H), 5.56(t, J = 7 \text{ Hz, } 1H), 3.71(s, 3H), \\
& \quad 2.9 - 2.86(m, 1H), 2.74 - 2.71(m, 1H), 2.2 - 2.0(m, 2H).
\end{align*}
\]

Example 12

N-Hydroxy-N-(3,4-dihydro-2H-1-benzopyran-3-yl)urea

\[
\begin{align*}
\text{m. p.:} & \quad 167.9 - 168.5 ^\circ C \\
\text{IR:} & \quad (\text{KBr}): 3430, 3145, 1668 \text{ cm}^{-1}
\end{align*}
\]

\[
\begin{align*}
\text{NMR:} & \quad (270 \text{ MHz, DMSO-}d_6) \delta : 9.30(s, 1H), 7.12-7.04(m, 2H), 6.84(dt, J = 1 \text{ and } 8 \text{ Hz, } 1H), \\
& \quad 6.76(d, J = 8 \text{ Hz, } 1H), 6.49(s, 2H), 4.41-4.37(m, 1H), 4.17-4.11(m, 1H), 3.87(t, J = \\
& \quad 10 \text{ Hz, } 1H), 3.05(dd, J = 11 \text{ and } 16 \text{ Hz, } 1H), 2.68(dd, J = 4 \text{ and } 16 \text{ Hz, } 1H).
\end{align*}
\]
Example 13  N-(1-Benzyl-1,2,3,4-tetrahydroquinolin-6-yl)methyl-N-hydroxyacetamide

m.p.: 166-167 °C (dec)

IR: (KBr, cm⁻¹) 3125 2920 2850 1604 1510

NMR: (270MHz, CDCl₃)

δ 8.30 (br s, 1H)
7.23-7.35 (m, 5H)
6.91 (br s, 2H)
6.46 (d, 1H, J= 8Hz)
4.64 (s, 2H)
4.47 (s, 2H)
3.37 (t, 2H, J= 6Hz)
2.81 (t, 2H, J= 6Hz)
2.17 (s, 3H)
2.01 (quin, 2H, J= 6Hz)

Example 14  N-Hydroxy-N-(3,4-dihydro-2H-1-benzopyran-2-yl)methylurea

m.p.: 124.4 - 125.4 °C

IR:

(KBr): 3465, 3200, 1663, 1631, 1583, 752 cm⁻¹

NMR:

(270 MHz, DMSO-d₆) δ : 9.47(s, 1H), 7.04(t, J = 8 Hz, 2H), 6.78(dd, J = 1 and 8 Hz, 1H), 6.72(d, J = 8 Hz, 1H), 6.34(br. s, 2H), 4.22(m, 1H), 3.64(dd, J = 6 and 14 Hz, 1H),
Example 15

N-Hydroxy-N-(3,4-dihydro-2H-1-benzopyran-2-yl)methylacetamide

\[ \text{m.p.: 120.5 - 120.8 °C} \]

IR:
(KBr): 3150, 2845, 1618, 1600, 1584, 749 cm\(^{-1}\)

NMR:
(270 MHz, CDCl\(_3\)) \(\delta\): 8.45 (br. s, 1H), 7.12 - 7.04 (m, 2H), 6.88 - 6.75 (m, 2H), 4.42 - 1.5 (m, 1H), 4.0 - 3.75 (m, 2H), 2.95 - 2.80 (m, 2H), 2.20 (s, 3H), 2.15 - 1.95 (m, 1H), 1.85 - 1.75 (m, 1H)

Example 16

N-Hydroxy-N-(2-indan-1-ylethyl)urea

m.p.: 89.0-89.9°C

IR: (KBr) \(\nu\) 3430, 1635.

NMR:
(270 MHz, CDCl\(_3\)) \(\delta\): 7.12-7.25 (m, 4H), 5.26 (br s, 2H), 3.55-3.76 (m, 2H), 3.07-3.21 (m, 1H), 2.76-2.97 (m, 2H), 2.14-2.38 (m, 2H), 1.63-1.79 (m, 3H).
Example 17

N-Hydroxy-N-(2-phenyl-3,4-dihydro-2H-benzopyran-6-yl)methylurea

\[
\begin{align*}
\text{Ph} & \quad \text{N} & \quad \text{O} & \quad \text{NH}_2 \\
\text{OH}
\end{align*}
\]

m.p.: 163.8-164.5 °C

E.A.:  
Calcd. : C 68.44 %  H 6.08%  N 9.39 %  Found : C 68.68 %  H 6.21%  N 9.10 %

IR: (KBr, cm\(^{-1}\))  
3525  
3415  
1647  
1490

NMR: (270MHz, DMSO-d\(_6\))  
\(\delta\) 9.25 (s, 1H)  
7.31-7.46 (m, 5H)  
7.02 (br s, 2H)  
6.76 (d, 1H, J= 6Hz)  
6.29 (br s, 2H)  
5.10 (dd, 1H, J=2, 10Hz)  
4.41 (s, 2H)  
2.88-3.03 (m, 1H)  
2.63-2.76 (m, 1H)  
2.11-2.22 (m, 1H)  
1.91-2.07 (m, 1H)
Example 18

N-Hydroxy-N-(6-methoxyindan-1-yl)urea

\[
\begin{array}{c}
\text{OCH}_3 \\
\text{H} \\
\text{N} \\
\text{NH}_2 \\
\text{O}
\end{array}
\]

m. p.: 160.0 - 160.4 °C

IR:
(KBr): 3465, 3190, 1653, 1572, 1489, 1451 cm\(^{-1}\)

NMR:
(270 MHz, DMSO-\(d_6\)) \(\delta\) : 8.95(s, 1H), 7.08(d, J = 8 Hz, 1H), 6.75(dd, J = 2 and 8 Hz, 1H), 6.72(d, J = 2 Hz, 1H), 6.42(s, 2H), 5.62(t, J = 7 Hz, 1H), 3.71(s, 3H), 2.9 - 2.78(m, 1H), 2.7 - 2.6(m, 1H), 2.2 - 2.0(m, 2H).

Example 19

N-Hydroxy-N-(6-methoxyindan-1-yl)acetamide

\[
\begin{array}{c}
\text{OCH}_3 \\
\text{H} \\
\text{N} \\
\text{CH}_3
\end{array}
\]

m. p.: 153.2 - 154.2 °C

IR:
(KBr): 2850, 1610, 1586 cm\(^{-1}\)

NMR:
(270 MHz, DMSO-\(d_6\)) \(\delta\) : 9.45(s, 1H), 7.13(d, J = 8 Hz, 1H), 6.78(dd, J = 2 and 8 Hz, 1H), 6.64(d, J = 2 Hz, 1H), 5.90(t, 7 Hz, 1H), 3.71(s, 3H), 2.95 - 2.82(m, 1H), 2.76 - 2.64(m, 1H), 2.25 - 2.0(m, 2H), 2.06(s, 3H)
Example 20

-23-

N-Hydroxy-N-(5-benzyloxyindan-1-yl)acetamide

\[
\text{m.p. : } 143.5 - 144.0 ^\circ \text{C}
\]

IR:

(KBr): 3200, 1603 cm\(^{-1}\)

NMR:

(270 MHz, DMSO-\(d_6\)) \(\delta\) : 9.40(s, 1H), 7.45 - 7.31(m, 5H), 7.01(d, J = 8 Hz, 1H), 6.88(d, J = 2 Hz, 1H), 6.81(dd, J = 2 and 8 Hz, 1H), 5.89(t, J = 7 Hz, 1H), 5.08(s, 2H), 3.00 - 2.86(m, 1H), 2.82 - 2.66(m, 1H), 2.25 - 2.0(m, 2H), 2.04(s, 3H)

Example 21

N-Hydroxy-N-(5-benzyloxyindan-1-yl)urea

\[
\text{m.p. : } 165.0 - 166.5 ^\circ \text{C}
\]

IR:

(KBr): 3455, 3260, 1651, 1617, 1573, 1419, 734 cm\(^{-1}\)

NMR:

(270 MHz, DMSO-\(d_6\)) delta: 8.90(s, 1H), 7.45-7.3(m, 5H), 7.06 (d, J=8Hz, 1H), 6.85(d, J=2Hz, 1H), 6.80 (dd, J=2 and 8Hz, 1H), 6.36(s, 2H), 5.59(t, J=7Hz, 1H), 5.06(s, 2H), 2.96-2.8(m, 1H), 2.76-2.62(m, 1H), 2.22-2.04(m, 2H)
Example 22

N-(3,4-Dihydro-2H-benzopyran-6-yl)methyl-N-hydroxyurea

\[ \text{IR: (KBr, cm}^{-1}\text{)} \]
\[ 3440, 1639, 1497 \]

\[ \text{NMR: (270MHz, DMSO-d}_6\text{)} \]
\[ \delta \]
\[ 9.22 (s, 1H) \]
\[ 6.94-6.97 (m, 2H) \]
\[ 6.65 (d, 1H, J=9Hz) \]
\[ 6.27 (br s, 2H) \]
\[ 4.37 (s, 2H) \]
\[ 4.09 (t, 2H, J=5Hz) \]
\[ 2.70 (t, 2H, J=6Hz) \]
\[ 1.86-1.94 (m, 2H) \]

Example 23

N-Hydroxy-N-(6-methylindan-1-yl)acetamide

\[ \text{IR: (KBr): 2850, 1600, 1430 cm}^{-1}\text{) } \]

\[ \text{NMR: (270 MHz, DMSO-d}_6\text{)} \]
\[ \delta \]
\[ 9.44(s, 1H), 7.11(d, J=8 Hz, 1H), 7.02(d, J=8 Hz, 1H), \]
\[ 6.92(s, 1H), 5.93(t, J=7 Hz, 1H), 2.96 - 2.84(m, 1H), 2.8 - 2.65(m, 1H), \]
Example 24

N-(3,4-Dihydro-2H-benzopyran-6-yl)methyl-N-hydroxyacetamide

\[
\begin{align*}
\text{m.p.:} & \quad 115-118^\circ C \\
\text{IR: (KBr, cm}^{-1}\text{)} & \quad 3435 \quad 1499 \\
& \quad 2935 \quad 1251 \\
& \quad 1619 \\
& \quad 1599 \\
\text{NMR: (270MHz, CDCl}_3\text{)} \\
\delta & \quad 8.34 \text{ (br s, 1H)} \\
& \quad 6.94-7.06 \text{ (m, 2H)} \\
& \quad 6.78 \text{ (d, 1H, J= 8Hz)} \\
& \quad 4.70 \text{ (s, 2H)} \\
& \quad 4.18 \text{ (t, 2H, J=5Hz)} \\
& \quad 2.78 \text{ (t, 2H, J=6Hz)} \\
& \quad 2.18 \text{ (s, 3H)} \\
& \quad 1.94-2.06 \text{ (m, 2H)}
\end{align*}
\]
Example 25  N-Hydroxy-N-(5-methylindan-1-yl)urea

**STRUCTURE:**

```
Me
OH
N
NH2
```

m. p.: 172.9-174.6°C

IR: ν (KBr): 3460, 1660, 1570, 1460 cm⁻¹.

NMR: δ (DMSO-d₆):

8.89 (s, 1H), 7.08-6.93 (m, 3H), 6.36 (s, 2H),
5.62 (t, J=7.7Hz, 1H), 2.95-2.80 (m, 1H), 2.77-2.62 (m, 1H),
2.26 (s, 3H), 2.23-1.98 (m, 2H)

Example 26  N-Hydroxy-N-(5-chloroindan-1-yl)urea

**STRUCTURE:**

```
Cl
OH
N
NH2
```

m. p.: 169.4-170.8°C

IR: ν (KBr): 3480, 1655, 1530 cm⁻¹.

NMR: δ (DMSO-d₆):

9.01 (s, 1H), 7.28-7.11 (m, 3H), 6.43 (s, 2H),
5.63 (t, J=7.5Hz, 1H), 2.97-2.85 (m, 1H), 2.82-2.59 (m, 1H),
2.28-2.04 (m, 2H).
Example 27  
N-Hydroxy-N-[1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylacetamide  

**STRUCTURE:**

![Chemical Structure](image)

**mp:** 96.3-96.5°C/dec.

**IR (KBr) cm⁻¹:** 1610, 1600

**NMR (DMSO) δ:**

9.70 (s, 1H), 7.19-7.27 (m, 1H), 6.75-6.84 (m, 5H), 6.38 (d, J= 8.2 Hz, 1H), 4.45 (s, 2H), 4.43 (s, 2H), 3.72 (s, 3H), 3.25-3.53* (2H), 2.66-2.75 (m, 2H), 1.98 (s, 3H), 1.84-1.97 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆

---

Example 28  
N-[1-(4-Chlorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methyl-N-hydroxyacetamide  

**STRUCTURE:**

![Chemical Structure](image)

**mp:** 163-166 °C (dec)

**IR (KBr) cm⁻¹:** 3145, 2940, 2875, 1612, 1602, 1509 cm⁻¹

**NMR (CDCl₃) δ:**

8.31 (br s, 1H), 7.26 (d, 2H, J= 1.5Hz), 7.19 (d, 2H, J= 1.5Hz), 6.91 (br s, 2H), 6.40 (d, 1H, J= 8Hz), 4.64 (s, 2H), 4.42 (s, 2H), 3.35 (t, 2H, J= 6Hz), 2.80 (t, 2H, J= 6Hz), 2.17 (s, 3H), 2.03 (quin, 2H, J= 6Hz)
Example 29  
N-Hydroxy-N-[5-(2-quinolylmethoxy)indan-1-yl]urea

**STRUCTURE:**

![Structure Image]

**mp:** 182.8-184.1°C

**IR (KBr) cm⁻¹:** 3480, 3200, 1650, 1570, 1490, 1430, 1330, 1280, 1140, 920

**NMR (DMSO-d₆) δ:**

8.92(s, 1H), 8.40(d, J=8.43Hz, 1H), 8.00(t, J=8.43Hz, 2H), 7.78(m, 1H),
7.62(m, 2H), 7.07(d, J=8.43Hz, 1H), 6.87(m, 2H), 6.35(s, 2H),
5.59(m, 1H), 5.33(s, 2H), 2.85(m, 1H), 2.69(m, 1H), 2.13(m, 2H)

Example 30  
N-Hydroxy-N-[1-(3-methoxybenzyl)-8-chloro-1,2,3,4-tetrahydro-quinolin-6-yl]methylacetamide

**STRUCTURE:**

![Structure Image]

**mp:** amorphous

**IR (KBr) cm⁻¹:** 2930, 1610, 1475, 1255 cm⁻¹

**NMR (CDCl₃) δ:**

9.90 (s, 1H), 7.28 (dd, 1H, J=8.1, 7.7Hz), 7.08-7.13 (m, 3H), 6.95
(d, 1H, J=1.8Hz), 6.85 (dd, 1H, J=8.1, 1.8Hz), 4.75 (s, 2H), 4.12 (s,
2H), 3.75 (s, 3H), 2.82-2.86 (m, 2H), 2.74-2.79 (m, 2H), 2.03 (s, 3H),
1.73-1.79 (br, 2H).
### Example 31

**N-Hydroxy-N-[4-[(3,4-dihydro-2H-benzopyran)6-yl]3-buten-2-yl]acetamide**

**STRUCTURE:**

![Structure of N-Hydroxy-N-[4-[(3,4-dihydro-2H-benzopyran)6-yl]3-buten-2-yl]acetamide](image)

- **mp:** 90-93°C
- **IR:** ν (Nujol): 1610, 1590, 1490, 1240, 1170, 1060, 1005, 970, 820 cm⁻¹
- **NMR:** δ (CDCl₃-DMSO-d₆): 8.95 (s, 1H), 7.10 (d, J = 8.4 Hz, 1H), 7.05 (s, 1H), 6.70 (d, J = 8.4 Hz, 1H), 6.42 (d, J = 15.7 Hz, 1H), 6.12 (d, J = 6.6, 15.7 Hz, 1H), 5.29 (m, 1H), 4.16 (t, J = 5.1 Hz, 2H), 2.75 (t, J = 6.2 Hz, 2H), 2.14 (s, 3H), 1.99 (m, 2H), 1.37 (br d, 3H)

### Example 32

**N-Hydroxy-N-(4-phenoxyindan-1-yl)acetamide**

**STRUCTURE:**

![Structure of N-Hydroxy-N-(4-phenoxyindan-1-yl)acetamide](image)

- **mp:** 141.4 - 143.1 °C
- **IR:** ν (KBr): 2850, 1585, 1465, 1245, 770 cm⁻¹
- **NMR:** δ (DMSO-d₆): 9.51 (s, 1H), 7.36 (t, J = 8 Hz, 2H), 7.22 (t, J = 8 Hz, 1H), 7.10 (t, J = 8 Hz, 1H), 6.95 (d, J = 8 Hz, 3H), 6.79 (d, J = 8 Hz, 1H), 6.01 (t, J = 7 Hz, 1H), 2.9 - 2.76 (m, 1H), 2.68 - 2.56 (m, 1H), 2.3 - 2.0 (m, 2H), 2.07 (s, 3H)
Example 33

**N-Hydroxy-N-(5-phenoxyindan-1-yl)acetamide**

**STRUCTURE:**

![Structure](image)

**mp:** 111.0 - 111.5 °C

**IR:** ν (KBr): 3450, 3150, 2700, 1605, 1590, 1485, 1250, 780, 695 cm\(^{-1}\)

**NMR:** δ (DMSO-d6): 9.48 (s, 1H), 7.38 (t, J = 8 Hz, 2H), 7.14 (t, J = 8 Hz, 2H), 6.98 (dd, J = 8 and 2 Hz, 2H), 6.85 (s, 1H), 6.83 (d, J = 8 Hz, 1H), 5.94 (t, J = 7 Hz, 1H), 3.0 - 2.9 (m, 1H), 2.85 - 2.7 (m, 1H), 2.3 - 2.05 (m, 2H), 2.05 (s, 3H)
<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-[(1-(4-fluorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methyl]urea</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

**STRUCTURE:**

```
\( \text{N-Hydroxy-N-} [\text{1-(4-fluorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl}] \text{methylurea} \)
```

<table>
<thead>
<tr>
<th>m. p.</th>
<th>141.4-141.6°C/dec.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR (KBr)</td>
<td>3500, 1645</td>
</tr>
</tbody>
</table>

**NMR:**

8 (DMSO): 9.14 (s, 1H), 7.23-7.32 (m, 2H), 7.09-7.18 (m, 2H), 6.77-6.85 (m, 2H), 6.39 (d, J= 8.1 Hz, 1H), 6.20 (s, 2H), 4.44 (s, 2H), 4.29 (s, 2H), 3.23-3.37 (2H), 2.70 (t, J= 6.2 Hz, 2H), 1.85-1.95 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*

<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-{1-(1-benzoyl-1,2,3,4-tetrahydroquinolin-6-yl)ethyl}urea</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

**STRUCTURE:**

```
\( \text{N-Hydroxy-N-} [\text{1-(1-benzoyl-1,2,3,4-tetrahydroquinolin-6-yl)ethyl}] \text{urea} \)
```

<table>
<thead>
<tr>
<th>m. p.</th>
<th>180.7-181.0°C/dec.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR (KBr)</td>
<td>3450, 1670, 1610</td>
</tr>
</tbody>
</table>

**NMR:**

8 (DMSO): 9.01 (s, 1H), 7.32-7.43 (m, 5H), 7.15 (s, 1H), 6.84-6.90 (m, 1H), 6.75-6.81 (m, 1H), 6.26 (s, 2H), 5.20 (q, J= 7.0 Hz, 1H), 3.71 (t, J= 6.2 Hz, 2H), 2.79 (t, J= 6.6 Hz, 2H), 1.86-1.99 (m, 2H), 1.34 (d, J= 7.0 Hz, 3H)
Example 36

N-Hydroxy-N-{1-(1-benzoyl-1,2,3,4-tetrahydroquinolin-7-yl)ethyl}urea

STRUCTURE:

\[
\text{N} - \text{H} - \text{O} - \text{N} - \text{N} - \text{O} - \text{NH}_2 - 1/5\text{H}_2\text{O}
\]

m. p. : 161.4-161.7°C/dec.

IR: \(\nu\) (KBr):

3500, 1652, 1610

NMR: \(\delta\) (DMSO):

8.85 (s, 1H), 7.26-7.43 (m, 5H), 7.08 (d, J = 8.1 Hz, 1H), 6.93 (dd, J = 7.7 Hz, 1.5 Hz, 1H), 6.69 (s, 1H), 6.16 (s, 2H), 4.94 (q, J = 7.0 Hz, 1H), 3.64-3.86 (m, 2H), 2.78 (t, J = 6.6 Hz, 2H), 1.88-2.01 (m, 2H), 0.91 (d, J = 7.0 Hz, 3H)

Example 37

N-Hydroxy-N-(1-allyl-1,2,3,4-tetrahydroquinolin-6-yl)methylurea

STRUCTURE:

\[
\text{N} - \text{H} - \text{O} - \text{N} - \text{NH}_2
\]

m. p. : 114.3-114.6°C/dec.

IR: \(\nu\) (KBr):

3440, 1665, 1640, 1610

NMR: \(\delta\) (DMSO):

9.14 (s, 1H), 6.85 (d, J = 8.4 Hz, 1H), 6.81 (s, 1H), 6.45 (d, J = 8.4 Hz, 1H), 6.21 (s, 2H), 5.73-5.89 (m, 1H), 5.08-5.19 (m, 2H), 4.30 (s, 2H), 3.79-3.88 (m, 2H), 3.21 (t, J = 5.7 Hz, 2H), 2.66 (t, J = 6.2 Hz, 2H), 1.80-1.91 (m, 2H)
**Example 38**

**N-Hydroxy-N-[(1-(4-methybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea**

**STRUCTURE:**

![Structure of N-Hydroxy-N-[(1-(4-methybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea](image)

**m. p.:** 156.6-156.8°C/dec.

**IR: v (KBr):** 3520, 3400, 1650, 1615

**NMR: δ (DMSO):**

9.13 (s, 1H), 7.12 (s, 4H), 6.82 (s, 1H), 6.78 (d, J = 8.4 Hz, 1H), 6.38 (d, J = 8.4 Hz, 1H), 6.19 (s, 2H), 4.40 (s, 2H), 4.28 (s, 2H), 3.25-3.41*(2H), 2.70 (t, J = 6.2 Hz, 2H), 2.26 (s, 3H), 1.85-1.96 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*

**Example 39**

**N-Hydroxy-N-(1-benzyl-1,2,3,4-tetrahydroquinaldin-6-yl)methylurea**

**STRUCTURE:**

![Structure of N-Hydroxy-N-(1-benzyl-1,2,3,4-tetrahydroquinaldin-6-yl)methylurea](image)

**m. p.:** 141.8-142.1°C/dec.

**IR: v (KBr):** 3420, 1673, 1640, 1615

**NMR: δ (DMSO):**

9.13 (s, 1H), 7.17-7.36 (m, 5H), 6.87 (s, 1H), 6.76 (d, J = 8.4 Hz, 1H), 6.22 (d, J = 8.4 Hz, 1H), 6.19 (s, 2H), 4.47 (d, J = 5.1 Hz, 2H), 4.28 (s, 2H), 3.50-3.65 (m, 1H), 2.58-2.90 (m, 2H), 1.71-2.00 (m, 2H), 1.11 (d, J = 6.6 Hz, 3H)
<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-(1-(1-phenylethyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td></td>
</tr>
<tr>
<td>STRUCTURE:</td>
<td>![Structure Image]</td>
</tr>
<tr>
<td>m. p. :</td>
<td>125.0-125.3°C/dec.</td>
</tr>
<tr>
<td>IR: v (KBr):</td>
<td>3520, 3400, 1650, 1615</td>
</tr>
<tr>
<td>NMR: δ (DMSO):</td>
<td>9.14 (s, 1H), 7.18-7.38 (m, 5H), 6.79-6.87 (m, 2H), 6.59 (d, J = 9.2 Hz, 1H), 6.21 (s, 2H), 5.08 (q, J = 7.0 Hz, 1H), 4.30 (s, 2H), 2.94-3.25 (m, 2H), 2.61-2.71 (m, 2H), 1.65-1.92 (m, 2H), 1.50 (d, J = 7.0 Hz, 3H)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-(1-(2-phenylethyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>41</td>
<td></td>
</tr>
<tr>
<td>STRUCTURE:</td>
<td>![Structure Image]</td>
</tr>
<tr>
<td>m. p. :</td>
<td>132.4-132.8°C/dec.</td>
</tr>
<tr>
<td>IR: v (KBr):</td>
<td>3480, 1641</td>
</tr>
<tr>
<td>NMR: δ (DMSO):</td>
<td>9.26 (s, 1H), 7.14-7.33 (m, 5H), 6.91 (d, J = 8.4 Hz, 1H), 6.80 (s, 1H), 6.56 (d, J = 8.4 Hz, 1H), 6.20 (s, 2H), 4.31 (s, 2H), 3.34-3.45 (m, 2H), 3.14 (t, J = 5.3 Hz, 2H), 2.69-2.80 (m, 2H), 2.60 (t, J = 6.2 Hz, 2H), 1.66-1.83 (m, 2H)</td>
</tr>
</tbody>
</table>
Example N-Hydroxy-N-1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea·HCl·2/3H₂O

STRUCTURE:

\[ \text{N-Hydroxy-N-1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea·HCl·2/3H₂O} \]

m. p. : 97.4-100.2°C/dec.

IR: ν (KBr): 1650

NMR: δ (DMSO):

7.24 (t, J = 8.1 Hz, 1H), 6.77-6.90 (m, 5H), 6.43-6.53 (m, 1H), 4.45 (s, 2H),
4.32 (s, 2H), 3.71 (s, 3H), 3.33 (t, J = 5.5 Hz, 2H), 2.72 (t, J = 5.9 Hz, 2H),
1.85-1.99 (m, 2H) ppm

*This peak was hidden by H₂O in DMSO-d₆

Example N-Hydroxy-N-1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea

STRUCTURE:

\[ \text{N-Hydroxy-N-1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea} \]

m. p. : 120.7-121.0°C/dec.

IR: ν (KBr): 3500, 1640

NMR: δ (DMSO):

9.13 (s, 1H), 7.16-7.24 (m, 1H), 6.72-6.83 (m, 5H), 6.34 (d, J = 8.4 Hz, 1H),
6.17 (s, 2H), 4.40 (s, 2H), 4.27 (s, 2H), 3.68 (s, 3H), 3.17-3.46 (2H),
2.68 (t, J = 6.2 Hz, 2H), 1.80-1.95 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆
### Example 44

**N-Hydroxy-N-{1-(2-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl}methylurea**

**Structure:***

```
\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{NH}_2 \\
\text{MeO}
\end{array}
\]
```

**M. p.:** 104.2-104.8°C/dec.

**IR: v (KBr):** 3420, 1670

**NMR: δ (DMSO):**

- 9.14 (s, 1H), 7.22 (t, J = 7.4 Hz, 1H), 7.01 (d, J = 7.7 Hz, 2H), 6.82-6.89 (m, 2H), 6.77 (d, J = 8.1 Hz, 1H), 6.15-6.24 (m, 3H), 4.37 (s, 2H), 4.29 (s, 2H), 3.83 (s, 3H), 3.25-3.45 (2H), 2.73 (t, J = 6.0 Hz, 2H), 1.86-1.98 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*

### Example 45

**N-Hydroxy-N-{1-(3-trifluoromethylbenzyl)-1,2,3,4-tetrahydroquinolin-6-yl}methylurea**

**Structure:***

```
\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{NH}_2 \\
\text{CF}_3
\end{array}
\]
```

**M. p.:** 133.7-133.8°C/dec.

**IR: v (KBr):** 3500, 1618

**NMR: δ (DMSO):**

- 9.16 (s, 1H), 7.50-7.63 (m, 4H), 6.85 (s, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.37 (d, J = 8.4 Hz, 1H), 6.21 (s, 2H), 4.56 (s, 2H), 4.30 (s, 2H), 3.27-3.46 (2H), 2.73 (t, J = 6.2 Hz, 2H), 1.86-1.99 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*
Example N-Hydroxy-N-{1-(3,5-dimethoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl}methylurea

**Structure:**

```
O
N    O
   NH
   OH
OMe OMe
```

**m.p.:** 152.5-153.0°C/dec.

**IR: v (KBr):** 3500, 1652

**NMR: δ (DMSO):**

9.16 (s, 1H), 6.83 (s, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.33-6.41 (m, 4H), 6.20 (s, 2H), 4.38 (s, 2H), 4.29 (s, 2H), 3.70 (s, 6H), 3.28-3.51 (2H), 2.71 (t, J = 6.0 Hz, 2H), 1.83-1.96 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*

---

Example N-Hydroxy-N-{1-(3-chlorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl}methylurea

**Structure:**

```
O
N    O
   NH
   OH
Cl
```

**m.p.:** 119.7-121.6°C/dec.

**IR: v (KBr):** 3480, 1638

**NMR: δ (DMSO):**

9.15 (s, 1H), 7.35 (t, J = 7.3 Hz, 1H), 7.25-7.32 (m, 2H), 7.20 (d, J = 7.3 Hz, 1H), 6.84 (s, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 8.4 Hz, 1H), 6.21 (s, 2H), 4.47 (s, 2H), 4.30 (s, 2H), 3.26-3.45 (2H), 2.72 (t, J = 6.2 Hz, 2H), 1.85-1.93 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*
Example 48  N-Hydroxy-N-[1-(3-pentyloxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea

Structure:

m. p.: 130.7-131.8°C/dec.

IR: ν (KBr): 3500, 1640

NMR: δ (DMSO):
9.14 (s, 1H), 7.17-7.25 (m, 1H), 6.74-6.85 (m, 5H), 6.37 (d, J = 8.1 Hz, 1H), 6.20 (s, 2H), 4.41 (s, 2H), 4.29 (s, 2H), 3.91 (t, J = 6.4 Hz, 2H), 3.26-3.50* (2H), 2.71 (t, J = 6.2 Hz, 2H), 1.85-1.96 (m, 2H), 1.61-1.74 (m, 2H), 1.26-1.44 (m, 4H), 0.88 (t, J = 7.3 Hz, 3H)
*This peak was hidden by H₂O in DMSO-d₆

Example 49  N-Hydroxy-N-[1-(3-fluorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea

Structure:

m. p.: 123.5-123.9°C/dec.

IR: ν (KBr): 3420, 1662, 1615

NMR: δ (DMSO):
9.15 (s, 1H), 7.32-7.42 (m, 1H), 6.99-7.12 (m, 3H), 6.84 (s, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 8.4 Hz, 1H), 6.20 (s, 2H), 4.47 (s, 2H), 4.29 (s, 2H), 3.24-3.53* (2H), 2.72 (t, J = 6.2 Hz, 2H), 1.86-1.98 (m, 2H)
*This peak was hidden by H₂O in DMSO-d₆
### Example 50

**N-Hydroxy-N-\{(1-(2-fluorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl) methylurea**

**Structure:**

![Structure](image)

**m. p.:** 134.7-134.9°C/dec.

**IR:** ν (KBr): 3500, 3400, 1650, 1615

**NMR: 8 (DMSO):**

- 9.14 (s, 1H), 7.08-7.35 (m, 4H), 6.84 (s, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.37 (d, J = 8.4 Hz, 1H), 6.21 (s, 2H), 4.50 (s, 2H), 4.29 (s, 2H), 3.28-3.38 (m, 2H), 2.72 (t, J = 6.2 Hz, 2H), 1.86-1.97 (m, 2H)

### Example 51

**N-Hydroxy-N-\{(1-(3-(2-propoxy)benzyl)-1,2,3,4-tetrahydroquinolin-6-yl) methylurea**

**Structure:**

![Structure](image)

**m. p.:** 134.4-134.5°C/dec.

**IR:** ν (KBr): 3500, 1640

**NMR: 8 (DMSO):**

- 9.13 (s, 1H), 7.19 (t, J = 7.7 Hz, 1H), 6.72-6.85 (m, 5H), 6.38 (d, J = 8.1 Hz, 1H), 6.20 (s, 2H), 4.49-4.61 (m, 1H), 4.41 (s, 2H), 4.29 (s, 2H), 3.26-3.36 (m, 2H), 2.71 (t, J = 6.0 Hz, 2H), 1.84-1.93 (m, 2H), 1.23 (d, J = 6.2 Hz, 6H)
**Example 52**  
N-Hydroxy-N-\{1-(3-allyloxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

![Chemical Structure](image)

**m. p.:** 120.8-121.5°C/dec.

**IR:** ν (KBr): 3490, 1630

**NMR:** δ (DMSO):

<table>
<thead>
<tr>
<th>Peak</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.13</td>
<td>(s, 1H)</td>
</tr>
<tr>
<td>7.18-7.26</td>
<td>(m, 1H)</td>
</tr>
<tr>
<td>6.76-6.85</td>
<td>(m, 5H)</td>
</tr>
<tr>
<td>6.37</td>
<td>(d, J = 8.1 Hz, 1H)</td>
</tr>
<tr>
<td>6.20</td>
<td>(s, 2H)</td>
</tr>
<tr>
<td>6.01</td>
<td>(ddt, J = 17.2 Hz, 10.2 Hz, 5.1 Hz, 1H)</td>
</tr>
<tr>
<td>5.36</td>
<td>(dtt, J = 17.2 Hz, 1.8 Hz, 1.8 Hz, 1H)</td>
</tr>
<tr>
<td>5.23</td>
<td>(dtt, J = 10.2 Hz, 1.8 Hz, 1.8 Hz, 1H)</td>
</tr>
<tr>
<td>4.52</td>
<td>(ddt, J = 5.1 Hz, 1.5 Hz, 1.5 Hz, 2H)</td>
</tr>
<tr>
<td>4.42</td>
<td>(s, 2H)</td>
</tr>
<tr>
<td>4.29</td>
<td>(s, 2H)</td>
</tr>
<tr>
<td>3.24-3.41</td>
<td><em>(2H)</em></td>
</tr>
<tr>
<td>2.71</td>
<td>(t, J = 6.4 Hz, 2H)</td>
</tr>
<tr>
<td>1.85-1.97</td>
<td>(m, 2H)</td>
</tr>
</tbody>
</table>

*This peak was hidden by H₂O in DMSO-d₆*

---

**Example 53**  
N-Hydroxy-N-\{1-(3-methoxyphenylethyl)-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

![Chemical Structure](image)

**m. p.:** 126.0-126.7°C/dec.

**IR:** ν (KBr): 3500, 3450, 3200, 1670, 1640, 1615

**NMR:** δ (DMSO):

<table>
<thead>
<tr>
<th>Peak</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.13</td>
<td>(s, 1H)</td>
</tr>
<tr>
<td>7.25</td>
<td>(t, J = 7.7 Hz, 1H)</td>
</tr>
<tr>
<td>6.77-6.91</td>
<td>(m, 5H)</td>
</tr>
<tr>
<td>6.57</td>
<td>(d, J = 9.2 Hz, 1H)</td>
</tr>
<tr>
<td>6.20</td>
<td>(s, 2H)</td>
</tr>
<tr>
<td>5.03</td>
<td>(q, J = 6.5 Hz, 1H)</td>
</tr>
<tr>
<td>4.30</td>
<td>(s, 2H)</td>
</tr>
<tr>
<td>3.77</td>
<td>(s, 3H)</td>
</tr>
<tr>
<td>3.25-3.44</td>
<td><em>(2H)</em></td>
</tr>
<tr>
<td>2.67-2.71</td>
<td>(m, 2H)</td>
</tr>
<tr>
<td>1.68-1.91</td>
<td>(m, 2H)</td>
</tr>
<tr>
<td>1.48</td>
<td>(d, J = 6.5 Hz, 3H)</td>
</tr>
</tbody>
</table>

*This peak was hidden by H₂O in DMSO-d₆*
Example 54  
N-Hydroxy-N-\{1-(3-cyanobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

![Chemical Structure](Image)

**m. p.:** 140.2-141.6°C/dec.

**IR: v (KBr):** 3430, 3340, 2220, 1640

**NMR: δ (DMSO):**

9.14 (s, 1H), 7.71 (ddd, J= 7.7 Hz, 1.4 Hz, 1.4 Hz, 1H), 7.67 (s, 1H), 7.59 (ddd, J= 7.7 Hz, 1.4 Hz, 1.4 Hz, 1H), 7.53 (t, J= 7.7 Hz, 1H), 6.84 (d, J= 2.2 Hz, 1H), 6.80 (dd, J= 8.1 Hz, 2.2 Hz, 1H), 6.33 (d, J= 6.1 Hz, 1H), 6.21 (s, 2H), 4.52 (s, 2H), 4.29 (s, 2H), 3.24-3.43*2H), 2.66-2.78 (m, 2H), 1.87-1.98 (m, 2H)

*This peak was hidden by H2O in DMSO-d6

Example 55  
N-Hydroxy-N-\{1-(3-phenylpropyl)-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

![Chemical Structure](Image)

**m. p.:** 113.1-113.8°C/dec.

**IR: v (KBr):** 3500, 1635

**NMR: δ (DMSO):**

9.13 (s, 1H), 7.14-7.33 (m, 5H), 6.83 (dd, J= 8.2 Hz, 1.9 Hz, 1H), 6.78 (d, J= 1.9 Hz, 1H), 6.39 (d, J= 8.2 Hz, 1H), 6.20 (s, 2H), 4.29 (s, 2H), 3.15-3.28 (m, 4H), 2.56-2.69 (m, 4H), 1.71-1.90 (m, 4H)
Example

N-Hydroxy-N-\{1-(4-cyanobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

\[
\begin{align*}
\text{STRUCTURE:} \\
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{NH}_2 \\
\text{OH} \\
\end{array} \\
\text{-0.4H}_2\text{O}
\end{align*}
\]

\text{m. p.:} \\
141.7-143.2^\circ\text{C/dec.}

\text{IR: } \nu \text{ (KBr):} \\
3500, 2220, 1640

\text{NMR: } \delta \text{ (DMSO):} \\
9.16 \text{ (s, 1H), } 7.78 \text{ (d, } J = 8.4 \text{ Hz, 2H), } 7.43 \text{ (d, } J = 8.4 \text{ Hz, 2H), } 6.85 \text{ (d, } J = 1.8 \text{ Hz, 1H), } 6.78 \text{ (dd, } J = 8.4 \text{ Hz, 1.8 Hz, 1H), } 6.29 \text{ (d, } J = 8.4 \text{ Hz, 1H), } 6.21 \text{ (s, 2H), } 4.55 \text{ (s, 2H), } 4.29 \text{ (s, 2H), } 3.25-3.56* \text{(2H), } 2.72 \text{ (t, } J = 6.4 \text{ Hz, 2H), } 1.87-1.99 \text{ (m, 2H)}

*This peak was hidden by H\text{\textsubscript{2}}O in DMSO-\text{d\textsubscript{6}}

Example

N-Hydroxy-N-\{(1,2,3,4-tetrahydroquinolin-6-yl)methylurea

\[
\begin{align*}
\text{STRUCTURE:} \\
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{NH}_2 \\
\text{OH} \\
\end{array}
\end{align*}
\]

\text{m. p.:} \\
\sim 121.0-121.6^\circ\text{C/dec.}

\text{IR: } \nu \text{ (KBr):} \\
3490, 3390, 1640

\text{NMR: } \delta \text{ (DMSO):} \\
9.11 \text{ (s, 1H), } 6.73-6.79 \text{ (m, 2H), } 6.34 \text{ (d, } J = 8.8 \text{ Hz, 1H), } 6.19 \text{ (s, 2H), } 5.51 \text{ (s, 1H), } 4.27 \text{ (s, 2H), } 3.09-3.18 \text{ (m, 2H), } 2.62 \text{ (t, } J = 6.2 \text{ Hz, 2H), } 1.70-1.82 \text{ (m, 2H)}
<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-[1-(3-methoxycarbonylbenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td><img src="image1" alt="Structure" /></td>
</tr>
<tr>
<td>m. p.</td>
<td>146.5-147.3°C/dec.</td>
</tr>
<tr>
<td>IR: ν (KBr):</td>
<td>3490, 3390, 1720, 1710, 1650, 1630</td>
</tr>
<tr>
<td>NMR: δ (DMSO):</td>
<td></td>
</tr>
<tr>
<td>9.14 (s, 1H), 7.86 (s, 1H), 7.80-7.85 (m, 1H), 7.51-7.56 (m, 1H), 7.47 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 1.1 Hz, 1H), 6.79 (dd, J = 8.1 Hz, 1.1 Hz, 1H), 6.36 (d, J = 8.1 Hz, 1H), 6.20 (s, 2H), 4.53 (s, 2H), 4.29 (s, 2H), 3.83 (s, 3H), 3.26-3.40 (m, 2H), 2.68-2.78 (m, 2H), 1.87-1.98 (m, 2H)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-[1-{2-(3-methoxyphenyl)ethyl}-1,2,3,4-tetrahydroquinolin-6-yl]methylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>59</td>
<td><img src="image2" alt="Structure" /></td>
</tr>
<tr>
<td>m. p.</td>
<td>108.0-108.7°C/dec.</td>
</tr>
<tr>
<td>IR: ν (KBr):</td>
<td>3420, 3330, 1675, 1640, 1615</td>
</tr>
<tr>
<td>NMR: δ (DMSO):</td>
<td></td>
</tr>
<tr>
<td>9.15 (s, 1H), 7.21 (t, J = 8.1 Hz, 1H), 6.92 (dd, J = 8.4 Hz, 1.8 Hz, 1H), 6.80-6.86 (m, 3H), 6.77 (dd, J = 8.1 Hz, 2.2 Hz, 1H), 6.59 (d, J = 8.4 Hz, 1H), 6.21 (s, 2H), 4.32 (s, 2H), 3.74 (s, 3H), 3.37-3.48 (m, 2H), 3.14-3.22 (m, 2H), 2.70-2.79 (m, 2H), 2.63 (t, J = 6.2 Hz, 2H), 1.75-1.86 (m, 2H)</td>
<td></td>
</tr>
<tr>
<td>Example</td>
<td>N-Hydroxy-N-[1-(3-methoxymethylbenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methyleurea</td>
</tr>
<tr>
<td>---------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Structure:</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>m. p.</td>
<td>94.9-95.2°C/dec.</td>
</tr>
<tr>
<td>IR: ν (KBr):</td>
<td>3420, 1645</td>
</tr>
<tr>
<td>NMR: δ (DMSO):</td>
<td>9.13 (s, 1H), 7.29 (t, J= 7.5 Hz, 1H), 7.12-7.22 (m, 3H), 6.83 (d, J= 1.9 Hz, 1H), 6.79 (dd, J= 8.4 Hz, 1.9 Hz, 1H), 6.38 (d, J= 8.4 Hz, 1H), 6.20 (s, 2H), 4.45 (s, 2H), 4.38 (s, 2H), 4.29 (s, 2H), 3.28-3.39*(2H), 3.27 (s, 3H), 2.71 (t, J=6.4 Hz, 2H), 1.85-1.96 (m, 2H)</td>
</tr>
<tr>
<td>*This peak was hidden by H₂O in DMSO-d₆</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-[1-(2-cyanobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methyleurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure:</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>m. p.</td>
<td>140.3-140.6°C/dec.</td>
</tr>
<tr>
<td>IR: ν (KBr):</td>
<td>3400, 1675, 1640, 1615</td>
</tr>
<tr>
<td>NMR: δ (DMSO):</td>
<td>9.15 (s, 1H), 7.86 (d, J= 7.7 Hz, 1H), 7.64 (td, J= 7.7 Hz, 1.0 Hz, 1H), 7.44 (t, J= 7.7 Hz, 1H), 7.37 (d, J= 7.7 Hz, 1H), 6.87 (s, 1H), 6.80 (d, J= 8.5 Hz, 1H), 6.29 (d, J= 8.5 Hz, 1H), 6.21 (s, 2H), 4.63 (s, 2H), 4.30 (s, 2H), 3.24-3.43*(2H), 2.74 (t, J= 6.0 Hz, 2H), 1.87-2.00 (m, 2H)</td>
</tr>
<tr>
<td>*This peak was hidden by H₂O in DMSO-d₆</td>
<td></td>
</tr>
</tbody>
</table>
Example N-Hydroxy-N-[1-(3-carbamoylbenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea

**STRUCTURE:**

```
  N
 /|
/  \
O   
\   
\  
\ 
CONH₂
```

**m. p.:** 117.6-120.0°C/dec.

**IR: v (KBr):** 3490, 3330, 3180, 1670, 1620

**NMR: δ (DMSO):**
- 9.13 (s, 1H), 7.95 (s, 1H), 7.68-7.80 (m, 2H), 7.30-7.43 (m, 3H),
- 6.84 (d, J = 2.2 Hz, 1H), 6.79 (dd, J = 8.4 Hz, 2.2 Hz, 1H), 6.37 (d, J = 8.4 Hz, 1H),
- 6.20 (s, 2H), 4.49 (s, 2H), 4.29 (s, 2H), 3.26-3.44*(2H), 2.72 (t, J = 6.2 Hz, 2H),
- 1.87-1.98 (m, 2H)

*This peak was hidden by H₂O in DMSO-d₆*

Example N-(1-Phenyl-1,2,3,4-tetrahydroquinolin-6-yl)methyl-N-hydroxyurea

**STRUCTURE:**

```
  N
 /|
/  \
O   
\   
\  
\ 
CONH₂
```

**m. p.:** 89-90°C

**IR: v (KBr):** 3440, 1646, 1595, 1566, 1498, 1490 cm⁻¹

**NMR: δ (CDCl₃):**
- 7.06-7.38 (m, 5H), 7.04 (br s, 1H), 6.91 (dd, 1H, J = 8, 2Hz),
- 6.68 (d, 1H, J = 8Hz), 5.92 (br s, 1H), 5.20 (br s, 2H), 4.56 (s, 2H),
- 3.61 (t, 2H, J = 6Hz), 2.84 (t, 2H, J = 6Hz), 2.04 (quin, 2H, J = 6Hz)
Example 64  N-Hydroxy-N-(3-methoxy-1-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)methylurea

**STRUCTURE:**

![Chemical Structure Image]

**m. p.:** 132.1-132.5°C/dec.

**IR: v (KBr):** 3480, 1652

**NMR: δ (DMSO):**

9.22 (s, 1H), 7.35 (t, J = 7 Hz, 2H), 7.20 (d, J = 8 Hz, 2H), 7.06 (t, J = 7 Hz, 1H),
6.98 (s, 1H), 6.84 (d, J = 8 Hz, 1H), 6.60 (d, J = 8 Hz, 1H), 6.25 (s, 2H),
4.36 (s, 2H), 3.76-3.85 (m, 1H), 3.70 (dd, J = 9 Hz, 1Hz, 1H),
3.51 (dd, J = 13 Hz, 6 Hz, 1H), 3.26 (s, 3H), 3.04 (dd, J = 16 Hz, 4 Hz, 1H),
2.75 (dd, J = 16 Hz, 6 Hz, 1H)

Example 65  N-Hydroxy-N-(3-allyloxy-1-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)methylurea

**STRUCTURE:**

![Chemical Structure Image]

**m. p.:** (amorphous solid)

**IR: v (KBr):** 3500, 1650

**NMR: δ (DMSO):**

9.23 (s, 1H), 7.34 (t, J = 7.3 Hz, 2H), 7.19 (d, J = 7.3 Hz, 2H),
7.06 (t, J = 7.0 Hz, 1H), 6.99 (s, 1H), 6.84 (d, J = 8.4 Hz, 1H),
6.61 (d, J = 8.4 Hz, 1H), 6.26 (s, 2H), 5.84 (ddt, J = 15.4 Hz, 10.3 Hz, 5.1 Hz, 1H),
5.19 (dt, J = 15.4 Hz, 1.5 Hz, 1.5 Hz, 1H), 5.08 (d, J = 10.3 Hz, 1H), 4.36 (s, 2H),
3.87-4.07 (m, 3H), 3.71 (dd, J = 13 Hz, 4 Hz, 1H), 3.52 (dd, J = 13 Hz, 6 Hz, 1H),
3.05 (dd, J = 15 Hz, 4 Hz, 1H), 2.76 (dd, J = 15 Hz, 6 Hz, 1H)
<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-[(7-methoxy-1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td><strong>STRUCTURE:</strong></td>
</tr>
<tr>
<td></td>
<td>![Structure Diagram]</td>
</tr>
<tr>
<td></td>
<td><strong>m. p.:</strong> 124.2-126.8°C/dec.</td>
</tr>
<tr>
<td></td>
<td><strong>IR: v (KBr):</strong> 3500, 1640, 1620</td>
</tr>
<tr>
<td></td>
<td><strong>NMR: δ (DMSO):</strong></td>
</tr>
<tr>
<td></td>
<td>9.11 (s, 1H), 7.24 (t, J = 8.6 Hz, 1H), 6.74-6.89 (m, 4H), 6.20 (s, 2H), 6.09 (s, 1H), 4.46 (s, 2H), 4.34 (s, 2H), 3.72 (s, 3H), 3.53 (s, 3H), 3.27-3.35 (m, 2H), 2.62 (t, J = 2.6 Hz, 2H), 1.82-1.94 (m, 2H)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-[(7-chloro-1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td><strong>STRUCTURE:</strong></td>
</tr>
<tr>
<td></td>
<td>![Structure Diagram]</td>
</tr>
<tr>
<td></td>
<td><strong>m. p.:</strong> 157.0-158.1°C/dec.</td>
</tr>
<tr>
<td></td>
<td><strong>IR: v (KBr):</strong> 3500, 1650, 1610</td>
</tr>
<tr>
<td></td>
<td><strong>NMR: δ (DMSO):</strong></td>
</tr>
<tr>
<td></td>
<td>9.27 (s, 1H), 7.25 (t, J = 8.1 Hz, 1H), 6.93 (s, 1H), 6.76-6.84 (m, 3H), 6.38 (s, 1H), 6.32 (s, 2H), 4.45 (s, 2H), 4.44 (s, 2H), 3.72 (s, 3H), 3.25-3.41*(2H), 2.69 (t, J = 6.2 Hz, 2H), 1.84-1.96 (m, 2H)</td>
</tr>
<tr>
<td></td>
<td><strong>(This peak was hidden by H₂O in DMSO-d₆)</strong></td>
</tr>
</tbody>
</table>
Example 68  
N-Hydroxy-N-[1-(3-difluoromethoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methyl-N'-ethyleurea

**STRUCTURE:**

![Structure Diagram]

**m. p.:** 113.9-114.2°C/dec.

**IR: v (KBr):** 3450, 1635

**NMR: δ (DMSO):**

9.05 (s, 1H), 7.37 (t, J= 8.1 Hz, 1H), 7.21 (t, J= 74.2 Hz, 1H), 7.11 (d, J= 8.1 Hz, 1H), 7.00-7.06 (m, 2H), 6.76-6.85 (m, 3H), 6.36 (d, J= 8.4 Hz, 1H), 4.47 (s, 2H), 4.28 (s, 2H), 3.27-3.39*(2H), 3.06 (quint, J= 6.3 Hz, 2H), 2.67-2.77 (m, 2H), 1.86-1.97 (m, 2H), 0.99 (t, J= 7.1Hz, 3H)  
*This peak was hidden by H₂O in DMSO-d₆

Example 69  
N-Hydroxy-N-[1-(3-difluoromethoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea

**STRUCTURE:**

![Structure Diagram]

**m. p.:** 115.3-115.6°C/dec.

**IR: v (KBr):** 3410, 3330, 1675, 1640, 1620

**NMR: δ (DMSO):**

9.14 (s, 1H), 7.37 (t, J= 8.4 Hz, 1H), 7.21 (t, J= 74.2 Hz, 1H), 7.11 (d, J= 7.7 Hz, 1H), 7.00-7.06 (m, 2H), 6.84 (d, J= 2.2 Hz, 1H), 6.80 (dd, J= 8.4 Hz, 2.2 Hz, 1H), 6.36 (d, J= 8.4 Hz, 1H), 6.21 (s, 2H), 4.47 (s, 2H), 4.29 (s, 2H), 3.28-3.39*(2H), 2.71 (t, J= 6.0 Hz, 2H), 1.85-1.98 (m, 2H)  
*This peak was hidden by H₂O in DMSO-d₆
Example N-(1-(4-Chlorobenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methyl- 
N-hydroxyurea

**STRUCTURE:**

mp: 145-146 °C (dec)

IR (KBr) cm⁻¹: 3400, 1644, 1552, 1508 cm⁻¹

NMR (CDCl₃) δ: 7.28 (d, 2H, J = 1.5Hz), 7.18 (d, 2H, J = 1.5Hz), 6.94-7.00 (m, 2H), 
6.40 (d, 1H, J = 8Hz), 5.53 (br s, 1H), 5.17 (br s, 2H), 4.54 (s, 2H), 
4.42 (s, 2H), 3.35 (t, 2H, J = 6Hz), 2.80 (t, 2H, J = 6Hz), 
2.03 (quin, 2H, J = 6Hz)

Example N-(1-(4-Methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methyl- 
N-hydroxyurea

**STRUCTURE:**

mp: 140-143 °C (dec)

IR (KBr) cm⁻¹: 3515, 3390, 1647, 1615, 1554, 1512, 1458, 1250 cm⁻¹

NMR (DMSO) δ: 9.13 (br s, 1H), 7.17 (d, 2H, J = 1.5Hz), 6.87 (d, 2H, J = 1.5Hz), 
6.78-6.84 (m, 2H), 6.42 (d, 1H, J = 8Hz), 4.38 (s, 2H), 4.29 (s, 2H), 
3.31 (s, 3H), 3.30 (br s, 2H), 2.69 (t, 2H, J = 6Hz), 
1.89 (quin, 2H, J = 6Hz)
Example N-Hydroxy-N-[(3-trifluoromethylbenzyl)-8-fluoro-1,2,3,4-tetrahydroquinolin-6-yl]methyleurea

**STRUCTURE:**

```
\[
\text{\begin{center}
\includegraphics[width=0.3\textwidth]{structure1.png}
\end{center}}
\]
```

**m. p.:** 148.5-149.5°C

**IR: v (KBr):** 3500, 1645, 1625, 1325, 1130 cm⁻¹

**NMR: δ (DMSO):**

9.31 (s, 1H), 7.56-7.72 (m, 4H), 6.83 (dd, 1H, J=13.9, 1.8Hz), 6.78 (br, 1H), 6.33 (s, 2H), 4.38 (s, 2H), 4.34 (s, 2H), 2.93-3.01 (m, 2H), 2.72 (t, 2H, J=6.2Hz), 1.74-1.83 (br, 2H)

Example N-Hydroxy-N-[(3-difluoromethoxybenzyl)-8-fluoro-1,2,3,4-tetrahydroquinolin-6-yl]methyleurea

**STRUCTURE:**

```
\[
\text{\begin{center}
\includegraphics[width=0.3\textwidth]{structure2.png}
\end{center}}
```

**m. p.:** 109-110°C

**IR: v (KBr):** 3495, 1645, 1625, 1115 cm⁻¹

**NMR: δ (DMSO):**

9.31 (s, 1H), 7.40 (dd, 1H, J=7.9, 7.9Hz), 7.22-7.26 (m, 1H), 7.22 (t, 1H, J=74.2Hz), 7.17 (br, 1H), 7.05-7.09 (m, 1H), 6.77-6.85 (m, 2H), 6.33 (s, 2H), 4.38 (s, 2H), 4.28 (s, 2H), 2.98-3.02 (2H), 2.70 (t, 2H, J=6.2Hz), 1.77 (br, 2H)
Example 74  
N-Hydroxy-N-[3-{1-(3-methoxybenzyl)-1,2,3,4-tetrahydro-quinolin-6-yl}propyl]urea

[Chemical Structure Image]

m.p.: 95-96°C

IR: ν (KBr): 3465, 1630, 1515 cm⁻¹

NMR: δ (DMSO):
9.19 (s, 1H), 7.19-7.25 (m, 1H), 6.68-6.83 (m, 5H), 6.35 (d, 1H, J=8.0Hz)
6.22 (s, 2H), 4.40 (s, 2H), 3.71 (s, 3H), 3.26-3.32 (4H), 2.70 (t, 2H, J=6.4Hz), 2.36 (t, 2H, J=7.5Hz), 1.88-1.93 (m, 2H), 1.65-1.71 (m, 2H)

Example 75  
N-Hydroxy-N-{1-(3-cyanobenzyl)-8-fluoro-1,2,3,4-tetrahydro-quinolin-6-yl}methylurea

[Chemical Structure Image]

m.p.: 141-142°C

IR: ν (KBr): 3500, 2230, 1640, 1630, 1495 cm⁻¹

NMR: δ (DMSO):
9.32 (s, 1H) 7.71-7.79 (m, 3H), 7.57 (dd, 1H, J=7.7, 7.7Hz), 6.77-6.85 (m, 2H), 6.33 (s, 2H), 4.38 (s, 2H) 4.31 (s, 2H), 3.00 (t, 2H, J=5.3Hz), 2.71 (t, 2H, J=6.2Hz), 1.72 -1.85 (m, 2H)
Example N-Hydroxy-N-\{1-cyclohexylmethyl-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

```
\begin{align*}
\text{N}-\text{H} \quad \text{O} \\
\text{N} \quad \text{NH}_2
\end{align*}
```

m. p.: 111-112°C

IR: ν (KBr): 3490, 2925, 1640, 1515 cm⁻¹

NMR: δ (DMSO): 9.13 (s, 1H), 6.85(dd, 1H, J=8.4, 2.2Hz), 6.78 (d, 1H, J=2.2Hz), 6.40 (d, 1H, J=8.4Hz), 6.20 (s, 2H), 4.29 (s, 2H), 3.24 (t, 2H, J=5.5Hz), 3.00 (d, 2H, J=6.6Hz), 2.64 (t, 2H, J=6.2Hz), 1.66-1.83 (m, 8H), 1.10-1.25 (m, 3H), 0.85-0.95 (m, 2H)

Example N-Hydroxy-N-\{1-(pyridin-3-yl)methyl-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

```
\begin{align*}
\text{N} \quad \text{O} \\
\text{N} \quad \text{NH}_2
\end{align*}
```

m. p.: 62-68°C (amorphous)

IR: ν (KBr): 3490, 1655, 1650, 1515, 785 cm⁻¹

NMR: δ (DMSO): 9.15 (s, 1H), 8.48 (d, 1H, J=1.8Hz), 8.44 (dd, 1H, J=4.8, 1.5Hz), 7.63 (ddd, 1H, J=7.7, 1.8, 1.5Hz), 7.33 (dd, 1H, J=7.7, 4.8Hz), 6.79-6.84 (m, 2H), 6.43 (d, 1H, J=8.4Hz), 6.21 (s, 2H), 4.51 (s, 2H), 4.29 (s, 2H), 3.30-3.37 (2H), 2.71 (t, 2H, J=6.2Hz), 1.87-1.96 (m, 2H)
**Example** N-Hydroxy-N-\{1-(3-methoxybenzyl)-7-methyl-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

![Chemical Structure](image)

m. p.: 142-143°C

**IR:** ν (KBr): 3500, 1635, 1516, 1484, 1337 cm⁻¹

**NMR:** δ (DMSO): 9.11 (s, 1H), 7.20-7.26 (m, 1H), 6.78-6.83 (m, 4H), 6.28 (s, 1H), 6.20 (s, 2H), 4.42 (s, 2H), 4.33 (s, 2H), 3.72 (s, 3H), 3.29-3.33 (2H), 2.66 (m, 2H), 2.08 (s, 3H), 1.86-1.90 (br, 2H)

**Example** N-Hydroxy-N-\{1-(3-methoxybenzyl)-5-methyl-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

**STRUCTURE:**

![Chemical Structure](image)

m. p.: 123.5-125°C

**IR:** ν (KBr): 3490, 1640, 1575, 1455 cm⁻¹

**NMR:** δ (DMSO): 9.02 (s, 1H), 7.19-7.25 (m, 1H), 6.75-6.83 (m, 4H), 6.28 (d, 1H, J=8.4Hz), 6.18 (s, 2H), 4.41 (s, 2H), 4.37 (s, 2H), 3.71 (s, 3H), 3.27-3.31 (2H), 2.61-2.66 (m, 2H), 2.10 (s, 3H), 1.92-1.96 (br, 2H).
Example N-Hydroxy-N-{1-(3-methoxybenzyl)-8-methyl-1,2,3,4-tetrahydroqui-nolin-6-yl}methylurea

**STRUCTURE:**

![Chemical Structure](image)

m. p.: 138-139°C

IR: v (KBr): 3505, 3390, 1660, 1600, 1260 cm⁻¹

NMR: δ (DMSO):

9.24 (s, 1H), 7.29 (dd, 1H, J=7.9, 7.9Hz), 7.05-7.08 (m, 2H), 6.82-6.89 (m, 3H), 6.28 (s, 2H), 4.38 (s, 2H), 3.94 (s, 2H), 3.76 (s, 3H), 2.84-2.87 (m, 2H), 2.70-2.75 (m, 2H), 2.22 (s, 3H), 1.7-1.76 (br, 2H).

---

Example N-Hydroxy-N-{1-(3-methoxybenzyl)-7-fluoro-1,2,3,4-tetrahydroqui-nolin-6-yl}methylurea

**STRUCTURE:**

![Chemical Structure](image)

m. p.: 150-151°C

IR: v (KBr): 3490, 3200, 1645, 1520, 1280 cm⁻¹

NMR: δ (DMSO):

9.20 (s, 1H), 7.21-7.27 (m, 1H), 6.88 (d, 1H, J=8.8Hz), 6.79-6.81 (m, 3H), 6.26 (s, 2H), 6.15 (d, 1H, J=13.6Hz), 4.44 (s, 2H), 4.35 (s, 2H), 3.72 (s, 3H), 3.29-3.37 (2H), 2.65-2.69 (m, 2H), 1.87-1.92 (m, 2H).
Example 82  N-Hydroxy-N-\{1-(3-methoxybenzyl)-8-fluoro-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

STRUCTURE:

\[\text{Chemical Structure Image}\]

m. p.: 141-142°C

IR: \(v\) (KBr): 3505, 3390, 1660, 1494, 1260 cm\(^{-1}\)

NMR: \(\delta\) (DMSO):

- 9.30 (s, 1H), 7.25 (dd, 1H, J=8.1, 7.7Hz), 6.90-6.94 (m, 2H), 6.76-6.84 (m, 3H), 6.32 (s, 2H), 4.37 (s, 2H), 4.25 (s, 2H), 3.73 (s, 3H), 2.98-3.02 (m, 2H), 2.66-2.71 (m, 2H), 1.73-1.77 (m, 2H).

Example 83  N-Hydroxy-N-\{1-(3-methoxybenzyl)-8-chloro-1,2,3,4-tetrahydroquinolin-6-yl\}methylurea

STRUCTURE:

\[\text{Chemical Structure Image}\]

m. p.: 95-97°C (amorphous)

IR: \(v\) (KBr): 3490, 1650, 1470 cm\(^{-1}\)

NMR: \(\delta\) (DMSO):

- 9.36 (s, 1H), 7.28 (dd, 1H, J= 8.1, 7.7 Hz), 7.08-7.15 (m, 3H), 6.96 (d, 1H, J= 1.8Hz), 6.85 (dd, 1H, J=8.1, 1.8Hz), 6.36 (s, 2H), 4.41 (s, 2H), 4.11 (s, 2H), 3.75 (s, 3H), 2.82-2.86 (m, 2H), 2.76 (t, 2H, J=6.6Hz), 1.73-1.77 (br, 2H)
Example N-Hydroxy-N-(1-(thiophen-2-yl)methyl-1,2,3,4-tetrahydroquinolin-6-yl)methylurea

**STRUCTURE:**

m. p.: 135-136°C (dec.)

IR: v (KBr): 3470, 1625, 1515 cm⁻¹

NMR: δ (DMSO): 9.16 (s, 1H), 7.35 (dd, 1H, J=4.8, 1.5Hz), 7.01 (br, 1H), 6.96 (dd, 1H, J=4.8, 3.7Hz), 6.82-6.87 (m, 2H), 6.64, (d, 1H, J=8.4Hz), 6.21 (s, 2H), 4.62 (s, 2H), 4.30 (s, 2H), 3.28-3.32 (2H), 2.66 (t, 2H, J=6.7Hz), 1.85-1.90 (br, 2H).

Example N-Hydroxy-N-(1-(3-methoxybenzyl)-5-fluoro-1,2,3,4-tetrahydroquinolin-6-yl)methylurea

**STRUCTURE:**

m. p.: 141-142°C

IR: v (KBr): 3460, 1645, 1635, 1435 cm⁻¹

NMR: δ (DMSO): 9.19 (s, 1H), 7.20-7.26 (m, 1H), 6.87 (dd, 1H, J=8.6, 8.6Hz), 6.78-6.82 (m, 3H), 6.27 (d, 1H, J=8.6Hz), 6.24 (s, 2H), 4.45 (s, 2H), 4.38 (s, 2H), 3.71 (s, 3H), 3.29-3.34 (2H), 2.67 (t, 2H, J=6.2Hz), 1.88-1.93 (m, 2H)
Example 66  
**N-Hydroxy-N-(2-(trans-indan-1-ylidene)ethyl)urea**

**STRUCTURE:**

![Structure of N-Hydroxy-N-(2-(trans-indan-1-ylidene)ethyl)urea](image)

**m. p.:** 134-136°C

**IR: v:** (nujol) 1615, 1570, 1170, 1130, 860

**NMR: 8**

(CDCl₃-DMSO-d₆): 9.17 (s, 1H), 7.46 (m, 1H), 7.23 (m, 1H), 7.18 (m, 2H), 6.09 (m, 1H), 5.49 (s, 2H), 4.29 (d, J=7.3Hz, 2H), 2.99 (t, J=5.1Hz, 2H), 2.85 (d, J=5.1Hz, 2H)

---

Example 87  
**N-Hydroxy-N-(5-phenoxyindan-1-yl)urea**

**STRUCTURE:**

![Structure of N-Hydroxy-N-(5-phenoxyindan-1-yl)urea](image)

**mp:** 163.1 - 164.0 °C

**IR: v (KBr):** 3450, 3300, 1680, 1655, 1485, 1245 cm⁻¹

**NMR: 5 (DMSO-d₆):** 8.98 (s, 1H), 7.37 (t, J = 8 Hz, 2H), 7.13 (t, J = 8 Hz, 1H), 7.11 (t, J = 8 Hz, 1H), 6.97 (d, J = 8 Hz, 2H), 6.82 (s, 1H), 6.81 (d, J = 8 Hz, 1H), 6.84 (s, 2H), 5.64 (t, J = 7 Hz, 1H), 2.95 - 2.85 (m, 1H), 2.76 - 2.65 (m, 1H), 2.25 - 2.05 (m, 2H)
### Example 88

**N-Hydroxy-N-(6-phenoxyindan-1-yl)urea**

**Structure:**

![Structure](image)

**mp:** 146.5 - 147.7 °C

**IR:** ν (KBr): 3495, 3320, 1650, 1630, 1485, 1240, 690 cm\(^{-1}\)

**NMR:** δ (DMSO-d\(_6\)): 9.01 (s, 1H), 7.33 (t, J = 8 Hz, 2H), 7.21 (t, J = 8 Hz, 1H), 7.09 (t, J = 8 Hz, 1H), 6.94 (d, J = 8 Hz, 2H), 6.86 (dd, J = 8 and 2 Hz, 1H), 6.78 (d, J = 2 Hz, 1H), 6.43 (s, 2H), 5.71 (t, J = 8 Hz, 1H), 2.95 - 2.84 (m, 1H), 2.82 - 2.68 (m, 1H), 2.25 - 2.05 (m, 2H)

### Example 89

**N-Hydroxy-N-(7-phenoxyindan-1-yl)urea**

**Structure:**

![Structure](image)

**mp:** 157.6 - 158.8 °C

**IR:** ν (KBr): 3500, 3350, 3190, 1645, 1585, 1465, 1250, 765, 695 cm\(^{-1}\)

**NMR:** δ (DMSO-d\(_6\)): 8.87 (s, 1H), 7.35 (dt, J = 8 and 2 Hz, 2H), 7.17 (t, J = 8 Hz, 1H), 7.1 (t, J = 8 Hz, 1H), 7.01 (dd, J = 8 and 2 Hz, 2H), 6.98 (t, J = 7 Hz, 1H), 6.53 (d, J = 8 Hz, 1H), 6.14 (s, 2H), 5.82 (dd, J = 8 and 2 Hz, 1H), 3.1 - 2.95 (m, 1H), 2.85 - 2.7 (m, 1H), 2.3 - 2.15 (m, 1H), 2.08 - 1.96 (m, 1H)
Example 90  N-Hydroxy-N-(4-phenoxyindan-1-yl)urea

 STRUCTURE:

 mp: 166.6 - 168.1 °C

 IR: ν (KBr): 3480, 3330, 3200, 1660, 1570, 1470, 1245, 780, 745 cm⁻¹

 NMR: δ (DMSO-d₆): 9.0 (s, 1H), 7.38 (t, J = 8 Hz, 2H), 7.19 (t, J = 8 Hz, 1H), 7.07 (t, J = 8 Hz, 1H), 6.97 (t, J = 8 Hz, 1H), 6.86 (d, J = 8 Hz, 2H), 6.79 (d, J = 8 Hz, 1H), 6.41 (s, 2H), 5.64 (t, J = 7 Hz, 1H), 2.85 - 2.72 (m, 1H), 2.65 - 2.5 (m, 1H), 2.25 - 2.05 (m, 2H)

Example 91  N-Hydroxy-N-[4-[(3,4-dihydro-2H-benzopyran)6-yl]3-buten-2-yl]urea

 STRUCTURE:

 m. p.: 138-140°C

 IR: ν (nujol) 3440, 1640, 1250, 1060, 970, 815 cm⁻¹

 NMR: δ (DMSO-d₆); 9.67 (s, 1H), 7.76 (m, 2H), 7.34 (d, J=8.8Hz, 1H), 7.02 (d, J=15.1Hz, 1H), 6.99 (s, 2H), 6.78 (d d, J=6.6Hz, 1H), 5.45 (m, 1H), 4.79 (t, J=6.2Hz, 2H), 3.40 (t, J=6.2Hz, 2H), 2.57 (m, 2H), 1.88 (d, J=7.0Hz, 3H)
Example N-Hydroxy-N-\{(5-(3-methoxyphenoxy)indan-1-yl)urea

**STRUCTURE:**

\[
\begin{array}{c}
\text{OCH}_3 \\
\text{O} \\
\text{N} \\
\text{NH}_2
\end{array}
\]

**m.p.:** 143.1-144.6°C

**IR:** ν (KBr): 3450, 3300, 3200, 2900, 1660, 1580, 1360, 1340, 1250, 870 cm⁻¹

**NMR:** δ (DMSO-d₆):

8.97(s, 1H), 7.26(t, J=8.43Hz, 1H), 7.14(d, J=8.43Hz, 1H), 6.83(br.s, 1H), 6.82(d, J=6.60Hz, 1H), 6.68(d, J=9.16Hz, 1H), 6.52(m, 2H), 6.40(br.s, 2H), 5.64(t, J=7.33Hz, 1H), 3.73(s, 3H), 2.87(m, 1H), 2.74(m, 1H), 2.16(m, 2H)

---

Example N-Hydroxy-N-\{(5-(3-fluorophenoxy)indan-1-yl)urea

**STRUCTURE:**

\[
\begin{array}{c}
\text{F} \\
\text{O} \\
\text{N} \\
\text{NH}_2
\end{array}
\]

**m.p.:** 150.2-153.2°C

**IR:** ν (KBr): 3450, 3000-3400, 1680, 1610, 1580, 1480, 1260, 1140, 960 cm⁻¹

**NMR:** δ (DMSO-d₆):

8.99(s, 1H), 7.39(m, 1H), 7.18(d, J=8.06Hz, 1H), 6.87(m, 5H), 6.41(br.s, 2H), 5.65(t, J=7.33Hz, 1H), 2.87(m, 1H), 2.74(m, 1H), 2.17(m, 2H)
Example N-Hydroxy-N-(5-(4-phenylphenoxy)inden-1-yl)urea

**Structure:**

![Chemical Structure](image)

- m. p.: 167.9-169.2°C
- IR: ν (KBr): 3500, 3300, 2900, 1630, 1550, 1490, 1250, 1010, 980, 690 cm⁻¹
- NMR: δ (DMSO-d₆):
  - 9.00(s, 1H), 7.65(m, 4H), 7.45(m, 2H), 7.34(m, 1H)
  - 7.18(d, J=8.42Hz, 1H), 7.05(m, 2H), 6.87(m, 2H), 6.42(br.s, 2H)
  - 5.66(t, J=7.36Hz, 1H), 2.91(m, 1H), 2.76(m, 1H), 2.17(m, 2H)

Example N-Hydroxy-N-(5-(3,4-dimethylenedioxyphenoxy)inden-1-yl)urea

**Structure:**

![Chemical Structure](image)

- m. p.: 173.2-174.0°C
- IR: ν (KBr): 3450, 3200, 2900, 1650, 1570, 1480, 1240, 1040, 920 cm⁻¹
- NMR: δ (DMSO-d₆):
  - 8.95(s, 1H), 7.11(m, 1H), 6.89(d, J=8.42Hz, 1H), 6.76(m, 2H)
  - 6.68(d, J=2.56Hz, 1H), 6.45(dd, J=2.20, 8.06Hz, 1H), 6.38(br.s, 2H)
  - 6.03(br.s, 2H), 5.62(t, J=6.96Hz, 1H), 2.87(m, 1H), 2.72(m, 1H)
  - 2.13(m, 2H)
Example N-Hydroxy-N-[5-(4-fluorophenoxy)indan-1-yl]urea

**STRUCTURE:**

![Chemical Structure](image)

**m. p.:** 175.2-176.6°C

**IR:** ν (KBr): 3460, 3250, 2950, 1650, 1580, 1500, 1430, 1320, 1200 cm⁻¹

**NMR:** δ (DMSO-d₆):

<table>
<thead>
<tr>
<th>Chemical Shift</th>
<th>Multiplicity</th>
<th>J (Hz)</th>
<th>Coupled Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.97(s, 1H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.18(m, 3H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.02(m, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.79(m, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.39(br.s, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.39(t, J=7.32Hz, 1H)</td>
<td>2.87(m, 1H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.72(m, 1H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.15(m, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Example N-Hydroxy-N-[5-(3-fluoro-4-methoxyphenoxy)indan-1-yl]urea

**STRUCTURE:**

![Chemical Structure](image)

**m. p.:** 166.3-167.5°C

**IR:** ν (KBr): 3200-3500, 2950, 1660, 1510, 1490, 1440, 1260, 1150, 970 cm⁻¹

**NMR:** δ (DMSO-d₆):

<table>
<thead>
<tr>
<th>Chemical Shift</th>
<th>Multiplicity</th>
<th>J (Hz)</th>
<th>Coupled Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.97(s, 1H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.14(m, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.97(dd, J=2.57, 12.09Hz, 1H)</td>
<td>6.79(m, 3H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.39(br.s, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.62(t, J=7.33Hz, 1H)</td>
<td>3.81(s, 3H)</td>
<td>2.86(m, 1H)</td>
<td></td>
</tr>
<tr>
<td>2.73(m, 1H)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.14(m, 2H)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Example \textit{N}-Hydroxy-\textit{N}-(5-(3-trifluoromethylphenoxy)indan-1-yl)urea

\textbf{STRUCTURE:}

\begin{center}
\includegraphics[width=0.5\textwidth]{structure1.png}
\end{center}

\textbf{m. p.:} 164.0-165.1°C

\textbf{IR: \textit{v} (KBr):} 3450, 3300, 2900, 1650, 1630, 1320, 800 cm\(^{-1}\)

\textbf{NMR: \textit{\delta} (DMSO-d\(_6\)):}

\begin{itemize}
\item 9.00 (s, 1H), 7.60(t, J=7.70Hz, 1H), 7.46(d, J=7.70Hz, 1H),
\item 7.23(m, 3H), 6.90(m, 2H), 6.42(s, 2H), 5.66(t, J=7.33Hz, 1H),
\item 2.89(m, 1H), 2.76(m, 1H), 2.18(m, 2H)
\end{itemize}

---

Example \textit{N}-Hydroxy-\textit{N}-(5-(3-methylphenoxy)indan-1-yl)urea

\textbf{STRUCTURE:}

\begin{center}
\includegraphics[width=0.5\textwidth]{structure2.png}
\end{center}

\textbf{m. p.:} 163.9-165.4°C

\textbf{IR: \textit{v} (KBr):} 3450, 3000-3400, 2850, 1660, 1570, 1480, 1260, 1150, 950 cm\(^{-1}\)

\textbf{NMR: \textit{\delta} (DMSO-d\(_6\)):}

\begin{itemize}
\item 8.97(s, 1H), 7.24(t, J=7.70Hz, 1H), 7.14(d, J=8.79Hz, 1H),
\item 6.93(d, J=7.32Hz, 1H), 6.78(m, 4H), 6.40(br.s, 2H),
\item 5.64(t, J=8.06Hz, 1H), 2.88(m, 1H), 2.73(m, 1H), 2.28(s, 3H),
\item 2.14(m, 2H)
\end{itemize}
Example N-Hydroxy-N-\{(5-(4-methoxyphenoxy)indan-1-yl)urea

**STRUCTURE:**

![Structure Image]

**m.p.: 159.0-160.2°C**

**IR: ν (KBr): 3450, 3300, 2800-3000, 1670, 1650, 1580, 1500, 1240, 1030, 920, 910 cm\(^{-1}\)**

**NMR: \(δ\) (DMSO-\(d_6\)):**

- 8.94(s, 1H), 7.10(d, \(J=7.70\)Hz, 1H), 6.95(m, 4H), 6.71(m, 2H),
- 6.38(br.s, 2H), 5.61(t, \(J=6.96\)Hz, 1H), 3.74(s, 3H),
- 2.86(m, 1H), 2.71(m, 1H), 2.13(m, 2H)

---

Example N-Hydroxy-N-\{(5-(3-fluoro-4-methylphenoxy)indan-1-yl)urea

**STRUCTURE:**

![Structure Image]

**m.p.: 156.1-157.5°C**

**IR: ν (KBr): 3450, 3200, 2950, 1660, 1580, 1450, 1280, 1150, 1100, 960, 910 cm\(^{-1}\)**

**NMR: \(δ\) (DMSO-\(d_6\)):**

- 8.97(s, 1H), 7.26(t, \(J=8.79\)Hz, 1H), 7.15(d, \(J=8.79\)Hz, 1H),
- 6.77(m, 4H), 6.40(br.s, 2H), 5.64(t, \(J=6.96\)Hz, 1H),
- 2.87(m, 1H), 2.74(m, 1H), 2.16(m, 2H)
Example N-Hydroxy-N-\{5-(3,4-difluorophenoxy)indan-1-yl\}urea

**STRUCTURE:**

\[
\begin{align*}
\text{F} & \quad \text{O} \\
\text{F} & \quad \text{N} & \quad \text{NH}_2 \\
\text{OH} & \\
\end{align*}
\]

**m. p.:** 167.9-169.1°C

**IR:** \(v\) (KBr): 3450, 3250, 1660, 1520, 1490, 1420, 1250, 1150, 960, 940 cm\(^{-1}\)

**NMR:** \(\delta\) (DMSO-\(d_6\)):

8.99(s, 1H), 7.43(m, 1H), 7.14(m, 2H), 6.83(m, 3H), 6.41(br.s, 2H), 5.64(t, 7.33Hz, 1H), 2.88(m, 1H), 2.75(m, 1H), 2.16(m, 2H)

Example N-Hydroxy-N-(5-cinnamoyloxyindan-1-yl)urea

**STRUCTURE:**

\[
\begin{align*}
\text{C} & \quad \text{O} \\
\text{N} & \quad \text{NH}_2 \\
\text{OH} & \\
\end{align*}
\]

**m. p.:** 170.0-171.3°C

**IR:** \(v\) (KBr): 3450, 3200, 2850, 1680, 1580, 1500, 1460, 1250, 1150, 970 cm\(^{-1}\)

**NMR:** \(\delta\) (DMSO-\(d_6\)):

8.90(bs, 1H), 7.50(m, 2H), 7.36(m, 3H), 7.06(d, J=8.43Hz, 1H), 6.77(m, 3H), 6.65(m, 1H), 6.35(br.s, 2H), 5.59(t, J=6.59Hz, 1H), 4.69(d, J=5.86Hz, 2H), 2.89(m, 1H), 2.73(m, 1H), 2.14(m, 2H)
Example N-Hydroxy-N-[5-(5-trifluoromethyl-2-pyridyloxy)indan-1-yl]urea

104

STRUCTURE:

\[
\begin{array}{c}
\text{CF}_3 \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{NH}_2 \\
\text{OH}
\end{array}
\]

m. p. : 155.0-156.3°C

IR: \( \nu \) (KBr): 3450, 3200, 2900, 1670, 1610, 1580, 1490, 1420, 1390, 1130, 1080, 940 cm\(^{-1}\)

NMR: \( \delta \) (DMSO-d\(_6\)):

\[
\begin{align*}
9.05 & (s, 1H), \quad 8.55 & (m, 1H), \quad 8.20 & (dd, J=2.56, 8.06Hz, 1H), \\
7.20 & (d, J=8.43Hz, 2H), \quad 6.98 & (m, 2H), \quad 6.43 & (br.s, 2H), \\
5.67 & (t, J=7.33Hz, 1H), \quad 2.90 & (m, 1H), \quad 2.76 & (m, 1H), \quad 2.14 & (m, 2H)
\end{align*}
\]

Example N-Hydroxy-N-[5-(3-chloro-2-pyridyloxy)indan-1-yl]urea

105

STRUCTURE:

\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{Cl} \\
\text{N} \\
\text{NH}_2 \\
\text{OH}
\end{array}
\]

m. p. : 169.3-170.4°C

IR: \( \nu \) (KBr): 3450, 3350, 2900, 1630, 1580, 1420, 1250, 1130, 1040, 940 cm\(^{-1}\)

NMR: \( \delta \) (DMSO-d\(_6\)):

\[
\begin{align*}
9.50 & (s, 1H), \quad 8.05 & (m, 2H), \quad 7.16 & (m, 2H), \quad 6.94 & (m, 2H), \\
6.42 & (br.s, 2H), \quad 5.67 & (t, J=7.32Hz, 1H), \quad 2.89 & (m, 1H), \\
2.77 & (m, 1H), \quad 2.17 & (m, 2H)
\end{align*}
\]
Example 106

N-Hydroxy-N\{5-(4-chlorophenoxy)indan-1-yl\}urea

STRUCTURE:

\[ \text{Structure Image} \]

m. p.: 178.2-179.0°C

IR: ν (KBr): 3470, 3270, 1660, 1580, 1485, 1420, 1250 cm\(^{-1}\).

NMR: δ (DMSO-d\(_6\)):

8.98 (s, 1H), 7.37-7.45 (m, 2H), 7.17 (d, J=7.7Hz, 1H),
7.03-6.95 (m, 2H), 6.88-6.82 (m, 2H), 6.41 (s, 2H),
5.65 (t, J=7.5Hz, 1H), 2.96-2.85 (m, 1H), 2.80-2.66 (m, 1H),
2.24-2.07 (m, 2H).

Example 107

N-Hydroxy-N\{5-(2-pyridloxy)indan-1-yl\}urea

STRUCTURE:

\[ \text{Structure Image} \]

m. p.: 161.6-162.8°C

IR: ν (KBr): 3490, 3200, 1665, 1470, 1430 cm\(^{-1}\).

NMR: δ (DMSO-d\(_6\)):

8.17 (s, 1H), 7.30-7.25 (m, 1H), 7.01-6.92 (m, 1H),
6.33-6.20 (m, 2H), 6.16-5.99 (m, 3H), 5.56 (s, 2H),
4.81 (t, J=7.5Hz, 1H), 2.15-2.01 (m, 1H), 1.96-1.83 (m, 1H),
1.44-1.20 (m, 2H).
<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-{5-(4-methylphenoxy)indan-1-yl}urea</th>
</tr>
</thead>
<tbody>
<tr>
<td>108</td>
<td></td>
</tr>
</tbody>
</table>

**STRUCTURE:**

![Chemical Structure](image)

**m. p.:** 163.0-163.7°C

**IR:** ν (Nujol): 3460, 3190, 1665, 1575, 1224 cm⁻¹.

**NMR:** δ (DMSO-d₆):

8.98 (s, 1H), 7.18 (d, J=8.5Hz, 2H), 7.13 (d, J=9.0Hz, 1H),
6.89 (d, J=8.5Hz, 2H), 6.77 (d, J=6.0Hz, 2H), 6.40 (s, 2H),
5.63 (t, J=7.5Hz, 1H), 2.94-2.83 (m, 1H), 2.77-2.65 (m, 1H),
2.28 (s, 3H), 2.23-2.05 (m, 2H).

<table>
<thead>
<tr>
<th>Example</th>
<th>N-Hydroxy-N-{5-(3-phenylpropyloxy)indan-1-yl}urea</th>
</tr>
</thead>
<tbody>
<tr>
<td>109</td>
<td></td>
</tr>
</tbody>
</table>

**STRUCTURE:**

![Chemical Structure](image)

**m. p.:** 160.5-162.0°C

**IR:** ν (Nujol): 3460, 3200, 1670, 1244, 1039 cm⁻¹.

**NMR:** δ (DMSO-d₆):

8.90 (s, 1H), 7.32-7.15 (m, 5H), 7.04 (d, J=8.0Hz, 1H),
6.75-6.70 (m, 2H), 6.35 (s, 2H), 5.59 (t, J=7.5Hz, 1H),
3.92 (t, J=6.5Hz, 2H), 2.89-2.83 (m, 1H), 2.76-2.67 (m, 3H),
2.21-1.94 (m, 4H).
Example N-Hydroxy-N-\{5-(2-thiazolyloxy)indan-1-y1\}urea

**STRUCTURE:**

```
  N
 / \  \
O   O
\    /  O
  \  /   
   \/
    OH
```

m. p. : 138.1-139.9°C

**IR: v (KBr):** 3450, 3000-3400, 2950, 1670, 1570, 1440, 1240, 1160, 940 cm⁻¹

**NMR: δ (DMSO-d₆):**

9.40(s, 1H), 7.27(d, J=3.66Hz, 1H), 7.15(m, 4H),
6.44(br.s, 2H), 5.67(t, J=7.69Hz, 1H), 2.91(m, 1H),
2.79(m, 1H), 2.18(m, 2H).

---

Example N-Hydroxy-N-\{5-(4-tetrahydroxyloxy)indan-1-y1\}urea

**STRUCTURE:**

```
O
\  / O
  / O
\ /   
  OH
```

m. p. : 152.4-153.9°C

**IR: v (KBr):** 3450, 3200, 2950, 2850, 1670, 1580, 1490, 1450, 1240, 1140,
1150, 1090, 1070, 990, 860, 810 cm⁻¹

**NMR: δ (DMSO-d₆):**

8.89(s, 1H), 7.39(d, J=8.06Hz, 1H), 6.80(br.s, 1H),
6.74(d, J=8.43Hz, 1H), 6.35(br.s, 2H), 5.58(t, J=6.96Hz, 1H),
4.50(m, 1H), 3.83(m, 2H), 3.43(m, 2H),
2.87(m, 1H), 2.70(m, 1H), 2.11(m, 2H), 1.94(m, 2H),
1.55(m, 2H).
Example N-Hydroxy-N-{5-(6-methoxy-2-pyridyloxy) indan-1-yl}urea

STRUCTURE:

\[
\text{CH}_3O-N\text{O} \quad \text{OH} \quad \text{NH}_2
\]

mp: \hspace{1cm} 128.2-128.7^\circ C

IR (Nujol) cm\(^{-1}\): \hspace{1cm} 3460, 3190, 1245, 1143, 1037

NMR (DMSO-d\(_6\)) \(\delta\): \hspace{1cm} 9.03 (s, 1H), 7.70 (t, J=8.0Hz, 1H), 7.18 (d, J=8.0Hz, 1H), 6.97 (s, 1H), 6.93 (dd, J=2.0 and 8.0Hz, 1H) 6.52 (d, J=8.0Hz, 1H), 6.42 (s, 2H), 6.37 (d, J=8.0Hz, 1H), 5.67 (t, J=7.5Hz, 1H), 3.71 (s, 3H), 2.98-2.87 (m, 1H), 2.81-2.70 (m, 1H), 2.27-2.08 (m, 2H).

Example N-Hydroxy-N-{5-(3,4-dimethoxyphenoxy) indan-1-yl}urea

STRUCTURE:

\[
\text{CH}_3O \quad \text{OH} \quad \text{NH}_2
\]

mp: \hspace{1cm} 148.1-149.3^\circ C

IR (KBr) cm\(^{-1}\): \hspace{1cm} 3450, 3200, 2850, 1670, 1580, 1520, 1470, 1450, 1230, 1150, 1110, 1020, 960

NMR (DMSO-d\(_6\)) \(\delta\): \hspace{1cm} 8.94(s, 1H), 7.11(d, J=8.06Hz, 1H), 6.93(d, J=8.79Hz, 1H) 6.74(m, 3H), 6.94(dd, J=2.92, 8.79Hz, 1H), 6.38(br.s, 2H), 5.62(t, J=6.96Hz, 1H), 3.73(s, 3H), 3.72(s, 3H), 2.84(m, 1H), 2.71(m, 1H), 2.14(m, 2H)
1. A compound of the formula

\[
\begin{align*}
\text{R}^4 & \quad \text{O} \quad \text{N} \quad \text{R}^1 \\
\text{Z} & \\
\text{(A)}_m \\
\text{Y}_n
\end{align*}
\]

wherein

\(\text{R}^1\) is hydrogen, C1 to C4 alkyl, C2 to C4 alkenyl, alkylthioalkyl, alkoxyalkyl or \(\text{-NR}^2\text{R}^3\);

\(\text{R}^2\) and \(\text{R}^3\) are each independently hydrogen, C1 to C4 alkyl, hydroxyl, aryl or substituted aryl wherein the substituent or substituents are selected from the group consisting of halo, nitro, cyano, C1 to C12 alkyl, C1 to C12 alkoxy, C1 to C12 halosubstituted alkyl, C1 to C12 hydroxy-substituted alkyl, C1 to C12 alkoxy carbonyl, aminocarbonyl, C1 to C12 alkyaminocarbonyl, C1 to C12 dialkylaminocarbonyl and C1 to C12 alkylsulfonyl, with the proviso that \(\text{R}^2\) and \(\text{R}^3\) are not both hydroxyl;

\(\text{R}^4\) is hydrogen, a pharmaceutically acceptable cation, aroyl or C1 to C12 alkanoyl;

\(\text{X}\) is a chemical bond, oxygen, sulfur or \(\text{N}\text{R}^5\);

\(\text{R}^5\) is hydrogen, C1 to C6 alkyl, C3 to C6 alkenyl, C1 to C6 alkanoyl, aryl, arylalkyl or aroyl;

\(\text{m}\) is 0 or 1;

\(\text{n}\) is 1 to 3;

\(\text{A}\) is C1 to C6 alkylene, C2 to C6 alkenylene or C2 to C6 alkylidene;

each \(\text{Y}\) is independently hydrogen, halogen, hydroxy, cyano, C1 to C12 alkyl, halosubstituted alkyl, hydroxysubstituted alkyl, C2 to C12
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alkenyl, C1 to C12 alkoxy, C3 to C12 alkenyloxy, C3 to C8 cycloalkyl, C1 to C8 thioalkyl, C1 to C12 alkoxy carbonyl, C1 to C12 arylalkoxycarbonyl, aminocarbonyl, C1 to C12 alkylaminocarbonyl, C1 to C12 dialkylaminocarbonyl, C1 to C12 arylalkyl amino, C1 to C12 arylalkylaminocarbonyl, alkoxyalkyl, aryl, aryloxy, aroyl, C1 to C12 arylalkyl, C2 to C12 arylalkeny1, C1 to C12 arylalkoxy or C1 to C12 arylthioalkoxy wherein said aryl, aryloxy, aroyl, arylalkyl, arylalkeny1, arylalkoxy and arylthioalkoxy may be optionally substituted with a substituent or substituents selected from the group consisting of halo, nitro, cyano, C1 to C12 alkyl, halosubstituted alkyl and C1 to C12 alkoxy; and

Z is oxygen or sulfur.

2. A compound according to Claim 1 wherein R^6 is H.

3. A compound according to Claim 2 wherein Z is O.

4. A compound according to Claim 3 wherein R^1 is NH_2.

5. A compound according to Claim 4 wherein X is NR^5.

6. A compound according to Claim 5 having the structure

![Chemical Structure](image)

7. A compound according to Claim 6 wherein R^5 is aryl or arylalkyl.
8. A compound according to Claim 4 wherein X is a chemical bond.

9. A compound according to Claim 8 having the structure

10. A compound according to Claim 9 wherein Y is aryloxy.

11. A compound according to Claim 10 wherein Y is phenoxy or substituted phenoxy.

12. A compound according to Claim 3 which is N-hydroxy-N-(5-phenoxyindan-1-yl)acetamide.

13. A compound according to Claim 7 which is N-hydroxy-N-[1-(3-methoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea;
    - N-hydroxy-N-[1-(3-trifluoromethylbenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea;
    - N-hydroxy-N-[1-(3,5-dimethoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea;
    - N-hydroxy-N-[1-(3-allyloxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl]methylurea;
    - N-(1-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)methyl-N-hydroxyurea;
    - N-hydroxy-N-(3-methoxy-1-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)methylurea;
    - N-hydroxy-N-(3-allyloxy-1-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)methylurea;
14. A compound according to Claim 10 which is N-hydroxy-N-[1-(3-methoxybenzyl)-8-fluoro-1,2,3,4-tetrahydroquinolin-6-yl)methylurea; 
N-hydroxy-N-[1-(3-difluoromethoxybenzyl)-1,2,3,4-tetrahydroquinolin-6-yl)methylurea; or 
N-hydroxy-N-[1-(3-difluoromethoxybenzyl)-8-fluoro-1,2,3,4-tetrahydroquinolin-6-yl)methylurea.

15. A compound according to Claim 11 which is N-hydroxy-N-[5-(5-trifluoromethyl-2-pyridyloxy)indan-1-yl]urea;
N-hydroxy-N-[5-(2-thiazolyloxy)indan-1-yl]urea; or 
N-hydroxy-N-[5-(6-methoxy-2-pyridyloxy)indan-1-yl]urea.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a lipoxygenase-inhibiting amount of a compound according to Claim 1, 4, 7 or 10.

17. A method of treating inflammatory conditions in a mammal comprising administering to said mammal an effective amount of a compound according to Claim 7 or 10.

18. A method of inhibiting lipoxygenase activity in a mammal comprising administering to said mammal a lipoxygenase-inhibiting amount of a compound according to Claim 7 or 10.

19. A method of inhibiting lipoxygenase activity in a mammal comprising administering to said mammal a pharmaceutical composition according to Claim 16.
20. A method of making a compound according to Claim 3, wherein $R^1$ is CH$_3$, comprising the steps:

(A) preparing a diacetyl of the formula

\[
\begin{array}{c}
OAc \\
Q-(A)_m-N \\
\mid \\
CH_3 \\
Q \\
\end{array}
\]

from an hydroxylamine of the formula

\[
\begin{array}{c}
OH \\
Q-(A)_m-NH \\
\end{array}
\]

wherein $Q$ represents

\[
\begin{array}{c}
Y_n \quad \text{[Diagram]} \\
\end{array}
\]

by reacting said hydroxylamine with acetyl chloride or acetic anhydride with a base in a non-reactive solvent;

(B) isolating the diacetyl;

(C) subjecting the diacetyl to selective hydrolysis by reaction with a base to produce said compound; and

(D) isolating said compound.

21. A method according to Claim 20 wherein the base of step (A) is selected from triethylamine and pyridine; the non-reactive solvent is selected from methylene chloride, chloroform, tetrahydrofuran, benzene and toluene; and the base of step (C) is selected from ammonia, ammonium hydroxide, sodium hydroxide, potassium hydroxide and lithium hydroxide.
22. A method of making a compound according to Claim 4 comprising treating an hydroxylamine of the formula

\[
\text{OH} \\
Q-(A)_m-NH
\]

wherein Q represents

with trimethylsilyl isocyanate in a non-reactive solvent and isolating said compound.

23. A method according to Claim 22 wherein the non-reactive solvent is selected from tetrahydrofuran, dioxane, methylene chloride and benzene.

24. A method of making a compound according to Claim 4 comprising the steps:

(A) treating an hydroxylamine of the formula

\[
\text{OH} \\
Q-(A)_m-NH
\]

wherein Q represents

with gaseous hydrogen chloride in a non-reactive solvent;

(B) subsequent treatment with phosgene and aqueous ammonia; and

(C) isolating said compound.

25. A method according to Claim 24 wherein said solvent is selected from benzene and toluene.
INTERNATIONAL SEARCH REPORT

I. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC: C 07 C 259/06, A 61 K 31/16, C 07 C 275/64, C 07 D 215/12,
C 07 D 215/18, 311/60, 311/58, A 61 K 31/17, 31/35, 31/47

II. FIELDS SEARCHED

Minimum Documentation Searched

Classification/System Classification Symbols
IPC C 07 C 259/00, 275/00, C 07 D 215/00, 311/00

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in the Fields Searched

III. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Category</th>
<th>Citation of Document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to Claim No.</th>
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<td>EP, A, 0292699 (ABBOTT LABORATORIES) 30 November 1988 see the whole document</td>
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<td>A</td>
<td>EP, A, 0279281 (ABBOTT LABORATORIES) 24 August 1988 see the whole document</td>
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<td>A</td>
<td>GB, A, 2191194 (E.R. SQUIBB &amp; SONS) 9 December 1987 see the whole document</td>
<td>1-16, 20-25</td>
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* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"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
"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.
"Z" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search
24th July 1991

Date of Mailing of this International Search Report
09 SEP 1991

International Searching Authority
EUROPEAN PATENT OFFICE

Signature of Authorized Officer

Form PCT/ISA/210 (second sheet) (January 1985)
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V. OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. Claim numbers 17-19, because they relate to subject matter not required to be searched by this Authority, namely:

See PCT Rule 39.1(iv)
Methods for treatment of the human or animal body by means of surgery or therapy, as well as diagnostic methods.

2. Claim numbers ..., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claim numbers ..., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This international Searching Authority found multiple inventions in this international application as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remarz on Protest
□ The additional search fees were accompanied by applicant's protest.
□ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (supplemental sheet (2)) (January 1985)
ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. US 9102674
SA 47217

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 27/08/91. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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