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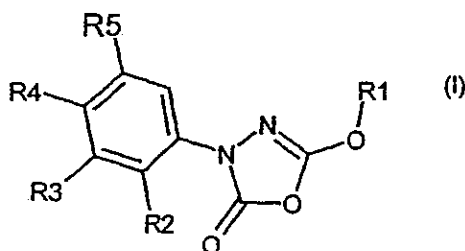
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(54) Title: SUBSTITUTED 3-PHENYL-5-ALKOXI-1,3,4-OXDIAZOL-2-ONE AND USE THEREOF FOR INHIBITING HORMONE-SENSITIVE LIPASE

(54) Bezeichnung: SUBSTITUIERTE 3-PHENYL-5-ALKOXI-1,3,4-OXDIAZOL-2-ONE (UND) IHRE VERWENDUNG ZUR HEMMUNG DER HORMONSENSITIVEN LIPASE



CONH, $n = 1$ or 2 , R^7 = hydrogen, substituted C_1 - C_{18} -alkyl, C_2 - C_{18} -alkenyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyl, C_3 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, C_5 - C_8 -cycloalkyl, C_6 - C_{10} -aryl- C_2 - C_6 -alkenyl, C_6 - C_{10} -aryl, diphenyl, diphenyl- C_1 - C_4 -alkyl, indanyl or the group Het-(CH_2)_r, with $r = 0, 1, 2$ or 3 and Het = a saturated and unsaturated 5-7 membered heterocycle which can be benzoannellated and substituted. The invention also relates to a method for producing the same. The inventive compounds have an inhibitory effect on hormone-sensitive lipase, HSL.

(57) Zusammenfassung: Es werden substituierte 3-Phenyl-5-alkoxi-1,3,4-oxdiazol-2-one der Formel (1) beschrieben, worin R^1 substituiertes C_1 - C_6 -Alkyl und C_3 - C_9 -Cycloalkyl, R^2 , R^3 , R^4 und R^5 Wasserstoff, Halogen, Nitro, C_1 - C_4 -Alkyl, C_1 - C_9 -Alkyloxy, substituiertes C_6 - C_{10} -Aryl- C_1 - C_4 -alkyloxy, C_6 - C_{10} -Aryloxy, C_6 - C_{10} -Aryl, C_3 - C_8 -Cycloalkyl oder O - C_3 - C_8 -Cycloalkyl, oder 2-Oxo-pyrrolidin-1-yl, 2,5-Dimethylpyrrol-1-yl oder NR^6 -A- R^7 , bedeuten, mit der Massgabe, dass R^2 , R^3 , R^4 und R^5 nicht gleichzeitig Wasserstoff bedeuten und mindestens einer der Reste R^2 , R^3 , R^4 oder R^5 für den Rest 2-Oxo-pyrrolidin-1-yl, 2,5-Dimethylpyrrol-1-yl oder NR^6 -A- R^7 steht, mit R^6 = Wasserstoff, C_1 - C_4 -Alkyl oder substituiertes C_6 - C_{10} -Aryl- C_1 - C_4 -alkyl, A = eine einfache Bindung, CO_n , SO_n oder CONH, $n = 1$ oder 2 , R^7 = Wasserstoff, substituiertes C_1 - C_{18} -Alkyl, C_2 - C_{18} -alkenyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyl, C_3 - C_8 -Cycloalkyl- C_1 - C_4 -alkyl, C_5 - C_8 -Cycloalkyl, C_6 - C_{10} -Aryl- C_2 - C_6 -alkenyl, C_6 - C_{10} -Aryl, Diphenyl, Diphenyl- C_1 - C_4 -alkyl, Indanyl, oder die Gruppe Het-(CH_2)_r, mit $r = 0, 1, 2$ oder 3 und Het = gesättigter oder ungesättigter 5-7-gliedriger Heterocyclus, der benzoannelliert und substituiert sein kann, bedeuten sowie ein Verfahren zu deren Herstellung. Die Verbindungen zeigen eine hemmende Wirkung an der hormonsensitiven Lipase, HSL.

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Description:

SUBSTITUTED 3-PHENYL-5-ALKOXY-1,3,4-OXDIAZOL-2-ONES AND THEIR USE
FOR INHIBITING HORMONE-SENSITIVE LIPASE

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The invention relates to substituted 3-phenyl-5-alkoxy-1,3,4-oxdiazol-2-ones which show an inhibitory effect on hormone-sensitive lipase, HSL.

10

Certain 5-alkoxy-1,3,4-oxdiazol-2-ones with an ortho-substituted phenyl ring as substituent or with fused-on five- or six-membered rings have anthelmintic (DE-A 26 04 110) and insecticidal effects (DE-A 26 03 877, EP-B 0 048 040, EP-B 0 067 471).

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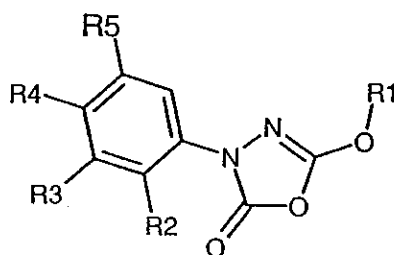
Certain 5-phenoxy-1,3,4-oxdiazol-2-ones with an ortho-substituted phenyl ring as substituents show an endoparasitocidal effect (EP-A 0 419 918).

The aim of the invention was now to find compounds which show an inhibitory effect on hormone-sensitive lipase, HSL.

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In a first aspect of the present invention, there is provided a compound of the formula

1

1

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in which the meanings are:

R^1 C_1 - C_6 -alkyl, C_3 - C_9 -cycloalkyl, it being possible for both groups to be substituted one or more times by phenyl, C_1 - C_4 -alkyloxy, S- C_1 - C_4 -alkyl,

$N(C_1-C_4\text{-alkyl})_2$, and for phenyl in turn to be substituted one or more times by halogen, $C_1-C_4\text{-alkyl}$, $C_1-C_4\text{-alkyloxy}$, nitro, CF_3 ; and

R^2 , R^3 , R^4 and R^5 independently of one another hydrogen, halogen, nitro,

$C_1-C_4\text{-alkyl}$, $C_1-C_9\text{-alkyloxy}$;

5 $C_6-C_{10}\text{-aryl-}C_1-C_4\text{-alkyloxy}$, $C_6-C_{10}\text{-aryloxy}$, $C_6-C_{10}\text{-aryl}$, $C_3-C_8\text{-cycloalkyl}$ or $O-C_3-C_8\text{-cycloalkyl}$, each of which may be substituted once, twice or three times by halogen, CF_3 , $C_1-C_4\text{-alkyloxy}$ or $C_1-C_4\text{-alkyl}$;

2-oxopyrrolidin-1-yl, 2,5-dimethylpyrrol-1-yl or $NR^6\text{-A-R}^7$,

10 with the proviso that R^2 , R^3 , R^4 and R^5 are not simultaneously hydrogen, and at least one of the radicals R^2 , R^3 , R^4 or R^5 is the radical 2-oxopyrrolidin-1-yl, 2,5-dimethylpyrrol-1-yl or $NR^6\text{-A-R}^7$, with

R^6 hydrogen, $C_1-C_4\text{-alkyl}$ or $C_6-C_{10}\text{-aryl-}C_1-C_4\text{-alkyl}$, where aryl may be

15 substituted by halogen, CF_3 , $C_1-C_8\text{-alkyloxy}$ or $C_1-C_4\text{-alkyl}$;

A a single bond, CO_n , SO_n or $CONH$;

n 1 or 2;

R^7 hydrogen;

20 $C_1-C_{18}\text{-alkyl}$ or $C_2-C_{18}\text{-alkenyl}$, each of which may be substituted once to three times by $C_1-C_4\text{-alkyl}$, halogen, CF_3 , $C_1-C_4\text{-alkyloxy}$, $N(C_1-C_4\text{-alkyl})_2$, $-COOH$, $C_1-C_4\text{-alkyloxycarbonyl}$, $C_6-C_{12}\text{-aryl}$, $C_6-C_{12}\text{-aryloxy}$, $C_6-C_{12}\text{-arylcarbonyl}$, $C_6-C_{10}\text{-aryl-}C_1-C_4\text{-alkyloxy}$ or oxo, where aryl in turn may be substituted by halogen, $C_1-C_4\text{-alkyl}$, aminosulfonyl or methylmercapto;

25 $C_6-C_{10}\text{-aryl-}C_1-C_4\text{-alkyl}$, $C_5-C_8\text{-cycloalkyl-}C_1-C_4\text{-alkyl}$, $C_5-C_8\text{-cycloalkyl}$, $C_6-C_{10}\text{-aryl-}C_2-C_6\text{-alkenyl}$, $C_6-C_{10}\text{-aryl}$, diphenyl, diphenyl- $C_1-C_4\text{-alkyl}$, indanyl, each of which may be substituted once or twice by $C_1-C_{18}\text{-alkyl}$, $C_1-C_{18}\text{-alkyloxy}$, $C_3-C_8\text{-cycloalkyl}$, $COOH$, hydroxyl, $C_1-C_4\text{-alkylcarbonyl}$, $C_6-C_{10}\text{-aryl-}C_1-C_4\text{-alkyl}$, $C_6-C_{10}\text{-aryl-}C_1-C_4\text{-alkyloxy}$, $C_6-C_{10}\text{-aryloxy}$, nitro, cyano, $C_6-C_{10}\text{-aryl}$, fluorosulfonyl, $C_1-C_6\text{-alkyloxycarbonyl}$, $C_6-C_{10}\text{-arylsulfonyloxy}$, pyridyl, $NHSO_2\text{-}$

30 $C_6-C_{10}\text{-aryl}$, halogen, CF_3 or OCF_3 , where alkyl may be substituted again by $C_1-C_4\text{-alkyloxycarbonyl}$, CF_3 or carboxyl, and aryl by halogen, CF_3 or $C_1-C_4\text{-alkyloxy}$;

or the group $Het-(CH_2)_r$,

with $r = 0, 1, 2$ or 3 and Het = saturated or unsaturated 5-7-membered heterocycle which may be benzo-fused and substituted by C_1 - C_4 -alkyl, C_6 - C_{10} -aryl, halogen, C_1 - C_4 -alkyloxy, C_1 - C_4 -alkyloxycarbonyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkylmercapto or nitro, where benzo-fused aryl may in turn be substituted by halogen, C_1 - C_4 -alkyloxy or CF_3 and alkyl in arylalkyl by methoxy and CF_3 ,

and their pharmacologically suitable salts and acid addition salts.

- 10 Said aryl radicals may optionally be substituted one or more times by C_1 - C_9 -alkyl, C_1 - C_8 -alkyloxy, halogen, trifluoromethyl. Said cycloalkyl radicals may optionally be substituted one or more times by C_1 - C_4 -alkyl, C_6 - C_{10} -aryl, and said alkyl radicals may be substituted by hydroxyl, di- C_1 - C_4 -alkylamino and fluorine. Halogen is fluorine, chlorine, bromine, preferably fluorine and chlorine. Alkyl, alkenyl, alkyloxy etc. may be branched or unbranched.

Preferred compounds of the formula 1 are those in which:

R^1 is C_1 - C_4 -alkyl; and/or

R^5 is hydrogen; and/or

- 20 R^2 is hydrogen, halogen, C_1 - C_4 -alkyl, C_1 - C_9 -alkyloxy or amino.

Further preferred compounds of the formula 1 are those in which

- 30 R^3 is hydrogen, C_1 - C_4 -alkyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy which may optionally be substituted in the aryl moiety by halogen, or is NR^6 -A- R^7 with

25 R^6 = hydrogen or benzyl,

A = single bond and

R^7 = C_6 - C_{10} -aryl- C_1 - C_4 -alkyl which may be substituted by halogen, CF_3 , cyano, phenyl- C_1 - C_4 -alkyloxy, CF_3 -phenoxy, C_5 - C_8 -cycloalkyl or fluorosulfonyloxy;

- 30 C_1 - C_{12} -alkyl which may be substituted by C_1 - C_4 -alkyloxy, phenyl, CF_3 or phenyl- C_1 - C_4 -alkyloxy;

C_2 - C_{12} -alkenyl or the group Het- $(CH_2)_r$, with $r = 0$ or 1 , and Het = saturated or unsaturated 5-7-membered heterocycle which may be benzo-fused and substituted by C_1 - C_4 -alkyl or halogen.

Additionally preferred compounds of the formula 1 are those in which:

R^4 is hydrogen, 2-oxopyrrolidin-1-yl, 2,5-dimethylpyrrol-1-yl or C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy which may be substituted by halogen, and/or

5 compounds of the formula 1 in which:

R^4 is NR^6 -A- R^7 , with

R^6 = hydrogen or methyl,

A = single bond and

R^7 = hydrogen;

10 C_1 - C_{12} -alkyl which may be substituted once or twice by halogen;

C_2 - C_{18} -alkenyl which may be substituted once or twice by C_1 - C_4 -alkyl or

C_1 - C_4 -alkyloxycarbonyl;

C_6 - C_{10} -aryl- C_1 - C_4 -alkyl which may be substituted by halogen, C_1 - C_6 -alkyloxy,

CF_3 , cyano, C_5 - C_6 -cycloalkyl, C_1 - C_4 -alkyloxycarbonyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyl,

15 C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy, where aryl may again be substituted by halogen or CF_3 ;

C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl;

or the group $Het-(CH_2)_r$,

with $r = 1, 2$ or 3 and Het = saturated or unsaturated 5-7-membered

20 heterocycle which may be substituted by halogen, C_1 - C_4 -alkyloxy or

C_1 - C_4 -alkyloxycarbonyl, and/or

compounds of the formula 1 in which:

R^4 is NR^6 -A- R^7 , with

25 R^6 = hydrogen,

A = -CO- and

R^7 = C_1 - C_{18} -alkyl which may be substituted by halogen, phenyl, phenoxy, phenylcarbonyl or C_1 - C_4 -alkyloxycarbonyl, where phenoxy in turn may be substituted by methyl, halogen or methylmercapto;

30 C_2 - C_{18} -alkenyl which may be substituted by C_6 - C_{10} -aryl;

C_6 - C_{10} -aryl which may be substituted by halogen, C_1 - C_8 -alkyl, phenyl-

C_1 - C_4 -alkyl, CF_3 , OCF_3 , fluorosulfonyl, C_1 - C_4 -alkyloxycarbonyl, phenoxy,

where aryl in turn may be substituted by C_1 - C_4 -alkyloxy;

C₆-C₁₀-aryl-C₁-C₄-alkyl where alkyl may be substituted by methoxy or CF₃ and aryl by halogen;

or the group Het-(CH₂)_r,

with r = 0 and Het = saturated or unsaturated 5-7-membered heterocycle

5 which may be benzo-fused and substituted by C₁-C₄-alkyl, halogen,

C₁-C₄-alkyloxy, halophenyl or halobenzylmercapto, where benzo-fused aryl

may in turn be substituted by halogen or methoxy, and/or

compounds of the formula 1 in which:

10 R⁴ is NR⁶-A-R⁷, with

R⁶ = hydrogen,

A = -CO₂- and

R⁷ = C₁-C₁₈-alkyl which is substituted by CF₃ or phenyl;

C₆-C₁₀-aryl;

15 C₆-C₁₀-aryl-C₁-C₄-alkyl which is substituted by C₁-C₄-alkyl, halogen, CF₃ or OCF₃, benzyloxy or phenyl;

or the group Het-(CH₂)_r,

with r = 0 or 1 and Het = saturated or unsaturated 5-7-membered heterocycle

which may be benzo-fused and substituted by C₁-C₄-alkyl or benzyl, and/or

20 R⁴ is NR⁶-A-R⁷, with

R⁶ = hydrogen,

A = -SO₂- and

R⁷ = C₁-C₆-alkyl which may be substituted by CF₃;

C₂-C₄-alkenyl which may be substituted by phenyl;

25 C₆-C₁₀-aryl which may be substituted by C₁-C₆-alkyl, halogen, C₁-C₄-alkyloxy or benzyl;

diphenyl-C₁-C₄-alkyl substituted by halogen;

or the group Het-(CH₂)_r,

with r = 0 and Het = saturated or unsaturated 5-7-membered heterocycle,

30 and/or

compounds of the formula 1 in which:

R⁴ is NR⁶-A-R⁷, with

R⁶ = hydrogen,

A = -CO-NH- and

R^7 = C₁-C₁₀-alkyl which may be substituted by C₁-C₄-alkyloxycarbonyl, N(C₁-C₄-alkyl)₂ or phenyl which may in turn be substituted by halogen or aminosulfonyl;

5 C₆-C₁₀-aryl which may be substituted by C₁-C₆-alkyl, C₁-C₆-alkyloxy, C₁-C₆-alkyloxycarbonyl, phenoxy, OCF₃, benzyl or pyridyl, where alkyl may again be substituted by C₁-C₄-alkyloxycarbonyl or carboxyl;

C₅-C₈-cycloalkyl which may be substituted by hydroxyl, or indanyl; or the group Het-(CH₂)_r,

10 with r = 0 or 1 and Het = saturated or unsaturated 5-7-membered heterocycle which may be substituted by benzyl.

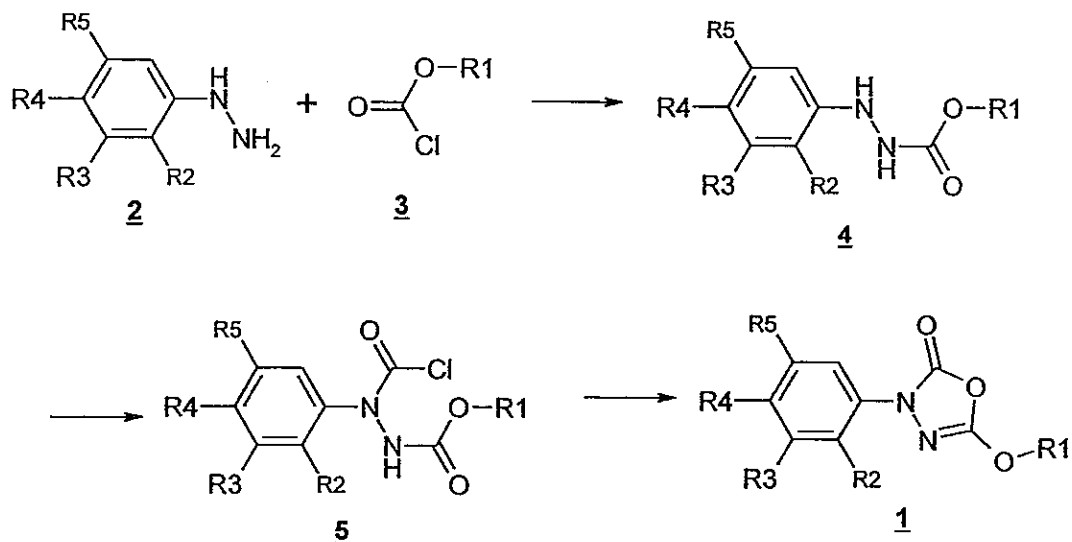
Particularly preferred compounds of the formula 1 are those in which R¹ is methyl.

15 Very particularly preferred compounds of the formula 1 are those in the group mentioned in Examples 21, 22, 27, 28, 30 to 34, 36 to 42, 53, 54, 58, 60, 62, 65, 69, 71, 74, 92, 97, 107, 116, 128, 130, 136, 139, 142, 152, 166 and 171.

The compounds of the invention of the formula 1 have a surprising inhibitory effect
20 on hormone-sensitive lipase, HSL, an allosteric enzyme in adipocytes, which is inhibited by insulin and is responsible for the breakdown of fats in fat cells and for the transfer of fat constituents into the blood stream. Inhibition of this enzyme thus corresponds to an insulin-like effect of the compounds of the invention, which eventually leads to a reduction of free fatty acids in the blood and of blood glucose.

25 They can thus be employed for metabolic derangements such as, for example, for non-insulin-dependent diabetes mellitus, for diabetic syndrome and for direct damage to the pancreas.

The compounds of the invention, of the formula 1, can be prepared in various ways by methods known per se. In a second aspect of the present invention, there is provided a process for preparing compounds of the formula 1 as defined in the first aspect which comprises



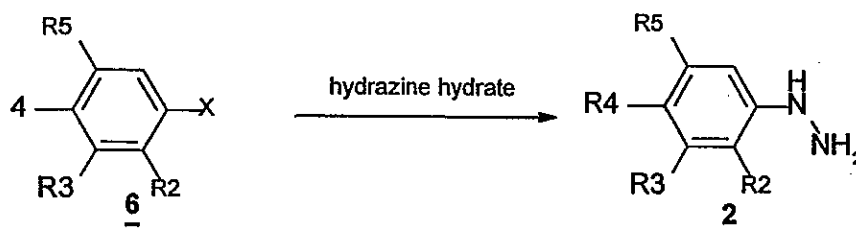
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reacting hydrazines of the formula 2 with chloroformate esters of the formula 3 or other reactive carbonic ester derivatives, in which R¹, R², R³, R⁴ and R⁵ are as defined in the first aspect, to give the compounds of the formula 4, which are

acylated with phosgene, carbonyldiimidazole, diphosgene or triphosgene, cyclized and converted where appropriate, converted by further chemical modification of the radicals R²-R⁵, such as, for example, by reduction of nitro to amino radicals and subsequent acylation or alkylation, into compounds of the formula 1. Since acids are usually liberated in these reactions, promotion is advisable by adding bases such as pyridine, triethylamine, sodium hydroxyde solution or alkali metal carbonates. The reactions can be carried out in wide temperature ranges. It has proved advantageous as a rule to operate at 0°C to the boiling point of the solvent used. Examples of solvents employed are methylene chloride, THF, DMF, toluene, ethyl acetate, n-heptane, dioxane, diethyl ether.

20

The hydrazines of the formula 2 can be prepared by known methods, for example by diazotization of the corresponding anilines and



subsequent reduction by known methods or by nucleophilic substitution of suitably substituted phenyl derivatives 6 (X = F, Cl, Br, I, OSO₂CF₃) with hydrazine hydrate.

- 5 Such suitable phenyl derivatives may be nitro-substituted halobenzenes, preferably fluoro- and chloronitrobenzenes, from which the compounds of the invention can be prepared by known methods at a suitable point in the synthetic route by reduction and reaction with acylating or alkylating agents such as, for example, acid chlorides, anhydrides, isocyanates, chloroformic esters, sulfonyl chlorides or alkyl and arylalkyl
- 10 halides, or by reductive alkylation with aldehydes.

The effect of the compounds of the invention, of the formula 1, was tested using the following enzyme assay system:

15 Enzyme preparation:

Preparation of partially purified HSL:

- Isolated rat fat cells are obtained from epididymal adipose tissue from untreated male rats (Wistar, 220-250 g) by collagenase treatment according to published
- 20 methods (e.g. S. Nilsson et al., Anal. Biochem. 158, 1986, 399 – 407; G. Fredrikson et al., J. Biol. Chem. 256, 1981, 6311 – 6320; H. Tornquist et al., J. Biol. Chem. 251, 1976, 813 – 819). The fat cells from 10 rats are washed three times by flotation with 50 ml each time of homogenization buffer (25 ml tris/HCl, pH 7.4, 0.25 M sucrose, 1 mM EDTA, 1 mM DTT, 10 µg/ml leupeptin, 10 µg/ml antipain, 20 µg/ml pepstatin)
- 25 and finally taken up in 10 ml of homogenization buffer. The fat cells are homogenized in a Teflon-in-glass homogenizer (Braun-Melsungen) by 10 strokes at 1 500 rpm and 15°C. The homogenate is centrifuged (Sorvall SM24 tubes, 5 000 rpm, 10 min, 4°C). The supernatant between the fatty layer at the top and the pellet is removed and the centrifugation is repeated. The supernatant resulting
- 30 therefrom is recentrifuged (Sorvall SM24 tubes, 20 000 rpm, 45 min, 4°C). The

subnatant is removed and mixed with 1 g of heparin-Sepharose (Pharmacia-Biotech, CL-6B, 5 × washed with 25 mM tris/HCl, pH 7.4, 150 mM NaCl). After the mixture has been incubated at 4°C for 60 min (shaking at 15-min intervals), it is centrifuged (Sorvall SM24 tubes, 3 000 rpm, 10 min, 4°C). The supernatant is adjusted to pH 5.2
5 by adding glacial acetic acid and incubated at 4°C for 30 min. The precipitates are collected by centrifugation (Sorvall SS34, 12 000 rpm, 10 min, 4°C) and suspended in 2.5 ml of 20 mM tris/HCl, pH 7.0, 1 mM EDTA, 65 mM NaCl, 13% sucrose, 1 mM DTT, 10 µg/ml leupeptin/pepstatin/antipain. The suspension is dialyzed against 25 mM tris/HCl, pH 7.4, 50% glycerol, 1 mM DTT, 10 µg/ml leupeptin, pepstatin,
10 antipain at 4°C overnight and then loaded onto a hydroxy apatite column (0.1 g per 1 ml of suspension, equilibrated with 10 mM potassium phosphate, pH 7.0, 30% glycerol, 1 mM DTT). The column is washed with four volumes of equilibration buffer at a flow rate of 20 to 30 ml/h. The HSL is eluted with one volume of equilibration buffer containing 0.5 M potassium phosphate, and then dialyzed (see above) and
15 concentrated 5- to 10-fold by ultrafiltration (Amicon Diaflo PM 10 filter) at 4°C. The partially purified HSL can be stored at -70°C for 4 to 6 weeks.

Assay:

To prepare the substrate, 25-50 µCi of [³H]trioleoylglycerol (in toluene), 6.8 µmol of
20 unlabeled trioleoylglycerol and 0.6 mg of phospholipids (phosphatidylcholine/ phosphatidylinositol 3:1 w/v) are mixed, dried with N₂ and then taken up in 2 ml of 0.1 M KP_i (pH 7.0) by ultrasonic treatment (Branson 250, microtip, setting 1-2, 2 × 1 min at 1-min intervals). After addition of 1 ml of KP_i and renewed ultrasonic treatment (4 × 30 sec on ice in 30-sec intervals), 1 ml of 20% BSA (in KP_i) is added
25 (final concentration of trioleoylglycerol 1.7 mM). For the reaction, 100 µl of substrate solution are pipetted into 100 µl of HSL solution (HSL prepared as above, diluted in 20 mM KP_i, pH 7.0, 1 mM EDTA, 1 mM DTT, 0.02% BSA, 20 µg/ml pepstatin, 10 µg/ml leupeptin) and incubated at 37°C for 30 min. Addition of 3.25 ml of methanol/chloroform/heptane (10:9:7) and of 1.05 ml of 0.1 M K₂CO₃, 0.1 M boric
30 acid (pH 10.5) is followed by thorough mixing and finally centrifugation (800 × g, 20 min). After phase separation, one equivalent of the upper phase (1 ml) is removed and the radioactivity is determined by liquid scintillation measurement.

Evaluation:

Substances are normally tested in four independent mixtures. The inhibition of the HSL enzymatic activity by a test substance is determined by comparing with an uninhibited control reaction. The IC_{50} is calculated via an inhibition plot with at least 10 concentrations of the test substance. The data are analyzed using the software package GRAPHIT, Elsevier-BIOSOFT.

The compounds showed the following effect in this assay:

Compound of Example No.	IC_{50} (μM)
21	10
22	1
27	10
28	6
30	1
31	10
32	3
33	0.2
34	1
36	10
37	1
38	1
39	1
40	10
41	0.1
42	1
53	1
54	1
58	0.8
60	0.2
62	0.3
65	1
69	0.03

71	0.02
74	0.04
92	0.25
97	0.03
107	0.12
116	0.1
128	0.6
130	0.5
136	0.5
139	0.4
142	0.2
152	0.2
166	0.2
171	0.6

The following examples illustrate the preparation methods in detail without restricting them.

Examples:

Example 1:

3-Methyl-4-nitrophenylhydrazine

- 5 5 g of hydrazine hydrate are slowly added dropwise to a solution of 15.9 g of 2-methyl-4-fluoronitrobenzene in 10 ml of N-methylpyrrolidone at room temperature, and the mixture is heated with stirring at 65°C for 4 hours. The product is precipitated by adding 70 ml of water and is filtered off with suction and recrystallized from isopropanol.
- 10 Yield: 13.3 g m.p.: 138°C

The following examples were prepared in an analogous way:

Example 2:

3-Fluoro-4-nitrophenylhydrazine

- 15 M.p.: 130°C

Example 3:

2-Chloro-4-nitrophenylhydrazine

M.p.: 144°C

20

Example 4:

2-Methyl-4-nitrophenylhydrazine

M.p.: 135°C

- 25 Example 5:

3-(4-Fluorobenzyloxy)-2-nitrophenylhydrazine

M.p.: 164°C

- 30 The starting compound 2-fluoro-4-(4-fluorobenzyloxy)nitrobenzene (m.p.: 99°C) was prepared by alkylation of 3-fluoro-4-nitrophenol with 4-fluorobenzyl chloride in DMF in the presence of potassium carbonate.

Example 6:

3-(4-Fluorobenzyloxy)-4-nitrophenylhydrazine (intermediate)

M.p.: 145°C

5 Example 7:

4-(4-Chlorophenoxy)-3-nitroaniline

1.4 g of potassium carbonate are added to a solution of 1.29 g of 4-chlorophenol in 8 ml of DMF and, after stirring for 30 minutes, 1.6 g of 4-fluoro-3-nitroaniline are added, and the mixture is stirred at 100°C for 3 hours. After cooling, 80 ml of water are added and, after briefly stirring, the precipitate is filtered off with suction and dried in vacuo at 40°C.

Yield: 2.0 g; m.p.: 101°C

15 Example 8:

4-(4-Chlorophenoxy)-3-nitrophenylhydrazine

A solution of 0.52 g of sodium nitrite in 5 ml of water is added dropwise to a stirred mixture consisting of 1.9 g of 4-(4-chlorophenoxy)-3-nitroaniline, 25 ml of concentrated hydrochloric acid and 25 ml of ethanol cooled to 0°C, and the mixture is then stirred at 0°C for 60 min and subsequently added dropwise to a suspension of 8.5 g of tin dichloride dihydrate in 8 ml of concentrated HCl. The precipitate is filtered off with suction, washed with water, suspended in 200 ml of water under nitrogen and decomposed with 100 ml of 30% strength sodium hydroxide solution at 10-15°C. The oil which forms is extracted by shaking with ethyl acetate and washed with water, and the organic phase is dried with sodium sulfate. The product is then precipitated with isopropanolic HCl, filtered off with suction and dried in vacuo.

Yield: 1.1 g; m.p.: 221°C

30 Example 9:

Methyl N'-(4-nitro-2-methylphenyl)hydrazinoformate

0.43 ml of methyl chloroformate was cautiously added dropwise to a mixture consisting of 0.84 g of 2-methyl-4-nitrophenylhydrazine, 15 ml of NMP and 2 ml of

pyridine while cooling in ice, and the mixture was then stirred for 2 hours while slowly warming to RT. After dilution with 50 ml of water, the mixture was stirred over night and the solid was dried in vacuo at 40°C.

Yield: 0.81 g; m.p.: 153°C

5

The following examples were prepared in an analogous way:

Example 10:

Methyl N'-(4-nitrophenyl)hydrazinoformate (intermediate)

10 M.p.: 179°C

Example 11:

Methyl N'-(3-fluoro-4-nitrophenyl)hydrazinoformate

M.p.: 127.4°C

15

Example 12:

Methyl N'-(3-methyl-4-nitrophenyl)hydrazinoformate

M.p.: 159°C

20 Example 13:

Methyl N'-(2-chloro-4-nitrophenyl)hydrazinoformate

M.p.: 156°C

Example 14:

25 Methyl N'-(3-(4-fluorobenzyloxy)-4-nitrophenyl)hydrazinoformate (intermediate)

M.p.: 166°C

Example 15:

Methyl N'-(3-(4-fluorobenzyloxy)-2-nitrophenyl)hydrazinoformate

30 M.p.: 193°C

Example 16:

Methyl N'-(4-(4-chlorophenoxy)-3-nitrophenyl)hydrazinoformate

M.p.: 147°C

Example 17:

Methyl N'-(3-piperidino-4-nitrophenyl)hydrazinoformate (-)

M.p.: 131°C

5

The latter compound and the compound of Example 18 were prepared by reacting methyl N'-(3-fluoro-4-nitrophenyl)hydrazinoformate with piperidine and N-benzylpiperazine, respectively, in NMP at 80°C.

10 Example 18:

Methyl N'-(3-(N-benzylpiperazino)-4-nitrophenyl)hydrazinoformate

M.p.: 156°C

Example 19:

15 5-Methoxy-3-(4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

2.5 g of methyl N'-(4-nitrophenyl)hydrazinoformate and 5 ml of pyridine were taken up in 15 ml of methylene chloride and, while stirring and cooling in ice, 3 ml of a 20% strength solution of phosgene in toluene were added dropwise. This mixture was left to stand at room temperature over night and was diluted with a further 10 ml of methylene chloride and then washed 3 times with water. After drying over sodium sulfate, the mixture was concentrated in vacuo, and the product was purified by column chromatography (silica gel, solvents: methanol:methylene chloride = 2:98) and recrystallized from isopropanol.

25 Yield: 1.5 g m.p.: 151°C

The following examples were prepared in analogy to Example 4:

Example 20:

30 5-Methoxy-3-(3-methyl-4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 112°C

Example 21:

5-Methoxy-3-(4-(4-chlorophenoxy-3-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

5 Example 22:

5-Methoxy-3-(3-(4-fluorobenzyloxy)-2-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 99°C

Example 23:

10 5-Methoxy-3-(2-methyl-4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 111°C

Example 24:

5-Methoxy-3-(3-(4-fluorobenzyloxy)-4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

15 M.p.: 137°C

Example 25:

5-Methoxy-3-(4-aminophenyl)-3-H-(1,3,4)oxdiazol-2-one

20 A mixture consisting of 1.4 g of 5-methoxy-3-(4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one, 0.5 g of Pd/C and 20ml of methanol is hydrogenated under atmospheric pressure at room temperature until the calculated amount of hydrogen has been taken up. The catalyst is then filtered off, and the solution is concentrated in vacuo. The remaining semisolid residue is stirred with isopropanol and filtered off with suction.

25 Yield: 0.75g; m.p.: 85°C

Example 26:

5-Methoxy-3-(2-amino-4-(4-fluorobenzyloxy)phenyl)-3-H-(1,3,4)oxdiazol-2-one

30 M.p.: oil

Example 27:

5-Methoxy-3-(3-amino-4-(4-chlorophenoxy)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 133°C

Example 28:

5-Methoxy-3-(4-amino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 114°C

5

Example 29:

5-Methoxy-3-(4-amino-3-(4-fluorobenzyloxy)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 195°C

10 Example 30:

5-Methoxy-3-(4-(4-chlorophenylacetyl-amino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

201 mg of 4-chlorophenylacetyl chloride are added dropwise to a mixture consisting of 200 mg of 5-methoxy-3-(4-aminophenyl)-3-H-(1,3,4)oxdiazol-2-one, 20 ml of methylene chloride and 0.1 ml of pyridine cooled in ice, and the mixture is stirred at room temperature for 5 hours. Volatiles are removed in vacuo, and the residue is stirred with water and the solid is filtered off with suction and dried at 40°C in vacuo. Yield: 318 mg; m.p.: 161°C

20 The following examples were prepared in an analogous way:

Example 31:

5-Methoxy-3-(4-(4-chlorophenylacetyl-amino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

25 M.p.: 190°C

Example 32:

5-Methoxy-3-(4-octanoylamino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 110°C

30

Example 33:

5-Methoxy-3-(4-(4-heptylbenzoylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 155°C

Example 34:

5-Methoxy-3-(4-(4-butylphenylsulfonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 135°C

5 Example 35:

5-Methoxy-3-(4-(4-chlorobutanoylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 137°C

Example 36:

10 5-Methoxy-3-(4-pivaloylamino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 157°C

Example 37:

15 5-Methoxy-3-(4-(4-chlorophenylsulfonylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 147°C

Example 38:

20 5-Methoxy-3-(4-(1-naphthylsulfonylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 123°C

Example 39:

25 5-Methoxy-3-(4-(2-phenylethenylsulfonylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 129°C

Example 40:

30 5-Methoxy-3-(4-(2,2,2-trifluoroethylsulfonylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 151°C

Example 41:

5-Methoxy-3-(4-(benzyloxycarbonylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 115°C

5

Example 42:

5-Methoxy-3-(4-(3,4-dichlorophenylaminocarbonylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 210°C

10

The latter compound was obtained by reacting 5-methoxy-3-(4-amino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one with equimolar amounts of 3,4-dichlorophenyl isocyanate in toluene at 50°C.

15 Example 43:

5-Methoxy-3-(4-(4-chlorophenylsulfonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 169°C

Example 44:

20 5-Methoxy-3-(4-(2-chlorophenylsulfonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 171°C

Example 45:

5-Methoxy-3-(4-(3-chlorophenylsulfonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

25 M.p.: 141°C

Example 46:

5-Methoxy-3-(4-(4-chlorophenylacetyl amino)-3-(4-fluorobenzyloxy)phenyl)-3-H-(1,3,4)oxdiazol-2-one

30 M.p.: 167°C

Example 47:

5-Methoxy-3-(4-benzylsulfonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 153°C

Example 48:

5-Methoxy-3-(4-(-2-(4'-chlorobiphenyl)ethyl)sulfonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

5 M.p.: 165°C

Example 49:

5-Methoxy-3-(4-isopropylsulfonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 190°C

10

Example 50:

5-Methoxy-3-(4-dimethylamino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 71°C

15 The latter compound was obtained by reacting 5-methoxy-3-(4-amino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one with paraformaldehyde/formic acid in DMF at room temperature and was purified by column chromatography (silica gel, ethyl acetate:n-heptane = 1:1).

20 Example 51:

5-Methoxy-3-(4-(4-chlorobenzylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

25 The latter compound was obtained by reacting 5-methoxy-3-(4-amino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one with 4-chlorobenzaldehyde/sodium borohydride in methanol/methylene chloride at room temperature and was purified by column chromatography (silica gel, ethyl acetate:n-heptane = 1:1).

Example 52:

30 5-Methoxy-3-(4-(2-oxopyrrolidin-1-yl)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

The latter compound was prepared by reacting 5-methoxy-3-(4-(4-chlorobutanoylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one with sodium

hydride in dioxane at room temperature and purifying the crude product by column chromatography (silica gel, methylene chloride:methanol = 98:2).

Example 53:

5 5-Methoxy-3-(4-(4-oxopent-2-en-2-ylamino)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 143°C

10 The latter compound was obtained by reacting 5-methoxy-3-(4-amino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one with equimolar amounts of acetylacetone in glacial acetic acid at 80°C and was isolated by precipitation by adding water and filtration.

Example 54:

15 5-Methoxy-3-(4-(2,5-dimethylpyrrol-1-yl)-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one
M.p.: oil

20 The latter compound was obtained by reacting 5-methoxy-3-(4-amino-3-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one with equimolar amounts of acetonylacetone in glacial acetic acid at 80°C. Working up took place by dilution with water, extraction by shaking with ethyl acetate and column chromatography (silica gel, methylene chloride) of the crude product obtained after concentration of the dried organic phase.

Example 55:

25 5-Methoxy-3-(3-(4-fluorobenzyloxy)-4-methylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one
M.p.: 98°C

30 The latter compound was obtained as by-product of the hydrogenation of 5-methoxy-3-(3-(4-fluorobenzyloxy)-4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one with platinum dioxide as catalyst in methanol at room temperature under atmospheric pressure and after filtering off the catalyst, concentrating the reaction mixture and column chromatography (silica gel, methylene chloride).

The compounds of Examples 56-199 were prepared analogously to the previous examples.

Example 56:

5 5-Methoxy-3-(3-aminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 95°C

Example 57:

5-Methoxy-3-(3-dibenzylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

10 M.p.: 71°C

Example 58:

5-Methoxy-3-(3-benzylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

15

Example 59:

5-Methoxy-3-(4-(pyrid-2-yl)aminocarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 81°C

20 Example 60:

5-Methoxy-3-(3-(4-fluorobenzyloxy)-4-benzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

25 Example 61:

5-Methoxy-3-(4-amino-2-methylphenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

Example 62:

30 5-Methoxy-3-(3-methyl-4-(2-chlorobenzyloxycarbonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 161°C

Example 63:

5-Methoxy-3-(4-amino-2-chlorophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 126°C

5 Example 64:

5-Methoxy-3-(2-chloro-4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 92°C

Example 65:

10 5-Methoxy-3-(2-methyl-4-benzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 112°C

Example 66:

5-Methoxy-3-(2-methyl-4-(4-trifluoromethoxybenzoylamino)phenyl)-3-H-

15 (1,3,4)oxdiazol-2-one

M.p.: 150°C

Example 67:

5-Methoxy-3-(2-chloro-4-benzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

20 M.p.: 150°C

Example 68:

5-Methoxy-3-(3-fluoro-4-nitrophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 127°C

25

Example 69:

5-Methoxy-3-(4-(4-*t*-butylbenzoylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 173°C

30 Example 70:

5-Methoxy-3-(4-(4-chlorobenzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 177°C

Example 71:

5-Methoxy-3-(2-chloro-4-(4-heptylbenzoylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 135°C

5 Example 72:

5-Methoxy-3-(4-(3,4-dichlorobenzoylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 200°C

Example 73:

10 5-Methoxy-3-(4-(2-(4-chlorophenoxy)-2-methylpropionylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 153°C

Example 74:

15 5-Ethoxy-3-(3-methyl-4-benzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 94°C

Example 75:

5-Isopropoxy-3-(3-methyl-4-benzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-

20 2-one

M.p.: 119°C

Example 76:

5-Isopropoxy-3-(3-methyl-4-butyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

25 M.p.: 114°C

Example 77:

5-Isopropoxy-3-(3-methyl-4-(3-chlorophenylaminocarbonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

30 M.p.: 201°C

Example 78:

5-tert-Butoxy-3-(3-methyl-4-benzyloxycarbonylaminophenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 113°C

Example 79:

5-Methoxy-3-(3-methyl-4-phenoxy-carbonylamino-phenyl)-3-H-(1,3,4)oxdiazol-2-one

5 M.p.: 145°C

Example 80:

5-Methoxy-3-(3-methyl-4-(pyrid-3-yl-carbonylamino)-phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

10

Example 81:

5-Methoxy-3-(3-methyl-4-(indan-2-ylaminocarbonylamino)-phenyl)-3-H-

(1,3,4)oxdiazol-2-one

M.p.: 206°C

15

Example 82:

5-Methoxy-3-(3-methyl-4-(pyrid-3-ylmethylaminocarbonylamino)-phenyl)-3-H-

(1,3,4)oxdiazol-2-one

M.p.: 229°C

20

Example 83:

5-Methoxy-3-(3-methyl-4-(pyrid-3-ylmethoxycarbonylamino)-phenyl)-3-H-

(1,3,4)oxdiazol-2-one

M.p.: 232°C

25

Example 84:

5-Methoxy-3-(3-fluoro-4-benzyloxycarbonylamino-phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

30

Example 85:

5-Methoxy-3-(3-fluoro-4-(4-trifluoromethylbenzoylamino)-phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: oil

Example 86:

5-Methoxy-3-(3-benzyloxy-4-(4-trifluoromethylbenzoylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 159°C

5

Example 87:

5-Methoxy-3-(3-fluoro-4-(4-tert-butylbenzoylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 144°C

10 Example 88:

5-Methoxy-3-(3-methyl-4-(2,2,2-trifluoroethoxycarbonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 141°C

15 Example 89:

5-Methoxy-3-(3-methyl-4-piperidinocarbonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 154°C

Example 90:

20 5-Methoxy-3-(4-(6-methoxybenzofuran-2-yl-carbonylamino)phenyl)-3-H-(1,3,4)oxdiazol-2-one

M.p.: 191°C

25 Further examples which were prepared by the processes described above and were characterized by mass spectroscopy (M+1):

Example No.	Chemical name:	M+1	Mol. wt.
91	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3-methyl-benzenesulfonamide	362	361.4
92	3,4-Dimethoxy-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-phenyl]benzenesulfonamide	408	407.4
93	Quinoline-8-sulfonic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	399	398.4
94	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-5-nitro-isophthalic acid monomethyl ester	415	414.3

95	3-(2-Chlorophenyl)-5-methylisoxazole-4-carboxylic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	427	426.8
96	3,3,3-Trifluoro-2-methoxy-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2-phenylpropionamide	424	423.3
97	2-Fluoro-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-benzamide	330	329.3
98	Tetradecanoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	418	417.5
99	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2-phenethylbenzamide	416	415.4
100	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2-(4-methoxyphenoxy)-5-nitrobenzamide	479	478.4
101	2-(4-Benzyloxyphenyl)-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]acetamide	432	431.4
102	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3,3,3-triphenylpropionamide	492	491.5
103	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3,5-bis-trifluoromethylbenzamide	448	447.3
104	4-Cyano-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-benzamide	337	336.3
105	Nonanoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-amide	348	347.4
106	Methyl 9-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-carbamoyl]nonanoate	406	405.4
107	Undecanoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	376	375.5
108	4-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]carbamoyl]-benzenesulfonyl fluoride	394	393.3
109	11-Phenoxyundecanoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	468	467.6
110	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2,3-diphenylpropionamide	416	415.4
111	4-Chloro-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2-methylbenzamide	360	359.8
112	6-Chloro-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-nicotinamide	347	346.7
113	5-Fluoro-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2-methylbenzamide	344	343.3
114	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-2,4,6-trimethylbenzamide	354	353.4
115	N-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3-naphthalen-2-ylacrylamide	388	387.4
116	5-Oxo-5-phenylpentanoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	382	381.4
117	3-(2,4-Dichlorobenzylsulfanyl)thiophene-2-carboxylic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	509	508.4
118	2-Fluoro-N-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-4-trifluoromethylbenzamide	398	397.3
119	1-Hexyl-3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	335	334.4
120	1-(4-Bromophenyl)-3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	406	405.2
121	1-[3-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3-(2-methoxyphenyl)urea	357	356.3

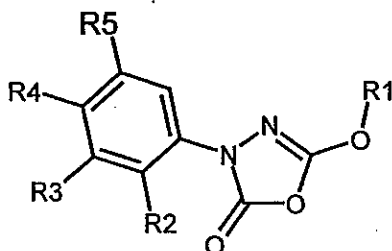
122	Ethyl 2-[3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]ureido]-3-phenylpropionate	427	426.4
123	1-(2,6-Diisopropylphenyl)-3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	411	410.5
124	1-[3-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3-octylurea	363	362.4
125	1-(4-Fluorobenzyl)-3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-phenyl]urea	359	358.3
126	1-(2-Ethylphenyl)-3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-phenyl]urea	355	354.4
127	Ethyl 6-[3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-ureido]hexanoate	393	392.4
128	1-(2,6-Dimethoxyphenyl)-3-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	387	386.4
129	5-Methoxy-3-[4-[(thiophen-3-ylmethyl)amino]phenyl]-3H-[1,3,4]oxdiazol-2-one	304	303.3
130	4-[[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]methyl]-benzonitrile trifluoroacetate	437	436.3
131	3-[4-(2-Bromo-4,5-dimethoxybenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one	437	436.3
132	3-[4-(3-Ethoxy-4-methoxybenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	486	485.4
133	Methyl 4-[[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]-methyl]benzoate trifluoroacetate	470	469.4
134	4-[[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]-methyl]phenyl acetate	356	355.3
135	5-Methoxy-3-[4-(pentafluorophenylmethylamino)phenyl]-3H-[1,3,4]oxdiazol-2-one	388	387.3
136	3-[4-(4-Benzyloxybenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	518	517.5
137	3-[4-(3,3-Dichlorononylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	517	516.3
138	2-[[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]-methyl]benzonitrile	323	322.3
139	3-[4-(Cyclohexylmethylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one	304	303.4
140	5-Methoxy-3-[4-(2,3,5-trichlorobenzylamino)phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	515	514.7
141	3-[4-(5-Bromo-2-fluorobenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	509	508.2
142	3-[4-(4-Hexyloxybenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	512	511.5
143	5-Methoxy-3-[4-[3-(3-trifluoromethylphenoxy)benzylamino]phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	572	571.4
144	3-[4-[(2-Chloroquinolin-3-ylmethyl)amino]phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	497	496.8
145	Methyl 3-methoxy-5-[[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]methyl]pyridine-2-carboxylate trifluoroacetate	501	500.4
146	4-[[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]-methyl]phenyl benzenesulfonate	454	453.5
147	2-(2,6-Dimethyl-4-methylsulfanylphenoxy)-N-[3-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]acetamide	416	415.5
148	1-(2,4-Difluorophenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	363	362.3

149	1-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3-(4-phenoxyphenyl)urea	419	418.4
150	1-(2,6-Difluorophenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	363	362.3
151	1-Butyl-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	307	306.3
152	1-(2-Ethoxyphenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	371	370.4
153	1-(2,6-Dibromo-4-fluorophenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	503	502.1
154	1-(4-Butoxyphenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	399	398.4
155	1-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-3-(4-trifluoromethoxyphenyl)urea	411	410.3
156	1-Benzyl-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	341	340.3
157	1-(3-Fluorophenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	345	344.3
158	Ethyl 6-[3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-ureido]hexanoate	393	392.4
159	1-Biphenyl-4-yl-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]urea	403	402.4
160	Butyl 2-[3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-ureido]benzoate	427	426.4
161	5-Methoxy-3-[3-(7-methoxy-3,7-dimethyloctylamino)phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	492	491.5
162	5-Methoxy-3-[3-[(thiophen-2-ylmethyl)amino]phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	418	417.4
163	3-(3-Hexylaminophenyl)-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	406	405.4
164	5-Methoxy-3-[3-(3-phenylpropylamino)phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	440	439.4
165	5-Methoxy-3-(3-undecylaminophenyl)-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	476	475.5
166	5-Methoxy-3-[3-[3-(3-trifluoromethylphenoxy)benzylamino]phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	572	571.4
167	3-[3-[(2-Chloroquinolin-3-ylmethyl)amino]phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	497	496.8
168	4-[[3-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]-methyl]phenyl 4-fluorobenzenesulfonate trifluoroacetate	586	585.5
169	5-Methoxy-3-[3-(3,4,5-trifluorobenzylamino)phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	466	465.3
170	3-[3-(3,5-Bistrifluoromethylbenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	548	547.3
171	3-(3-Dec-4-enylaminophenyl)-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	460	459.5
172	3-[3-(3-Cyclopentyl-2-phenethyloxybenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	600	599.6
173	4-[[3-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenylamino]methyl]-benzonitrile trifluoroacetate	437	436.3
174	5-Methoxy-3-[3-[(6-methylpyridin-2-ylmethyl)amino]phenyl]-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	427	426.3
175	3-[3-(2-Benzylloxyethylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	456	455.4

176	3-[3-(2,6-Difluorobenzylamino)phenyl]-5-methoxy-3H-[1,3,4]oxdiazol-2-one trifluoroacetate	448	447.3
			M.p. °C
177	Dodecanoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	93	
178	Octadec-9-enoic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]-amide	67	
179	2-Methoxyethyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	117	
180	1-(4-Hydroxycyclohexyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]urea	220	
181	1,1-Dibutyl-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]urea	Oil	
182	5-Methoxybenzofuran-2-carboxylic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]amide	199	
183	4-Methylpiperazine-1-carboxylic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]amide	Oil	
184	1-Methylpiperidin-4-yl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	235	
185	Cyclohexyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	163	
186	4-Benzylpiperidine-1-carboxylic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]amide	146	
187	1-(2-Diisopropylaminoethyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]urea	136	
188	4-(2-{3-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]ureido}ethyl)benzenesulfonamide	200	
189	1-(1-Benzylpiperidin-4-yl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]urea	198	
190	1-(4-Isopropylphenyl)-3-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]urea	200	
191	2-{3-[4-(5-Methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]ureido}-3-methylbutyric acid	246	
192	1,2,3,4-Tetrahydronaphth-1-yl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	159	
193	1-Phenylethyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	Oil	
194	4-Isopropylbenzyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	88	
195	4-Trifluoromethoxybenzyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	82	
196	3,5-Dichlorobenzyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	169	
197	Biphenyl-2-ylmethyl [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]carbamate	138	
198	5-Chlorobenzofuran-2-carboxylic acid-[4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)-2-methylphenyl]amide	210	
199	5-Chlorobenzofuran-2-carboxylic acid [4-(5-methoxy-2-oxo-[1,3,4]oxdiazol-3-yl)phenyl]amide	209	

Patent claims:

1. A compound of the formula 1

**1**

in which the meanings are:

R^1 C_1 - C_6 -alkyl, C_3 - C_9 -cycloalkyl, it being possible for both groups to be substituted one or more times by phenyl, C_1 - C_4 -alkyloxy, S- C_1 - C_4 -alkyl, N(C_1 - C_4 -alkyl)₂, and for phenyl in turn to be substituted one or more times by halogen, C_1 - C_4 -alkyl, C_1 - C_4 -alkyloxy, nitro, CF₃; and

R^2 , R^3 , R^4 and R^5 independently of one another hydrogen, halogen, nitro, C_1 - C_4 -alkyl, C_1 - C_9 -alkyloxy;

C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy, C_6 - C_{10} -aryloxy, C_6 - C_{10} -aryl, C_3 - C_8 -cycloalkyl or O- C_3 - C_8 -cycloalkyl, each of which may be substituted once, twice or three times by halogen, CF₃, C_1 - C_4 -alkyloxy or C_1 - C_4 -alkyl; 2-oxopyrrolidin-1-yl, 2,5-dimethylpyrrol-1-yl or NR⁶-A-R⁷,

with the proviso that R^2 , R^3 , R^4 and R^5 are not simultaneously hydrogen, and at least one of the radicals R^2 , R^3 , R^4 or R^5 is the radical 2-oxopyrrolidin-1-yl, 2,5-dimethylpyrrol-1-yl or NR⁶-A-R⁷, with

R^6 hydrogen, C_1 - C_4 -alkyl or C_6 - C_{10} -aryl- C_1 - C_4 -alkyl, where aryl may be substituted by halogen, CF₃, C_1 - C_8 -alkyloxy or C_1 - C_4 -alkyl;

A a single bond, CO_n, SO_n or CONH;

n 1 or 2;

R^7 hydrogen;

C₁-C₁₈-alkyl or C₂-C₁₈-alkenyl, each of which may be substituted once to three times by C₁-C₄-alkyl, halogen, CF₃, C₁-C₄-alkyloxy, N(C₁-C₄-alkyl)₂, -COOH, C₁-C₄-alkyloxycarbonyl, C₆-C₁₂-aryl, C₆-C₁₂-aryloxy, C₆-C₁₂-arylcarbonyl, C₆-C₁₀-aryl-C₁-C₄-alkyloxy or oxo, where aryl in turn may be substituted by

halogen, C₁-C₄-alkyl, aminosulfonyl or methylmercapto; C₆-C₁₀-aryl-C₁-C₄-alkyl, C₅-C₈-cycloalkyl-C₁-C₄-alkyl, C₅-C₈-cycloalkyl, C₆-C₁₀-aryl-C₂-C₆-alkenyl, C₆-C₁₀-aryl, diphenyl, diphenyl-C₁-C₄-alkyl, indanyl, each of which may be substituted once or twice by C₁-C₁₈-alkyl, C₁-C₁₈-alkyloxy, C₃-C₈-cycloalkyl, COOH, hydroxyl, C₁-C₄-alkylcarbonyl, C₆-C₁₀-aryl-C₁-C₄-alkyl, C₆-C₁₀-aryl-C₁-C₄-alkyloxy, C₆-C₁₀-aryloxy, nitro, cyano, C₆-C₁₀-aryl, fluorosulfonyl, C₁-C₆-alkyloxycarbonyl, C₆-C₁₀-arylsulfonyloxy, pyridyl, NHSO₂-C₆-C₁₀-aryl, halogen, CF₃ or OCF₃, where alkyl may be substituted again by C₁-C₄-alkyloxycarbonyl, CF₃ or carboxyl, and aryl by halogen, CF₃ or C₁-C₄-alkyloxy;

or the group Het-(CH₂)_r,

with $r = 0, 1, 2$ or 3 and Het = saturated or unsaturated 5-7-membered heterocycle which may be benzo-fused and substituted by C₁-C₄-alkyl, C₆-C₁₀-aryl, halogen, C₁-C₄-alkyloxy, C₁-C₄-alkyloxycarbonyl, C₆-C₁₀-aryl-C₁-C₄-alkyl, C₆-C₁₀-aryl-C₁-C₄-alkylmercapto or nitro, where benzo-fused aryl may in turn be substituted by halogen, C₁-C₄-alkyloxy or CF₃ and alkyl in arylalkyl by methoxy and CF₃,

and the pharmacologically suitable salts and acid addition salts thereof.

2. A compound of the formula 1 as claimed in claim 1, in which R¹ is C₁-C₄-alkyl.
3. A compound of the formula 1 as claimed in claim 1 or 2, in which R¹ is methyl.
4. A compound of the formula 1 as claimed in claims 1 to 3, in which R⁵ is hydrogen.
5. A compound of the formula 1 as claimed in claims 1 to 4, in which R² is hydrogen, halogen, C₁-C₄-alkyl, C₁-C₉-alkyloxy or amino.

6. A compound of the formula 1 as claimed in claims 1 to 5, in which R^3 is hydrogen, C_1 - C_4 -alkyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy which may optionally be substituted in the aryl moiety by halogen, or is NR^6 -A- R^7 with
 R^6 = hydrogen or benzyl,
 5 A = single bond and
 R^7 = C_6 - C_{10} -aryl- C_1 - C_4 -alkyl which may be substituted by halogen, CF_3 , cyano, phenyl- C_1 - C_4 -alkyloxy, CF_3 -phenoxy, C_5 - C_8 -cycloalkyl or fluorosulfonyloxy;
 C_1 - C_{12} -alkyl which may be substituted by C_1 - C_4 -alkyloxy, phenyl, CF_3 or
 10 phenyl- C_1 - C_4 -alkyloxy;
 C_2 - C_{12} -alkenyl or the group $Het-(CH_2)_r$, with $r = 0$ or 1 , and Het = saturated or unsaturated 5-7-membered heterocycle which may be benzo-fused and substituted by C_1 - C_4 -alkyl or halogen.
- 15 7. A compound of the formula 1 as claimed in claims 1 to 6, in which R^4 is hydrogen, 2-oxopyrrolidin-1-yl, 2,5-dimethylpyrrol-1-yl or C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy which may be substituted by halogen.
8. A compound of the formula 1 as claimed in claims 1 to 7, in which
 20 R^4 is NR^6 -A- R^7 , with
 R^6 = hydrogen or methyl,
 A = single bond and
 R^7 = hydrogen;
 C_1 - C_{12} -alkyl which may be substituted once or twice by halogen;
 25 C_2 - C_{18} -alkenyl which may be substituted once or twice by C_1 - C_4 -alkyl or C_1 - C_4 -alkyloxycarbonyl;
 C_6 - C_{10} -aryl- C_1 - C_4 -alkyl which may be substituted by halogen, C_1 - C_6 -alkyloxy, CF_3 , cyano, C_5 - C_6 -cycloalkyl, C_1 - C_4 -alkyloxycarbonyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyl, C_6 - C_{10} -aryl- C_1 - C_4 -alkyloxy, where aryl may again be substituted by halogen or
 30 CF_3 ;
 C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl;
 or the group $Het-(CH_2)_r$,

with $r = 1, 2$ or 3 and Het = saturated or unsaturated 5-7-membered heterocycle which may be substituted by halogen, C_1 - C_4 -alkyloxy or C_1 - C_4 -alkyloxycarbonyl.

- 5 9. A compound of the formula 1 as claimed in claims 1 to 8, in which
 R^4 is NR^6 -A- R^7 , with
 R^6 = hydrogen,
A = -CO- and
10 R^7 = C_1 - C_{18} -alkyl which may be substituted by halogen, phenyl, phenoxy, phenylcarbonyl or C_1 - C_4 -alkyloxycarbonyl, where phenoxy in turn may be substituted by methyl, halogen or methylmercapto;
 C_2 - C_{18} -alkenyl which may be substituted by C_6 - C_{10} -aryl;
 C_6 - C_{10} -aryl which may be substituted by halogen, C_1 - C_8 -alkyl, phenyl-
15 C_1 - C_4 -alkyl, CF_3 , OCF_3 , fluorosulfonyl, C_1 - C_4 -alkyloxycarbonyl, phenoxy, where aryl in turn may be substituted by C_1 - C_4 -alkyloxy;
 C_6 - C_{10} -aryl- C_1 - C_4 -alkyl where alkyl may be substituted by methoxy or CF_3 and aryl by halogen;
or the group Het-(CH_2) r ,
with $r = 0$ and Het = saturated or unsaturated 5-7-membered heterocycle
20 which may be benzo-fused and substituted by C_1 - C_4 -alkyl, halogen, C_1 - C_4 -alkyloxy, halophenyl or halobenzylmercapto, where benzo-fused aryl may in turn be substituted by halogen or methoxy.

10. A compound of the formula 1 as claimed in claims 1 to 9, in which
25 R^4 is NR^6 -A- R^7 , with
 R^6 = hydrogen,
A = -CO₂- and
 R^7 = C_1 - C_{18} -alkyl which is substituted by CF_3 or phenyl;
 C_6 - C_{10} -aryl;
30 C_6 - C_{10} -aryl- C_1 - C_4 -alkyl which is substituted by C_1 - C_4 -alkyl, halogen, CF_3 or OCF_3 , benzyloxy or phenyl;
or the group Het-(CH_2) r ,
with $r = 0$ or 1 and Het = saturated or unsaturated 5-7-membered heterocycle
which may be benzo-fused and substituted by C_1 - C_4 -alkyl or benzyl.

11. A compound of the formula 1 as claimed in claims 1 to 10, in which

R^4 is NR^6-A-R^7 , with

R^6 = hydrogen,

A = $-SO_2-$ and

R^7 = C_1-C_6 -alkyl which may be substituted by CF_3 ;

C_2-C_4 -alkenyl which may be substituted by phenyl;

C_6-C_{10} -aryl which may be substituted by C_1-C_6 -alkyl, halogen, C_1-C_4 -alkyloxy or benzyl;

diphenyl- C_1-C_4 -alkyl substituted by halogen;

or the group $Het-(CH_2)_r$,

with $r = 0$ and Het = saturated or unsaturated 5-7-membered heterocycle.

12. A compound of the formula 1 as claimed in claims 1 to 11, in which

R^4 is NR^6-A-R^7 , with

R^6 = hydrogen,

A = $-CO-NH-$ and

R^7 = C_1-C_{10} -alkyl which may be substituted by C_1-C_4 -alkyloxycarbonyl,

$N(C_1-C_4-alkyl)_2$ or phenyl which may in turn be substituted by halogen or aminosulfonyl;

C_6-C_{10} -aryl which may be substituted by C_1-C_6 -alkyl, C_1-C_6 -alkyloxy,

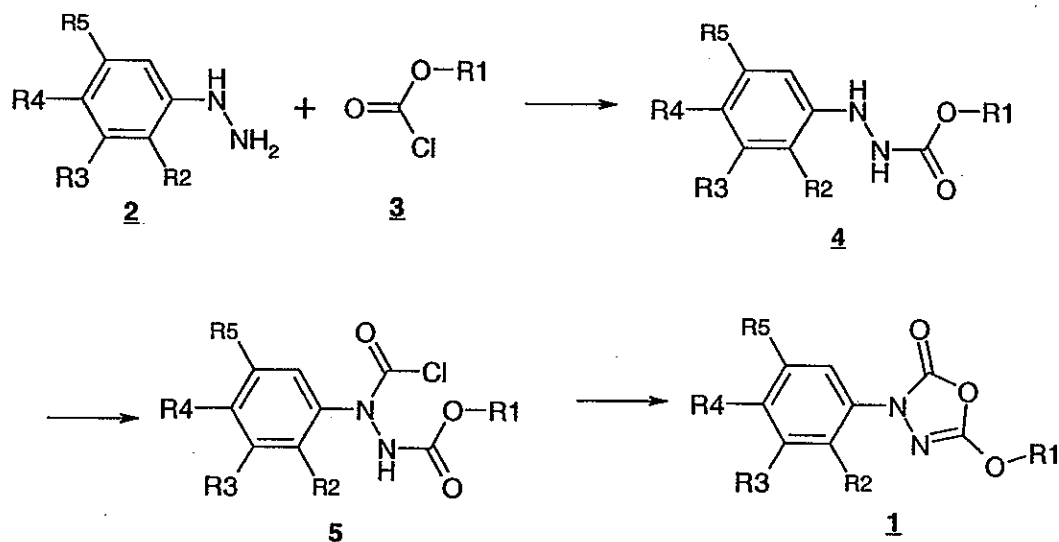
C_1-C_6 -alkyloxycarbonyl, phenoxy, OCF_3 , benzyl or pyridyl, where alkyl may again be substituted by C_1-C_4 -alkyloxycarbonyl or carboxyl;

C_5-C_8 -cycloalkyl which may be substituted by hydroxyl, or indanyl;

or the group $Het-(CH_2)_r$,

with $r = 0$ or 1 and Het = saturated or unsaturated 5-7-membered heterocycle which may be substituted by benzyl.

13. A process for preparing compounds of the formula 1 as claimed in claims 1 to 12, which comprises



reacting hydrazines of the formula 2 with chloroformic esters of the formula 3 or other reactive carbonic ester derivatives in which R¹, R², R³, R⁴ and R⁵ are as defined in claims 1 to 12 to give the compounds of the formula 4, which are acylated with phosgene, carbonyldiimidazole, diphosgene or triphosgene, cyclized and, where appropriate, converted by further chemical modification of the radicals R²-R⁵ such as, for example, by reduction of nitro to amino radicals and subsequent acylation or alkylation into the compounds of the formula 1.

14. A compound of the formula 1 as claimed in claims 1 to 12 for use in a pharmaceutical with an inhibitory effect on hormone-sensitive lipase, HSL.
15. A compound of the formula 1 as claimed in claims 1 to 12 for use in a pharmaceutical for treating non-insulin-dependent diabetes mellitus or diabetic syndrome.
16. A pharmaceutical for treating non-insulin-dependent diabetes mellitus or diabetic syndrome comprising at least one compound of the formula 1 as claimed in claims 1 to 12.