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Yield: 56%

¹H-NMR (400MHz, DMSO) δ ppm: 1.15-1.40 (m, 5H), 1.55-1.65 (m, 1H), 1.70-1.83 (m, 4H), 2.60-2.75 (m, 3H), 3.52 (s, 3H), 3.55-3.63 (m, 4H), 3.78 (t, 2H), 3.80-3.90 (m, 2H), 7.70 (dd, 2H), 7.82 (dd, 2H), 10.28 (t, 1H).

To a solution of 4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N(2-morpholin-4-yl-ethyl)thiobenzamide (1.12 mmol, 500 mg) in THF (20 ml), sodium hydride (60% dispersion in mineral oil, 1.12 mmol, 44 mg) was added and the mixture was warmed at reflux during one hour. After cooling at room temperature, methyl iodide (1.35 mmol, 84 μ l) was added and the mixture was warmed 4 hours at reflux and then overnight at room temperature. The mixture was concentrated under reduced pressure to give a crude material which was solubilized in ethanol (50 ml). To this solution, cyanamide (1.8 mmol, 75 mg) and triethylamine (0.9 mmol, 125 μ l) were added and the mixture was stirred 2 days at reflux. Mercury(II)chloride (1.68 mmol, 457 mg) and cyanamide (2.35 mmol, 100 mg) were added and the reaction was allowed to stir 3 days at room temperature. The mixture was concentrated under reduced pressure and the residue was diluted in ethyl acetate and filtered through celite. The filtrate was concentrated under vacuum. The residue was chromatographed on silica gel using a gradient of dichloromethane containing from 0 to 5% methanol to afford the title compound.

Yield: 17%

¹H-NMR (400MHz, DMSO) δ ppm: 1.18-1.42 (m, 5H), 1.55-1.65 (m, 1H), 1.70-1.85 (m, 4H), 2.40-2.50 (m, 4H), 2.50-2.60 (m, 2H), 2.60-2.70 (m, 1H), 3.45-3.55 (m, 2H), 3.55 (s, 3H), 3.55-3.65 (m, 4H), 7.68 (dd, 2H), 7.52 (dd, 2H), 9.15 (t, 1H).

MS (m/z) / M+1 = 454

HPLC (uv purity, λ = 214 nm) = 95%

35

Example I37.29: R1= cyclohexyl, R2= methyl, R3= 4-N-(2-pyrrolidin-1-yl-ethyl)-benzamide



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4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide

Compound I37.29 was prepared by the procedure described in example I37.23 using appropriate intermediates and reagents

5 (I37 and 1-(2-aminoethyl)pyrrolidine).

The residue was purified by silica gel chromatography eluting with a gradient of dichloromethane containing from 0 to 14% methanol to afford the desired product.

Yield: 26%

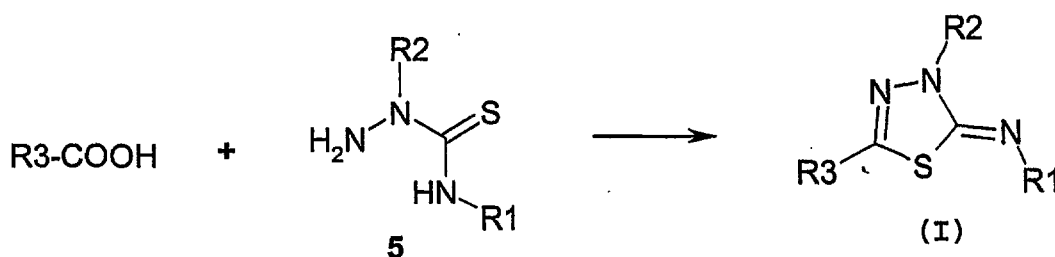
10 $^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 1.20-1.45 (m, 5H), 1.60-1.87 (m, 9H), 2.45-2.70 (m, 7H), 3.35-3.45 (m, 2H), 3.60 (s, 3H), 7.73 (dd, 2H), 7.95 (dd, 2H), 8.55 (t, 1H).

MS (m/z) / M+1= 414

HPLC (uv purity, λ = 214 nm)= 99.9%

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Protocol D :



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EXAMPLE I: PROTOCOL D

Example I15: R1= cyclohexyl, R2= methyl, R3= 4-methylsulfonyl-phenyl

25 Cyclohexyl-[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine

To a mixture of 4-methylsulfonyl-benzoic acid (2.5 mmol, 500 mg), 2-methylthiosemicarbazide 5a (2.5 mmol, 468 mg) in anhydrous dioxane (5 mL) at 65°C, POCl₃ (3 mmol, 280 μ l) was added and the mixture was warmed at 95°C for 5 hours. The solvent was removed by distillation under reduced pressure to give a crude material which was basified at pH 8-7 with a saturated solution of NaHCO₃. The aqueous phase was

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extracted with dichloromethane. The organic layer was washed with saturated solution of NaCl, dried over magnesium sulfate, filtered and distilled to give a residue which was purified by silica gel chromatography (eluted with a gradient of cyclohexane/ethyl acetate finishing with the ratio 80/20) to afford 230 mg of the title compound.

Yield: 26%

¹H-NMR (400MHz, DMSO) δ ppm: 1.25-1.45 (m, 5H), 1.65-1.75 (m, 1H), 1.75-1.95 (m, 4H), 1.70-1.80 (m, 1H), 3.35 (s, 3H), 3.65(s, 3H), 8.05(dd, 4H).

MS (m/z) / M+1= 352.5

HPLC (uv purity, λ= 214 nm): 95.3%

The compounds of the following examples were prepared by the procedure described in example I15 using appropriate intermediates and reagents:

I15.1	[3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-dimethyl-amine
I15.2	Cyclohexyl-[5-(3-methoxy-4-nitro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine

Example I38: R1= cyclohexyl, R2= Me, R3= 3-pyridyl

Cyclohexyl-(3-methyl-5-pyridin-3-yl-3H-[1,3,4]thiadiazol-2-ylidene)-amine

Compound I38 was prepared by the procedure described in example I15 (protocol D) using appropriate intermediates and reagents.

The title product was isolated by chromatography on silica gel eluting with cyclohexane containing from 0 to 10% ethylacetate.

Yield= 0.06 g, 13.5%

¹H-NMR (400MHz, DMSO) δ ppm: 1.20-1.44 (m, 5H), 1.59-1.64 (b, 1H), 1.73-1.83 (b, 4H), 2.61-2.70 (b, 1H), 3.54 (s, 3H), 7.50-7.53 (m, 1H), 8.04 (d, 1H), 8.63-8.67 (m, 1H), 8.85 (s, 1H).

MS (m/z) / M+1= 275/276

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HPLC (uv purity, $\lambda = 214$ nm) = 95.87%

Example I39: R1= cyclohexyl, R2= methyl, R3= 3-sulfamoyl-phenyl

5 3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide

Compound I39 was prepared by the procedure described in example I15 (protocol D) using appropriate intermediates and reagents.

10 The title product was isolated by chromatography on silica gel eluting with dichloromethane containing from 0 to 5% methanol.

Yield= 8.0 %

¹H-NMR (400MHz, DMSO) δ ppm: 1.18-1.41 (m, 5H), 1.58-1.63 (m, 1H), 1.73-1.84 (m, 4H), 2.60-2.67 (m, 1H), 3.56 (s, 3H), 7.48 (s, 2H), 7.67 (t, 1H), 7.82-7.90 (m, 2H), 8.12 (s, 1H).

MS (m/z) / M+1= 353/354

HPLC (uv purity, $\lambda = 214$ nm) = 97.55%

20 Example I40: R1= cyclohexyl, R2= methyl, R3= benzo[1,3]dioxol-5-yl

(5-Benzo[1,3]dioxol-5-yl-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene)-cyclohexyl-amine

Compound I40 was prepared by the procedure described in example I15 (protocol D) using appropriate intermediates and reagents.

The title product was isolated by chromatography on silica gel eluting with cyclohexane containing from 0 to 15% ethylacetate.

30 Yield: 27%

¹H-NMR (400MHz, DMSO) δ ppm: 1.20-1.45 (m, 5H), 1.60-1.70 (m, 1H), 1.70-1.85 (m, 4H), 2.60-2.70 (m, 1H), 3.50 (s, 3H), 6.15 (s, 2H), 7.00 (d, 1H), 7.15 (d, 1H), 7.25 (s, 1H)

MS (m/z) / M+1= 318

35 HPLC (uv purity, $\lambda = 214$ nm): 99.9%

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Example I41: R1= cyclohexyl, R2= methyl, R3= 3,4,5-trimethoxyphenyl

Cyclohexyl-[3-methyl-5-(3,4,5-trimethoxy-phenyl)-3H-[1,3,4]thiadiazol-2-ylidene]-amine

- 5 Compound I41 was prepared by the procedure described in example I15 (protocol D) using appropriate intermediates and reagents.

The title product was isolated by chromatography on silica gel eluting with heptane containing from 0 to 20%
10 diethylether.

Yield: 26%

¹H-NMR (400MHz, DMSO) δ ppm: 1.15-1.50 (m, 5H), 1.55-1.65 (m, 1H), 1.70-1.85 (m, 4H), 2.65-2.70 (m, 1H), 3.50 (s, 3H), 3.70 (s, 3H), 3.85 (s, 6H), 6.90 (s, 2H)

15 MS (m/z) / M+1= 364.49

HPLC (uv purity, λ= 214 nm): 99.9%

EXAMPLE I: PROTOCOL A

- 20 Example I42 : R1= cyclopentyl, R2= methyl, R3= 4-cyano-phenyl

4-(5-Cyclopentylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzonitrile

- To a suspension of 1,3,4-thiadiazolium perchlorate (3c)
25 (0.86 mmol, 300 mg) in ethanol (20 ml), cyclopentylamine (1.03 mmol, 102 μl) and triethylamine (1.03 mmol, 264 μl) were added, and the mixture was stirred at reflux overnight. The mixture was concentrated by distillation of the solvent and the crude material was solubilized in ethyl acetate. The
30 inorganic salts were removed by extraction with water. The organic layer was washed with water and a solution of NaCl, dried under magnesium sulphate, filtered, and distilled to give a residue which was chromatographed on silica gel column (using a gradient of solvent ethyl acetate-
35 cyclohexane starting with a ratio 0/100 to 20/80) to isolate 210 mg of the pure product.

Yield= 85.7%

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¹H-NMR (400MHz, DMSO) δ ppm: 1.40-1.95 (m, 8H), 3.15-3.25 (m, 1H), 3.50 (s, 3H), 7.80 (dd, 2H), 7.92 (dd, 2H).

MS (m/z) / M+1= 285

- 5 **Example I43: R1= cycloheptyl, R2 = methyl, R3= 4-cyanophenyl**
4-(5-Cycloheptylimino-4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl)-benzonitrile

The compound I43 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents
10 (protocol A). The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 20% ethylacetate.

Yield= 70.6%

¹H-NMR (400MHz, DMSO) δ ppm: 1.40-1.85 (m, 12H), 2.75-2.85 (m, 1H), 3.50 (s, 3H), 7.80 (dd, 2H), 7.90 (dd, 2H).

15 MS (m/z) / M+1= 313

- Example I44: R1= 4-fluorophenyl, R2= Methyl, R3= 4-cyano-**
phenyl
20 **4-[5-(4-Fluoro-phenylimino)-4-methyl-4,5-dihydro-**
[1,3,4]thiadiazol-2-yl]-benzonitrile

The compound I44 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). The residue was purified by chromatography on
25 silica gel eluting with a gradient of cyclohexane containing from 0 to 20% ethylacetate.

Yield= 71.1%

¹H-NMR (400MHz, DMSO) δ ppm: 3.72 (s, 3H), 7.03-7.10 (m, 2H), 7.16-7.25 (m, 2H), 7.83 (dd, 2H), 7.93 (dd, 2H).

30 MS (m/z) / M+1= 311

- Example I45: R1= 3-phenol, R2= methyl, R3= 4-cyano-phenyl**
4-[5-(3-Hydroxy-phenylimino)-4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl]-benzonitrile

35 The compound I45 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). The residue was purified by chromatography on

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silica gel eluting with a gradient of dichloromethane containing from 0 to 20% methanol.

Yield = 99%

¹H-NMR (400MHz, DMSO) δ ppm: 3.70 (s, 3H), 6.41-6.55 (m, 3H), 7.15 (t, 1H), 7.82 (dd, 2H), 7.91 (dd, 2H), 9.42 (s, 1H).

MS (m/z) / M+1= 309

Example I46: R1= 4-fluoro-3-benzoic acid, R2= methyl, R3= 4-cyano-phenyl

5- [5- (4-Cyano-phenyl)-3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino]-2-fluoro-benzoic acid

The compound I46 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). In this particular case, the residue was precipitated in ethylacetate to afford the pure product.

Yield= 65.5%

¹H-NMR (400MHz, DMSO) δ ppm: 3.74 (s, 3H), 7.24-7.37 (m, 3H), 7.44-7.51 (m, 1H), 7.85 (dd, 2H), 7.94 (dd, 2H), 13.31 (b, 1H).

MS (m/z) / M+1= 355

Example I47: R1= 4-methyl-cyclohexyl, R2= methyl, R3= 4-cyano-phenyl

I47a : 4- [4-Methyl-5- (cis-4-methyl-cyclohexylimino)-4,5-dihydro- [1,3,4]thiadiazol-2-yl]-benzonitrile

I47b : 4- [4-Methyl-5- (trans-4-methyl-cyclohexylimino)-4,5-dihydro- [1,3,4]thiadiazol-2-yl]-benzonitrile

The compound I47 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 20% ethylacetate to give the cis and trans isomers.

Yield= 68.6%

Compound cis: I47a

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¹H-NMR (400MHz, DMSO) δ ppm: 0.92 (d, 3H), 1.38-1.68 (m, 9H), 2.85-2.92 (m, 1H), 3.55 (s, 3H), 7.80 (dd, 2H), 7.92 (dd, 2H).

MS (m/z) / M+1= 313

5 **Compound trans:I47b**

¹H-NMR (400MHz, DMSO) δ ppm: 0.88 (d, 3H), 0.94-1.09 (m, 2H), 1.30-1.45 (m, 3H), 1.64-1.83 (m, 4H), 2.48-2.60 (m, 1H), 3.52 (s, 3H), 7.80 (dd, 2H), 7.92 (dd, 2H).

MS (m/z) / M+1= 313

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Example I48: R1= trans-4-hydroxycyclohexyl, R2= methyl, R3= 4-cyano-phenyl

4-[5-(trans-4-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

15 The compound I48 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). Using 0.86 mmol of thiadiazolium, an excess of trans-4-aminocyclohexanol hydrochloride (7.7 mmol) and 8.6 mmol of triethylamine. The residue was purified by
20 chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 30% ethylacetate.

Yield= 74%

¹H-NMR (400MHz, DMSO) δ ppm: 1.18-1.42 (m, 4H), 1.73-1.89 (m, 4H), 2.52-2.62 (m, 1H), 3.40-3.50 (m, 1H), 3.53 (s, 3H),
25 4.50 (s, 1H), 7.80 (dd, 2H), 7.92 (dd, 2H).

MS (m/z) / M+1= 315

HPLC (uv purity, λ= 214 nm)= 99.9%

30 **Example I49: R1= exo-2-norbornyl, R2= methyl, R3= 4-cyano-phenyl**

4-[5-(Bicyclo[2.2.1]hept-2-ylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

The compound I49 was prepared by the procedure described in example I48 using the appropriate intermediates and reagents
35 (protocol A). The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 8% ethylacetate.

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Yield= 64%

¹H-NMR (400MHz, DMSO) δ ppm: 1.10-1.20 (m, 3H), 1.26-1.35 (m, 1H), 1.40-1.53 (m, 2H), 1.56-1.61 (m, 1H), 1.70-1.79 (m, 1H), 2.09-2.14 (m, 1H), 2.24-2.29 (m, 1H), 2.71-2.78 (m, 1H), 3.52 (s, 3H), 7.80 (dd, 2H), 7.91 (dd, 2H).

MS (m/z) / M+1= 311

HPLC (uv purity, λ= 214 nm)= 99.2%

Example I50: R1= (1R*, 2R*)-2-hydroxy-cyclohexyl, R2= methyl, R3= 4-cyano-phenyl

4-[5-((1R*, 2R*)-2-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

The compound I50 was prepared by the procedure described in example I48 using the appropriate intermediates and reagents (protocol A). The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 50% ethylacetate.

Yield= 74%

¹H-NMR (400MHz, DMSO) δ ppm: 1.15-1.40 (m, 5H), 1.58-1.75 (m, 3H), 1.80-1.90 (m, 1H), 2.38-2.49 (m, 1H), 3.30-3.40 (m, 1H), 3.55 (s, 3H), 4.50 (s, 1H), 7.80 (dd, 2H), 7.92 (dd, 2H).

MS (m/z) / M+1= 315

HPLC (uv purity, λ= 214 nm)= 99.9%

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Example I51: R1= (1R*, 2S*)-2-hydroxycyclohexyl, R2= methyl, R3= 4-cyano-phenyl

4-[5-((1R*, 2S*)-2-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

Compound I51 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). 1,3,4-thiadiazolium perchlorate (0.287 mmol, 100 mg) in ethanol (6 ml), cis-2-aminocyclohexanol hydrochloride (2.58 mmol, 390 mg) and triethylamine (2.87 mmol, 400 μl) were added. The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 30% ethylacetate.

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Yield= 72%

¹H-NMR (400MHz, DMSO) δ ppm: 1.15-1.80 (m, 8H), 2.83-2.97 (m, 1H), 3.52-3.70 (m, 4H), 4.10-4.20 (m, 1H), 7.80 (dd, 2H), 7.94 (dd, 2H).

5 MS (m/z) / M+1= 315

HPLC (uv purity, λ = 214 nm) = 98.7%

Examples I52-a and I52-b : R1= 3-hydroxycyclohexyl, R2= methyl, R3= 4-cyano-phenyl

10 I52-a: 4-[5-((1R*, 3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

I52-b: 4-[5-((1R*, 3S*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

The compounds I52-a and I52-b were prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). A mixture of 1,3,4-thiadiazolium perchlorate (3c) (3.5 mmol, 1.22 g) in ethanol (80 ml), racemic-3-aminocyclohexanol (4.2 mmol, 485 mg) and triethylamine (4.2 mmol, 587 μl) was stirred at reflux during 4H. The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 60% ethylacetate to give 120 mg of the trans isomer and 260 mg cis isomer.

1R*, 3R* isomer (I52a)

25 Yield = 11%.

¹H-NMR (400MHz, DMSO) δ ppm: 1.35-1.50 (m, 2H), 1.50-1.70 (m, 6H), 3.04-3.12 (m, 1H), 3.54 (s, 3H), 3.88-3.96 (m, 1H), 4.44 (d, 1H), 7.80 (dd, 2H), 7.94 (dd, 2H).

30 1R*, 3S* isomer (I52b)

¹H (400MHz, DMSO) δ ppm: 1.03-1.30 (m, 4H), 1.64-1.78 (m, 2H), 1.78-1.87 (m, 1H), 1.98-2.04 (m, 1H), 2.58-2.70 (m, 1H), 3.40-3.58 (m, 4H), 4.61 (s, 1H), 7.44 (s, 1H), 7.70 (dd, 2H), 7.95 (dd, 2H), 8.07 (s, 1H).

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Example I53: R1= (1R*, 3R*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-(methylsulfonyl)phenyl

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(1R*, 3R*)) -3-[5-(4-Methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-cyclohexanol

The compound I53 was prepared by the procedure described in example I42 using the appropriate intermediates and reagents (protocol A). A mixture of 1,3,4-thiadiazolium perchlorate (3b) (1 mmol, 400 mg), ethanol (25 ml), 3-aminocyclohexanol (1.2 mmol, 140 mg) and triethylamine (2.5 mmol, 350 μ l) was stirred at reflux during 3H. The residue was purified by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 50% ethylacetate. The product was then purified by HPLC on Kromasil C18 column with a gradient of acetonitrile/water 95/5 to 5/95 to give the pure product.

Yield= 10%

$^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 1.30-1.69 (m, 8H), 3.00-3.10 (m, 1H), 3.21 (s, 3H), 3.52 (s, 3H), 3.82-3.95 (m, 1H), 4.35 (d, 1H), 7.85 (dd, 2H), 7.98 (dd, 2H)

MS (m/z) / M+1= 367/369

HPLC (uv purity, λ = 214 nm)= 98.9%

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Example I54: R1= (1R*, 3R*)-3-Hydroxy-cyclohexyl, R2= methyl, R3= 4-benzoic acid

4-[5-(1R*, 3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzoic acid

To a solution of I52a (3.18 mmol, 1 g) in isopropanol (20ml), a solution of KOH [6N] (15.9 mmol, 2.6 ml) was added and the mixture was stirred at reflux during 4 days. The mixture was acidified to pH= 6-7 with a solution of HCl and concentrated under reduced pressure to give the carboxylic acid derivative I54.

^1H (400MHz, DMSO) δ ppm : 1.32-1.70 (m, 8H), 3.03-3.12 (m, 1H), 3.50 (s, 3H), 3.85-3.95 (m, 1H), 4.35-4.50 (m, 1H), 7.75 (dd, 2H), 8.00 (dd, 2H), 13.15 (s, 1H)

Example I55: R1= (1R*, 3R*)-3-hydroxycyclohexyl, R2= methyl, R3= 4-[N-(2-morpholin-4-yl-ethyl)]benzamide

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4-[5-((1R*, 3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide

Compound I55 was prepared by the procedure described in example I37.11 using I54 as a starting material.

The residue was purified by silica gel chromatography using a gradient of dichloromethane containing 0 to 4% methanol, to give the desired product.

Yield: 14%

¹H-NMR (400MHz, DMSO): δ ppm: 1.35-1.70 (m, 8H), 2.35-2.52 (m, 6H), 3.02-3.12 (m, 1H), 3.32-3.45 (m, 2H), 3.50-3.62 (m, 7H), 3.88-3.95 (m, 1H), 4.40 (d, 1H) 7.72 (dd, 2H), 7.92 (dd, 2H), 8.50 (s, 1H).

MS (m/z) / M+1= 446.

HPLC (uv purity, λ= 214 nm)= 96.6%

Example I56: R1= trans-4-hydroxycyclohexyl, R2 = methyl, R3= 4-benzoic acid

4-[5-(trans-4-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzoic acid

To a solution of I48 (1.9 mmol, 600 mg) in ethanol (15 ml) and isopropanol (15 ml), a solution of KOH [6N] (5.7 mmol, 960 μl) was added and stirred at reflux during 7H. The mixture was acidified to pH = 6-7 with a solution of HCl and then concentrated under reduced to give the carboxylic acid derivative I56.

¹H-RMN (400MHz, DMSO) δ ppm: 1.22-1.32 (m, 2H), 1.60-1.80 (b, 2H), 1.90-2.04 (m, 4H), 3.41-3.50 (m, 1H), 4.00 (s, 3H), 7.80-7.90 (m, 2H), 8.00-8.10 (m, 2H), 11.00 (s, 1H).

Example I57: R1= trans-4-hydroxy-cyclohexyl, R2= methyl, R3= 4-(N-2-hydroxy-1,1-dimethyl-ethyl)benzamide

4-[5-(trans-4-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-N-(2-hydroxy-1,1-dimethyl-ethyl)-

benzamide

Compound I57 was prepared by the procedure described in example I37.11 using I56 as a starting material. The residue

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was purified by silica gel chromatography using a gradient of dichloromethane containing 0 to 9% methanol, to give the expected product.

Yield: 20%

5 ^1H -NMR (400MHz, DMSO): δ ppm: 1.15-1.45 (m, 10H), 1.70-1.90 (m, 4H), 2.50-2.60 (m, 1H), 3.40-3.55 (m, 6H), 4.50 (d, 1H) 4.85 (d, 1H), 7.60 (s, 1H), 7.70 (dd, 2H), 7.89 (dd, 2H).

MS (m/z) / M+1= 405

HPLC (uv purity, λ = 214 nm)= 99.9%

10

Example I58: R1= (1R*, 3R*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-(N-2-hydroxy-1,1-dimethyl-ethyl)benzamide
4-[5-((1R*, 3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-N-(2-hydroxy-1,1-dimethyl-ethyl)-benzamide

15

Compound I58 was prepared by the procedure described in example I55 using appropriate intermediates and reagents (I54 and 1,1-dimethyl-2-ethanolamine).

20

The residue was purified by silica gel chromatography using a gradient of dichloromethane containing 0 to 5% methanol, to give the desired product.

Yield: 58%

25

^1H -NMR (400MHz, DMSO): δ ppm: 1.20-1.70 (m, 14H), 3.02-3.12 (m, 1H), 3.40-3.60 (m, 5H), 3.85-3.95 (m, 1H), 4.40 (d, 1H), 4.85 (d, 1H), 7.60 (s, 1H), 7.68 (dd, 2H), 7.85 (dd, 2H)

MS (m/z) / M+1= 405

HPLC (uv purity, λ = 214 nm)= 94.4%

30

Example I59: (1R*, 3R*)-3-hydroxycyclohexyl, R2= methyl, R3= 4-(N-tert-butyl)-benzamide
N-tert-Butyl-4-[5-((1R*, 3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide

35

Compound I59 was prepared by the procedure described in example I55 using appropriate intermediates and reagents (I54 and isobutylamine). The residue was purified by silica gel chromatography using a gradient of dichloromethane containing 0 to 10%.

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Yield: 33%

¹H-NMR (400MHz, DMSO): δ ppm: 1.30-1.70 (m, 17H), 3.02-3.12 (m, 1H), 3.50 (s, 3H), 3.85-3.95 (m, 1H), 4.40 (d, 1H), 7.68 (dd, 2H), 7.80-7.90 (m, 3H).

5 MS (m/z) / M+1= 389

HPLC (uv purity, λ = 214 nm)= 94.1%

Example I60: R1= (1R*, 3R*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-[N-(1,1-dimethyl-3-oxo-butyl)]-benzamide
10 N-(1,1-dimethyl-3-oxo-butyl)-4-[5-(1R*, 3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide

To a suspension of diacetoamine hydrogenoxalate (3 mmol, 616 mg) in DMF (6 ml) under nitrogen atmosphere, morpholine
15 resin [3.47 mmol/g] (7 mmol, 2 g) was added, and the mixture was stirred at room temperature during 30 minutes and then filtered. A mixture of acid I54 (0.6 mmol), the filtrate, N,N-diisopropylethylamine (1.32 mmol, 227 μ l), benzotriazol-1-yloxytris(dimethylamino) phosphonium hexafluorophosphate
20 (0.72 mmol, 318 mg), 1-hydroxy-7-azabenzotriazole (0.3 mmol, 82 mg) was stirred at room temperature during 4H. The mixture was concentrated and then diluted in dichloromethane. The organic layer was washed with a saturated solution of ammonium chloride, a saturated solution of NaHCO₃,
25 with water, brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography using a gradient of dichloromethane containing 0 to 8% methanol. The compound was purified by HPLC (Kromasil C18 column) eluting with
30 acetonitrile/water 95/5 to 5/95 to give the desired product.
Yield: 10%

¹H-NMR (400MHz, DMSO): δ ppm: 1.30-1.70 (m, 14H), 2.05 (s, 3H), 2.92-3.10 (m, 3H), 3.50 (s, 3H), 3.85-3.95 (m, 1H), 4.40 (d, 1H), 7.68 (dd, 2H), 7.85 (dd, 2H), 7.95 (s, 1H).

35 MS (m/z) / M+1= 431

HPLC (uv purity, λ = 214 nm)= 99.3%

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Example I61: R1= (1R*,3R*)-3-hydroxy-cyclohexyl, R2= methyl,
R3= 4-[N-(2-cyano-1,2,2-trimethyl-ethyl)]-benzamide
N-(2-Cyano-1,2,2-trimethyl-ethyl)-4-[5-((1R*, 3R*)-3-
hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-
5 [1,3,4]thiadiazol-2-yl]-benzamide

Compound I61 was prepared by the procedure described in
example I55 using appropriate intermediates and reagents
(I54 and 2-amino-2,3-dimethylbutanenitrile).

The residue was purified by silica gel chromatography using
10 a gradient of cyclohexane containing 0 to 70% ethylacetate,
to give the title product.

Yield: 8%

¹H-NMR (400MHz, DMSO): δ ppm: 0.95 (d, 3H), 1.10 (d, 3H),
1.30-1.70 (m, 11H), 2.45-2.65 (m, 1H), 3.00-3.10 (m, 1H),
15 3.50 (s, 3H), 3.85-3.95 (m, 1H), 4.40 (d, 1H), 7.70 (dd,
2H), 7.90 (d, 2H), 8.65 (s, 1H).

MS (m/z) / M+1= 428

HPLC (uv purity, λ= 214 nm)= 99.4%

20 Example I62: R1= (1R*, 3R*)-3-hydroxy-cyclohexyl, R2=
methyl, R3= 4-(N-1-methoxycarbonyl-cyclopropyl)-benzamide
1-{4-[5-((1R*,3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-
dihydro-[1,3,4]thiadiazol-2-yl]-benzoylamino}-
cyclopropanecarboxylic acid methyl ester

25 Compound I62 was prepared by the procedure described in
example I37.24 using appropriate intermediates and reagents
(I55 and 1-aminocyclopropane-1-carboxylic acid, methylester
hydrochloride)

The residue was purified once by silica gel chromatography
30 using a gradient of dichloromethane containing 0 to 10%
methanol and by HPLC (Hypersil Column) with a gradient
acetonitrile/water 95/5 to 5/95 to afford the desired
product.

Yield: 32%

35 ¹H-NMR (400MHz, DMSO): δ ppm: 1.12-1.20 (m, 2H), 1.33-1.50
(m, 4H), 1.50-1.70 (m, 6H), 3.03-3.12 (m, 1H), 3.52 (s, 3H),

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3.60 (s, 1H), 3.89-3.98 (m, 1H), 4.40 (d, 1H), 7.72 (dd, 2H), 7.94 (d, 2H), 9.17 (s, 1H).

MS (m/z) / M+1= 431

HPLC (uv purity, λ = 214 nm)= 97.9%

5

**Example I63: R1= cyclopentyl, R2= methyl, R3= 4-benzamide
4-(5-Cyclopentylimino-4-methyl-4,5-dihydro-[1,3,4]
thiadiazol-2-yl)-benzamide**

To a solution of compound I42 (0.53 mmol, 150 mg) in ethanol
10 (17 ml), a solution of Na₂CO₃ [3N] (5.6 mmol, 1.88 ml) and a
solution of H₂O₂ at 30% in water (1.54 ml) were added. The
solution was stirred overnight at room temperature. To the
mixture, was added a solution of H₂O₂ at 30% in water (770
15 μ l) and the solution was allowed to stir at room temperature
during two days (reaction to completion). The resultant
mixture was concentrated by distillation of the solvent and
the crude material was precipitated in water. The
precipitate was filtered off, washed several times with
water and dried to give the pure product.

20 Yield= 53.4%

¹H-NMR (400MHz, DMSO) δ ppm: 1.43-1.95 (m, 8H), 3.18-3.28
(m, 1H), 3.52 (s, 3H), 7.44 (s, 1H), 7.70 (dd, 2H), 7.95
(dd, 2H), 8.05 (s, 1H).

MS (m/z) / M+1= 303

25 HPLC (uv purity, λ = 214 nm)= 98.04%

**Example I64: R1= cycloheptyl, R2= methyl, R3= 4-benzamide
4-(5-Cycloheptylimino-4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl)-benzamide**

30 Compound I64 was prepared by the procedure described in
example I63 using appropriate intermediates (I43) and
reagents.

The precipitate was filtered, washed several times with
water and dried to give the pure product.

35 Yield= 59.88%

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¹H-NMR (400MHz, DMSO) δ ppm: 1.40-1.83 (m, 12H), 2.78-2.85 (m, 1H), 3.52 (s, 3H), 7.44 (s, 1H), 7.72 (dd, 2H), 7.97 (dd, 2H), 8.07 (s, 1H).

MS (m/z) / M+1= 331

5 HPLC (uv purity, λ= 214 nm)= 98.98%

Example I65: R1= 4-fluoro-phenyl, R2= methyl, R3= 4-benzamide

10 **4-[5-(4-Fluoro-phenylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide**

Compound I65 was prepared by the procedure described in example I63 using appropriate intermediates I44 and reagents.

15 The precipitate was filtered, washed several times with water and dried to give the pure product.

Yield= 72.43%

¹H-NMR (400MHz, DMSO) δ ppm: 3.72 (s, 3H), 7.02-7.40 (m, 2H), 7.15-7.24 (m, 2H), 7.44 (s, 1H), 7.72 (dd, 2H), 7.95 (dd, 2H), 8.05 (s, 1H).

20 MS (m/z) / M+1= 329

HPLC (uv purity, λ= 214 nm)= 97.7%

Example I66: R1= 3-hydroxy-phenyl, R2= methyl, R3= 4-benzamide

25 **4-[5-(3-Hydroxy-phenylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide**

Compound I66 was prepared by the procedure described in example I63 using appropriate intermediates (I45) and reagents.

30 The precipitate was filtered, washed several times with water and dried to give the pure product.

Yield= 59.84%

35 ¹H-NMR (400MHz, DMSO) δ ppm: 3.70 (s, 3H), 6.44-6.52 (m, 3H), 7.18 (t, 1H), 7.44 (s, 1H), 7.75 (dd, 2H), 7.97 (dd, 2H), 8.06 (s, 1H), 9.40 (s, 1H).

MS (m/z) / M+1= 327

HPLC (uv purity, λ= 214 nm)= 99.68%

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Example I67: R1= 4-fluoro-3-benzoic acid, R2= methyl, R3= 4-benzamide

5 5- [5- (4-Carbamoyl-phenyl) -3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino]-2-fluoro-benzoic acid

Compound I67 was prepared by the procedure described in example I63 using appropriate intermediate (I46) and reagents.

10 The precipitate was filtered, washed several times with water and dried to give the pure product.

Yield= 44.41%

¹H-NMR (400MHz, DMSO) δ ppm: 3.72 (s, 3H), 7.25-7.32 (m, 2H), 7.43-7.50 (m, 2H), 7.78 (dd, 2H), 7.95 (dd, 2H), 8.05 (s, 1H), 13.30 (b, 1H).

15 MS (m/z) / M+1= 373

HPLC (uv purity, λ = 214 nm)= 90.52%

Example I68: R1= trans-4-methyl-cyclohexyl, R2= methyl, R3= 4-benzamide

20 4- [4-Methyl-5- (trans-4-methyl-cyclohexylimino) -4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide

Compound I68 was prepared by the procedure described in example I63 using appropriate intermediates (I47b) and reagents.

25 The precipitate was filtered, washed several times with water and dried to give the pure product.

Yield= 52.53%

30 ¹H-NMR (400MHz, DMSO) δ ppm: 0.90 (d, 3H), 0.95-1.08 (m, 2H), 1.30-1.45 (m, 3H), 1.67-1.85 (m, 4H), 2.50-2.60 (m, 1H), 3.52 (s, 3H), 7.44 (s, 1H), 7.72 (dd, 2H), 7.95 (dd, 2H), 8.05 (s, 1H).

MS (m/z) / M+1= 331

HPLC (uv purity, λ= 214 nm)= 99.7%

35 Example I69: R1= trans-4-hydroxy-cyclohexyl, R2= methyl, R3= 4-benzamide

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4- [5- (trans-4-Hydroxy-cyclohexylimino) -4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl] -benzamide

To a suspension of I48 (0.477 mmol, 150 mg) in ethanol (17 ml), a solution of Na₂CO₃ [3N] (5.1 mmol, 1.7 ml) and a
5 solution of H₂O₂ at 30% in water (1.4 ml) were added and the mixture was stirred overnight at room temperature. This mixture was poured into water before extraction with ethyl acetate. The organic layer was washed with water and with a
10 saturated solution of NaCl, dried over magnesium sulfate, filtered and distilled to give a residue which was purified by silica gel chromatography (eluted with a gradient of dichloromethane/methanol 100/0 to 98/2) to afford the pure product.

Yield= 31%

15 ¹H-NMR (400MHz, DMSO) δ ppm: 1.20-1.42 (m, 4H), 1.75-1.90 (m, 4H), 2.50-2.63 (m, 1H), 3.40-3.52 (m, 1H), 3.50 (s, 3H), 4.55 (s, 1H), 7.44 (s, 1H), 7.72 (dd, 2H), 7.98 (dd, 2H), 8.07 (s, 1H).

MS (m/z) / M+1= 332/333

20 HPLC (uv purity, λ= 214 nm)= 97.3%

Example I70: R1= bicyclo[2.2.1]hept-2-yl, R2= methyl, R3= 4-benzamide

25 4- [5- (Bicyclo[2.2.1]hept-2-ylimino) -4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl] -benzamide

Compound I70 was prepared by the procedure described in example I69 using appropriate intermediates (I49) and reagents.

30 The residue was purified by silica gel chromatography (eluted with a gradient of dichloromethane/methanol 100/0 to 90/10) to afford the desired product.

Yield= 66%

35 ¹H-NMR (400MHz, DMSO) δ ppm: 1.10-1.25 (m, 3H), 1.28-1.40 (m, 1H), 1.40-1.67 (m, 4H), 2.10-2.18 (m, 1H), 2.25-2.32 (m, 1H), 2.70-2.80 (m, 1H), 3.52 (s, 3H), 7.50 (s, 1H), 7.72 (dd, 2H), 7.97 (dd, 2H), 8.10 (s, 1H).

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MS (m/z) / M+1= 329

HPLC (uv purity, λ = 214 nm)= 99.9%

Example I71: R1= (1R*,2R*)-2-hydroxy-cyclohexyl, R2= methyl,
5 R3= 4-benzamide

4- [5- ((1R*,2R*)-2-hydroxy-cyclohexylimino)-4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl]-benzamide

Compound I71 was prepared by the procedure described in
example I69 using appropriate intermediates (I50) and
10 reagents.

The residue was purified by silica gel chromatography
(eluted with a gradient of dichloromethane/methanol 100/0 to
90/10) to afford the pure product.

Yield= 44%

15 ¹H-NMR (400MHz, DMSO) δ ppm: 1.20-1.39 (m, 4H), 1.60-1.75
(m, 3H), 1.80-1.90 (m, 1H), 2.35-2.45 (m, 1H), 3.50 (s, 3H),
4.55 (s, 1H), 7.50 (s, 1H), 7.72 (dd, 2H), 7.96 (dd, 2H),
8.05 (s, 1H).

MS (m/z) / M+1=333

20 HPLC (uv purity, λ = 214 nm)= 97.4%

Example I72: R1= (1R*,2S*)-2-hydroxy-cyclohexyl, R2= methyl,
R3= 4-benzamide

4- [5- ((1R*,2S*)-2-Hydroxy-cyclohexylimino)-4-methyl-4,5-
25 dihydro- [1,3,4]thiadiazol-2-yl]-benzamide

To a suspension of I51 (0.16 mmol, 50 mg) in DMSO (100 μ l),
K₂CO₃ (0.022 mmol, 3 mg), a solution of H₂O₂ at 30% in water
(20 μ l) was added and the mixture was stirred overnight at
room temperature. To this mixture, water was added and the
30 solution was allowed to stir 15 minutes. The precipitate was
filtered off and dried under reduced pressure to give the
desired product.

Yield= 68%

35 ¹H-NMR (400MHz, DMSO) δ ppm: 1.25-1.38 (m, 2H), 1.40-1.80
(m, 6H), 2.85-2.90 (m, 1H), 3.57 (s, 3H), 3.60-3.68 (m, 1H),
4.10 (d, 1H), 7.40 (s, 1H), 7.70 (dd, 2H), 7.95 (dd, 2H),
8.05 (s, 1H).

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MS (m/z) / M+1= 333

HPLC (uv purity, λ = 214 nm)= 98.8%

**Example I73: R1= (1R*,3R*)-3-hydroxy-cyclohexyl, R2= methyl,
R3= 4-benzamide**

4-[5-((1R*,3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide

Compound I73 was prepared by the procedure described in example I69 using appropriate intermediates (I52-a) and reagents.

The mixture was concentrated under reduced pressure and stirred in water several hours, filtered and dried under vacuum to afford the desired product.

Yield= 70%

¹H-NMR (400MHz, DMSO) δ ppm: 1.30-1.70 (m, 8H), 3.10 (s, 1H), 3.52 (s, 3H), 3.93 (s, 1H), 4.42 (d, 1H), 7.43 (s, 1H), 7.70 (dd, 2H), 7.96 (dd, 2H), 8.05 (s, 1H).

MS (m/z) / M+1=333

HPLC (uv purity, λ = 214 nm)= 98.3%

Example I74: R1= (1R*,3S*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-benzamide

4-[5-((1R*,3S*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide

Compound I74 was prepared by the procedure described in example I69 using appropriate intermediates (I52-b) and reagents.

The mixture was concentrated under reduced pressure and stirred in water several hours, filtered and dried under vacuum to afford the desired product.

Yield= 83%

¹H-NMR (400MHz, DMSO) δ ppm: 1.05-1.30 (m, 4H), 1.65-1.78 (m, 2H), 1.78-1.88 (m, 1H), 1.95-2.05 (m, 1H), 3.40-3.58 (m, 4H), 4.60 (s, 1H), 7.45 (s, 1H), 7.70 (dd, 2H), 7.95 (dd, 2H), 8.05 (s, 1H).

MS (m/z) / M+1=333

HPLC (uv purity, λ = 214 nm)= 99.4%

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Example I74.1: R1= 3-oxo-cyclohexyl, R2= methyl, R3= 4-benzamide

4-[4-Methyl-5-(3-oxo-cyclohexylimino)-4,5-dihydro-
5 [1,3,4]thiadiazol-2-yl]-benzamide

To a solution of I74 (0.15 mmol, 50 mg) in dichloromethane (0.5 ml), tetrapropylammoniumperruthenate (0.5% mol, 3 mg), 4-methylmorpholine-N-oxide (0.22 mmol, 28 mg) and molecular sieve (500 mg/mol, 75 mg) were added and the mixture was
10 stirred at room temperature overnight. The mixture was filtered through a pad of silica gel (eluted with dichloromethane/methanol 100/0 to 95/5), the filtrate was concentrated under reduced pressure and washed with diethylether to afford the pure product.

15 Yield= 18%

¹H-NMR (400MHz, DMSO) δ ppm: 1.63-1.82 (m, 2H), 1.89-2.10 (m, 2H), 2.21-2.50 (m, 4H), 3.15-3.30 (m, 1H), 3.52 (s, 3H), 7.45 (s, 1H), 7.70 (dd, 2H), 7.98 (dd, 2H), 8.08 (s, 1H).

MS (m/z) / M+1=331

20 HPLC (uv purity, λ= 214 nm)= 98.7%

Example I75: R1= 3,3-difluoro-cyclohexyl, R2= methyl, R3= 4-benzamide

4-[5-(3,3-Difluoro-cyclohexylimino)-4-methyl-4,5-dihydro-
25 [1,3,4]thiadiazol-2-yl]-benzamide

To a solution of I52-b (0.318 mmol, 100 mg) in dichloromethane (1 ml) was added tetrapropylammonium perruthenate (0.5 %mol, 6 mg), 4-methylmorpholine-N-oxide (0.477 mmol, 56 mg) and molecular sieve (500 mg/mol, 160
30 mg). The mixture was stirred at room temperature for 3H, filtered through silica gel (eluted with cyclohexane/ethyl acetate 100/0 to 60/40) and concentrated under reduced pressure to afford 4-[4-Methyl-5-(3-oxo-cyclohexylimino)-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

35 Yield = 90%

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¹H-NMR (400MHz, DMSO) δ ppm: 1.60-1.80 (m, 2H), 1.87-2.10 (m, 2H), 2.21-2.30 (m, 3H), 2.55-2.60 (m, 1H), 3.15 (s, 1H), 3.52 (s, 3H), 7.82 (dd, 2H), 7.92 (dd, 2H).

To a solution of this ketone (0.288 mmol, 90 mg) in
5 dichloromethane (0.5 ml), a solution of deoxo-fluor (0.49 mmol, 90 µl) in dichloromethane (1 ml) and ethanol (0.346 mmol, 5 µl) was added and the mixture was stirred overnight at room temperature. The mixture was poured into a saturated solution of NaHCO₃ (pH=7), and the aqueous layer was
10 extrated with dichloromethane. The organic layer was washed with water and brine, dried with magnesium sulfate, filtered and concentrated under reduced pressure to give a residue wich was purified by silica gel chromatography (eluted with a gradient of cyclohexane/ethyl acetate 100/0 to 80/20) to
15 afford the pure di-fluoro compound : 4-[5-(3,3-Difluoro-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile

Yield = 12%

¹H-RMN (400MHz, DMSO) δ ppm: 1.40-1.55 (m, 2H), 1.78-1.90
20 (m, 4H), 1.95-2.09 (m, 1H), 2.15-2.28 (m, 1H), 2.80-2.90 (m, 1H), 3.55 (s, 3H), 7.82 (dd, 2H), 7.92 (dd, 2H).

To a solution of this di-fluoro derivative (0.036 mmol, 12 mg) in ethanol (1.6 ml) a solution of Na₂CO₃ [3N] (0.6 mmol, 200 µl), and a solution of H₂O₂ at 30% in water (150 µl) were
25 added and the mixture was stirred at 40°C overnight. Then, a solution of H₂O₂ at 30% in water (130 µl) was added and the solution was allowed to stir 12 h at 40°C. The mixture was concentrated under reduced pressure. The residue was stirred in water several hours, filtered, washed with ether and
30 dried under vaccum to give the desired compound.

Yield= 40%

¹H-NMR (400MHz, DMSO) δ ppm: 1.33-1.53 (m, 2H), 1.70-1.90 (m, 4H), 1.90-2.05 (m, 1H), 2.15-2.28 (m, 1H), 2.80-2.90 (m, 1H), 3.55 (s, 3H), 7.48 (s, 1H), 7.72 (dd, 2H), 7.96 (dd,
35 2H), 8.08 (s, 1H)

MS (m/z) / M+1=353

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HPLC (uv purity, $\lambda = 214$ nm) = 98.7%

Example I76: R1= (1R*,3R*)-3-fluoro-cyclohexyl, R2= methyl, R3= 4-benzamide

5 4-[5-((1R*,3R*)-3-Fluoro-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide

To a solution of I52-b (1.59 mmol, 500 mg) in dichloromethane (4 ml), 4-morpholinisulfurtrifluoride (3.18 mmol, 390 μ l) was added at -15°C dropwise under nitrogen
10 atmosphere. The mixture was warmed at room temperature during 30 minutes and poured into a saturated solution of NaHCO₃ (pH=7). The aqueous phase was extracted with dichloromethane. The organic layer was washed with water and brine, dried over magnesium sulfate, filtered and
15 concentrated under reduce pressure to give a residue wich was purified by silica gel chromatography (eluted with a gradient of cyclohexane/ethyl acetate 100/0 to 70/30) to afford 4-[5-(Cyclohex-3-enylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile and a mono-fluoro
20 intermediate (4-[5-((trans)-3-Fluoro-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile):

Yield= 14%

¹H-NMR (400MHz, DMSO) δ ppm: 1.40-1.50 (m, 1H), 1.58-1.85 (m, 6H), 1.92-2.05 (m, 1H), 2.95-3.05 (m, 1H), 3.55 (s, 3H),
25 4.95 (d, 1H), 7.83 (dd, 2H), 7.95 (dd, 2H).

To a solution of this fluoro intermediate (0.2 mmol, 65 mg) in ethanol (8.7 ml) a solution of Na₂CO₃ [3N] (2.61 mmol, 870 μ l) and a solution of H₂O₂ at 30% in water (705 μ l) were added and the mixture was stirred overnight at 40°C. A
30 solution of H₂O₂ at 30% in water (705 μ l) was added and the reaction was allowed to stir for 10h at 40°C. The mixture was concentrated under reduced pressure. The residue was stirred in water several hours, filtered, washed with ether and dried under vaccum to give the title product I76.

35 Yield= 58%

¹H-NMR (400MHz, DMSO) δ ppm: 1.35-1.52 (m, 1H), 1.52-1.90 (m, 6H), 1.90-2.08 (m, 1H), 2.93-3.08 (m, 1H), 3.55 (s, 3H),

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5.00 (d, 1H), 7.50 (s, 1H), 7.78 (dd, 2H), 7.99 (dd, 2H),
8.10 (s, 1H).

MS (m/z) / M+1= 335

HPLC (uv purity, λ = 214 nm)= 96.6%

5

Example I77: R1= 3-cyclohexene, R2= methyl, R3= 4-benzamide
4-[5-(Cyclohex-3-enylimino)-4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl]-benzamide

To a solution of 4-[5-(Cyclohex-3-enylimino)-4-methyl-4,5-
10 dihydro-[1,3,4]thiadiazol-2-yl]-benzonitrile from protocol
I76 (0.94 mmol, 280 mg) in ethanol (41 ml), a solution of
Na₂CO₃ [3N] (12.3 mmol, 4.1 ml), and a solution of H₂O₂ at
30% in water (3.33 ml) were added. The mixture was stirred
overnight at room temperature and concentrated under reduced
15 pressure. The residue was stirred in water several hours,
filtered, and dried under vacuum to afford the pure product.
Yield= 64%

¹H-NMR (400MHz, DMSO) δ ppm: 1.48-1.65 (m, 1H), 1.72-2.35
(m, 5H), 2.82-2.92 (m, 1H), 3.55 (s, 3H), 5.65 (t, 2H), 7.50
20 (s, 1H), 7.71 (dd, 2H), 7.95 (dd, 2H), 8.09 (s, 1H)

MS (m/z) / M+1= 315

HPLC (uv purity, λ = 214 nm)= 96.1%

Example I78: R1= (1R*,3R*)-3-hydroxy-cyclohexyl, R2= methyl,
25 R3= 4-(1H-tetrazol-5-yl)-phenyl
(1R*,3R*)-3-{3-Methyl-5-[4-(1H-tetrazol-5-yl)-phenyl]-3H-
[1,3,4]thiadiazol-2-ylideneamino}-cyclohexanol

To a solution of I52-a (1.27 mmol, 400 mg) in toluene (3
ml), sodium azide (1.65 mmol, 108 mg) and triethylamine
30 hydrochloride (1.65 mmol, 228 mg) were added and the mixture
was warmed at reflux during 24 hours. The reaction mixture
was cooled at room temperature, acidified with a solution of
HCl [0.1N], and then basified at pH=6-7 with a saturated
solution of NaHCO₃. The aqueous phase was extracted with
35 dichloromethane and the organic layer was washed with a
saturated solution of NaCl, dried over magnesium sulfate,
filtered and concentrated under reduced pressure. The

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residue was chromatographed on silica gel column using a gradient of dichloromethane containing from 0 to 20% methanol to afford the title compound.

Yield: 50%

5 $^1\text{H-NMR}$ (400MHz, DMSO): δ ppm: 1.30-1.70 (m, 8H), 3.00-3.15 (m, 1H), 3.50 (s, 3H), 3.85-3.98 (m, 1H), 4.40 (s, 1H), 7.75 (dd, 2H), 8.10 (d, 2H).

MS (m/z) / M+1 = 358

HPLC (uv purity, λ = 214 nm) = 99.9%

10

Example I79: R1= 3-(6-hydroxy)-benzoic acid, R2= methyl, R3= 4-chloro-phenyl

3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-hydroxy-benzoic acid

15 The title compound was prepared by the procedure described in example I3 using ethanol as solvent and appropriate intermediates and reagents. The residue was twice chromatographed on silica gel eluting with dichloromethane containing from 0 to 7% of methanol. The isolated product
20 was washed with water to afford the desired product.

Yield= 9.7%

$^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 3.62 (s, 3H), 6.80 (t, 1H), 7.12 (d, 1H), 7.40-7.46 (m, 3H), 7.59 (d, 2H).

MS (m/z) / M+1 = 362/364.

25 HPLC (uv purity, λ = 214 nm): 98.36%

Example I80 : R1= 3-benzoic acid, R2= methyl, R3= 4-cyano-phenyl

30 **3-[5-(4-cyano-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid**

A suspension of 1,3,4-thiadiazolium perchlorate (3c) (4.873 mmol, 1.70 g), 3-aminobenzoic acid (4.87 mmol, 0.668 g) and triethylamine (4.873 mmol, 0.679 ml) in ethanol (20 ml) was refluxed for 3.5h. On cooling, the solid formed was filtered
35 off and washed with cold EtOH and ether. The solid was dried under reduced pressure to give 1.25 g of the expected compound.

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Yield= 76.2%

¹H-NMR (400MHz, DMSO) δ ppm: 3.87 (s, 3H), 7.39-7.42 (m, 1H), 7.60-7.65 (m, 1H), 7.70 (s, 1H), 7.78-7.82 (m, 1H), 7.96-8.00 (d, 2H), 8.00-8.04 (d, 2H).

5 MS (m/z) / M+1 = 337/338

HPLC (uv purity, λ= 214 nm)= 93.22%

Example I80.1: R1= 3-benzoic acid, R2= methyl, R3= 4-benzamide

10 **3-[5-(4-carbamoyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid**

Concentrated sulfuric acid (19.8 mmol, 1.06 ml) and water (0.13 ml) were respectively added, at 0°C, to I80 (0.595 mmol, 0.200 g) and the reaction mixture was heated at 80°C
15 for 1h30. Then, ice was added to the mixture and the formed precipitate was filtered off and purified by chromatography on silica gel, eluting with a mixture of acetic acid/dichloromethane/methanol (1.5/85/13.5). The isolated product was triturated in methanol and the solid was
20 filtered off and dried under vacuum to give the title product.

Yield=34%

¹H-NMR (400MHz, DMSO) δ ppm: 3.76 (s, 3H), 7.30 (d, 1H), 7.46-7.55 (m, 2H), 7.62 (s, 1H), 7.67 (d, 1H), 7.80 (d, 2H),
25 7.99 (d, 2H), 8.09 (s, 1H), 12.90-13.02 (d, 1H).

MS (m/z) / M+1= 355/356

HPLC (uv purity, λ= 214 nm): 96.37%

Example I81: R1= 4-fluoro-3-benzoic acid, R2= methyl, R3= 4-(methylsulfonyl)-phenyl

30 **2-Fluoro-5-[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid**

I81 was prepared by the procedure described in example I4 (protocol A) with the appropriate reagents and using 1.0 eq
35 of triethylamine. The reaction mixture was concentrated and the residue was purified by silica gel chromatography

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eluting with dichloromethane and then a mixture of dichloromethane/ MeOH/AcOH (98 /1.8 /0.2).

Yield= 13%

¹H-NMR (400MHz, DMSO) δ ppm: 3.19 (s, 3H), 3.57 (s, 3H),
5 7.11-7.19 (m, 2H), 7.31-7.34 (m, 1H), 3.50 , 7.79 (d, 2H),
7.85 (d, 2H), 13.08-13.14 (b, 1H).

MS (m/z) / M+1 = 408/409

HPLC (uv purity, λ= 214 nm)= 98.3%

10 **Example I82: R1= 3-carboxylic acid cyclohexyl, R2= methyl, R3= 4-(methylsulfonyl)-phenyl**

3-[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-

[1,3,4]thiadiazol-2-ylideneamino]-cyclohexanecarboxylic acid

I82 was prepared by the procedure described in example I4
15 with the appropriate reagents and using 1.0 eq of triethylamine. The mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by silica gel chromatography eluting with CHCl₃/MeOH (93/7) to afford 15 mg of the desired product.

20 Yield= 1.52%

¹H-NMR (400MHz, DMSO) δ ppm: 1.02-1.24 (m, 4H), 1.58-1.70 (m, 3H), 1.80-1.86 (m, 1H), 2.12-2.19 (m, 1H), 2.44-2.52 (m, 1H), 3.06 (s, 3H), 3.36 (s, 3H), 7.70 (d, 2H), 7.82 (d, 2H), 11.82-11.90 (b, 1H).

25 MS (m/z) / M+1 = 395/396

HPLC (uv purity, λ= 214 nm): 98.76%

Example I83: R1= piperidin-1-yl, R2= methyl, R3= 4-(methylsulfonyl)-phenyl

30 **[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-piperidin-1-yl amine**

To a suspension of 1,3,4-thiadiazolium perchlorate (3b) (1.26 mmol, 0.5 g) in ethanol (6 ml) were added 1-aminopiperidine (2.5 mmol, 0.3 ml) then triethylamine (2.5
35 mmol, 0.4 ml) and the mixture was maintained at 70°C for 3 hours. The mixture was concentrated under reduced pressure. The residue was taken into dichloromethane, washed twice

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with water, concentrated under reduced pressure and purified by chromatography on silica gel (99:1 DCM/MeOH) to give 0.2 g of the title compound.

Yield = 45%.

5 $^1\text{H-NMR}$ (400MHz, CDCl_3) δ ppm: 1.46 (s, 2H), 1.68-1.71 (m, 4H), 2.77 (s, 4H), 3.07 (s, 3H), 3.65 (s, 3H), 7.81-7.83 (dd, 2H), 7.95-7.97 (dd, 2H).

MS (m/z) / M+1= 353.46.

HPLC (uv purity, λ = 214 nm)= 97.4%

10

Example I84: R1= tetrahydro-pyran-4-yl, R2= methyl, R3= 4-(methylsulfonyl)-phenyl

[5-(4-Methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-(tetrahydro-pyran-4-yl)-amine

15 To a suspension of 1,3,4-thiadiazolium perchlorate (3b) (0.7 mmol, 0.3 g) in ethanol (4 ml) were added 4-aminotetrahydropyran (1.4 mmol, 0.3 g) and triethylamine (3 mmol, 0.4 ml). The mixture was maintained for 3 hours at 70°C, concentrated under reduced pressure. The residue was
20 taken into dichloromethane, washed once with water, concentrated under reduced pressure and purified by chromatography on silica gel (99:1 DCM/MeOH) and washed with ethyl acetate and heptane to give 23 mg of the expected compound.

25 Yield= 30%.

$^1\text{H-NMR}$ (400MHz, CDCl_3) δ ppm: 1.68-1.85 (m, 4H), 2.88-2.95 (m, 1H), 3.07 (s, 3H), 3.47-3.57 (m, 2H), 3.65 (s, 3H), 4.01-4.06 (m, 2H), 7.81 (d, 2H), 7.97 (d, 2H).

MS (m/z) / M+1= 354.03

30 HPLC (uv purity, λ = 214 nm)= 100%.

Example I85: R1= 3-benzoic acid, R2= methyl, R3= 4-acetylamino-phenyl

35 3-[5-(4-Acetylamino-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid

A suspension of 1,3,4-thiadiazolium triflate (3d) (0.7 mmol, 0.3 g), triethylamine (2.1 mmol, 0.3 ml) and 3-

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acetamidobenzoic acid (0.6 mmol, 0.077 g) in ethanol (20 ml) was refluxed overnight. The mixture was concentrated under reduced pressure, purified by chromatography on silica gel (95:5 DCM /MeOH) and washed with MeOH to give 0.01 g of a white solid.

Yield= 5%

¹H-NMR (400MHz, DMSO) δ ppm: 2.06 (s, 3H), 2.71 (s, 3H), 7.26 (d, 1H), 7.47 (t, 1H), 7.60-7.70 (m, 6H), 10.18 (s, 1H).

MS (m/z) / M+1=368.95

HPLC (uv purity, λ= 214 nm)= 98%

Example I86: R1= trans-4-hydroxy-cyclohexyl, R2= methyl, R3= 4-acetylamino-phenyl

N-{4-[5-(trans-4-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide

A mixture of trans-4-aminocyclohexanol (0.28 mmol, 0.04 g), triethylamine (0.39 mmol, 0.06 ml) and 3-methyl-2-methylthio[1,3,4]thiadiazolium triflate (3d) (0.14 mmol, 0.05 g) were refluxed in ethanol (1ml) overnight. The mixture was concentrated under reduced pressure. The residue was taken into dichloromethane, washed once with water, concentrated under reduced pressure and purified by chromatography on silica gel (95:5 DCM /MeOH) to give 0.014g of a white solid.

Yield= 30%

¹H-NMR (400MHz, DMSO) δ ppm: 1.23-1.38 (m, 4H), 1.76-1.86 (m, 4H), 2.06 (s, 3H), 2.45-2.60 (m, 1H), 4.52 (d, 1H), 3.38-3.44 (m, 1H), 3.47 (m, 3H), 7.58 (d, 2H), 7.68 (d, 2H), 10.15 (s, 1H).

MS (m/z) / M+1 = 346.87

HPLC (uv purity, λ= 214 nm)= 98.5%

Example I87: R1= (1R*,3S*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-acetylamino-phenyl

N-{4-[5-((1R*,3S*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide

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I87 was prepared by the procedure described in example I86 (protocol A).

I87 was purified by chromatography on silica gel with AcOEt:Cyclohexane (80:20) and washed with MeOH to give 0.15g of the expected compound.

Yield= 20%

¹H-NMR (400MHz, DMSO) δ ppm: 1.10-1.30 (m, 4H), 1.55-2.00 (m, 4H), 2.10 (s, 3H), 2.60 (m, 1H), 3.50 (m, 1H), 3.50 (s, 3H), 4.6 (d, 1H), 7.60 (dd, 2H), 7.60 (dd, 2H), 10.15 (s, 1H).

M+1 = 347.1

Example I88: R1= (1R*,3R*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-acetylamino-phenyl

N-{4-[5-((1R*,3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide

To a suspension of I87 (0.4 mmol, 0.15 g) in DCM (2 ml) containing 4Å molecular sieves (0.216 g), N-methyl morpholine oxide (0.65 mmol, 0.76 g) under nitrogen atmosphere was added tetrapropylammonium perruthenate (10% mol equiv., 15 mg). The resulting mixture was stirred overnight, filtered, washed with methanol and concentrated under reduced pressure. The residue was purified by chromatography on silica gel with DCM:MeOH (95:5) to give 0.1 g of a ketone intermediate: N-{4-[4-Methyl-5-(3-oxo-cyclohexylimino)-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide

Yield= 71%

¹H-NMR (400MHz, DMSO) δ ppm: 1.25 (m, 1H), 1.60-1.75 (m, 2H), 1.85-2 (m, 2H), 2.05 (s, 3H), 2.3 (m, 3H), 3.15 (m, 1H), 3.5 (s, 3H), 7.55 (dd, 2H), 7.70 (dd, 2H), 10.15 (s, 1H).

To a solution of this ketone intermediate (0.15 mmol, 0.05 g) in THF (2 ml) at -70°C under nitrogen atmosphere was added a 1M solution of L-Selectride in THF (0.2 mmol, 0.2 mL). The resulting mixture was allowed to warm up to room temperature over 1 hour, diluted with dichloromethane, washed with water and concentrated under reduced pressure.

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The residue was purified by chromatography on silica gel with AcOEt:Cyclohexane (80:20) to give 30 mg of the expected product.

Yield= 60%

5 $^1\text{H-NMR}$ (400MHz, CDCl_3) δ ppm: 1.25-1.30 (m, 3H), 1.72-1.78 (m, 5H), 2.20 (s, 3H), 3.11-3.14 (m, 1H), 3.58 (s, 3H), 4.13 (m, 1H), 7.20 (s, 1H), 7.52-7.60 (m, 4H).

MS (m/z) / M+1= 347.21

HPLC (uv purity, λ = 214 nm)= 98%

10

Example I89 : R1= (1R*,3R*)-3-hydroxy-cyclohexyl, R2= methyl, R3= 4-acetylamino-pyridin-3-yl

N-{5-[5-((1R*,3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-pyridin-2-yl}-acetamide

15 The compound I89 was prepared by the procedure described in example I4 (protocol A).

To a suspension of 1,3,4-thiadiazolium perchlorate (3e) (0.5 mmol, 2 g) in ethanol (20 ml) were added triethylamine (1.5 mmol, 2 ml) followed by 3-aminocyclohexanol (0.8 mmol, 0.9 ml) and the mixture was maintained at 70°C overnight, concentrated under reduced pressure. The residue was taken into dichloromethane, washed twice with water, concentrated under reduced pressure and purified by chromatography on silica gel (20:80 cyclohexane /EtOAc) to give 0.03g of a white solid.

25

Yield= 17%

$^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 1.37-1.65 (m, 8H), 2.11 (s, 3H), 3.03-3.08 (m, 1H), 3.50 (s, 3H), 3.91-3.92 (m, 1H), 4.41 (d, 1H), 8.01-8.03 (dd, 1H), 8.17 (d, 1H), 8.55 (d, 1H), 10.75 (s, 1H).

30

MS (m/z) / M+1= 348.3

HPLC (uv purity, λ = 214 nm)= 99.2%

Example I90: R1= 3-cyano-phenyl, R2= methyl, R3= 4-chloro-phenyl

35

3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzonitrile

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To a suspension of I6.11 (4.14 mmol, 1.43 g) in pyridin (20 mL) was added benzoyl chloride (8.28 mmol, 964 μ L). The mixture was heated at reflux for 2 days.

The solvent was concentrated under reduced pressure, the reaction mixture was retaken in an aqueous solution of NaHCO₃ and the crude product was extracted with dichloromethane. The compound was purified by chromatography on silica gel (eluted with cyclohexane/ethyl acetate: 80/20 to 70/30) to give 1.25 g of the expected compound (92%).

¹H-NMR (400 MHz, DMSO) δ ppm: 3.8 (s, 3H), 7.40 (d, 1H), 7.48 (s, 1H), 7.52-7.60 (m, 4H), 7.73 (d, 2H).

MS (m/z) / M+1 = 327/329

HPLC (uv purity, λ = 245nm) = 99.4%

Example I90.1: R1 = 3-(1H-Tetrazol-5-yl)-phenyl, R2 = methyl, R3 = 4-chloro-phenyl

[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene] - [3-(1H-tetrazol-5-yl)-phenyl] - amine

A mixture of I90 (1.22 mmol, 0.4 g), sodium azide (1.59 mmol, 0.1 g) and triethylamine hydrochloride (1.59 mmol, 0.22 g) in toluene (7 mL) was heated at 90°C with stirring under nitrogen atmosphere. After cooling, the reaction mixture was poured in water and extracted with dichloromethane. To the aqueous layer, aqueous HCl 0.1N was added until the pH is acidic (CAUTION! This has to be done under a well ventilated hood). The precipitate was filtered, washed with ether and the resulting compound was cristallized in dichloromethane containing few drops of methanol to give 0.1 g of the desired compound

Yield: 24%

¹H-NMR (400 MHz, DMSO) δ ppm: 3.8 (s, 3H), 7.28 (d, 1H), 7.55 (d, 2H), 7.60 (t, 1H), 7.70-7.77 (m, 4H)

MS (m/z) / M+1 = 370/372

HPLC (uv purity, λ = 245 nm) = 99.7%

Example I90.2: R1 = 3-(N-Hydroxycarbamimidoyl)-phenyl, R2 = methyl, R3 = 4-chloro-phenyl

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3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-N-hydroxy-benzamidine

To a mixture of I90 (1.53 mmol, 0.5 g) and hydroxylamine hydrochloride (2.29 mmol, 0.156 g) in ethanol (13 mL) was added sodium hydroxyde (2.29 mmol, 0.09 g) dissolved in the minimum of water. The reaction mixture was heated at reflux for 24h with stirring. After cooling, the precipitate is filtered, washed with ethanol and dried under vacuum at 45°C to give 0.54 g of the desired compound

Yield: 98%

¹H-NMR (400 MHz, DMSO) δ ppm: 3.8 (s, 3H), 5.76 (bs, 2H), 7.05 (dd, 1H), 7.34-7.4 (m, 3H), 7.54 (d, 2H), 7.70 (d, 2H), 9.6 (s, 1H).

MS (m/z) / M+1 = 360/362

HPLC (uv purity, λ = 245 nm) = 97.3%

Example I90.3: R1 = 3-(5-hydroxy-[1,2,4]oxadiazol-3-yl)-phenyl, R2 = methyl, R3 = 4-chloro-phenyl

3-{3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-phenyl}-[1,2,4]oxadiazol-5-ol

A mixture of I90.2 (2.78 mmol, 0.1 g) and 1,1'-carbonyldiimidazole (5.56 mmol, 0.9 g) in anhydrous THF (2 mL) was heated at reflux for 5h. After cooling, the reaction mixture was concentrated and poured in water.

Dichloromethane was added and the precipitate was filtered and washed with methanol. The resulting mixture was purified by chromatography on silica gel (eluent dichloromethane/methanol: 98/2 + 1% acetic acid) to give 0.03 g of the desired product.

Yield: 28%

¹H-NMR (400 MHz, DMSO) δ ppm: 3.8 (s, 3H), 7.20 (dt, 1H), 7.50-7.55 (m, 5H), 7.70 (d, 2H).

MS (m/z) / M+1 = 386/388

HPLC (uv purity, λ = 245 nm) = 98.2%

EXAMPLE I: PROTOCOL C

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Example I91: R1= cyclohexyl, R2= methyl, R3= 3-methyl-4-bromo-phenyl

5 [5-(4-Bromo-3-methyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine

I91 was prepared by the procedure described in example I18 (Protocol C) using appropriate intermediates and reagents.

Yield= 50.4 %

10 ¹H-NMR (400MHz, CDCl₃) δ ppm: 1.21-1.51 (m, 5H), 1.64-1.70 (m, 1H), 1.78-1.89 (m, 4H), 2.38 (s, 3H), 2.56-2.64 (m, 1H), 3.55 (s, 3H), 7.28 (d, 1H), 7.47 (s, 1H), 7.54 (d, 1H).

MS (m/z) / M+1= 366/368

15 Example I91.1: R1= cyclohexyl, R2= methyl, R3= 3-methyl-4-cyano-phenyl

4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methyl-benzonitrile

20 To a solution of I91 (7.370 mmol, 2.7 g) in N-methyl-2-pyrrolidone (17ml), copper cyanide (13.267 mmol, 1.19 g) was added and the mixture was heated at reflux for 3h. The mixture was cooled at room temperature, basified with a solution of aqueous ammonia (2N) and stirred 10h at room temperature. The suspension was then filtered through Celite and the aqueous layer was extracted with ethyl acetate,

25 washed with water and brine, dried (MgSO₄), filtered and then concentrated under reduced pressure. The residue was purified by chromatography on silica gel, eluting with a gradient of dichloromethane containing from 0 to 1% of methanol.

30 Yield= 54.8

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.22-1.59 (m, 5H), 1.64-1.67 (m, 1H), 1.77-1.87 (m, 4H), 2.57-2.67 (m, 4H), 3.60 (s, 3H), 7.52 (d, 1H), 7.56 (s, 1H), 7.63 (d, 1H).

35 Example I91.2: R1= cyclohexyl, R2= methyl, R3= 3-methyl-4-benzamide

4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methyl-benzamide

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To a solution of I91.1 (0.320 mmol, 0.1 g) in ethanol (17 ml), an aqueous solution of sodium carbonate 3N (3.424 mmol, 1.14 ml) then a solution of hydrogen peroxide (5.60 ml) were added. The suspension was stirred for 2 days at room temperature, then heated at 40°C for 8h. The mixture was poured into a solution of Na₂S₂O₅ and evaporated to dryness then the crude material was diluted with water and extracted with dicloromethane. The organic layer was washed with water and brine, dried over MgSO₄, filtered and concentrated under reduced pressure.

Yield: 70%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.22-1.51 (m, 5H), 1.60-1.68 (m, 1H), 1.81-1.91 (m, 4H), 2.52 (s, 3H), 2.59-2.69 (m, 1H), 3.60 (m, 3H), 5.64-5.83 (b, 2H), 7.49 (s, 2H), 7.48 (s, 1H).

MS (m/z) / M+1= 331/332.

HPLC (uv purity, λ= 214 nm): 97.28%

Example I92: R1= cyclohexyl, R2= methyl, R3= 4-bromo-3-methoxy-phenyl

[5-(4-Bromo-3-methoxy-phenyl)-3-methyl-2,3-dihydro-[1,3,4]thiadiazol-2-yl]-cyclohexyl-amine

To a mixture of 3-hydroxybenzoic acid (14.480 mmol, 2 g) in acetic acid (14.5 ml) and sulfuric acid (1.5 ml) at 50°C, a solution of bromine (15.204 mmol, 0.780 ml) in acetic acid (7.2 ml) was added and stirred 30 min at 100°C. The reaction was allowed to room temperature and diluted with water. The aqueous layer was extracted with ethylacetate, washed with water and brine, dried (MgSO₄), filtered and concentrated under reduced pressure to give the 4-Bromo-2-hydroxy-benzoic acid (yield =100%).

To a solution of 4-bromo-3-hydroxybenzoic acid (14.480 mmol, 2.600 g) in acetone (180 ml), potassium carbonate (62.988 mmol, 8.710 g) and dimethylsulfate (31.422 mmol, 2.970 ml) were added. The reaction was stirred at room temperature for 30 min and evaporated to dryness. The residue was then diluted with water and extracted with ethylacetate. The collected organic layer was washed with water and brine,

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dried (MgSO₄), filtered and concentrated under reduced pressure. 4-Bromo-3-methoxy-benzoic acid methyl ester was isolated by chromatography on silica gel eluting with cyclohexane containing from 0 to 20% ethylacetate (yield=

5 47%).

To a solution of 4-Bromo-3-methoxy-benzoic acid methyl ester (6.875 mmol, 1.676 ml) in a mixture 1/1 of THF/ MeOH (15ml), lithium hydroxyde (7.553 mmol, 0.180 g) was added and the reaction was stirred at room temperature overnight before

10 distillation of volatiles. The residue was diluted with water, acidified with a solution of HCl (1N) and stirred for 1h. The formed precipitate was filtered off, washed with water and petroleum ether to give 4-Bromo-3-methoxy-benzoic acid (Yield = 56%).

15 The title compound was prepared by procedure as described in example I17 (protocol C) starting from 4-Bromo-3-methoxy-benzoic acid. In this particular case, methyltrifluoromethanesulfonate (1.2eq) was added once and the basic aqueous layer was extracted with DCM. The crude

20 was chromatographed on silica gel eluting with cyclohexane containing from 0 to 10% ethylacetate. The oil obtained was triturated in diethylether and the formed white solid was isolated by filtration.

Yield = 26% (overall, the 2 steps).

25 ¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.46 (m, 5H), 1.60-1.68 (m, 1H), 1.77-1.88 (m, 4H), 2.58-2.68 (m, 1H), 3.59 (s, 3H), 3.96 (s, 3H), 7.02 (d, 1H), 7.22 (s, 1H), 7.53 (d, 1H)

Example I92.1: R1= cyclohexyl, R2= methyl, R3= 3-methoxy-4-

30 **benzamide**

4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-benzamide

I92 was reacted with copper cyanide by the procedure described in example I91-1 and the formed intermediate was

35 transformed to I92.1 following the following protocol:

To a heterogeneous solution of this material (0.9134 mmol, 0.300 g) in ethanol (50 ml), a solution of sodium carbonate (3N) (9.773 mmol, 3.258 ml) and hydrogen peroxide (13.3 ml)

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were added and the reaction was heated at 40°C for 1.5 days. The mixture was poured into a saturated solution of $\text{Na}_2\text{S}_2\text{O}_5$ and the solution was concentrated under reduced pressure. The residue was diluted with water, extracted with dichloromethane and the organic layer was washed with water and brine, dried over MgSO_4 , filtered and then evaporated to dryness. The crude material was purified by chromatography on silica gel eluting with dichloromethane containing from 0 to 4% methanol.

10 Yield: 25%

^1H -NMR (400MHz, CDCl_3) δ ppm: 1.20-1.50 (m, 5H), 1.76-1.88 (m, 4H), 2.59-2.69 (m, 1H), 3.60 (s, 3H), 4.02 (s, 3H), 5.80-5.90 (b, 1H), 7.25 (d, 1H), 7.34 (s, 1H), 7.62-7.67 (b, 1H), 8.23 (d, 1H).

15 MS (m/z) / M+1= 347/348

HPLC (uv purity, λ = 214 nm): 97.61%

Example I92.2: R1= cyclohexyl, R2= methyl, R3= 3-hydroxy-4-benzamide

20 **4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-hydroxy-benzamide**

To a mixture of I92.1 and n-tetrabutylammonium iodide (0.433 mmol, 0.160 g) in anhydrous dichloromethane (2 ml) under nitrogen atmosphere at -78°C, a solution of BCl_3 1N in dichloromethane (0.433 mmol, 0.433 ml) was added and the reaction mixture was allowed to stir at -78°C for 10 min followed by 2h at 0°C and 1h30 at room temperature. Then, a solution of BCl_3 1N in dichloromethane (0.433 mmol, 0.433 ml) was added. After an additionnal 1h30 of stirring at room temperature, the reaction was quenched with water and basified with a saturated solution of sodium bicarbonate before extraction with dichloromethane. The organic layer was washed with brine, dried over MgSO_4 , filtered and evaporated to dryness. The residue was chromatographed on silica gel eluting with dichloromethane containing from 0 to 4% of methanol to give the desired product.

35 Yield= 26%

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¹H-NMR (400MHz, CDCl₃) δ ppm: 1.21-1.50 (m, 5H), 1.63-1.70 (m, 1H), 1.80-1.90 (m, 4H), 2.58-2.68 (m, 1H), 3.60 (s, 3H), 5.70-6.20 (b, 2H), 7.18 (s, 1H), 7.24 (d, 1H), 7.38 (d, 1H), 12.25 (s, 1H).

5 MS (m/z) / M+1= 333/334

HPLC (uv purity, λ= 214 nm): 96.54%

Example I93: R1= cyclohexyl, R2= methyl, R3= 3-nitro-4-methoxycarbonyl-phenyl

10 **4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-nitro-benzoic acid methyl ester**

I93 was prepared by the procedure described in example I21 (protocol C) using the appropriate intermediates and reagents. In this particular case, triethylamine was not
15 used and the expected product was isolated by filtration after treatment with a saturated solution of NaHCO₃.

Yield= 77%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.48 (m, 5H), 1.64-1.70 (m, 1H), 1.80-1.90 (m, 4H), 5.58-5.66 (m, 1H), 3.63 (s, 3H),
20 3.82 (s, 3H), 7.80-7.84 (m, 2H), 8.11 (s, 1H).

Example I93.1: R1= cyclohexyl, R2= methyl, R3= 3-amino-4-methoxycarbonyl-phenyl

25 **2-Amino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester**

To a solution of I93 (1.328 mmol, 0.500 g) in ethanol (20 ml), tin chloride dihydrate (6.641 mmol, 1.495 g) was added and the mixture was heated at reflux for 5h then allowed to stand at room temperature overnight. The mixture was
30 evaporated to dryness and the crude material was basified with a saturated solution of sodium carbonate before extraction with dichloromethane. The organic layer was washed with brine, dried over MgSO₄, filtered and concentrated under vacuum. The residue was chromatographed on
35 silica gel eluting with dichloromethane containing from 0 to 2% of methanol to afford the desired compound.

Yield: 65%

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¹H-NMR (400MHz, CDCl₃) δ ppm: 1.21-1.49 (m, 5H), 1.60-1.69 (m, 1H), 1.80-1.90 (m, 4H), 2.58-2.67 (m, 1H), 3.60 (s, 3H), 3.89 (s, 3H), 5.77-5.83 (b, 2H), 7.88-7.92 (m, 2H), 7.89 (d, 1H).

5 MS (m/z) / M+1= 347/349

HPLC (uv purity, λ= 214 nm): 98.31%

Example I93.2: R1= cyclohexyl, R2= methyl, R3= 3-acetylamino-4-methoxycarbonyl-phenyl

10 **2-Acetylamino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester**

To a suspension of I93.1 (0.144 mmol, 0.05 g) in anhydrous toluene (2 ml) at 0°C, triethylamine (0.150 mmol, 0.015 ml) and acetic anhydride (0.160 mmol, 0.015 ml) were added. The
15 reaction was allowed to stir at room temperature for 3 days and 5.4 more equivalents of acetic anhydride and triethylamine were added. After 2 days of stirring at room temperature the mixture was evaporated to dryness and the residue was chromatographed on silica gel eluting with
20 dichloromethane containing from 0 to 1% of methanol.

Yield = 89%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.21-1.49 (m, 5H), 1.60-1.67 (m, 1H), 1.76-1.88 (m, 4H), 2.28 (s, 3H), 2.60-2.70 (m, 1H), 3.60 (s, 3H), 3.93 (s, 3H), 7.45 (d, 1H), 8.03 (d, 1H), 8.98
25 (s, 1H), 11.10 (s, 1H).

MS (m/z) / M+1= 389/390

HPLC (uv purity, λ=214 nm): 96.93%

Example I93.3: R1= cyclohexyl, R2= methyl, R3= 3-amino-4-benzamide
30

2-Amino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide

I93 was modified following the procedure described in example I37.3 to afford the amide derivative with an overall
35 yield 84%. The reduction of the nitro group to give I93.3 was performed as described in example I93.1. In this particular case, the reactional mixture was basified with a

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saturated solution of sodium carbonate then distilled. The crude was diluted in water and extracted with dichloromethane. The aqueous phase, saturated with brine, was then extracted with ethylacetate and the organic layer was dried over MgSO_4 , filtered and evaporated to dryness to give a residue which was purified by two consecutive chromatographies on silica gel, eluting first with dichloromethane/methanol (93/7) and the second purification made eluting with a gradient of cyclohexane containing from 0 to 40% ethylacetate.

Yield= 10%

$^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 1.27-1.40 (m, 5H), 1.56-1.62 (m, 1H), 1.70-1.80 (m, 4H), 2.58-2.65 (m, 1H), 3.50 (s, 3H), 6.73-6.78 (m, 3H), 7.00 (s, 1H), 7.10-7.20 (b, 1H), 7.61 (d, 1H), 7.75-7.85 (b, 1H).

MS (m/z) / M+1= 332/333

HPLC (uv purity, λ = 214 nm): 95.83%

Example I93.4: R1= cyclohexyl, R2= methyl, R3= 4-oxo-3,4-dihydro-quinazoline-7-yl

7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-3H-quinazolin-4-one

A mixture of I93.1 (1.443 mmol, 0.500 g) and formamide (4 ml) was stirred and heated at reflux for 2h before cooling at room temperature. The mixture was diluted with water and the precipitate was collected by filtration. The precipitate was washed with water and petroleum ether and purified by chromatography on silica gel, eluting with dichloromethane containing from 0 to 3% of methanol followed by an isocratic elution with dichloromethane/methanol (93/7).

Yield= 20%

$^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 1.20-1.40 (m, 5H), 1.55-1.64 (m, 1H), 1.70-1.83 (m, 4H), 2.63-2.71 (m, 1H), 3.56 (s, 3H), 7.73 (s, 1H), 7.00 (s, 1H), 7.80 (d, 1H), 8.12-8.19 (m, 3H), 12.30-12.40 (b, 1H).

MS (m/z) / M+1= 342/343

HPLC (uv purity, λ = 214 nm): 95.19%

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Example I93.5: R1= cyclohexyl, R2= methyl, R3= 4-amino-quinazoline-7-yl

5 7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-quinazolin-4-ylamine

A mixture of I93.4 (0.264 mmol, 0.090 g), thionyl chloride (2 ml) and a catalytic amount of dimethylformamide was refluxed for 2h before distillation of solvents under reduced pressure. To the residue, a solution of NH₃ (0.5N) in dioxan (4 ml) was added and the mixture was heated in a sealed tube at 80°C for 4 days. The mixture was then evaporated to dryness and the crude was diluted in a solution of acetic acid (0.1 ml AcOH in 10 mmol H₂O), and extracted with dichloromethane to remove the impurities. The aqueous phase was then basified with a solution NaOH (0.1N) and then extracted with dichloromethane. The organic layer was washed with water, brine, dried over MgSO₄, filtered and concentrated under reduced pressure to give the desired product.

20 Yield= 7.5%.

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.29-1.50 (m, 5H), 1.60-1.69 (m, 1H), 1.79-1.90 (m, 4H), 2.65-2.72 (m, 1H), 3.65 (s, 3H), 5.60-5.70 (b, 2H), 7.75 (d, 1H), 7.90 (s, 1H), 7.98 (d, 1H), 8.67 (s, 1H).

25 MS (m/z) / M+1= 341/343

HPLC (uv purity, λ= 214 nm): 99.99%

Example I93.6: R1= cyclohexyl, R2= methyl, R3= 2,4-Dioxo-1,2,3,4-tetrahydro-quinazoline-7-yl

30 7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-1H-quinazoline-2,4-dione

To a solution of I93.3 in THF (4ml), carbonyldiimidazole (0.464 mmol, 0.080 g) was added and the reaction was heated at reflux overnight. Carbonyldiimidazole (0.464 mmol, 0.080 g) was added and the mixture was kept at reflux for 24h. Then, the solvent was distilled and the residue was purified by chromatography on silica gel, eluting with a gradient of cyclohexane containing from 15 to 30%. The chromatographed

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product was solubized in ethylacetate and the organic layer was washed with water. The collected organic layer was washed with brine, dried over MgSO_4 , filtered and evaporated to dryness to give the title product.

5 Yield= 13.3%

$^1\text{H-NMR}$ (400MHz, DMSO) δ ppm: 1.28-1.39 (m, 5H), 1.56-1.64 (m, 1H), 1.72-1.82 (m, 4H), 2.62-2.67 (m, 1H), 3.54 (s, 3H), 7.41-7.43 (m, 2H), 7.94 (d, 1H), 11.17 (s, 1H), 11.36 (s, 1H).

10 MS (m/z) / M+1 = 358/359

HPLC (uv purity, λ = 214 nm): 96.70%

Example I94: R1= cyclohexyl, R2= methyl, R3= 3-methoxy-4-sulfamoyl-phenyl

15 **4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-benzenesulfonamide**

The title compound was prepared by the procedure described in example I19 (protocol C) using the appropriate intermediates and reagents. The residue was purified by
20 chromatography on silica gel, eluting with dicloromethane containing from 0 to 2% of methanol.

Yield= 59%

$^1\text{H-NMR}$ (400MHz, CDCl_3) δ ppm: 1.21-1.49 (m, 5H), 1.63-1.69 (m, 1H), 1.77-1.87 (m, 4H), 2.59-2.67 (m, 1H), 3.60 (s, 3H),
25 4.06 (s, 3H), 5.02 (s, 2H), 7.20 (d, 1H), 7.40 (s, 1H), 7.90 (d, 1H).

MS (m/z) / M+1 = 384/386

HPLC (uv purity, λ = 214 nm): 99.99%

30 **Example I95: R1= cyclohexyl, R2= methyl, R3= 4-methoxy-3-sulfamoyl-phenyl**

5-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-benzenesulfonamide

The title compound was prepared by procedure as described in
35 example I18 (protocol C) using the appropriate intermediates and reagents.

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In this particular case, the residue obtained after extraction and distillation was triturated with methanol and the precipitate was filtered off and purified by silica gel chromatography, eluting with a mixture of cyclohexane/ethylacetate (1/1).

Yield= 9%.

$^1\text{H-NMR}$ (400MHz, CDCl_3) δ ppm: 1.30-1.50 (m, 5H), 1.62-1.70 (m, 1H), 1.80-1.90 (m, 4H), 2.58-2.65 (m, 1H), 3.58 (s, 3H), 4.02 (s, 3H), 5.10 (s, 2H), 7.09 (d, 1H), 7.80 (d, 1H), 8.12 (s, 1H).

MS (m/z) / M+1 = 383/384

HPLC (uv purity, λ = 214 nm): 99.38%

Example I96: R1= 3-methoxycarbonyl-phenyl, R2= methyl, R3= 3-cyano-phenyl

3- [5- (3-Cyano-phenyl) -3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino]-benzoic acid methyl ester

To a solution of 7j (1.25 mmol, 0.42 g) in anhydrous dioxane (14 mL), was added methyltrifluoromethane sulfonate (1.5 mmol, 142 μl). The resultant mixture was stirred for 24h at room temperature. To this solution was added methyltrifluoromethane sulfonate (0.45 mmol, 43 μl) to ensure completion of the reaction. The solvent was removed by distillation under reduced pressure to give a crude material which was basified with an aqueous saturated solution of NaHCO_3 and extracted with dichloromethane. The organic layer was dried over Na_2SO_4 , filtered and concentrated. The crude material was purified by 2 successive flash chromatographies (eluent: dichloromethane/methanol 95/5 and cyclohexane/ethyl acetate 90/10) to give the desired compound 0.23 g (yield 53%).

$^1\text{H-NMR}$ (400 MHz, DMSO) δ ppm: 3.75 (s, 3H), 3.86 (s, 3H), 7.34 (d, 1H), 7.54 (t, 1H), 7.61 (s, 1H), 7.67-7.70 (m, 2H), 7.94 (d, 1H), 8.02 (d, 1H), 8.12 (s, 1H).

MS (m/z) / M+1: 351/353

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Example I96.1: R1= 3-benzoic-acid, R2= methyl, R3= 3-cyano-phenyl

3-[5-(3-Cyano-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid

- 5 A mixture of I96 (3 mg, 8.56 mmol) and potassium hydroxyde (1N in water, 12.8 mmol, 12.8mL) in tetrahydrofuran (90 ml) was stirred at room temperature overnight. The reaction mixture was heated at reflux for 1h. After cooling, the reaction mixture is concentrated, water is added (2 mL) and
- 10 a solution of HCl (1N in water, 12.8 mmol, 12.8 mL) is added. The precipitate is collected by filtration and washed succesively with water and with ether before being dried under vacuum at 45°C. The compound was purified by flash chromatography (eluent: dichloromethane/methanol 99/1 +1%
- 15 acetic acid) to give 2.38 g of the title product
- Yield: 83%

¹H-NMR (400 MHz , DMSO) δ ppm : 3.8 (s, 3H), 7.31 (d, 1H), 7.51 (t, 1H), 7.61 (s, 1H), 7.65-7.69 (m, 2H), 7.93 (d, 1H), 8.01 (d, 1H), 8.11 (s, 1H), 13.06 (s, 1H).

20 MS (m/z) / M+1 = 337/338

HPLC (uv purity, λ = 245 nm): 99.6%

Example I97: R1= 3-methoxycarbonyl-phenyl, R2= methyl, R3= 2-pyridyl

25 3-[3-Methyl-5-pyridin-2-yl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid methyl ester

- To a solution of 7k (1.76 mmol, 0.55 g) in anhydrous dioxane (14 mL) and triethylamine (1.76 mmol, 264 μ L), methyltrifluoromethane sulfonate (1.76 mmol, 199 μ L) was
- 30 added. The resultant mixture was stirred for 24h. To this solution was added methyltrifluoromethane sulfonate (0.53 mmol, 60 μ L) and triethylamine (0.53 mmol, 79.2 μ L) to allow reaction to completion. The solvent was removed by distillation under reduced pressure to give a crude material
- 35 which was basified with an aqueous saturated solution of NaHCO₃ and extracted with dichloromethane. The organic layer was dried over Na₂SO₄, filtered and concentrated. The crude

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material was purified by filtration on silica gel (eluent: dichloromethane) to give the desired compound.

Yield: 28%

¹H-NMR (400 MHz, DMSO) δ ppm: 3.76 (s, 3H), 3.86 (s, 3H),
5 7.35 (dd, 1H), 7.48-7.54 (m, 2H), 7.64-7.68 (m, 2H), 7.96-
8.00 (m, 2H), 8.58 (d, 1H).

MS (m/z) / M+1: 327/329

Example I97.1: R1 = 3-benzoic-acid, R2= methyl, R3= 2-pyridyl
10 **3- [3-Methyl-5-pyridin-2-yl-3H-[1,3,4]thiadiazol-2-**
ylideneamino]-benzoic acid

A mixture of I97 (16 g, 0.49 mmol) and potassium hydroxyde
(1N in water, 0.58 mmol, 0.58 mL) in tetrahydrofuran (3mL)
was stirred at room temperature for 48h. The reaction
15 mixture was heated at reflux for 2h. After cooling, the
reaction mixture is concentrated, water is added (5 mL), the
aqueous layer was extrated with dichloromethane and
neutralized with a solution of HCl (0.1N in water). The
precipitate is collected by filtration and washed
20 successively with water and with ether before being dried
under vacuum at 45°C to give 0.08 g of the title product.

Yield: 54%

¹H-NMR (400 MHz, DMSO) δ ppm: 3.8 (s, 3H), 7.31 (d, 1H),
7.47-7.49 (m, 2H), 7.64-7.66 (m, 2H), 7.96-7.98 (m, 2H), 8.58
25 (d, 1H)

MS (m/z) / M+1= 313/314/315

HPLC (uv purity, λ = 245 nm): 97.6%

Example I98: R1= 3-benzoic-acid, R2= methyl, R3= 4-Chloro-3-
30 **sulfamoyl-phenyl**

3- [5-(4-Chloro-3-sulfamoyl-phenyl)-3-methyl-3H-
[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid

I98 was prepared by the procedure described in example I96.1
using the appropriate intermediates and reagents. In this
35 particular case, the ester intermediate was basified with
triethylamine. The title product was isolated by

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chromatography on silica gel, eluting with ethylacetate / cyclohexane (15/85).

Yield=19% (2 steps)

¹H-NMR (400MHz, DMSO) δ ppm: 3.73 (s, 3H), 3.85 (s, 3H),
5 7.35 (d, 1H), 7.54 (t, 1H), 7.62 (s, 1H), 7.70 -7.80 (m, 4H), 7.86 (d, 1H), 8.24 (s, 1H).

MS (m/z) / M+1 = 439/441

Then, A solution (1N) of potassium hydroxide (1.139mmol,
10 1.14ml) was added to a solution of the ester derivative (0.456mmol, 0.2g) in THF (5ml) and the mixture was stirred overnight. The reaction mixture was evaporated to dryness and the residue was diluted in ethanol and acidified with a solution (6.9N) of HCl in ethanol (0.165ml). The mixture was
15 stirred at RT for 5h and the solvent was distilled under reduced pressure. The crude material was chromatographed on silica gel, eluting with a gradient of dichloromethane containing from 5 to 25% methanol. The isolated product was solubilized in THF and filtered through a pad of silica gel
20 and the filtrate was evaporated to dryness to afford the desired product.

Yield = 37%.

¹H-NMR (400MHz, CDCl₃) δ ppm: 3.74 (s, 3H), 7.24 (d, 1H),
7.45 (t, 1H), 7.62 (s, 1H), 7.66 (d, 1H), 7.73-7.80 (m, 3H),
25 7.84 (d, 1H), 8.23 (s, 1H).

MS (m/z) / M+1= 425/427

HPLC (uv purity, λ= 214 nm): 94.86%

30 EXAMPLE I: PROTOCOL D

**Example I99: R1= cyclohexyl, R2= methyl, R3= 4-cyano-phenyl
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-
2-yl)-benzonitrile**

35 Compound I99 was prepared by the procedure described in exemple I15 (protocol D).

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To a mixture of 4-cyanobenzoic acid (74.8 mmol, 11 g), 2-methylthiosemicarbazide 5a (74.8 mmol, 13.42 g) in anhydrous dioxane (110 mL) at 70°C, POCl₃ (89.65 mmol, 76.76 ml) was added and the mixture was warmed at 95°C for 4 hours. The solvent was removed by distillation under reduced pressure to give a crude material which was basified at pH 8-7 with a saturated solution of NaHCO₃. The aqueous phase was extracted with dichloromethane. The organic layer was washed with water and saturated solution of NaCl, dried over magnesium sulfate, filtered and distilled to give a residue which was purified by silica gel chromatography (eluted with a gradient of cyclohexane/ethyl acetate finishing with the ratio 90/10) to afford 8.5 g of the title compound.

Yield: 42%

¹H-NMR (400MHz, DMSO) δ ppm: 1.15-1.40 (m, 5H), 1.55-1.65 (m, 1H), 1.70-1.83 (m, 4H), 2.57-2.70 (m, 1H), 3.55 (s, 3H), 7.82 (dd, 2H), 7.93 (dd, 2H).

Example I99.1: R1= cyclohexyl, R2= methyl, R3= 4-(1H-tetrazol-5-yl)-phenyl

Cyclohexyl-{3-methyl-5-[4-(1H-tetrazol-5-yl)-phenyl]-3H-[1,3,4]thiadiazol-2-ylidene}-amine

To a solution of I99 (1.67 mmol, 500 mg) in toluene (2 ml), sodium azide (2.18 mmol, 142 mg), triethylamine hydrochloride (2.18 mmol, 300 mg) were added and the mixture was warmed at reflux during 24 hours. The reaction mixture was cooled at room temperature, acidified with a solution of HCl [0.1N], and then basified at pH=6-7 with a saturated solution of NaHCO₃. The aqueous phase was extracted with ethyl acetate and the organic layer was washed with a saturated solution of NaCl, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel column using a gradient of dichloromethane containing from 0 to 20% methanol to afford the title compound.

Yield: 61%

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¹H-NMR (400MHz, DMSO) δ ppm: 1.20-1.42 (m, 5H), 1.55-1.65 (m, 1H), 1.70-1.85 (m, 4H), 2.60-2.72 (m, 1H), 3.55 (s, 3H), 7.85 (dd, 2H), 8.13 (dd, 2H)

MS (m/z) / M+1 = 341/342

5 HPLC (uv purity, λ = 214 nm) = 99.9%

**Example I100: R1= cyclohexyl, R2= methyl, R3= 4-nitro-phenyl
Cyclohexyl-[3-methyl-5-(4-nitro-phenyl)-3H-[1,3,4]
thiadiazol-2-ylidene]-amine**

10 I100 was prepared as described in example I15 (protocol D) using the appropriate reagents. The crude material was purified by silica gel chromatography eluting with a gradient of cyclohexane containing from 0 to 10% ethylacetate.

15 Yield: 40%

¹H-NMR (400MHz, DMSO) δ ppm: 1.20-1.40 (m, 5H), 1.57-1.64 (m, 1H), 1.72-1.83 (m, 4H), 2.61-2.91 (m, 1H), 3.56 (s, 3H), 7.89 (d, 2H), 8.29 (d, 2H).

MS (m/z) / M+1 = 319/320

20

Example I100.1: R1= cyclohexyl, R2= methyl, R3= 4-amino-phenyl

4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenylamine

25 Tin chloride dihydrate (93.278 mmol, 20.987 g) was added to a solution I100 (18.656 mmol, 5.940 g) in ethanol at 70°C and the mixture was refluxed for 1h30. The mixture was then filtered on Celite and the filtrate was evaporated to dryness. The crude material was basified with a saturated
30 solution of sodium bicarbonate then extracted with ethyl acetate. The organic layer was washed with water and brine, dried over MgSO₄, filtered and then evaporated to dryness. The residue was filtered through a pad of silica gel with a mixture of dichloromethane/methanol (95/5).

35 Yield= 62%

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¹H-NMR (400MHz, CDCl₃) δ ppm: 1.19-1.37 (m, 5H), 1.56-1.63 (m, 1H), 1.70-1.80 (b, 4H), 2.56-2.74 (m, 1H), 3.44 (s, 3H), 5.60 (s, 2H), 6.58 (d, 2H), 7.29 (d, 2H).

MS (m/z) / M+1 = 289/290

5 HPLC (uv purity, λ = 214 nm): 97.61%

Example I100.2: R1= cyclohexyl, R2= methyl, R3= 4-(N-cyano-N'-(2-dimethylaminoethyl)carboximidamide)-phenyl

10 **[5-(4-(N-cyano-N'-(2-dimethylaminoethyl)-carboximidamide)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexylamine**

To a solution of diphenylcyanocarbonimide (0.364 mmol, 0.087 mmol) in acetonitrile (1 ml) at 70°C, I100.1 (0.347 mmol, 0.1 g) was added and the reaction mixture was heated
15 at 80°C for 15h. 1eq. of carbonimide was added and the mixture was kept at 80°C for an additional 5h before evaporation of volatiles. The residue was mixed with ethanol (2 ml) and N,N-dimethylethylene diamine (0.34 mmol, 0.038 mg). The mixture was stirred at room temperature for 15h and
20 heated at reflux for 5h. On cooling to room temperature, the precipitate formed was filtered off and purified by silica gel chromatography eluting with a gradient of dichloromethane containing from 2 to 5% methanol.

Yield= 32%

25 ¹H-NMR (400MHz, CDCl₃) δ ppm: 1.16-1.41 (m, 5H), 1.50-1.70 (m, 1H), 1.80-1.91 (m, 4H), 2.35 (s, 6H), 2.50-2.60 (m, 3H), 3.31-3.38 (m, 2H), 3.55 (s, 3H), 6.00-6.10 (b, 1H), 7.30 (d, 2H), 7.52 (d, 2H).

MS (m/z) / M+1 = 427/428

30 HPLC (uv purity, λ = 214 nm): 97.23%

Example I100.3: R1= cyclohexyl, R2= methyl, R3= 4-acetamide-phenyl

35 **N-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-acetamide**

To a solution of I100.1 (0.347 mmol, 0.1 g) in presence of triethylamine (0.361 mmol, 0.051 ml) in anhydrous toluene (3

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ml) at 0°C, acetic anhydride (0.382 mmol, 0.036 ml) was added and the reaction mixture was stirred at room temperature for 20h and then concentrated to dryness. The residue was mixed with a saturated solution of sodium bicarbonate and then the aqueous mixture was extracted with dichloromethane. The organic layer was washed with water, brine, dried over MgSO₄, filtered and evaporated to dryness. The residue was purified by silica gel chromatography eluting with a mixture of methanol/dichloromethane (2/98).

Yield=22%.

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.22-1.45 (m, 5H), 1.58-1.68 (m, 1H), 1.80-1.88 (m, 4H), 2.21 (s, 3H), 2.58-2.64 (m, 1H), 3.60 (3H, s), 7.20 (s, 1H), 7.52-7.62 (m, 4H).

MS (m/z) / M+1 = 331:332

HPLC (uv purity, λ= 214 nm): 95.24%

Example I100.4: R1= cyclohexyl, R2= methyl, R3= 4-(bis-ethylesulfonyl-amino)-phenyl

[5-(4-(bis-ethylsulfonylamino)-phenyl)-3-methyl-3H-

[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine

To a solution of I100.1 (0.347 mmol, 0.1 g) in dichloromethane (5 ml) with triethylamine (0.520 mmol, 0.072 ml), chlorosulfonyl chloride (0.590 mmol, 0.057 ml) was added at 0°C and the mixture was stirred at room temperature for 4h30 before evaporation to dryness under reduced pressure. The crude material was purified by silica gel chromatography eluting with a gradient of dichloromethane containing from 0 to 5% methanol.

Yield= 76%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.52 (m, 11H), 1.61-1.68 (m, 1H), 1.80-1.89 (m, 4H), 2.59-2.68 (m, 1H), 3.58-3.64 (m, 7H), 7.40 (d, 2H), 7.70 (d, 2H).

MS (m/z) / M+1= 473/475

HPLC (uv purity, λ= 214 nm): 98.68%

Example I100.5: R1= cyclohexyl, R2= methyl, R3= 4-(1-(2-dimethylaminoethyl)amino-2-nitro-vinylamino)-phenyl

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[5-(4-(1-(2-dimethylaminoethyl)amino-2-nitro-vinylamino)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexylamine

To a solution of 1,1-bis(methylthio)-2-nitroethylene (1.041 mmol, 0.172 g) in acetonitrile (1 ml), at 75°C, I100.1 (0.347 mmol, 0.1 g) was added and the reaction was heated at reflux for 7h. The reaction mixture was then evaporated to dryness and the crude material was purified by silica gel chromatography eluting with a gradient of dichloromethane containing from 0 to 5% of methanol to give the desired intermediate (0.09 g, yield: 64%).

A mixture of ethylenediamine (0.133 mmol, 0.017 ml) and this intermediate (0.111 mmol, 0.045 g) in ethanol (2 ml) was heated at reflux for 3h. The mixture was concentrated under reduce pressure to give a residue which was purified by silica gel chromatography eluting with dichloromethane containing 2% methanol.

Yield= 90%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.23-1.49 (m, 5H), 1.65-1.70 (m, 1H), 1.78-1.88 (m, 4H), 2.45 (s, 6H), 2.57-2.71 (m, 3H), 3.51-3.61 (m, 5H), 6.66 (s, 1H), 7.09 (d, 2H), 7.60 (d, 2H), 10.55-10.62 (b, 1H), 12.28-12.40 (b, 1H).

MS (m/z) / M+1= 446/447

HPLC (uv purity, λ= 214 nm): 99.34%

25

Example I100.6: R1= cyclohexyl, R2= methyl, R3= 4-(1-amino-2-nitro-vinylamino)-phenyl

(E)-N¹-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-2-nitro-ethene-1,1-diamine

The title product was prepared by the procedure described in example I100.5 using a solution of ammonia (2N) in methanol (80 eq) instead of ethylenediamine.

The desired product was isolated by chromatography on silica gel, eluting with a gradient of dichloromethane containing from 2 to 4 % methanol.

Yield= 83%

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¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.47 (m, 5H), 1.62-1.67 (m, 1H), 1.76-1.87 (m, 4H), 2.60-2.66 (m, 1H), 3.60 (m, 3H), 6.70 (s, 1H), 7.24 (d, 2H), 7.67 (d, 2H).

MS (m/z) / M+1 = 375/376

5 HPLC (uv purity, λ= 214 nm): 94.09%

Example I100.7: R1= cyclohexyl, R2= methyl, R3= 4-(N-cyano-N'-methyl-carboximidamide)-phenyl

10 **[5-(N-cyano-N'-methyl-4-carboximidamide-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine**

To a solution of diphenylcyanocarbonimidate (0.364 mmol, 0.087 g) in acetonitrile (1 ml) at 70°C, I100-1 (0.347 mmol, 0.1 g) was added and the mixture was heated at 80°C for 15h. One equivalent of diphenylcyanocarbonimidate was added and
15 the mixture was stirred for 5h. The mixture was concentrated under reduced pressure to give the intermediate which was used without further purification. The intermediate (0.416 mmol, 0.300 g) in a solution (2N) of methylamine in MeOH (32.890 mmol, 16.64 ml) was refluxed for 8h then allowed to
20 stand at room temperature for 2 days. The mixture was evaporated to dryness and the residue was purified by chromatography on silica gel, eluting with a gradient of dichloromethane containing from 0 to 4% of methanol to give the desired product.

25 Yield: 29%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.45 (m, 5H), 1.62-1.67 (m, 1H), 1.76-1.87 (m, 4H), 2.57-2.67 (m, 1H), 2.90 (d, 3H), 3.60 (m, 3H), 4.90-5.01 (b, 1H), 7.17-7.28 (m, 3H), 7.69 (d, 2H).

30 MS (m/z) / M+1= 370/371

HPLC (uv purity, λ= 214 nm): 99.99%

Example I100.8: R1= cyclohexyl, R2= methyl, R3= 4-(N-cyano-N'-amino-carboximidamide)-phenyl

35 **[5-(4-(N-cyano-N'-amino-carboximidamide)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine**

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The title product was prepared by the procedure described in example I100.7 using the same intermediate (0.416 mmol, 0.300 g) and a solution (2N) of ammonia in methanol (32.89 mmol, 16.64 ml). The desired product was purified by chromatography on silica gel eluting with a gradient of dichloromethane containing from 0 to 7% methanol.

Yield= 67%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.46 (m, 5H), 1.60-1.66 (m, 1H), 1.78-1.88 (m, 4H), 2.55-2.65 (m, 1H), 3.58 (m, 3H), 6.10 (s, 2H), 7.42 (d, 2H), 7.55 (d, 2H), 8.71 (s, 1H).

MS (m/z) / M+1 = 356/357

HPLC (uv purity, λ= 214 nm): 97.39%

Example I100.9: R1= cyclohexyl, R2= methyl, R3= 4-ethylsulfonylamino-phenyl

Ethanesulfonic acid [4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-amide

Ethylsulfonyl chloride (0.416 mmol, 0.040 ml) was added to a solution of I100.1 (0.347 mmol, 0.10 g) in dichloromethane at 0°C. The mixture was stirred for 12 h at room temperature then basified with a saturated solution of sodium bicarbonate. The organic layer was collected and concentrated under reduce pressure. The crude material was reacted with 1,1-bis(methylthio)-2-nitroethylene (2.690 mmol, 0.445 g, 10 eq) at reflux in acetonitrile (5 ml) for 24 h. The solvent was then distilled under reduced pressure and the residue was purified by silica gel chromatography eluting with dichloromethane containing a gradient from 0 to 10% methanol.

Yield= 15%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.24-1.44 (m, 8H), 1.62-1.68 (m, 1H), 1.78-1.87 (m, 4H), 2.59-2.65 (m, 1H), 3.14-3.19 (q, 2H), 3.60 (s, 3H), 6.44 (s, 2H), 7.23 (dd, 2H), 7.61 (dd, 2H).

MS (m/z) / M+1= 381/383

HPLC (uv purity, λ= 214 nm): 99.22%

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Example I100.10: R1= cyclohexyl, R2= methyl, R3= 4-Ureido-phenyl

[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]

5 thiadiazol-2-yl)-phenyl]-urea

To a solution of I100.1 (0.348 mmol, 0.100 g) in THF (1 ml), trimethylsilyl isocyanate (0.416 mmol, 0.488 ml) was added and the mixture was stirred at room temperature for 10 h and water was added. The organic layer was extracted with
10 ethylacetate, washed with water, brine, dried over MgSO₄, filtered and then evaporated to dryness. The crude product was purified by chromatography on silica gel, eluting with a gradient of dichloromethane containing from 0 to 4% of methanol.

15 Yield= 13%

¹H-NMR (400MHz, DMSO) δ ppm: 1.24-1.39 (m, 5H), 1.53-1.57 (m, 1H), 1.69-1.80 (m, 4H), 2.57-2.65 (m, 1H), 3.47 (s, 3H), 5.92 (s, 2H), 7.50 (s, 4H), 8.79 (s, 1H).

MS (m/z) / M+1= 332/333

20 HPLC (uv purity, λ= 214 nm): 92.50%

Example I100.11: R1= cyclohexyl, R2= methyl, R3= 4-[3-(2-dimethylamino-ethyl)-ureido]-phenyl

1-[4-(Cyclohexylimino-methyl-4,5-dihydro-[1,3,4]thiadiazol-
25 2-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea

To a solution of I100.1 (0.347 mmol, 0.100 g) with triethylamine (1.041 mmol, 0.145 ml) in dichloromethane anhydrous (5 ml), was added a solution of phosgene (20% in toluene) (1.024 mmol, 0.487 ml) at 0°C. The mixture was
30 stirred at 0°C for 10 min then allowed to raise to room temperature for 1h and N,N-dimethyl-ethylene diamine (0.694 mmol, 0.076 ml) was added. After 20 h of stirring at room temperature, the mixture was basified with a saturated solution of sodium bicarbonate then extracted with
35 dichloromethane. The organic phase was washed with water, brine, dried over MgSO₄ and evaporated under reduced pressure. The residue was chromatographed on silica gel

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eluting with a mixture dichloromethane/methanol (95/5) to afford the tittle product.

Yield= 11%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.50 (m, 5H), 1.70-1.75 (m, 1H), 1.78-1.90 (m, 4H), 2.33 (s, 6H), 2.58-2.68 (m, 3H), 3.30-3.40 (b, 2H), 3.60 (s, 3H), 5.37-5.47 (b, 1H), 7.40 (d, 2H), 7.55 (d, 2H).

MS (m/z) / M+1 = 403/404

HPLC (uv purity, λ= 214 nm): 99.99%

10

Example I101: R1= cyclohexyl, R2= methyl, R3= 3-chloro-4-sulfamoyl-phenyl

2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide

15 The title compound was prepared by the procedure described in example I15 (protocol D) using the appropriate intermediates and reagents.

The desired product was isolated by chromatography on silica gel, eluting with a gradient of cyclohexane containing from 0 to 30% ethylacetate.

20

Yield: 23%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.21-1.49 (m, 5H), 1.60-1.69 (m, 1H), 1.79-1.87 (m, 4H), 2.59-2.69 (m, 1H), 3.60 (m, 3H), 5.10 (s, 2H), 7.58 (d, 1H), 7.80 (s, 1H), 8.10 (d, 1H).

25 MS (m/z) / M+1 = 388/389

HPLC (uv purity, λ= 214 nm): 98.32%

Example I102: R1=cyclohexyl, R2= methyl, R3= 3-chloro-4-methoxycarbonyl-phenyl

30 **2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester**

I102 was prepared by procedure as described in example I15 (protocol D) using the appropriate intermediates and reagents. The desired product was isolated by chromatography on silica gel eluting with a gradient of cyclohexane containing from 0 to 7% ethylacetate. (yield : 12%)

35

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¹H-NMR (400MHz, CDCl₃) δ ppm: 1.21-1.48 (m, 5H), 1.60-1.67 (m, 1H), 1.78-1.87 (m, 4H), 2.58-2.66 (m, 1H), 3.60 (s, 3H), 4.93 (s, 3H), 7.55 (d, 1H), 7.71 (s, 1H), 7.86 (d, 1H).

5 **Example I102.1: R1= cyclohexyl, R2= methyl, R3= 3-chloro-4-benzamide**

2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide

To a solution of I102 (0.391 mmol, 0.147 g) in a mixture of
10 THF/ MeOH (2 ml) (1/1), Lithium hydroxyde (0.430 mmol, 0.010 g) was added and the reaction mixture was allowed to stir for 15h at room temperature. Lithium hydroxyde (0.430 mmol, 0.010 g) was added and the reaction was stirred for 24 h before evaporation to dryness. The crude material was
15 acidified with a solution of HCl (1N), stirred at room temperature for 3h and the mixture was then concentrated to dryness.

Toluene (5 ml) was added to the residue (0.273 mmol, 0.120 g) followed by an addition of thionyl chloride (0.820 mmol, 20 0.598 ml) and the mixture was heated at reflux overnight before distillation of volatiles under reduced pressure. The residue was poured into THF (5 ml) and cooled to 0°C then a solution of concentrated ammonia (6.833 mmol, 0.448 ml) was added. The reaction was allowed to stir at room temperature
25 for 3 h and then the solvent was distilled. The residue was purified by chromatography on silica gel, eluting with dicloromethane containing from 0 to 1% methanol.

Yield: 63% (overall)

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.48 (m, 5H), 1.62-1.69
30 (m, 1H), 1.79-1.88 (b, 4H), 2.58-2.67 (m, 1H), 3.60 (m, 3H), 5.86-5.93 (b, 1H), 6.38-6.48 (b, 1H), 7.57 (d, 1H), 7.70 (s, 1H), 7.87 (d, 1H).

MS (m/z) / M+1= 351/353

HPLC (uv purity, λ= 214 nm): 96.60%

35

Example I103: R1= cyclohexyl, R2= methyl, R3= 4-chloro-3-benzamide

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2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide

The title compound was prepared by the procedure described in example I102.1 using the appropriate intermediates and reagents (protocol D).

Yield: 47%

¹H-NMR (400MHz, CDCl₃) δ ppm: 1.20-1.42 (m, 5H), 1.60-1.69 (m, 1H), 1.77-1.89 (b, 4H), 2.55-2.65 (m, 1H), 3.60 (m, 3H), 5.89-6.00 (b, 1H), 6.30-6.40 (b, 1H), 7.46 (d, 1H), 7.68 (d, 1H), 8.00 (s, 1H).

MS (m/z) / M+1 = 351/353

HPLC (uv purity, λ= 214 nm): 98.70%

15 PROTOCOL E: Intermediate 8

**R1= cyclohexyl, R2= methyl, R3= 4-methoxycarbonyl-phenyl
1-(4-methoxycarbonyl-benzoyl)-2-methyl-4-cyclohexyl-thiosemicarbazide**

To a stirred solution of 5a (2.517 mmol, 0.456 g) in pyridine (6ml), methyl-4-chloro carbonyl benzoate (2.517mmol, 0.500g) was added. The mixture was stirred 24h at RT, and then the pyridine was distilled under reduced pressure. The residue was poured into water and extracted with dichloromethane. The organic layer was washed with water, brine, dried over MgSO₄ and concentrated to dryness to afford 1.10g of product.

¹H-NMR (400MHz, DMSO) δ ppm: 1.15-1.25 (m, 5H), 1.51-1.61 (m, 1H), 1.61-1.71 (m, 2H), 1.71-1.87 (m, 2H), 3.28 (s, 3H), 3.9 (s, 3H), 4.10-4.21 (m, 1H), 8.00-8.10 (m, 4H), 8.59 (d, 1H), 10.79 (s, 1H).

EXAMPLE I : PROTOCOL E

**Example I104: R1= cyclohexyl, R2= methyl, R3= 4-methoxycarbonyl-phenyl
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-benzoic acid methyl ester**

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A stirred mixture of the previous intermediate 8 (2.517 mmol, 1.10 g) and methanol (50 ml) was warmed until a homogeneous solution was obtained then mercury oxide (10.068 mmol, 2.18 g) was added. After 18h at reflux, 3 more equivalents of HgO were added and the reaction was kept at reflux for an additionnal 6h then allowed to cool down to RT. The reaction was filtered through a pad of Celite and the filtrate was evaporated under reduced pressure. The crude material was purified by chromatography on silica gel eluting with cyclohexane containing from 10 to 20% ethylacetate.

Yield= 44%

¹H-NMR (400MHz, DMSO) δ ppm: 1.1-1.4 (m, 5H), 1.53-1.61 (m, 1H), 1.69-1.80 (m, 1H), 3.30 (s, 3H), 3.40-3.48 (m, 1H), 3.88 (s, 3H), 3.85 (d, 2H), 7.96 (d, 2H), 8.08 (d, 2H).
MS (m/z) / M+1 =316/318

Example 104.1: R1= cyclohexyl, R2= methyl, R3= 4-benzamide 4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-benzamide

The title compound was prepared by procedure described in example I37.3. The desired product was isolated by chromatography on silica gel eluting with dichloromethane containing from 1 to 2 % methanol.

Yield= 26 % (overall)

¹H-NMR (400MHz, DMSO) δ ppm: 1.17-1.40 (m, 5H), 1.58-1.64 (m, 1H), 1.70-1.80 (m, 4H), 3.30 (s, 3H), 3.41-3.51 (m, 1H), 7.50-7.55 (b, 1H), 7.80 (d, 2H), 8.00 (d, 2H), 8.10-8.18 (b, 1H).

MS (m/z) / M+1 =301/302

HPLC (uv purity, λ = 214 nm) = 99.9%

The compounds of formula (I) disclosed in the examples are summarized in the following table:

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Example	Structure
I1	
I1,1	
I1,2	
I1,3	
I1,4	
I1,5	
I1,6	
I1,7	

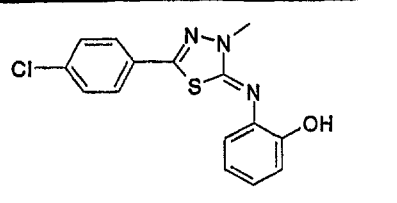
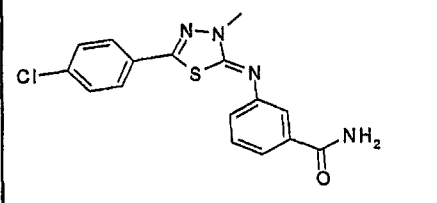
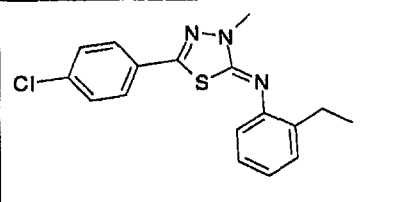
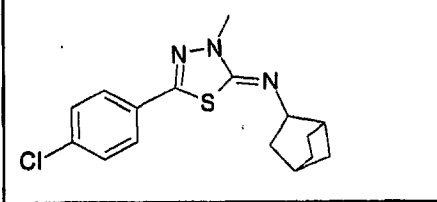
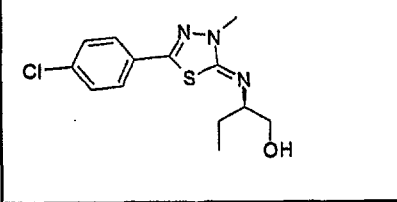
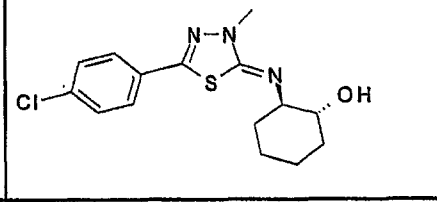
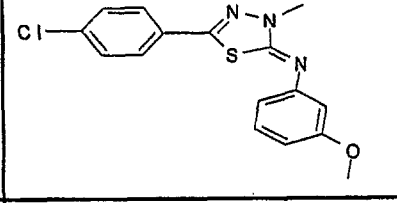
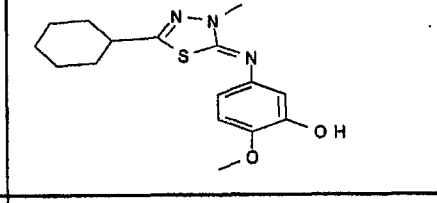
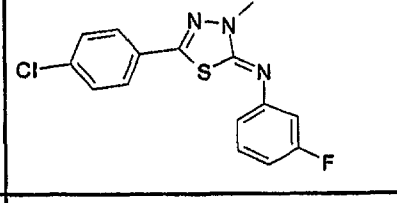
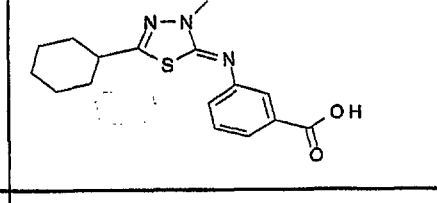
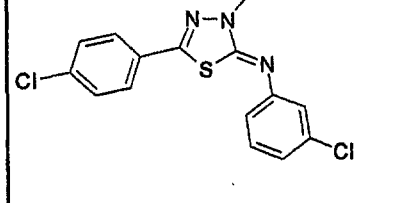
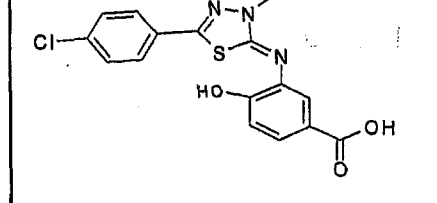
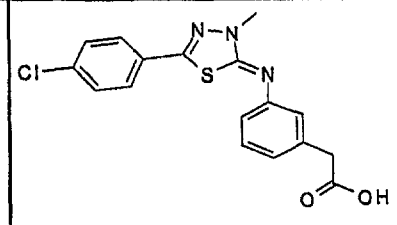
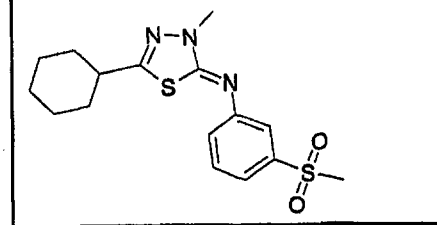
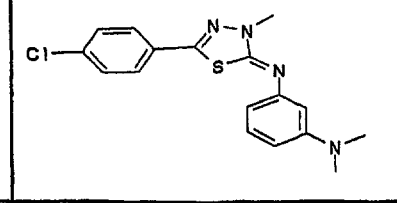
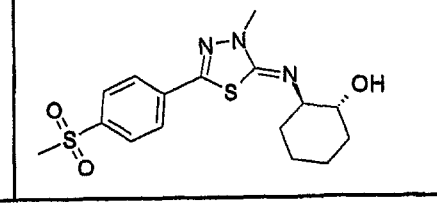
Example	Structure
I1,8	
I1,9	
I1,10	
I2	
I2,1	
I2,2	
I3	
I3,1	

Example	Structure
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I3,3	
I3,4	
I3,5	
I3,6	
I3,7	
I3,8	
I3,9	

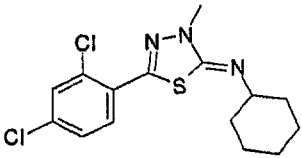
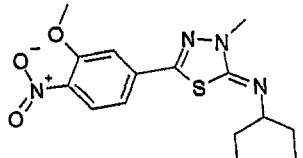
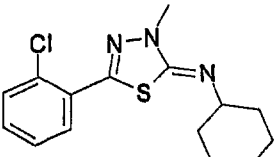
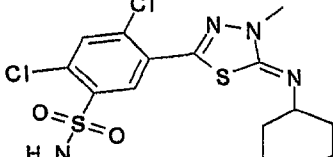
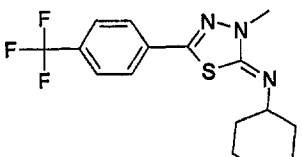
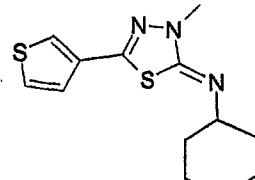
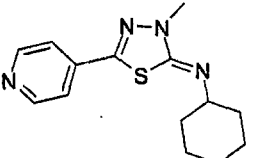
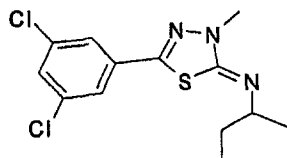
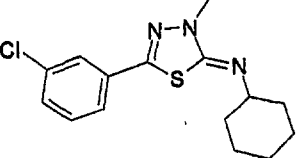
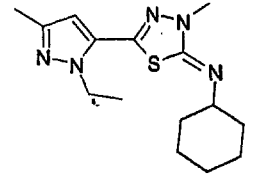
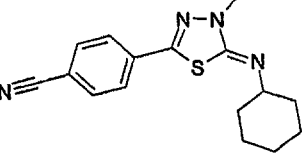
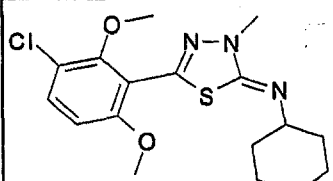
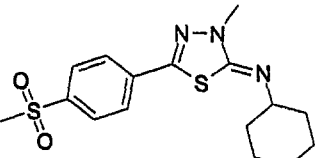
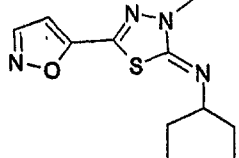
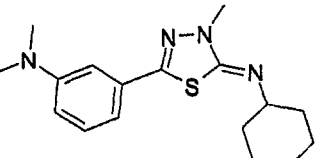
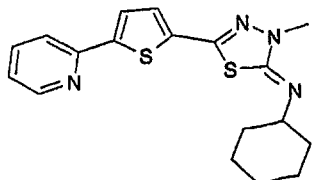
Example	Structure
I3,10	
I3,11	
I3,12	
I3,13	
I3,14	
I3,15	
I3,16	
I3,17	

Example	Structure	Example	Structure
I3,18		I3,26	
I3,19		I4	
I3,20		I4,1	
I3,21		I4,2	
I3,22		I5	
I3,23		I6	
I3,24		I6,1	
I3,25		I6,2	

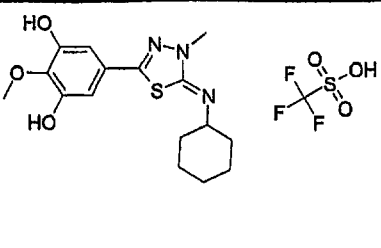
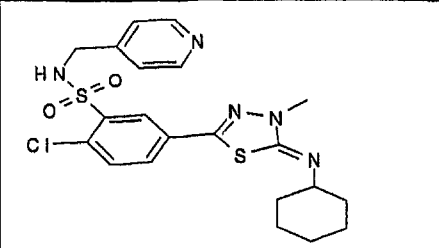
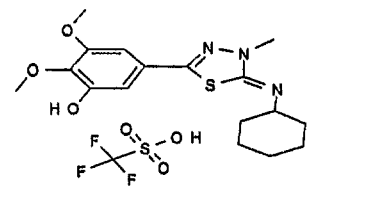
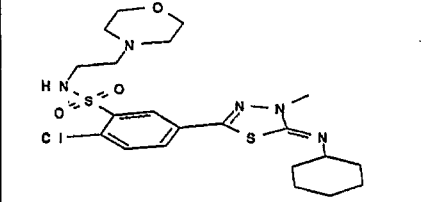
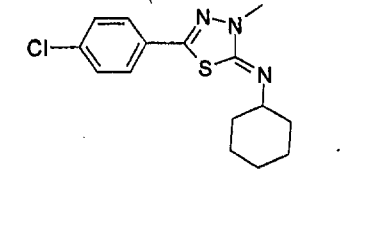
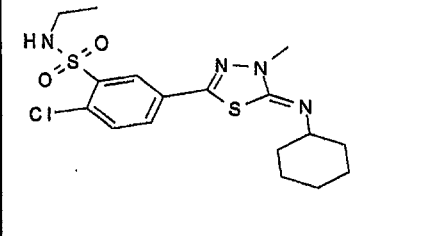
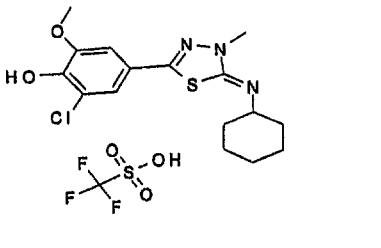
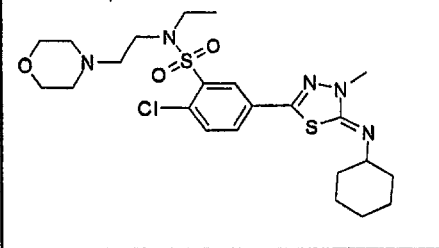
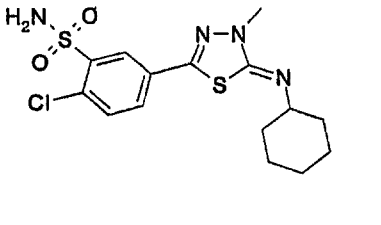
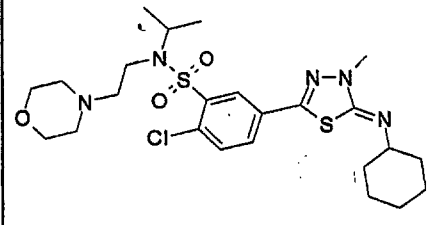
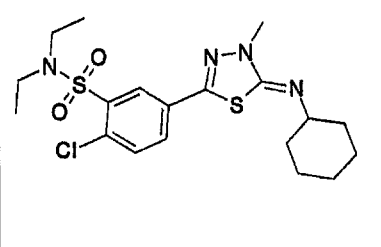
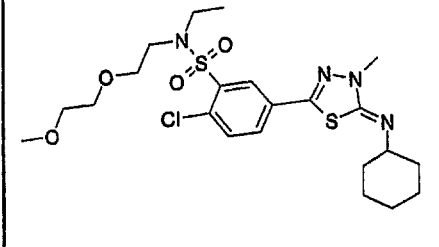
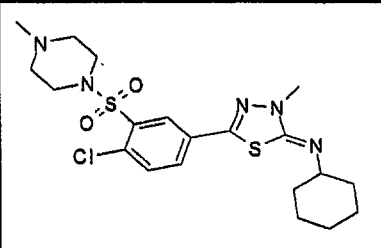
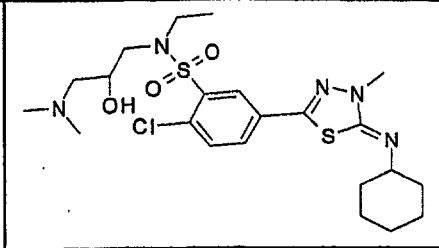
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I6,3		I6,11	
I6,4		I7	
I6,5		I8	
I6,6		I8,1	
I6,7		I8,2	
I6,8		I8,3	
I6,9		I8,4	
I6,10		I9	

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I10		I15,2	
I10,1		I16	
I11		I17	
I12		I17,1	
I13		I17,2	
I14		I18	
I15		I18,1	
I15,1		I18,2	

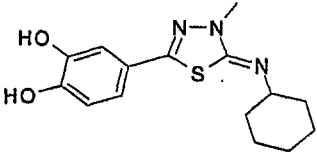
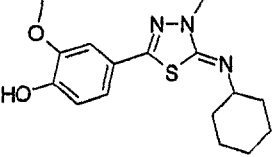
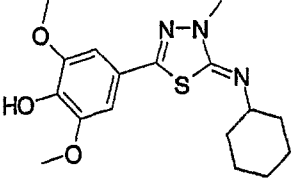
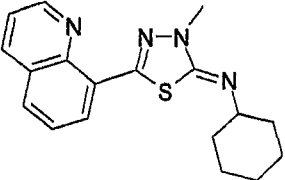
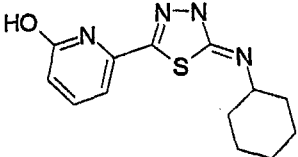
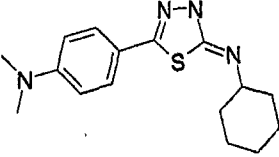
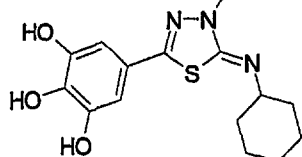
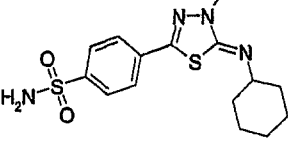
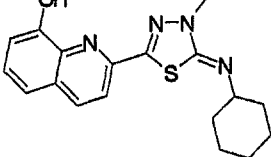
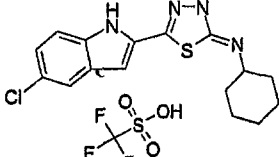
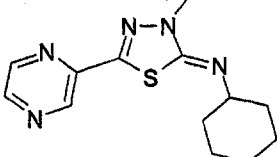
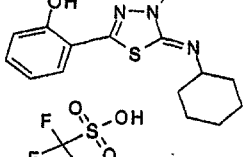
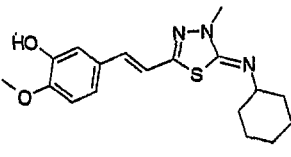
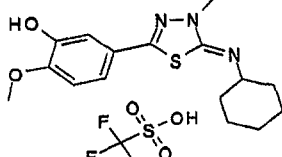
185

I18,3		I19,3	
I18,4		I19,4	
I18,5		I19,5	
I18,6		I19,6	
I119		I19,7	
I19,1		I19,8	
I19,2		I19,9	

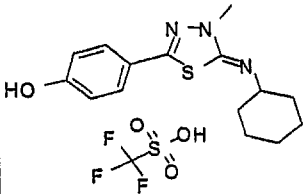
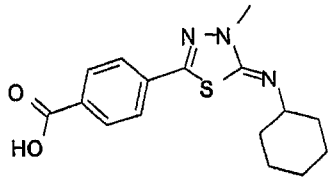
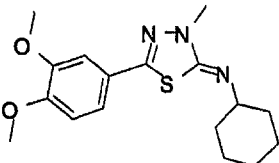
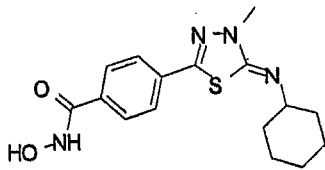
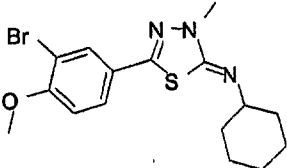
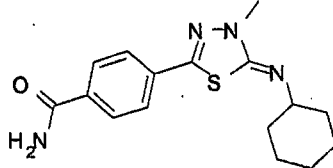
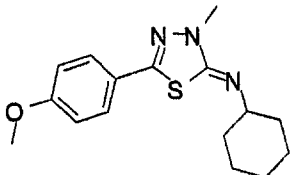
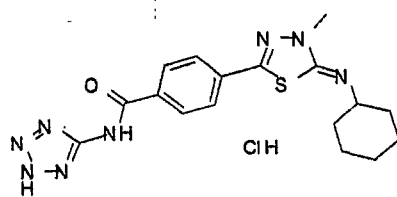
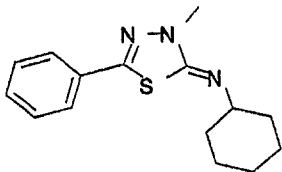
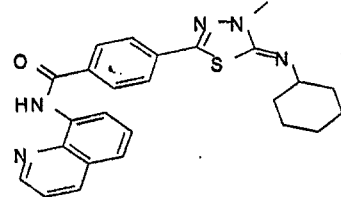
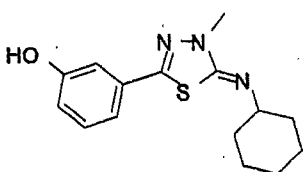
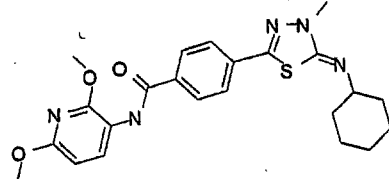
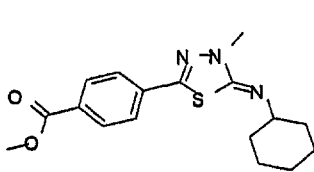
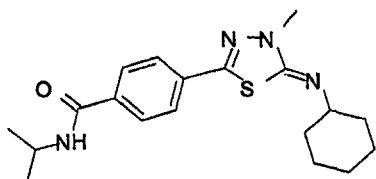
186

I19,10		I20.2	
I19,11		I20.3	
I19,12		I21	
I19,13		I21,1	
I19,14		I21,2	
I20		I21,3	
I20,1		I21,4	

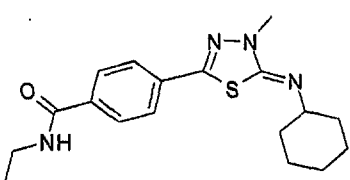
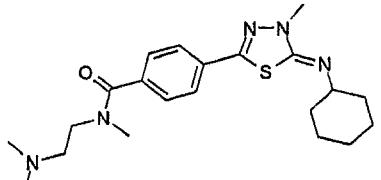
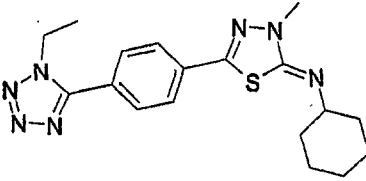
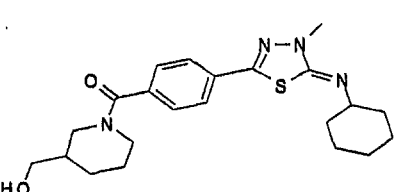
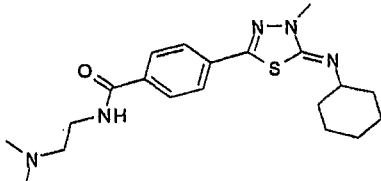
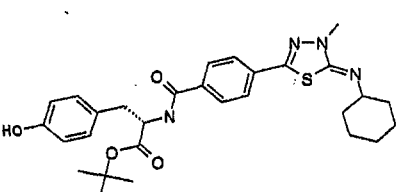
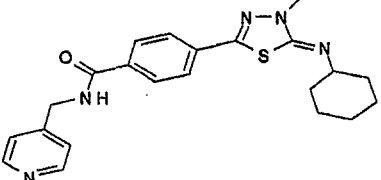
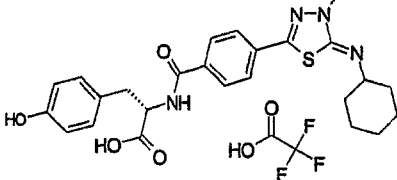
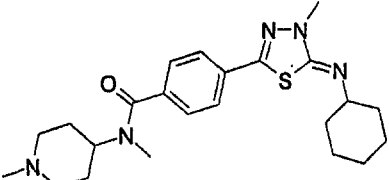
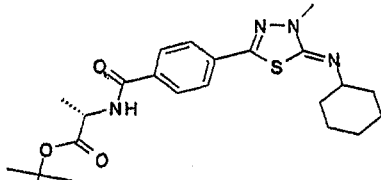
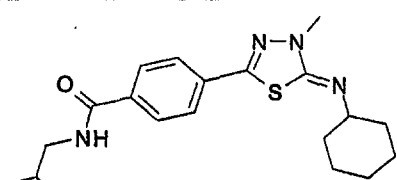
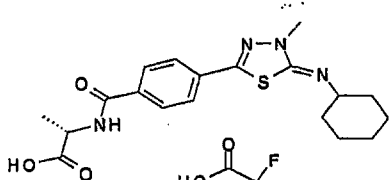
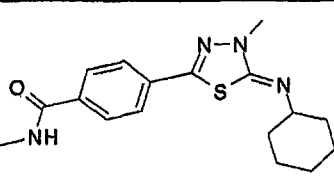
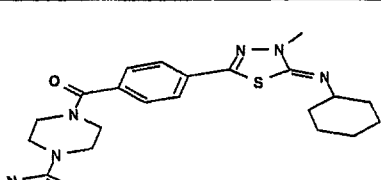
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I22		I27	
I23		I28	
I23,1		I29	
I23,2		I30	
I24		I31	
I25		I31,1	
I26		I32	

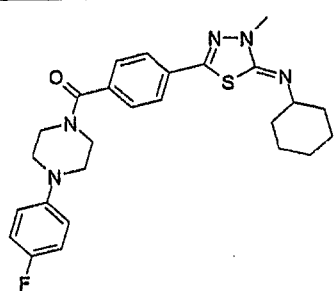
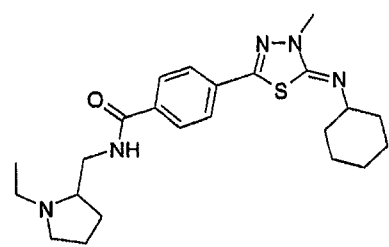
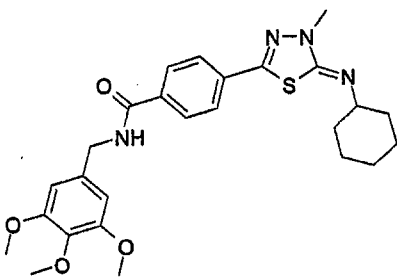
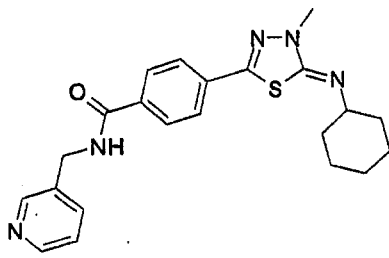
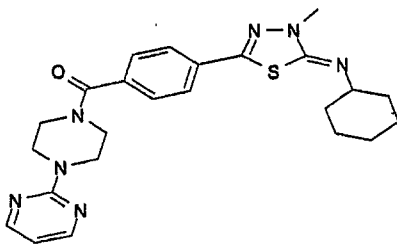
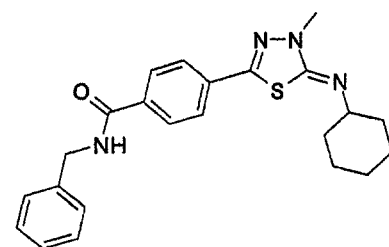
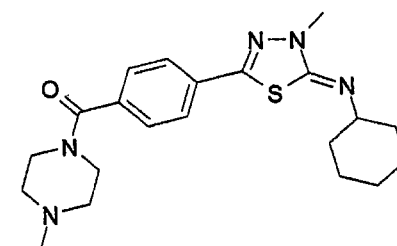
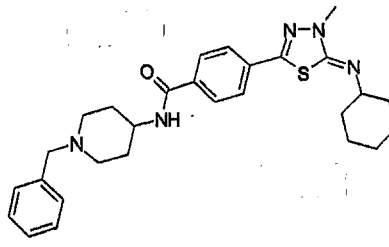
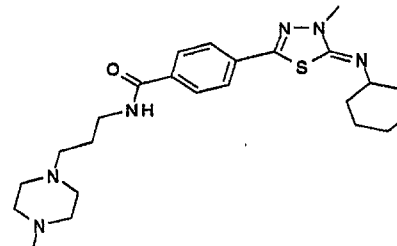
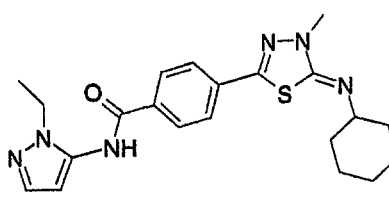
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I33		I37,1	
I34		I37,2	
I35		I37,3	
I35,1		I37,4	
I35,2		I37,5	
I36		I37,6	
I37		I37,7	

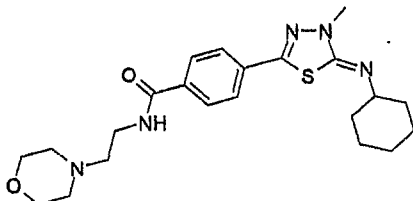
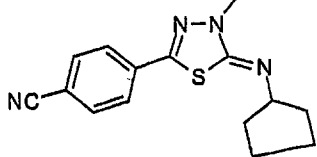
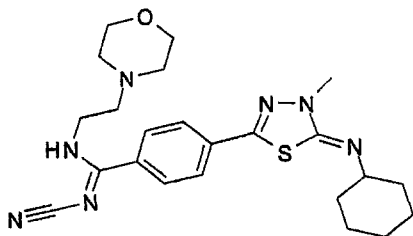
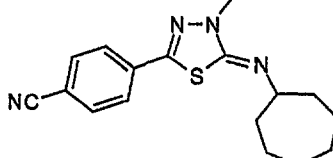
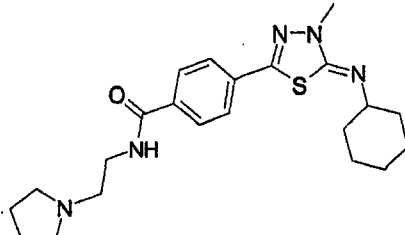
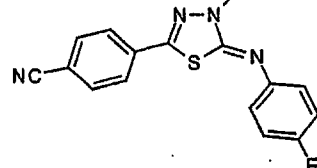
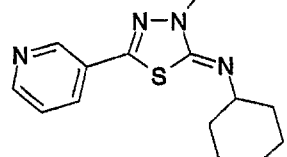
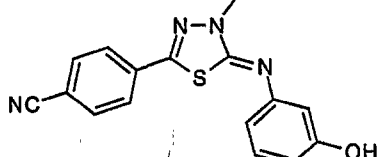
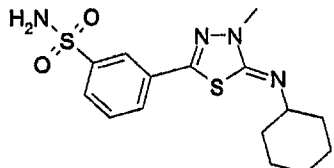
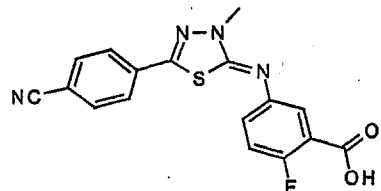
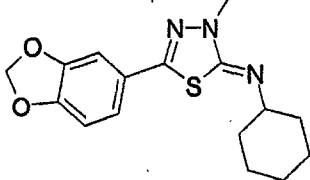
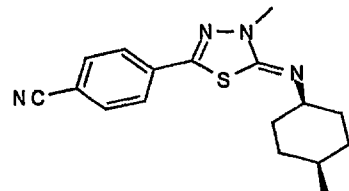
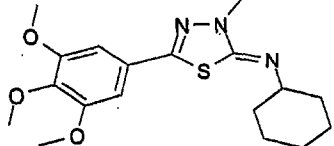
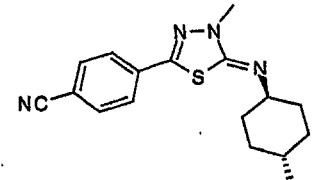
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I37,8		I37,13-1	
I37,8-1		I37,14	
I37,9		I37,15	
I37,10		I37,15-a	
I37,11		I37,16	
I37,12		I37,16-a	
I37,13		I37,17	

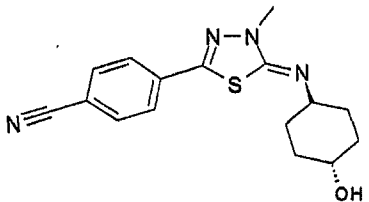
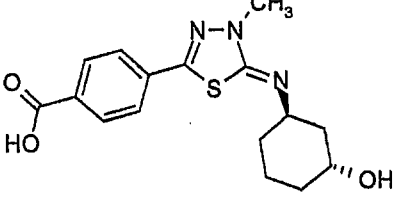
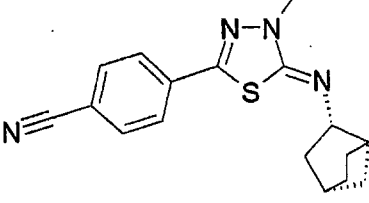
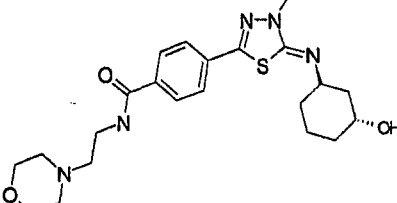
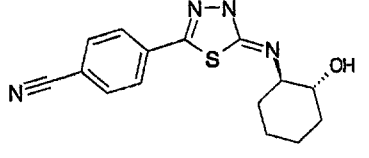
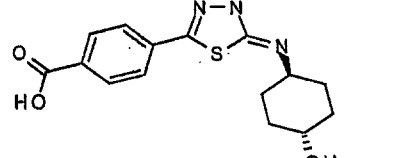
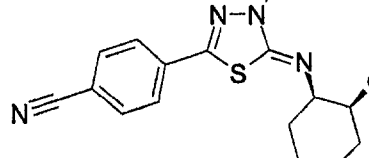
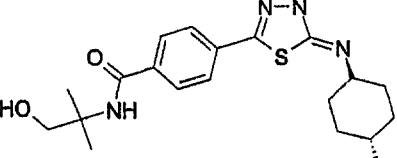
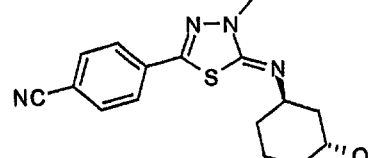
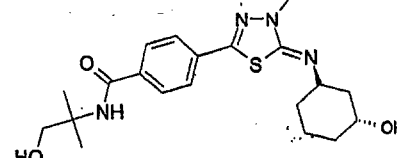
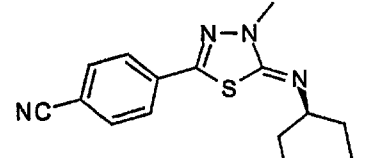
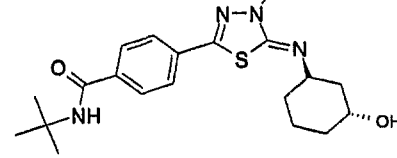
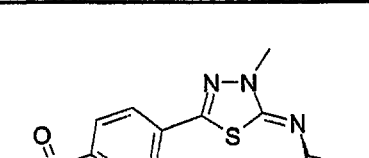
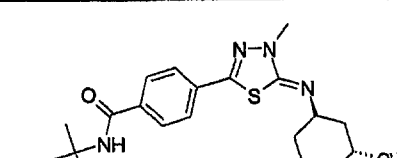
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I37,18		I37,23	
I37,19		I37,24	
I37,20		I37,25	
I37,21		I37,26	
I37,22		I37,27	

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I37,28		I42	
I37,28-1		I43	
I37,29		I44	
I38		I45	
I39		I46	
I40		I47-a	
I41		I47-b	

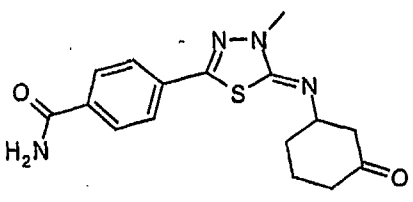
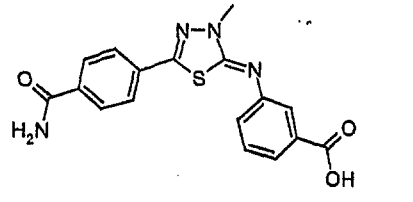
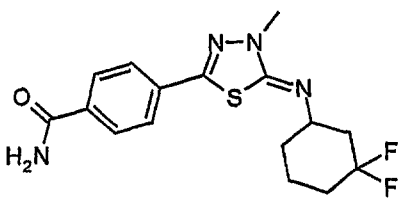
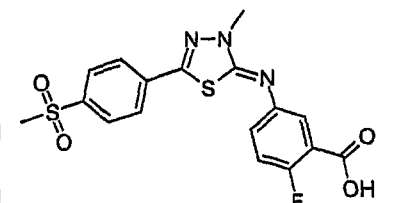
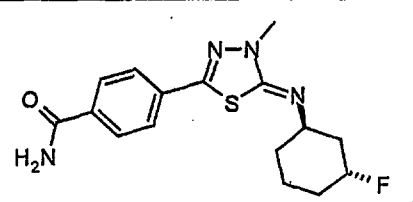
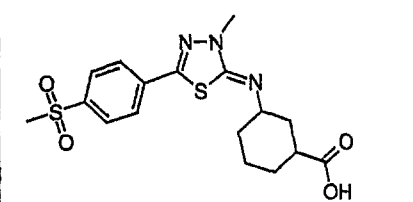
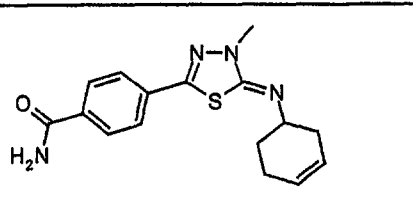
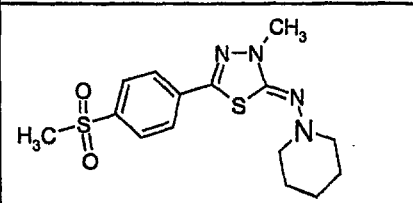
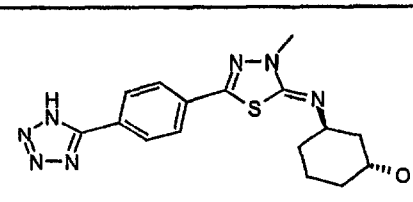
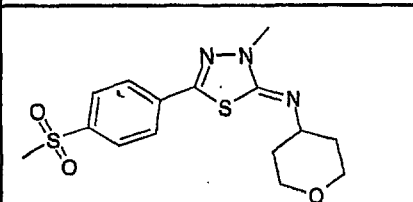
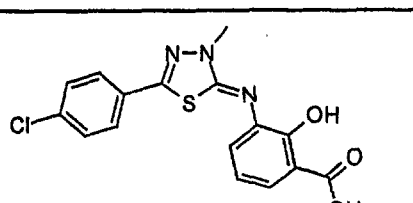
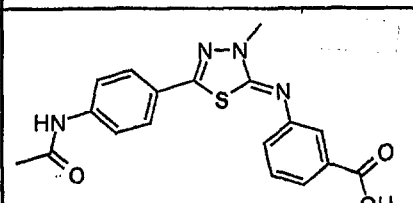
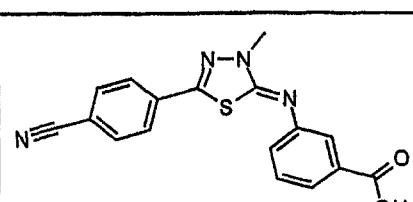
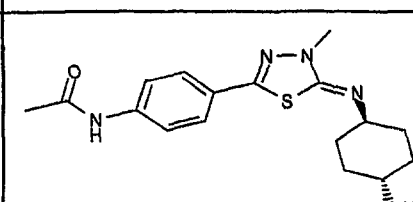
192

I48		I54	
I49		I55	
I50		I56	
I51		I57	
I52-a		I58	
I52-b		I59	
I53		I60	

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I61		I68	
I62		I69	
I63		I70	
I64		I71	
I65		I72	
I66		I73	
I67		I74	

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I74,1		I80,1	
I75		I81	
I76		I82	
I77		I83	
I78		I84	
I79		I85	
I80		I86	

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I87		I91	
I88		I91,1	
I89		I91,2	
I90		I92	
I90,1		I92,1	
I90,2		I92,2	
I90,3		I93	

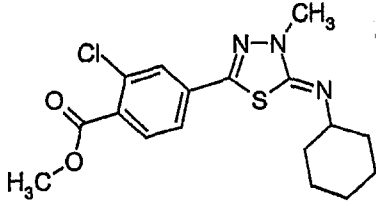
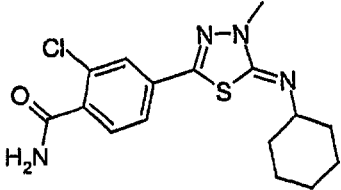
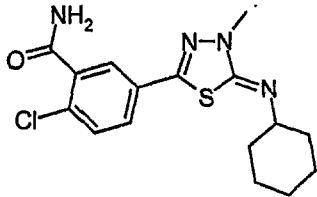
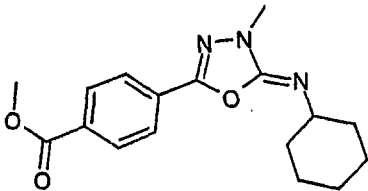
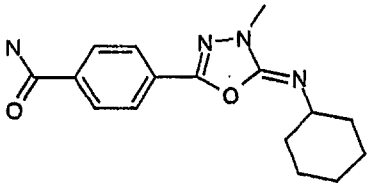
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I93,1		I95	
I93,2		I96	
I93,3		I96,1	
I93,4		I97	
I93,5		I97,1	
I93,6		I98	
I94		I99	

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I99,1		I100,6	
I100		I100,7	
I100,1		I100,8	
I100,2		I100,9	
I100,3		I100,10	
I100,4		I100,11	
I100,5		I101	

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I102	
I102,1	
I103	
I104	
I104,1	

Biological results

In vitro inhibition of the phosphodiesterase 7 and of other phosphodiesterases

The capacity of the compounds of the invention to inhibit cyclic nucleotide phosphodiesterases was evaluated by measuring their IC₅₀ (concentration necessary to inhibit the enzymatic activity by 50 %).

PDE3A3, PDE4D3, PDE7A1 were cloned and expressed in insect cells Sf21 using the baculovirus expression system. The source of PDE103 and of PDE503 were human cell lines

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(respectively TPH1 human monocytes and MCF7 human caucasian breast adenocarcinoma). The various types of phosphodiesterases were obtained partially purified on an anion exchange column (Mono Q) according to a method adapted from Lavan B.E., Lakey T., Houslay M.D. Biochemical Pharmacology, 1989, 38 (22), 4123-4136.

Measurement of the enzymatic activity for the various types of PDE was then made according to a method adapted from W.J. Thompson et al. 1979, Advances in Cyclic Nucleotide Research, Vol. 10 : 69-92, ed. G. Brooker et al. Raven Press, NY.

The substrate used was cGMP for PDE1 and PDE5 and cAMP for PDE 3, PDE 4 and PDE 7. The substrate concentration was 0.2 μ M for PDE 1, PDE 3 and PDE 5, 0,25 μ M for PDE 4 and 50nM for PDE 7.

The enzymatic reaction was stopped after 1 hour for PDE 1, PDE 3 and PDE 5 and 10 minutes for PDE 4 and PDE 7.

In order to determine their IC₅₀, compounds of the invention were assayed at 8 concentrations ranging from 0.03nM to 100 μ M for PDE 4 and PDE 7 and at 6 concentration ranging from 0,1 μ M to 30 μ M for PDE 1, 3 and 5.

The IC₅₀ (μ M) were determined for some of the compounds of the invention, and the results are summarised in the following table:

Compounds	IC ₅₀ (PDE7)	Compounds	IC ₅₀ (PDE7)
I1	0,15	I27	0,46
I2,1	0,13	I28	0,23
I3,25	1,20	I29	0,30
I4	0,15	I30	0,14
I7	1,05	I31	0,23
I8	0,45	I32	0,23
I9	0,28	I33	0,24
I10,1	1,30	I34	0,63
I11	0,98	I35	0,58
I12	0,29	I36	0,29
I13	0,70	I37	0,23

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Compounds	IC ₅₀ (PDE7)	Compounds	IC ₅₀ (PDE7)
I14	0,27	I37,1	0,55
I15	0,14	I37,2	1,2
I17,1	1,30	I37,3	0,062
I18,2	0,32	I37,4	0,15
I18,3	0,061	I37,5	0,093
I18,4	0,092	I37,6	0,097
I18,5	1,20	I37,7	0,086
I19	0,07	I37,8	0,064
I21	0,15	I37,9	0,075
I21,1	0,87	I37,10	0,044
I22	1	I37,11	0,072
I23	0,85	I38	0,34
I24	0,36	I39	0,2
I25	0,47	I40	0,45
I26	0,4	I41	1,3

These results show that the compounds of the invention inhibit PDE7 at very low concentrations, with some IC₅₀ values lower than 100nM. The results of the assays with
5 other PDE (1, 3, 4 and 5) show IC₅₀ values often superior to 10 μ M.

It demonstrates that compounds of the invention are strong and selective PDE7 inhibitors.

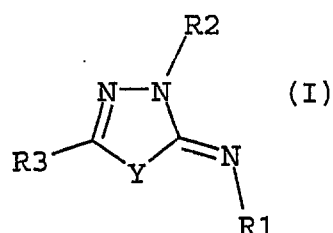
10 References

- M. Akbar Ali, S.E. Livingston, and D.J. Philipps, Inorganica Chimica Acta , 6, 11 (1972)
- P. Molina, A. Tarraga, A. Espinosa ; Synthesis, 690 (1988)
- 15 - P. Molina, A. Tarraga, A. Espinosa ; Heterocycles, vol.29, N°12 (1989)
- R. Noto, P. Lo`Meo, M. Gruttadauria, G. Werber ; J. Heterocyclic Chem., 33, 863 (1996)
- patent: Gulf oil corporation, WO 77 12352
- 20 - patent: Bayer AG, DE 44 18 066 A1.
- patent: Gulf oil corporation, WO 80 1507

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CLAIMS

1. A compound having the following formula (I),



in which

- Y is O or S;

- R1 is:

- 10 C₄-C₁₀ alkyl,
 C₂-C₁₀ alkenyl,
 C₂-C₁₀ alkynyl,
 cycloalkyl,
 cycloalkenyl,
 15 heterocycle,
 aryl,

or a bicyclic group;

each optionally substituted with one or several groups X₁-R₄, identical or different, in which:

- 20 - X₁ is:

a single bond, lower alkylene, C₂-C₆ alkenylene, cycloalkylene, arylene or divalent heterocycle, and,

- R₄ is:

- 25 1) H, =O, NO₂, CN, halogen, lower haloalkyl, lower alkyl, carboxylic acid bioisostere,
 2) COOR₅, C(=O)R₅, C(=S)R₅, SO₂R₅, SOR₅, SO₃R₅, SR₅, OR₅,
 3) C(=O)NR₇R₈, C(=S)NR₇R₈, C(=CH-NO₂)NR₇R₈, C(=N-CN)NR₇R₈,
 30 C(=N-SO₂NH₂)NR₇R₈, C(=NR₇)NHR₈, C(=NR₇)R₈, C(=NR₉)NHR₈, C(=NR₉)R₈, SO₂NR₇R₈ or NR₇R₈ in which R₇ and R₈ are the same or different and are

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selected from OH, R_5 , R_6 , $C(=O)NR_5R_6$, $C(=O)R_5$, SO_2R_5 , $C(=NR_9)NHR_{10}$, $C(=NR_9)R_{10}$, $C(=CH-NO_2)NR_9R_{10}$, $C(=N-SO_2NH_2)NR_9R_{10}$, $C(=N-CN)NR_9R_{10}$ or $C(=S)NR_9R_{10}$;

5 - R2 is:

lower alkyl,
 C_2-C_{10} alkenyl,
 C_4-C_{10} alkynyl,
cycloalkyl,
10 cycloalkenyl,
heterocycle,
aryl;

each optionally substituted with one or several groups which are the same or different and which are selected from:

15 1) H, carboxylic acid bioisostere, lower haloalkyl, halogen,
2) $COOR_5$, OR_5 , SO_2R_5 ,
3) $SO_2NR_{11}R_{12}$, $C(=O)NR_{11}R_{12}$ or $NR_{11}R_{12}$ in which R_{11} and R_{12} are the same or different and are selected
20 from OH, R_5 , R_6 , $C(=O)NR_5R_6$, $C(=O)R_5$, SO_2R_5 , $C(=S)NR_9R_{10}$, $C(=CH-NO_2)NR_9R_{10}$, $C(=N-CN)NR_9R_{10}$, $C(=N-SO_2NH_2)NR_9R_{10}$, $C(=NR_9)NHR_{10}$ or $C(=NR_9)R_{10}$;

- R3 is $X_2-R'_3$ wherein:

25 - X_2 is a single bond or,
a group selected from C_1-C_4 alkylene, C_2-C_6 alkenylene, C_2-C_6 alkynylene, each optionally substituted with one or several groups which are the same or different and which are selected from:
30 1) H, C_1-C_3 alkyl, C_3-C_4 cycloalkyl, aryl, heterocycle, =O, CN,
2) OR_5 , $=NR_5$ or,
3) $NR_{13}R_{14}$ in which R_{13} and R_{14} are the same or different and are selected from R_5 , R_6 , $C(=O)NR_5R_6$,
35 $C(=O)R_5$, SO_2R_5 , $C(=S)NR_9R_{10}$, $C(=CH-NO_2)NR_9R_{10}$, $C(=NR_9)NHR_{10}$ or $C(=NR_9)R_{10}$;

- R'3 is:

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cycloalkyl,
 cycloalkenyl,
 aryl,
 heterocycle,

5 or a polycyclic group;

each optionally substituted with one or several groups X_3 - R_{17} ,
 identical or different, in which:

- X_3 is:

10 a single bond, lower alkylene, C_2 - C_6 alkenylene,
 C_2 - C_6 alkynylene, cycloalkylene, arylene, divalent
 heterocycle or a divalent polycyclic group, and,

- R_{17} is:

15 1) H, =O, NO_2 , CN, lower haloalkyl, halogen,
 cycloalkyl,
 2) $COOR_5$, $C(=O)R_5$, $C(=S)R_5$, SO_2R_5 , SOR_5 , SO_3R_5 , SR_5 ,
 OR_5 ,
 3) $C(=O)NR_{15}R_{16}$, $C(=S)NR_{15}R_{16}$, $C(=N-CN)NR_{15}R_{16}$, $C(=N-$
 $SO_2NH_2)NR_{15}R_{16}$, $C(=CH-NO_2)NR_{15}R_{16}$, $SO_2NR_{15}R_{16}$,
 $C(=NR_{15})NHR_{16}$, $C(=NR_{15})R_{16}$, $C(=NR_9)NHR_{16}$, $C(=NR_9)R_{16}$
 20 or $NR_{15}R_{16}$ in which R_{15} and R_{16} are the same or
 different and are selected from OH, R_5 , R_6 ,
 $C(=O)NR_5R_6$, $C(=O)R_5$, SO_2R_5 , $C(=S)NR_9R_{10}$, $C(=CH-$
 $NO_2)NR_9R_{10}$, $C(=N-CN)NR_9R_{10}$, $C(=N-SO_2NH_2)NR_9R_{10}$,
 $C(=NR_9)NHR_{10}$ or $C(=NR_9)R_{10}$
 25 4) heterocycle optionally substituted with one or
 several groups R_5 ;

- R_5 and R_6 are the same or different and are selected
 from :

30 - H,
 - lower alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl;
 - X_4 -cycloalkyl, X_4 -cycloalkenyl, X_4 -aryl, X_4 -heterocycle
 or X_4 -polycyclic group, in which X_4 is a single bond,
 lower alkylene or C_2 - C_6 alkenylene;
 35 each optionally substituted with one or several groups
 which are the same or different and which are selected
 from:

- halogen, =O, $COOR_{20}$, CN, OR_{20} , lower alkyl

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optionally substituted with OR_{20} , O-lower alkyl optionally substituted with OR_{20} , $C(=O)$ -lower alkyl, lower haloalkyl, X_5-N-R_{18} in which X_5 is a single
 R_{19}

5 bond or lower alkylene and R_{18} , R_{19} and R_{20} are the same or different and are selected from H or lower alkyl;

- X_6 -heterocycle, X_6 -aryl, X_6 -cycloalkyl, X_6 -cycloalkenyl, X_6 -polycyclic group in which X_6 is
 10 selected from a single bond or lower alkylene, these groups being optionally substituted with one or several groups, identical or different, selected from halogens, $COOR_{21}$, OR_{21} , or $(CH_2)_nNR_{21}R_{22}$ in which n is 0, 1 or 2 and R_{21} and R_{22} are the same or different and
 15 are selected from H or lower alkyl;

- R_9 is selected from H, CN, OH, lower alkyl, O-lower alkyl, aryl, heterocycle, SO_2NH_2 or X_5-N-R_{18} in which X_5 is a
 R_{19}

single bond or lower alkylene and R_{18} and R_{19} are the same or
 20 different and are selected from H or lower alkyl;

- R_{10} is selected from hydrogen, lower alkyl, cyclopropyl or heterocycle;

or a pharmaceutically acceptable derivative thereof,

with the proviso that,

25 - when R_1 is phenyl, it bears at least one substituent other than H,

- when X_2 is a single bond and both R_1 and R'_3 are phenyl, each of R_1 and R'_3 bear at least one substituent other than H,

30 - when X_2 is a single bond and R'_3 is phenyl, R'_3 is not substituted by an ester or a carboxylic acid in the ortho position,

- the atom of R_3 which is linked to the thiadiazole group is a carbon atom,

35 with the exclusion of the following compounds,

1-Phenyl-1-[4-phenyl-5-(5-trifluoromethyl-2H-[1,2,4]triazol-3-ylimino)-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-methanone,

1-[4-Phenyl-5-(5-trifluoromethyl-2H-[1,2,4]triazol-3-

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- ylimino)-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-1-thiophen-2-yl-methanone,
 1-Phenyl-1-(4-phenyl-5-p-tolylimino-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-methanone,
 5 Cyclohexyl-[3-(2,4,6-trichloro-phenyl)-5-(2,3,3-trimethyl-cyclopent-1-enylmethyl)-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
 2-(3,5-Diphenyl-3H-[1,3,4]thiadiazol-2-ylideneamino)-1,4-diphenyl-but-2-ene-1,4-dione,
 10 2-[3-Phenyl-5-(1-phenyl-methanoyl)-3H-[1,3,4]thiadiazol-2-ylideneamino]-but-2-enedioic acid dimethyl ester,
 2-[5-(1-Phenyl-methanoyl)-3-p-tolyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-but-2-enedioic acid dimethyl ester, and,
 2-[3-(4-Chloro-phenyl)-5-(1-phenyl-methanoyl)-3H-
 15 [1,3,4]thiadiazol-2-ylideneamino]-but-2-enedioic acid dimethyl ester.

2. A compound according to claim 1 in which R1, R2, R3 and Y are as defined in claim 1 with the proviso that, when
 20 R2 is a phenyl, unsubstituted or substituted with 1 to 3 chlorine or with a methyl, then R3 does not represent C(=O)-phenyl, C(=O)-thienyl, phenyl or CH₂-(2,3,3-trimethyl-cyclopent-1-enyl).

25 3. A compound of formula (I) as defined in claim 1 or 2, in which R1 is:

C₄-C₆ alkyl,
 cycloalkyl,
 cycloalkenyl,
 30 heterocycle,
 aryl,

or a bicyclic group;

each optionally substituted with one or several groups X₁-R₄, identical or different, in which:

- 35 - X₁ is a single bond, a divalent heterocycle or a lower alkylene, and,
 - R₄ is selected from:
 1) H, =O, halogen, CN, lower haloalkyl, preferably

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CF₃, lower alkyl, carboxylic acid bioisostere,

2) COOR₅, SO₂R₅, OR₅, C(=O)R₅

3) C(=O)NR₇R₈, SO₂NR₇R₈ or NR₇R₈ in which R₇ and R₈ are the same or different and are selected from R₅, R₆, C(=O)NR₅R₆, C(=O)R₅, SO₂R₅, C(=NR₉)NHR₁₀, C(=NR₉)R₁₀ or C(=S)NR₉R₁₀,

wherein R₅ is selected from hydrogen or lower alkyl, optionally substituted with OH, and R₆, R₉ and R₁₀ are identical or different and are selected from hydrogen or lower alkyl.

4. A compound as defined in any one of claims 1 to 3 in which R₂ is lower alkyl.

5. A compound as defined in any one of claims 1 to 4 in which R₃ is X₂-R'₃ wherein,

- X₂ is a single bond, C₁-C₄ alkylene, C₂-C₆ alkenylene or C₂-C₆ alkynylene, and,

- R'₃ is:

cycloalkyl,

cycloalkenyl,

aryl,

heterocycle,

or a polycyclic group;

each optionally substituted with one or several groups X₃-R₁₇, identical or different, in which:

- X₃ is a single bond or lower alkylene, and,

- R₁₇ is:

1) H, =O, NO₂, CN, lower haloalkyl, halogen, cycloalkyl,

2) COOR₅, C(=O)R₅, C(=S)R₅, SO₂R₅, SOR₅, SO₃R₅, SR₅, OR₅,

3) C(=O)NR₁₅R₁₆, C(=S)NR₁₅R₁₆, C(=N-CN)NR₁₅R₁₆, C(=CH-NO₂)NR₁₅R₁₆, SO₂NR₁₅R₁₆, C(=NR₁₅)NHR₁₆,

C(=NR₁₅)R₁₆, C(=NR₉)NHR₁₆, C(=NR₉)R₁₆ or NR₁₅R₁₆ in which R₁₅ and R₁₆ are the same or different and are selected from OH, R₅, R₆, C(=O)NR₅R₆, C(=O)R₅, SO₂R₅, C(=S)NR₉R₁₀, C(=CH-NO₂)NR₉R₁₀, C(=N-CN)NR₉R₁₀,

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 $C(=NR_9)NHR_{10}$ or $C(=NR_9)R_{10}$,

4) heterocycle optionally substituted with one or several groups R_5 .

5 6. A compound as defined in any one of claims 1 to 5, in which R_1 is:

cycloalkyl, preferably cyclohexane,

cycloalkenyl,

aryl, preferably phenyl,

10 or a bicyclic group;

each optionally substituted with one or several groups X_1 - R_4 , identical or different, in which:

- X_1 is a single bond or a divalent heterocycle, and,

15 - R_4 is selected from:

1) H, halogen, CF_3 , $=O$,

2) $COOR_5$, OR_5 ,

3) $C(=O)NR_5R_6$.

wherein R_5 and R_6 are identical or different and
20 are selected from hydrogen or methyl.

7. A compound as defined in any one of claims 1 to 6, in which R_2 is CH_3 .

25 8. A compound as defined in any one of claims 1 to 7 in which R_3 is X_2 - R'_3 wherein,

- X_2 is a single bond, C_1 - C_4 alkylene or C_2 - C_6 alkenylene, and,

- R'_3 is:

30 cycloalkyl,

aryl, preferably phenyl,

heterocycle,

or a polycyclic group;

each optionally substituted with one or several groups X_3 - R_{17} ,

35 identical or different, in which:

- X_3 is a single bond or $-CH_2-$, and,

- R_{17} is:

1) H, CN, CF_3 , halogen, NO_2 ,

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- 2) COOR_5 , SO_2R_5 , OR_5 , $\text{C}(=\text{O})\text{R}_5$,
 3) $\text{C}(=\text{O})\text{NR}_{15}\text{R}_{16}$, $\text{SO}_2\text{NR}_{15}\text{R}_{16}$ or $\text{NR}_{15}\text{R}_{16}$ in which R_{15}
 and R_{16} are the same or different and are selected
 from OH , R_5 , R_6 , $\text{C}(=\text{O})\text{NR}_5\text{R}_6$, $\text{C}(=\text{O})\text{R}_5$, SO_2R_5 ,
 5 $\text{C}(=\text{S})\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{NR}_9)\text{NHR}_{10}$,
 $\text{C}(=\text{NR}_9)\text{R}_{10}$ or $\text{C}(=\text{N}-\text{CN})\text{NR}_9\text{R}_{10}$,
 4) heterocycle optionally substituted with one or
 several groups R_5 .

10 9. A compound according to claims 3, 4 and 5.

10. A compound according to claims 6, 7 and 8.

11. A compound as defined in claim 1 in which

15 R_1 is:

cyclohexane,
 phenyl
 or a bicyclic group;

each optionally substituted with one or several groups X_1-R_4 ,
 20 identical or different, in which:

- X_1 is a single bond or a divalent heterocycle,
 and,
- R_4 is selected from:
 - 1) H , halogen, CF_3 ,
 - 25 2) COOH , OH ,
 - 3) $\text{C}(=\text{O})\text{NR}_7\text{R}_8$ in which R_7 and R_8 are the same or
 different and are selected from H or lower alkyl,

R_2 is CH_3 , and,

30

R_3 is $\text{X}_2-\text{R}'_3$ wherein,

- X_2 is a single bond, C_1-C_4 alkylene or C_2-C_6
 alkenylene, and,
- R'_3 is:

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phenyl
 heterocycle,
 or a polycyclic group;

each optionally substituted with one or several groups X_3-R_{17} ,

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identical or different, in which:

- X_3 is a single bond, and,
- R_{17} is:
 - 1) CN, OH, CF_3 , =O, C_1 - C_6 alkoxy, halogen,
 - 2) $COOR_5$, SO_2R_5 ,
 - 3) $C(=O)NR_{15}R_{16}$, $SO_2NR_{15}R_{16}$ or $NR_{15}R_{16}$ in which R_{15} and R_{16} are the same or different and are selected from OH, $C(=O)R_5$, $C(=O)NR_5R_6$, R_5 or R_6 ,
 - 4) heterocycle optionally substituted with one or several groups R_5 .

12. A compound as defined in any one of claims 1 to 11 in which Y is S.

13. A compound as defined in any one of claims 1 to 11 in which Y is O.

14. A compound selected from the group consisting of:
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
(1R*, 2R*)-2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-cyclohexanecarboxylic acid,
(S)-2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-phenyl-ethanol,
2-{2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-phenyl}-ethanol,
{1-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-cyclopentyl}-methanol,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-cyclohexanecarboxylic acid,
5-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-fluoro-benzoic acid,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2,5,6-trifluoro-benzoic acid,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-propyl-amine,
(S)-2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-butan-1-ol,

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[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclobutyl-amine,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-azepan-2-one,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclopentyl-amine,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cycloheptyl-amine,
(S)-2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-3-methyl-butan-1-ol,
2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-methyl-propan-1-ol,
tert-Butyl-[5-(4-chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-isopropyl-amine,
4-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-(1-ethyl-propyl)-amine,
4-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-phenol,
N-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexane-1,2-diamine,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-(4-fluoro-phenyl)-amine,
N-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexane-1,4-diamine,
(1R*, 2S*)-2-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-cyclohexanol,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-(4-trifluoromethyl-phenyl)-amine,
3-[5-(4-Methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-phenol,
5-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-hydroxy-benzoic acid,

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(1-Aza-bicyclo[2.2.2]oct-3-yl) - [5- (4-chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] -amine,
2- [5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -phenol,
(R) - 2- [5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -butan-1-ol,
[5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] - (3-fluoro-phenyl) -amine,
(3-Chloro-phenyl) - [5- (4-chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] -amine,
{3- [5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -phenyl} -acetic acid,
3- [5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -benzamide,
Bicyclo[2.2.1]hept-2-yl - [5- (4-chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] -amine,
(1R*, 2R*) - 2- [5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -cyclohexanol,
5- (5-Cyclohexyl-3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino) -2-methoxy-phenol,
3- (5-Cyclohexyl-3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino) -benzoic acid,
3- [5- (4-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -4-hydroxy-benzoic acid,
(5-Cyclohexyl-3-methyl-3H- [1,3,4]thiadiazol-2-ylidene) - (3-methanesulfonyl-phenyl) -amine,
(1R*, 2R*) - 2- [5- (4-Methanesulfonyl-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylideneamino] -cyclohexanol,
Cyclohexyl - [5- (2,4-dichloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] -amine,
[5- (2-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] -cyclohexyl-amine,
Cyclohexyl - [3-methyl-5- (4-trifluoromethyl-phenyl) - 3H- [1,3,4]thiadiazol-2-ylidene] -amine,
Cyclohexyl - (3-methyl-5-pyridin-4-yl-3H- [1,3,4]thiadiazol-2-ylidene) -amine,
[5- (3-Chloro-phenyl) - 3-methyl-3H- [1,3,4]thiadiazol-2-ylidene] -cyclohexyl-amine,

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4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzonitrile,
Cyclohexyl-[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
[3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-dimethyl-amine,
Cyclohexyl-[5-(3-methoxy-4-nitro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
2,4-Dichloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide,
Cyclohexyl-(3-methyl-5-thiophen-3-yl-3H-[1,3,4]thiadiazol-2-ylidene)-amine,
Cyclohexyl-[5-(3,5-dichloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
Cyclohexyl-[5-(2-ethyl-5-methyl-2H-pyrazol-3-yl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
[5-(3-Chloro-2,6-dimethoxy-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
Cyclohexyl-(5-isoxazol-5-yl-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene)-amine,
Cyclohexyl-[3-methyl-5-(5-pyridin-2-yl-thiophen-2-yl)-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
5-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-2-methoxy-benzene-1,3-diol; compound with trifluoromethanesulfonic acid,
5-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-2,3-dimethoxy-phenol,
compound with trifluoro-methanesulfonic acid
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-6-methoxy-phenol; compound with 1,1,1-trifluoro-methanesulfonic acid,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N,N-diethylbenzenesulfonamide,

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{5-[4-Chloro-3-(4-methyl-piperazine-1-sulfonyl)-phenyl]-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene}-cyclohexyl-amine,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-pyridin-4-ylmethyl-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-morpholin-4-yl-ethyl)-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-N-(2-morpholin-4-yl-ethyl)-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-isopropyl-N-(2-morpholin-4-yl-ethyl)-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-N-[2-(2-methoxy-ethoxy)-ethyl]-benzenesulfonamide,
 C-Chloro-(cyclohexylimino-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(dimethylamino-hydroxy-propyl)-N-ethyl-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2,3-dihydroxy-propyl)-N-ethyl-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzenesulfonamide,
 2-Chloro-5-(cyclohexylimino-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-diethylamino-ethyl)-N-ethyl-benzenesulfonamide,
 2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-dimethylamino-propyl)-N-ethyl-benzenesulfonamide,
 [5-(4-Chloro-phenyl)-2-cyclohexylimino-[1,3,4]thiadiazol-3-yl]-acetic acid methyl ester,
 3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester,

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3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid,
3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-hydroxy-ethyl)-benzamide,
3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-methyl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzene-1,2-diol,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2,6-dimethoxy-phenol,
6-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-pyridin-2-ol,
5-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzene-1,2,3-triol,
2-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-quinolin-8-ol,
Cyclohexyl-(3-methyl-5-pyrazin-2-yl-3H-[1,3,4]thiadiazol-2-ylidene)-amine,
5-[(E)-2-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-vinyl]-2-methoxy-phenol,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-phenol,
Cyclohexyl-(3-methyl-5-quinolin-8-yl-3H-[1,3,4]thiadiazol-2-ylidene)-amine,
[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-dimethyl-amine,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide,
[5-(5-Chloro-1H-indol-2-yl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine; compound with trifluoro-methanesulfonic acid,
2-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenol; compound with 1,1,1-trifluoro-methanesulfonic acid,

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5-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-phenol,
compound with 1,1,1-trifluoro-methanesulfonic acid,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenol, compound with 1,1,1-trifluoro-methanesulfonic acid,
Cyclohexyl-[5-(3,4-dimethoxy-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
[5-(3-Bromo-4-methoxy-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
Cyclohexyl-[5-(4-methoxy-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
Cyclohexyl-(3-methyl-5-phenyl-3H-[1,3,4]thiadiazol-2-ylidene)-amine,
3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenol,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-hydroxy-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2H-tetrazol-5-yl)-benzamide hydrochloride salt,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-quinolin-8-yl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-(2,6-dimethoxy-pyridin-3-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-isopropyl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-ethyl-benzamide,
Cyclohexyl-{5-[4-(1-ethyl-1H-tetrazol-5-yl)-phenyl]-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene}-amine,

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4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-(2-dimethylamino-ethyl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-pyridin-4-ylmethyl-benzamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N,N-diethylbenzenesulfonamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-isobutyl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-methyl-benzamide,
4-(Cyclohexylimino-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-(2-dimethylamino-ethyl)-N-methyl-benzamide,
[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-phenyl]-1-(3-hydroxymethyl-piperidin-1-yl)-methanone,
2-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-benzoylamino]-3-(4-hydroxy-phenyl)-propionic acid tert-butyl ester,
2-([1-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-phenyl]-methanoyl]-amino)-3-(4-hydroxy-phenyl)-propionic acid, compound with 2,2,2-trifluoro-acetic acid,
(S)-2-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-benzoylamino]-propionic acid tert-butyl ester,
(S)-2-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-benzoylamino]-propionic acid; compound with 2,2,2-trifluoro-acetic acid,
[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-phenyl]-(4-pyridin-2-yl-piperazin-1-yl)-methanone,
[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-phenyl]-[4-(4-fluoro-phenyl)-piperazin-1-yl]-methanone,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-(3,4,5-trimethoxy-benzyl)-benzamide,

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[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-(4-pyrimidin-2-yl-piperazin-1-yl)-methanone,
[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-(4-methyl-piperazin-1-yl)-methanone,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-[3-(4-methyl-piperazin-1-yl)-propyl]-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(1-ethyl-pyrrolidin-2-ylmethyl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-pyridin-3-ylmethyl-benzamide,
N-Benzyl-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
N-(1-Benzyl-piperidin-4-yl)-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-ethyl-2H-pyrazol-3-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-morpholin-4-yl-ethyl)-benzamide,
[5-(4-((N-cyano-N'-ethylmorpholine)-carboximidamide)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene)-cyclohexyl-amine,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide,
Cyclohexyl-(3-methyl-5-pyridin-3-yl-3H-[1,3,4]thiadiazol-2-ylidene)-amine,
3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide,
(5-Benzo[1,3]dioxol-5-yl-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene)-cyclohexyl-amine,
Cyclohexyl-[3-methyl-5-(3,4,5-trimethoxy-phenyl)-3H-[1,3,4]thiadiazol-2-ylidene]-amine,

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4- (5-Cyclopentylimino-4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl) -benzonitrile,
4- (5-Cycloheptylimino-4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl) -benzonitrile,
4- [5- (4-Fluoro-phenylimino) -4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- (3-Hydroxy-phenylimino) -4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl] -benzonitrile,
5- [5- (4-Cyano-phenyl) -3-methyl-3H- [1,3,4]thiadiazol-2-
ylideneamino] -2-fluoro-benzoic acid,
4- [4-Methyl-5- (cis-4-methyl-cyclohexylimino) -4,5-dihydro-
[1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [4-Methyl-5- (trans-4-methyl-cyclohexylimino) -4,5-dihydro-
[1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- (trans-4-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- (Bicyclo[2.2.1]hept-2-ylimino) -4-methyl-4,5-dihydro-
[1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- ((1R*, 2R*) -2-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- ((1R*, 2S*) -2-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- ((1R*, 3R*) -3-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzonitrile,
4- [5- ((1R*, 3S*) -3-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzonitrile,
(1R*, 3R*)) -3- [5- (4-Methanesulfonyl-phenyl) -3-methyl-3H-
[1,3,4]thiadiazol-2-ylideneamino] -cyclohexanol,
4- [5- (1R*, 3R*) -3-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzoic acid,
4- [5- ((1R*, 3R*) -3-hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -N- (2-morpholin-4-yl-ethyl) -
benzamide,
4- [5- (trans-4-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -benzoic acid,
4- [5- (trans-4-Hydroxy-cyclohexylimino) -4-methyl-4,5-
dihydro- [1,3,4]thiadiazol-2-yl] -N- (2-hydroxy-1,1-dimethyl-
ethyl) -benzamide,

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4-[5-((1R*, 3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-N-(2-hydroxy-1,1-dimethylethyl)-benzamide,
N-tert-Butyl-4-[5-((1R*, 3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
N-(1,1-dimethyl-3-oxo-butyl)-4-[5-((1R*, 3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
N-(2-Cyano-1,2,2-trimethyl-ethyl)-4-[5-((1R*, 3R*)-3-hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
1-{4-[5-((1R*, 3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzoylamino}-cyclopropanecarboxylic acid methyl ester,
4-(5-Cyclopentylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cycloheptylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-[5-(4-Fluoro-phenylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-(3-Hydroxy-phenylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
5-[5-(4-Carbamoyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-fluoro-benzoic acid,
4-[4-Methyl-5-(4-methyl-cyclohexylimino)-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-(4-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-(Bicyclo[2.2.1]hept-2-ylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-((1R*, 2R*)-2-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-((1R*, 2S*)-2-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-((1R*, 3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-((1R*, 3S*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,

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4-[4-Methyl-5-(3-oxo-cyclohexylimino)-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-(3,3-Difluoro-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-((1R*,3R*)-3-Fluoro-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
4-[5-(Cyclohex-3-enylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-benzamide,
(1R*,3R*)-3-{3-Methyl-5-[4-(1H-tetrazol-5-yl)-phenyl]-3H-[1,3,4]thiadiazol-2-ylideneamino}-cyclohexanol,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-2-hydroxy-benzoic acid,
3-[5-(4-Cyano-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
3-[5-(4-carbamoyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
2-Fluoro-5-[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
3-[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-cyclohexanecarboxylic acid,
[5-(4-methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-piperidin-1-yl amine,
[5-(4-Methanesulfonyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-(tetrahydro-pyran-4-yl)-amine,
3-[5-(4-Acetylamino-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
N-{4-[5-(trans-4-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide,
N-{4-[5-((1R*,3S*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide,
N-{4-[5-((1R*,3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-phenyl}-acetamide,
N-{5-[5-((1R*,3R*)-3-Hydroxy-cyclohexylimino)-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl]-pyridin-2-yl}-acetamide,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzonitrile,

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[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-[3-(1H-tetrazol-5-yl)-phenyl]-amine,
3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-N-hydroxy-benzamidine,
3-{3-[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-phenyl}-[1,2,4]oxadiazol-5-ol,
[5-(4-Bromo-3-methyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methyl-benzonitrile,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methyl-benzamide,
[5-(4-Bromo-3-methoxy-phenyl)-3-methyl-2,3-dihydro-[1,3,4]thiadiazol-2-yl]-cyclohexyl-amine,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-hydroxy-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-nitro-benzoic acid methyl ester,
2-Amino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester,
2-Acetylamino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester,
2-Amino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-3H-quinazolin-4-one,
7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-quinazolin-4-ylamine,
7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-1H-quinazoline-2,4-dione,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-benzenesulfonamide,
5-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2-methoxy-benzenesulfonamide,
3-[5-(3-Cyano-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid methyl ester,

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3-[5-(3-Cyano-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
 3-[3-Methyl-5-pyridin-2-yl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
 3-[5-(4-Chloro-3-sulfamoyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
 4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzonitrile,
 Cyclohexyl-{3-methyl-5-[4-(1H-tetrazol-5-yl)-phenyl]-3H-[1,3,4]thiadiazol-2-ylidene}-amine,
 Cyclohexyl-[3-methyl-5-(4-nitro-phenyl)-3H-[1,3,4]thiadiazol-2-ylidene]-amine,
 4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenylamine,
 [5-(4-(N-cyano-N'-(2-dimethylaminoethyl)-carboximidamide)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
 N-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-acetamide,
 [5-(4-(bis-ethylsulfonylamino)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
 [5-(4-(1-(2-dimethylaminoethyl)amino-2-nitro-vinylamino)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
 (E)-N¹-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-2-nitro-ethene-1,1-diamine,
 [5-(N-cyano-N'-methyl-4-carboximidamide-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
 [5-(4-(N-cyano-N'-amino-carboximidamide)-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-cyclohexyl-amine,
 Ethanesulfonic acid [4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-amide,
 [4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-urea,
 1-[4-(Cyclohexylimino-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea,
 2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide,

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2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester,
2-Chloro-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-benzoic acid methyl ester, and,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-benzamide.

15. A compound according to claim 14, selected from the group consisting of:

5-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-2-methoxy-benzene-1,3-diol;
compound with trifluoro-methanesulfonic acid,
5-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-2,3-dimethoxy-phenol;
compound with trifluoro-methanesulfonic acid,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N,N-diethyl-benzenesulfonamide,
{5-[4-Chloro-3-(4-methyl-piperazine-1-sulfonyl)-phenyl]-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene}-cyclohexyl-amine,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-pyridin-4-ylmethyl-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-morpholin-4-yl-ethyl)-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-N-(2-morpholin-4-yl-

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ethyl)-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-isopropyl-N-(2-morpholin-4-yl)-ethyl)-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-N-[2-(2-methoxy-ethoxy)-ethyl]-benzenesulfonamide,
C-Chloro-(cyclohexylimino-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(dimethylamino-hydroxy-propyl)-N-ethyl-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2,3-dihydroxy-propyl)-N-ethyl-benzenesulfonamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-ethyl-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzenesulfonamide,
3-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-quinolin-8-yl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-(2,6-dimethoxy-pyridin-3-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-isopropyl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-ethyl-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-(2-dimethylamino-ethyl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N-pyridin-4-ylmethyl-benzamide,
2-Chloro-5-(5-cyclohexylimino-4-methyl-4,5-dihydro[1,3,4]thiadiazol-2-yl)-N,N-diethyl-benzenesulfonamide,

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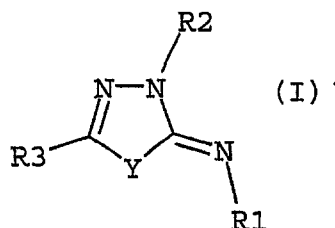
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-methyl-benzamide,
2-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoylamino]-3-(4-hydroxy-phenyl)-propionic acid tert-butyl ester,
(S)-2-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoylamino]-3-(4-hydroxy-phenyl)-propionic acid; compound with 2,2,2-trifluoroacetic acid,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(3,4,5-trimethoxy-benzyl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-[3-(4-methyl-piperazin-1-yl)-propyl]-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-pyridin-3-ylmethyl-benzamide,
N-(1-Benzyl-piperidin-4-yl)-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-ethyl-2H-pyrazol-3-yl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-morpholin-4-yl-ethyl)-benzamide,
4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide,
3-[5-(4-carbamoyl-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylideneamino]-benzoic acid,
[5-(4-Chloro-phenyl)-3-methyl-3H-[1,3,4]thiadiazol-2-ylidene]-[3-(1H-tetrazol-5-yl)-phenyl]-amine,
2-Amino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzoic acid methyl ester,
2-Amino-4-(5-cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-benzamide,
7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-3H-quinazolin-4-one,

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7-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-quinazolin-4-ylamine,,
 N-[4-(5-Cyclohexylimino-4-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-acetamide, and,
 1-[4-(Cyclohexylimino-methyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea.

16. Pharmaceutical composition comprising a compound of formula (I),

5



wherein:

- Y is O or S;
- R1 is:

10 C₁-C₁₀ alkyl,
 C₂-C₁₀ alkenyl,
 C₂-C₁₀ alkynyl,
 cycloalkyl,
 cycloalkenyl,
 15 heterocycle,
 aryl,

or a polycyclic group;

each optionally substituted with one or several groups X₁-R₄, identical or different, in which:

- 20 - X₁ is:
 a single bond, lower alkylene, C₂-C₆ alkenylene, cycloalkylene, arylene or a divalent heterocycle, and,
 - R₄ is:
 25 1) H, =O, NO₂, CN, halogen, lower haloalkyl, lower

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alkyl, carboxylic acid bioisostere,

2) COOR_5 , $\text{C}(=\text{O})\text{R}_5$, $\text{C}(=\text{S})\text{R}_5$, SO_2R_5 , SOR_5 , SO_3R_5 , SR_5 , OR_5 ,

5 3) $\text{C}(=\text{O})\text{NR}_7\text{R}_8$, $\text{C}(=\text{S})\text{NR}_7\text{R}_8$, $\text{C}(=\text{N}-\text{CN})\text{NR}_7\text{R}_8$, $\text{C}(=\text{N}-\text{SO}_2\text{NH}_2)\text{NR}_7\text{R}_8$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_7\text{R}_8$, $\text{C}(=\text{NR}_7)\text{NHR}_8$, $\text{C}(=\text{NR}_7)\text{R}_8$, $\text{C}(=\text{NR}_9)\text{NHR}_8$, $\text{C}(=\text{NR}_9)\text{R}_8$, $\text{SO}_2\text{NR}_7\text{R}_8$ or NR_7R_8 in which R_7 and R_8 are the same or different and are selected from OH , R_5 , R_6 , $\text{C}(=\text{O})\text{NR}_5\text{R}_6$, $\text{C}(=\text{O})\text{R}_5$, SO_2R_5 , $\text{C}(=\text{NR}_9)\text{NHR}_{10}$, $\text{C}(=\text{NR}_9)\text{R}_{10}$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{N}-\text{SO}_2\text{NH}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{N}-\text{CN})\text{NR}_9\text{R}_{10}$ or $\text{C}(=\text{S})\text{NR}_9\text{R}_{10}$;

10

- R_2 is:

lower alkyl,

 C_2 - C_{10} alkenyl,15 C_2 - C_{10} alkynyl,

cycloalkyl,

cycloalkenyl,

heterocycle,

aryl;

20 each optionally substituted with one or several groups which are the same or different and which are selected from:

1) H , carboxylic acid bioisostere, lower haloalkyl, halogen,2) COOR_5 , OR_5 , SO_2R_5 ,

25 3) $\text{SO}_2\text{NR}_{11}\text{R}_{12}$, $\text{C}(=\text{O})\text{NR}_{11}\text{R}_{12}$ or $\text{NR}_{11}\text{R}_{12}$ in which R_{11} and R_{12} are the same or different and are selected from OH , R_5 , R_6 , $\text{C}(=\text{O})\text{NR}_5\text{R}_6$, $\text{C}(=\text{O})\text{R}_5$, SO_2R_5 , $\text{C}(=\text{S})\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{N}-\text{CN})\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{N}-\text{SO}_2\text{NH}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{NR}_9)\text{NHR}_{10}$ or $\text{C}(=\text{NR}_9)\text{R}_{10}$;

30

- R_3 is $\text{X}_2-\text{R}'_3$ wherein:- X_2 is a single bond or,

a group selected from C_1 - C_4 alkylene, C_2 - C_6 alkenylene, C_2 - C_6 alkynylene, each optionally substituted with one or several groups which are the same or different and which are selected from:

35 1) H , C_1 - C_3 alkyl, C_3 - C_4 cycloalkyl, aryl, heterocycle, $=\text{O}$, CN ,

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2) OR_5 , $=\text{NR}_5$ or,

3) $\text{NR}_{13}\text{R}_{14}$ in which R_{13} and R_{14} are the same or different and are selected from R_5 , R_6 , $\text{C}(=\text{O})\text{NR}_5\text{R}_6$, $\text{C}(=\text{O})\text{R}_5$, SO_2R_5 , $\text{C}(=\text{S})\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{NR}_9)\text{NHR}_{10}$ or $\text{C}(=\text{NR}_9)\text{R}_{10}$;

- R'_3 is:

cycloalkyl,

cycloalkenyl,

aryl,

heterocycle,

or a polycyclic group;

each optionally substituted with one or several groups X_3 - R_{17} , identical or different, in which:

- X_3 is:

a single bond, lower alkylene, C_2 - C_6 alkenylene, cycloalkylene, arylene, a divalent heterocycle or a divalent polycyclic group, and,

- R_{17} is:

1) H , $=\text{O}$, NO_2 , CN , lower haloalkyl, halogen, carboxylic acid bioisostere, cycloalkyl,

2) COOR_5 , $\text{C}(=\text{O})\text{R}_5$, $\text{C}(=\text{S})\text{R}_5$, SO_2R_5 , SOR_5 , SO_3R_5 , SR_5 , OR_5 ,

3) $\text{C}(=\text{O})\text{NR}_{15}\text{R}_{16}$, $\text{C}(=\text{S})\text{NR}_{15}\text{R}_{16}$, $\text{C}(=\text{N}-\text{CN})\text{NR}_{15}\text{R}_{16}$, $\text{C}(=\text{N}-\text{SO}_2\text{NH}_2)\text{NR}_{15}\text{R}_{16}$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_{15}\text{R}_{16}$, $\text{SO}_2\text{NR}_{15}\text{R}_{16}$, $\text{C}(=\text{NR}_{15})\text{NHR}_{16}$, $\text{C}(=\text{NR}_{15})\text{R}_{16}$, $\text{C}(=\text{NR}_9)\text{NHR}_{16}$, $\text{C}(=\text{NR}_9)\text{R}_{16}$ or $\text{NR}_{15}\text{R}_{16}$ in which R_{15} and R_{16} are the same or different and are selected from OH , R_5 , R_6 , $\text{C}(=\text{O})\text{NR}_5\text{R}_6$, $\text{C}(=\text{O})\text{R}_5$, SO_2R_5 , $\text{C}(=\text{S})\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{CH}-\text{NO}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{N}-\text{CN})\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{N}-\text{SO}_2\text{NH}_2)\text{NR}_9\text{R}_{10}$, $\text{C}(=\text{NR}_9)\text{NHR}_{10}$ or $\text{C}(=\text{NR}_9)\text{R}_{10}$,

4) heterocycle optionally substituted with one or several groups R_5 ;

35 wherein,

- R_5 and R_6 are the same or different and are selected from :

- H ,

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- lower alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl;
- X₄-cycloalkyl, X₄-cycloalkenyl, X₄-aryl, X₄-heterocycle or X₄-polycyclic group, in which X₄ is a single bond, lower alkylene or C₂-C₆ alkenylene;

5 each optionally substituted with one or several groups which are the same or different and which are selected from:

- halogen, =O, COOR₂₀, CN, OR₂₀, lower alkyl optionally substituted with OR₂₀, O-lower alkyl optionally substituted with OR₂₀, C(=O)-lower alkyl, lower haloalkyl, X₅-N-R₁₈ in which X₅ is a single

$$\begin{array}{c} \text{R}_{19} \\ \diagup \end{array}$$

bond or lower alkyl and R₁₈, R₁₉ and R₂₀ are the same or different and are selected from H or lower alkyl;

- X₆-heterocycle, X₆-aryl, X₆-cycloalkyl, X₆-cycloalkenyl, X₆-polycyclic group in which X₆ is selected from a single bond or lower alkylene, these groups being optionally substituted with one or several groups, identical or different, selected from halogens, COOR₂₁, OR₂₁, or (CH₂)_nNR₂₁R₂₂ in which n is 0, 1 or 2 and R₂₁ and R₂₂ are the same or different and are selected from H or lower alkyl;

- R₉ is selected from H, CN, OH, lower alkyl, O-lower alkyl, aryl, heterocycle, SO₂NH₂ or X₅-N-R₁₈ in which X₅ is a

$$\begin{array}{c} \text{R}_{19} \\ \diagup \end{array}$$

single bond or lower alkylene and R₁₈ and R₁₉ are the same or different and are selected from H or lower alkyl;

- R₁₀ is selected from hydrogen, lower alkyl, cyclopropyl or heterocycle;

30 or a pharmaceutically acceptable derivative thereof, together with a pharmaceutically acceptable carrier, with the proviso that the compound of formula (I) is not 4-[2-Formylimino-5-(4-methoxy-phenyl)-[1,3,4]thiadiazol-3-yl]-butyric acid ethyl ester, or,
 35 4-[5-(4-Chloro-phenyl)-2-formylimino-[1,3,4]thiadiazol-3-yl]-butyric acid ethyl ester.

17. A pharmaceutical composition according to claim 16,

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comprising a compound of formula (I), in which R1, R2, R3 and Y are as defined in claim 18, with the proviso that when R1 is C(=O)-H, then R2 does not represent (CH₂)₃-C(=O)OCH₂CH₃.

5 18. Pharmaceutical composition comprising a compound of formula (I) according to any one of claims 1 to 15, together with a pharmaceutically acceptable carrier.

10 19. A pharmaceutical composition according to claim 16, 17 or 18, for the treatment of a disease for which treatment by a PDE7 inhibitor is relevant.

15 20. Method for the treatment of a disease for which treatment by a PDE7 inhibitor is relevant, comprising administering to a mammal, particularly a human, in need thereof, an effective amount of compound of formula (I) according any of claims 1 to 15.

20 21. Method according to claim 20, in which the disease to be treated is selected from T-cell-related diseases, autoimmune diseases, inflammatory diseases, respiratory diseases, CNS diseases, allergic diseases, endocrine or exocrine pancreas diseases, or gastrointestinal diseases.

25 22. Method according to claim 20, in which the disease to be treated is selected from visceral pain, inflammatory bowel disease, osteoarthritis, multiple sclerosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, acquired immune deficiency syndrome (AIDS) or graft
30 rejection.

35 23. Use of a compound of formula (I) according to any one of claims 1 to 15, for the manufacture of a medicament for the treatment of diseases for which treatment by a PDE7 inhibitor is relevant.

24. Use according to claim 23, in which the disease to be treated is selected from T-cell-related diseases,

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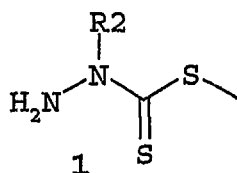
autoimmune diseases, inflammatory diseases, respiratory diseases, CNS diseases, allergic diseases, endocrine or exocrine pancreas diseases, or gastrointestinal diseases.

5 25. Use according to claim 23, in which the disease to be treated is selected from visceral pain, inflammatory bowel disease, osteoarthritis, multiple sclerosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, acquired immune deficiency syndrome (AIDS) or graft
10 rejection.

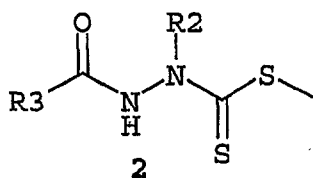
26. A compound of formula (I) as defined in any one of claims 1 to 15, as a medicament.

15 27. A process for the preparation of a 1,3,4-thiadiazole of formula (I) according to any one of claims 1 to 12, 14 or 15 in which Y is S, comprising the following steps:

(a) reaction of a substituted hydrazine R_2NHNH_2 in
20 which R_2 is as defined in claim 1, with carbon disulphide and MeX where X is a leaving group to obtain a compound of formula 1

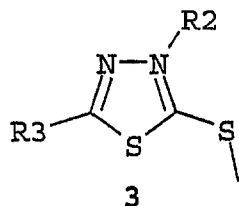


(b) reaction of the S-methyldithiocarbazate 1 with an
25 acyl chloride R_3COCl in which R_3 is as defined in claim 1 to obtain an acylated methyldithiocarbazate 2



(c) cyclization of the acylated methyldithiocarbazate 2 into a 1,3,4-thiadiazole 3

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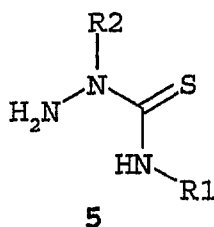


(d) reaction of the 1,3,4-thiadiazole 3 with an amine R_1NH_2 in which R_1 is as defined in claim 1, to obtain the compound of formula (I) in which Y is S,

5 (e) isolating the compound of formula (I).

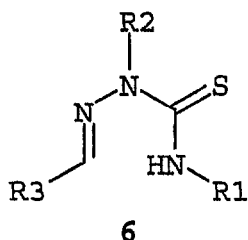
28. Process for the preparation of a 1,3,4-thiadiazole of formula (I) according to any one of claims 1 to 12, 14 or 15, in which Y is S, comprising the following steps:

10 (a) reaction of a substituted hydrazine R_2NHNH_2 in which R_2 is as defined in claim 1, with a substituted isothiocyanate $SCNR_1$ in which R_1 is as defined in claim 1, to obtain the substituted thiosemicarbazide 5



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(b) reaction of the thiosemicarbazide 5 with an aldehyde R_3CHO in which R_3 is as defined in claim 1, to obtain the thiosemicarbazone 6



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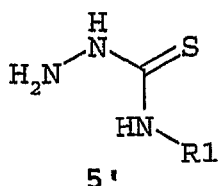
(c) cyclization of the thiosemicarbazone 6 into the compound of formula (I) in which Y is S,

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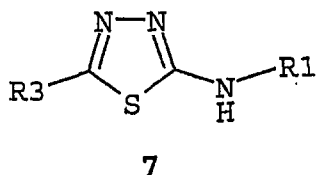
(d) isolating the compound of formula (I).

29. Process for the preparation of a 1,3,4-thiadiazole of formula (I) according to any one of claims 1 to 12, 14 or 15, in which Y is S, comprising the following steps:

(a) reaction of a carboxylic acid R_3COOH in which R_3 is as defined in claim 1, with the following thiosemicarbazide 5'



to obtain the 1,3,4-thiadiazole 7



(b) reaction of the 1,3,4-thiadiazole 7 with R_2X , in which R_2 is as defined in claim 1 and X is a leaving group to obtain the compound of formula (I) in which Y is S

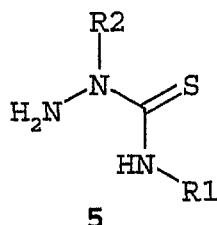
(c) isolating the compound of formula (I).

30. Process for the preparation of a 1,3,4-thiadiazole of formula (I) according to any one of claims 1 to 12, 14 or 15, comprising the following steps:

(a) reaction of a carboxylic acid R_3COOH , in which R_3 is as defined in claim 1, with the following thiosemicarbazide 5

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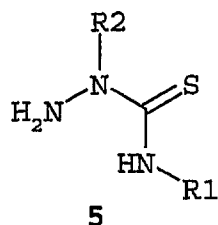
to obtain the final compound of formula I in which Y is S,

(b) isolating the compound of formula (I).

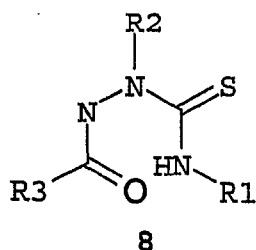
5

31. Process for the preparation of a 1,3,4-oxadiazole of formula (I) according to any one of claims 1 to 11 or 13, in which Y is O, comprising the following steps:

(a) reaction of a substituted hydrazine R_2NHNH_2 , in which R_2 is as defined in claim 1, with a substituted isothiocyanate $SCNR_1$, in which R_1 is as defined in claim 1, to obtain the substituted thiosemicarbazide 5,



(b) reaction of the thiosemicarbazide 5 with $R_3-C(=O)Cl$, in which R_3 is as defined in claim 1, to form the desired thiosemicarbazide 8



(c) cyclization of the thiosemicarbazide 8 into the final compound of formula I in which Y is O,

(d) isolating the compound of formula (I).

20