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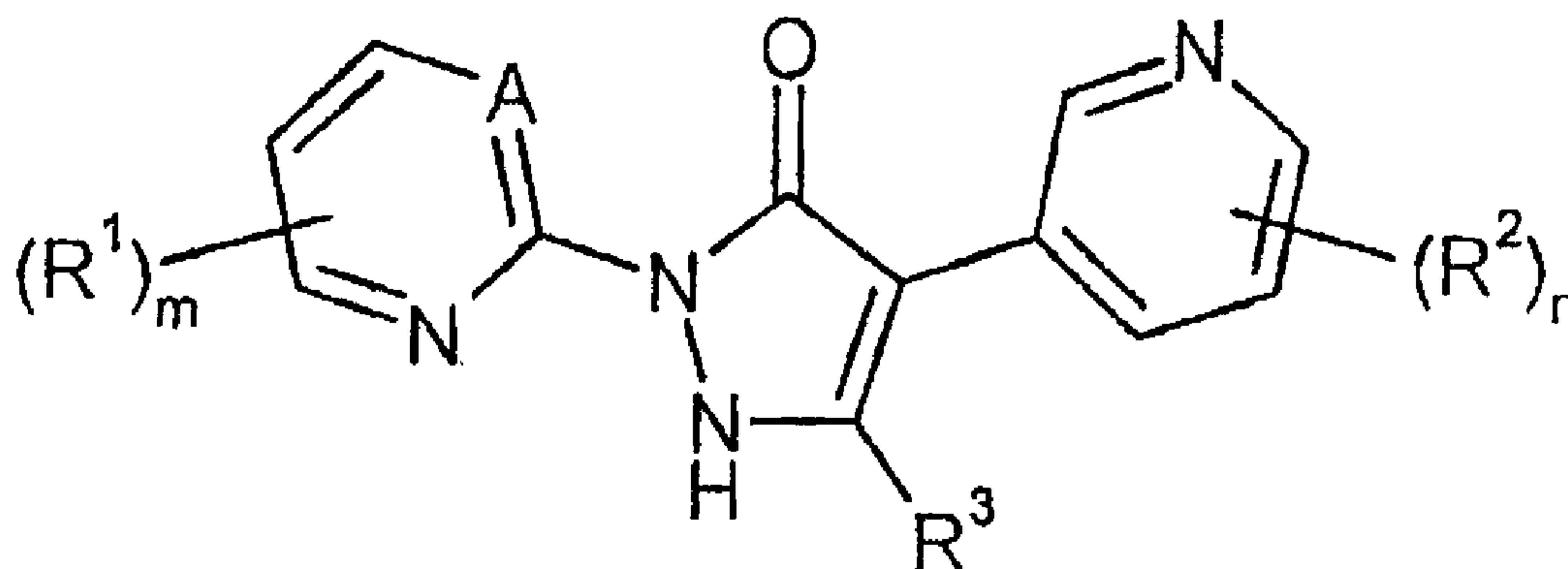
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(I)

(57) Abrégé/Abstract:

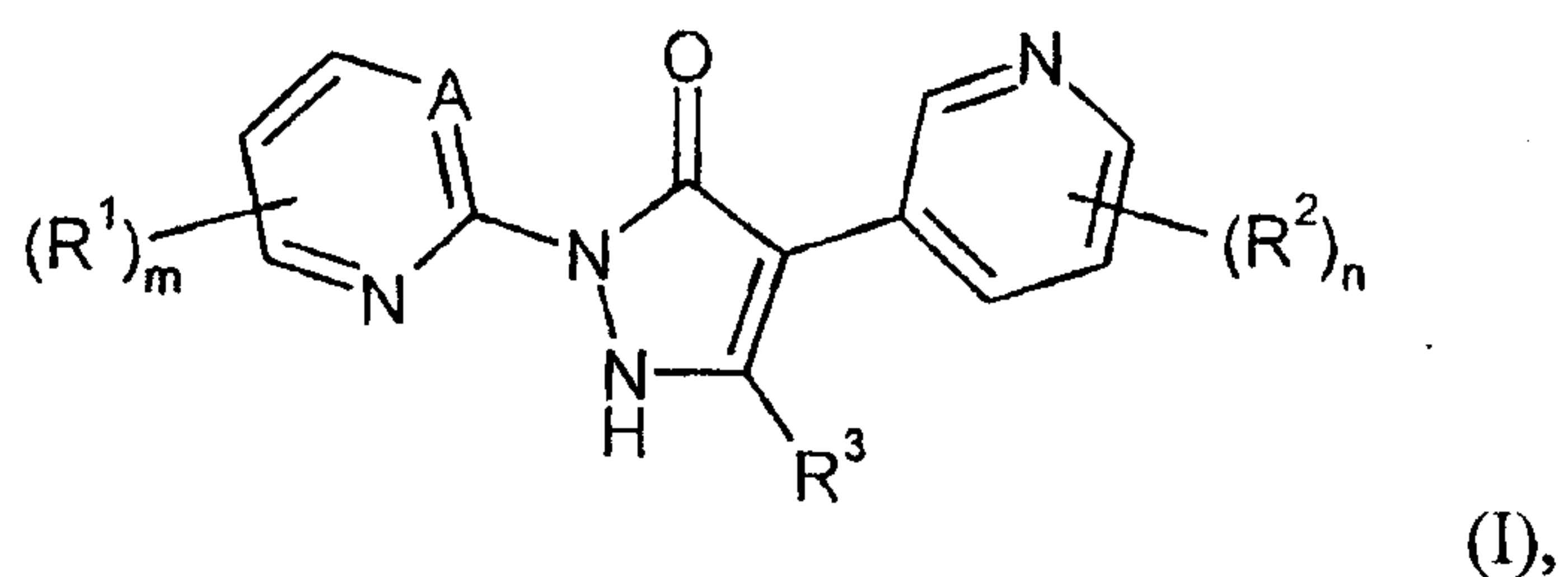
The present application relates to novel substituted dipyridyldihydropyrazolone derivatives of the general formula (I): (see formula I) processes for their preparation, their use for treatment and/or prophylaxis of diseases and their use for the preparation of medicaments for treatment and/or prophylaxis of diseases, in particular cardiovascular and hematological diseases and kidney diseases, and for promoting wound healing.

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ABSTRACT

The present application relates to novel substituted dipyridyldihydropyrazolone derivatives of the general formula (I):



- 5 processes for their preparation, their use for treatment and/or prophylaxis of diseases and their use for the preparation of medicaments for treatment and/or prophylaxis of diseases, in particular cardiovascular and hematological diseases and kidney diseases, and for promoting wound healing.

SUBSTITUTED DIPYRIDYL-DIHYDROPYRAZOLONES AND USE THEREOF

The present application relates to novel substituted dipyridyldihydropyrazolone derivatives, processes for their preparation, their use for treatment and/or prophylaxis of diseases and their use for the preparation of medicaments for treatment and/or prophylaxis of diseases, in particular
5 cardiovascular and hematological diseases and kidney diseases, and for promoting wound healing.

A deficient supply of oxygen to the human organism or its components which either impairs regular functioning of the organism or its components due to its duration and/or its extent or causes its functioning to break down completely is called hypoxia. Hypoxia can be caused by a reduction in the available oxygen in the air breathed in (for example during periods at a high
10 altitude), by disorders in external respiration (for example as a result of disturbed functioning of the lungs or obstruction of the respiratory tract), by a reduction in the cardiac output (for example in the event of cardiac insufficiency, acute right ventricular overloading with pulmonary embolism), by too low an oxygen transport capacity of the blood (for example as a result of an anemia or intoxication, for example with carbon monoxide), locally demarcated by a reduced
15 blood flow as a result of vascular occlusions (ischemia states typically for example of the heart, the lower extremities or the brain, diabetic macro- and microangiopathy) or also by an increased oxygen requirement of the tissue (for example as a result of increased muscular activity or local inflammations) [Eder, Gedigk (ed.), *Allgemeine Pathologie und pathologische Anatomie*, 33rd ed., Springer Verlag, Berlin, 1990]

20 The human organism is capable to a limited extent of adapting acutely and chronically to situations of reduced oxygen supply. In addition to an immediate response, which includes inter alia an increase in the cardiac output and respiratory output and a local dilation of blood vessels by vegetative-nervous control mechanisms, hypoxia brings about a change in the transcription of
25 numerous genes. The function of the gene products here serves to compensate the oxygen deficiency. Thus, expression of several enzymes of glycolysis and glucose transporter 1 is enhanced, as a result of which anaerobic ATP production increases and survival of the oxygen deficiency is rendered possible [Schmidt, Thews (ed.), *Physiologie des Menschen*, 27th ed., Springer Verlag, Berlin, 1997; Löffler, Petrides (ed.), *Biochemie und Pathobiochemie*, 7th ed.,
30 Springer Verlag, Berlin, 2003].

Hypoxia furthermore leads to enhanced expression of vascular endothelial cell growth factor, VEGF, as a result of which regeneration of blood vessels (angiogenesis) is stimulated in hypoxic tissues. The blood flow through ischemic tissue is thereby improved in the long term. This counter-
35 regulation is evidently only very inadequate in the case of various cardiovascular diseases and vascular occlusion diseases [overview in: Simons and Ware, *Therapeutic angiogenesis in cardiovascular disease*, Nat. Rev. Drug. Discov. 2 (11), 863-71 (2003)].

Furthermore, in cases of systemic hypoxia expression of the peptide hormone erythropoietin formed predominantly in the interstitial fibroblasts of the kidneys is enhanced. The formation of red blood cells in the bone marrow is thereby stimulated, and the oxygen transport capacity of the blood is therefore increased. This effect has been and is used by high-performance athletes in so-called high altitude training. A decrease in the oxygen transport capacity of the blood for example as a result of anemia after hemorrhaging usually causes an increase in erythropoietin production in the kidney. With certain forms of anemia, this regulatory mechanism may be disturbed or its normal value may be set lower. Thus for example in patients suffering from renal insufficiency, erythropoietin is indeed produced in the kidney parenchyma, but in significantly reduced amounts with respect to the oxygen transport capacity of the blood, which results in so-called renal anemia. Renal anemia in particular, but also anemias caused by tumors and HIV infection are conventionally treated by parenteral administration of recombinant human erythropoietin (rhEPO). No alternative therapy with an orally available medicament currently exists for this expensive therapy [overview in: Eckardt, *The potential of erythropoietin and related strategies to stimulate erythropoiesis*, Curr. Opin. Investig. Drugs 2(8), 1081-5 (2001); Berns, *Should the target hemoglobin for patients with chronic kidney disease treated with erythropoietic replacement therapy be changed?*, Semin. Dial. 18 (1), 22-9 (2005)]. Recent studies demonstrate that, in addition to its erythropoiesis-increasing action, erythropoietin also has a protective (anti-apoptotic) action, which is independent thereof, on hypoxic tissue, in particular the heart and the brain. Furthermore, according to recent studies therapy with erythropoietin reduces the average severity of morbidity in patients with cardiac insufficiency [overviews in: Caiola and Cheng, *Use of erythropoietin in heart failure management*, Ann. Pharmacother. 38 (12), 2145-9 (2004); Katz, *Mechanisms and treatment of anemia in chronic heart failure*, Congest. Heart. Fail. 10 (5), 243-7 (2004)].

The genes described above which are induced by hypoxia have the common feature that the increase in their expression under hypoxia is caused by the so-called hypoxia-inducible transcription factor (HIF). HIF is a heterodimeric transcription factor which comprises an alpha and a beta subunit. Three HIF alpha isoforms are described, of which HIF-1 alpha and HIF-2 alpha are highly homologous and are of importance for hypoxia-induced gene expression. While the beta subunit (of which 2 isoforms have been described), which is also called ARNT (aryl hydrocarbon receptor nuclear translocator), is expressed constitutively, expression of the alpha subunit depends on the oxygen content in the cell. Under normoxia, the HIF alpha protein is poly-ubiquitinated and then degraded proteasomally. Under hypoxia this degradation is inhibited, so that HIF alpha dimerizes with ARNT and can activate its target genes. The HIF dimer binds here to so-called hypoxia-responsible elements (HRE) in the regulatory sequences of its target genes. The HRE are defined by a consensus sequence. Functional HRE have been detected in the regulatory elements of numerous hypoxia-induced genes [overviews in: Semenza, *Hypoxia-inducible factor 1: oxygen*

homeostasis and disease pathophysiology, Trends Mol. Med. 7 (8), 345-50 (2001); Wenger and Gassmann, *Oxygen(es) and the hypoxia-inducible factor-1*, Biol. Chem. 378 (7), 609-16 (1997)].

The molecular mechanism on which this regulation of HIF alpha is based has been clarified by the works of several independent groups of researchers. The mechanism is conserved from species to species: HIF alpha is hydroxylated by a subclass of oxygen-dependent prolyl 4-hydroxylases, called PHD or EGLN, on two specific prolyl radicals (P402 and P564 of the human HIF-1 alpha subunit). The HIF prolyl 4-hydroxylases are iron-dependent, 2-oxoglutarate-converting dioxygenases [Epstein et al., *C. elegans EGL-9 and mammalian homologs define a family of dioxygenases that regulate HIF by prolyl hydroxylation*, Cell 107 (1), 43-54 (2001); Bruick and McKnight, *A conserved family of prolyl-4-hydroxylases that modify HIF*, Science 294 (5545), 1337-40 (2001); Ivan et al., *Biochemical purification and pharmacological inhibition of a mammalian prolyl hydroxylase acting on hypoxia-inducible factor*, Proc. Natl. Acad. Sci. U.S.A. 99 (21), 13459-64 (2002)]. The enzymes were annotated as prolyl hydroxylases for the first time in 2001 [Aravind and Koonin, *The DNA-repair protein AlkB, EGL-9, and leprecan define new families of 2-oxoglutarate- and iron-dependent dioxygenases*, Genome Biol. 2 (3), research0007.1-0007.8, Epub 2001 Feb 19].

The pVHL tumor suppressor protein, which together with elongin B and C forms the so-called VBC complex, which adapts the HIF alpha subunit to an E3 ubiquitin ligase, bonds to the prolyl-hydroxylated HIF alpha subunit. Since the prolyl 4-hydroxylation of the HIF alpha subunit and its subsequent degradation takes place as a function of the intracellular concentration of oxygen, HIF prolyl 4-hydroxylases have also been called a cellular oxygen sensor. Three isoforms of these enzymes have been identified: EGLN1/PHD2, EGLN2/PHD1 and EGLN3/PHD3. Two of these enzymes (EGLN2/PHD1 and EGLN3/PHD3) are induced transcriptionally even under hypoxia and are possibly responsible for the lowering of the HIF alpha levels to be observed under chronic hypoxia [overview in: Schofield and Ratcliffe, *Oxygen sensing by HIF hydroxylases*, Nat. Rev. Mol. Cell. Biol. 5 (5), 343-54 (2004)].

Selective pharmacological inhibition of HIF prolyl 4-hydroxylases brings about the increase in the gene expression of HIF-dependent target genes and is therefore beneficial for the therapy of numerous disease syndromes. In the case of diseases of the cardiovascular system in particular, an improvement in the course of the diseases is to be expected from induction of new blood vessels and the change in the metabolic situation of ischemic organs from aerobic to anaerobic ATP production. An improvement in the vascularization of chronic wounds promotes the healing process, especially in the case of poorly healing ulcera cruris and other chronic skin wounds. The induction of endogenous erythropoietin in certain disease forms, in particular in patients with renal anemia, is likewise a therapeutic goal to be aimed for.

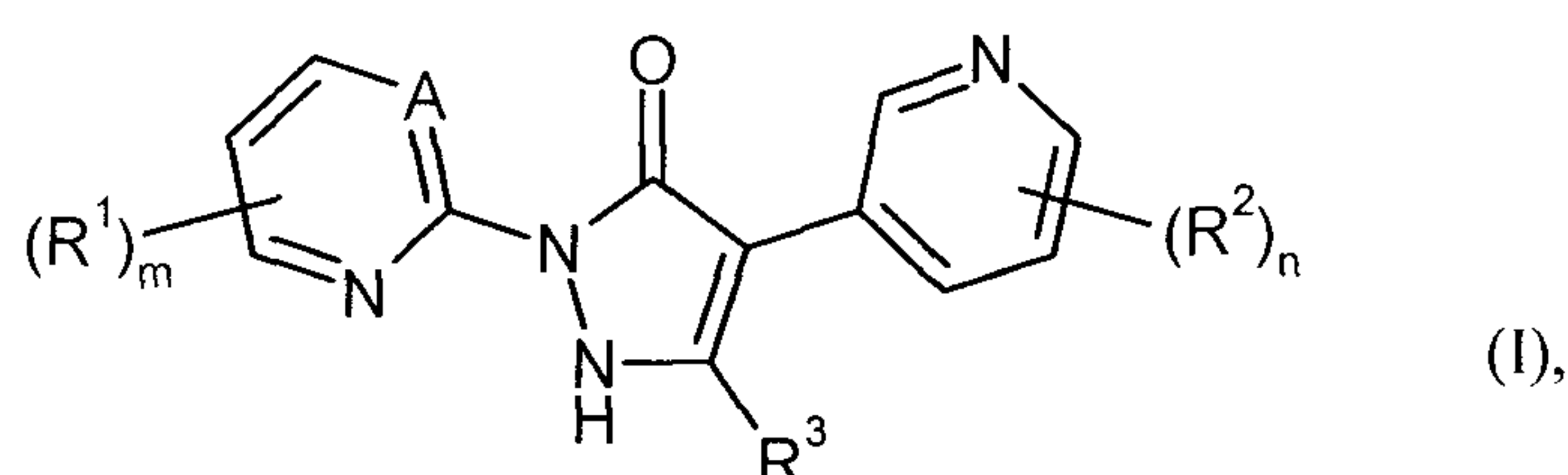
The HIF prolyl 4-hydroxylase inhibitors described hitherto in the scientific literature do not meet the requirements to be imposed on a medicament. These are either competitive oxoglutarate analogs (such as for example N-oxalylglycine), which are characterized by their very low action potency, and therefore in *in vivo* models have as yet shown no action in the sense of an induction of HIF target genes. Or they are iron-complexing agents (chelators), such as desferroxamine, which act as non-specific inhibitors of iron-containing dioxygenases and, although they bring about an induction of the target genes, such as for example erythropoietin, *in vivo*, evidently counteract erythropoiesis by complexing of the available iron.

10 The object of the present invention is to provide novel compounds which can be employed for treatment of diseases, in particular cardiovascular and hematological diseases.

In the context of the present invention, compounds are now described which act as specific inhibitors of HIF prolyl 4-hydroxylases and on the basis of this specific action mechanism bring about *in vivo*, after parenteral or oral administration, the induction of HIF target genes, such as for example erythropoietin, and the biological processes thereby caused, such as for example erythropoiesis.

2-Heteroaryl-4-aryl-1,2-dihydropyrazolones having a bactericidal and/or fungicidal action are disclosed in EP 165 448 and EP 212 281. The use of 2-heteroaryl-4-aryl-1,2-dihydropyrazolones as lipoxygenase inhibitors for treatment of respiratory tract, cardiovascular and inflammatory diseases is claimed in EP 183 159. 2,4-Diphenyl-1,2-dihydropyrazolones having a herbicidal activity are described in DE 2 651 008. The preparation and pharmacological properties of certain 2-pyridyl-1,2-dihydropyrazolones are reported in *Helv. Chim. Acta* 49 (1), 272-280 (1966). WO 96/12706, WO 00/51989 and WO 03/074550 claim further compounds having a dihydropyrazolone partial structure and their use for treatment of diseases, and WO 02/092573 describes pyrazol-4-ylpyridine and pyrazol-4-ylpyrimidine derivatives as kinase inhibitors. Heteroaryl-substituted pyrazole derivatives for treatment of pain and various CNS diseases are furthermore described in WO 03/051833 and WO 2004/089303. WO 2006/114213 has meanwhile disclosed 2,4-dipyridyl-1,2-dihydropyrazolones as inhibitors of HIF prolyl 4-hydroxylases.

The present invention provides compounds of the general formula (I)



in which

A represents CH or N,

R^1 and R^2 are identical or different and for each individual occurrence represent a substituent independently of one another selected from the group consisting of halogen, cyano, nitro, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, (C₁-C₆)-alkyl, (C₁-C₆)-alkoxy, (C₃-C₇)-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -C(=O)-R⁴, -C(=O)-OR⁵, -C(=O)-NR⁶R⁷, -O-C(=O)-R⁸, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -SO₂-R²⁰, -SO₂-NR²¹R²², -OR²³, -SR²⁴ and -NR²⁵R²⁶ in which

- (i) (C₁-C₆)-alkyl and (C₁-C₆)-alkoxy for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, (C₃-C₇)-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -C(=O)-R⁴, -C(=O)-OR⁵, -C(=O)-NR⁶R⁷, -O-C(=O)-R⁸, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -SO₂-R²⁰, -SO₂-NR²¹R²², -OR²³, -SR²⁴ and -NR²⁵R²⁶,

where the last-mentioned cycloalkyl, heterocycloalkyl, phenyl and heteroaryl radicals for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

- (ii) (C₃-C₇)-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of (C₁-C₆)-alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-R⁴, -C(=O)-OR⁵, -C(=O)-NR⁶R⁷, -O-C(=O)-R⁸, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -SO₂-R²⁰, -SO₂-NR²¹R²², -OR²³, -SR²⁴ and -NR²⁵R²⁶,

where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₇)-cycloalkyl, 4- to

7-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

(iii) $R^4, R^5, R^6, R^8, R^9, R^{12}, R^{14}, R^{16}, R^{19}, R^{20}, R^{21}, R^{23}, R^{24}$ and R^{25} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₇)-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl, where

(C₃-C₇)-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₇)-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

(iv) $R^7, R^{10}, R^{11}, R^{13}, R^{15}, R^{17}, R^{18}, R^{22}$ and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

(v) R^6 and R^7, R^9 and R^{10}, R^{11} and R^{12}, R^{13} and R^{14}, R^{15} and R^{16}, R^{16} and R^{17}, R^{18} and R^{19}, R^{21} and R^{22} and also R^{25} and R^{26} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino,

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hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m and n independently of one another represent the number 0, 1, 2 or 3,

where if R¹ or R² are present more than once, their meanings may in each case be identical or different,

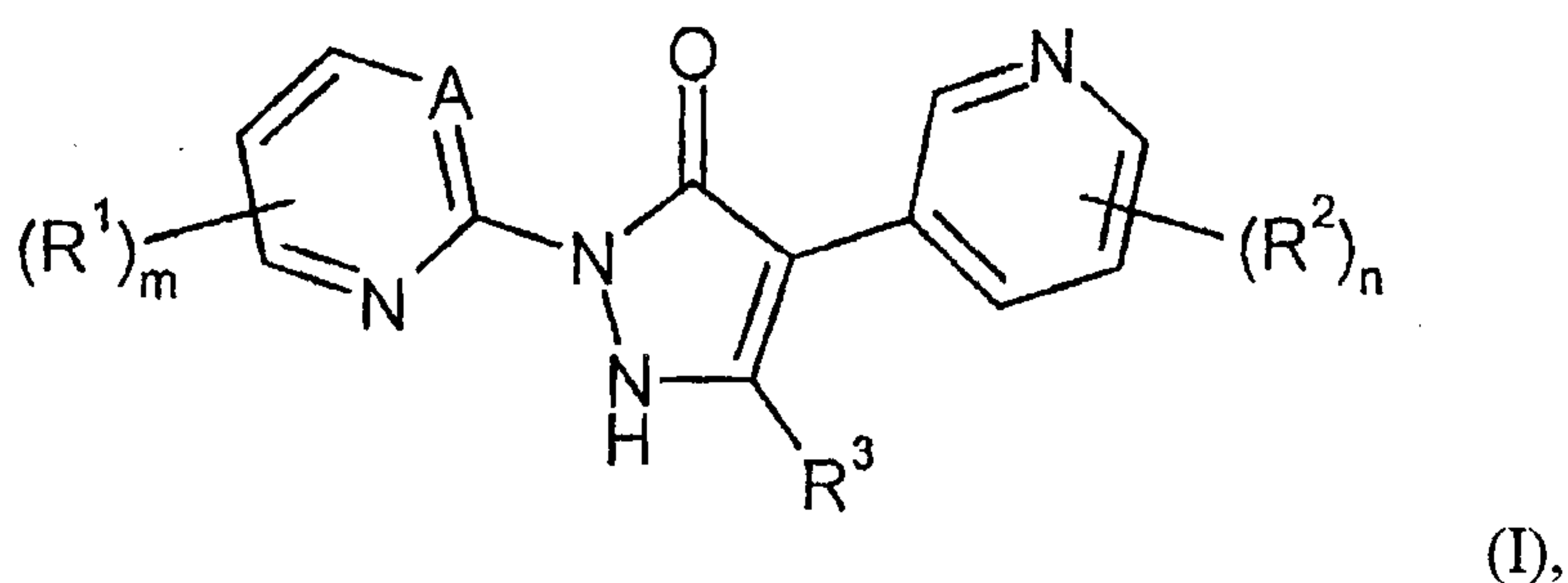
5 and

R³ represents hydrogen, (C₁-C₆)-alkyl or (C₃-C₇)-cycloalkyl,

and salts, solvates and solvates of the salts thereof.

More specifically, the present invention relates to:

[1] a compound of the formula (I)



10

in which

A represents CH,

R¹ represents a substituent selected from the group consisting of (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -O-C(=O)-NR⁹R¹⁰,

15 -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹ and -NR²⁵R²⁶

in which

(i) (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be mono- to trisubstituted by identical

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or different radicals selected from the group consisting of (C₁-C₆)-alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶,

- 5 where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,
- 10 (ii) R⁶, R⁹, R¹², R¹⁴, R¹⁶, R¹⁹, R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

- (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from
- 15 the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

- (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different
- 20 substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

- (iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen
- 25 and (C₁-C₆)-alkyl,

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where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

5 and/or in which

(iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A} and -NR^{25A}R^{26A} in which

(i) R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

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(iii) R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

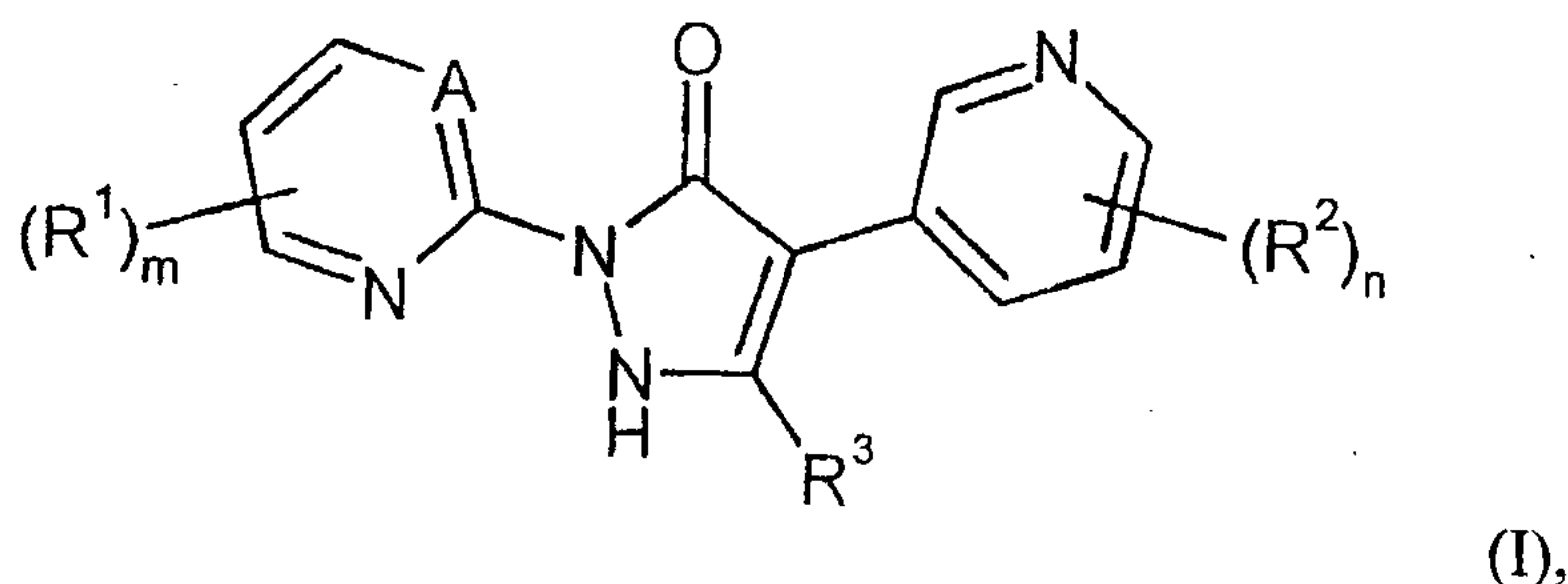
n represents the number 0 or 1

10 and

R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof;

[2] a compound of the formula (I)



15 in which

A represents CH,

R^1 represents a substituent selected from the group consisting of (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -O-C(=O)-NR⁹R¹⁰,

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$-\text{NR}^{11}-\text{C}(=\text{O})-\text{R}^{12}$, $-\text{NR}^{13}-\text{C}(=\text{O})-\text{OR}^{14}$, $-\text{NR}^{15}-\text{C}(=\text{O})-\text{NR}^{16}\text{R}^{17}$, $-\text{NR}^{18}-\text{SO}_2-\text{R}^{19}$ and $-\text{NR}^{25}\text{R}^{26}$
in which

(i) (C_3-C_6) -cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of (C_1-C_6) -alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, $-\text{C}(=\text{O})-\text{NR}^6\text{R}^7$, $-\text{O}-\text{C}(=\text{O})-\text{NR}^9\text{R}^{10}$, $-\text{NR}^{11}-\text{C}(=\text{O})-\text{R}^{12}$, $-\text{NR}^{13}-\text{C}(=\text{O})-\text{OR}^{14}$, $-\text{NR}^{15}-\text{C}(=\text{O})-\text{NR}^{16}\text{R}^{17}$, $-\text{NR}^{18}-\text{SO}_2-\text{R}^{19}$, $-\text{OR}^{23}$ and $-\text{NR}^{25}\text{R}^{26}$,

where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_1-C_4) -alkoxycarbonyl, (C_3-C_6) -cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

(ii) R^6 , R^9 , R^{12} , R^{14} , R^{16} , R^{19} , R^{23} and R^{25} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C_1-C_6) -alkyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl

and

(C_1-C_6) -alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_1-C_4) -alkoxycarbonyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl,

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(iii) R^7 , R^{10} , R^{11} , R^{13} , R^{15} , R^{17} , R^{18} and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

5 where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

10 (iv) R^6 and R^7 , R^9 and R^{10} , R^{11} and R^{12} , R^{13} and R^{14} , R^{15} and R^{16} , R^{16} and R^{17} , R^{18} and R^{19} and also R^{25} and R^{26} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-
15 alkoxycarbonyl,

R^2 represents a substituent selected from the group consisting of halogen, cyano, nitro, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, trifluoromethoxy, amino, hydroxycarbonyl and -C(=O)-NH- R^{7A} in which

(C₁-C₆)-alkyl and (C₁-C₆)-alkoxy for their part may be substituted by hydroxyl

20 and

R^{7A} represents hydrogen or (C₁-C₄)-alkyl,

m represents the number 1,

n represents the number 0 or 1

and

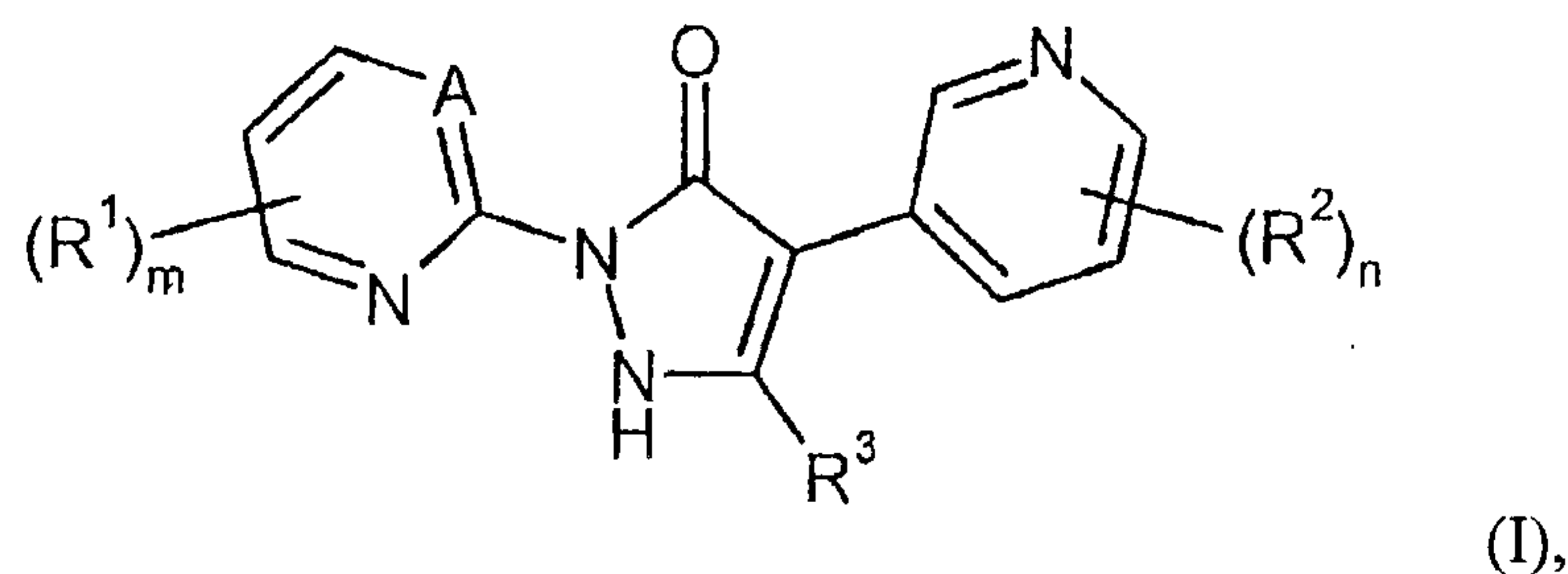
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R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof;

[3] a compound of the formula (I)



5 in which

A represents CH,

R^1 represents a substituent selected from the group consisting of (C₁-C₆)-alkyl, trifluoromethyl, halogen, cyano, nitro, hydroxyl, (C₁-C₆)-alkoxy, amino, hydroxycarbonyl, (C₁-C₆)-alkoxycarbonyl and -C(=O)-NH- R^7 in which

10 (C₁-C₆)-alkyl for its part may be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino or a group of the formula -NH-C(=O)- R^{12} , -NH-C(=O)-NH- R^{16} or -NH-SO₂- R^{19} in which

R^{12} , R^{16} and R^{19} each represent (C₁-C₆)-alkyl which may be substituted by hydroxyl or (C₁-C₄)-alkoxy,

15 and

R^7 represents hydrogen or (C₁-C₆)-alkyl which may be substituted by hydroxyl or (C₁-C₄)-alkoxy,

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R^2 represents a substituent selected from the group consisting of $-O-C(=O)-NR^{9A}R^{10A}$, $-NR^{11A}-C(=O)-R^{12A}$, $-NR^{13A}-C(=O)-OR^{14A}$, $-NR^{15A}-C(=O)-NR^{16A}R^{17A}$, $-NR^{18A}-SO_2-R^{19A}$ and $-NR^{25A}R^{26A}$ in which

(i) R^{9A} , R^{12A} , R^{14A} , R^{16A} , R^{19A} and R^{25A} independently of one another represent
 5 (C_1-C_6) -alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl or (C_1-C_4) -alkoxycarbonyl,

(ii) R^{10A} , R^{11A} , R^{13A} , R^{15A} , R^{17A} , R^{18A} and R^{26A} independently of one another
 10 represent hydrogen or (C_1-C_6) -alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl or (C_1-C_4) -alkoxycarbonyl,

and/or in which

(iii) R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which
 15 they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,

20 m represents the number 1,

n represents the number 1

and

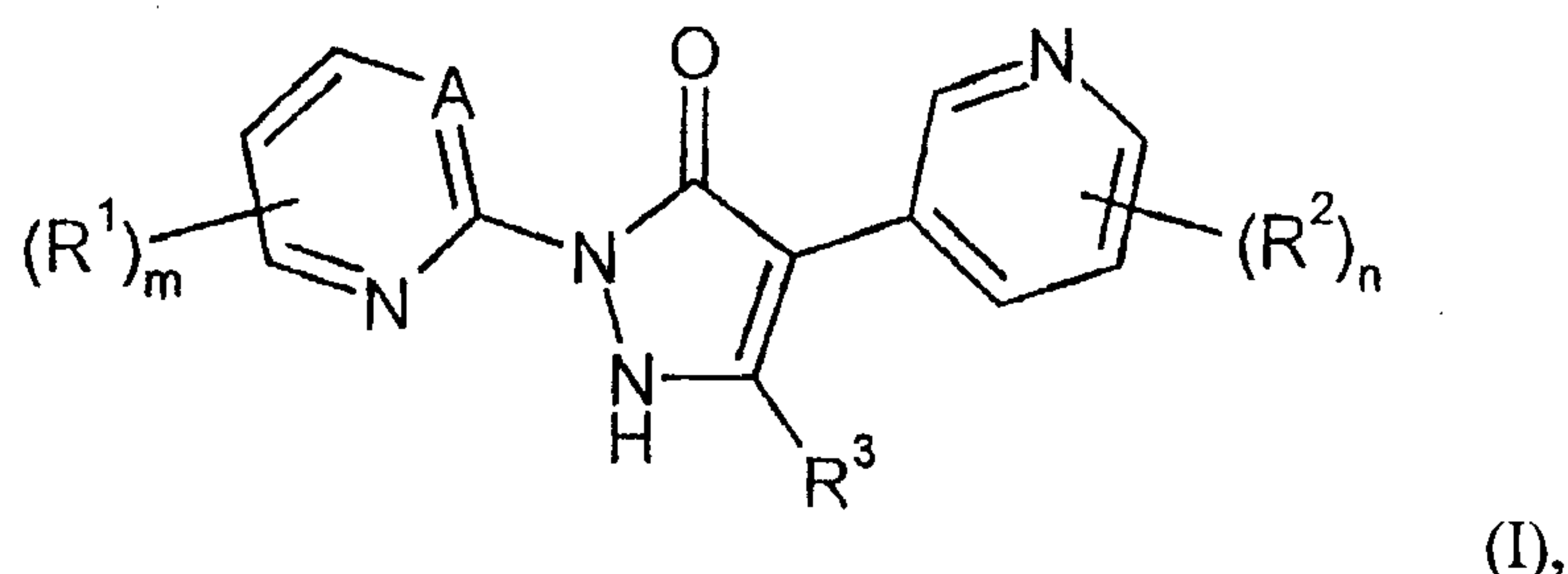
R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof;

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[4] a compound of the formula (I)



in which

A represents CH,

5 R^1 represents (C₁-C₆)-alkyl which

(i) is mono- or disubstituted by identical or different radicals from the group consisting of halogen, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -R¹¹-(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and

10 -NR²⁵R²⁶

and additionally may be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino or (C₁-C₄)-acylamino,

or

15 (ii) is disubstituted by identical or different radicals from the group consisting of hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and (C₁-C₄)-acylamino

in which

(a) the abovementioned cycloalkyl and heterocycloalkyl radicals for their part may in each case be substituted up to three times by identical or different substituents selected

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from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

(b) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

(c) R⁶, R⁹ and R¹⁴ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

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(d) R^{12} , R^{16} and R^{19} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in
 5 each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

10 (C₁-C₆)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(e) R^{23} and R^{25} independently of one another for each individual occurrence
 15 represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-
 20 alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-

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alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and/or in which

(f) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷,
 5 R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they
 are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to
 trisubstituted by identical or different substituents from the group consisting of halogen,
 cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo,
 amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-
 10 alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-
 alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl,
 -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-
 C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which

15 (i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl,
 hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-
 alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one
 another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano,
 20 trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-
 alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one
 another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by
 halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-
 25 (C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

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and/or in which

(iv) R^{6A} and R^{7A} , R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

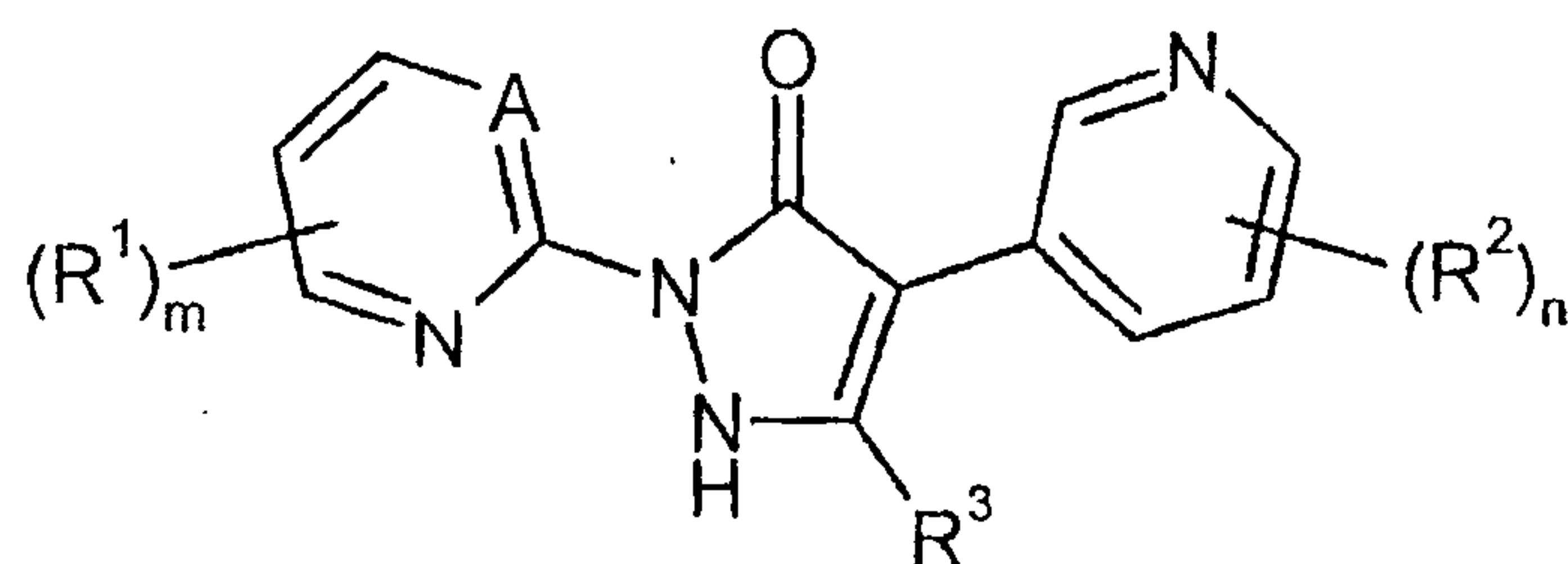
n represents the number 0 or 1

and

R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof;

[5] a compound of the formula (I)



(I),

in which

A represents CH,

R^1 represents (C₁-C₆)-alkoxy which is mono- or disubstituted by identical or different radicals selected from the group consisting of halogen, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4-

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to 6-membered heterocycloalkyl, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, $-C(=O)-NR^6R^7$, $-O-C(=O)-NR^9R^{10}$, $-NR^{11}-C(=O)-R^{12}$, $-NR^{13}-C(=O)-OR^{14}$, $-NR^{15}-C(=O)-NR^{16}R^{17}$, $-NR^{18}-SO_2-R^{19}$, $-OR^{23}$ and $-NR^{25}R^{26}$ in which

- (i) (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl for their part
 5 may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,
- (ii) $R^6, R^9, R^{12}, R^{14}, R^{16}, R^{19}, R^{23}$ and R^{25} independently of one another for each
 10 individual occurrence represent a radical selected from the group consisting of (C_1-C_6) -alkyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino,
 15 hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl

and

(C_1-C_6) -alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy,
 20 (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_1-C_4) -alkoxycarbonyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) $R^7, R^{10}, R^{11}, R^{13}, R^{15}, R^{17}, R^{18}$ and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C_1-C_6) -alkyl,

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where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

5 and/or in which

(iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which

(i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

20 (ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by

25

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halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

- (iv) R^{6A} and R^{7A}, R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A},
 5 R^{16A} and R^{17A}, R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the
 atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which
 may be mono- or disubstituted by identical or different substituents from the group consisting
 of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy,
 oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-
 10 alkoxycarbonyl,

m represents the number 1,

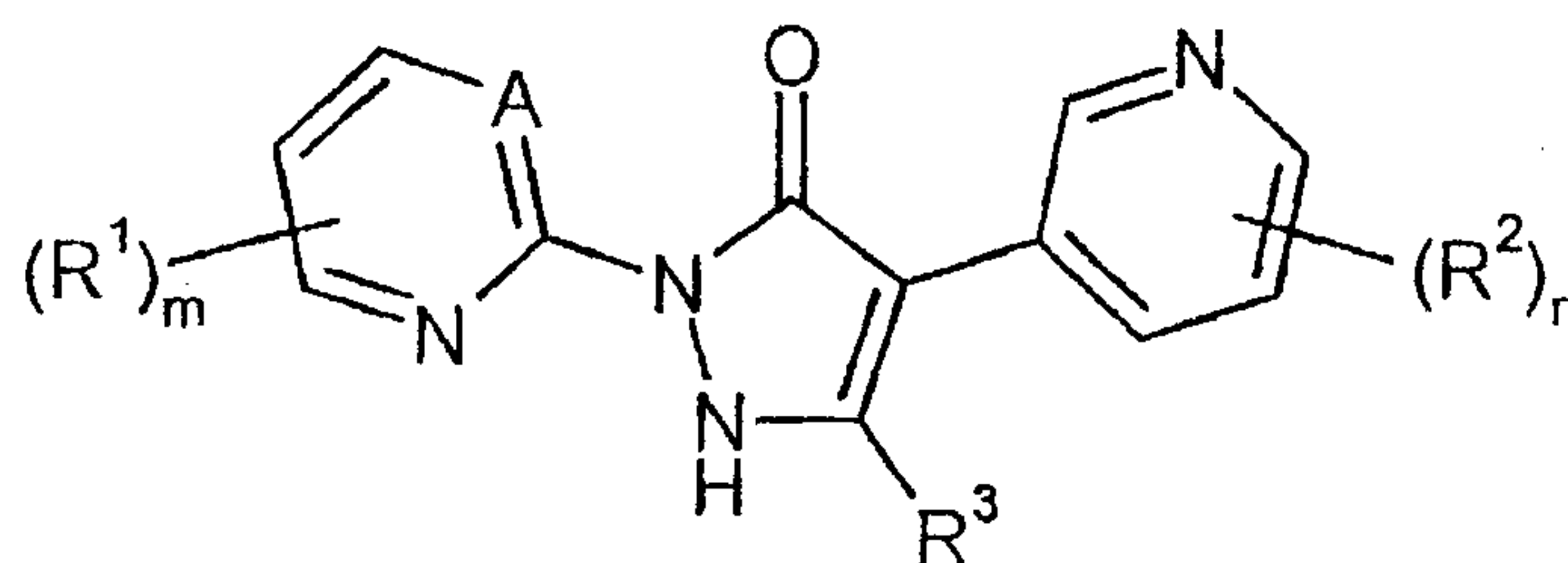
n represents the number 0 or 1

and

R³ represents hydrogen,

- 15 or a salt, solvate or solvate of the salt thereof; and

[6] a compound of the formula (I)



(I),

in which

A represents CH,

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R^1 represents the group $-C(=O)-NR^6R^7$

in which

(i) R^6 represents (C_3-C_6) -cycloalkyl or 4- to 6-membered heterocycloalkyl which may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,

or

represents (C_1-C_6) -alkyl which

(a) is mono- or disubstituted by identical or different radicals selected from the group consisting of halogen, cyano, trifluoromethyl, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_1-C_4) -alkoxycarbonyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl

and may additionally be substituted by hydroxyl or (C_1-C_4) -alkoxy,

or

(b) is disubstituted by hydroxyl and/or (C_1-C_4) -alkoxy,

and

R^7 represents hydrogen,

or in which

(ii) R^6 represents (C_1-C_6) -alkyl, (C_3-C_6) -cycloalkyl or 4- to 6-membered heterocycloalkyl, where

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(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl

and

R⁷ represents (C₁-C₆)-alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

or in which

(iii) R⁶ and R⁷ together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which

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(i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R^{6A} and R^{7A}, R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A}, R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

n represents the number 0 or 1

and

R³ represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

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Compounds according to the invention are the compounds of the formula (I) and their salts, solvates and solvates of the salts, the compounds included in the formula (I) of the formulae mentioned in the following and their salts, solvates and solvates of the salts, and the compounds included in the formula (I) and mentioned in the following as embodiment

5 examples and their salts, solvates and solvates of the salts, where the compounds included in the formula (I) and mentioned in the following are not already salts, solvates and solvates of the salts.

The compounds according to the invention can exist in stereoisomeric forms (enantiomers, diastereomers), depending on their structure. The invention therefore includes the enantiomers

10 or diastereomers and their particular mixtures. The stereoisomerically uniform constituents can be isolated from such mixtures of enantiomers and/or diastereomers in a known manner.

Where the compounds according to the invention can occur in tautomeric forms, the present invention includes all the tautomeric forms.

Preferred salts in the context of the present invention are physiologically acceptable salts of

15 the compounds according to the invention. Salts which are not themselves suitable for pharmaceutical uses but can be used, for example, for isolation or purification of the compounds according to the invention are also included.

Physiologically acceptable salts of the compounds according to the invention include acid addition salts of mineral acids, carboxylic acids and sulfonic acids, for example salts of

20 hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, benzenesulfonic acid, naphthalenedisulfonic acid, acetic acid, trifluoroacetic acid, propionic acid, lactic acid, tartaric acid, malic acid, citric acid, fumaric acid, maleic acid and benzoic acid.

Physiologically acceptable salts of the compounds according to the invention also include salts of conventional bases, such as, by way of example and preferably, alkali metal salts (for example sodium and potassium salts), alkaline earth metal salts (for example calcium and magnesium salts) and ammonium salts derived from ammonia or organic amines having 1 to 16 C atoms, such as, by way of example and preferably, ethylamine, diethylamine, triethylamine, ethyldiisopropylamine, monoethanolamine, diethanolamine, triethanolamine, dicyclohexylamine, dimethylaminoethanol, procaine, dibenzylamine, *N*-methylmorpholine, arginine, lysine, ethylenediamine and *N*-methylpiperidine.

Solvates in the context of the invention are described as those forms of the compounds according to the invention which form a complex in the solid or liquid state by coordination with solvent molecules. Hydrates are a specific form of solvates, in which the coordination takes place with water. Hydrates are preferred solvates in the context of the present invention.

The present invention moreover also includes prodrugs of the compounds according to the invention. The term "prodrugs" includes compounds which themselves can be biologically active or inactive, but are converted (for example metabolically or hydrolytically) into compounds according to the invention during their dwell time in the body.

In the context of the present invention, the substituents have the following meaning, unless specified otherwise:

(C₁-C₆)-Alkyl and (C₁-C₄)-alkyl in the context of the invention represent a straight-chain or branched alkyl radical having 1 to 6 or, respectively, 1 to 4 carbon atoms. A straight-chain or branched alkyl radical having 1 to 4 carbon atoms is preferred. There may be mentioned by way of example and preferably: methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, 1-ethylpropyl, *n*-pentyl and *n*-hexyl.

(C₁-C₆)-Alkoxy and (C₁-C₄)-alkoxy in the context of the invention represent a straight-chain or branched alkoxy radical having 1 to 6 or, respectively, 1 to 4 carbon atoms. A straight-chain or branched alkoxy radical having 1 to 4 carbon atoms is preferred. There may be mentioned by way of example and preferably: methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, *tert*-butoxy, *n*-pentoxy and *n*-hexoxy.

Mono-(C₁-C₆)-alkylamino and mono-(C₁-C₄)-alkylamino in the context of the invention represent an amino group with a straight-chain or branched alkyl substituent which contains 1 to 6 or, respectively, 1 to 4 carbon atoms. A straight-chain or branched monoalkylamino radical having 1 to 4 carbon atoms is preferred. There may be mentioned by way of example and preferably:

methylamino, ethylamino, *n*-propylamino, isopropylamino, *n*-butylamino, *tert*-butylamino, *n*-pentylamino and *n*-hexylamino.

Di-(C₁-C₆)-alkylamino and di-(C₁-C₄)-alkylamino in the context of the invention represent an amino group with two identical or different straight-chain or branched alkyl substituents which each contain 1 to 6 or, respectively, 1 to 4 carbon atoms. Straight-chain or branched dialkylamino radicals having in each case 1 to 4 carbon atoms are preferred. There may be mentioned by way of example and preferably: *N,N*-dimethylamino, *N,N*-diethylamino, *N*-ethyl-*N*-methylamino, *N*-methyl-*N*-*n*-propylamino, *N*-isopropyl-*N*-*n*-propylamino, *N,N*-diisopropylamino, *N*-*n*-butyl-*N*-methylamino, *N*-*tert*-butyl-*N*-methylamino, *N*-methyl-*N*-*n*-pentylamino and *N*-*n*-hexyl-*N*-methyl-
amino.

(C₁-C₄)-Acyl [(C₁-C₄)-alkanoyl] in the context of the invention represents a straight-chain or branched alkyl radical which has 1 to 4 carbon atoms, which carries a doubly attached oxygen atom in the 1-position and which is attached via the 1-position. Preference is given to an acyl radical having 1 to 4 carbon atoms. There may be mentioned by way of example and preferably: formyl, acetyl, propionyl, *n*-butyryl and isobutyryl.

(C₁-C₄)-Acylamino in the context of the invention represents an amino group having a straight-chain or branched acyl substituent which has 1 to 4 carbon atoms and is attached via the carbonyl group to the nitrogen atom. There may be mentioned by way of example and preferably: formylamino, acetylamino, propionylamino, *n*-butyrylamino and isobutyrylamino.

(C₁-C₆)-Alkoxy carbonyl and (C₁-C₄)-alkoxy carbonyl in the context of the invention represent a straight-chain or branched alkoxy radical having 1 to 6 or, respectively, 1 to 4 carbon atoms which is linked via a carbonyl group. A straight-chain or branched alkoxy carbonyl radical having 1 to 4 carbon atoms in the alkoxy group is preferred. There may be mentioned by way of example and preferably: methoxy carbonyl, ethoxy carbonyl, *n*-propoxy carbonyl, isopropoxy carbonyl, *n*-butoxy carbonyl and *tert*-butoxy carbonyl.

(C₃-C₇)-Cycloalkyl and (C₃-C₆)-cycloalkyl in the context of the invention represent a monocyclic, saturated carbocyclic radical having 3 to 7 or, respectively, 3 to 6 ring carbon atoms. There may be mentioned by way of example and preferably: cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

4- to 7-membered heterocycloalkyl in the context of the invention represents a monocyclic, saturated heterocycle having a total of 4 to 7 ring atoms which contains one or two ring heteroatoms from the group consisting of N, O and S and is attached via a ring carbon atom or, if

appropriate, a ring nitrogen atom. There may be mentioned by way of example: azetidiny, oxetanyl, thietanyl, pyrrolidinyl, pyrazolidinyl, tetrahydrofuranyl, thiolanyl, 1,3-oxazolidinyl, piperidinyl, piperazinyl, tetrahydropyranyl, tetrahydrothiopyranyl, 1,3-dioxanyl, 1,4-dioxanyl, morpholinyl, thiomorpholinyl, hexahydroazepinyl, hexahydro-1,4-diazepinyl. Preference is given
5 to a 4- to 6-membered heterocycloalkyl radical which has a total of 4 to 6 ring atoms and which contains one or two ring heteroatoms from the group consisting of N and O, such as, for example, pyrrolidinyl, tetrahydrofuranyl, piperidinyl, piperazinyl, tetrahydropyranyl and morpholinyl.

5- or 6-membered heteroaryl in the context of the invention represents an aromatic heterocyclic radical (heteroaromatic) having a total of 5 or, respectively, 6 ring atoms which contains up to four
10 identical or different ring heteroatoms from the group consisting of N, O and S and is linked via a ring carbon atom or optionally via a ring nitrogen atom. There may be mentioned by way of example: furyl, pyrrolyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl and triazinyl. 5- or 6-membered heteroaryl radicals having up to three ring heteroatoms
15 from the group consisting of N, O and S, such as, for example, furyl, thienyl, thiazolyl, oxazolyl, isothiazolyl, isoxazolyl, pyrazolyl, imidazolyl, triazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyridazinyl and pyrazinyl, are preferred.

Halogen in the context of the invention includes fluorine, chlorine, bromine and iodine. Fluorine, chlorine and bromine are preferred, and fluorine and chlorine are particularly preferred.

20 If radicals in the compounds according to the invention are substituted, the radicals can be mono- or polysubstituted, unless specified otherwise. In the context of the present invention, for all the radicals which occur several times, the meaning thereof is independent of one another. Substitution by one, two or three identical or different substituents is preferred. Substitution by one or two identical or different substituents is particularly preferred.

25 Compounds of the formula (I) which are preferred in the context of the present invention are those in which

A represents CH,

R¹ represents a substituent selected from the group consisting of (C₃-C₆)-cycloalkyl, 4- to 6-
membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -O-C(=O)-NR⁹R¹⁰,
30 -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹ and -NR²⁵R²⁶
in which

(i) (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered

heteroaryl for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of (C₁-C₆)-alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶,

where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

(ii) R⁶, R⁹, R¹², R¹⁴, R¹⁶, R¹⁹, R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

- (iv) R^6 and R^7 , R^9 and R^{10} , R^{11} and R^{12} , R^{13} and R^{14} , R^{15} and R^{16} , R^{16} and R^{17} , R^{18} and R^{19} and also R^{25} and R^{26} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,
- R^2 represents a substituent selected from the group consisting of -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A} and -NR^{25A}R^{26A} in which
- (i) R^{9A} , R^{12A} , R^{14A} , R^{16A} , R^{19A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,
- (ii) R^{10A} , R^{11A} , R^{13A} , R^{15A} , R^{17A} , R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,
- and/or in which
- (iii) R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,
- m represents the number 1,
- n represents the number 0 or 1
- and
- R^3 represents hydrogen,

and salts, solvates and solvates of the salts thereof.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

A represents CH,

5 R¹ represents a substituent selected from the group consisting of (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹ and -NR²⁵R²⁶ in which

10 (i) (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of (C₁-C₆)-alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶,

15 where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

20 (ii) R⁶, R⁹, R¹², R¹⁴, R¹⁶, R¹⁹, R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

25 (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

30 (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl,

(C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

5 where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

10 (iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of
15 halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, nitro, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, trifluoromethoxy, amino, hydroxycarbonyl and -C(=O)-NH-R^{7A} in which

20 (C₁-C₆)-alkyl and (C₁-C₆)-alkoxy for their part may be substituted by hydroxyl

and

R^{7A} represents hydrogen or (C₁-C₄)-alkyl,

m represents the number 1,

n represents the number 0 or 1

25 and

R³ represents hydrogen,

and salts, solvates and solvates of the salts thereof.

Preference in the context of the present invention is also given to compounds of the formula (I) in

which

A represents CH,

R¹ represents a substituent selected from the group consisting of (C₁-C₆)-alkyl, trifluoromethyl, halogen, cyano, nitro, hydroxyl, (C₁-C₆)-alkoxy, amino, hydroxycarbonyl, (C₁-C₆)-alkoxycarbonyl and -C(=O)-NH-R⁷ in which

(C₁-C₆)-alkyl for its part may be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino or a group of the formula -NH-C(=O)-R¹², -NH-C(=O)-NH-R¹⁶ or -NH-SO₂-R¹⁹ in which

R¹², R¹⁶ and R¹⁹ each represent (C₁-C₆)-alkyl which may be substituted by hydroxyl or (C₁-C₄)-alkoxy,

and

R⁷ represents hydrogen or (C₁-C₆)-alkyl which may be substituted by hydroxyl or (C₁-C₄)-alkoxy,

R² represents a substituent selected from the group consisting of -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A} and -NR^{25A}R^{26A} in which

(i) R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iii) R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A}, R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting

of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

5 n represents the number 0 or 1

and

R³ represents hydrogen,

and salts, solvates and solvates of the salts thereof.

Preference in the context of the present invention is also given to compounds of the formula (I) in
10 which

A represents CH,

R¹ represents (C₁-C₆)-alkyl which

(i) is mono- or disubstituted by identical or different radicals from the group consisting
of halogen, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocyclo-
15 alkyl, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-
C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and
-NR²⁵R²⁶

and additionally may be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-
C₄)-alkylamino, di-(C₁-C₄)-alkylamino or (C₁-C₄)-acylamino,

20 or

(ii) is disubstituted by identical or different radicals from the group consisting of
hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino
and (C₁-C₄)-acylamino

in which

25 (a) the abovementioned cycloalkyl and heterocycloalkyl radicals for their part may
in each case be substituted up to three times by identical or different substituents
selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl,
trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-

(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxy-carbonyl,

- (b) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

- (c) R⁶, R⁹ and R¹⁴ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxy-carbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

- (d) R¹², R¹⁶ and R¹⁹ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-

(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxy-carbonyl

and

5 (C₁-C₆)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cyclo-alkyl and 4- to 6-membered heterocycloalkyl,

10 (e) R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

15 (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxy-carbonyl

and

20 (C₁-C₆)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and/or in which

25 (f) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

30 R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-

alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl, $-C(=O)-NR^{6A}R^{7A}$, $-O-C(=O)-NR^{9A}R^{10A}$, $-NR^{11A}-C(=O)-R^{12A}$, $-NR^{13A}-C(=O)-OR^{14A}$, $-NR^{15A}-C(=O)-NR^{16A}R^{17A}$, $-NR^{18A}-SO_2-R^{19A}$, $-OR^{23A}$ and $-NR^{25A}R^{26A}$ in which

5 (i) (C_1-C_6) -alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl or (C_1-C_4) -alkoxycarbonyl,

10 (ii) R^{6A} , R^{9A} , R^{12A} , R^{14A} , R^{16A} , R^{19A} , R^{23A} and R^{25A} independently of one another represent (C_1-C_6) -alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl or (C_1-C_4) -alkoxycarbonyl,

15 (iii) R^{7A} , R^{10A} , R^{11A} , R^{13A} , R^{15A} , R^{17A} , R^{18A} and R^{26A} independently of one another represent hydrogen or (C_1-C_6) -alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl or (C_1-C_4) -alkoxycarbonyl,

and/or in which

20 (iv) R^{6A} and R^{7A} , R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,

m represents the number 1,

25 n represents the number 0 or 1

and

R^3 represents hydrogen,

and salts, solvates and solvates of the salts thereof.

Preference in the context of the present invention is also given to compounds of the formula (I) in

which

A represents CH,

R¹ represents (C₁-C₆)-alkoxy which is mono- or disubstituted by identical or different radicals selected from the group consisting of halogen, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶ in which

(i) (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

(ii) R⁶, R⁹, R¹², R¹⁴, R¹⁶, R¹⁹, R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino,

hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

5 (iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹
and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are
attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to
trisubstituted by identical or different substituents from the group consisting of
halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy,
trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino,
hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

10 R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-
alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl,
aminocarbonyl, -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-
C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in
which

15 (i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl,
trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkyl-
amino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent
20 (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano,
trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-
alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent
hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano,
trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-
25 alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R^{6A} and R^{7A}, R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A},
R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to
which they are attached may form a 5- or 6-membered heterocycloalkyl ring which
30 may be mono- or disubstituted by identical or different substituents from the group
consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy,

trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

n represents the number 0 or 1

5 and

R³ represents hydrogen,

and salts, solvates and solvates of the salts thereof.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

10 A represents CH,

R¹ represents the group -C(=O)-NR⁶R⁷

in which (i)

15 R⁶ represents (C₃-C₆)-cycloalkyl or 4- to 6-membered heterocycloalkyl which may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

or

represents (C₁-C₆)-alkyl which

20 (a) is mono- or disubstituted by identical or different radicals selected from the group consisting of halogen, cyano, trifluoromethyl, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl

and may additionally be substituted by hydroxyl or (C₁-C₄)-alkoxy,

25 or

(b) is disubstituted by hydroxyl and/or (C₁-C₄)-alkoxy,

and

R^7 represents hydrogen,

or in which (ii)

R^6 represents (C_1-C_6) -alkyl, (C_3-C_6) -cycloalkyl or 4- to 6-membered heterocycloalkyl,
5 where

(C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono-
10 (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxy-carbonyl

and

(C_1-C_6) -alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_1-C_4) -alkoxycarbonyl, (C_3-C_6) -cycloalkyl and 4- to 6-
15 membered heterocycloalkyl,

and

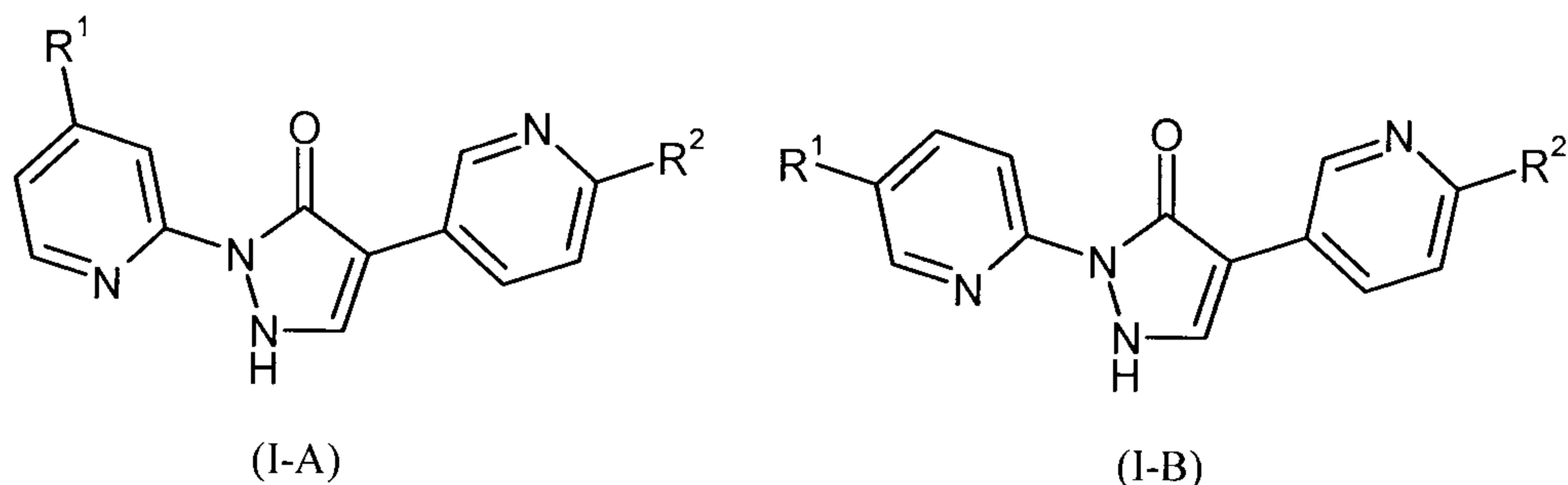
R^7 represents (C_1-C_6) -alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,
20

or in which (iii)

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- or 6-
25 membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,

- R^2 represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which
- (i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,
- (ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,
- (iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,
- and/or in which
- (iv) R^{6A} and R^{7A}, R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A}, R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,
- m represents the number 1,
- n represents the number 0 or 1
- and
- R³ represents hydrogen,
- and salts, solvates and solvates of the salts thereof.

Particular preference in the context of the present invention is also given to compounds of the formula (I-A) or (I-B)

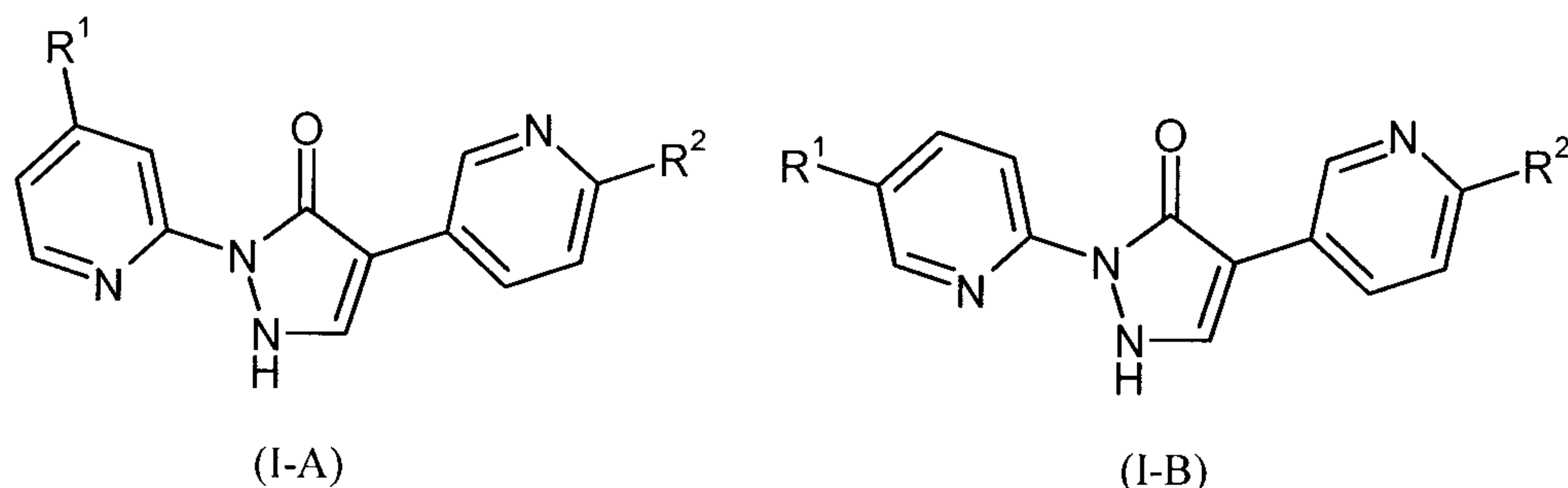


in which

- 5 R^1 represents 4- to 6-membered heterocycloalkyl, phenyl or 5- or 6-membered heteroaryl which may in each case be mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, bromine, cyano, (C_1-C_4) -alkyl, hydroxyl, amino, hydroxycarbonyl, $-OR^{23}$ and $-NR^{25}R^{26}$ in which
- 10 (C_1-C_4) -alkyl for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_3-C_6) -cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,
- 15 R^{23} and R^{25} independently of one another for each individual occurrence represent (C_1-C_4) -alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl,
- and
- 20 R^{26} for each individual occurrence represents hydrogen or (C_1-C_4) -alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino and hydroxycarbonyl,
- and
- 25 R^2 represents hydrogen, fluorine, chlorine, cyano, (C_1-C_4) -alkyl, trifluoromethyl,

hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl,
and salts, solvates and solvates of the salts thereof.

Particular preference in the context of the present invention is also given to compounds of the
formula (I-A) or (I-B)



in which

R¹ represents (C₁-C₆)-alkyl which

- (i) is mono- or disubstituted by identical or different radicals selected from the group
consisting of fluorine, chlorine, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-
membered heterocycloalkyl, hydroxycarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰,
-NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³
and -NR²⁵R²⁶

and may additionally be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-
C₄)-alkylamino, di-(C₁-C₄)-alkylamino or (C₁-C₄)-acylamino,

or

- (ii) is disubstituted by identical or different radicals selected from the group consisting of
hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino
and (C₁-C₄)-acylamino

in which

- (a) the above-mentioned cycloalkyl and heterocycloalkyl radicals for their part may
in each case be substituted up to three times by identical or different substituents
selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl,
trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino,
di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

- (b) R^7 , R^{10} , R^{11} , R^{13} , R^{15} , R^{17} , R^{18} and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₄)-alkyl,

where (C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

- (c) R^6 , R^9 and R^{14} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

- (d) R^{12} , R^{16} and R^{19} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, amino, mono-(C₁-C₄)-

alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

- (e) R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and/or in which

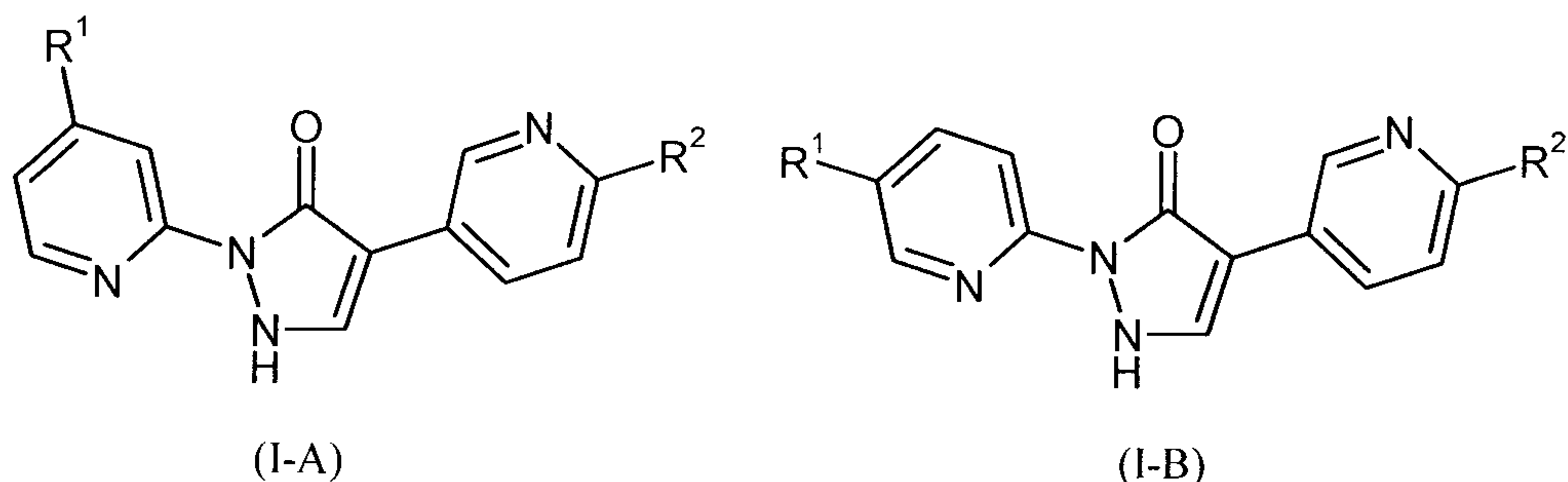
- (f) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and

- R² represents hydrogen, fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl,

and salts, solvates and solvates of the salts thereof.

Particular preference in the context of the present invention is also given to compounds of the formula (I-A) or (I-B)



in which

R^1 represents (C₁-C₆)-alkoxy which is mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxyl, amino, hydroxycarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶ in which

(i) (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

(ii) R⁶, R⁹, R¹², R¹⁴, R¹⁶, R¹⁹, R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each

individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₄)-alkyl,

where (C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and/or in which

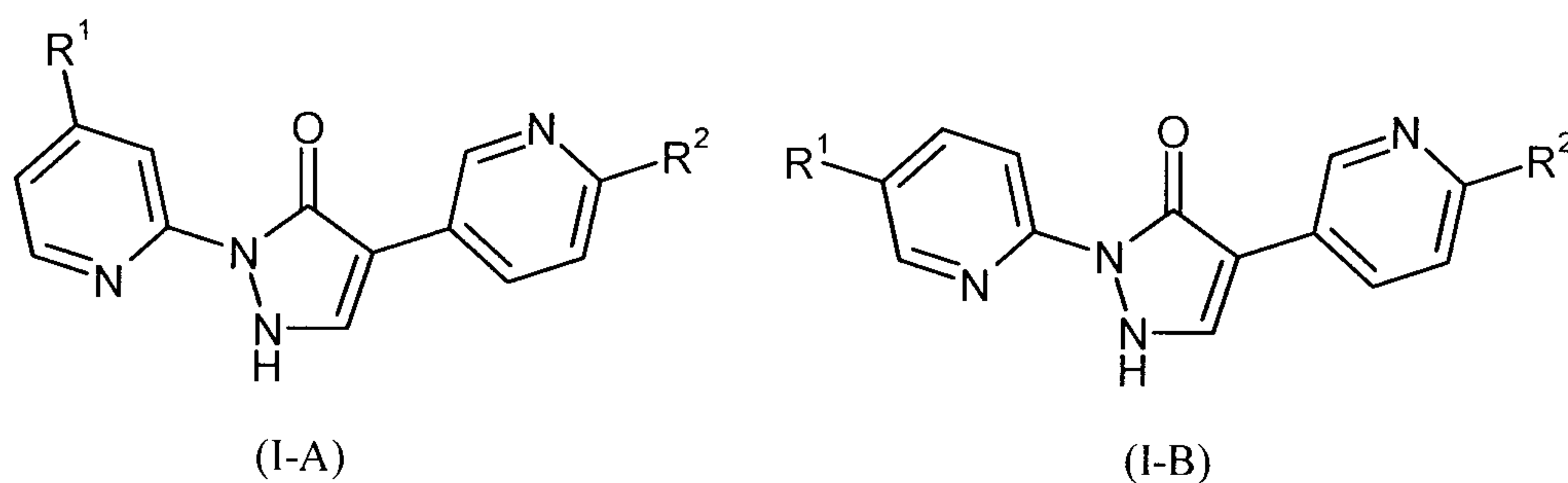
(iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and

R² represents hydrogen, fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl,

and salts, solvates and solvates of the salts thereof.

Particular preference in the context of the present invention is also given to compounds of the formula (I-A) or (I-B)



in which

R¹ represents the group -C(=O)-NR⁶R⁷

in which (i)

- 5 R⁶ represents (C₃-C₆)-cycloalkyl or 4- to 6-membered heterocycloalkyl which may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,
- or
- represents (C₁-C₆)-alkyl which
- 10 (a) is mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl
- and may additionally be substituted by hydroxyl or (C₁-C₄)-alkoxy,
- or
- (b) is disubstituted by hydroxyl and/or (C₁-C₄)-alkoxy,
- 15 and
- R⁷ represents hydrogen,
- or in which (ii)
- 20 R⁶ represents (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or 4- to 6-membered heterocycloalkyl, where
- (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl
- 25 and
- (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-

C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and

5 R⁷ represents (C₁-C₄)-alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

or in which (iii)

10 R⁶ and R⁷ together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and

15 R² represents hydrogen, fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl,

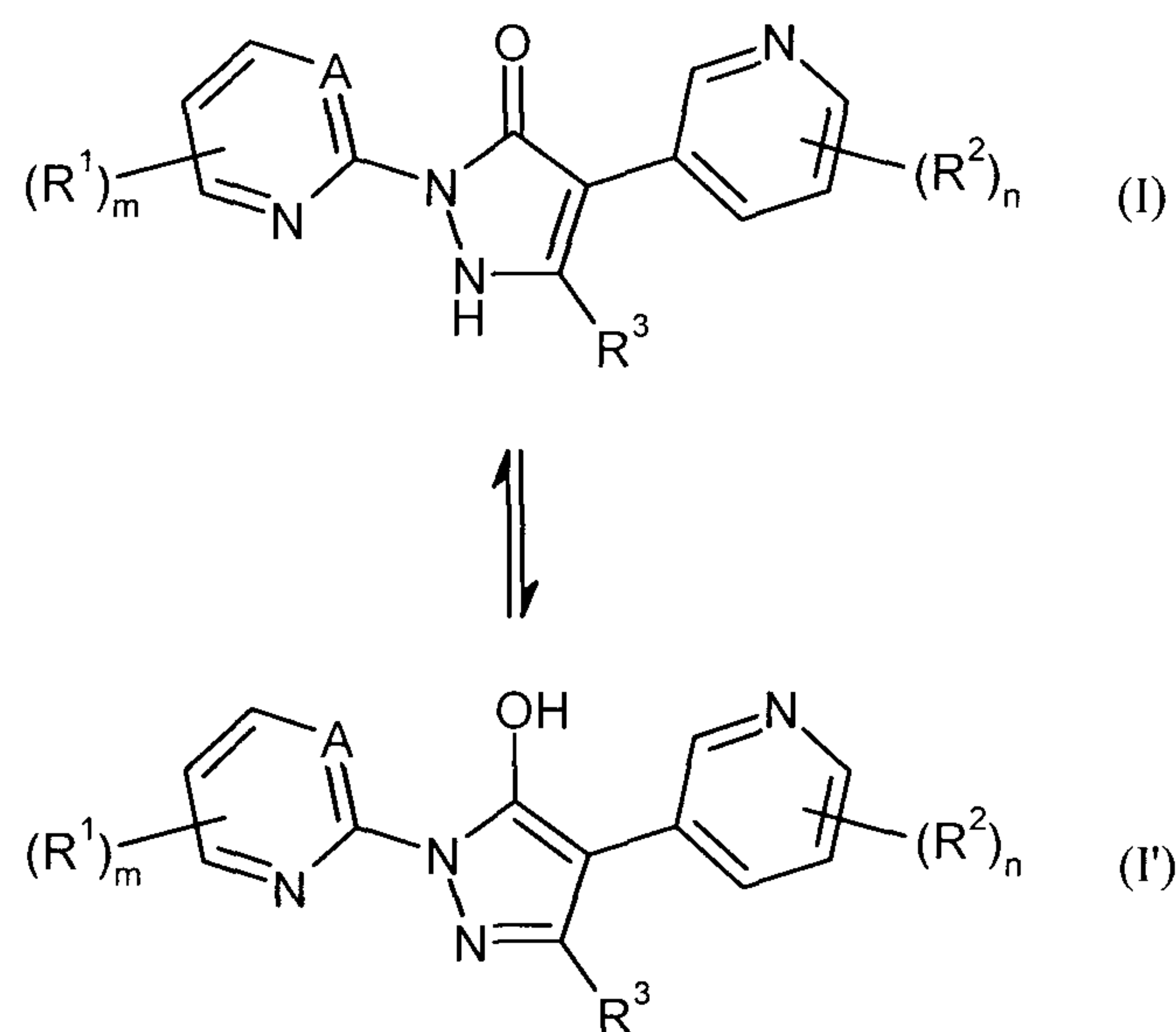
and their salts, solvates and solvates of the salts.

The radical definitions given in detail in the particular combinations or preferred combinations of radicals are also replaced as desired by radical definitions of other combinations, independently of the particular radical combinations given.

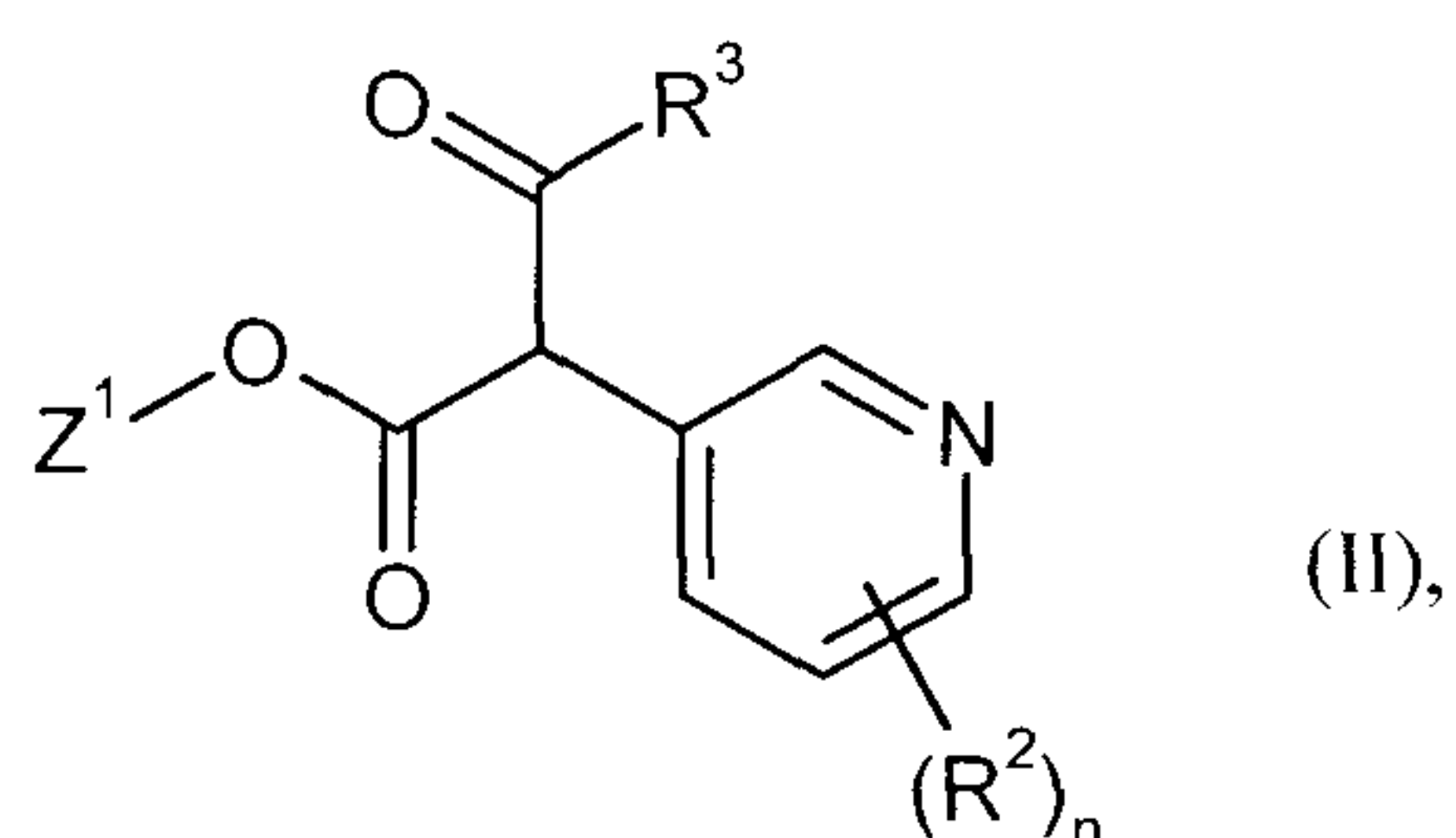
20 Combinations of two or more of the abovementioned preferred ranges are very particularly preferred.

The 1,2-dihydropyrazol-3-one derivatives of the formula (I) according to the invention can also be in the tautomeric 1*H*-pyrazol-5-ol form (I') (see Scheme 1 below); the two tautomeric forms are expressly incorporated into the present invention.

Scheme 1



The invention also provides a process for the preparation of the compounds of the formula (I) according to the invention, characterized in that a compound of the formula (II)

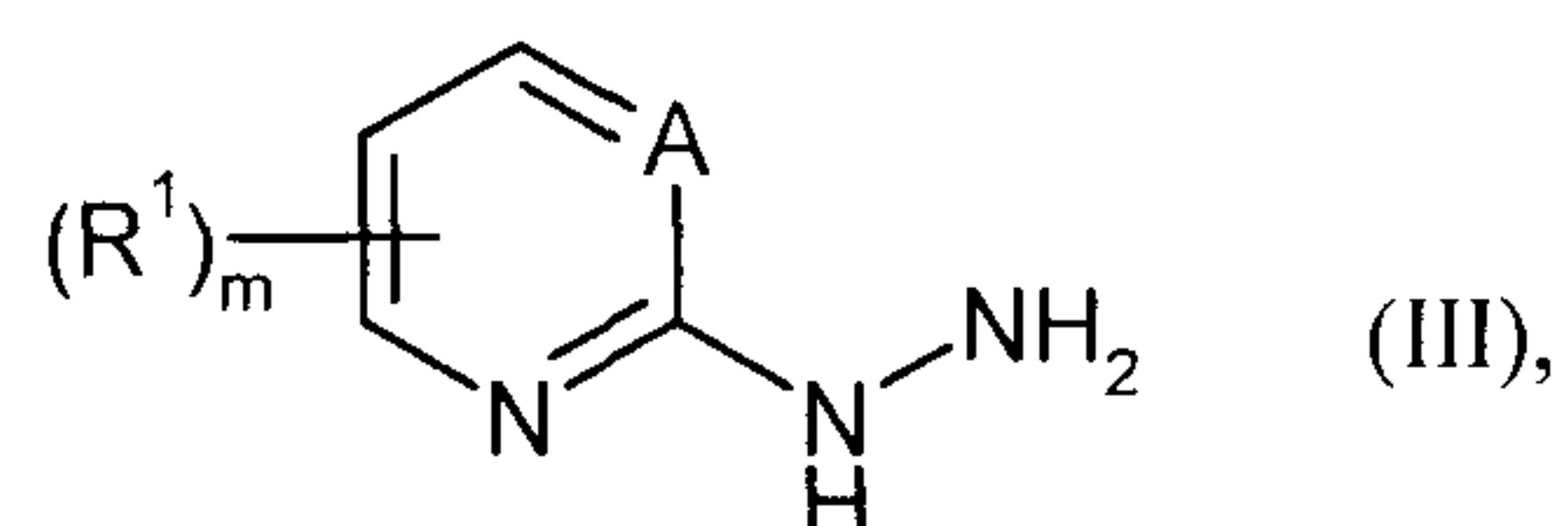


5

in which R^2 , R^3 and n have the meanings given above and

Z^1 represents methyl or ethyl,

is reacted in an inert solvent, if appropriate in the presence of an acid, with a compound of the formula (III)

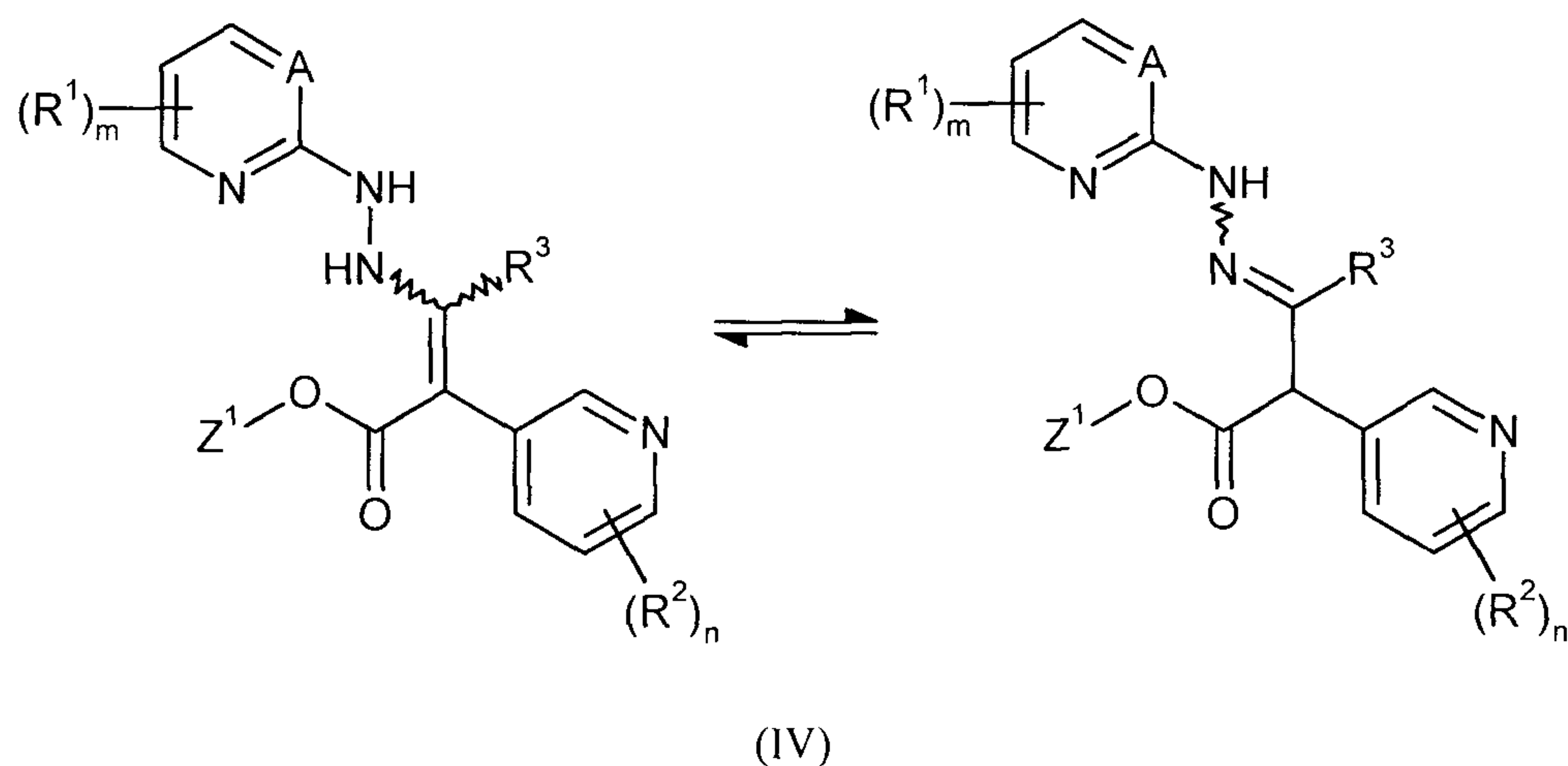


10

in which A , R^1 and m have the meanings given above,

to give compounds of the formula (IV)

- 34 -

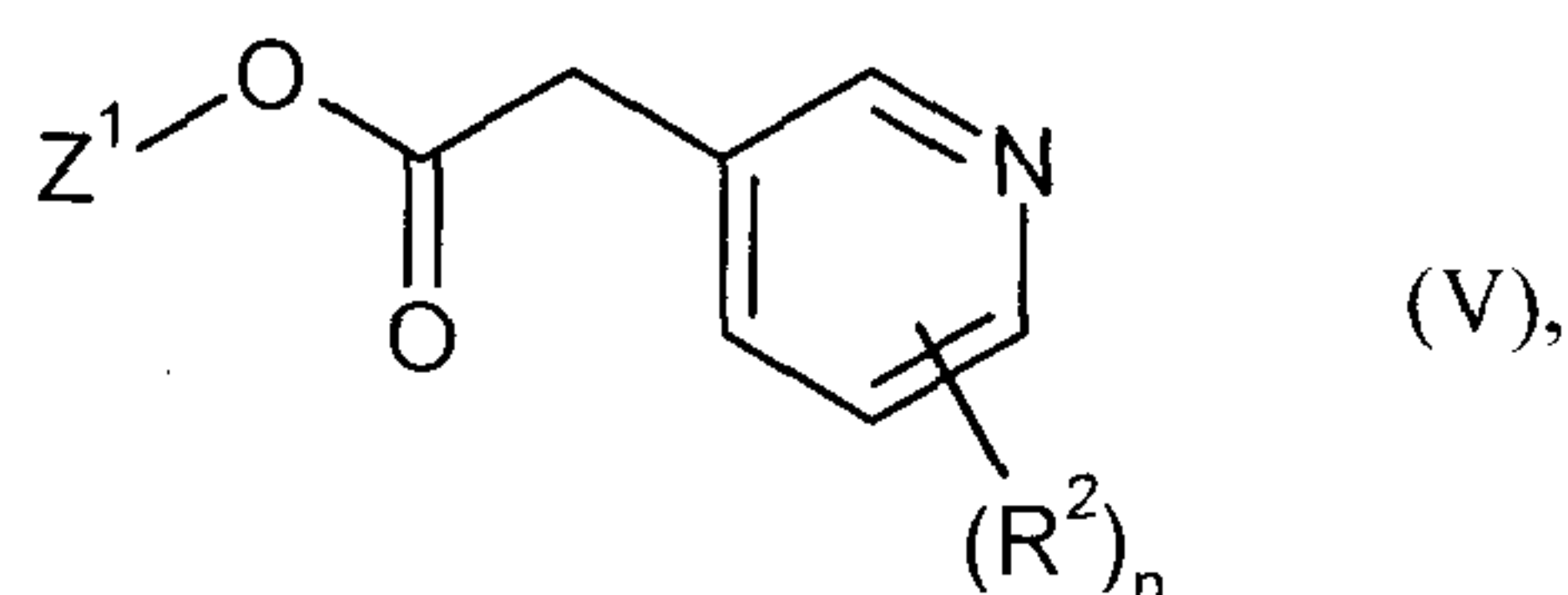


in which Z^1 , A, R^1 , R^2 , R^3 , m and n have the meanings given above,

which, already under these reaction conditions or in a subsequent reaction step under the influence
5 of a base, cyclize to give the compounds of the formula (I),

and the compounds of the formula (I) are, if appropriate with the appropriate (i) solvents and/or (ii) bases or acids, converted into their solvates, salts and/or solvates of the salts.

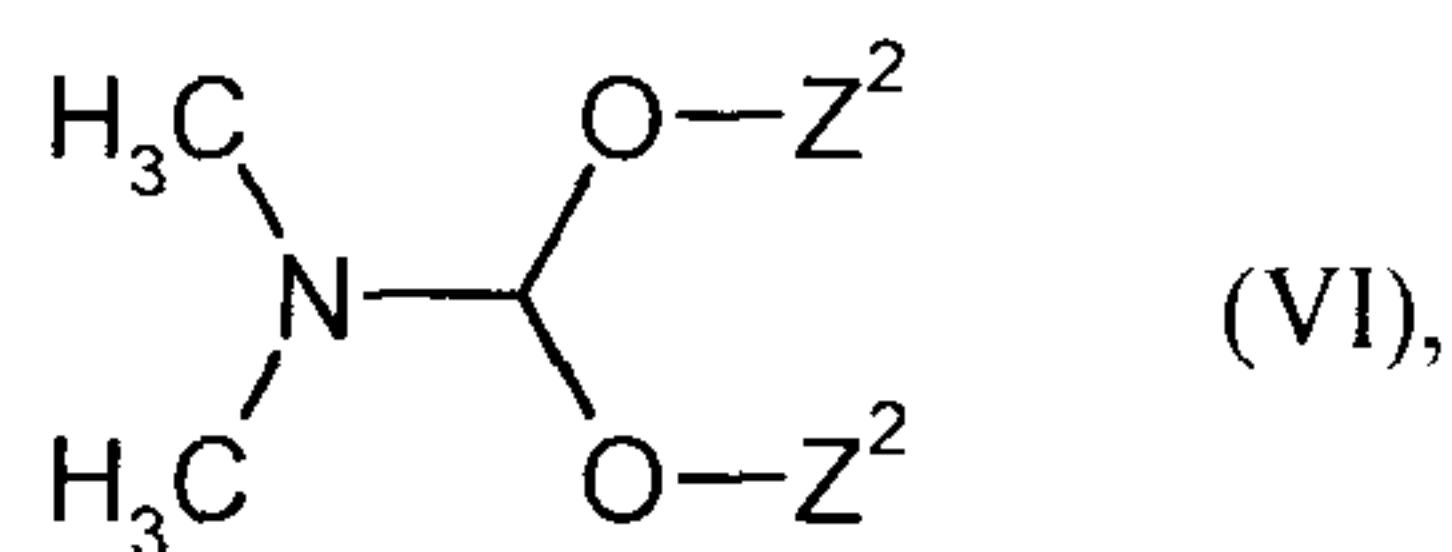
The compounds of the formula (I) according to the invention in which R^3 represents hydrogen can also be prepared by initially condensing a compound of the formula (V)



10

in which Z^1 , R^2 and n have the meanings given above,

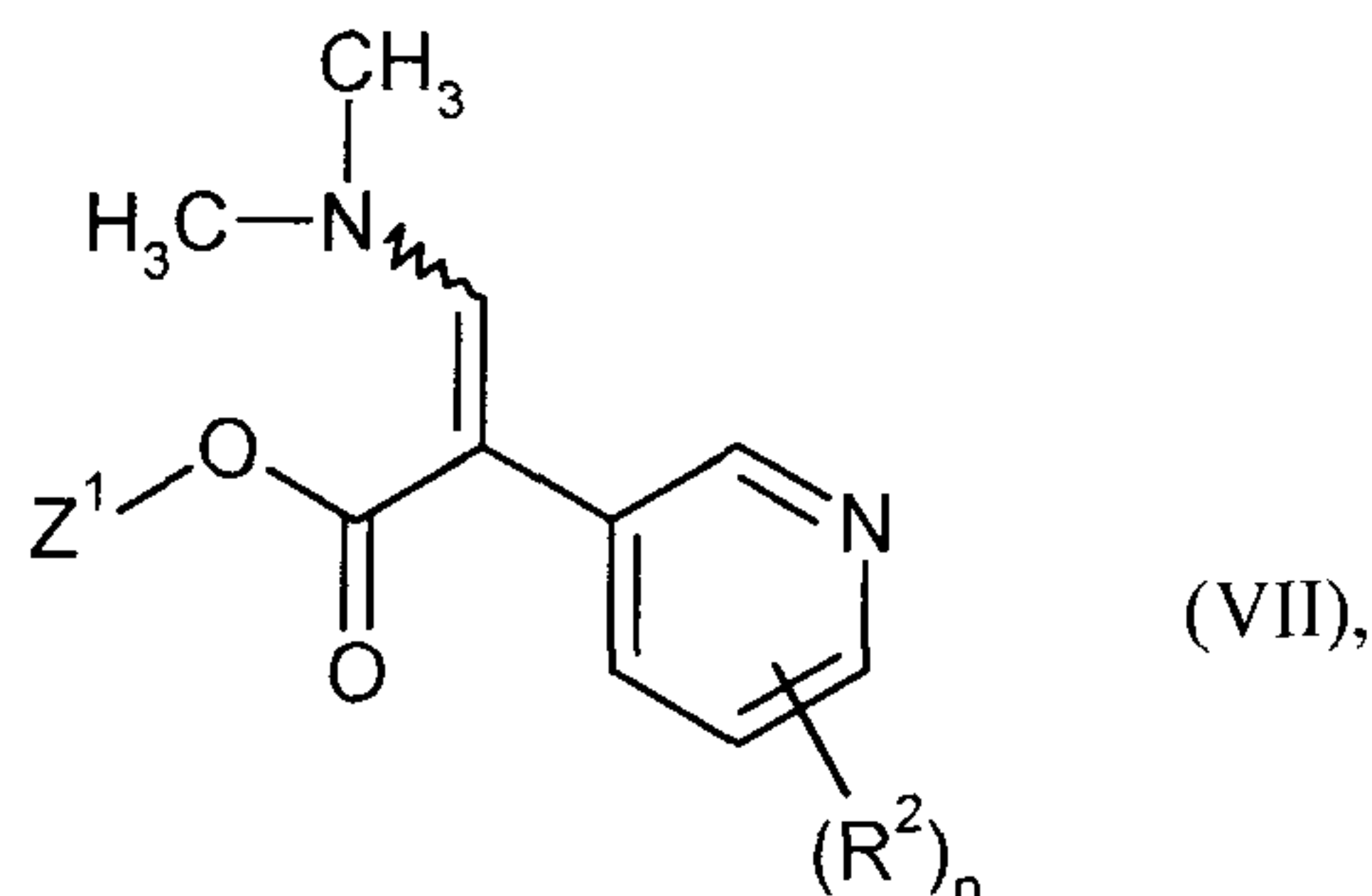
with a compound of the formula (VI)



in which

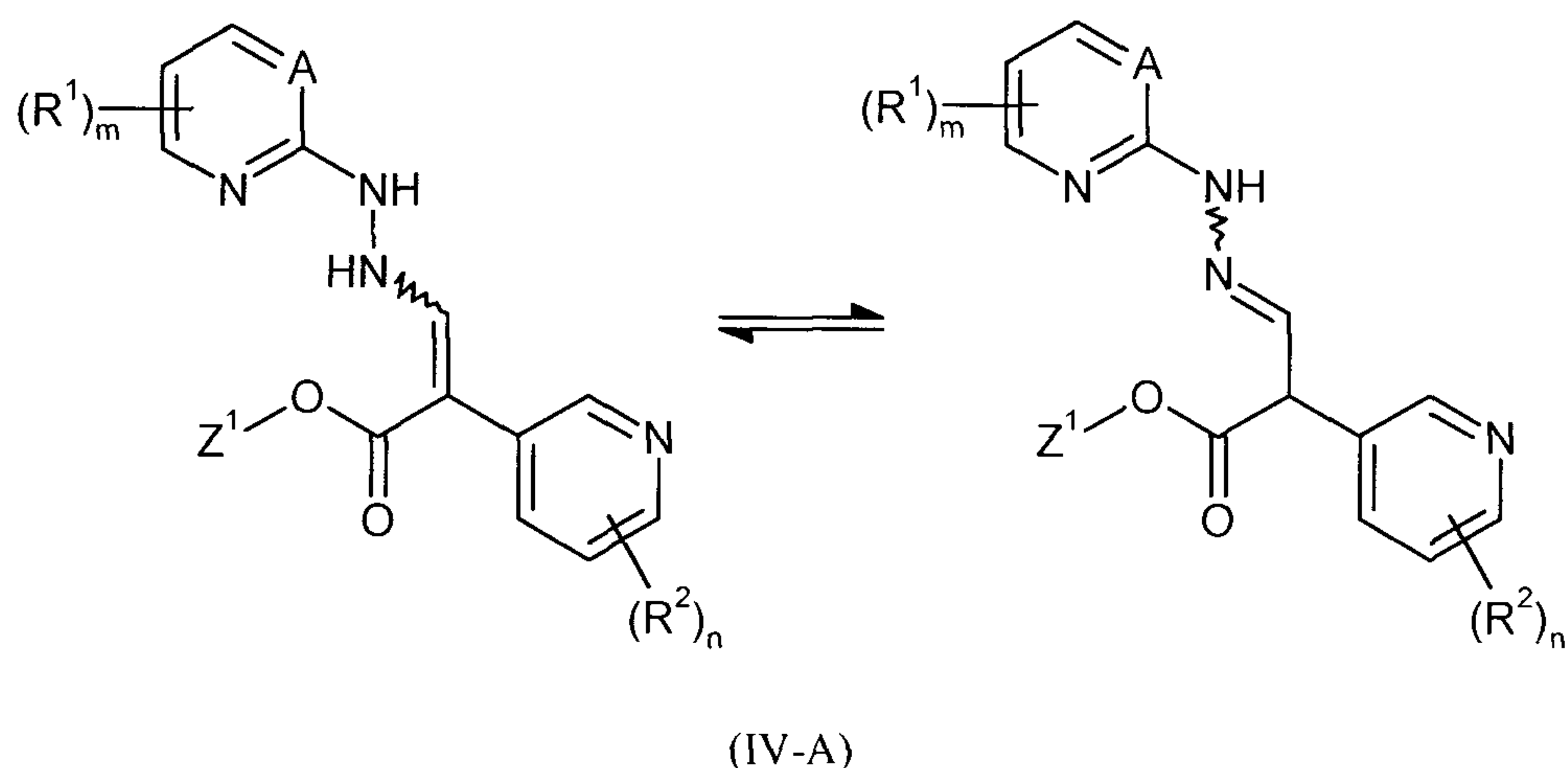
15 Z^2 represents methyl or ethyl,

to give compounds of the formula (VII)



in which Z^1 , R^2 and n have the meanings given above,

and then reacting in the presence of an acid with a compound of the formula (III) to give compounds of the formula (IV-A)



in which Z^1 , A , R^1 , R^2 , m and n have the meanings given above,

which, already under these reaction conditions or in a subsequent reaction step under the influence of a base, cyclize to give the compounds of the formula (I) in which R^3 represents hydrogen.

- 10 Further compounds according to the invention can optionally also be prepared by conversions of functional groups of individual substituents, in particular those listed under R^1 and R^2 , starting from the compounds of the formula (I) obtained by the above processes. These conversions are carried out by conventional methods known to the person skilled in the art and include, for example, reactions such as nucleophilic or electrophilic substitution, oxidation, reduction,
- 15 hydrogenation, transition metal-catalyzed coupling reactions, alkylation, acylation, amination, esterification, ester cleavage, etherification, ether cleavage, formation of carboxamides, sulfonamides, carbamates and ureas, and the introduction and removal of temporary protective groups.

Suitable inert solvents for the process steps (II) + (III) $\rightarrow$ (IV), (IV) $\rightarrow$ (I), (VII) + (III) $\rightarrow$ (IV-A) and (IV-A) $\rightarrow$ (I) are, in particular, ethers, such as diethyl ether, methyl tert-butyl ether, 1,2-dimethoxyethane, tetrahydrofuran and dioxane, or alcohols, such as methanol, ethanol, n-propanol, iso-propanol, n-butanol and tert-butanol. Methanol, ethanol tetrahydrofuran or mixtures of these
5 solvents are preferably employed.

The process step (V) + (VI) $\rightarrow$ (VII) is preferably carried out in dimethylformamide as a solvent or also in the presence of an excess of (VI) without a further solvent. The reaction can also optionally be carried out under microwave irradiation. The reaction in general takes place in a temperature range of from +20 °C to +150 °C, preferably at +80 °C to 120 °C [cf. also J.P. Bazureau et al.,
10 *Synthesis* 1998, 967; *ibid.* 2001 (4), 581].

Process steps (II) + (III) $\rightarrow$ (IV) and (VII) + (III) $\rightarrow$ (IV-A) can optionally advantageously be carried out with the addition of an acid. Conventional inorganic or organic acids are suitable for this, such as, for example, hydrogen chloride, acetic acid, trifluoroacetic acid, methanesulfonic acid, p-toluenesulfonic acid or camphor-10-sulfonic acid. Acetic acid or, in particular, camphor-
15 10-sulfonic acid or p-toluenesulfonic acid are preferably used.

The reaction (II) + (III) $\rightarrow$ (IV) is in general carried out in a temperature range of from 0°C to +100°C, preferably from +10°C to +50°C. The reaction (VII) + (III) $\rightarrow$ (IVA) is in general carried out in a temperature range of from +20°C to +120°C, preferably at +50°C to +100°C.

The process sequences (II) + (III) $\rightarrow$ (IV) $\rightarrow$ (I) and (VII) + (III) $\rightarrow$ (IV-A) $\rightarrow$ (I) can be carried
20 out under a two-stage reaction procedure or also as a one-pot reaction, without isolation of the intermediate stage (IV) or, respectively, (IV-A). For the latter variant, reaction of the components under microwave irradiation is suitable in particular; the reaction here is in general carried out in a temperature range of from +50°C to +200°C, preferably at +100°C to +180°C.

In some cases a cyclization to (I) also already occurs even during preparation of (IV) or,
25 respectively, (IV-A); the cyclization can then optionally be brought to completion by *in situ* treatment of the reaction mixture with a base.

Conventional inorganic or organic bases are suitable as the base for such a separate cyclization step (IV) $\rightarrow$ (I) or (IV-A) $\rightarrow$ (I). These include, in particular, alkali metal hydroxides, such as, for example, sodium or potassium hydroxide, alkali metal or alkaline earth metal carbonates, such as
30 sodium, potassium, calcium or cesium carbonate, alkali metal alcoholates, such as sodium or potassium methanolate, sodium or potassium ethanolate or sodium or potassium tert-butyrate, or alkali metal hydrides, such as sodium hydride. Sodium methanolate or ethanolate are preferably

used.

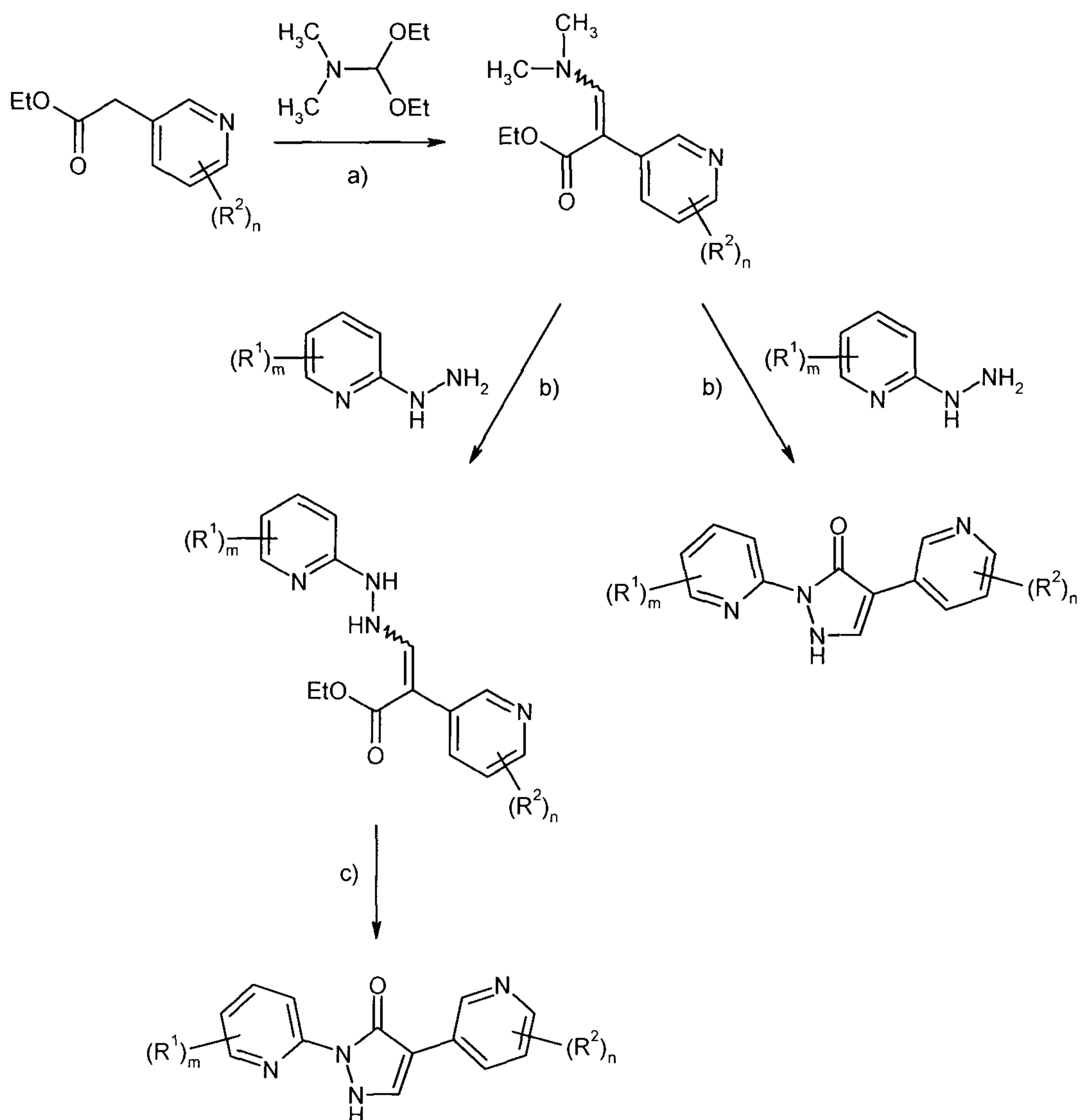
The base-induced reaction (IV) $\rightarrow$ (I) or (IV-A) $\rightarrow$ (I) is in general carried out in a temperature range of from 0°C to +60°C, preferably at 0°C to +30°C.

All the process steps can be carried out under atmospheric, elevated or reduced pressure (e.g. from
5 0.5 to 5 bar). In general, atmospheric pressure is applied.

The compounds of the formula (II) can be prepared by conventional methods from the literature for C-acylation of carboxylic acid esters from compounds of the formula (V). The compounds of the formulae (III), (V) and (VI) are commercially obtainable or known from the literature or can be prepared analogously to processes described in the literature.

10 The preparation of the compounds according to the invention can be illustrated by reaction scheme 2 below:

Scheme 2



[a): DMF, 16 h, +100°C; b): ethanol, cat. camphor-10-sulfonic acid, +78°C; c): NaOEt, ethanol, 1 h, RT].

- 5 The compounds according to the invention show an unforeseeable, valuable pharmacological action spectrum. They are therefore suitable for use as medicaments for treatment and/or prophylaxis of diseases in humans and animals.

The compounds according to the invention are distinguished as specific inhibitors of HIF prolyl 4-hydroxylases.

- 10 On the basis of their pharmacological properties, the compounds according to the invention can be employed for treatment and/or prophylaxis of cardiovascular diseases, in particular cardiac

insufficiency, coronary heart disease, angina pectoris, myocardial infarction, stroke, arteriosclerosis, essential, pulmonary and malignant hypertension and peripheral arterial occlusive disease.

The compounds according to the invention are furthermore suitable for treatment and/or
5 prophylaxis of blood formation disorders, such as for example idiopathic anemias, renal anemia and anemias accompanying a tumor disease (in particular an anemia induced by chemotherapy), an infection (in particular HIV infection) or another inflammatory disease, such as for example rheumatoid arthritis. The compounds according to the invention are moreover suitable for supporting treatment of anemias as a result of blood loss, iron deficiency anemia, vitamin
10 deficiency anemia (for example as a result of vitamin B12 deficiency or as a result of folic acid deficiency), hypoplastic and aplastic anemia or hemolytic anemia, or for supporting treatment of anemias as a result of iron utilization disorders (sideroachrestic anemia) or anemias as a result of other endocrine disorders (for example hypothyroidosis).

The compounds are furthermore suitable for increasing the hematocrit with the aim of obtaining
15 blood for autodonation of blood before operations.

The compounds according to the invention can moreover be used for treatment and/or prophylaxis of operation-related states of ischemia and consecutive symptoms thereof after surgical interventions, in particular interventions on the heart using a heart-lung machine (for example bypass operations, heart valve implants), interventions on the carotid arteries, interventions on the
20 aorta and interventions with instrumental opening or penetration of the skull cap. The compounds are furthermore suitable for general treatment and/or prophylaxis in the event of surgical interventions with the aim of accelerating wound healing and shortening the convalescence time.

The compounds are moreover suitable for treatment and prophylaxis of consecutive symptoms of acute and protracted ischemic states of the brain (for example stroke, birth asphyxia).

25 The compounds can furthermore be employed for treatment and/or prophylaxis of cancer and for treatment and/or prophylaxis of an impairment in the state of health occurring in the course of treatment of cancer, in particular after therapy with cytostatics, antibiotics and irradiations.

The compounds are furthermore suitable for treatment and/or prophylaxis of diseases of the rheumatic type and other disease forms to be counted as autoimmune diseases, and in particular for
30 treatment and/or prophylaxis of an impairment in the state of health occurring in the course of medicamentous treatment of such diseases.

The compounds according to the invention can moreover be employed for treatment and/or

prophylaxis of diseases of the eye (for example glaucoma), the brain (for example Parkinson's disease, Alzheimer's disease, dementia, chronic pain sensation), of chronic kidney diseases, renal insufficiency and acute renal failure and for promoting wound healing.

The compounds are moreover suitable for treatment and/or prophylaxis of general physical
5 weakness, up to cachexia, in particular occurring to an increased extent at a more elderly age.

The compounds are furthermore suitable for treatment and/or prophylaxis of sexual dysfunction.

The compounds are moreover suitable for treatment and/or prophylaxis of diabetes mellitus and its consecutive symptoms, such as for example diabetic macro- and microangiopathy, diabetic nephropathy and neuropathy.

10 The compounds according to the invention are moreover suitable for treatment and/or prophylaxis of fibrotic diseases for example of the heart, the lungs and the liver.

In particular, the compounds according to the invention are also suitable for prophylaxis and treatment of retinopathy in premature babies (retinopathia prematurorum).

The present invention moreover provides the use of the compounds according to the invention for
15 treatment and/or prevention of diseases, in particular the abovementioned diseases.

The present invention moreover provides the use of the compounds according to the invention for the preparation of a medicament for treatment and/or prevention of diseases, in particular the abovementioned diseases.

The present invention moreover provides a method for treatment and/or prevention of diseases, in
20 particular the abovementioned diseases, using an active amount of at least one of the compounds according to the invention.

The compounds according to the invention can be employed by themselves or, if required, in combination with other active compounds. The present invention moreover provides medicaments comprising at least one of the compounds according to the invention and one or more further
25 active compounds, in particular for treatment and/or prevention of the abovementioned diseases. Suitable active compounds in the combination which may be mentioned by way of example and preferably are: ACE inhibitors, angiotensin II receptor antagonists, beta receptor blockers, calcium antagonists, PDE inhibitors, mineralocorticoid receptor antagonists, diuretics, aspirin, iron supplements, vitamin B12 and folic acid supplements, statins, digitalis (digoxin) derivatives, tumor
30 chemotherapeutics and antibiotics.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an ACE inhibitor, such as, by way of example and preferably, enalapril, captopril, lisinopril, ramipril, delapril, fosinopril, quinoprol, perindopril or trandopril.

5 In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an angiotensin AII antagonist, such as, by way of example and preferably, losartan, candesartan, valsartan, telmisartan or embusartan.

10 In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a beta receptor blocker, such as, by way of example and preferably, propranolol, atenolol, timolol, pindolol, alprenolol, oxprenolol, penbutolol, bupranolol, metipranolol, nadolol, mepindolol, carazalol, sotalol, metoprolol, betaxolol, celiprolol, bisoprolol, carteolol, esmolol, labetalol, carvedilol, adaprolol, landiolol, nebivolol, epanolol or bucindolol.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a calcium antagonist, such as, by way of example and preferably, nifedipine, amlodipine, verapamil or diltiazem.

15 In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a phosphodiesterase (PDE) inhibitor, such as, by way of example and preferably, milrinone, amrinone, pimobendan, cilostazol, sildenafil, vardenafil or tadalafil.

20 In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a mineralocorticoid receptor antagonist, such as, by way of example and preferably, spironolactone, eplerenone, canrenone or potassium canrenoate.

25 In a preferred embodiment of the invention the compounds according to the invention are administered in combination with a diuretic, such as, by way of example and preferably, furosemide, bumetanide, torsemide, bendroflumethiazide, chlorthiazide, hydrochlorthiazide, hydroflumethiazide, methyclothiazide, polythiazide, trichlormethiazide, chlorthalidone, indapamide, metolazone, quinethazone, acetazolamide, dichlorphenamide, methazolamide, glycerin, isosorbide, mannitol, amiloride or triamterene.

30 In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an HMG-CoA reductase inhibitor from the class of statins, such as, by way of example and preferably, lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, rosuvastatin, cerivastatin or pitavastatin.

In a preferred embodiment of the invention, the compounds according to the invention are

administered in combination with a tumor chemotherapeutic, by way of example and preferably from the group consisting of platinum complexes, such as for example cisplatin and carboplatin, the alkylating agents, such as for example cyclophosphamide and chlorambucil, the antimetabolites, such as for example 5-fluorouracil and methotrexate, the topoisomerase inhibitors, such as for example etoposide and camptothecin, the antibiotics, such as for example doxorubicin and daunorubicin, or the kinase inhibitors, such as for example sorafenib and sunitinib.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an antibiotic, by way of example and preferably from the group consisting of penicillins, cephalosporins or quinolones, such as for example ciprofloxacin and moxifloxacin.

The present invention moreover provides medicaments which comprise at least one compound according to the invention, conventionally together with one or more inert, non-toxic, pharmaceutically suitable auxiliary substances, and the use thereof for the abovementioned purposes.

The compounds according to the invention can act systemically and/or locally. They can be administered in a suitable manner for this purpose, such as for example orally, parenterally, pulmonally, nasally, sublingually, lingually, buccally, rectally, dermally, transdermally, conjunctivally, otically or as an implant or stent.

The compounds according to the invention can be administered in suitable administration forms for these administration routes.

Administration forms which function according to the prior art, release the compounds according to the invention rapidly and/or in a modified manner and comprise the compounds according to the invention in crystalline and/or amorphized and/or dissolved form are suitable for oral administration, such as for example tablets (non-coated or coated tablets, for example coatings which are resistant to gastric juice or dissolve in a delayed manner or are insoluble and control the release of the compound according to the invention), tablets or films/wafers, films/lyophilizates or capsules which disintegrate rapidly in the oral cavity (for example hard or soft gelatin capsules), sugar-coated tablets, granules, pellets, powders, emulsions, suspensions, aerosols or solutions.

Parenteral administration can be effected with bypassing of an absorption step (for example intravenously, intraarterially, intracardially, intraspinally or intralumbally) or with inclusion of an absorption (for example intramuscularly, subcutaneously, intracutaneously, percutaneously or intraperitoneally). Administration forms which are suitable for parenteral administration are, inter

alia, injection and infusion formulations in the form of solutions, suspensions, emulsions, lyophilizates or sterile powders.

For the other administration routes, for example, inhalation medicament forms (inter alia powder inhalers, nebulizers), nasal drops, solutions or sprays, tablets, films/wafers or capsules for lingual, sublingual or buccal administration, suppositories, ear or eye preparations, vaginal capsules, aqueous suspensions (lotions, shaking mixtures), lipophilic suspensions, ointments, creams, transdermal therapeutic systems (for example patches), milk, pastes, foams, sprinkling powders, implants or stents are suitable.

Oral and parenteral administration are preferred, in particular oral and intravenous administration.

10 The compounds according to the invention can be converted into the administration forms mentioned. This can be effected in a manner known per se by mixing with inert, non-toxic, pharmaceutically suitable auxiliary substances. These auxiliary substances include inter alia carrier substances (for example microcrystalline cellulose, lactose, mannitol), solvents (for example liquid polyethylene glycols), emulsifiers and dispersing or wetting agents (for example sodium dodecyl sulfate, polyoxysorbitan oleate), binders (for example polyvinylpyrrolidone), synthetic and natural polymers (for example albumin), stabilizers (for example antioxidants, such as, for example, ascorbic acid), dyestuffs (for example inorganic pigments, such as, for example, iron oxides) and flavor and/or smell correctants.

20 In general, it has proved advantageous in the case of parenteral administration to administer amounts of from about 0.001 to 1 mg/kg, preferably about 0.01 to 0.5 mg/kg of body weight to achieve effective results. In the case of oral administration the dosage is about 0.01 to 100 mg/kg, preferably about 0.01 to 20 mg/kg and very particularly preferably 0.1 to 10 mg/kg of body weight.

25 Nevertheless it may be necessary to deviate from the amounts mentioned, and in particular depending on the body weight, administration route, individual behavior towards the active compound, nature of the formulation and point in time or interval at which administration takes place. Thus in some cases it may be sufficient to manage with less than the abovementioned minimum amount, while in other cases the upper limit mentioned must be exceeded. In the case where relatively large amounts are administered, it may be advisable to distribute these into several individual doses over the day.

30 The following embodiment examples illustrate the invention. The invention is not limited to the examples.

The percentage data in the following tests and examples are percentages by weight, unless stated

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otherwise; parts are parts by weight. The solvent ratios, dilution ratios and concentration data of liquid/liquid solutions in each case relate to the volume.

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A. ExamplesAbbreviations and acronyms:

aq.	aqueous solution
cat.	catalytic
d	day(s)
DCI	direct chemical ionization (in MS)
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
EI	electron impact ionization (in MS)
ESI	electrospray ionization (in MS)
Et	ethyl
GC-MS	gas chromatography-coupled mass spectroscopy
h	hour(s)
HPLC	high pressure, high performance liquid chromatography
conc.	concentrated
LC-MS	liquid chromatography-coupled mass spectroscopy
Meth.	method
min	minute(s)
MS	mass spectroscopy
NMR	nuclear magnetic resonance spectroscopy
R _t	retention time (in HPLC)
RT	room temperature
TFA	trifluoroacetic acid
THF	tetrahydrofuran

LC-MS, GC-MS and HPLC methods:5 Method 1:

Instrument: MicromassTM Platform LCZ mit HPLC AgilentTM Serie 1100; column: Thermo Hypersil GOLD 3 μ , 20 mm x 4 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 100% A → 0.2 min 100% A → 2.9 min 30% A → 3.1 min 10% A → 5.5 min 10% A; oven: 50°C; flow rate: 0.8 ml/min; UV detection: 210 nm.

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Method 2:

MS instrument type: Micromass ZQ; HPLC instrument type: HP 1100 Series; UV DAD; column: Phenomenex Synergi 2 μ Hydro-RP Mercury 20 mm x 4 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 90% A $\rightarrow$ 2.5 min 30% A $\rightarrow$ 3.0 min 5% A $\rightarrow$ 4.5 min 5% A; flow rate: 0.0 min 1 ml/min $\rightarrow$ 2.5 min/3.0 min/4.5 min 2 ml/min; oven: 50°C; UV detection: 210 nm.

Method 3:

MS instrument: Micromass TOF (LCT); HPLC instrument: Waters 2690; autosampler: Waters 2700; column: YMC-ODS-AQ, 50 mm x 4.6 mm, 3.0 μ m; mobile phase A: water + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid; gradient: 0.0 min 100% A $\rightarrow$ 0.2 min 95% A $\rightarrow$ 1.8 min 25% A $\rightarrow$ 1.9 min 10% A $\rightarrow$ 2.0 min 5% A $\rightarrow$ 3.2 min 5% A $\rightarrow$ 3.21 min 100% A $\rightarrow$ 3.35 min 100% A; oven: 40°C; flow rate: 3.0 ml/min; UV detection: 210 nm.

Method 4:

MS instrument: Waters ZQ 2000; HPLC instrument: Agilent 1100, 2-column system; autosampler: HTC PAL; column: YMC-ODS-AQ, 50 mm x 4.6 mm, 3.0 μ m; mobile phase A: water + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid; gradient: 0.0 min 100% A $\rightarrow$ 0.2 min 95% A $\rightarrow$ 1.8 min 25% A $\rightarrow$ 1.9 min 10% A $\rightarrow$ 2.0 min 5% A $\rightarrow$ 3.2 min 5% A $\rightarrow$ 3.21 min 100% A $\rightarrow$ 3.35 min 100% A; oven: 40°C; flow rate: 3.0 ml/min; UV detection: 210 nm.

Method 5:

Instrument: Micromass QuattroPremier with Waters UPLC Acquity; column: Thermo Hypersil GOLD 1.9 μ 50 mm x 1 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 90% A $\rightarrow$ 0.1 min 90% A $\rightarrow$ 1.5 min 10% A $\rightarrow$ 2.2 min 10% A; flow rate: 0.33 ml/min; oven: 50°C; UV detection: 210 nm.

25 Method 6:

Instrument: Micromass QuattroTM Micro MS with HPLC Agilent Serie 1100; column: Thermo Hypersil GOLD 3 μ 20 mm x 4 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 100% A $\rightarrow$ 3.0 min 10% A $\rightarrow$ 4.0 min 10% A $\rightarrow$ 4.01 min 100% A (flow rate 2.5 ml/min) $\rightarrow$ 5.00 min 100% A; oven: 50°C; flow rate: 2 ml/min; UV detection: 210 nm.

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Method 7:

MS instrument type: Waters ZQ; HPLC instrument type: Agilent 1100 Series; UV DAD; column: Thermo Hypersil GOLD 3 μ 20 mm x 4 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 100% A → 3.0 min 10% A → 4.0 min 10% A → 4.1 min 100% A; flow rate: 2.5 ml/min; oven: 55°C; UV detection: 210 nm.

Method 8:

MS instrument: Micromass TOF (LCT); HPLC instrument: Waters 2690; autosampler: Waters 2700; column: YMC-ODS-AQ, 3 μ , 50 mm x 4.6 mm; mobile phase A: water + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid; gradient: 0.0 min 100% A → 0.2 min 95% A → 1.8 min 25% A → 1.9 min 10% A → 2 min 5% A → 3.2 min 5% A → 3.21 min 100% A → 3.35 min 100% A; oven: 40°C; flow rate: 3 ml/min; UV detection: 210 nm.

Method 9:

MS instrument: Waters ZQ 2000; HPLC instrument: Agilent 1100, 2-column system; autosampler: HTC PAL; column: YMC-ODS-AQ, 50 mm x 4.6 mm, 3.0 μ m; mobile phase A: water + 0.1% formic acid, mobile phase B: acetonitrile + 0.1% formic acid; gradient: 0.0 min 100% A → 0.2 min 95% A → 1.8 min 25% A → 1.9 min 10% A → 2.0 min 5% A → 3.2 min 5% A → 3.21 min 100% A → 3.35 min 100% A; oven: 40°C; flow rate: 3.0 ml/min; UV detection: 210 nm.

Method 10:

Instrument: HP 1100 with DAD detection; column: KromasilTM 100 RP-18, 60 mm x 2.1 mm, 3.5 μ m; mobile phase A: 5 ml of perchloric acid (70% strength) / liter of water, mobile phase B: acetonitrile; gradient: 0 min 2% B → 0.5 min 2% B → 4.5 min 90% B → 6.5 min 90% B → 6.7 min 2% B → 7.5 min 2% B; flow rate: 0.75 ml/min; column temperature: 30°C; UV detection: 210 nm.

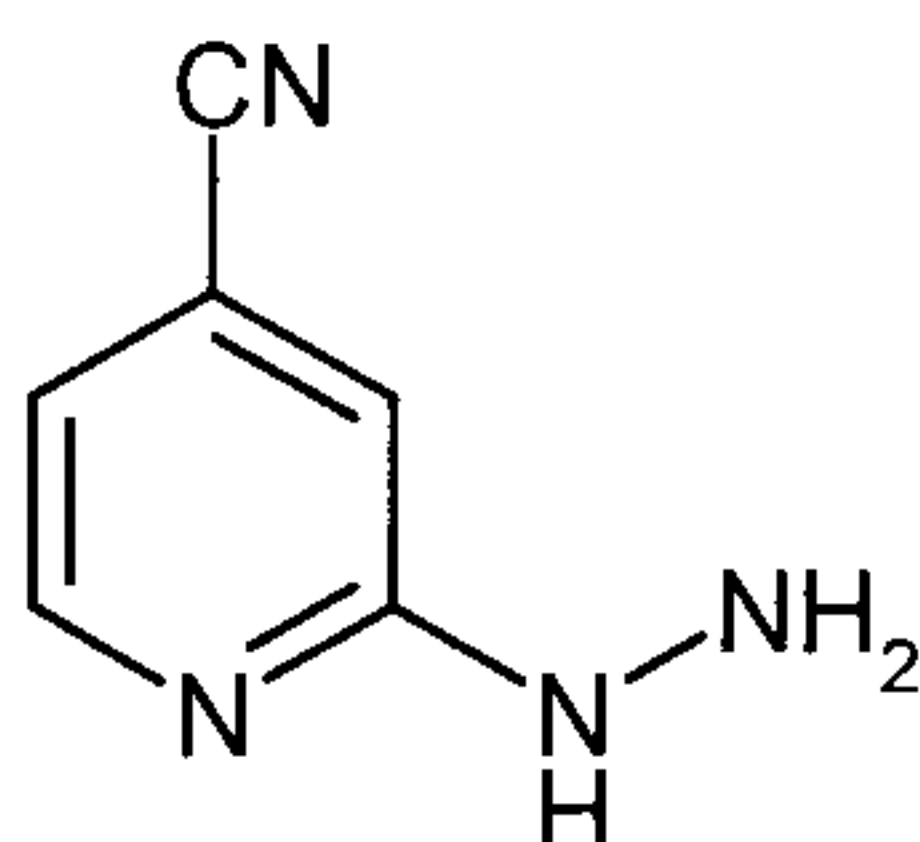
25 Method 11:

Instrument: Micromass GCT, GC6890; column: Restek RTX-35, 15 m x 200 μ m x 0.33 μ m; constant helium flow rate: 0.88 ml/min; oven: 70°C; inlet: 250°C; gradient: 70°C, 30°C/min → 310°C (maintained for 3 min).

Starting materials and intermediates:

Example 1A

2-Hydrazinoisonicotinonitrile



- 5 20.0 g (144 mmol) of 2-chloroisonicotinonitrile are initially charged in 150 ml of 1-butanol, 303 ml (303 mmol) of a 1 M solution of hydrazine hydrate in THF are added and the mixture is heated for 16 h (bath temperature 110°C). The mixture is concentrated and the residue is purified by flash chromatography on silica gel (mobile phase: dichloromethane/methanol 10:1).

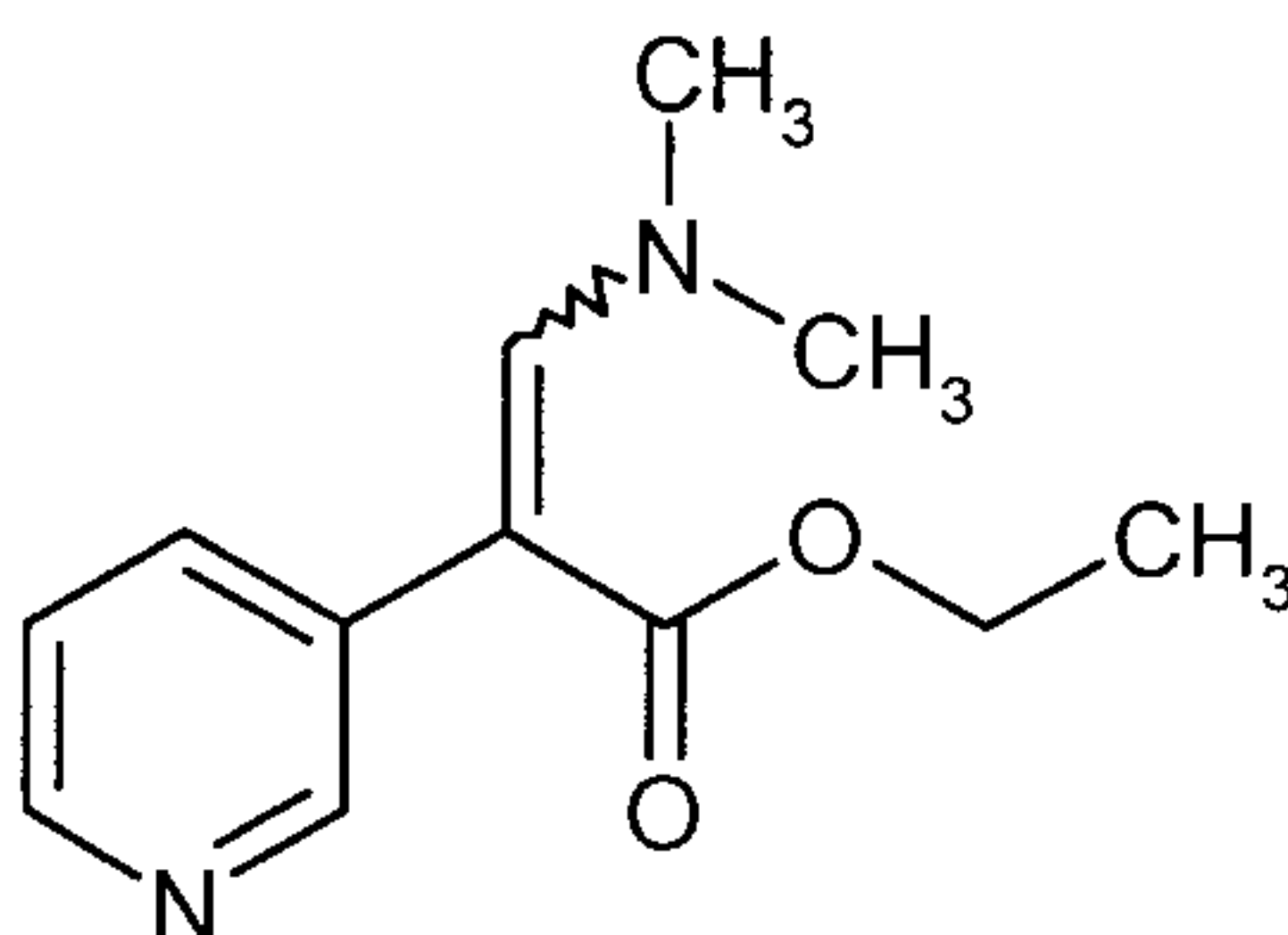
Yield: 9.48 g (49% of theory)

- 10 ¹H-NMR (400 MHz, DMSO-d₆): δ = 8.15 (d, 1H), 8.05 (s, 1H), 7.01 (s, 1H), 6.83 (dd, 1H), 4.30 (s, 2H).

LC-MS (Method 1): R_t = 0.52 min; MS (ESIpos): m/z = 135 [M+H]⁺.

Example 2A

Ethyl 3-(dimethylamino)-2-pyridin-3-ylacrylate



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- 37.4 g (226 mmol) of ethyl pyridin-3-ylacetate in 100 g (679 mmol) of dimethylformamide diethyl acetal are heated at 100°C overnight. After cooling, the mixture is concentrated and the residue is prepurified by flash chromatography on silica gel (mobile phase: gradient cyclohexane/ethyl acetate 1:1 → ethyl acetate/ethanol 9:1). The resulting product is subjected to fine purification by
20 vacuum distillation (1 mbar, 200°C bath temperature).

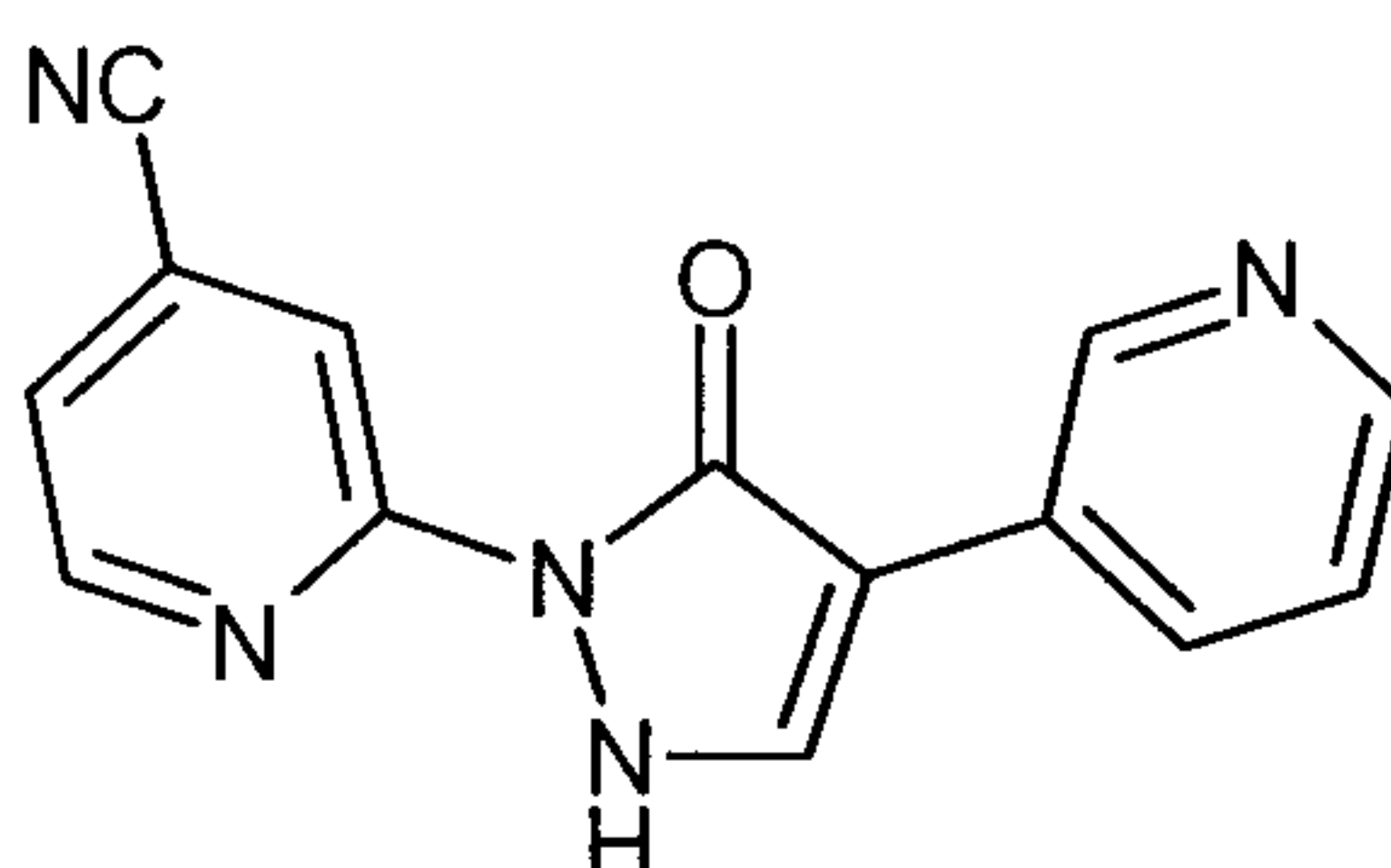
Yield: 35.0 g (70% of theory)

¹H-NMR (400 MHz, DMSO-d₆): δ = 8.37 (dd, 1H), 8.31 (dd, 1H), 7.59 (s, 1H), 7.51 (dt, 1H), 7.29 (ddd, 1H), 4.00 (q, 2H), 2.67 (s, 6H), 1.11 (t, 3H).

LC-MS (Method 1): R_t = 2.38 min; MS (ESIpos): m/z = 221 [M+H]⁺.

5 **Example 3A**

2-(4-Cyanopyridin-2-yl)-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one



545 mg (4.06 mmol) of the compound from Example 1A and 1.07 g (4.88 mmol) of the compound from Example 2A in 15 ml of glacial acetic acid are stirred at RT for 2 h. The mixture is concentrated and the residue is taken up in 300 ml of ethyl acetate and washed repeatedly with saturated sodium bicarbonate solution. The organic phase is dried over sodium sulfate, filtered and concentrated. The residue is taken up in 30 ml of ethanol, 1.33 g (4.88 mmol) of a 25% strength solution of sodium ethoxide in ethanol are added at RT and the mixture is stirred for 30 min. The pH is adjusted to 5 by addition of 1 M hydrochloric acid, and the solid formed is filtered off with suction, washed with diethyl ether and dried under high vacuum.

Yield: 890 mg (83% of theory)

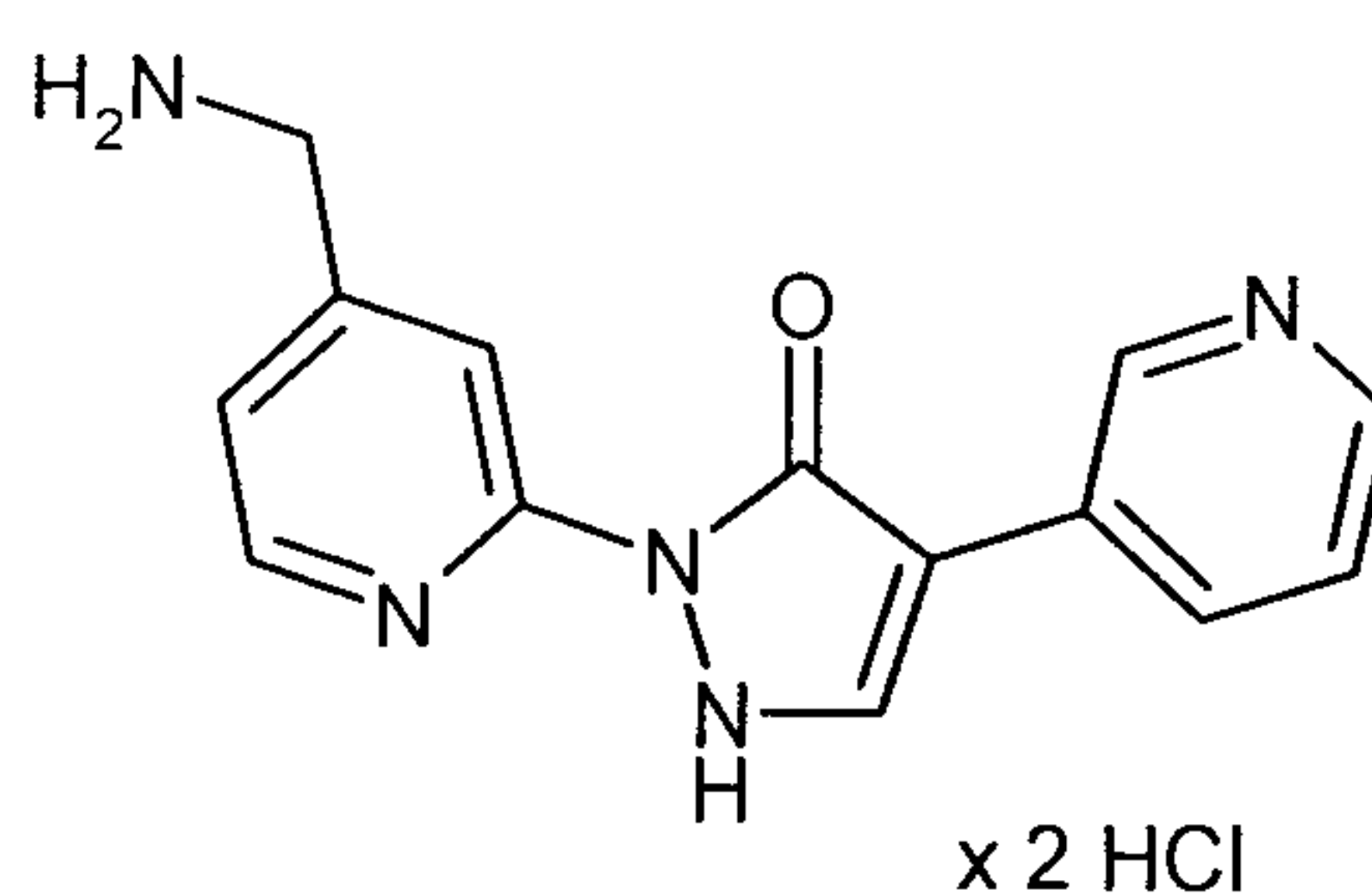
¹H-NMR (400 MHz, DMSO-d₆): δ = 9.01-8.98 (m, 2H), 8.54 (dd, 1H), 8.18 (dt, 1H), 8.01 (dd, 1H), 7.85 (s, 1H), 7.39 (dd, 1H), 7.14 (dd, 1H).

LC-MS (Method 2): R_t = 1.13 min; MS (ESIpos): m/z = 264 [M+H]⁺.

20 **Example 4A**

2-[4-(Aminomethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one dihydrochloride

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100 mg (380 μ mol) of the compound from Example 3A are dissolved in 10 ml of glacial acetic acid, 50.0 mg of catalyst (10% palladium on carbon) are added and the mixture is stirred under an atmosphere of hydrogen at atmospheric pressure and RT overnight. The reaction mixture is then
 5 filtered and concentrated, and the residue is purified by preparative HPLC (RP18-column; mobile phase: acetonitrile/water-gradient with addition of 0.1% conc. hydrochloric acid).

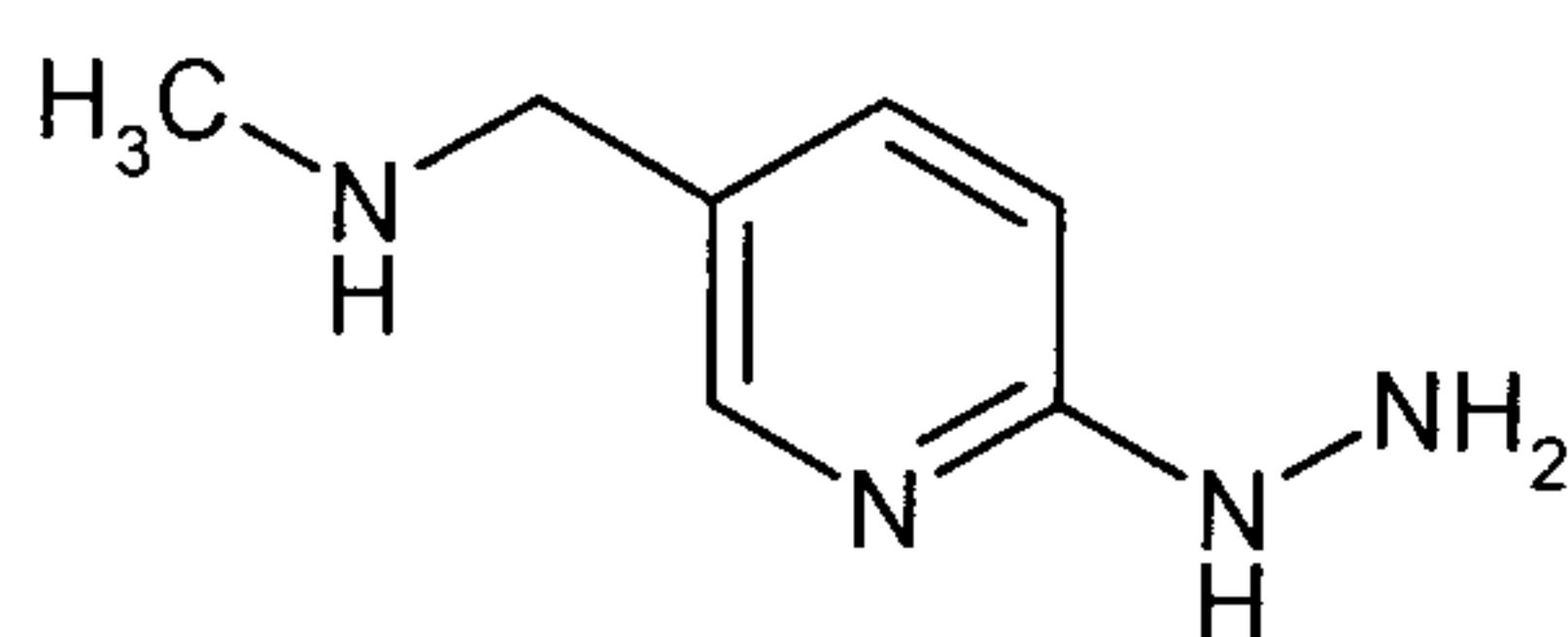
Yield: 64 mg (49% of theory)

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): δ = 9.38 (s, 1H), 8.93 (d, 1H), 8.79 (s, 1H), 8.75 (s, 3H), 8.64 (d, 1H), 8.56 (d, 1H), 8.48 (s, 1H), 7.99 (dd, 1H), 7.54 (d, 1H), 4.21 (q, 2H).

10 LC-MS (Method 1): R_t = 1.39 min; MS (ESIpos): m/z = 268 $[\text{M}+\text{H}]^+$.

Example 5A

1-(6-Hydrazinopyridin-3-yl)-*N*-methylethanamine



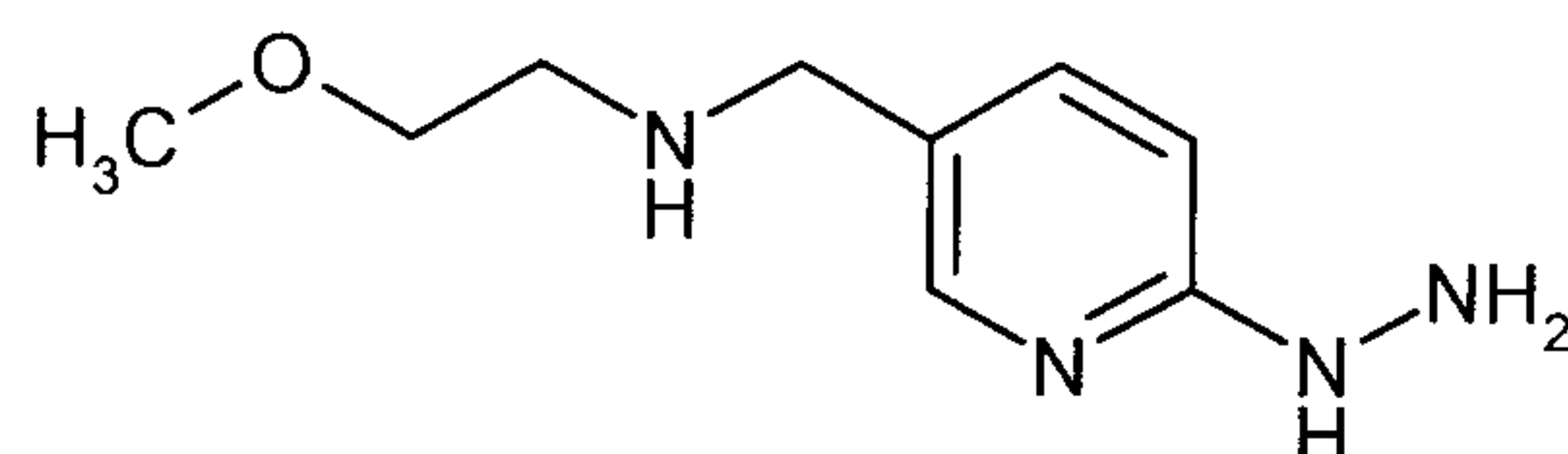
1.0 g (6.4 mmol) of 1-(6-chloropyridin-3-yl)-*N*-methylethanamine [for the preparation, see EP 0
 15 556 684-A1] are initially charged in 1.5 ml (1.6 g, 31.9 mmol) of hydrazine hydrate and stirred at boiling point at a bath temperature of 150°C for 12 h. The reaction solution is cooled and concentrated, and the residue is dried under reduced pressure. This gives 1.1 g of the title compound, which is used without any further purification.

LC-MS (Method 1): R_t = 0.52 min; MS (ESIpos): m/z = 153 $[\text{M}+\text{H}]^+$.

20 **Example 6A**

N-[(6-Hydrazinopyridin-3-yl)methyl]-2-methoxyethanamine

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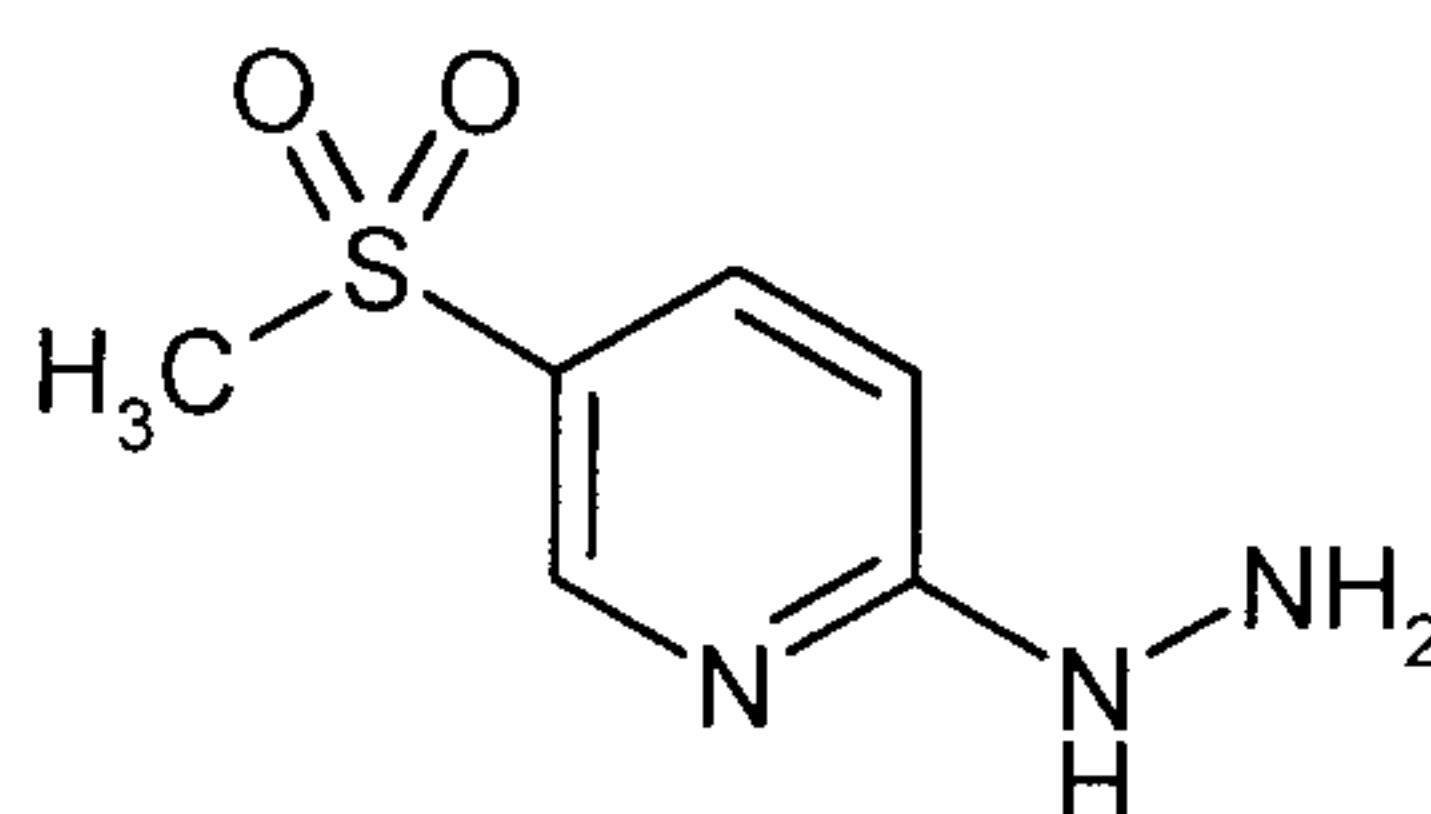
3.6 g (17.7 mmol) of *N*-[(6-chloropyridin-3-yl)methyl]-2-methoxyethanamine [prepared analogously to WO 2004/081007] are initially charged in 4.3 ml (4.4 g, 88.5 mmol) of hydrazine hydrate and stirred at boiling point at a bath temperature of 150°C for 16 h. The reaction solution
5 is cooled and concentrated, and the residue is purified by column chromatography on silica gel (mobile phase: acetonitrile/water 9:1).

Yield: 1.6 g (47% of theory)

LC-MS (Method 1): $R_t = 0.44$ min; MS (ESIpos): $m/z = 197$ $[M+H]^+$.

Example 7A

10 2-Hydrazino-5-(methylsulfonyl)pyridine



1.7 ml (1.7 g, 34.0 mmol) of hydrazine hydrate are added to 2.0 g (8.5 mmol) of 2,5-bis(methylsulfonyl)pyridine [Woods et al., J. Heterocycl. Chem. 1984, 21, 97-101] in 15 ml of ethanol, and the mixture is stirred under reflux for 4 h. For work-up, the reaction solution is cooled to 15°C, the
15 precipitated solid is filtered off, the filter residue is washed with ethanol and diethyl ether and the product is dried under reduced pressure.

Yield: 1.4 g (89% of theory)

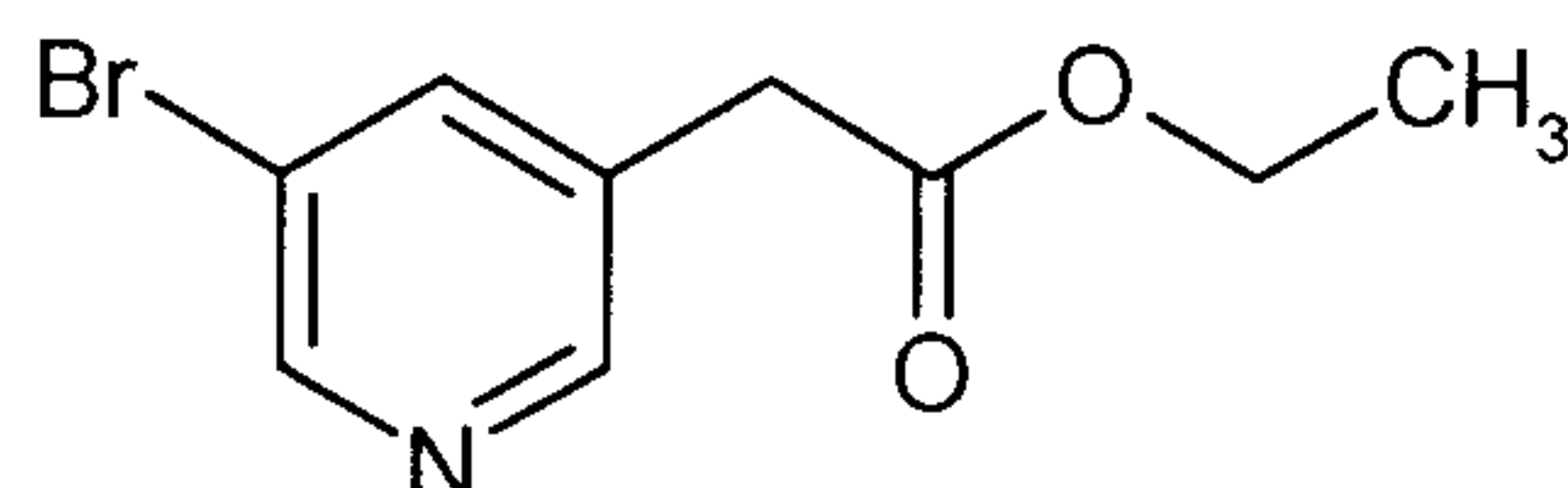
LC-MS (Method 1): $R_t = 0.51$ min; MS (ESIpos): $m/z = 188$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 8.56$ (s, 1H), 8.38 (d, 1H), 7.81 (dd, 1H), 6.79 (d, 1H), 4.42
20 (s, 2H), 3.11 (s, 3H).

Example 8A

Ethyl (5-bromopyridin-3-yl)acetate

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15 drops of concentrated sulfuric acid are added to 5.0 g (23.1 mmol) of (5-bromopyridin-3-yl)acetic acid in 30 ml of ethanol, and the mixture is heated under reflux for 16 h. After cooling to RT, the mixture is concentrated under reduced pressure and the residue is taken up in ethyl acetate
5 and washed with semiconcentrated sodium bicarbonate solution. The organic phase is dried over sodium sulfate, filtered and concentrated under reduced pressure.

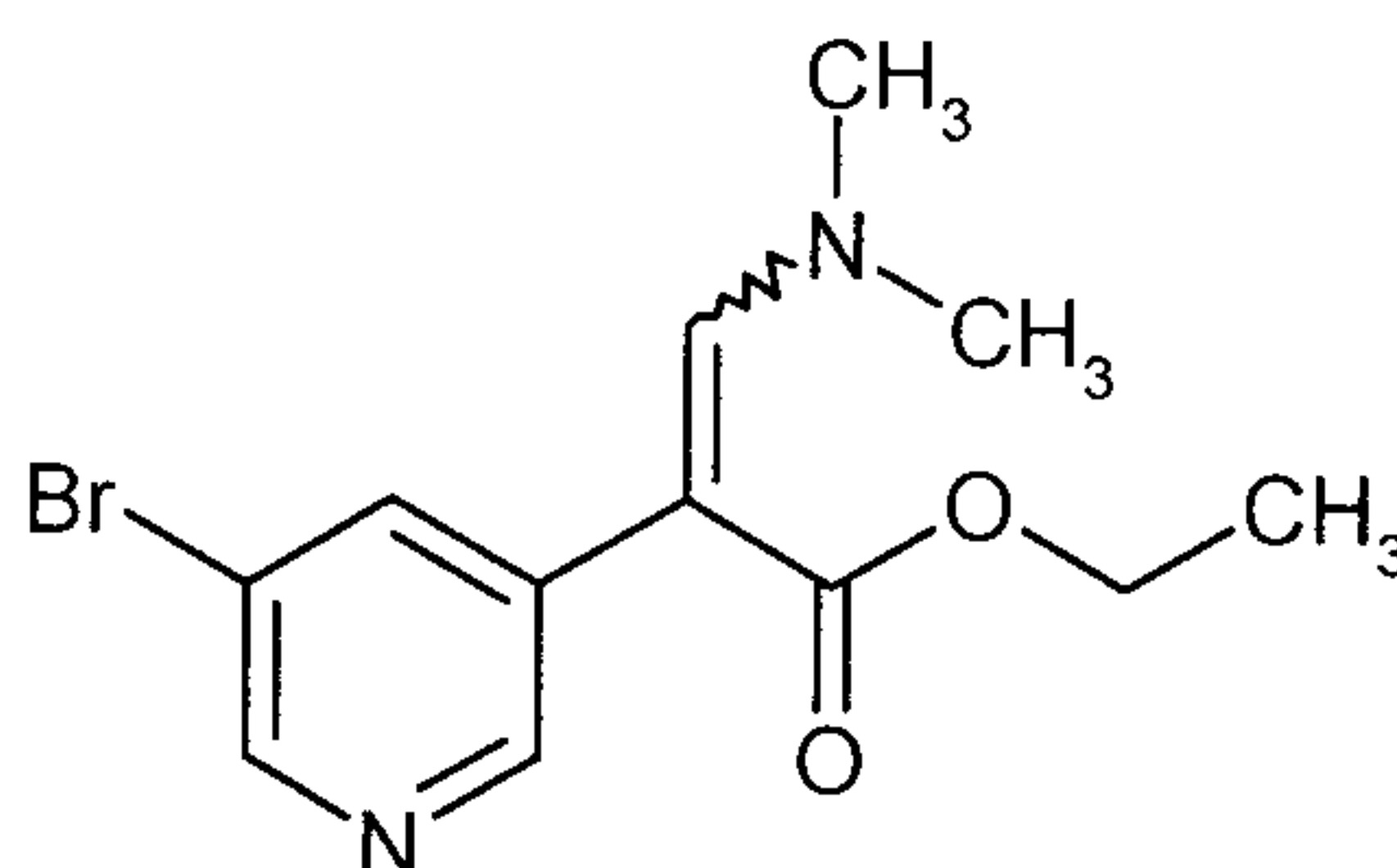
Yield: 5.2 g (91% of theory)

LC-MS (Method 2): $R_t = 1.48$ min; MS (ESIpos): $m/z = 244$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 8.61$ (d, 1H), 8.48 (d, 1H), 8.00 (dd, 1H), 4.10 (q, 2H), 3.33
10 (s, 2H), 1.20 (t, 3H).

Example 9A

Ethyl (2Z)-2-(5-bromopyridin-3-yl)-3-(dimethylamino)prop-2-enoate



5.1 g (20.8 mmol) of the compound from Example 8A in 7.1 ml (6.2 g, 41.8 mmol) of dimethyl-
15 formamide diethyl acetal are heated at 100°C for 16 h. After cooling, the mixture is concentrated under reduced pressure.

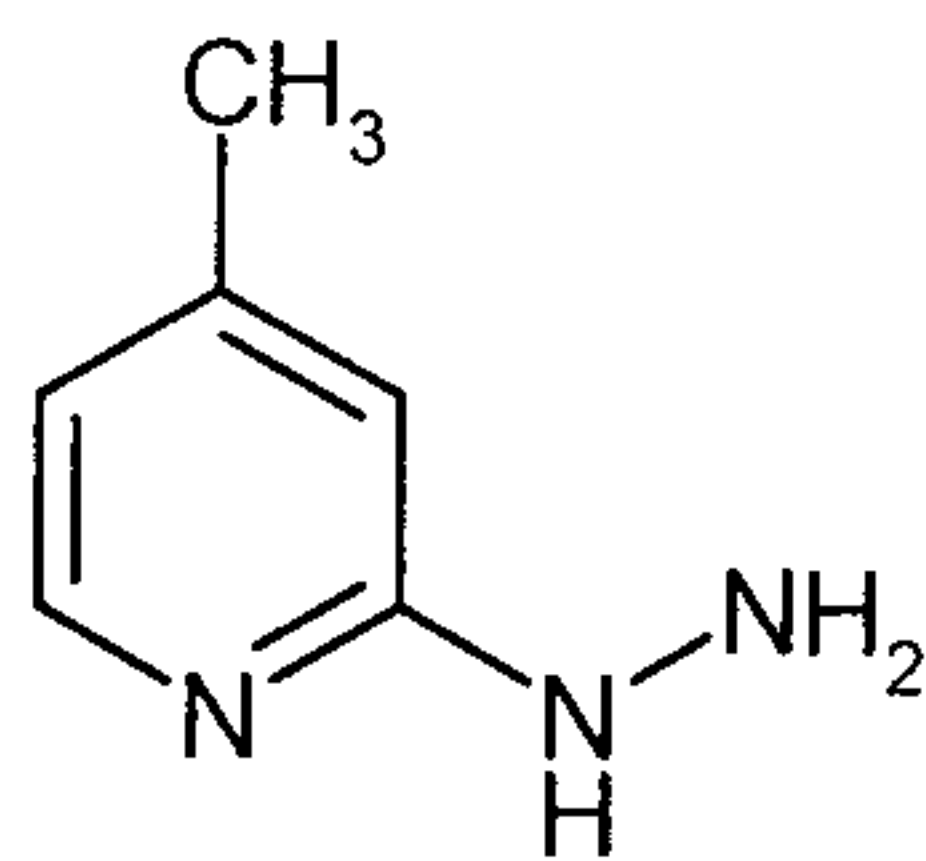
Yield: 6.1 g (73% of theory)

LC-MS (Method 6): $R_t = 1.86$ min; MS (ESIpos): $m/z = 299$ $[M+H]^+$.

Example 10A

20 2-Hydrazino-4-methylpyridine

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3.3 g (30.0 mmol) of 2-fluoro-4-methylpyridine are initially charged in 40 ml of ethylene glycol monoethyl ether, 14.6 ml (15.0 g, 300 mmol) of hydrazine hydrate are added to the solution and the mixture is stirred at boiling point (bath temperature 150°C) for 16 h. The reaction solution is then concentrated on a rotary evaporator, and the residue is added to 100 ml of water and extracted with ethyl acetate (three times 100 ml each). The combined organic phases are dried over sodium sulfate, filtered and concentrated. The residue obtained is dried under reduced pressure.

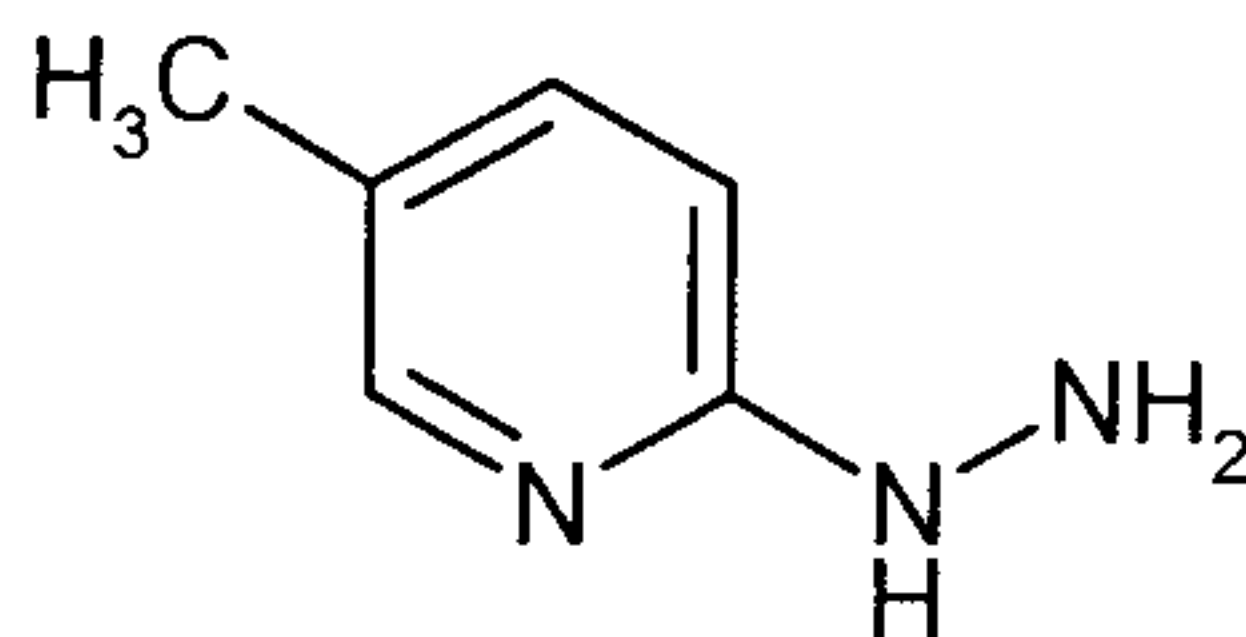
Yield: 1.90 g (51% of theory)

LC-MS (Method 1): $R_t = 0.80$ min; MS (ESIpos): $m/z = 124$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 7.83$ (d, 1H), 7.22 (s, 1H), 6.51 (s, 1H), 6.38 (d, 1H), 4.04 (s, 2H), 2.17 (s, 3H).

Example 11A

2-Hydrazino-5-methylpyridine



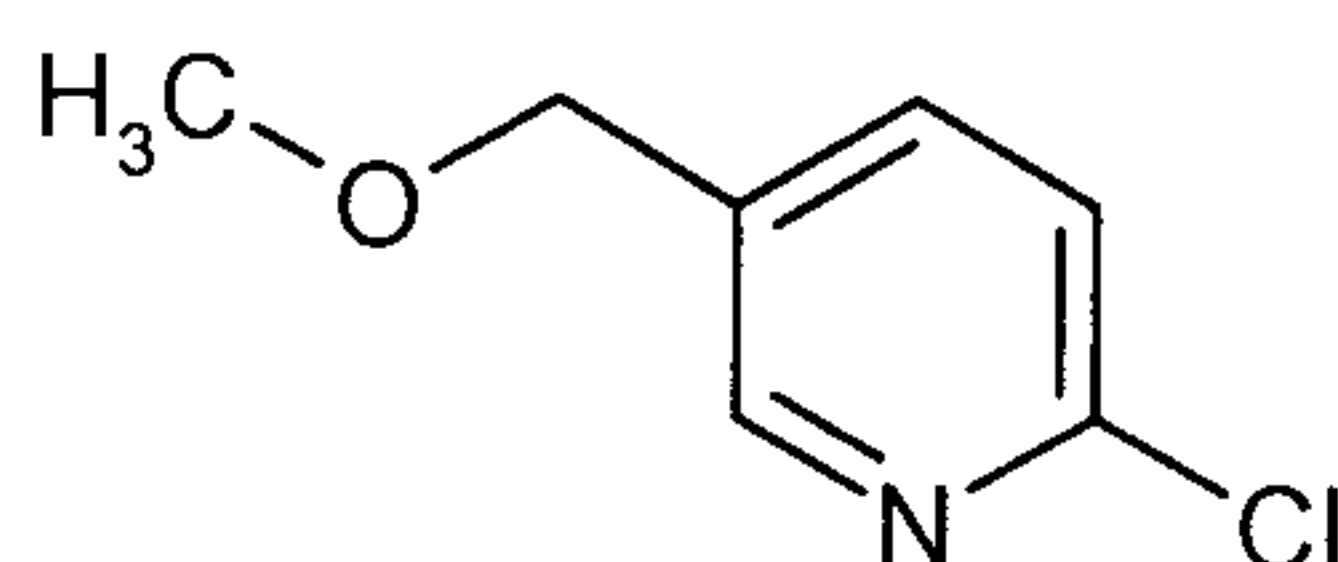
5.7 ml (5.9 g, 117.6 mmol) of hydrazine hydrate are added to 1.0 g (7.8 mmol) of 2-chloro-5-methylpyridine, and the mixture is stirred at boiling point (bath temperature 150°C) for 16 h. The reaction mixture is cooled and then concentrated on a rotary evaporator, and the residue is co-evaporated three times with in each case 10 ml of ethylene glycol monoethyl ether. The residue is then taken up in dichloromethane, the precipitate is separated off and the filtrate is concentrated under reduced pressure.

Yield: 644 mg (67% of theory)

LC-MS (Method 6): $R_t = 0.35$ min; MS (ESIpos): $m/z = 124$ $[M+H]^+$.

Example 12A

2-Chloro-5-(methoxymethyl)pyridine



2.6 g (23.0 mmol) of potassium *tert*-butoxide are dissolved in 50 ml of THF. 3.0 g (20.9 mmol) of
 5 (6-chloropyridin-3-yl)methanol are added, and the mixture is stirred at RT for 15 min. 4.4 g (31.3
 mmol) of iodomethane are then added slowly, and the mixture is stirred for about 30 min until the
 slightly exothermic reaction has subsided. The solvent is removed, and the residue is taken up in
 dichloromethane and washed twice with water. The organic phase is dried over magnesium sulfate
 and concentrated, and the residue is purified by column chromatography on silica gel (Biotage
 10 chromatography, mobile phase: cyclohexane/ethyl acetate 85:15).

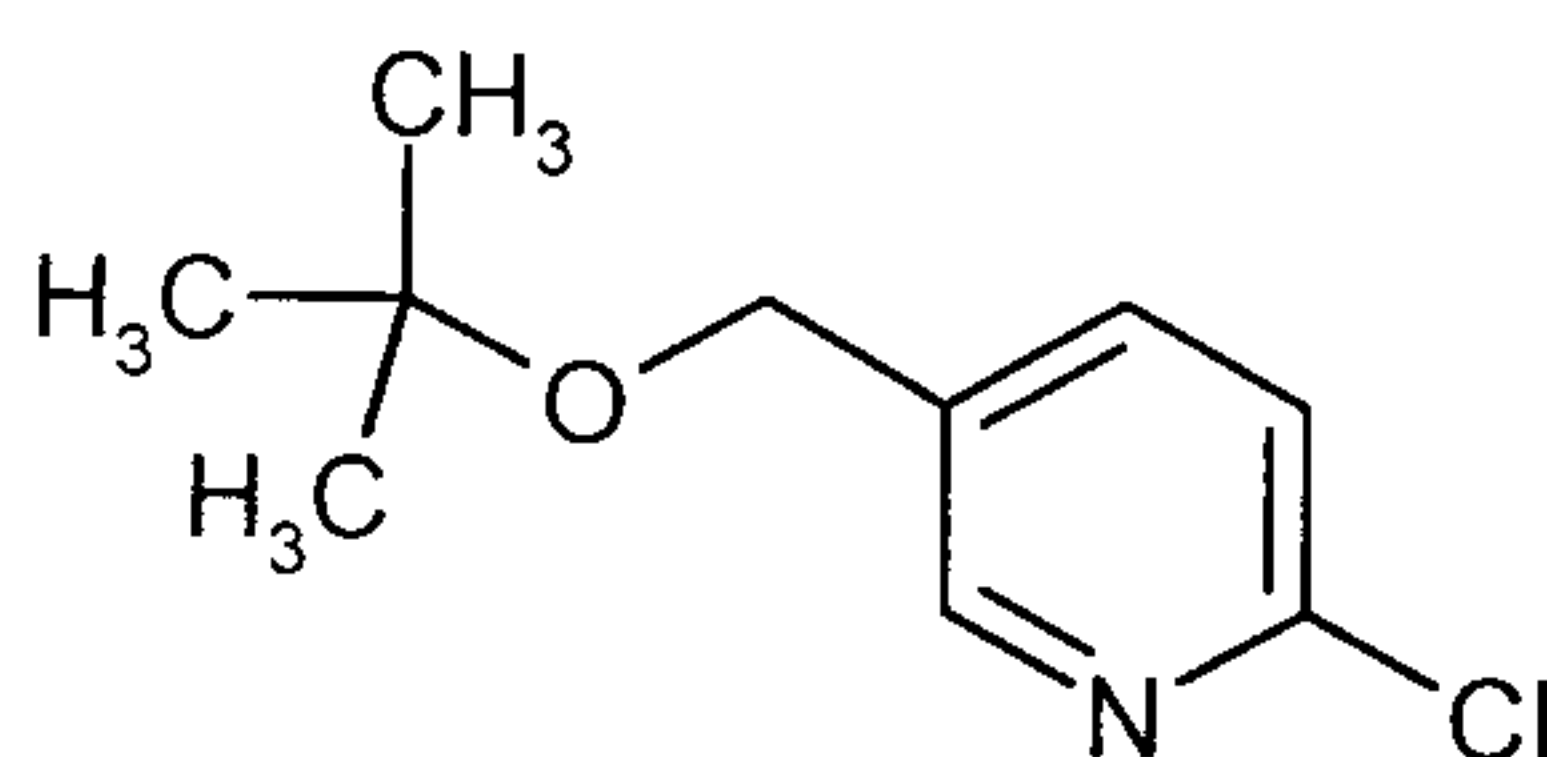
Yield: 2.2 g (68% of theory)

LC-MS (Method 1): $R_t = 2.62$ min; MS (ESIpos): $m/z = 158$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 8.34$ (d, 1H), 7.65 (dd, 1H), 7.32 (d, 1H), 4.45 (s, 2H), 3.41 (s,
 3H).

15 **Example 13A**

5-(*tert*-Butoxymethyl)-2-chloropyridine



7.2 g (50.0 mmol) of (6-chloropyridin-3-yl)methanol are initially charged in 50 ml of
 dichloromethane. 25.1 g (115.0 mmol) of di-*tert*-butyl dicarbonate and 1.1 g (5.0 mmol) of
 20 magnesium perchlorate are added, and the mixture is stirred at 40°C for 24 h. The mixture is then
 cooled to RT, a further 12.5 g (57.3 mmol) of di-*tert*-butyl dicarbonate and 600 mg (2.7 mmol) of
 magnesium perchlorate are added, and the mixture is stirred under reflux for another 2.5 h.
 Another 12.5 g (57.3 mmol) of di-*tert*-butyl dicarbonate are added, and the mixture is stirred under
 reflux for another 3 h. The mixture is then diluted with dichloromethane and washed once with
 25 water and once with saturated sodium chloride solution. The mixture is dried over magnesium

sulfate and concentrated, and the residue is purified by column chromatography on silica gel (mobile phase: cyclohexane/ethyl acetate 85:15).

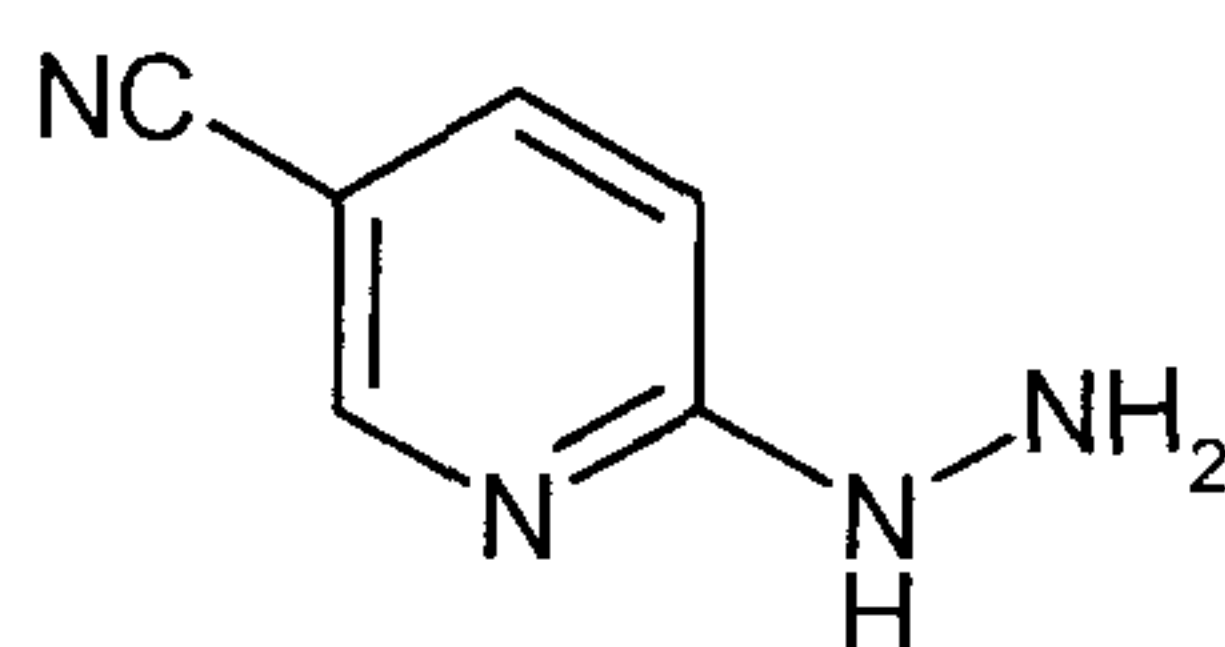
Yield: 7.9 g (79% of theory)

LC-MS (Method 5): $R_t = 1.12$ min; MS (ESIpos): $m/z = 200$ $[M+H]^+$;

- 5 $^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 8.35$ (d, 1H), 7.78 (dd, 1H), 7.48 (d, 1H), 4.45 (s, 2H), 1.22 (s, 9H).

Example 14A

6-Hydrazinopyridine-3-carbonitrile



- 10 90.3 g (1.8 mol) of hydrazine hydrate are added to 25.0 g (180.4 mmol) of 6-chloronicotinonitrile, and the mixture is stirred at a bath temperature of 100°C for 15 min. The reaction mixture is cooled to RT, diluted with water and stirred at RT for 30 min. The precipitate formed is filtered off, the filter residue is washed with water and the crystals are air-dried for 24 h and recrystallized once from ethyl acetate.

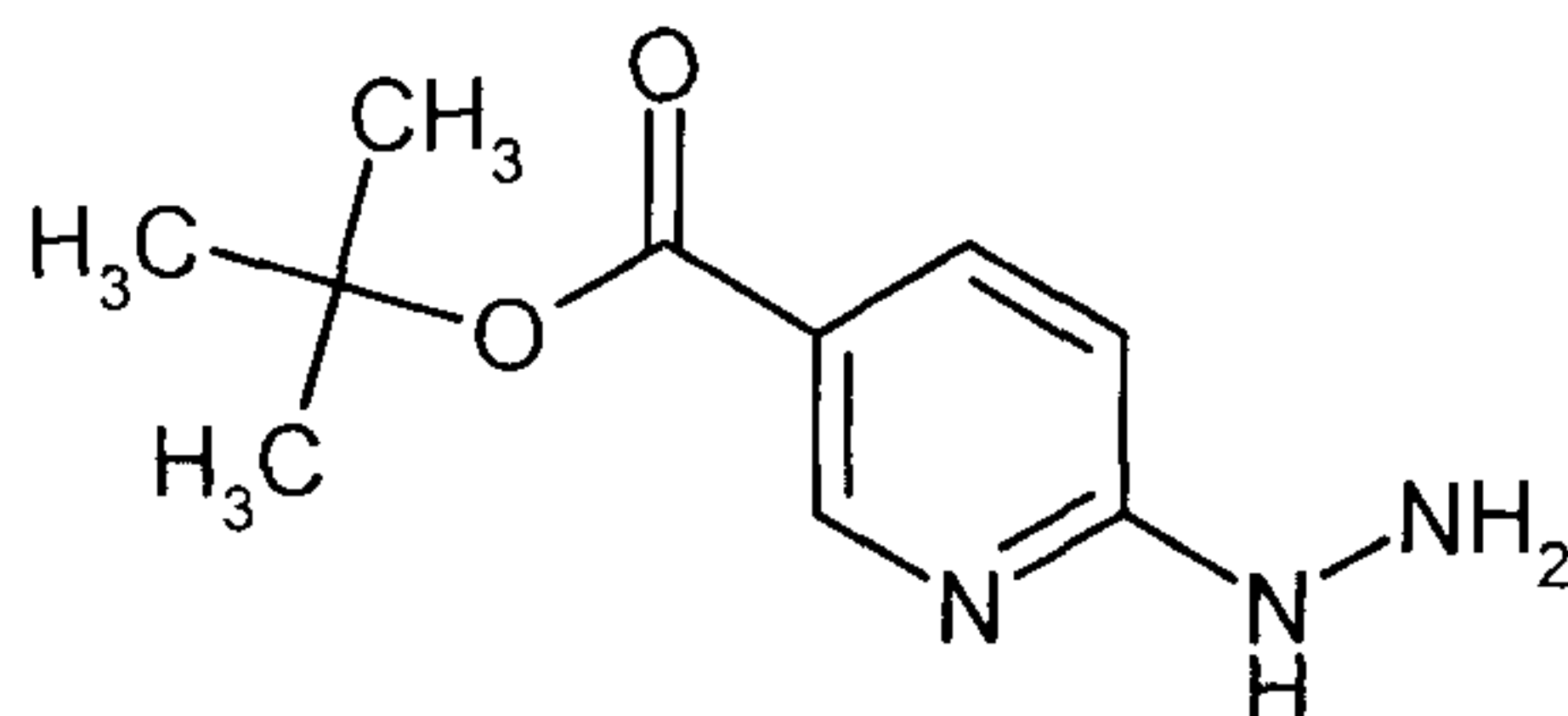
- 15 Yield: 18.7 g (77% of theory)

LC-MS (Method 1): $R_t = 0.51$ min; MS (ESIpos): $m/z = 135$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6) = 8.58 (s, 1H), 8.33 (s, 1H), 7.74 (d, 1H), 6.76 (br. s, 1H), 4.42 (s, 2H).

Example 15A

- 20 *tert*-Butyl 6-hydrazinopyridine-3-carboxylate



18.0 g (84.2 mmol) of *tert*-butyl 6-chloropyridine-3-carboxylate are initially charged in 85 ml of ethanol. 42.2 g (842.0 mmol) of hydrazine hydrate are added, and the mixture is stirred at 100°C for 2 h. The mixture is then concentrated, and the residue is taken up in a mixture of ethyl acetate and water. The phases are separated, and the organic phase is washed once with water and once
5 with saturated sodium chloride solution, dried over magnesium sulfate and concentrated again. The residue is triturated with petroleum ether, and the solid formed is filtered off and dried under high vacuum.

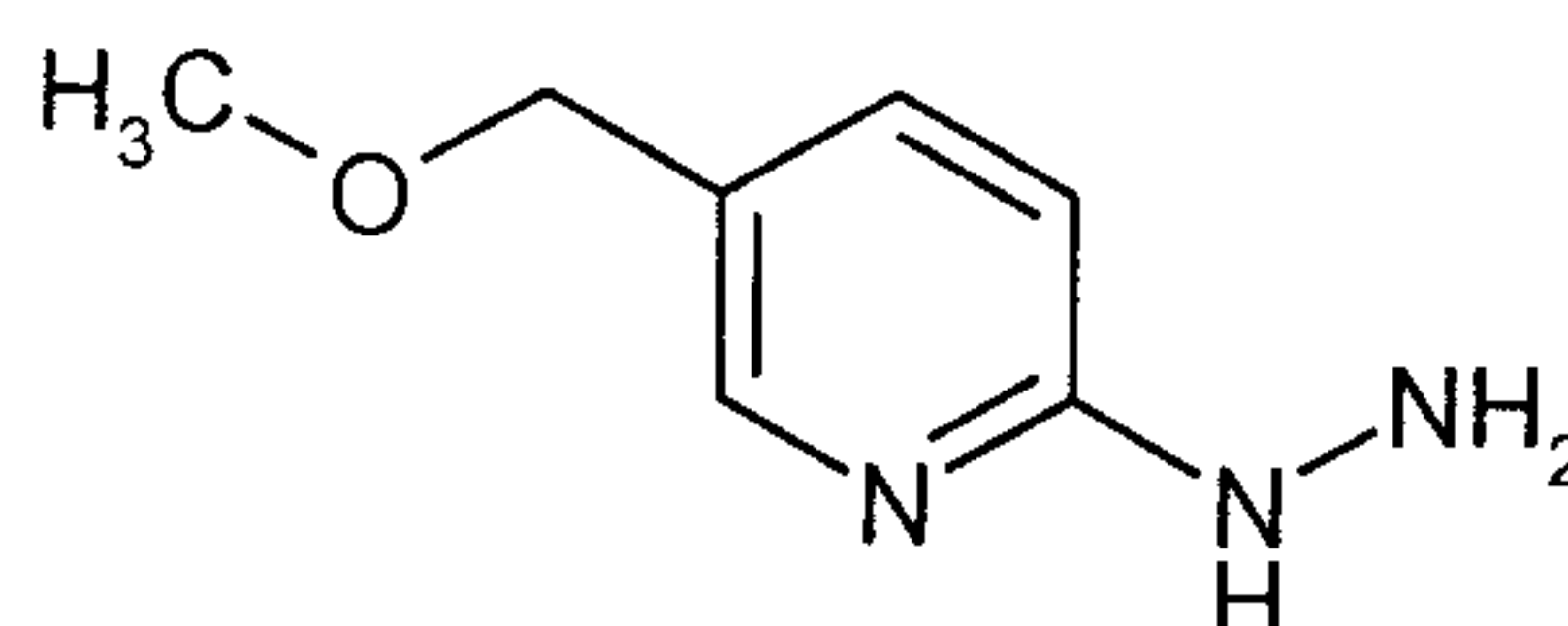
Yield: 16.4 g (78% of theory)

LC-MS (Method 1): $R_t = 2.30$ min; MS (ESIpos): $m/z = 210$ $[M+H]^+$;

10 $^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 8.49$ (d, 1H), 8.30 (s, 1H), 7.82 (dd, 1H), 6.70 (d, 1H), 4.35 (s, 2H), 1.50 (s, 9H).

Example 16A

2-Hydrazino-5-(methoxymethyl)pyridine



15 2.2 g (14.0 mmol) of the compound from Example 12A are initially charged in 10 ml of ethanol. 7.0 g (140.0 mmol) of hydrazine hydrate are added, and the mixture is stirred under reflux for 16 h. The reaction mixture is then reacted again in a single-mode microwave oven (CEM Explorer) at 150°C for 2 h. The mixture is then concentrated on a rotary evaporator, taken up in ethyl acetate, washed once with saturated sodium bicarbonate solution, dried over magnesium sulfate and
20 concentrated again, and the residue is dried under high vacuum.

Yield: 970 mg (45% of theory)

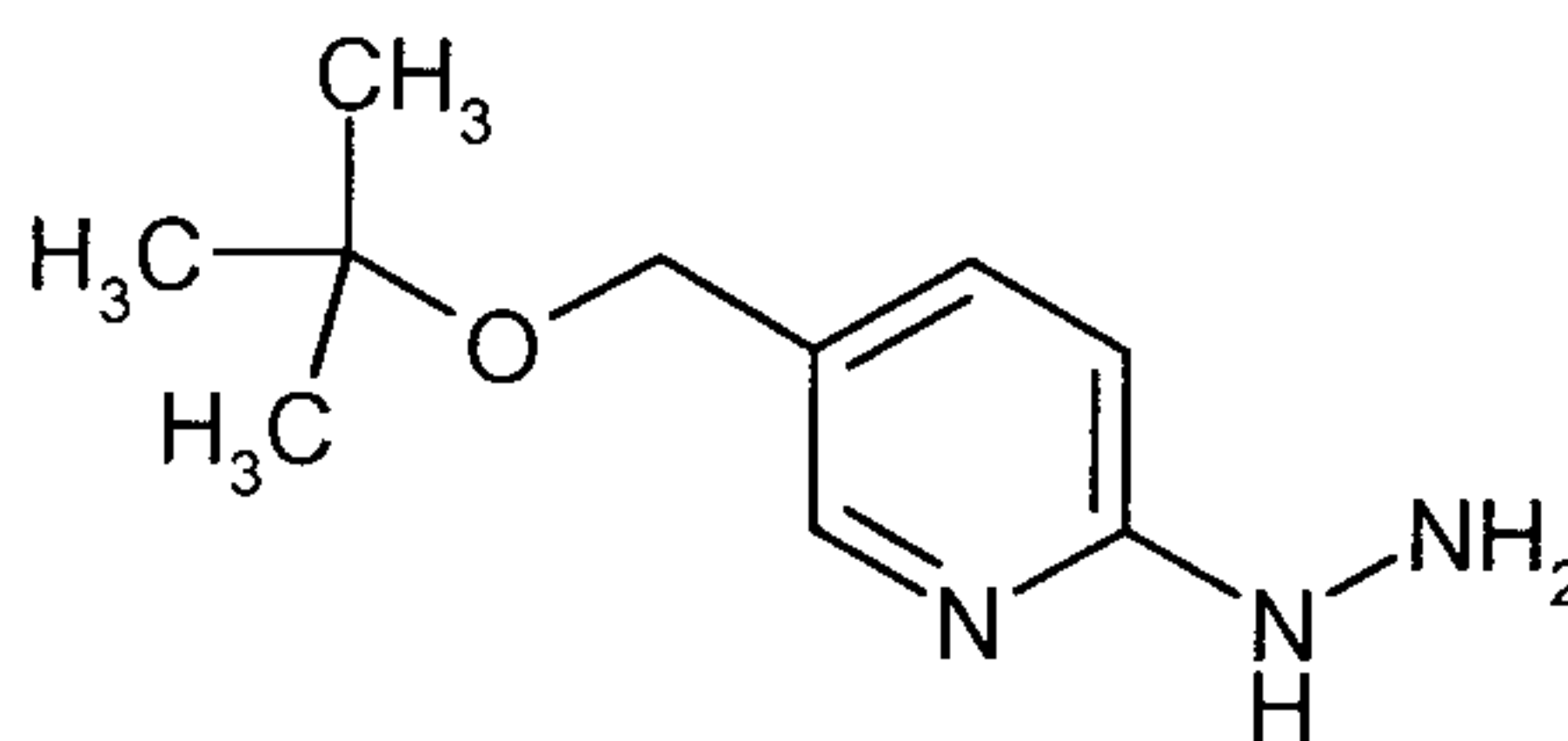
LC-MS (Method 7): $R_t = 0.20$ min; MS (ESIpos): $m/z = 154$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 8.09$ (d, 1H), 7.50 (dd, 1H), 6.70 (d, 1H), 6.00 (br. s, 1H), 4.32 (s, 2H), 3.75 (br. s., 2H), 3.35 (s, 3H).

25 **Example 17A**

5-(*tert*-Butoxymethyl)-2-hydrazinopyridine

- 57 -



7.9 g (40.0 mmol) of the compound from Example 13A are dissolved in 45 ml of ethanol. The solution is divided into three reaction vessels, and in each case 6.6 g (131.9 mmol) of hydrazine hydrate are added. Each reaction mixture is reacted in each case for 4 h at 170°C in a single-mode
5 microwave oven (CEM Explorer). The three mixtures are then combined, and the solvent is removed. The residue is taken up in ethyl acetate and washed once with saturated sodium bicarbonate solution. The aqueous phase is reextracted once with ethyl acetate. The two ethyl acetate phases are combined and washed once with saturated sodium chloride solution. The mixture is dried over magnesium sulfate and the solvent is removed. The residue is triturated with
10 petroleum ether, and the solid obtained is filtered off and dried under high vacuum.

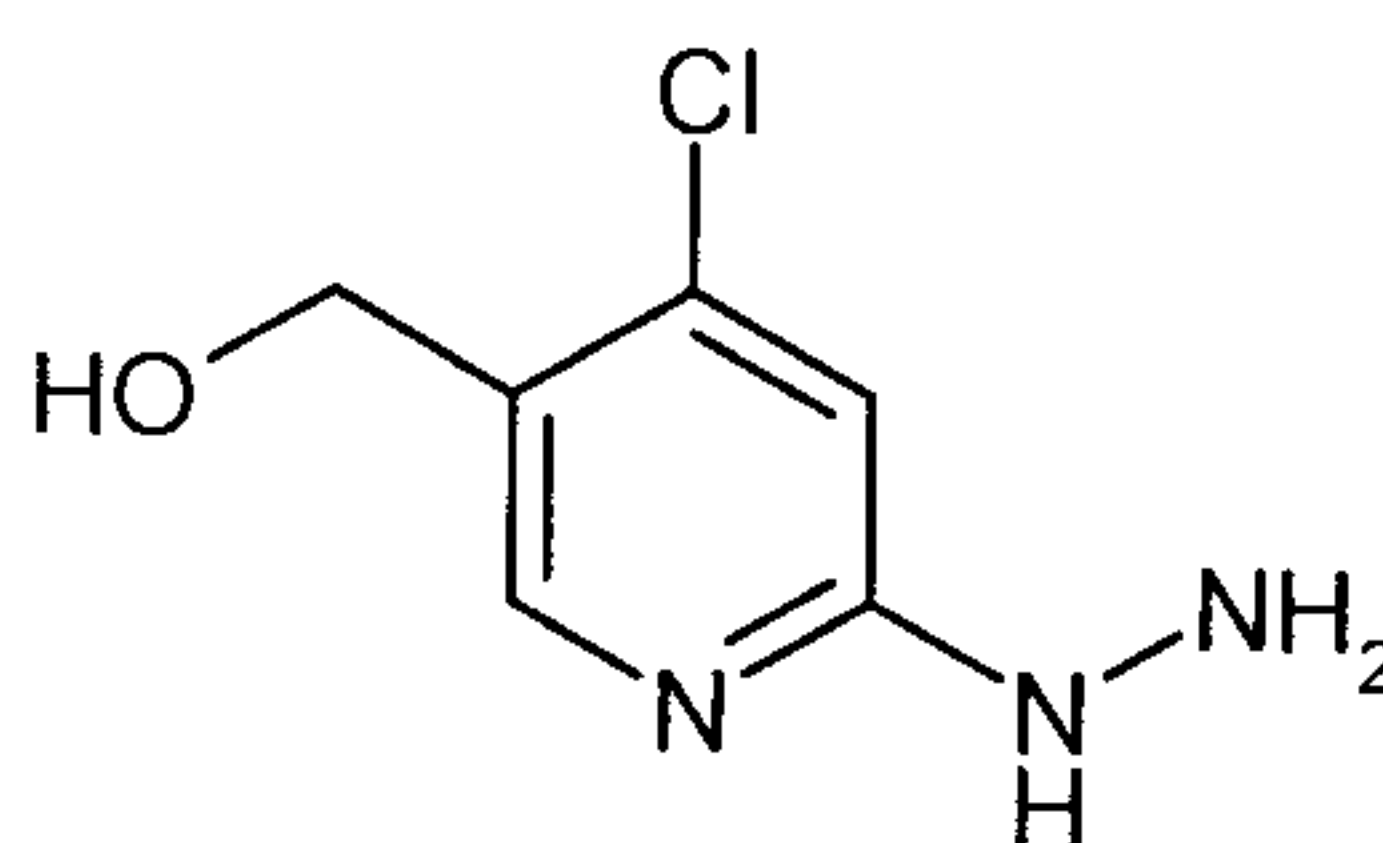
Yield: 1.6 g (21% of theory)

LC-MS (Method 5): $R_t = 0.77$ min; MS (ESIpos): $m/z = 196$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 8.09$ (d, 1H), 7.50 (d, 1H), 6.68 (d, 1H), 5.75 (br. s, 1H), 4.32 (s, 2H), 3.85 (br. s, 2H), 1.28 (s, 9H).

15 **Example 18A**

(4-Chloro-6-hydrazinopyridin-3-yl)methanol



500 mg (2.8 mmol) of (4,6-dichloropyridin-3-yl)methanol are initially charged in 2 ml of ethanol. 7.3 mg (14.0 mmol) of hydrazine hydrate are added, and the mixture is stirred at 100°C for 20 h.
20 The mixture is then allowed to cool to RT, the solid formed is filtered off and discarded and the mother liquor is concentrated on a rotary evaporator, which gives the title compound as a mixture with about 10% [4,6-bis(hydrazino)pyridin-3-yl]methanol.

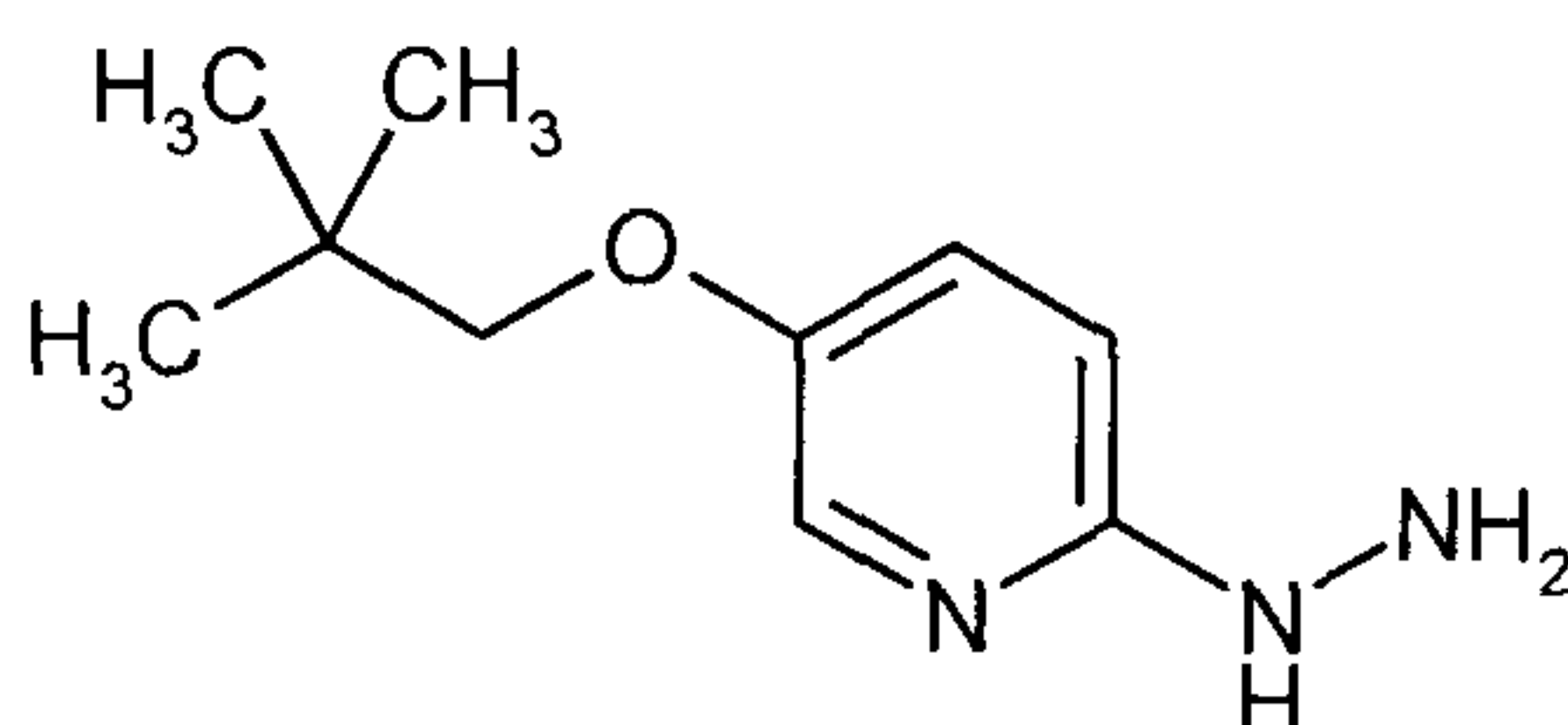
Yield: 450 mg (92% of theory)

LC-MS (Method 6): $R_t = 0.25$ min; MS (ESIpos): $m/z = 174$ $[M+H]^+$;

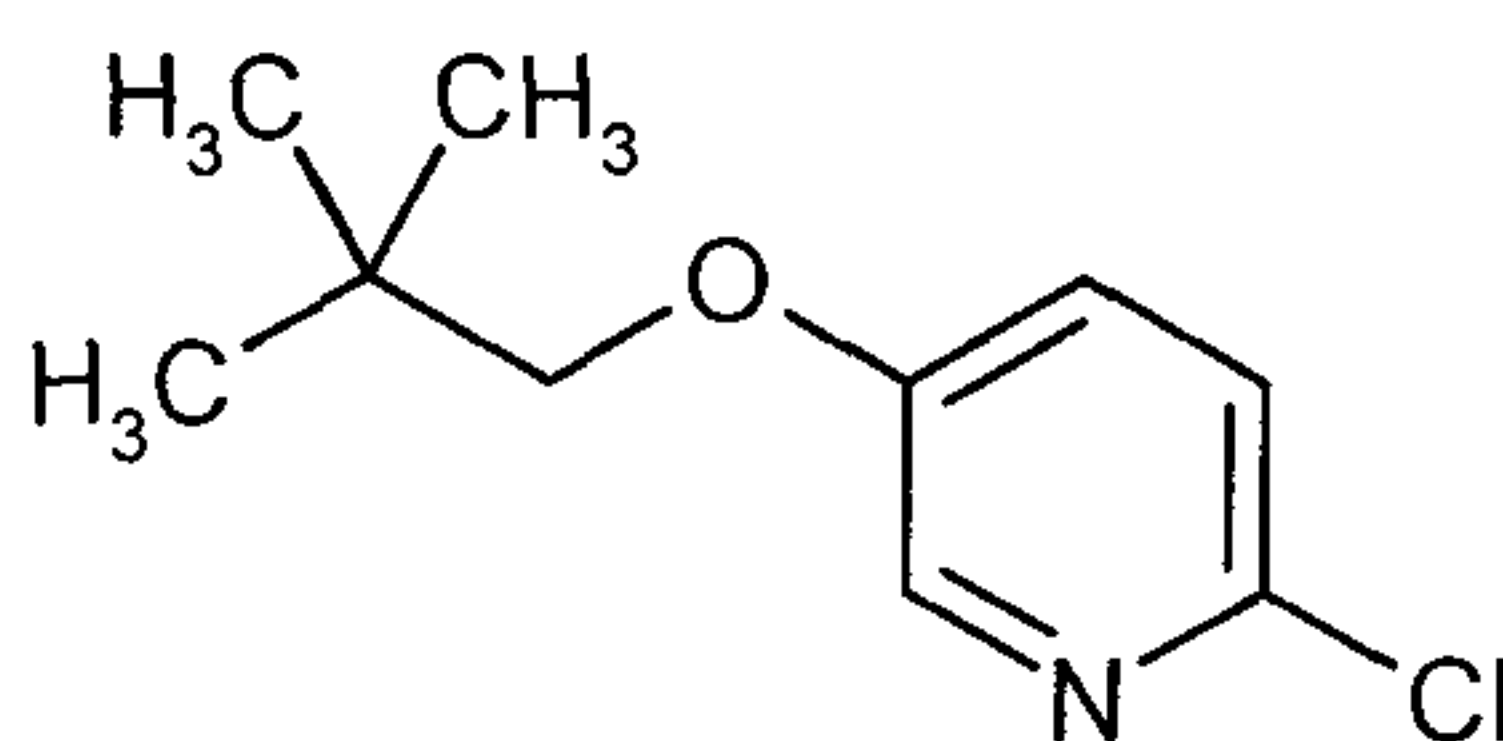
$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 7.75$ (s, 1H), 7.41 (s, 1H), 6.90 (s, 1H), 5.20 (br. s, 1H), 4.35 (br. s, 2H).

Example 19A

5 5-(2,2-Dimethylpropoxy)-2-hydrazinopyridine



Step a): 2-Chloro-5-(2,2-dimethylpropoxy)pyridine



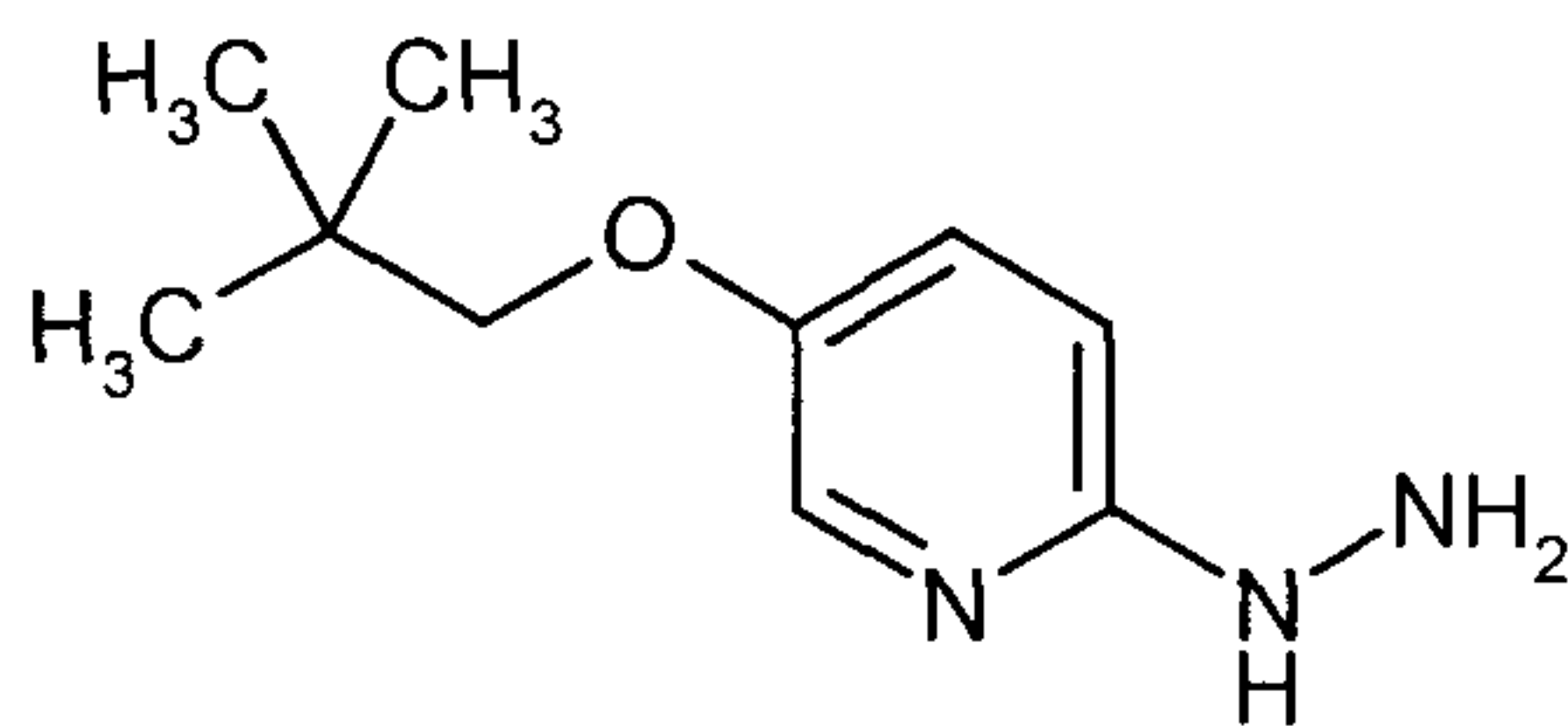
5.2 g (40.0 mmol) of 6-chloropyridin-3-ol, 11.9 g (60.0 mmol) of 1-iodo-2,2-dimethylpropane, 19.6
 10 g (60.0 mmol) of cesium carbonate and 120 ml of diethylene glycol dimethyl ether are divided into
 five portions of equal size and reacted portion-wise in a single-mode microwave oven (CEM
 Explorer) at 160°C for 4 h. The five reaction mixtures obtained are then combined, the solid is
 filtered off and washed with diethylene glycol dimethyl ether and filtrate and wash solutions are
 combined. Most of the solvent is removed, and 300 ml of water are added to the concentrated
 15 (about 50 ml) solution. The mixture is stirred for 30 min, and the solid obtained is filtered off,
 washed once with water and dried under high vacuum.

Yield: 7.0 g (88% of theory)

LC-MS (Method 6): $R_t = 2.47$ min; MS (ESIpos): $m/z = 200$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 8.05$ (d, 1H), 7.25-7.15 (m, 2H), 3.61 (s, 2H), 1.03 (s, 9H).

Step b): 5-(2,2-Dimethylpropoxy)-2-hydrazinopyridine



6.2 g (30.8 mmol) of 2-chloro-5-(2,2-dimethylpropoxy)pyridine together with 60 ml (1.2 mol) of hydrazine hydrate are divided into four portions of equal size, and in each case 10 ml of ethanol
5 are added. Each portion is reacted in a single-mode microwave oven (CEM Explorer) at 170°C (200 Watt) for in each case 12 h. The four mixtures are then combined, and the solvent is removed. The residue is taken up in ethyl acetate and washed in each case once with saturated sodium bicarbonate solution and saturated sodium chloride solution. The mixture is dried over magnesium sulfate and the solvent is removed under reduced pressure.

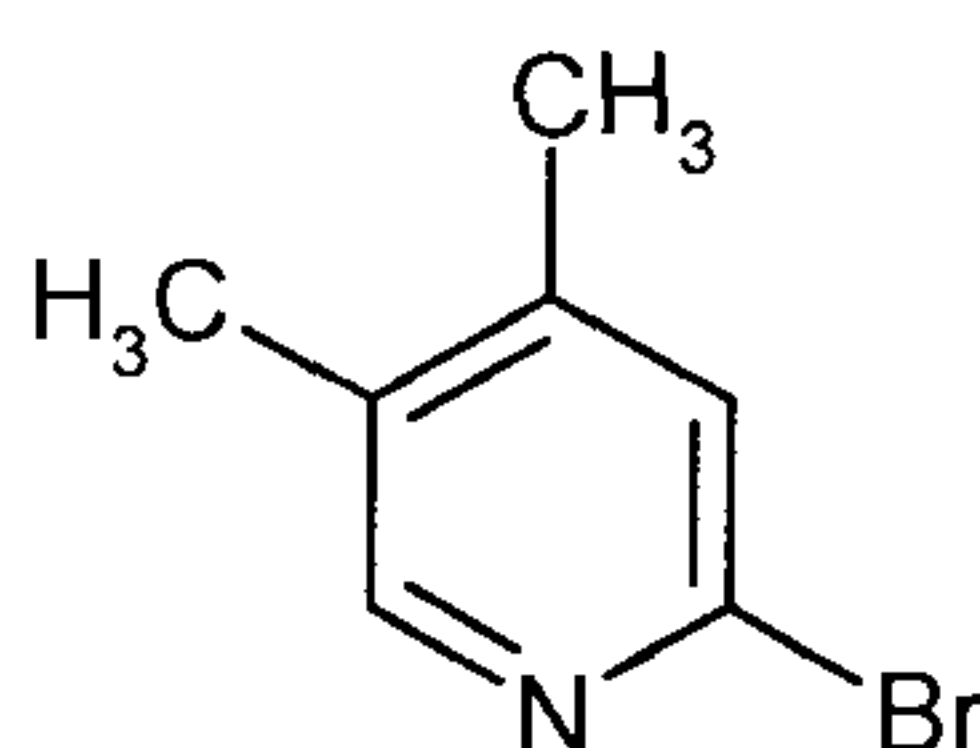
10 Yield: 6.0 g (76% of theory)

LC-MS (Method 6): $R_t = 1.28$ min; MS (ESIpos): $m/z = 196$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 7.84$ (s, 1H), 7.17 (dd, 1H), 6.68 (d, 1H), 5.54 (br. s, 1H), 3.80 (br. s, 2H), 3.56 (s, 2H), 1.02 (s, 9H).

Example 20A

15 2-Bromo-4,5-dimethylpyridine



71.3 g (0.8 mol) of 2-(dimethylamino)ethanol are initially charged in 500 ml of n-hexane, and the mixture is cooled to 0°C. 1.0 liter (1.6 mol) of n-butyllithium solution (1.6 M in n-hexane) is added slowly, and the mixture is stirred at 0°C for 15 min. A solution of 17.9 g (166.7 mmol) of 3,4-
20 lutidine in 500 ml of n-hexane is then added dropwise, and the mixture is stirred at 0°C for 1 h. The mixture is then cooled to -78°C, and a solution of 331.7 g (1.0 mol) of carbon tetrabromide in 1.0 liter of THF is added. The reaction mixture is stirred at -78°C for 1 h and then allowed to warm to RT. The mixture is cooled again to 0°C, and 1.5 liters of water are slowly added dropwise. The phases are separated, and the organic phase is washed with water, dried over magnesium sulfate

and concentrated under reduced pressure. The residue is initially prepurified on about 1 kg of silica gel (mobile phase: cyclohexane/ethyl acetate 9:1, then 7:3). The product-containing fractions are combined and concentrated under reduced pressure. The residue is then purified again on silica gel (mobile phase: cyclohexane/ethyl acetate 9:1). The product obtained in this manner contains about 5 10% of the regioisomeric 2-bromo-3,4-dimethylpyridine.

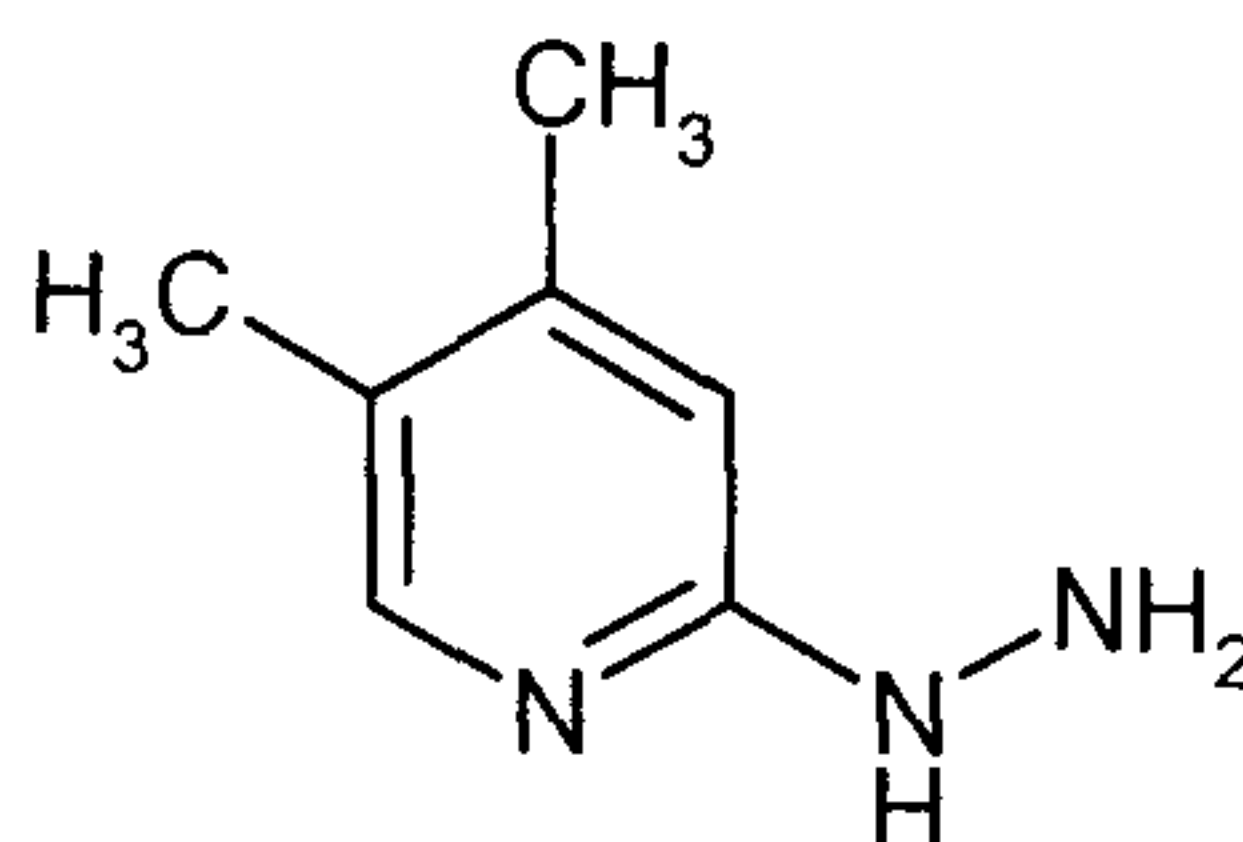
Yield: 6.7 g (20% of theory)

GC-MS (Method 11): $R_t = 4.24$ min; MS (ESIpos): $m/z = 187$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 8.07$ (s, 1H), 7.25 (s, 1H), 2.24 (s, 3H), 2.18 (s, 3H).

Example 21A

10 2-Hydrazino-4,5-dimethylpyridine



3.8 g (18.4 mmol, purity 90%) of the compound from Example 20A are initially charged in 12.5 ml of ethanol. 8.9 ml (9.2 g, 183.8 mmol) of hydrazine hydrate are added, and the mixture is reacted in a single-mode microwave oven (CEM Explorer) at 170°C (100 Watt) for 2 h. The reaction 15 solution is then concentrated, and the residue is taken up in ethyl acetate and washed in each case once with saturated sodium bicarbonate solution and saturated sodium chloride solution. The organic phase is dried over sodium sulfate, filtered and concentrated under reduced pressure.

Yield: 2.2 g (86% of theory)

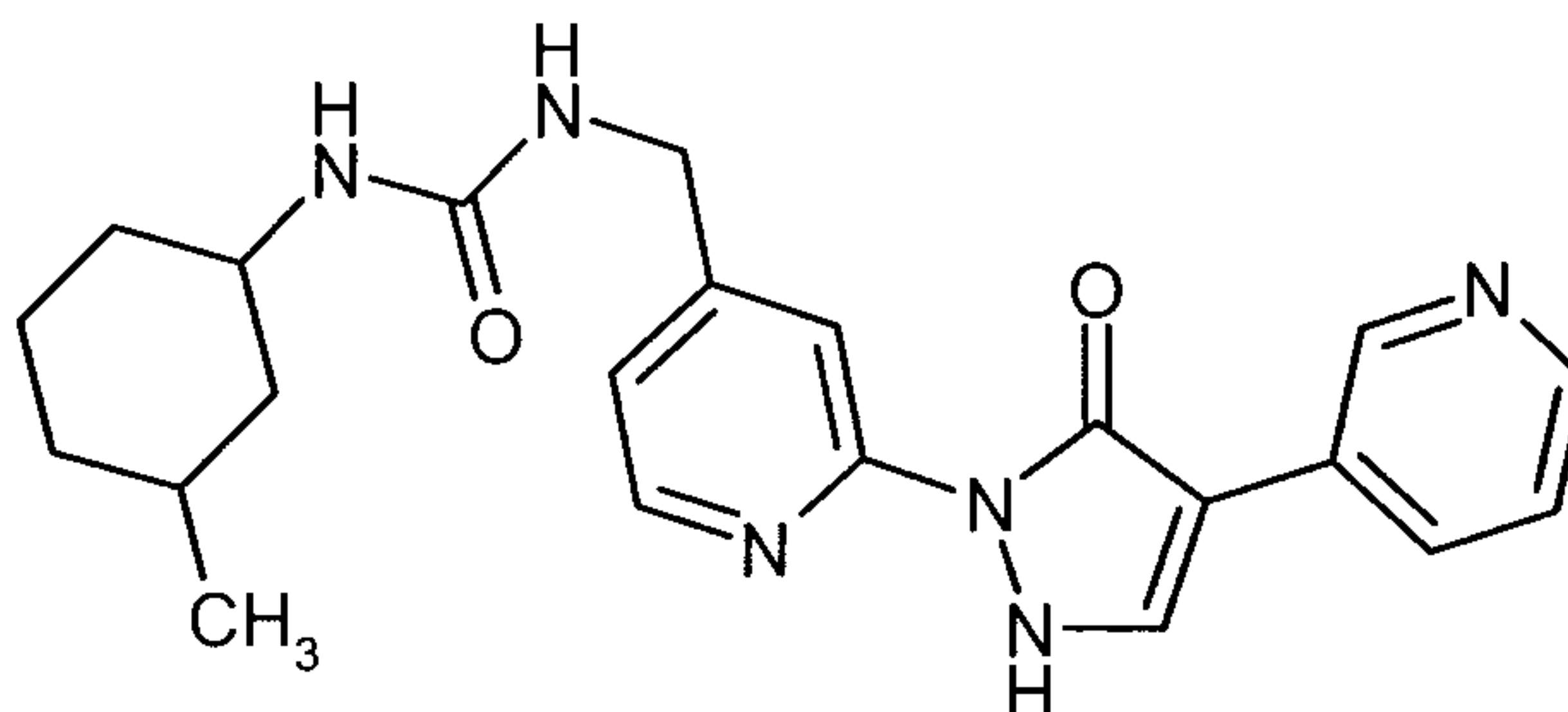
LC-MS (Method 6): $R_t = 0.75$ min; MS (ESIpos): $m/z = 138$ $[M+H]^+$;

20 $^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 7.86$ (s, 1H), 6.51 (s, 1H), 5.61 (br. s, 1H), 3.72 (br. s, 2H), 2.20 (s, 3H), 2.12 (s, 3H).

Exemplary examples:

Example 1

1-(3-Methylcyclohexyl)-3-{[2-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1*H*-pyrazol-1-yl)pyridin-4-yl]-methyl}urea



5

13.9 mg (100 μ mol) of 3-methylcyclohexyl isocyanate are initially charged, 34.0 mg (100 μ mol) of the compound from Example 4A, dissolved in 0.6 ml of 1,2-dichloroethane, and 25.8 mg (200 μ mol) of diisopropylethylamine are added and the mixture is stirred at RT overnight. The mixture is then concentrated, the residue is taken up in DMSO, the precipitate is filtered off and the filtrate is purified by preparative HPLC (Method 3).

10

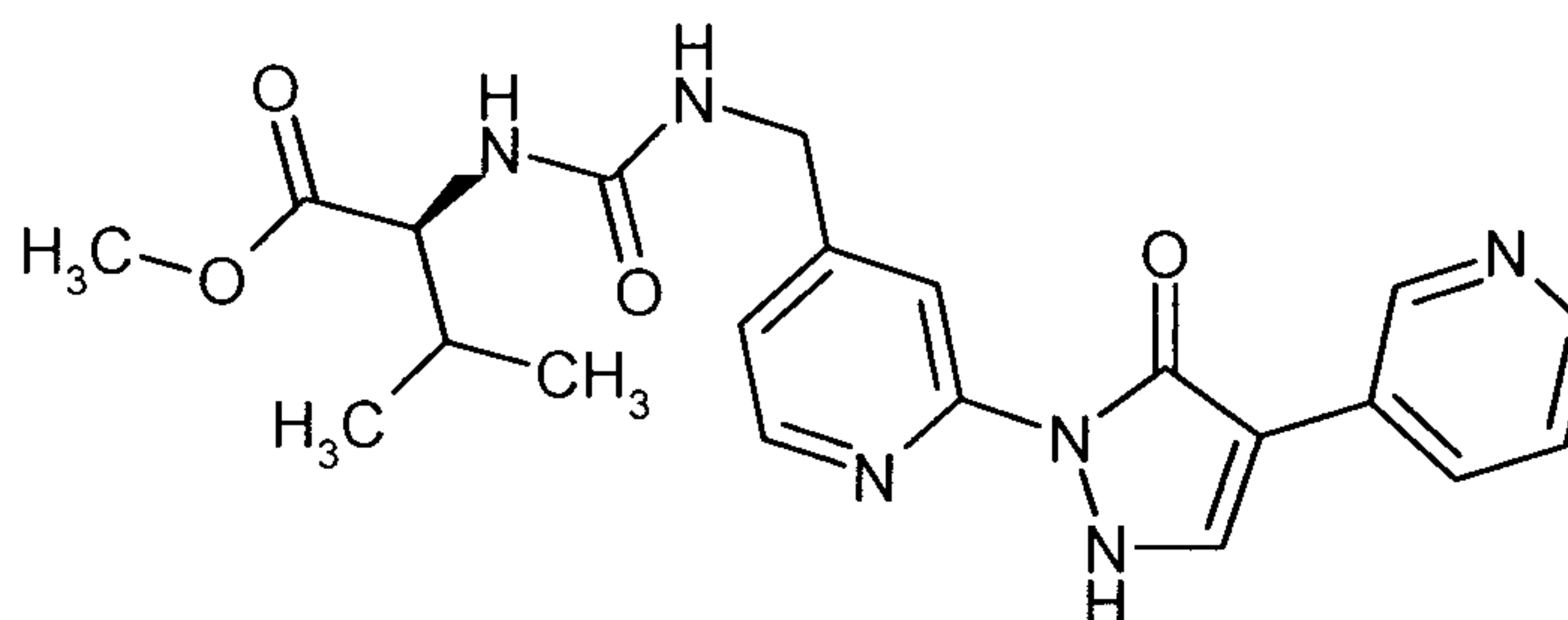
Yield: 5.7 mg (14% of theory)

LC-MS (Method 3): R_t = 1.40 min; MS (ESIpos): m/z = 407 $[M+H]^+$.

Example 2

Methyl *N*-({[2-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1*H*-pyrazol-1-yl)pyridin-4-yl]methyl}carbamoyl)-L-valinate

15



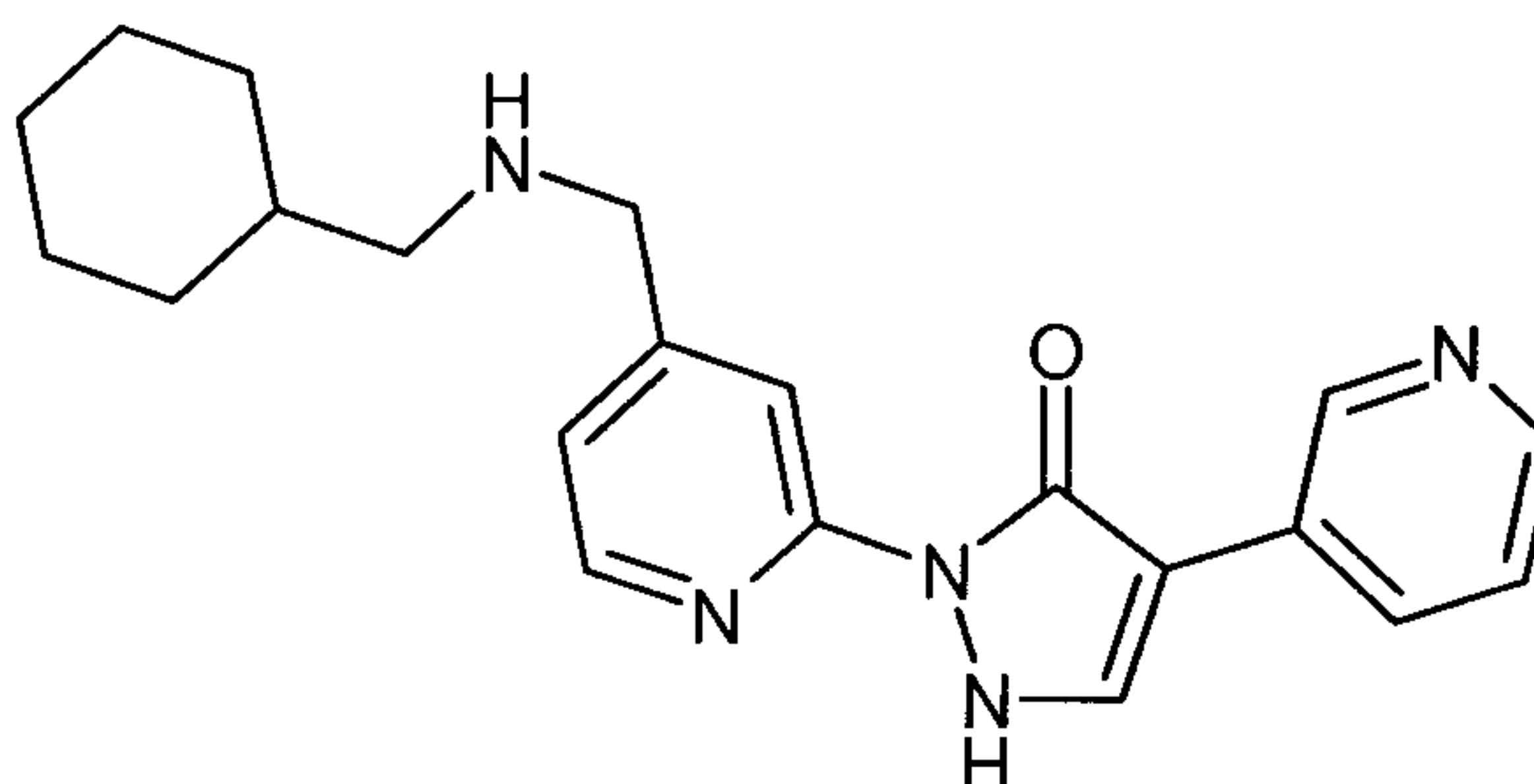
The title compound is obtained analogously to Example 1 starting with Example 4A and the appropriate isocyanate.

Yield: 7% of theory

LC-MS (Method 3): $R_t = 1.22$ min; MS (ESIpos): $m/z = 425$ $[M+H]^+$.

Example 3

2-(4-{[(Cyclohexylmethyl)amino]methyl}pyridin-2-yl)-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one



5

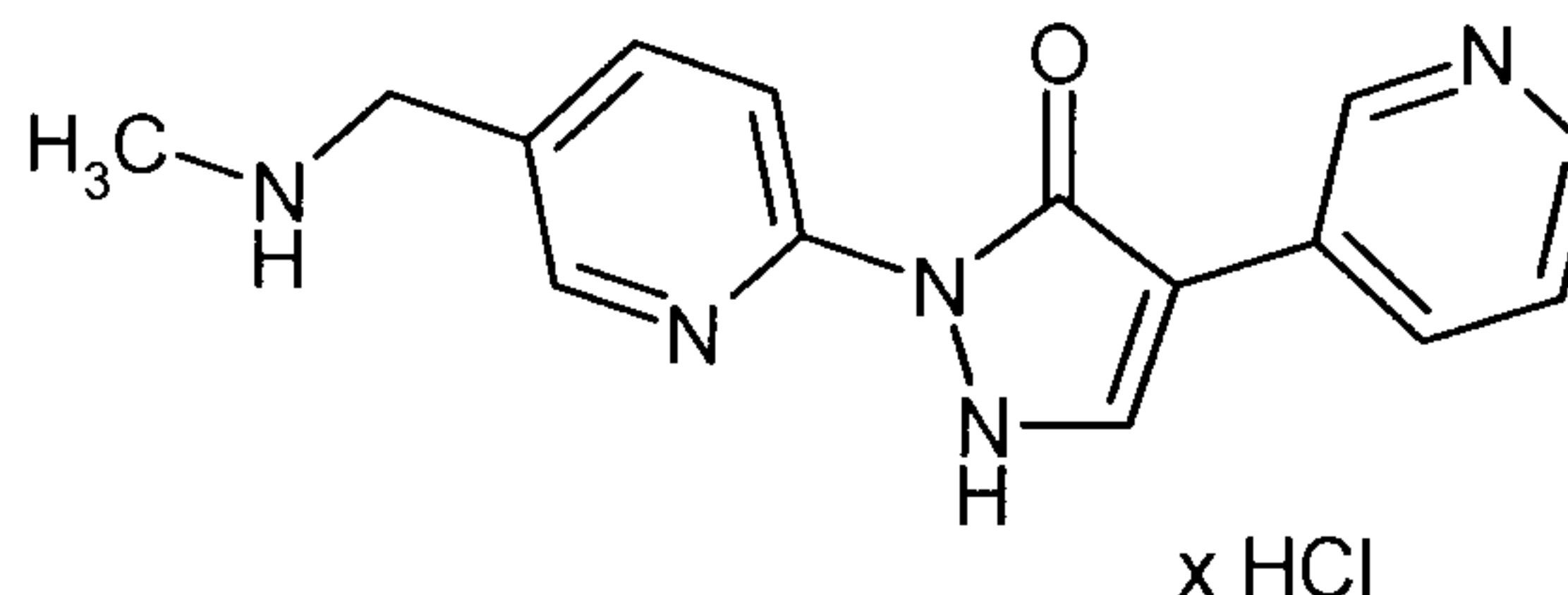
11.2 mg (100 μ mol) of cyclohexanecarbaldehyde are initially charged, 34.0 mg (100 μ mol) of the compound from Example 4A, dissolved in 0.6 ml of ethanol, and 25.8 mg (200 μ mol) of diisopropylethylamine are added and the mixture is stirred at RT overnight. 5.7 mg (150 μ mol) of sodium borohydride are then added, and the mixture is shaken at RT for 3 h. 100 μ l of water are then added, and the mixture is concentrated. The residue is taken up in DMSO, the precipitate is filtered off and the filtrate is purified by preparative HPLC (Method 4).

Yield: 2.6 mg (7% of theory)

LC-MS (Method 4): $R_t = 1.30$ min; MS (ESIpos): $m/z = 364$ $[M+H]^+$.

Example 4

2-{5-[(Methylamino)methyl]pyridin-2-yl}-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one hydrochloride



300 mg (1.4 mmol) of the compound from Example 2A and 207 mg (1.4 mmol) of the compound from Example 5A are dissolved in 2 ml of ethanol, and 47 mg (0.3 mmol) of p-toluenesulfonic acid are added. The mixture is heated under reflux for 24 h, then cooled to RT and purified directly by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with 0.1% formic acid

20

added to the water). The product-containing fractions are concentrated under reduced pressure, the residue is dissolved in 1.5 ml of ethanol and 0.5 ml of a 4 N solution of hydrogen chloride in dioxane is added. The mixture is stirred at RT for 30 min and then concentrated under reduced pressure, and the residue is dried under high vacuum.

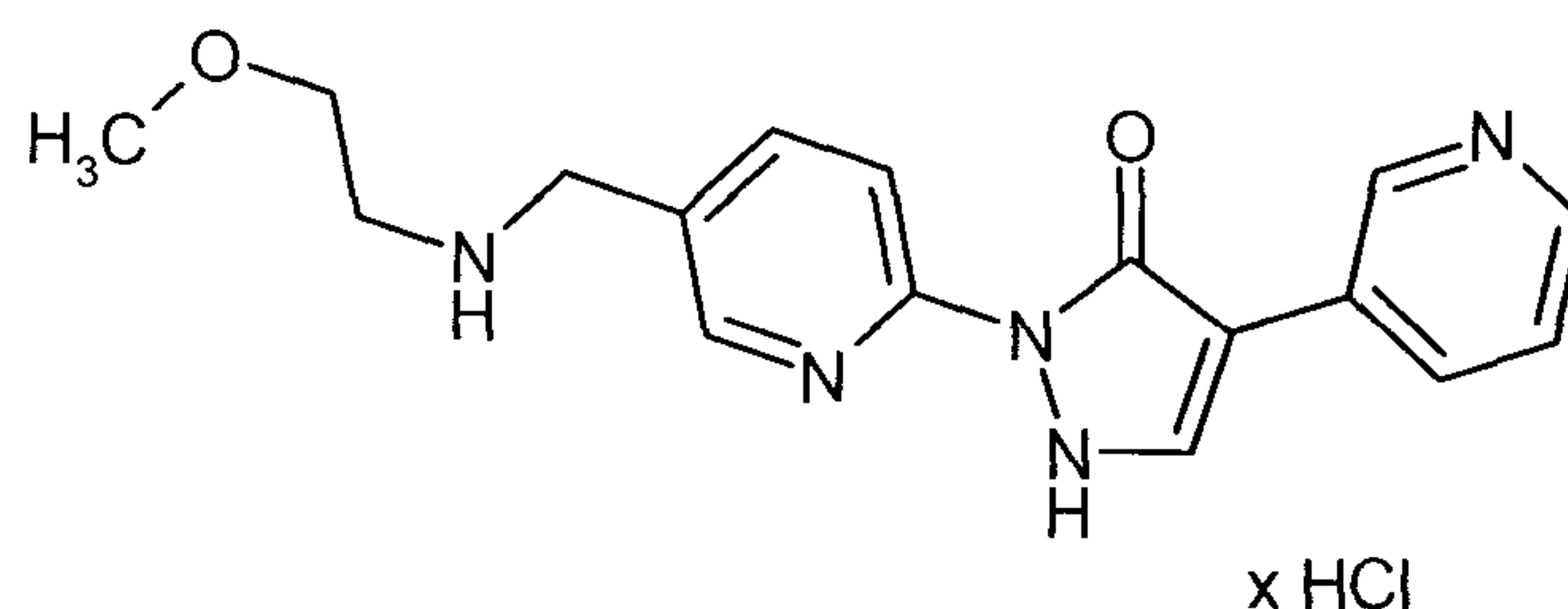
5 Yield: 25 mg (5% of theory)

LC-MS (Method 1): $R_t = 1.68$ min; MS (ESIpos): $m/z = 282$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.39$ - 9.35 (m, 1H), 8.90 (d, 1H), 8.81 (s, 1H), 8.67 (s, 1H), 8.62 (d, 1H), 8.47 (d, 1H), 8.20 (d, 1H), 7.94 (dd, 1H), 4.23 - 4.19 (m, 2H), 2.59 - 2.56 (m, 3H).

Example 5

10 2-(5-{[(2-Methoxyethyl)amino]methyl}pyridin-2-yl)-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one hydrochloride



200 mg (0.9 mmol) of the compound from Example 2A and 178 mg (0.9 mmol) of the compound from Example 6A are dissolved in 2 ml of ethanol, and 42 mg (0.2 mmol) of p-toluenesulfonic acid are added. The mixture is heated under reflux for 24 h and then cooled to RT and purified directly by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with 0.1% formic acid added to the water). The product-containing fractions are concentrated under reduced pressure, the residue is dissolved in 1 ml of ethanol and 0.5 ml of a 4 N solution of hydrogen chloride in dioxane is added. The mixture is stirred at RT for 30 min and then concentrated under reduced pressure, and the residue is dried under high vacuum.

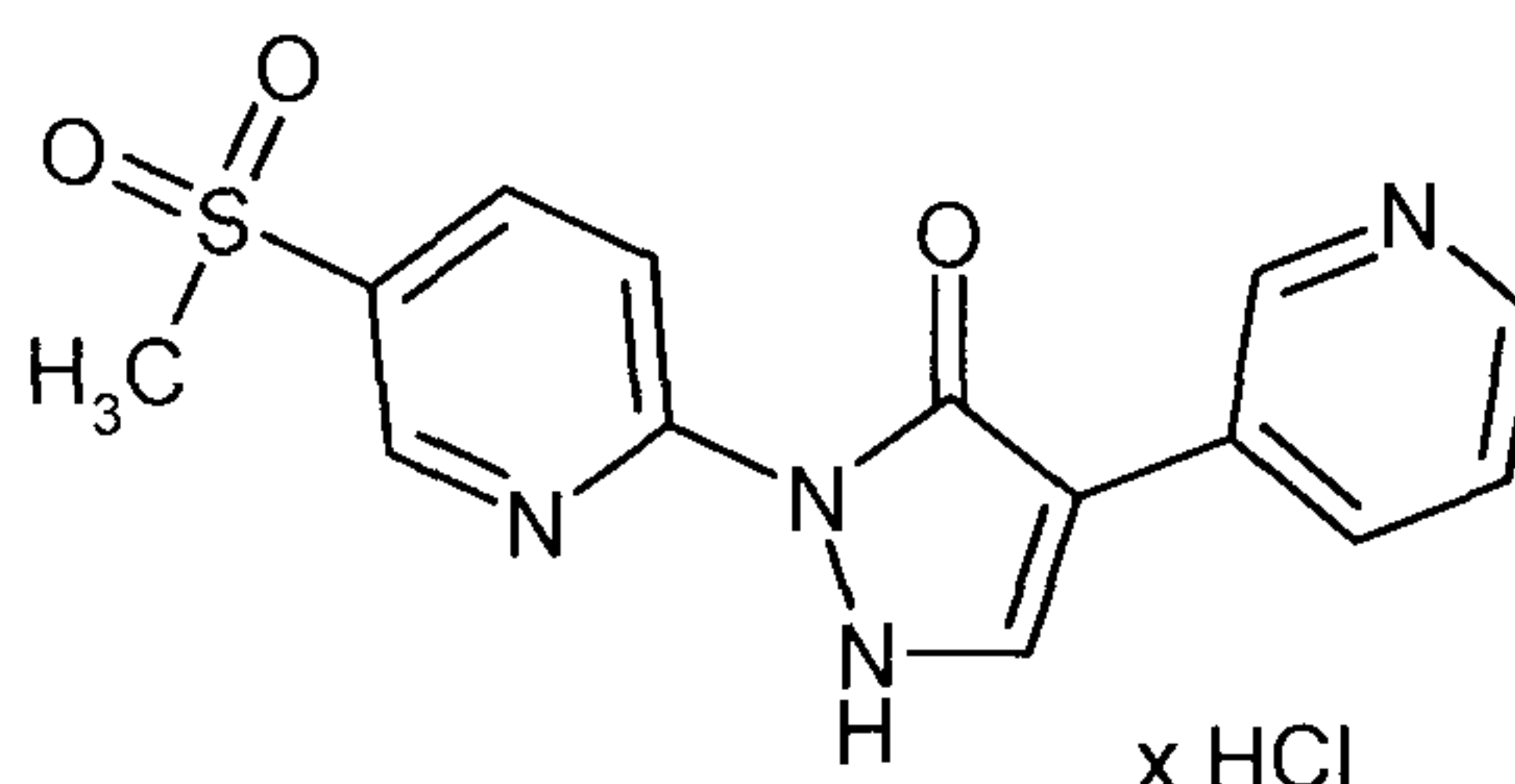
Yield: 10 mg (3% of theory)

HPLC (Method 10): $R_t = 2.84$ min; MS (ESIpos): $m/z = 326$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.47$ (br. s, NH), 9.40 (s, 1H), 8.96 (d, 1H), 8.84 (s, 1H), 8.67 (s, 1H), 8.65 (d, 1H), 8.47 (d, 1H), 8.24 (d, 1H), 8.00 (dd, 1H), 4.26 - 4.22 (m, 2H), 3.66 - 3.62 (m, 2H), 3.31 (s, 3H), 3.15 - 3.11 (m, 2H).

Example 6

2-[5-(Methylsulfonyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one hydrochloride



200 mg (0.9 mmol) of the compound from Example 2A and 170 mg (0.9 mmol) of the compound
5 from Example 6A are dissolved in 2 ml of ethanol, and 3 mg (0.2 mmol) of p-toluenesulfonic acid
are added. The mixture is heated under reflux for 24 h and then cooled to RT and purified directly
by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with 0.1% formic
acid added to the water). The product-containing fractions are concentrated under reduced
pressure, the residue is dissolved in 1 ml of ethanol and 0.5 ml of a 4 N solution of hydrogen
10 chloride in dioxane is added. The mixture is stirred at RT for 30 min and then concentrated under
reduced pressure, and the residue is dried under high vacuum.

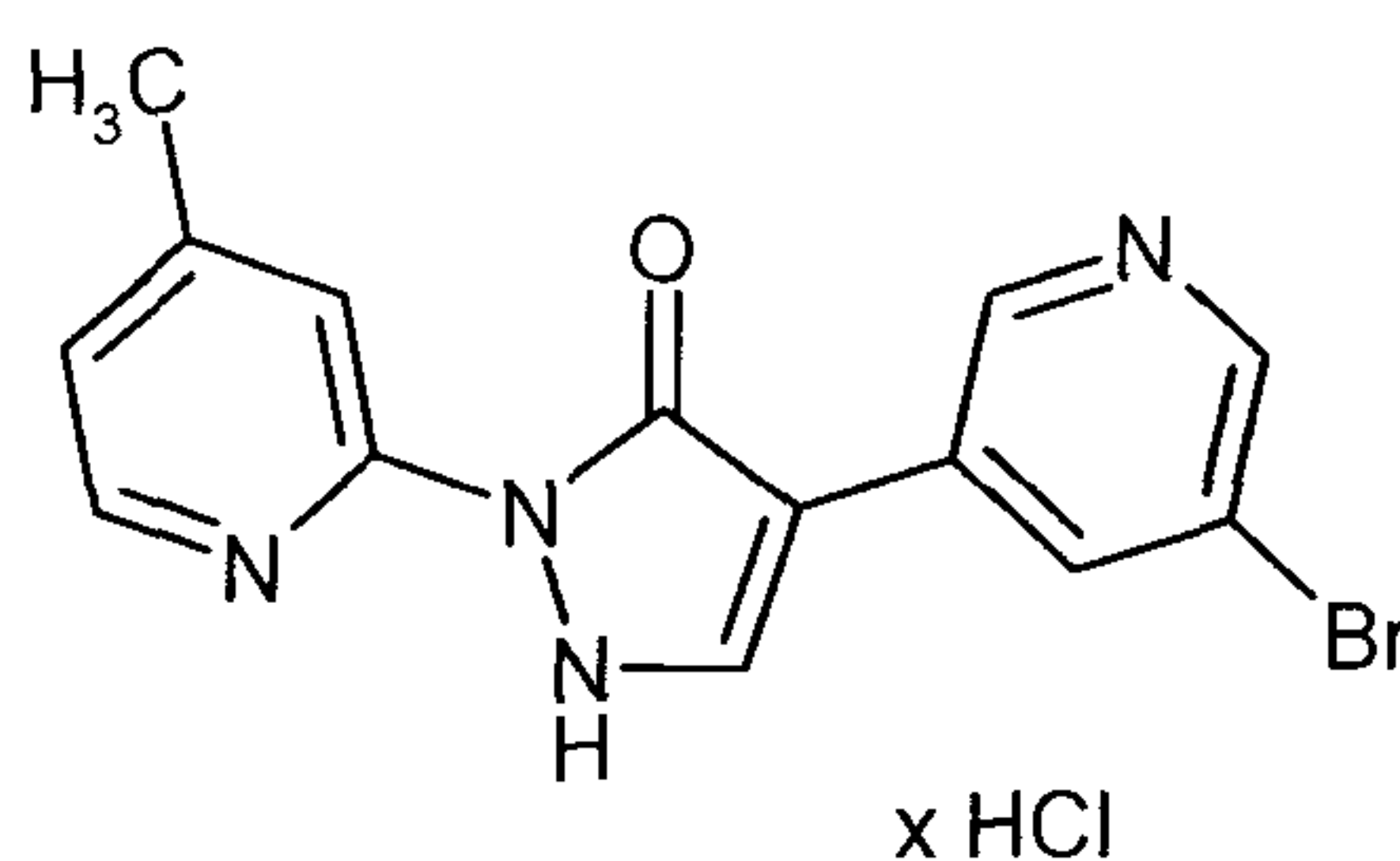
Yield: 224 mg (66% of theory)

LC-MS (Method 1): $R_t = 2.12$ min; MS (ESIpos): $m/z = 317$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.41$ (s, 1H), 8.99 (s, 1H), 8.98-8.94 (m, 2H), 8.71 (d, 1H),
15 8.66 (d, 1H), 8.53 (dd, 1H), 8.01 (dd, 1H), 3.37 (s, 3H).

Example 7

4-(5-Bromopyridin-3-yl)-2-(4-methylpyridin-2-yl)-1,2-dihydro-3H-pyrazol-3-one hydrochloride



1070 mg (3.6 mmol) of the compound from Example 9A and 441 mg (3.6 mmol) of the compound
20 from Example 10A are dissolved in 10 ml of ethanol, and 123 mg (0.7 mmol) of p-toluenesulfonic
acid are added. The mixture is heated under reflux for 24 h and then cooled to RT, and the

supernatant is decanted off. The residue is dissolved in 10 ml of ethanol, and 1 ml of a 4 N solution of hydrogen chloride in dioxane is added. The mixture is stirred at RT for 30 min and then concentrated under reduced pressure, and the residue is dried under high vacuum.

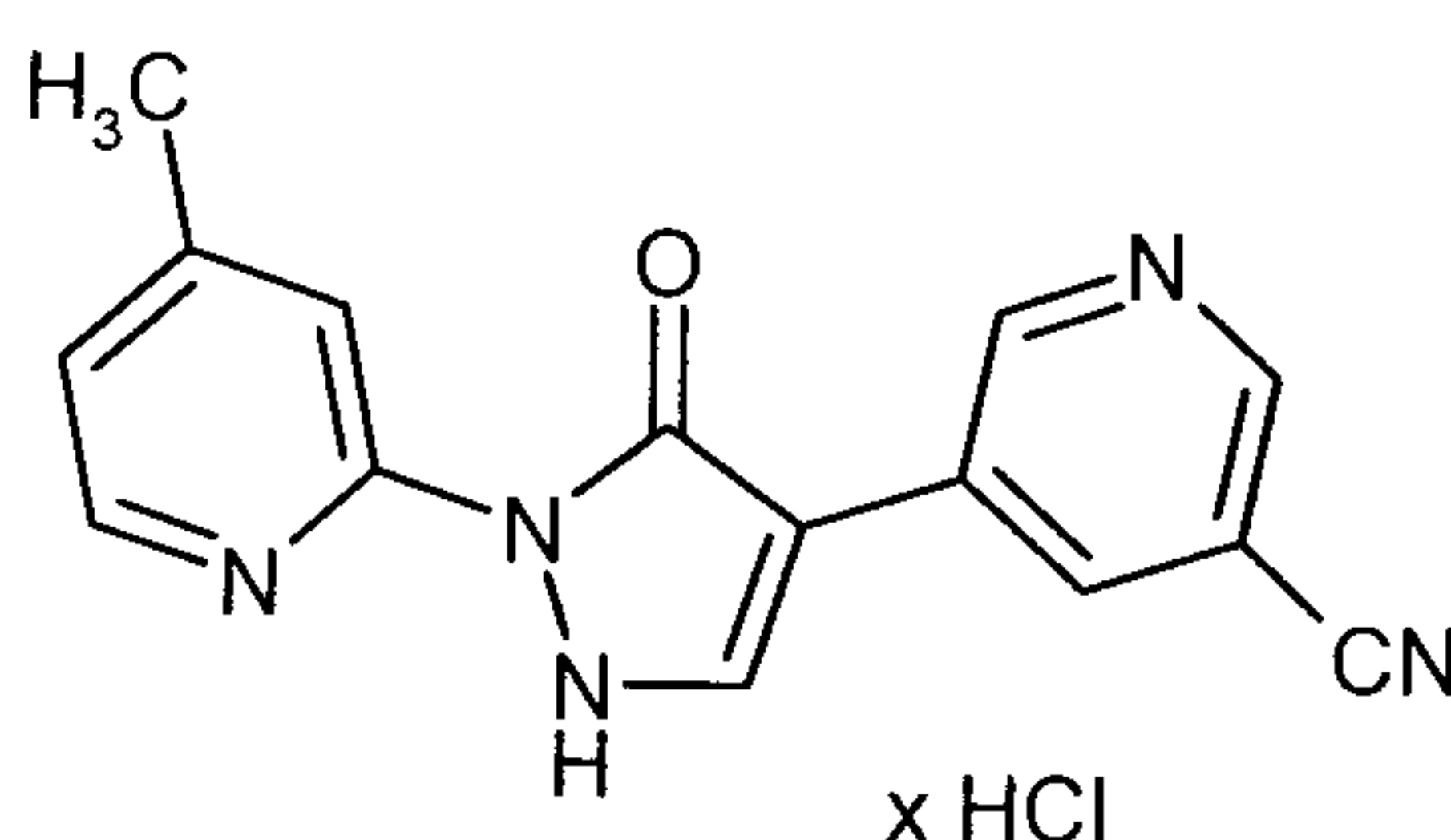
Yield: 470 mg (36% of theory)

5 LC-MS (Method 6): $R_t = 1.99$ min; MS (ESIpos): $m/z = 332$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.12$ (s, 1H), 8.66-8.62 (m, 1H), 8.53 (s, 1H), 8.51 (d, 1H), 8.35 (d, 1H), 8.16 (d, 1H), 7.24 (d, 1H), 2.46 (s, 3H).

Example 8

5-[2-(4-Methylpyridin-2-yl)-3-oxo-2,3-dihydro-1H-pyrazol-4-yl]pyridine-3-carbonitrile
10 hydrochloride



200 mg (0.5 mmol) of the compound from Example 7, 47 mg (0.4 mmol) of zinc cyanide and 19 mg (0.02 mmol) of tetrakis(triphenylphosphine)palladium(0) are reacted in 3 ml of DMF at 220°C in a single-mode microwave oven (Emrys Optimizer) for 50 min. The reaction mixture is then
15 concentrated under reduced pressure, the residue is taken up in 2 ml of ethanol and the mixture is adjusted with 1 N aqueous sodium hydroxide solution to pH 10. The mixture is extracted with ethyl acetate, the organic phase is dried over sodium sulfate and concentrated under reduced pressure and the residue is purified by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with 0.1% formic acid added to the water). The product-containing
20 fractions are concentrated under reduced pressure, the residue is dissolved in 1 ml of ethanol and 0.5 ml of a 4 N solution of hydrogen chloride in dioxane is added. The mixture is stirred at RT for 30 min and then concentrated under reduced pressure, and the residue is dried under high vacuum.

Yield: 12 mg (7% of theory)

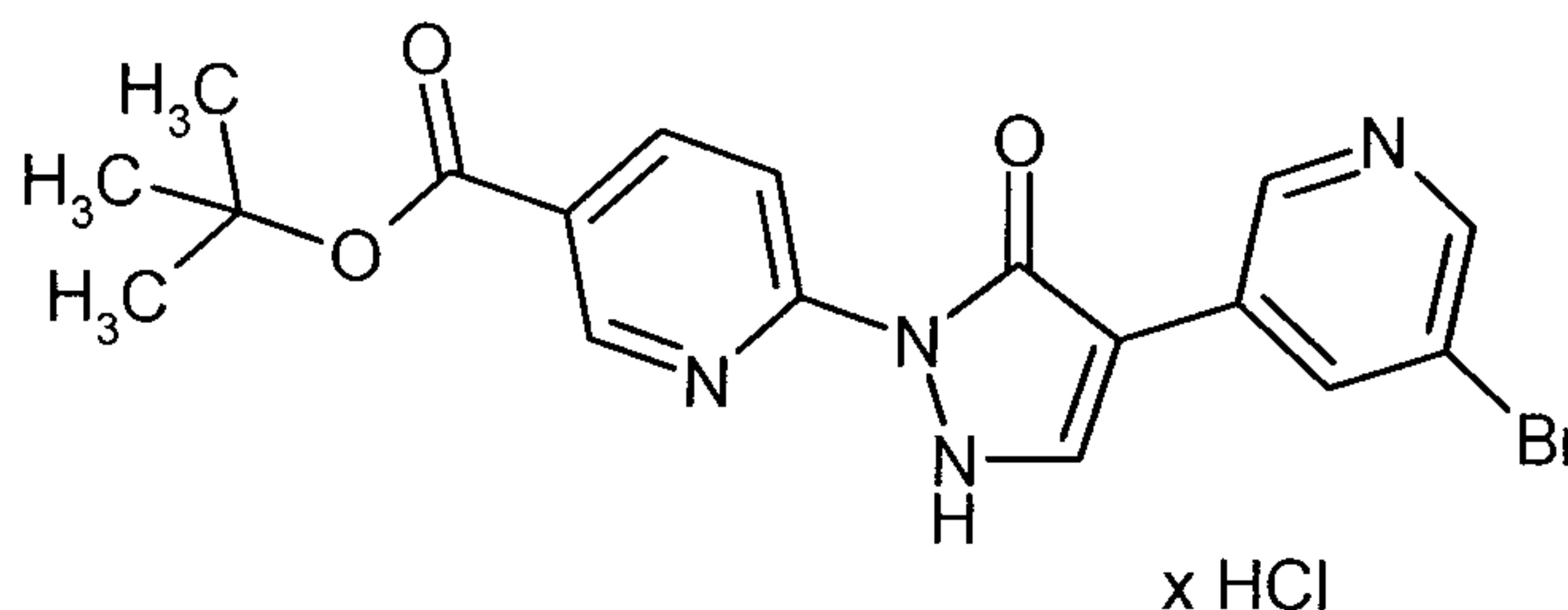
LC-MS (Method 6): $R_t = 1.79$ min; MS (ESIpos): $m/z = 278$ $[M+H]^+$;

25 $^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.38$ (s, 1H), 8.76 (s, 1H), 8.71 (s, 1H), 8.55 (s, 1H), 8.35 (d,

1H), 8.16 (d, 1H), 7.24 (d, 1H), 2.46 (s, 3H).

Example 9

tert-Butyl 6-[4-(5-bromopyridin-3-yl)-5-oxo-2,5-dihydro-1*H*-pyrazol-1-yl]pyridine-3-carboxylate hydrochloride



5

500 mg (1.7 mmol) of the compound from Example 9A and 350 mg (1.7 mmol) of the compound from Example 15A are dissolved in 2 ml of ethanol, and 58 mg (0.3 mmol) of *p*-toluenesulfonic acid are added. The mixture is heated under reflux for 24 h and then cooled to RT, and 0.5 ml of a 4 N solution of hydrogen chloride in dioxane is added. The mixture is stirred at RT for 30 min.

10 The precipitate is filtered off, washed with ethanol and diethyl ether and dried under high vacuum.

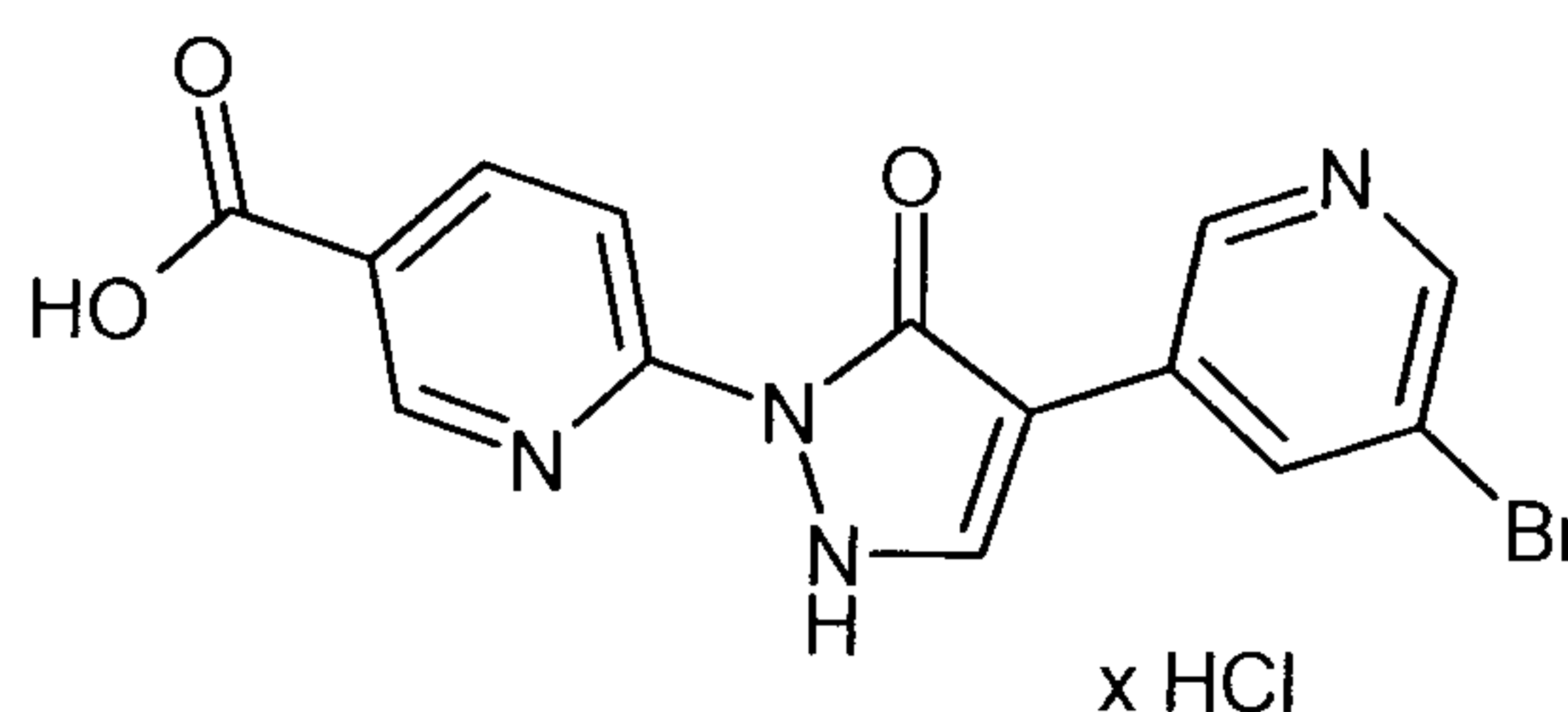
Yield: 425 mg (56% of theory)

LC-MS (Method 5): $R_t = 1.47$ min; MS (ESIpos): $m/z = 417$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.15$ (s, 1H), 8.91 (s, 1H), 8.74 (d, 1H), 8.64 (d, 1H), 8.52-8.49 (m, 2H), 8.43 (d, 1H), 1.58 (s, 9H).

15 **Example 10**

6-[4-(5-Bromopyridin-3-yl)-5-oxo-2,5-dihydro-1*H*-pyrazol-1-yl]pyridine-3-carboxylic acid hydrochloride



60 mg (0.1 mmol) of the compound from Example 9 are suspended in 2 ml of dichloromethane, and 0.5 ml of TFA is added. The mixture is stirred at RT for 4 h and then concentrated under reduced pressure, and 0.5 ml of a 4 N solution of hydrogen chloride in dioxane is added to the

20

residue. The mixture is stirred at RT for 30 min. The precipitate is filtered off, washed with diethyl ether and dried under high vacuum.

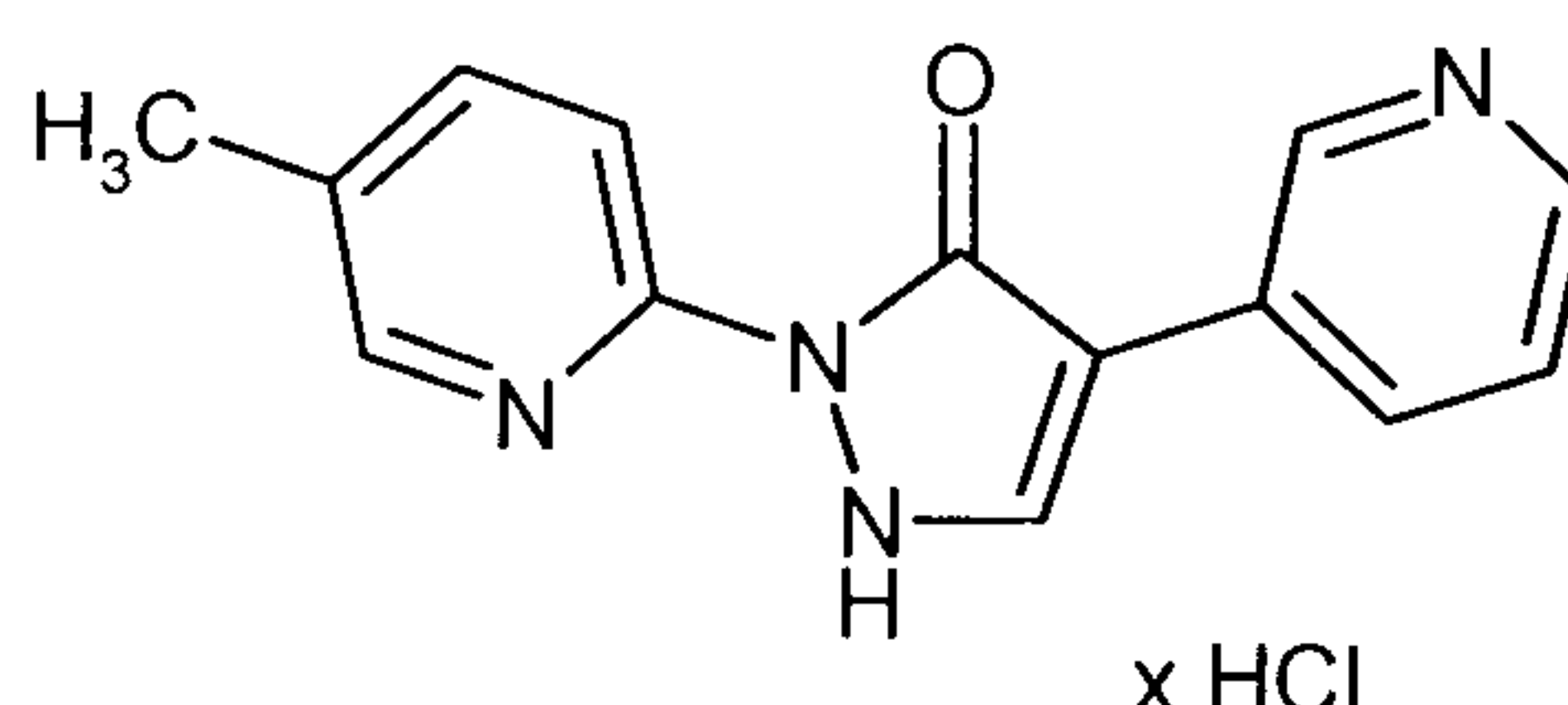
Yield: 37 mg (70% of theory)

LC-MS (Method 6): $R_t = 1.83$ min; MS (ESIpos): $m/z = 361$ $[M+H]^+$;

- 5 $^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.16$ (s, 1H), 8.97 (s, 1H), 8.75 (d, 1H), 8.66 (d, 1H), 8.52-8.47 (m, 2H), 8.46 (d, 1H).

Example 11

2-(5-Methylpyridin-2-yl)-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one hydrochloride



- 10 100 mg (0.5 mmol) of the compound from Example 9A and 62 mg (0.5 mmol) of the compound from Example 11A are dissolved in 1.5 ml of ethanol, and 16 mg (0.1 mmol) of p-toluenesulfonic acid are added. The mixture is heated under reflux for 24 h and then cooled to RT and concentrated under reduced pressure. The residue is taken up in 2 ml of ethanol, and 1 ml of a 4 N solution of hydrogen chloride in dioxane is added. The mixture is stirred at RT for 30 min. The precipitate is filtered off, washed with ethanol and diethyl ether and dried under high vacuum.
- 15

Yield: 66 mg (50% of theory)

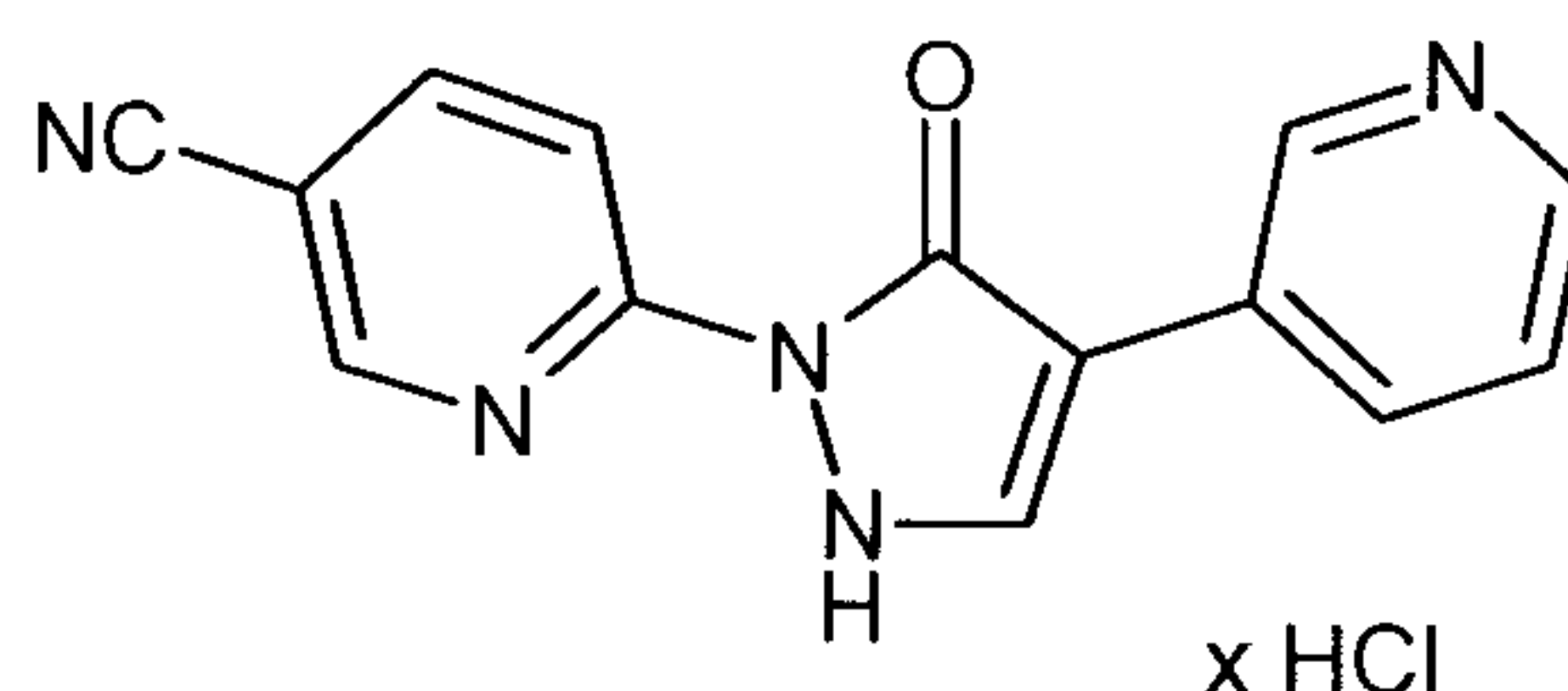
LC-MS (Method 6): $R_t = 1.07$ min; MS (ESIpos): $m/z = 253$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.31$ (s, 1H), 8.82 (d, 1H), 8.64 (s, 1H), 8.57 (d, 1H), 8.34 (d, 1H), 8.27 (d, 1H), 7.93 (dd, 1H), 7.89 (dd, 1H), 2.36 (s, 3H).

Example 12

6-(5-Oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carbonitrile hydrochloride

- 68 -



11.8 g (53.7 mmol) of the compound from Example 2A and 7.2 g (53.7 mmol) of the compound from Example 14A are initially charged in 175 ml of ethanol. 2.0 g (10.7 mmol) of p-toluenesulfonic acid monohydrate are added, and the mixture is stirred under reflux for 16 h. The mixture is then cooled to 0°C, and the solid formed is filtered off and dried under high vacuum. The solid is stirred in a 4 N solution of hydrogen chloride in dioxane for 30 min, and the precipitate is filtered off again and dried under high vacuum.

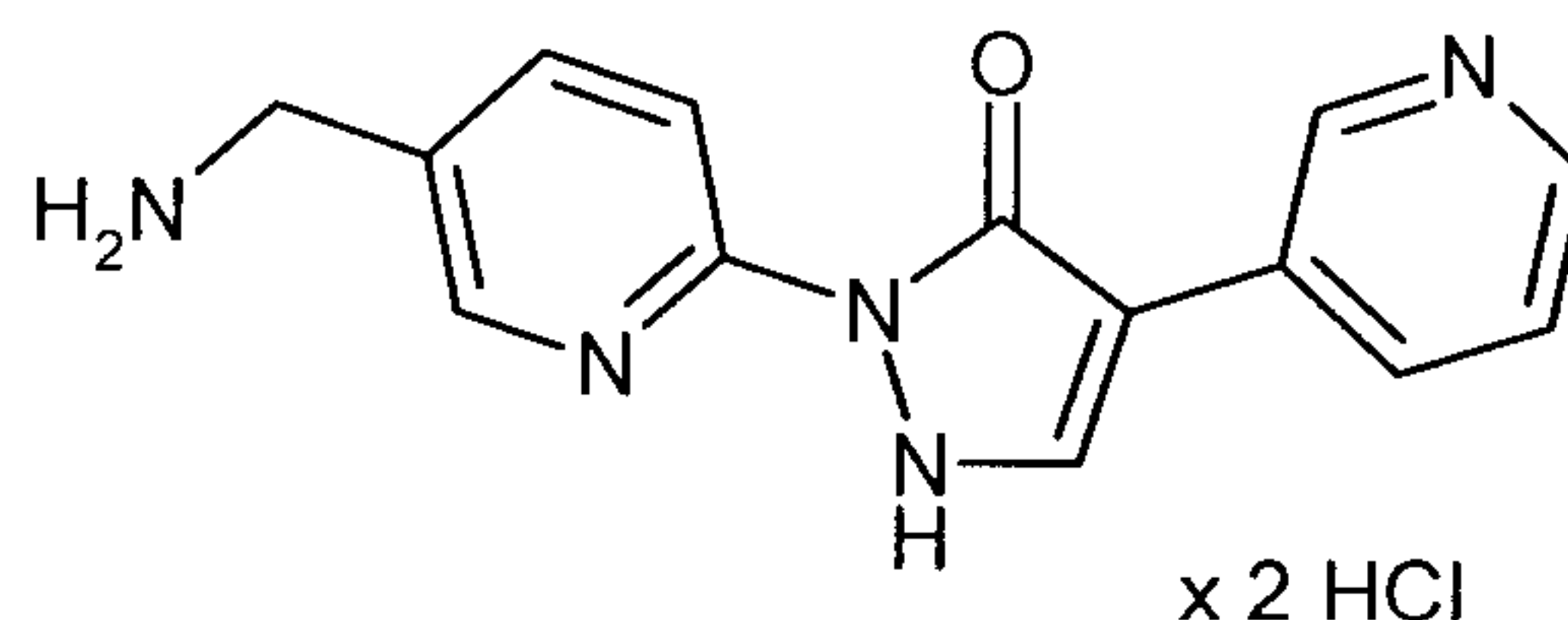
Yield: 10.8 g (67% of theory)

LC-MS (Method 1): $R_t = 2.22$ min; MS (ESIpos): $m/z = 264$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.40$ (s, 1H), 9.02-8.96 (m, 3H), 8.68-8.61 (m, 2H), 8.49 (dd, 1H), 8.00 (dd, 1H).

Example 13

2-[5-(Aminomethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one dihydrochloride



10.0 g (38.0 mmol) of the compound from Example 12 are initially charged in 300 ml of acetic acid. 20 ml of a 4 N solution of hydrogen chloride in dioxane and 5.0 g (4.7 mmol) of palladium on carbon (10%) are added and the mixture is hydrogenated at RT under atmospheric pressure for 96 h. Water is then added until the organic solid formed has gone back into solution, and the catalyst is filtered off through silica gel. The filtrate is concentrated and the residue is purified by column chromatography on silica gel (mobile phase: cyclohexane/ethyl acetate mixture). The product obtained is then stirred in a 4 N solution of hydrogen chloride in dioxane for 30 min, and the solid is filtered off and dried under high vacuum. The solid is then dissolved in about 300 ml of water, and the solution is lyophilized.

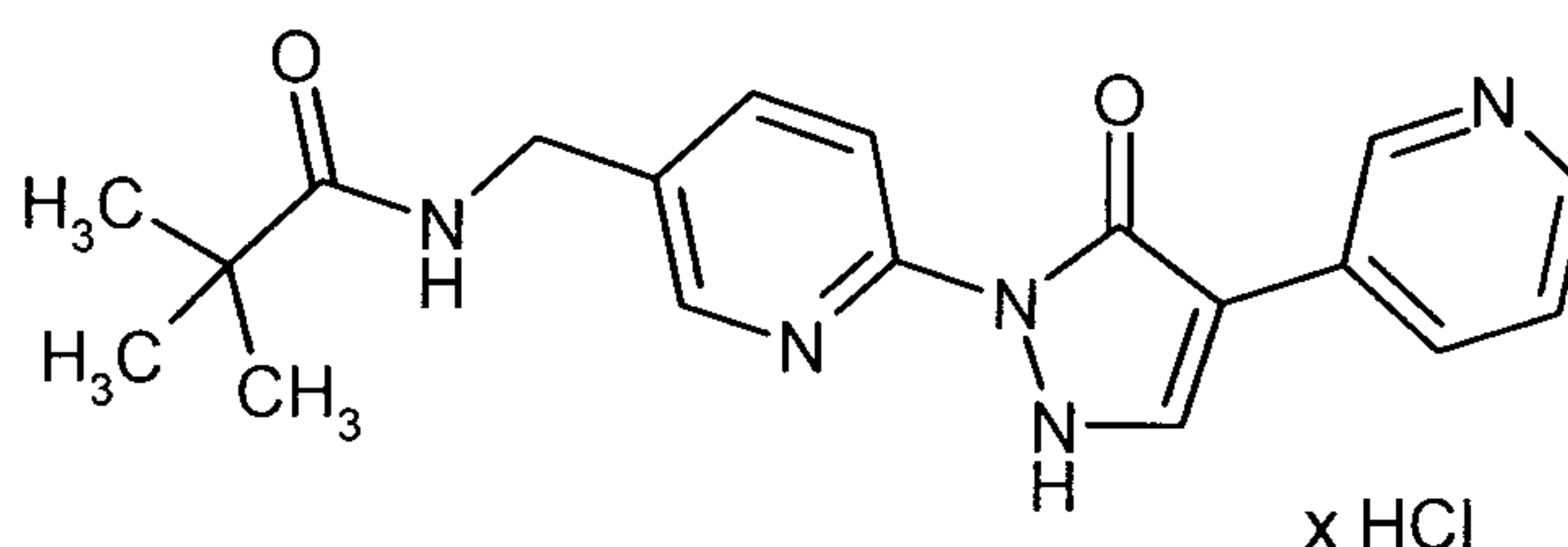
Yield: 8.7 g (67% of theory)

LC-MS (Method 6): $R_t = 0.71$ min; MS (ESIpos): $m/z = 268$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.42$ (s, 1H), 9.04 (d, 1H), 8.87 (s, 1H), 8.68-8.53 (m, 4H), 8.45 (d, 1H), 8.20 (d, 1H), 8.05 (dd, 1H), 4.12 (d, 2H).

Example 14

- 5 2,2-Dimethyl-*N*-{[6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1*H*-pyrazol-1-yl)pyridin-3-yl]methyl}-propanamide hydrochloride



- 100 mg (0.3 mmol) of the compound from Example 13 are suspended in 3 ml of dichloromethane. 152 mg (1.2 mmol) of *N,N*-diisopropylethylamine (Hünig base) are added, and the mixture is stirred at RT for 5 min. 43 mg (0.4 mmol) of 2,2-dimethylpropanoyl chloride are then added, and the mixture is stirred at RT for 16 h. The mixture is then concentrated on a rotary evaporator, the residue is taken up in 5 ml of dioxane and 1 ml 1 N aqueous sodium hydroxide solution is added. This mixture is then purified by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with addition of 0.1% TFA to the water). The product-containing fractions are combined and concentrated on a rotary evaporator. The residue is dissolved in 1 N hydrochloric acid, and the solution is lyophilized. The solid is then stirred in *tert*-butyl methyl ether for 30 min, filtered off and dried under high vacuum.

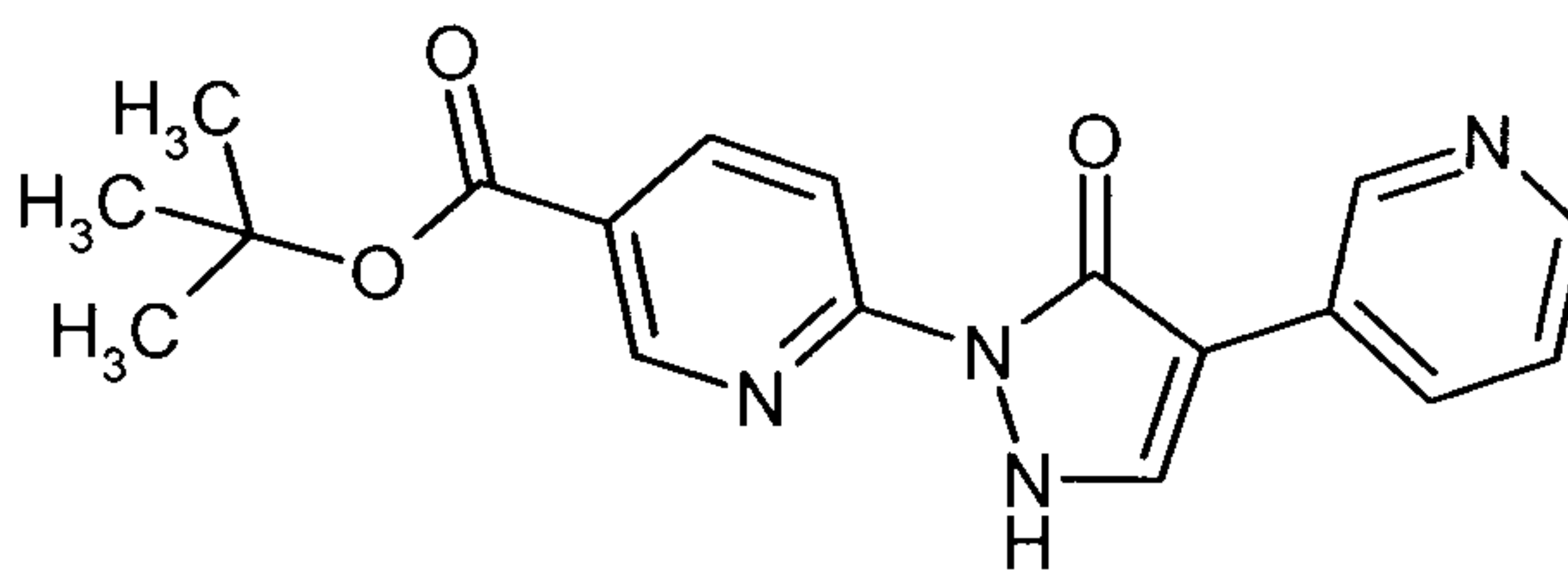
Yield: 71 mg (62% of theory)

LC-MS (Method 1): $R_t = 2.37$ min; MS (ESIpos): $m/z = 352$ $[M+H]^+$;

- 20 $^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.39$ (s, 1H), 9.00 (d, 1H), 8.87 (s, 1H), 8.63 (d, 1H), 8.33 (m, 2H), 8.27 (t, 1H), 8.05 (dd, 1H), 7.93 (dd, 1H), 4.33 (d, 2H), 1.12 (s, 9H).

Example 15

tert-Butyl 6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1*H*-pyrazol-1-yl)pyridine-3-carboxylate



2.2 g (10.0 mmol) of the compound from Example 2A are initially charged in 50 ml of ethanol. 2.1 g (10.0 mmol) of the compound from Example 15A and 380 mg (2.0 mmol) of p-toluenesulfonic acid are added, and the mixture is stirred under reflux for 16 h. The mixture is then cooled to 0°C, and the solid formed is filtered off and washed once with a little ethanol (batch 1). The mother liquor is concentrated and the residue is triturated with a little ethanol. The solid obtained is filtered off and washed once with ethanol (batch 2). The two solids batches are combined and dried under high vacuum. The solid is then stirred in *tert*-butyl methyl ether for 30 min, filtered off again and dried under high vacuum.

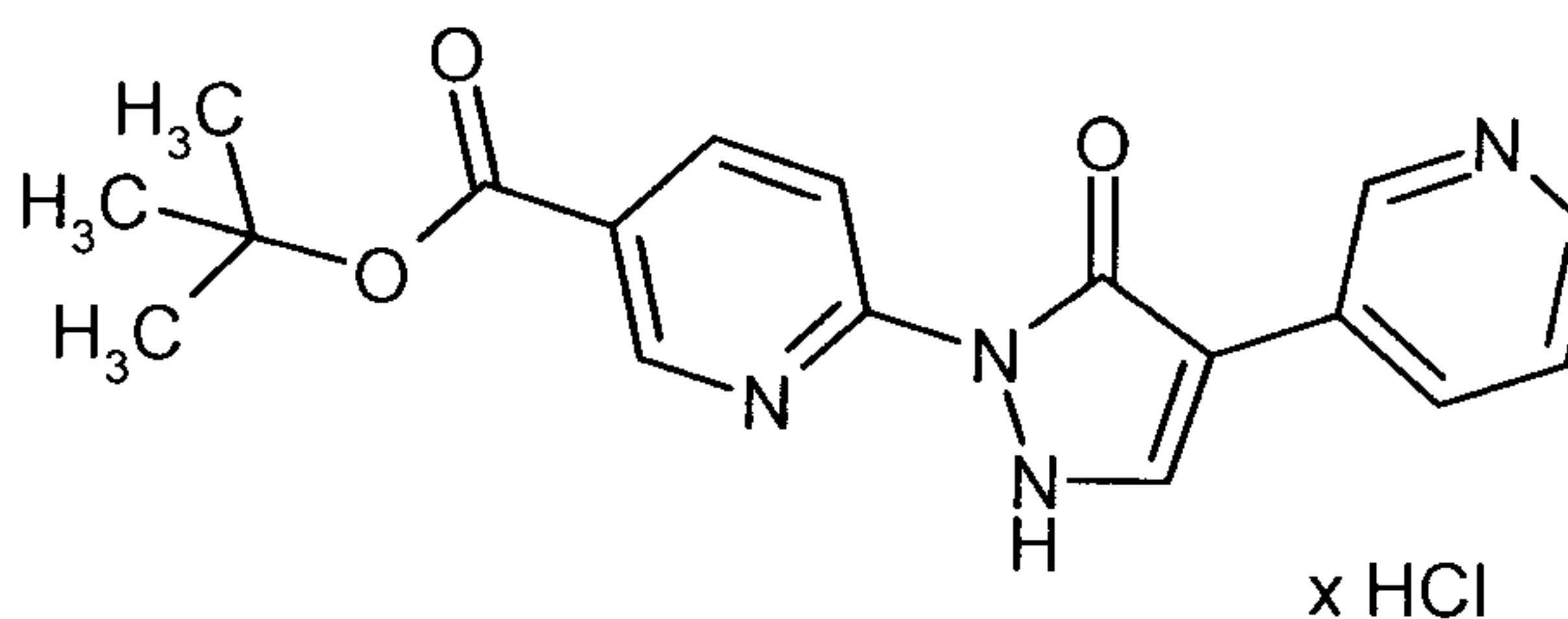
Yield: 2.7 g (79% of theory)

LC-MS (Method 5): $R_t = 0.93$ min; MS (ESIpos): $m/z = 339$ $[M+H]^+$;

¹H-NMR (400 MHz, DMSO-*d*₆): $\delta = 9.11$ (d, 1H), 8.91 (d, 1H), 8.57 (s, 1H), 8.51-8.49 (m, 1H), 8.40 (dd, 1H), 8.37-8.35 (m, 1H), 8.28 (d, 1H), 7.37 (dd, 1H), 1.58 (s, 9H).

Example 16

tert-Butyl 6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1*H*-pyrazol-1-yl)pyridine-3-carboxylate hydrochloride



100 mg (0.3 mmol) of the compound from Example 15 are stirred in a 4 N solution of hydrogen chloride in dioxane at RT for 30 min. The solid is then filtered off and dried under high vacuum.

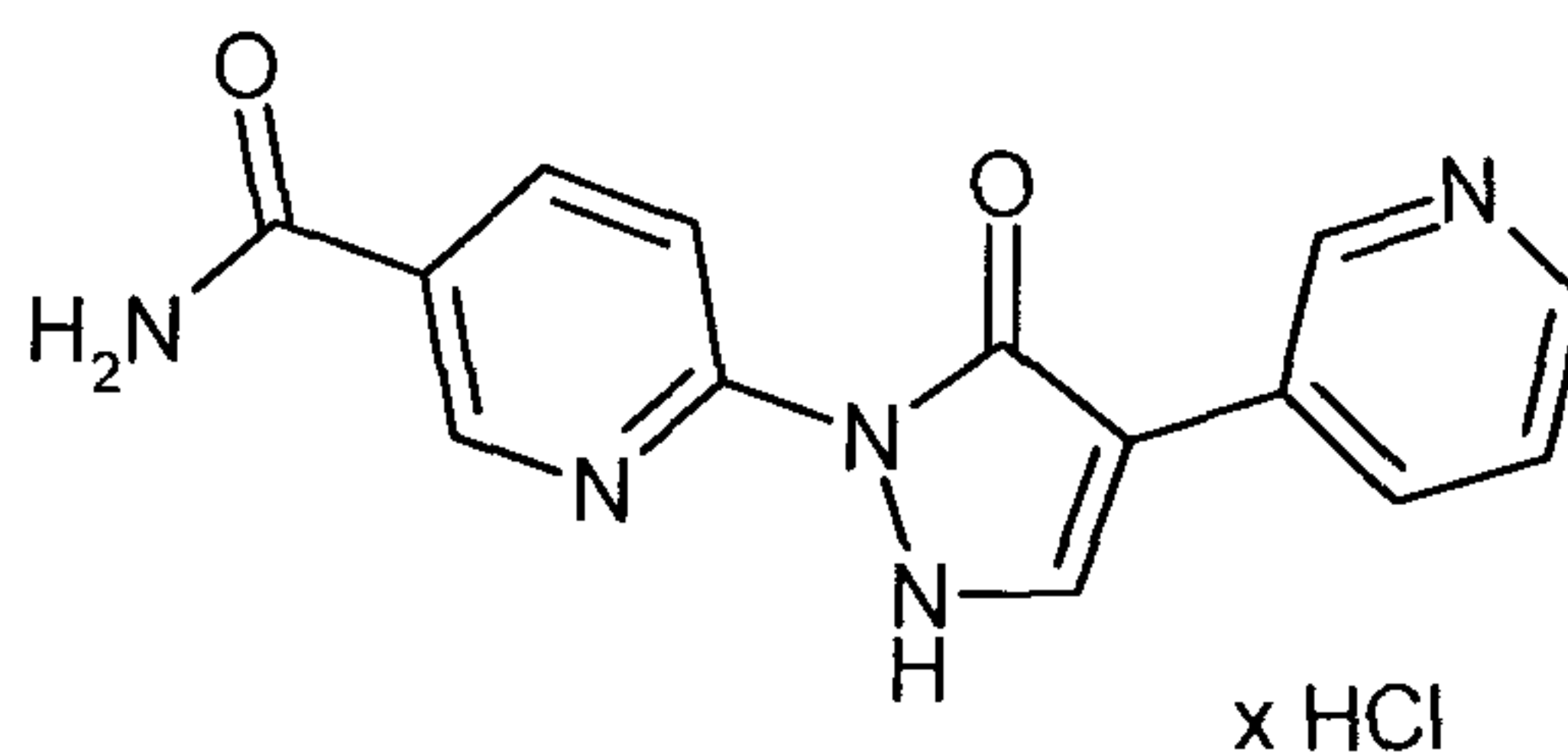
Yield: 90 mg (81% of theory)

LC-MS (Method 1): $R_t = 3.04$ min; MS (ESIpos): $m/z = 339$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): δ = 9.39 (s, 1H), 8.99-8.86 (m, 3H), 8.65 (d, 1H), 8.55 (d, 1H), 8.45 (d, 1H), 8.00 (dd, 1H), 1.57 (s, 9H).

Example 17

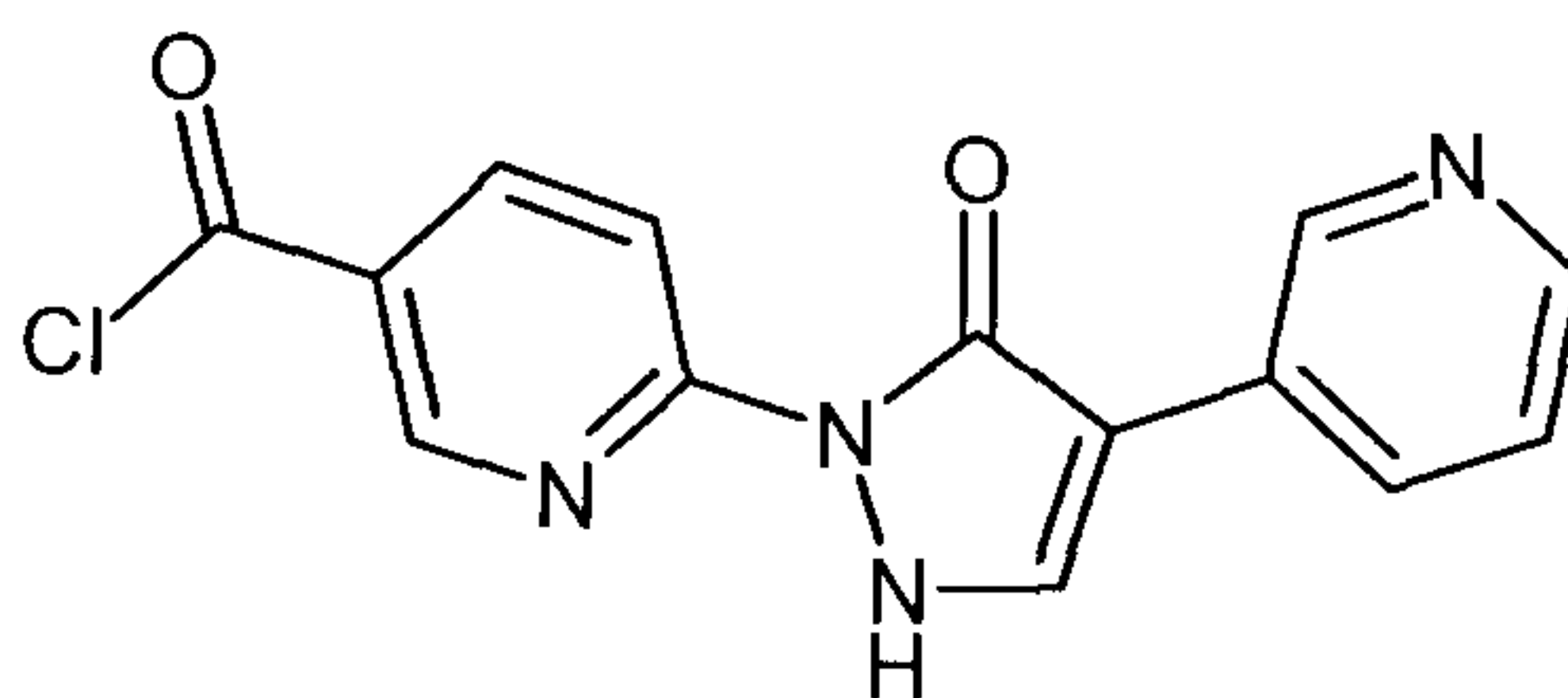
6-(5-Oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carboxamide hydrochloride



5

Step a):

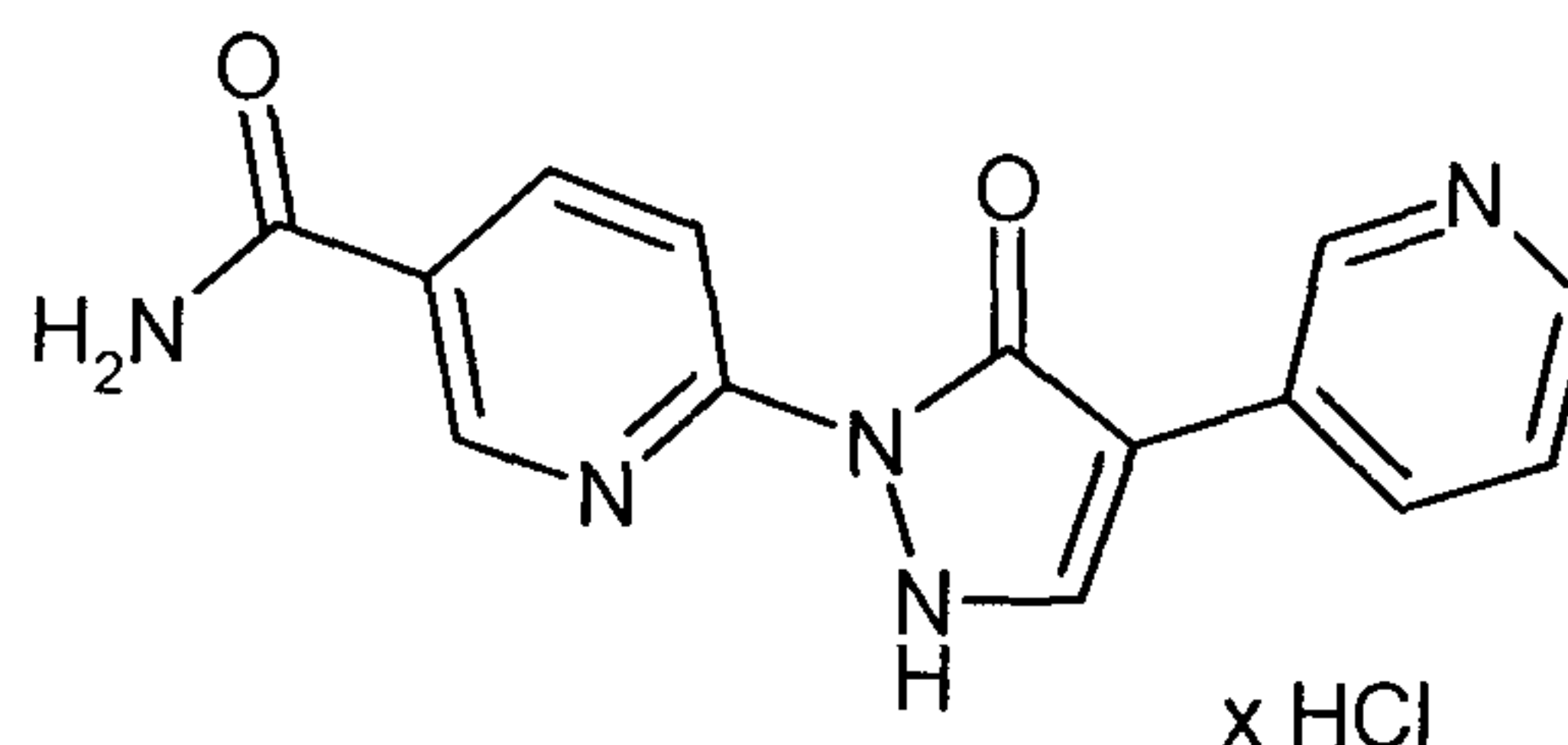
6-(5-Oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carbonyl chloride



2.5 g (8.9 mmol) of 6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carboxylic acid [WO 2006/114213, Example 39] are initially charged in 50 ml of dichloromethane. With stirring, 0.1 ml of DMF and then slowly 2.2 g (17.7 mmol) of oxalyl chloride are added at RT. After the evolution of gas has ceased, the mixture is stirred under reflux for 1 h. The mixture is then concentrated on a rotary evaporator, the residue is dried under high vacuum and the acid chloride obtained in this manner is used directly for the subsequent step.

15 Step b):

6-(5-Oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carboxamide hydrochloride



337 mg (1.0 mmol) of 6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carbonyl chloride are suspended in 5 ml of dioxane. Slowly and with stirring, 4 ml of a 5 N solution of ammonia in dioxane are then added, and the mixture is stirred at RT for 16 h. The mixture is then concentrated, and the residue is taken up in DMSO and purified by preparative HPLC (RP18 column; mobile phase: acetonitrile/ water gradient with 0.1% TFA added to the water). The product-containing fractions are combined and concentrated on a rotary evaporator. The residue is dissolved in 1 N hydrochloric acid, and the solution is then lyophilized.

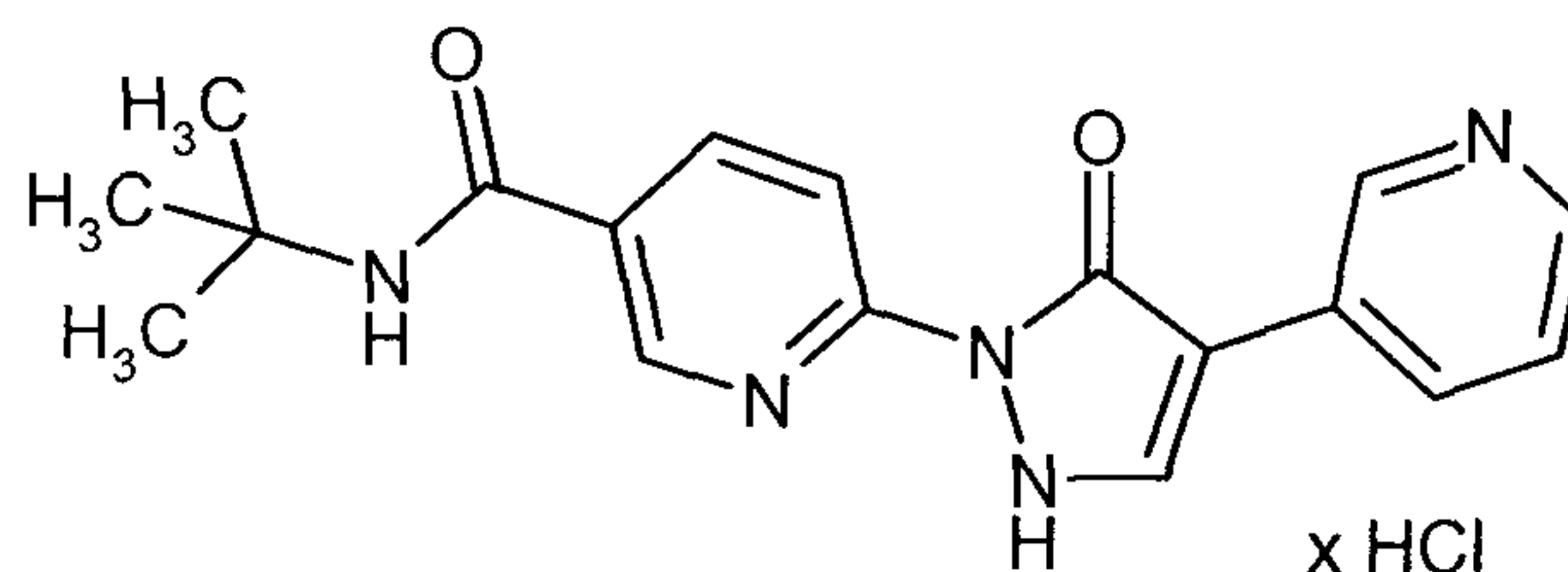
Yield: 47 mg (15% of theory)

LC-MS (Method 1): $R_t = 2.01$ min; MS (ESIpos): $m/z = 282$ $[M+H]^+$;

¹H-NMR (400 MHz, DMSO- d_6): $\delta = 9.41$ (s, 1H), 9.00-8.95 (m, 2H), 8.48 (s, 1H), 8.65 (d, 1H), 8.56-8.42 (m, 2H), 8.23 (s, 1H), 8.03 (t, 1H), 7.63 (s, 1H).

Example 18

N-tert-Butyl-6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carboxamide hydrochloride



15

337 mg (1.0 mmol) of 6-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridine-3-carbonyl chloride from Example 17 (Step a) are initially charged, a solution of 293 mg (4.0 mmol) of *tert*-butylamine in 15 ml of THF is added and the mixture is stirred at RT for 1 h. The mixture is then concentrated on a rotary evaporator, and the residue is purified by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with 0.1% TFA added to the water). The product-containing fractions are combined and concentrated. The residue is dissolved in 1 N hydrochloric acid, and the solution is then lyophilized.

Yield: 47 mg (12% of theory)

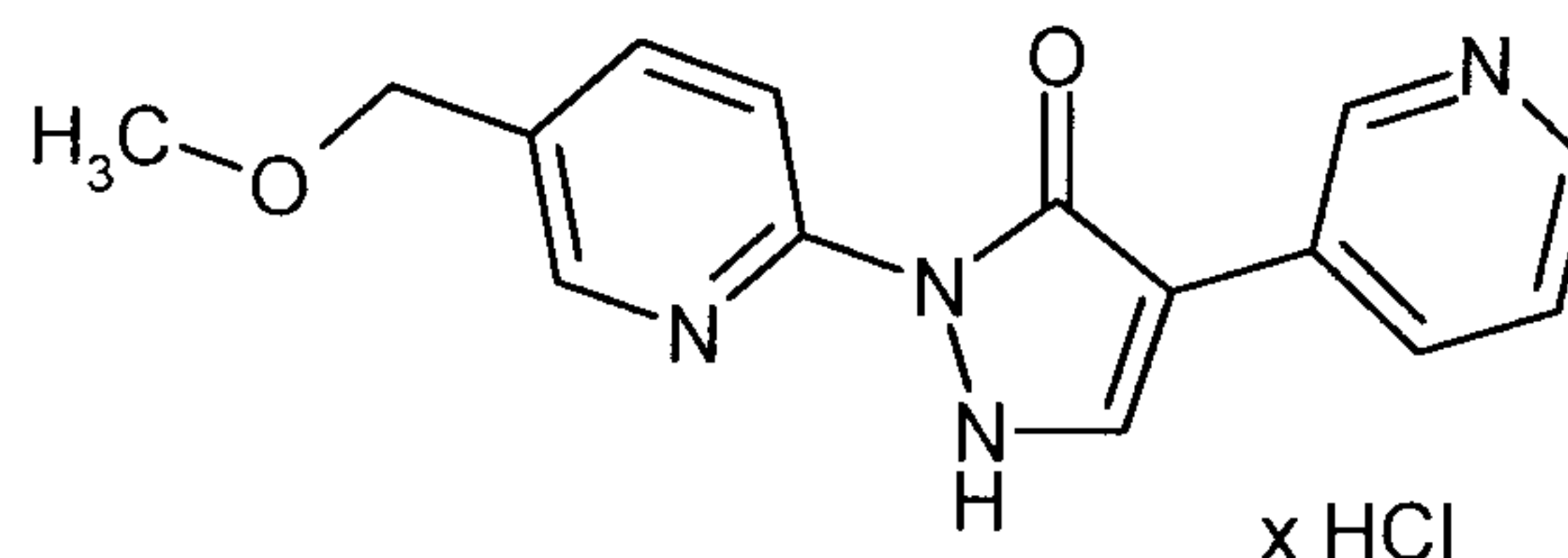
LC-MS (Method 1): $R_t = 2.50$ min; MS (ESIpos): $m/z = 338$ $[M+H]^+$;

¹H-NMR (400 MHz, DMSO- d_6): $\delta = 9.41$ (s, 1H), 8.99 (d, 1H), 8.88 (s, 2H), 8.64 (d, 1H), 8.51-8.39 (m, 2H), 8.09 (s, 1H), 8.03 (t, 1H), 1.40 (s, 9H).

25

Example 19

2-[5-(Methoxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one hydrochloride



661 mg (3.0 mmol) of the compound from Example 2A and 460 mg (3.0 mmol) of the compound
5 from Example 16A are initially charged in 10 ml of ethanol. 114 mg (0.6 mmol) of p-toluenesulfonic acid are added, and the mixture is stirred under reflux for 16 h. The mixture is allowed to cool to RT, and the solid formed is filtered off and washed once with ethanol (batch 1). The mother liquor is concentrated and the residue is purified by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with 0.1% TFA added to the water) (batch 2). Both
10 batches are combined and dissolved in 1 N hydrochloric acid, and the solution is then lyophilized.

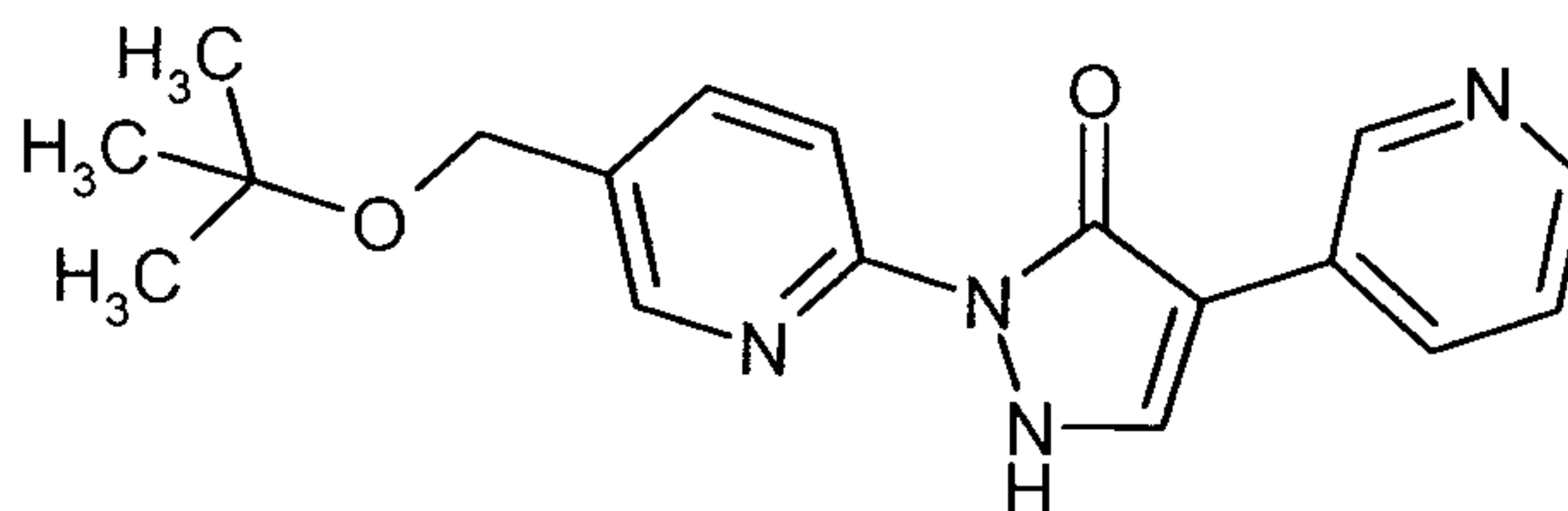
Yield: 625 mg (65% of theory)

LC-MS (Method 7): $R_t = 1.08$ min; MS (ESIpos): $m/z = 283$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.41$ (s, 1H), 9.01 (d, 1H), 8.80 (s, 1H), 8.65 (d, 1H), 8.44 (d, 1H), 8.40 (d, 1H), 8.06-8.04 (m, 2H), 4.50 (s, 2H), 3.34 (s, 3H).

15 **Example 20**

2-[5-(*tert*-Butoxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one



661 mg (3.0 mmol) of the compound from Example 2A and 586 mg (3.0 mmol) of the compound
from Example 17A are initially charged in 10 ml of ethanol. 114 mg (0.6 mmol) of p-toluene-
20 sulfonic acid are added, and the mixture is stirred under reflux for 16 h. The mixture is then allowed to cool to RT, and the solid formed is filtered off, washed once with ethanol and dried under high vacuum. The solid is then stirred in *tert*-butyl methyl ether for 30 min, filtered off again and dried under high vacuum (batch 1). The filtrates and wash solutions obtained beforehand are

combined and concentrated, and the residue is stirred in saturated sodium bicarbonate solution. The solid obtained is filtered off and washed once with water, and the filter residue is then purified by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with addition of 0.1% TFA to the water). The product fractions are combined and concentrated (batch 2).

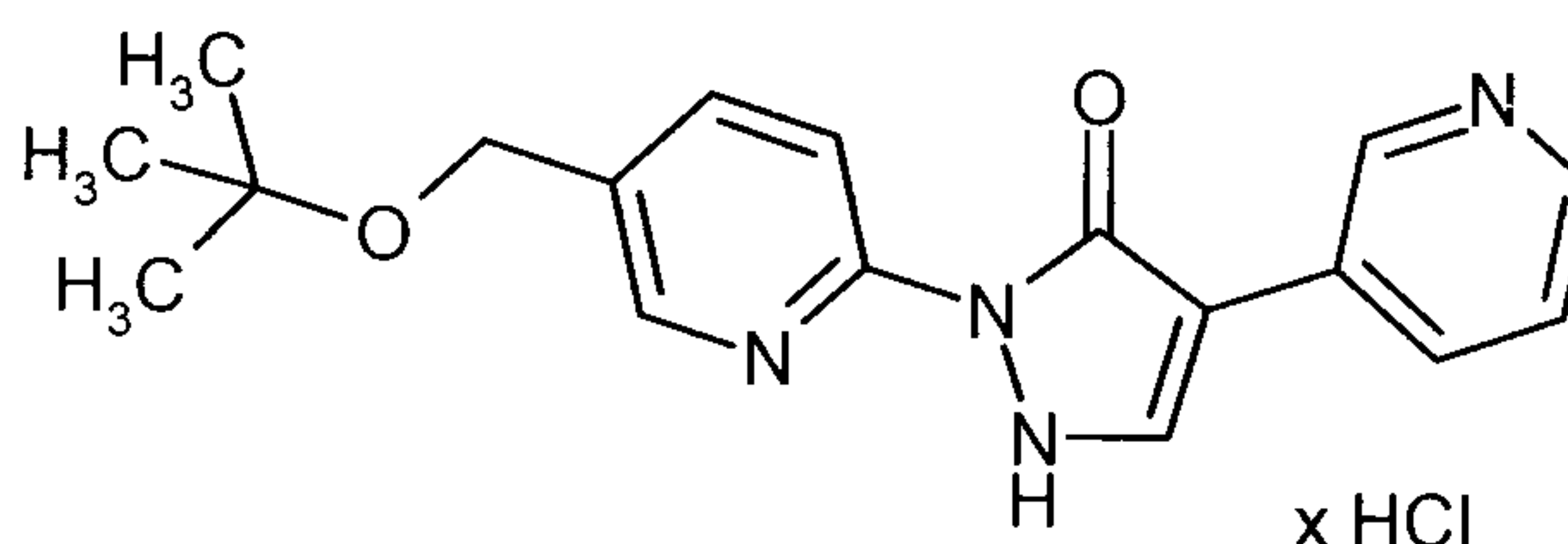
5 Yield: together 487 mg (50% of theory)

LC-MS (Method 5): $R_t = 0.82$ min; MS (ESIpos): $m/z = 325$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.08$ (s, 1H), 8.41 (s, 2H), 8.37 (d, 1H), 8.24 (d, 2H), 7.98 (d, 1H), 8.38 (dd, 1H), 4.49 (s, 2H), 1.25 (s, 9H).

Example 21

10 2-[5-(*tert*-Butoxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3*H*-pyrazol-3-one hydrochloride



400 mg (1.2 mmol) of the compound from Example 20 are stirred in 20 ml of a 4 N solution of hydrogen chloride in dioxane at RT for 30 min. The solid is filtered off and dried under high vacuum. It is then dissolved in water, and the solution is lyophilized. The lyophilizate is once more
15 stirred with 10 ml of a 4 N solution of hydrogen chloride in dioxane for 30 min. The solid is filtered off, washed once with *tert*-butyl methyl ether and dried under high vacuum.

Yield: 306 mg (69% of theory)

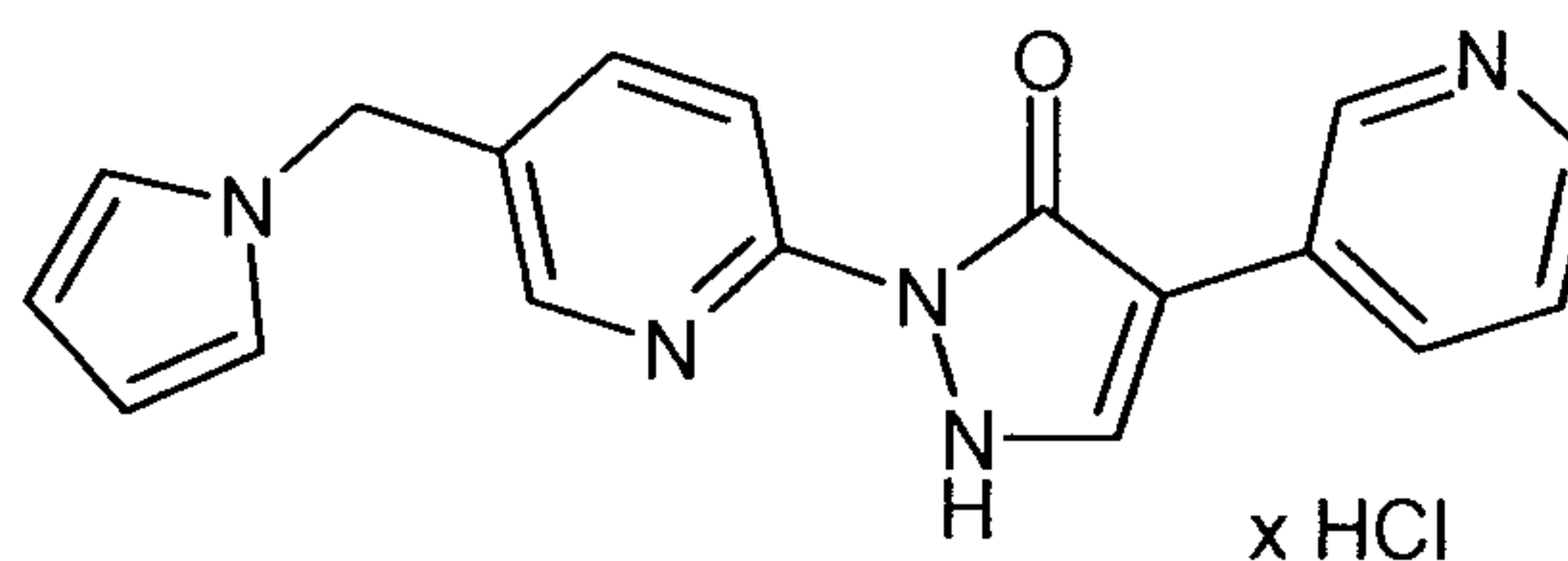
LC-MS (Method 5): $R_t = 0.81$ min; MS (ESIpos): $m/z = 325$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.38$ (s, 1H), 8.94 (d, 1H), 8.73 (s, 1H), 8.61 (d, 1H), 8.43 (s,
20 1H), 4.35 (d, 1H), 8.01-7.99 (m, 2H), 4.49 (s, 2H), 1.25 (s, 9H).

Example 22

4-Pyridin-3-yl-2-[5-(1*H*-pyrrol-1-ylmethyl)pyridin-2-yl]-1,2-dihydro-3*H*-pyrazol-3-one hydrochloride

- 75 -



565 mg (9.4 mmol) of acetic acid are initially charged in 0.3 ml of water. 744 mg (9.4 mmol) of pyridine are added slowly. 191 mg (0.6 mmol) of the compound from Example 13 and 74 mg (0.6 mmol) of 2,5-dimethoxytetrahydrofuran are then added, and the mixture is stirred at 100°C for 16 h. The mixture is then concentrated on a rotary evaporator, 3 ml of acetonitrile and 3 ml of 1 N hydrochloric acid are added and the mixture is stirred at RT for 30 min. The solid formed is filtered off, washed once with water and dried under high vacuum.

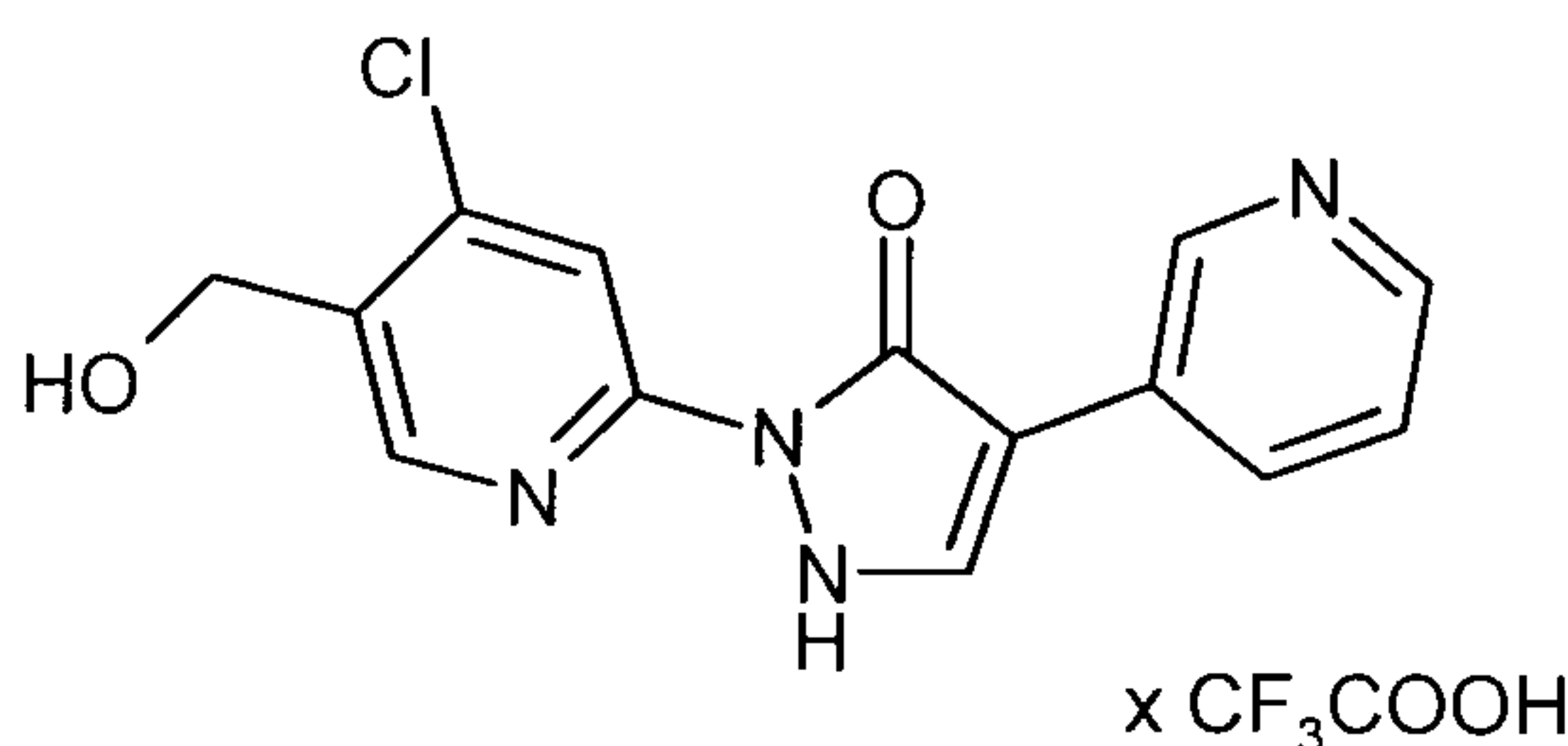
Yield: 150 mg (76% of theory)

LC-MS (Method 5): $R_t = 0.74$ min; MS (ESIpos): $m/z = 318$ $[\text{M}+\text{H}]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.35$ (s, 1H), 8.88 (d, 1H), 8.73 (s, 1H), 8.60 (d, 1H), 8.48 (s, 1H), 8.35 (d, 1H), 7.97-7.86 (m, 2H), 6.90 (s, 2H), 6.05 (s, 2H), 5.70 (s, 2H).

Example 23

2-[4-Chloro-5-(hydroxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one trifluoroacetate



15

345 mg (1.6 mmol) of the compound from 2A, 272 mg (1.6 mmol) of the compound from Example 18A and 60 mg (0.3 mmol) of p-toluenesulfonic acid are initially charged in a mixture of 10 ml of THF and 5 ml of ethanol. The mixture is reacted at 150°C in a single-mode microwave oven (CEM Explorer) for 3 h. The mixture is then concentrated on a rotary evaporator, and the residue is taken up in a mixture of 5 ml of methanol and 4 ml of 1 N hydrochloric acid. The product is purified twice successively by preparative HPLC (RP18 column; mobile phase: acetonitrile/water gradient with addition of 0.1% TFA to the water).

20

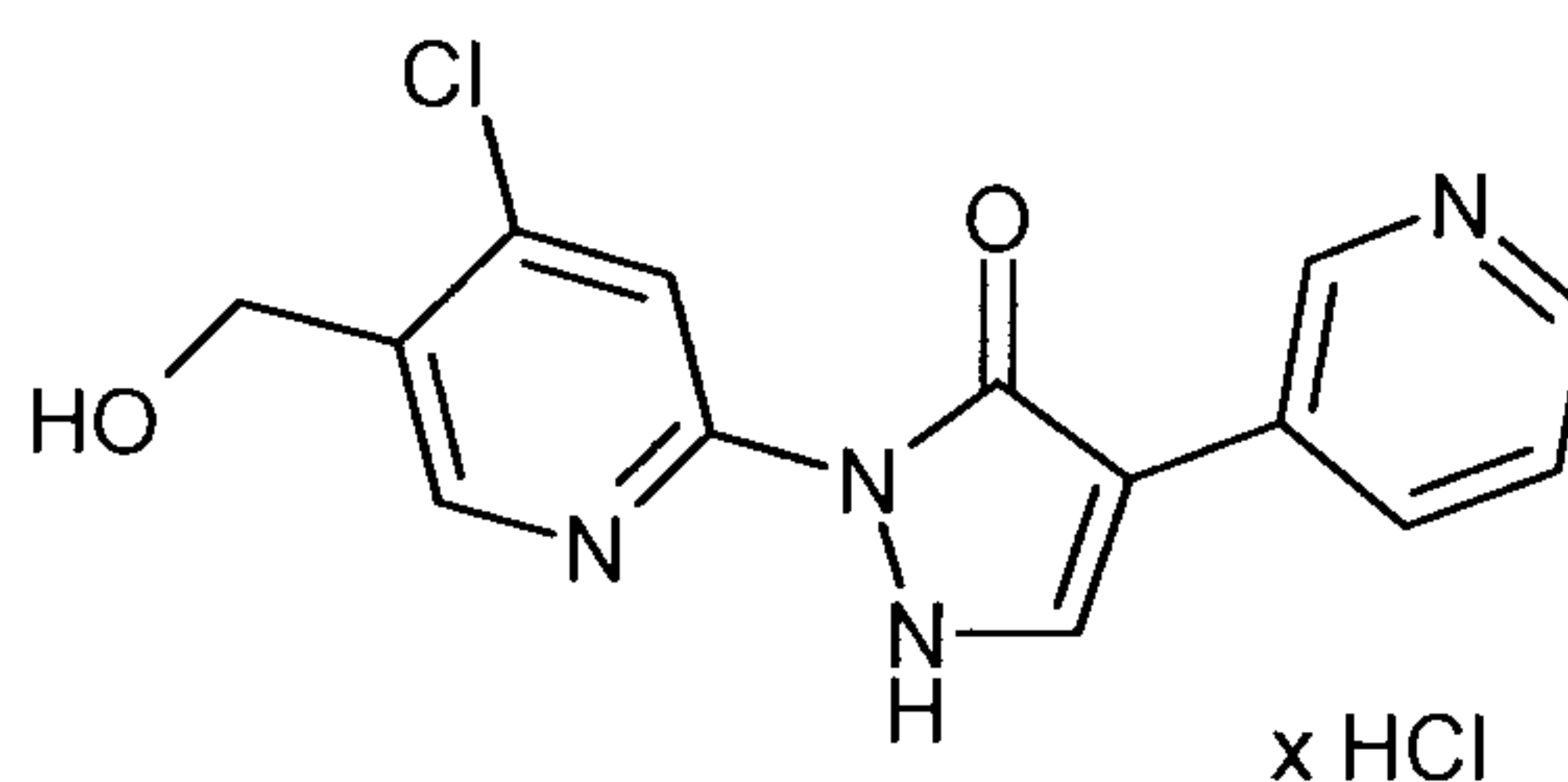
Yield: 16 mg (2% of theory)

LC-MS (Method 6): $R_t = 1.04$ min; MS (ESIpos): $m/z = 303$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.38$ (s, 1H), 8.64 (d, 1H), 8.48 (s, 1H), 8.33 (d, 1H), 8.20 (s, 1H), 7.96 (s, 1H), 7.77 (dd, 1H), 4.57 (s, 2H).

Example 24

- 5 2-[4-Chloro-5-(hydroxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3*H*-pyrazol-3-one
hydrochloride



12 mg (0.03 mmol) of the compound from Example 23 are stirred in 1.5 ml of a 4 N solution of
hydrogen chloride in dioxane for 30 min. The mixture is then decanted, the residue is stirred in
10 *tert*-butyl methyl ether and decanted off again, and the solid that remains is initially air-dried and
then dried under high vacuum.

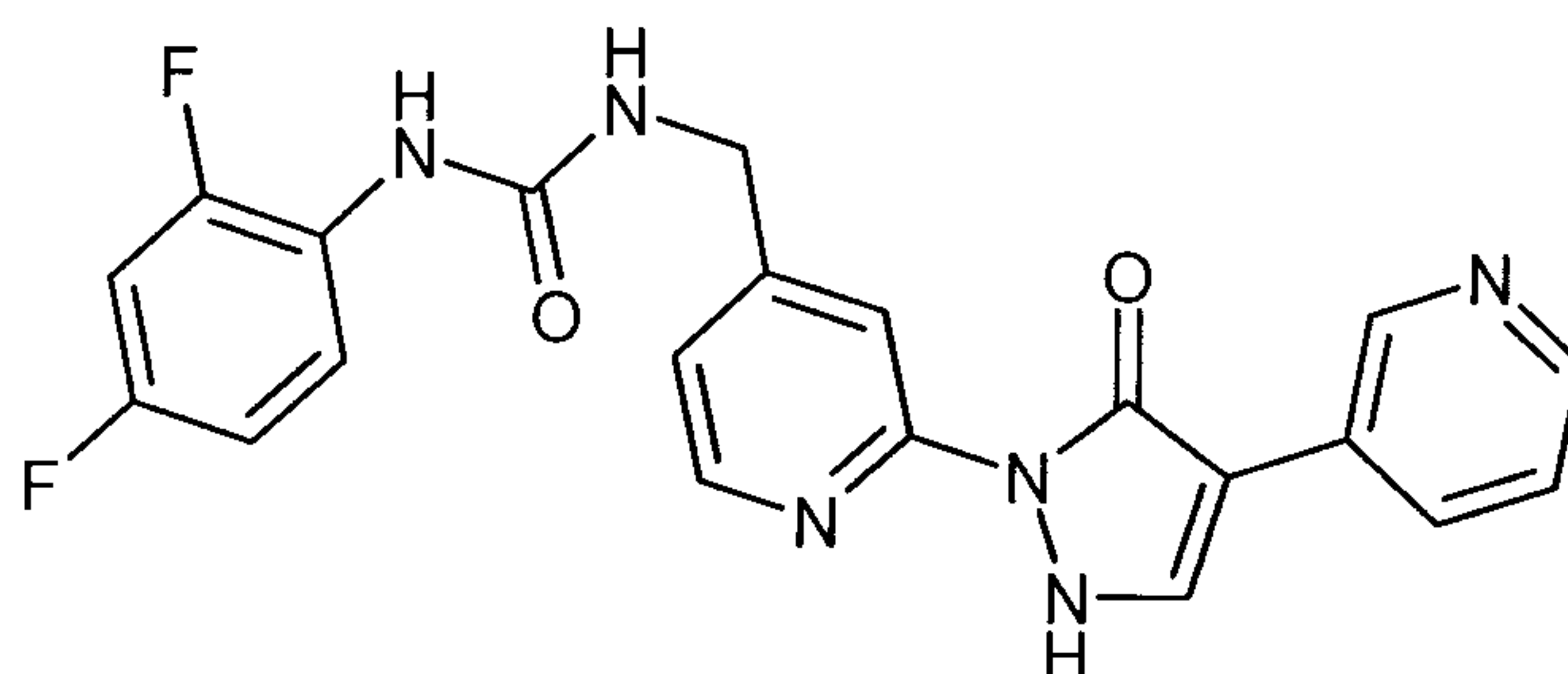
Yield: 10 mg (95% of theory)

LC-MS (Method 6): $R_t = 1.06$ min; MS (ESIpos): $m/z = 303$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.31$ (s, 1H), 8.90 (d, 1H), 8.66 (s, 1H), 8.63 (d, 2H), 8.03
15 (dd, 1H), 7.69 (s, 1H), 4.61 (s, 2H).

Example 25

1-(2,4-Difluorophenyl)-3-{[2-(5-oxo-4-pyridin-3-yl-2,5-dihydro-1*H*-pyrazol-1-yl)pyridin-4-yl]-
methyl}urea



2.7 g (10 mmol) of the compound from Example 4A are dissolved in 60 ml of 1,2-dichloroethane and provided as a stock solution.

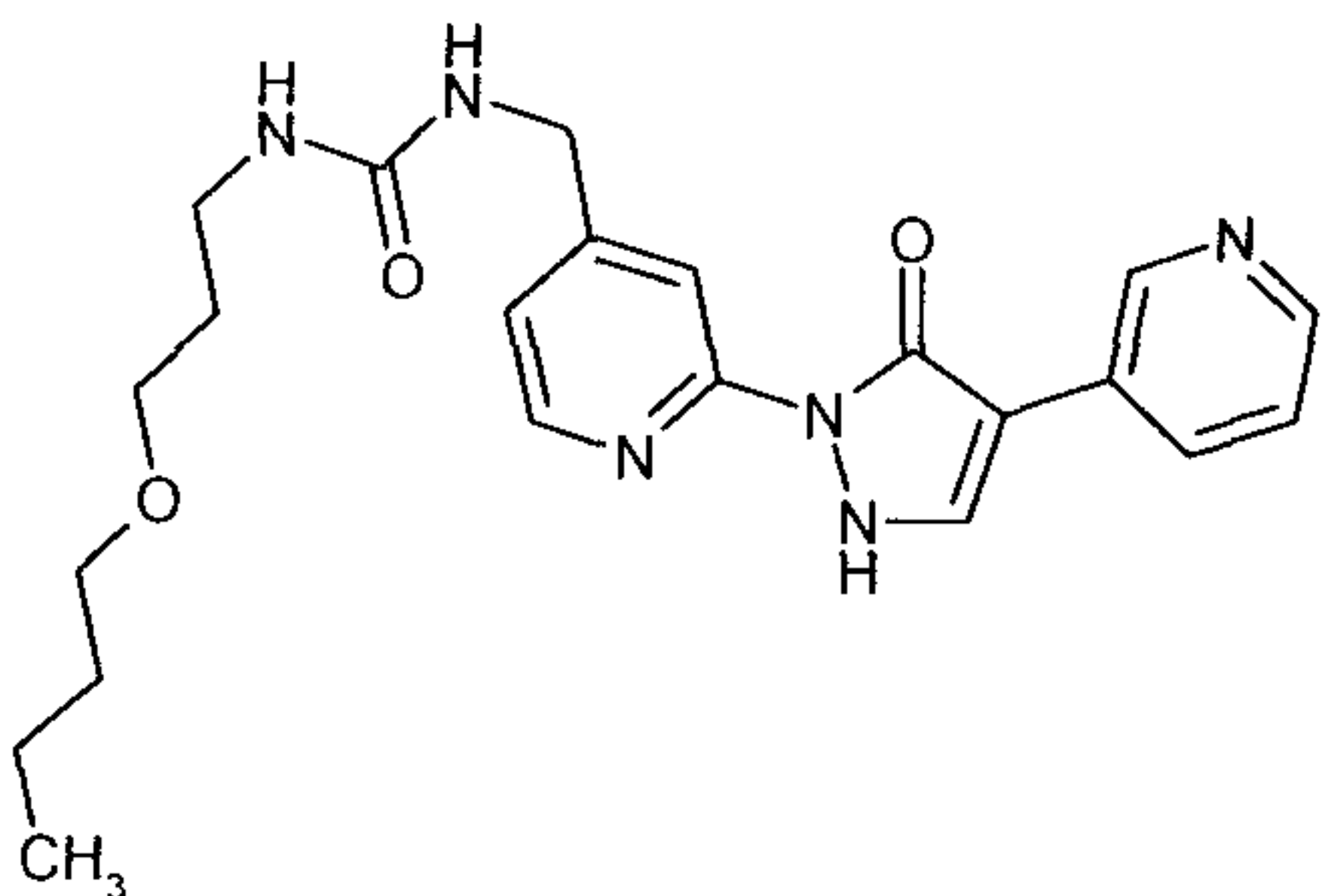
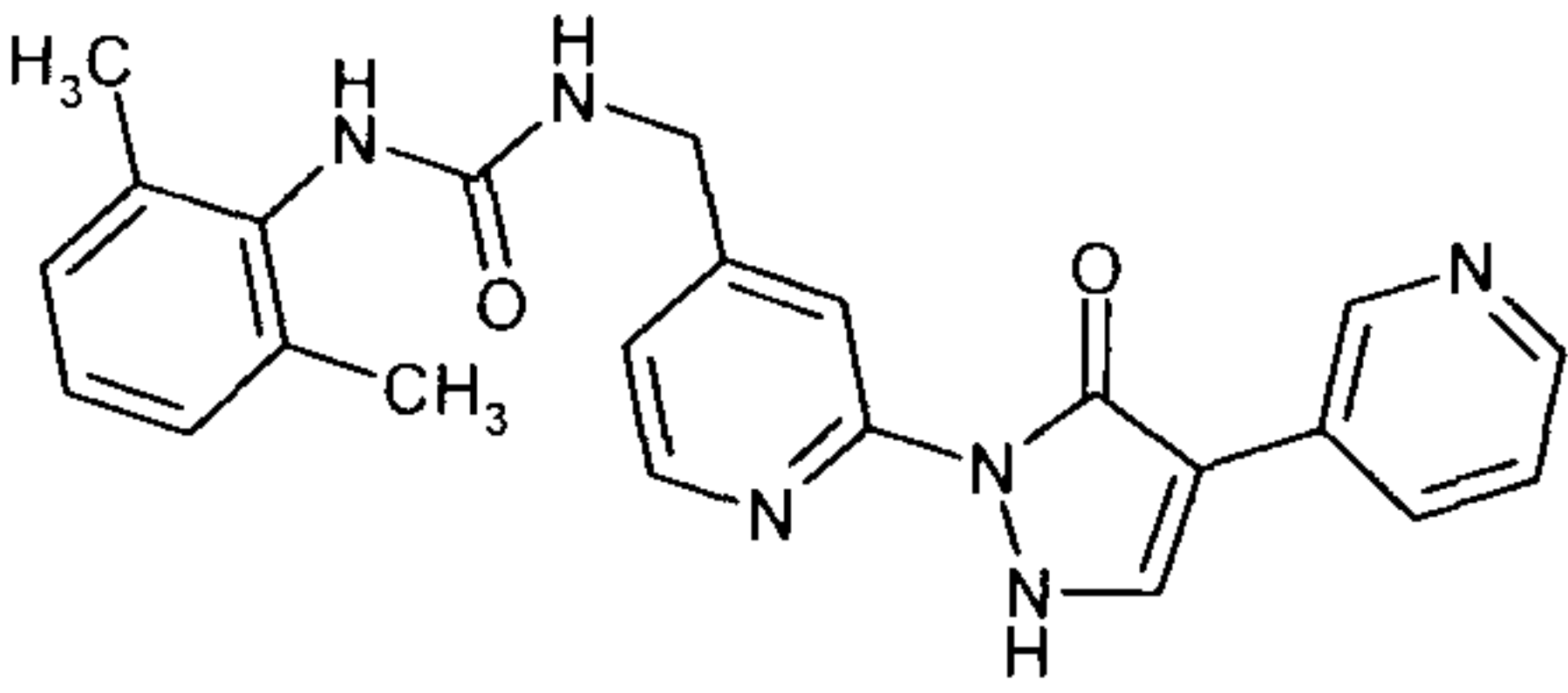
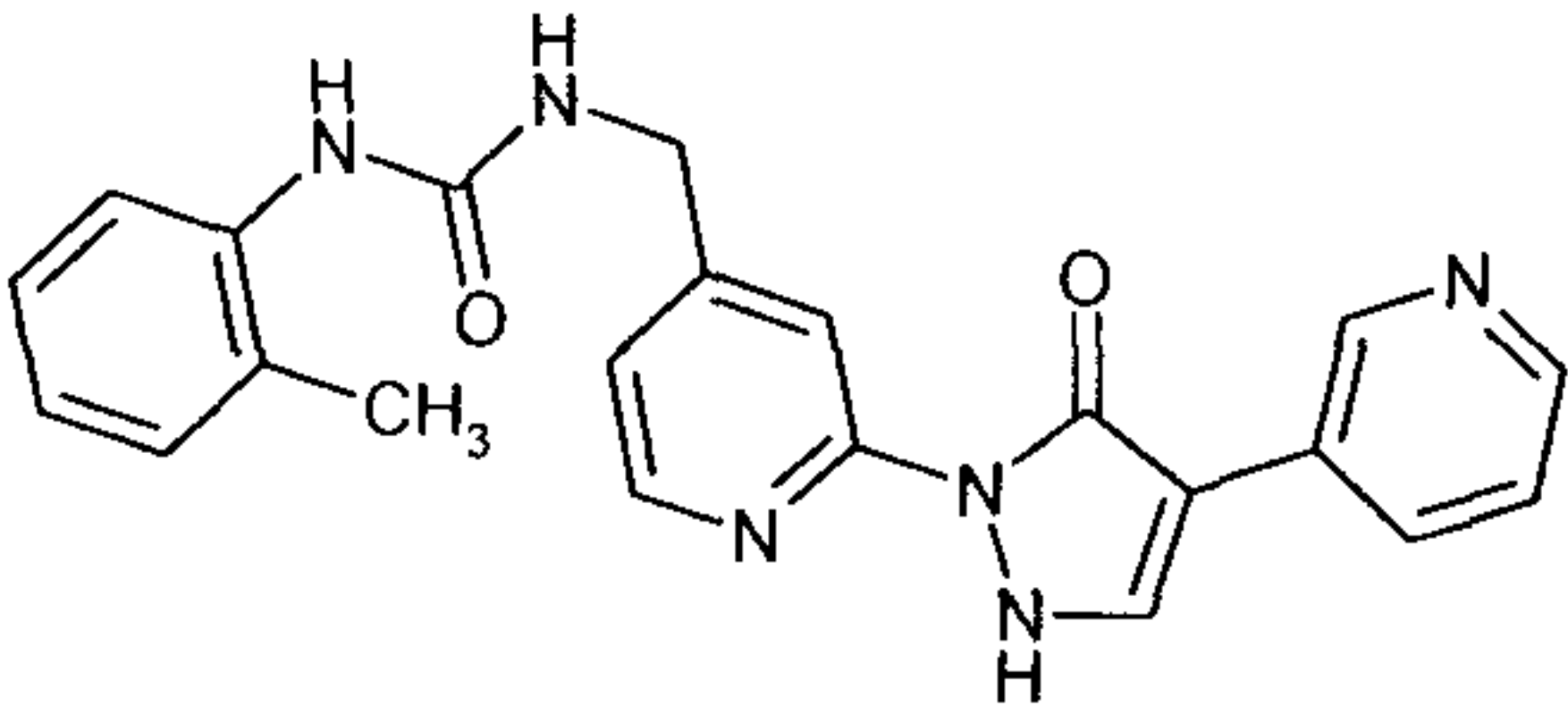
16 mg (0.1 mmol) of 2,4-difluoro-1-isocyanatobenzene are initially charged, and 600 μ l (0.1 mmol) of the above stock solution and 26 mg (0.2 mmol) of *N,N*-diisopropylethylamine (Hünig base) are added. The reaction mixture is stirred at RT for 16 h. For work-up, the solvent is removed under reduced pressure, the residue is taken up in DMSO and filtered and the filtrate is purified directly by preparative LC-MS (Method 8). The product fractions are concentrated under reduced pressure and the residue is dried.

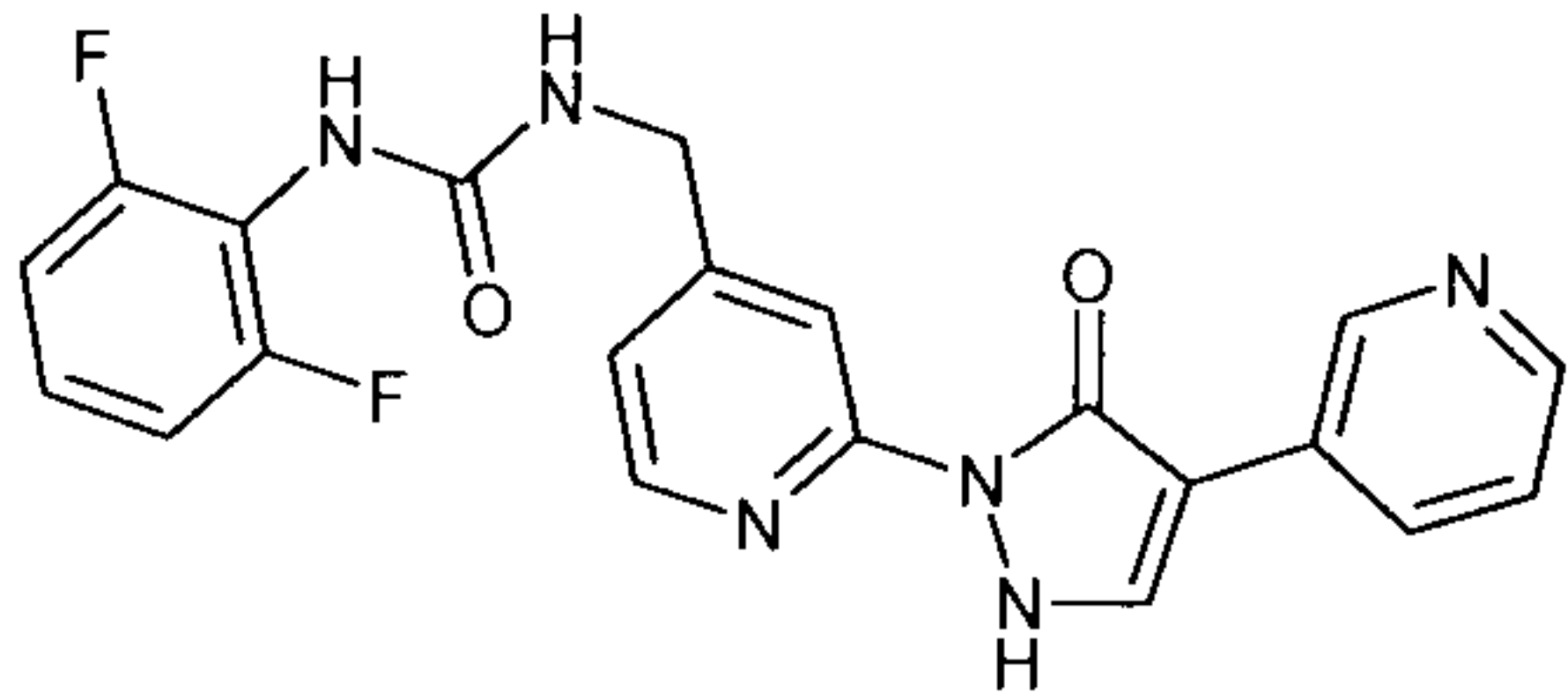
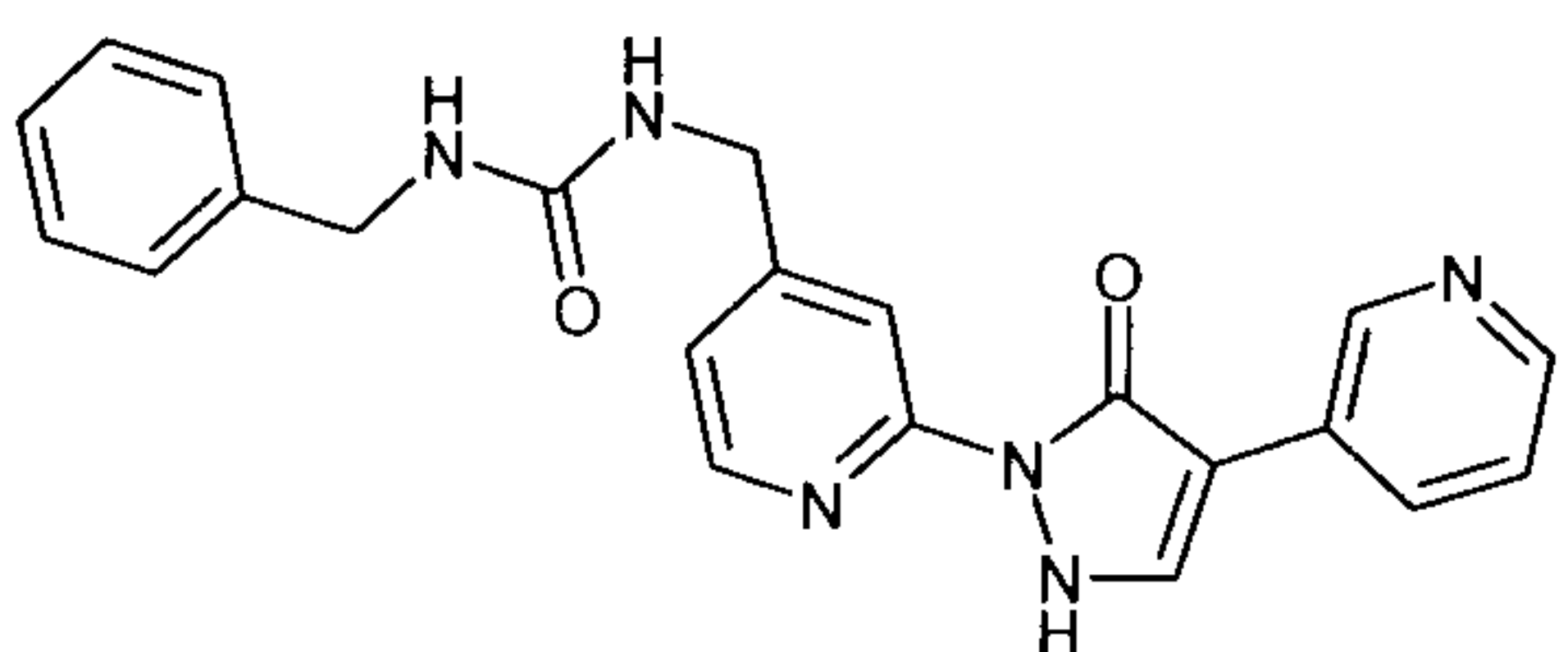
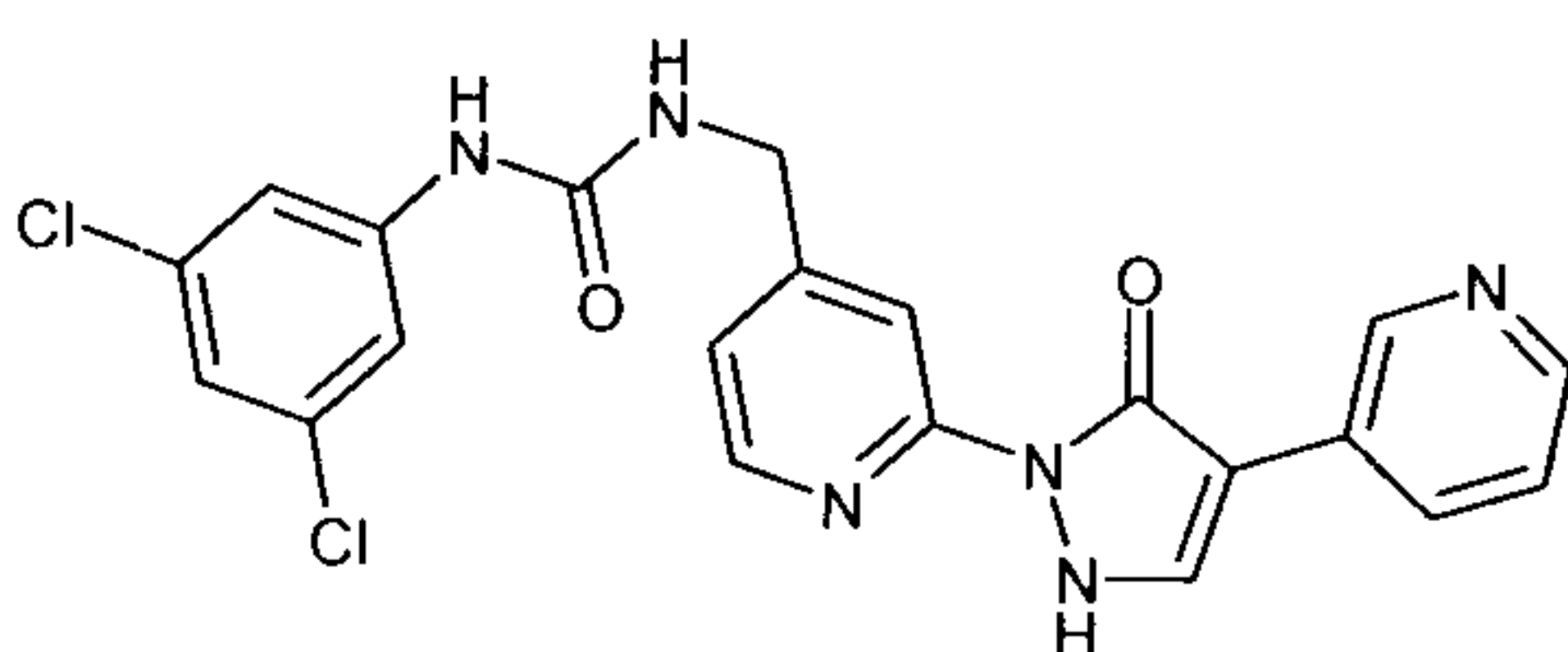
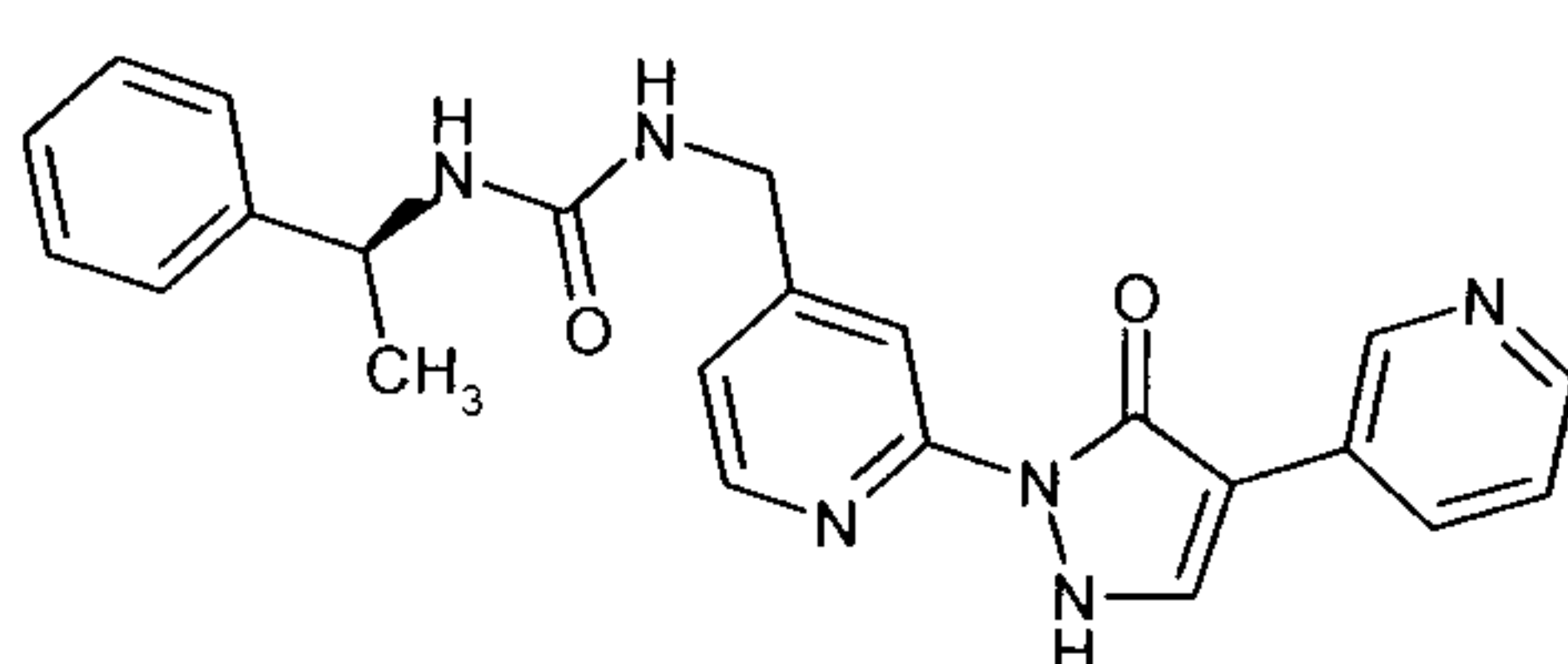
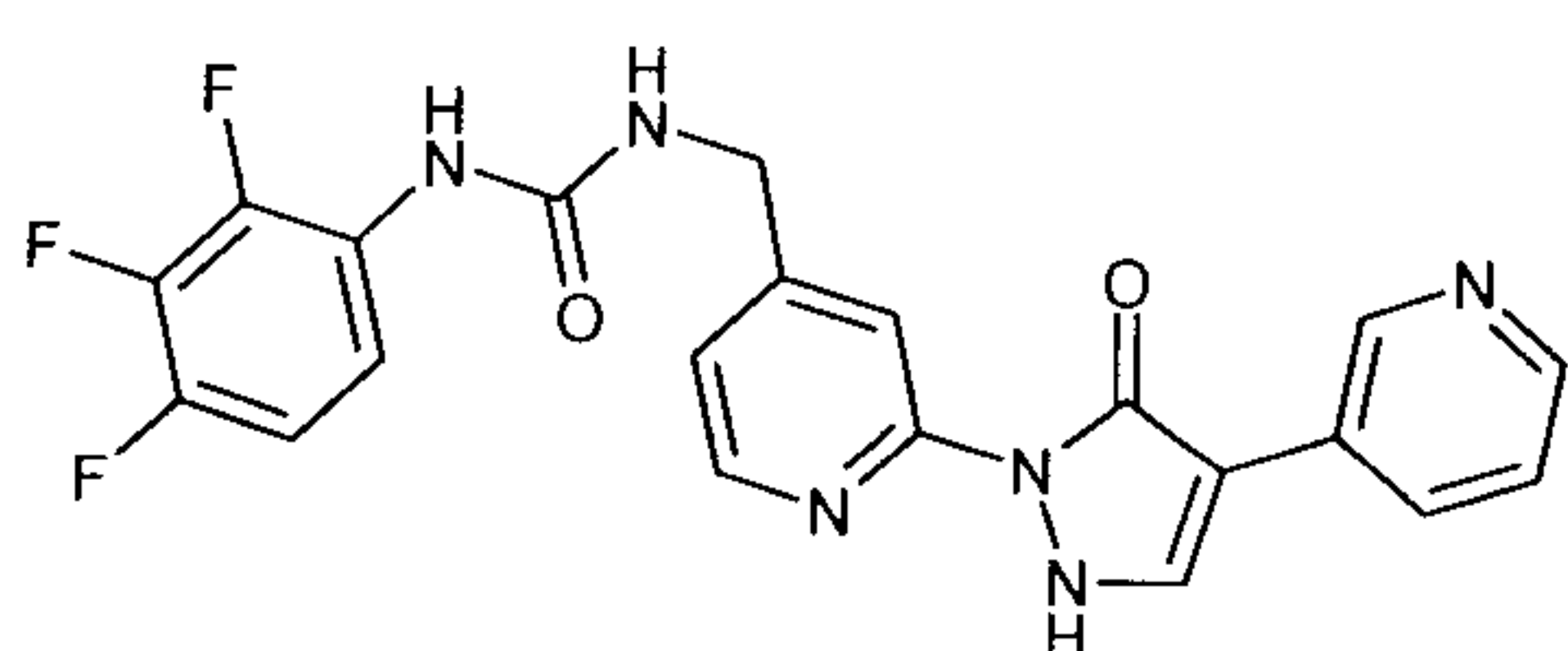
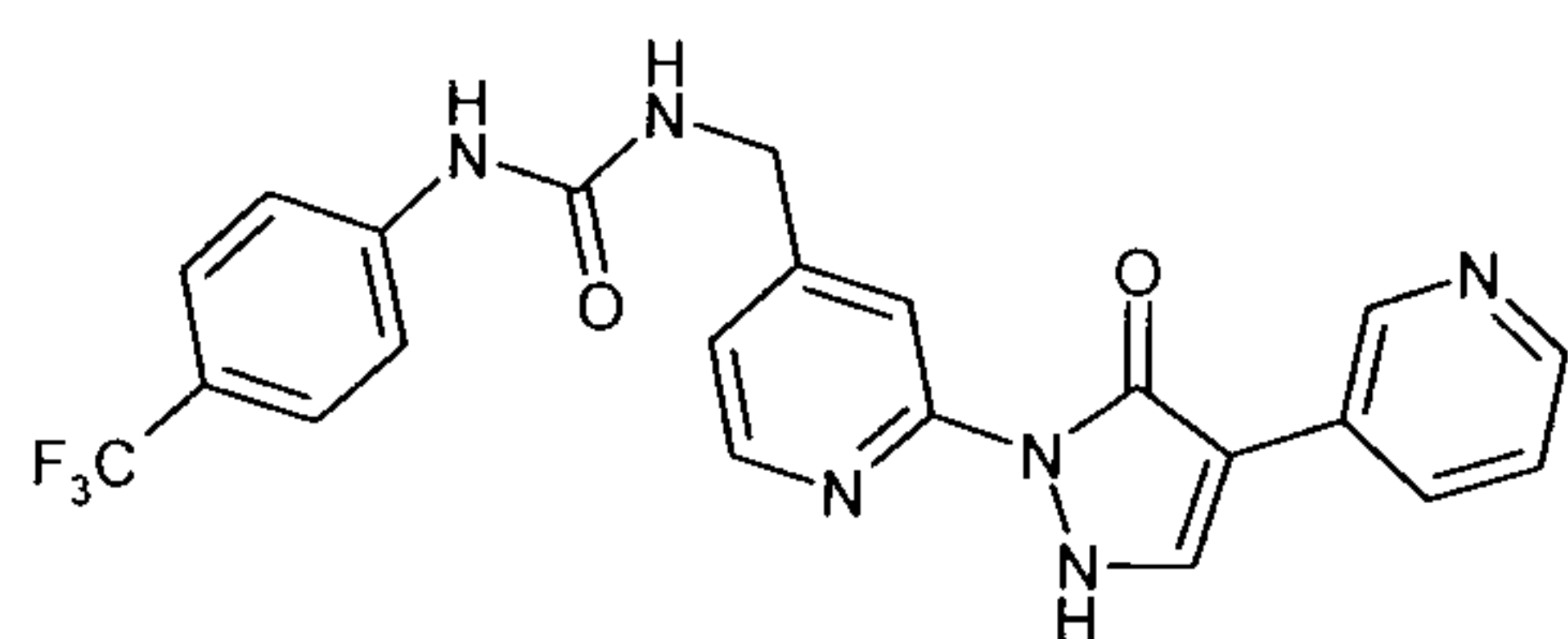
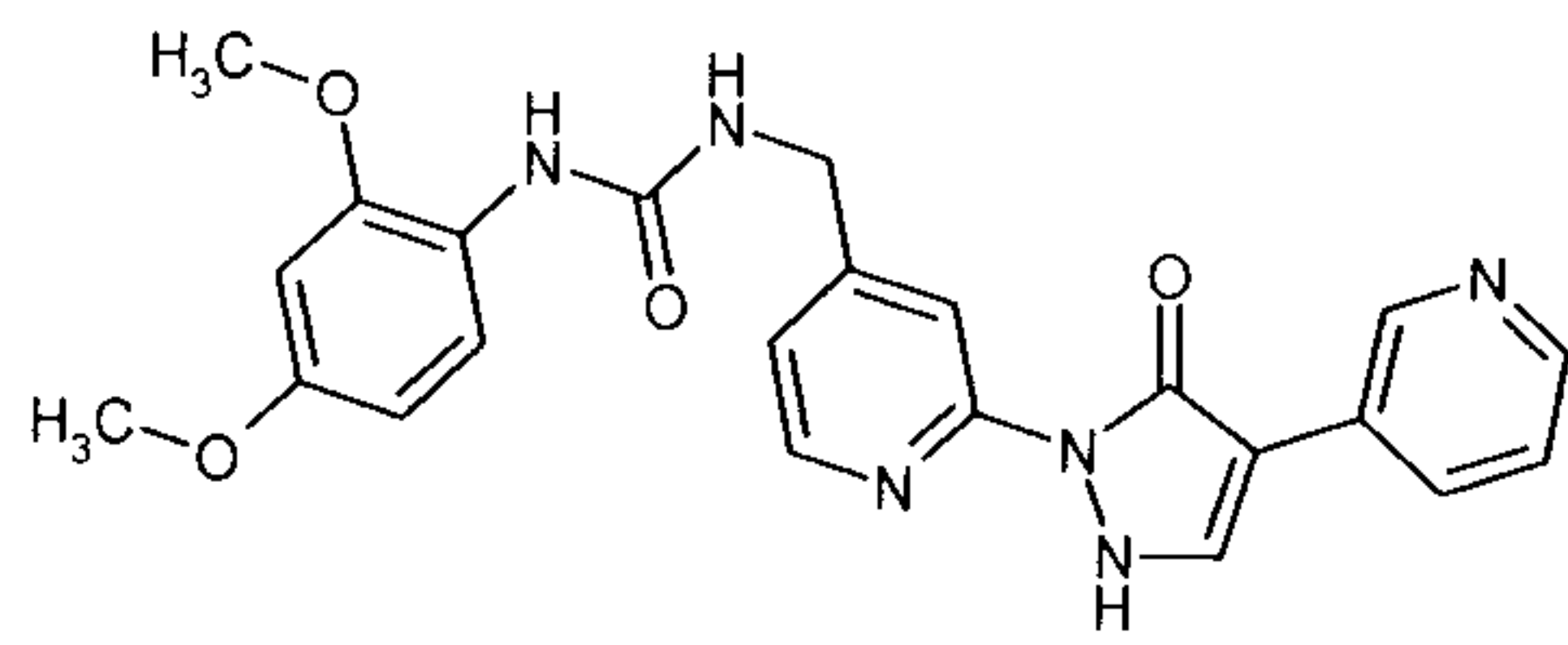
Yield: 3 mg (10% of theory)

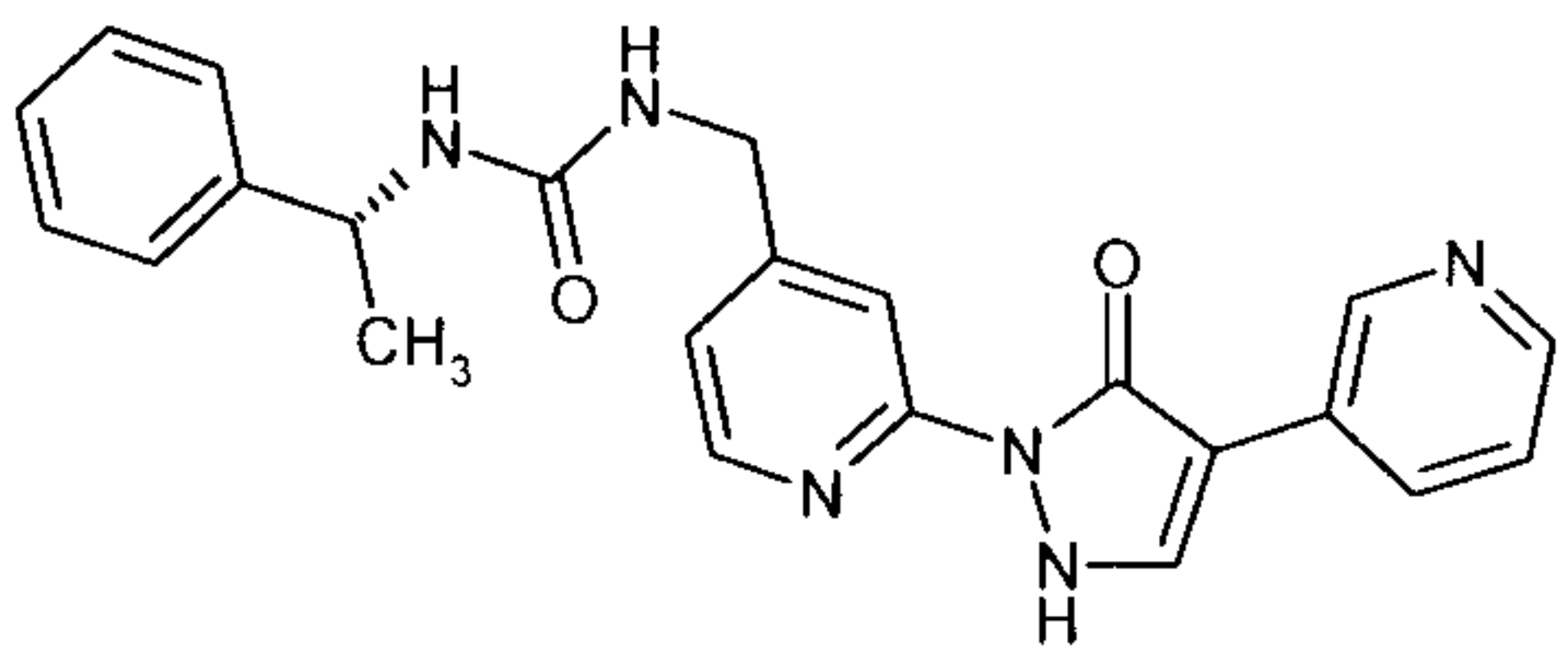
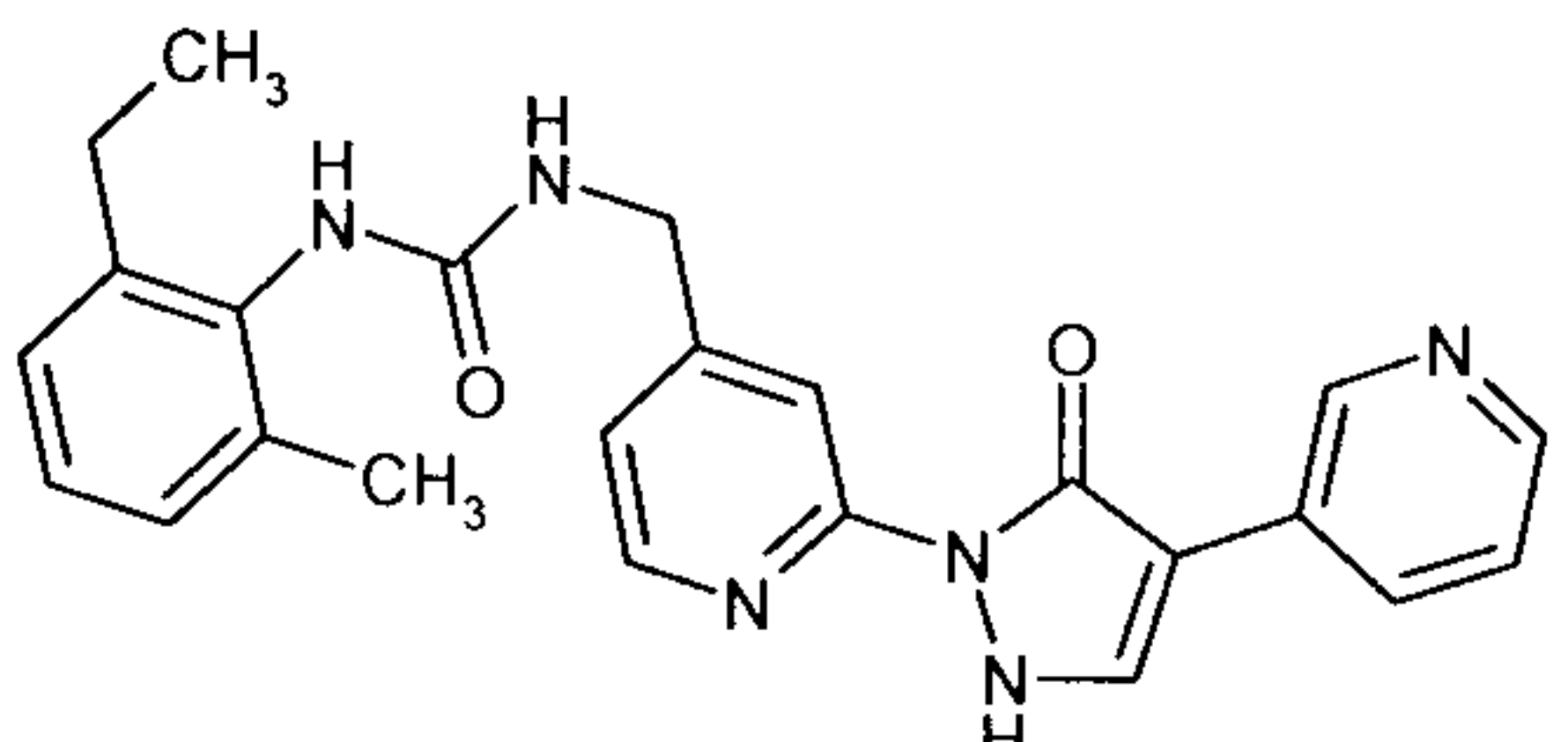
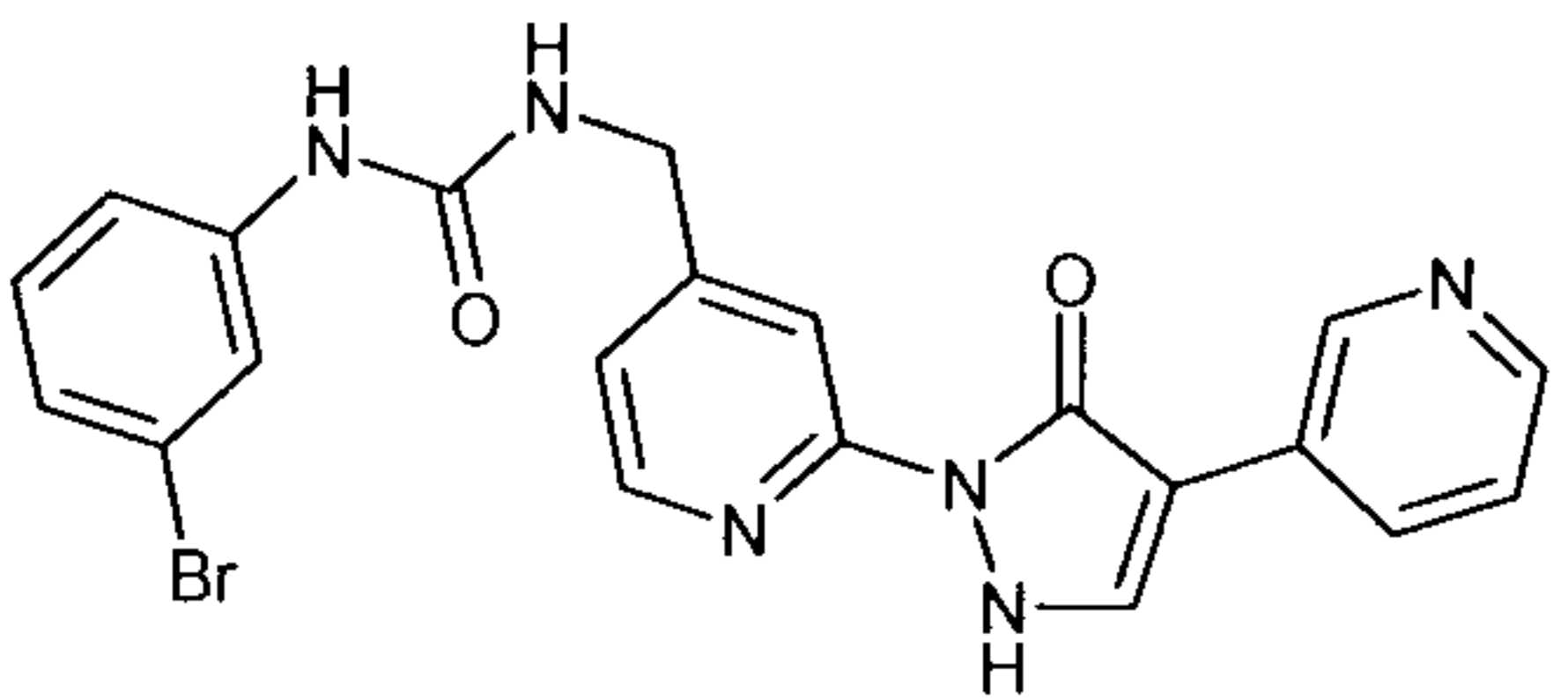
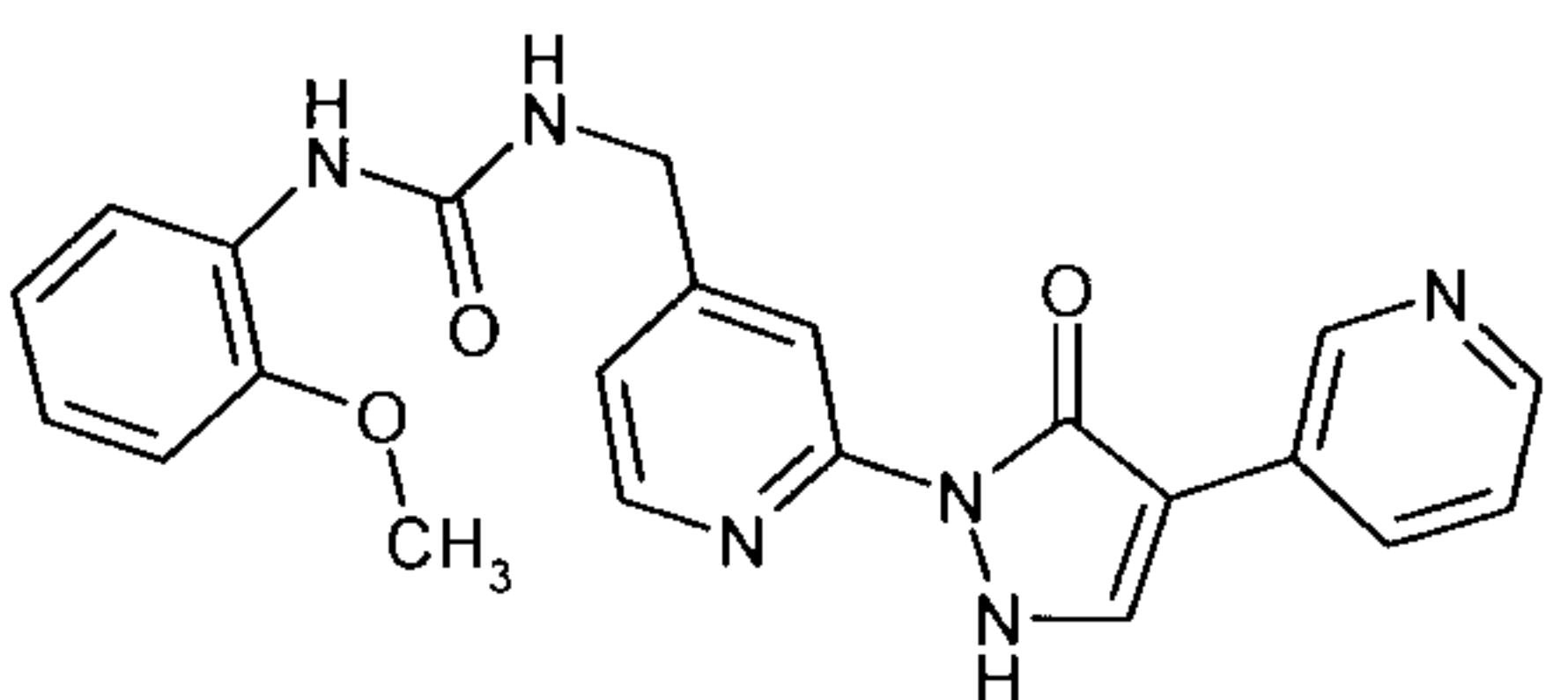
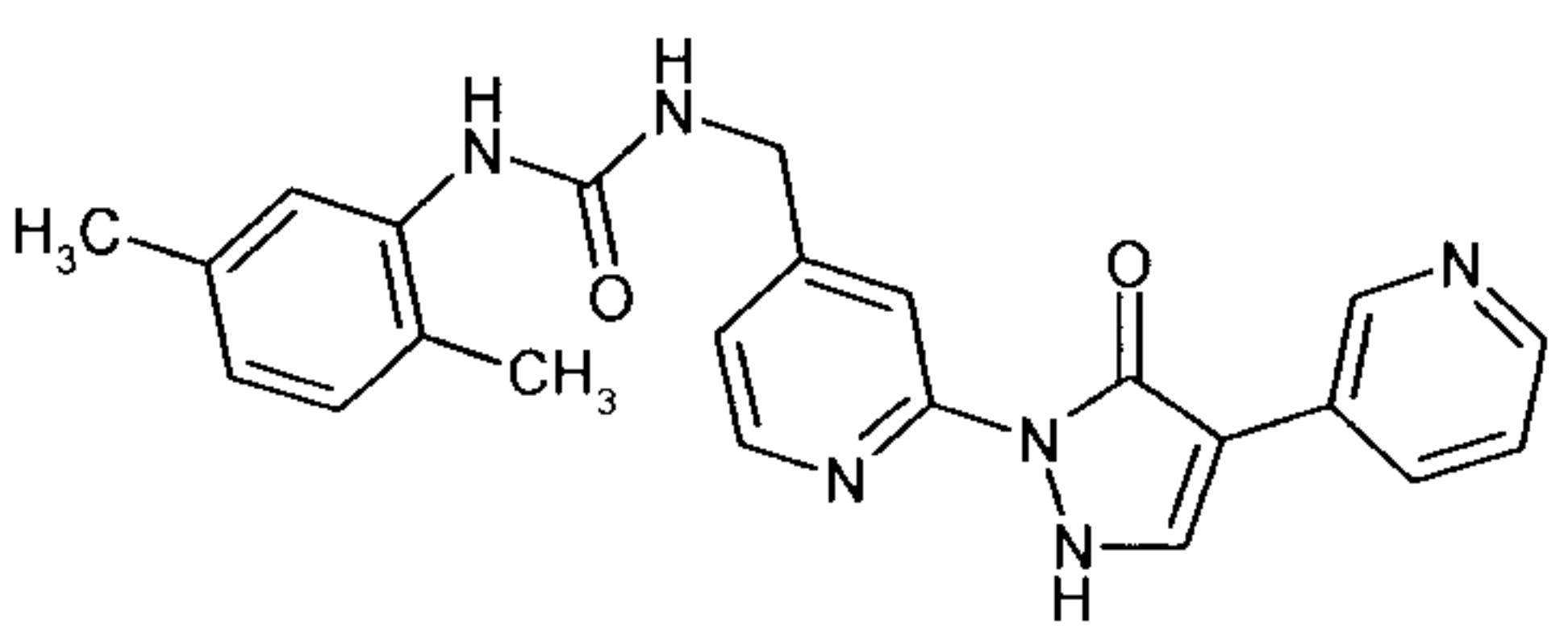
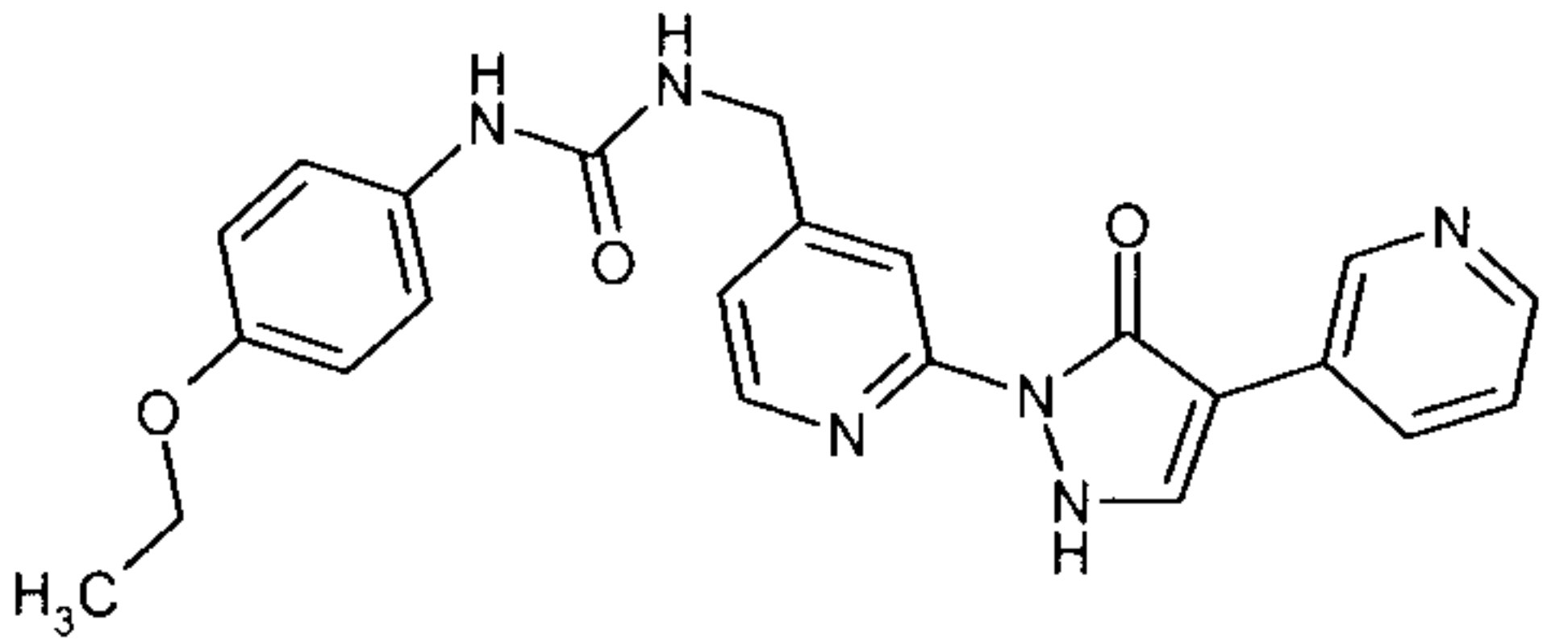
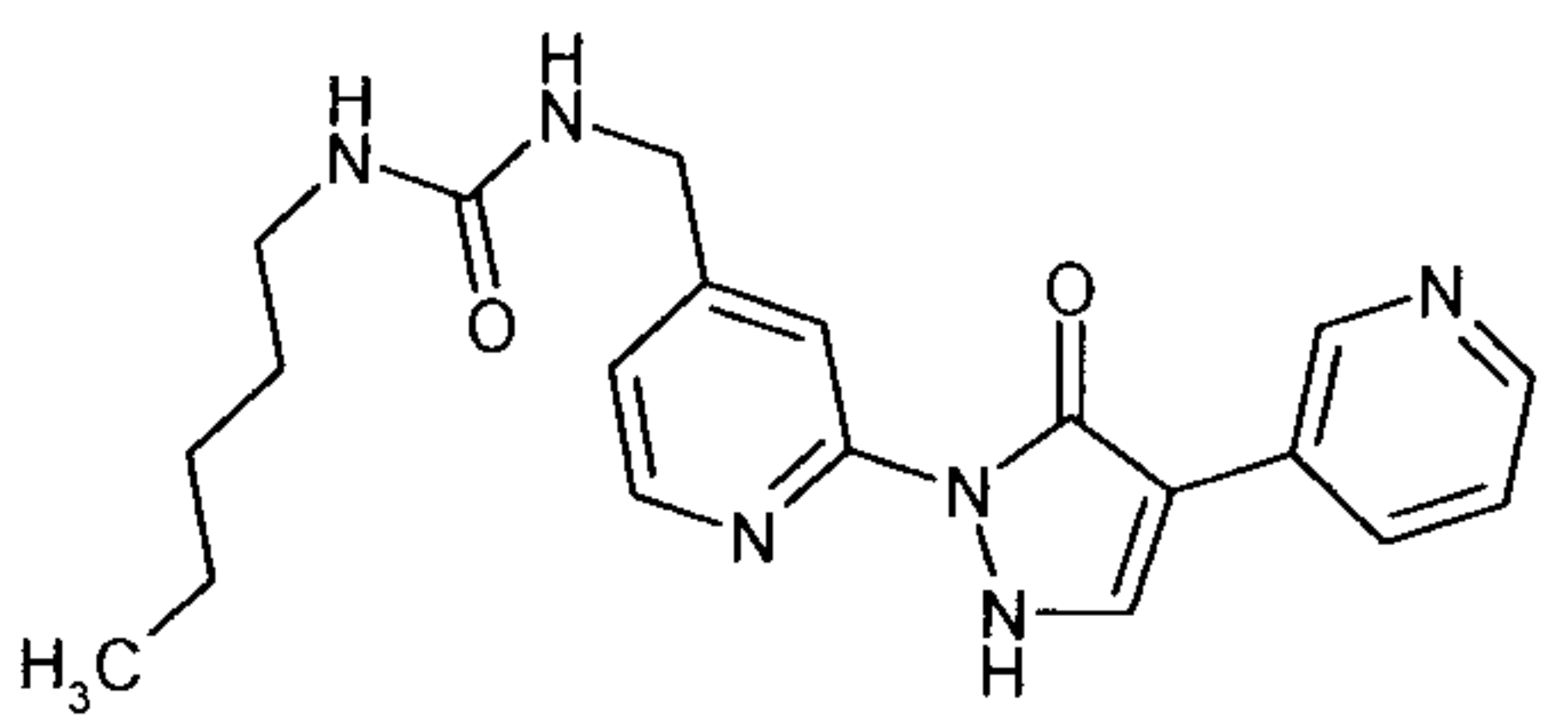
10 LC-MS (Method 8): $R_t = 1.33$ min; MS (ESIpos): $m/z = 423$ $[M+H]^+$.

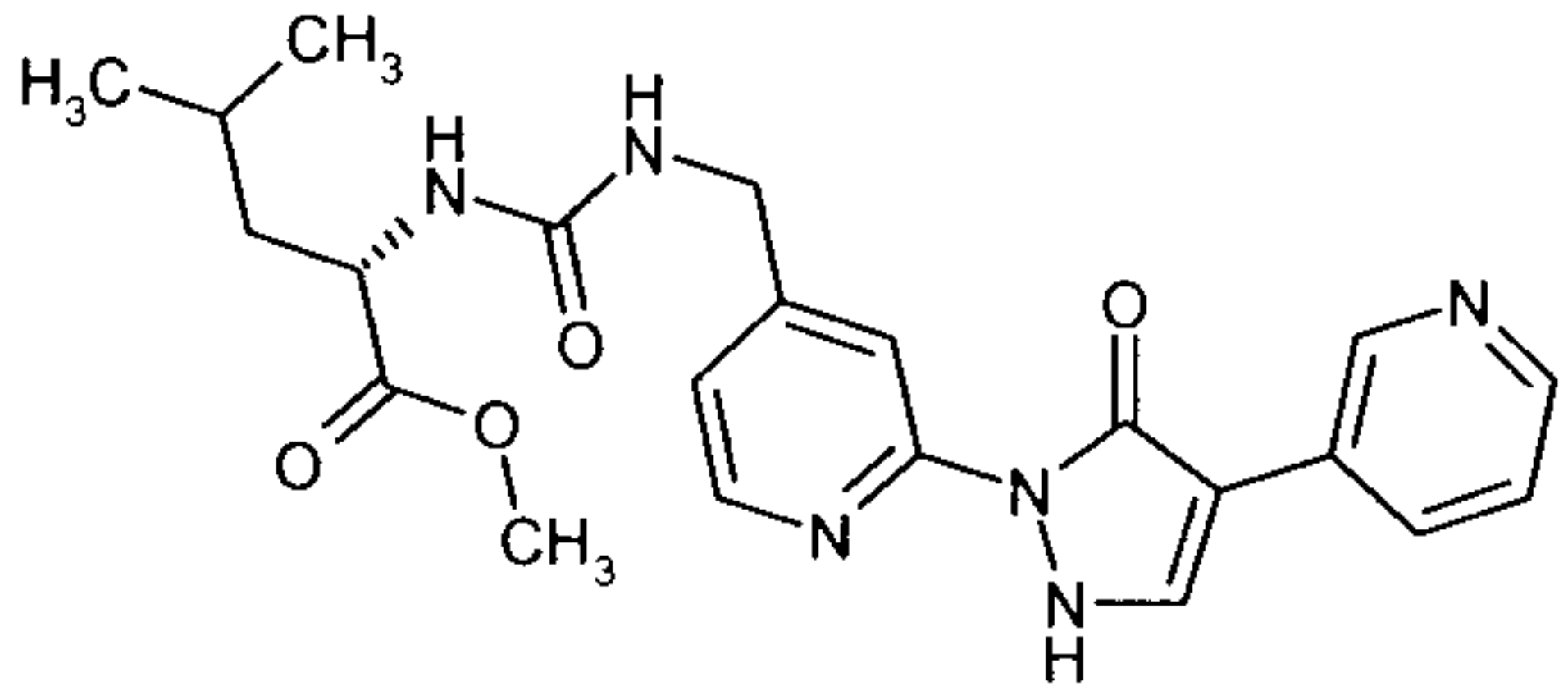
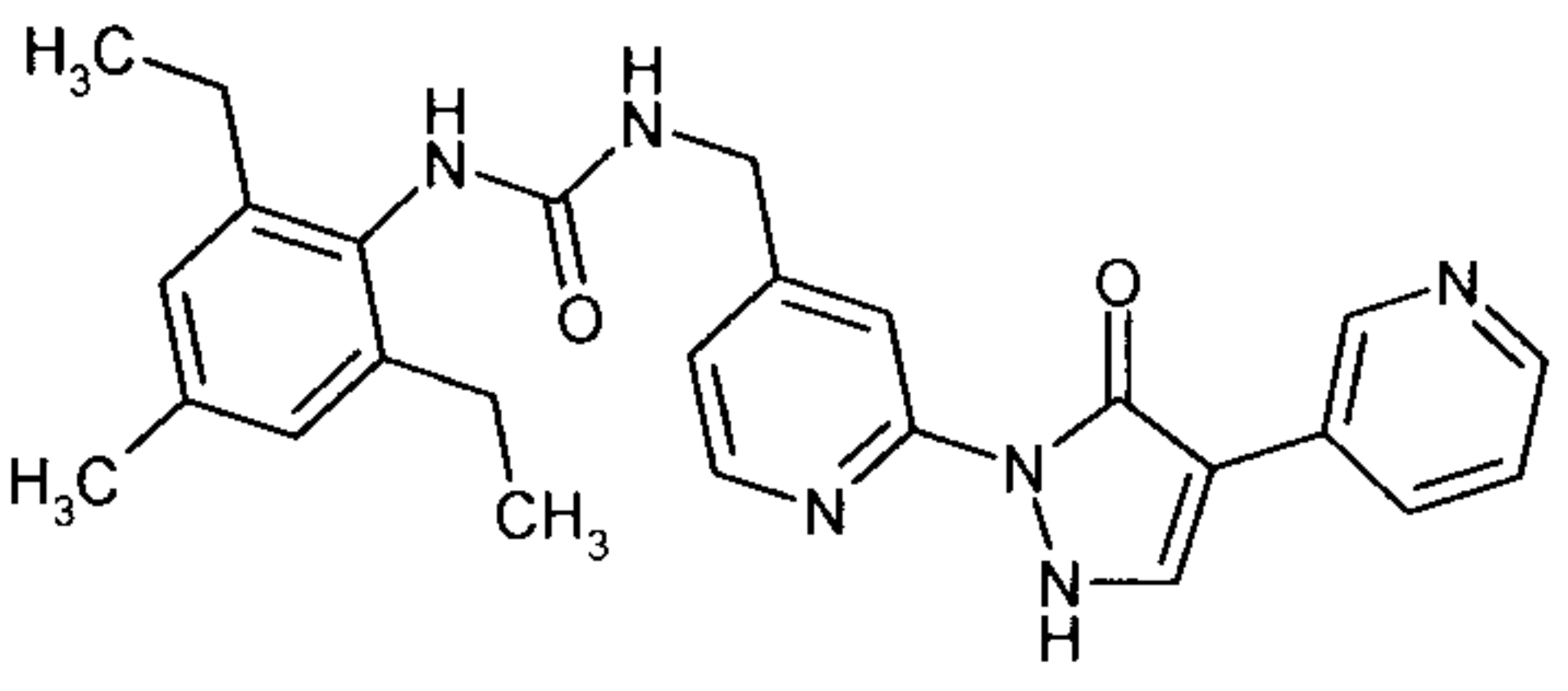
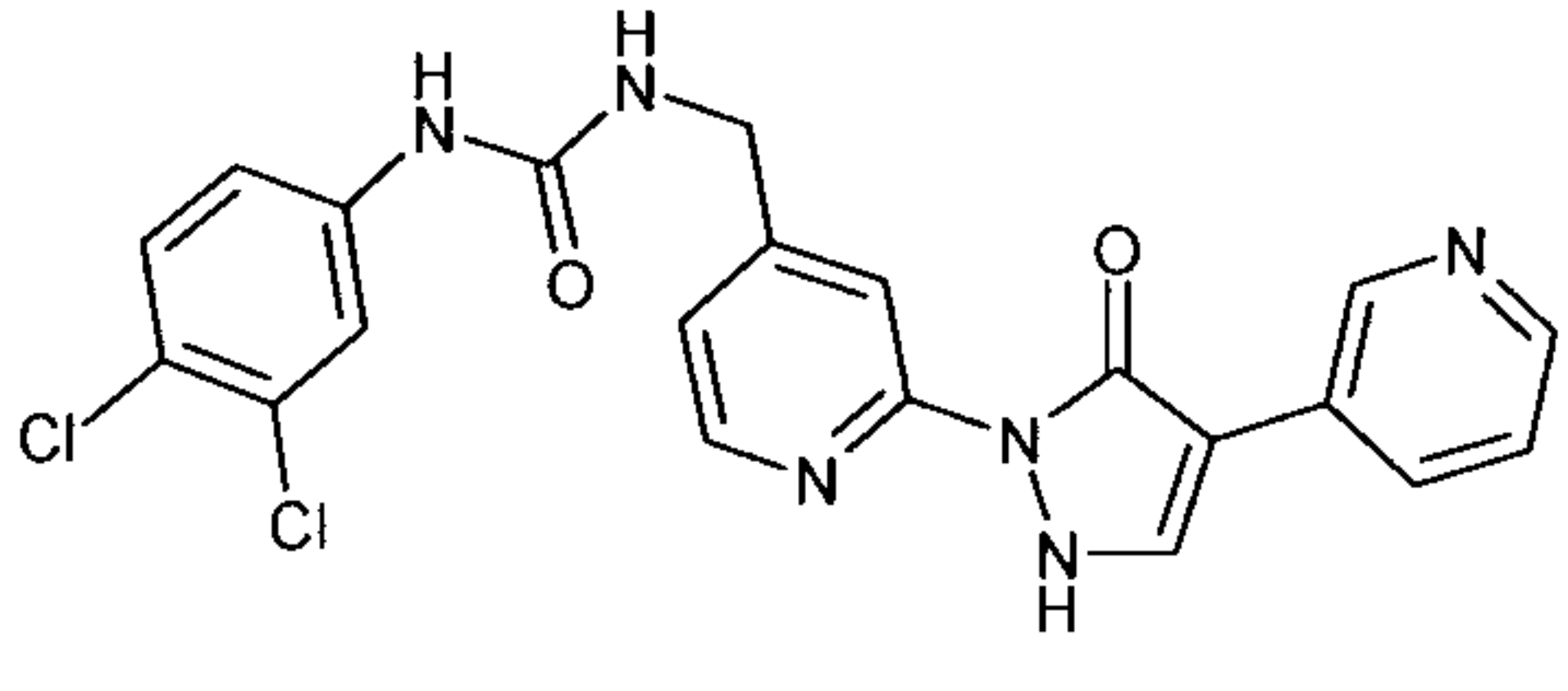
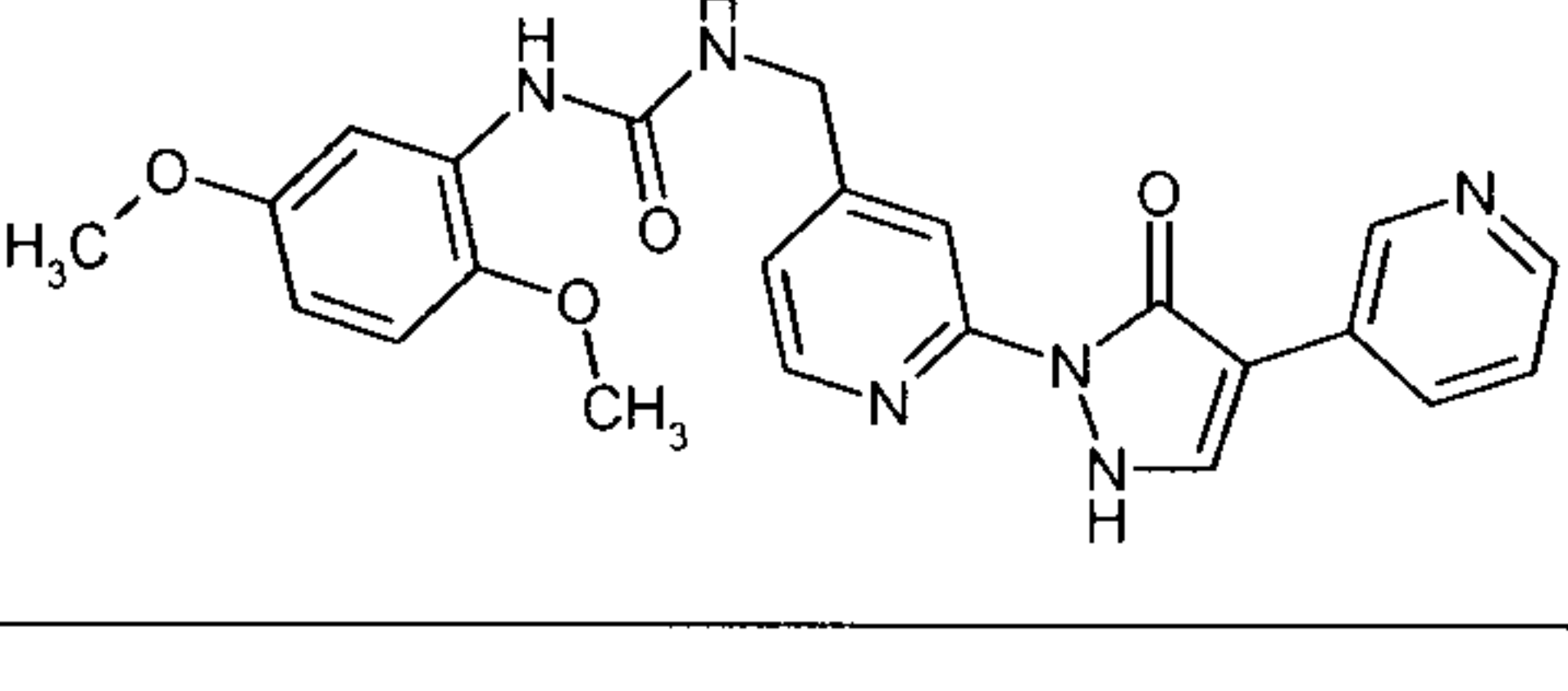
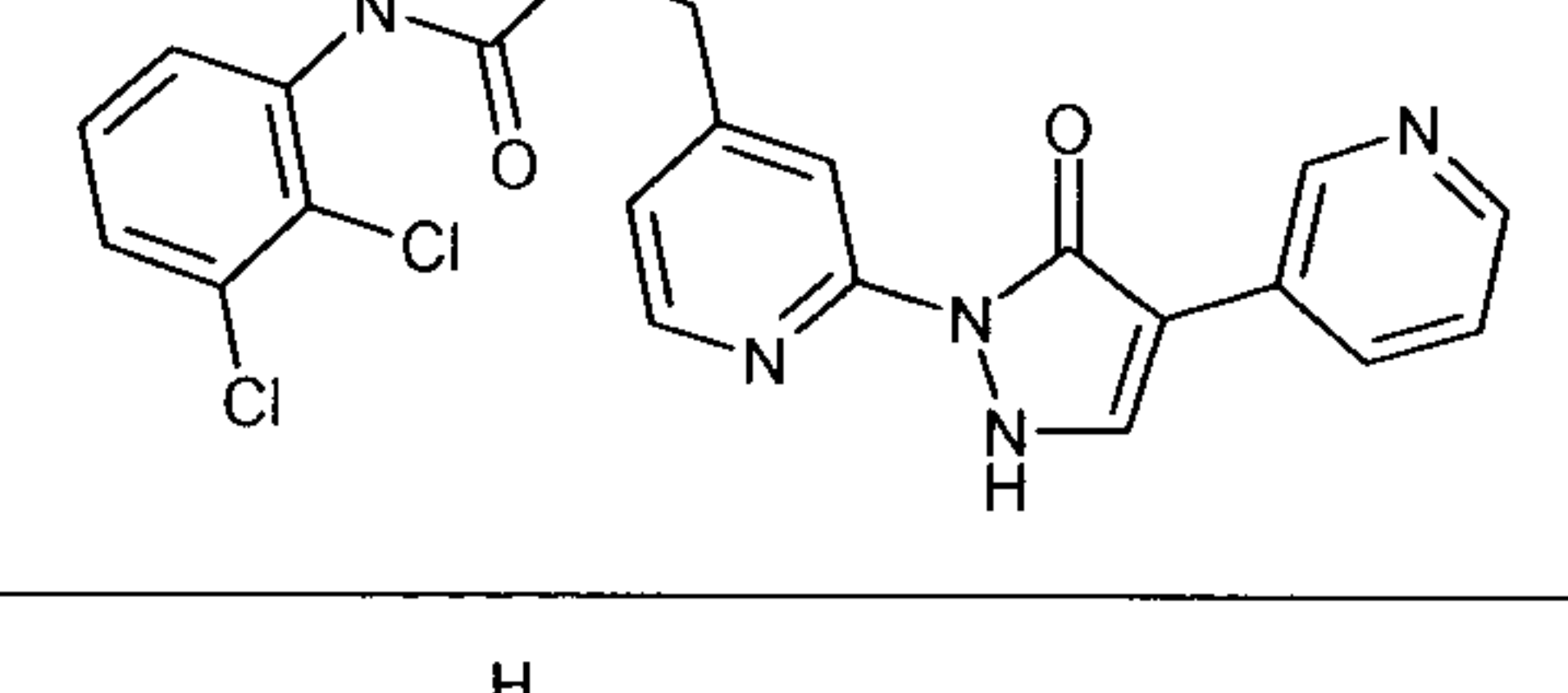
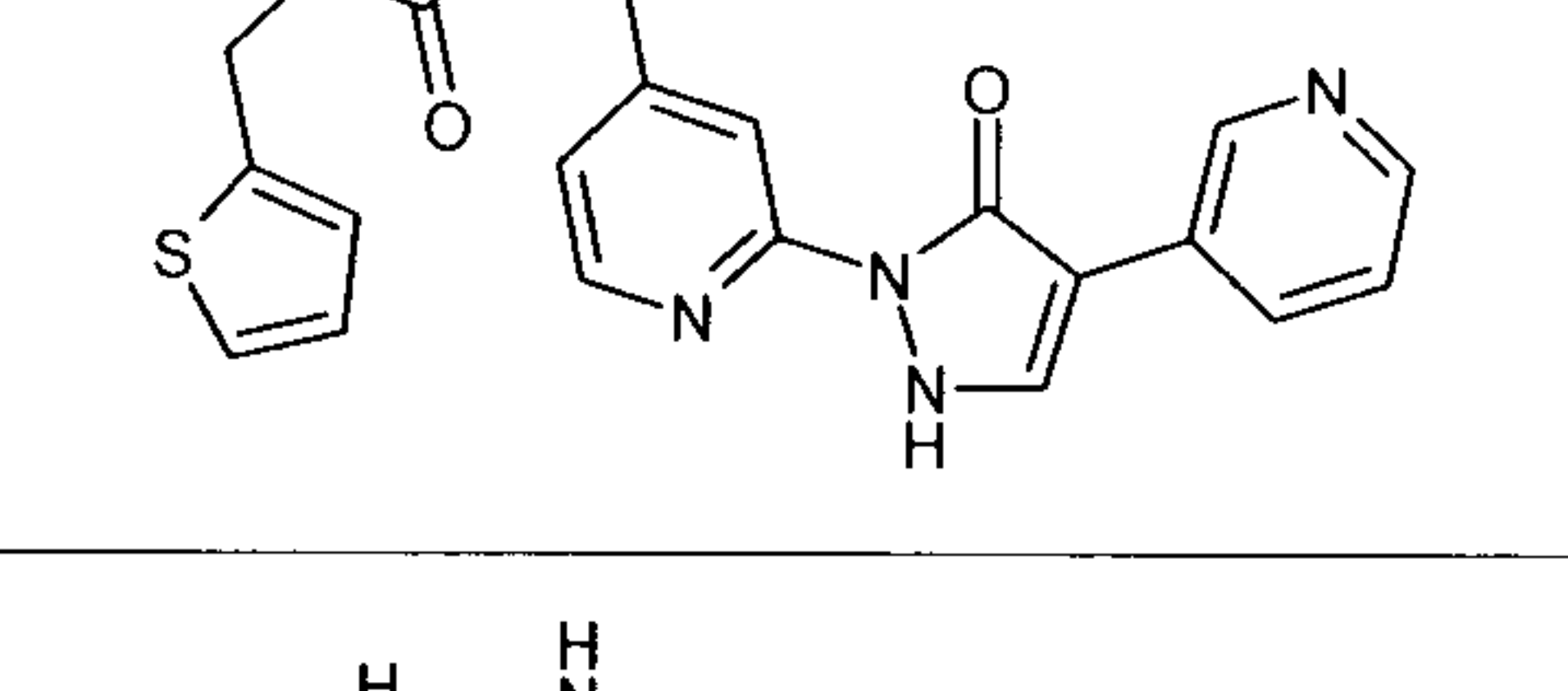
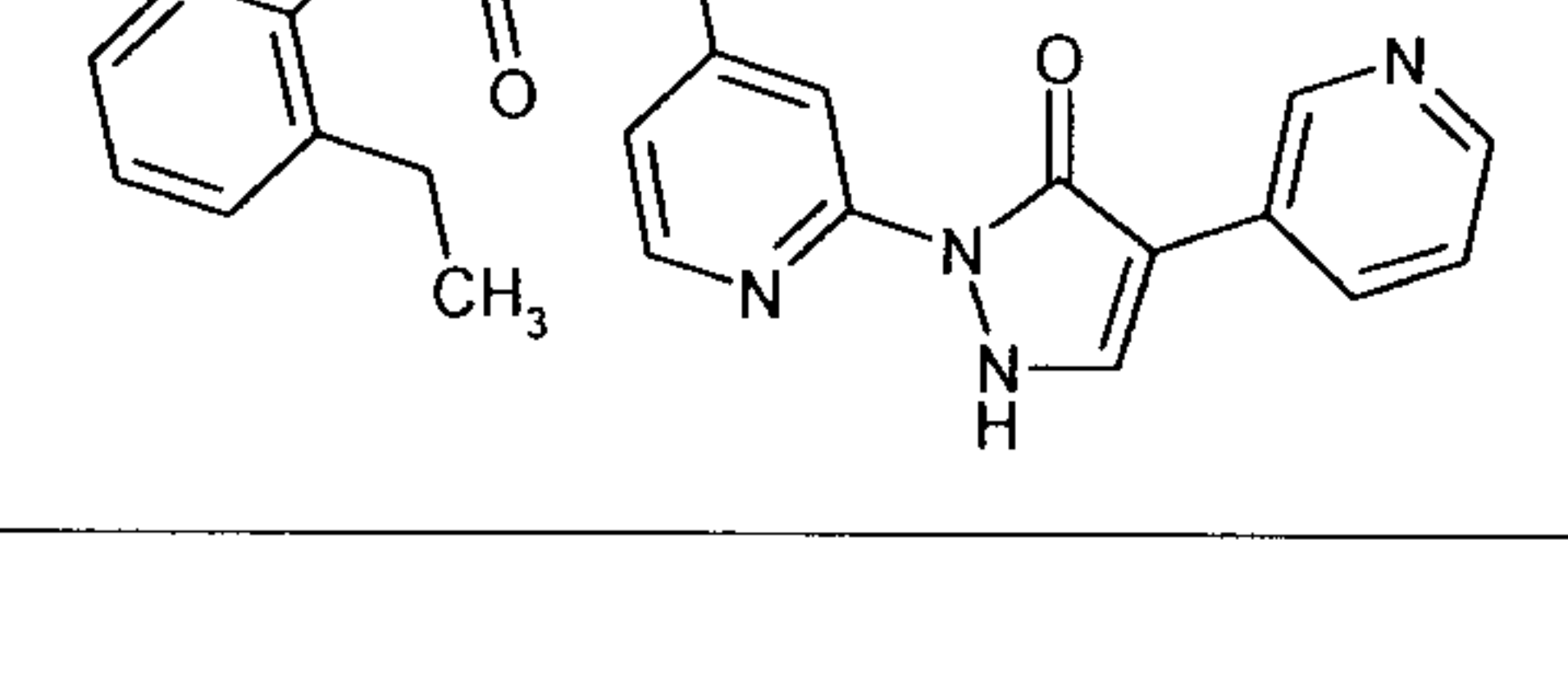
The compounds listed in Table 1 are prepared analogously to the procedure of Example 25 from 0.1 mmol of the compound from Example 4A and 0.1 mmol of the appropriate isocyanate:

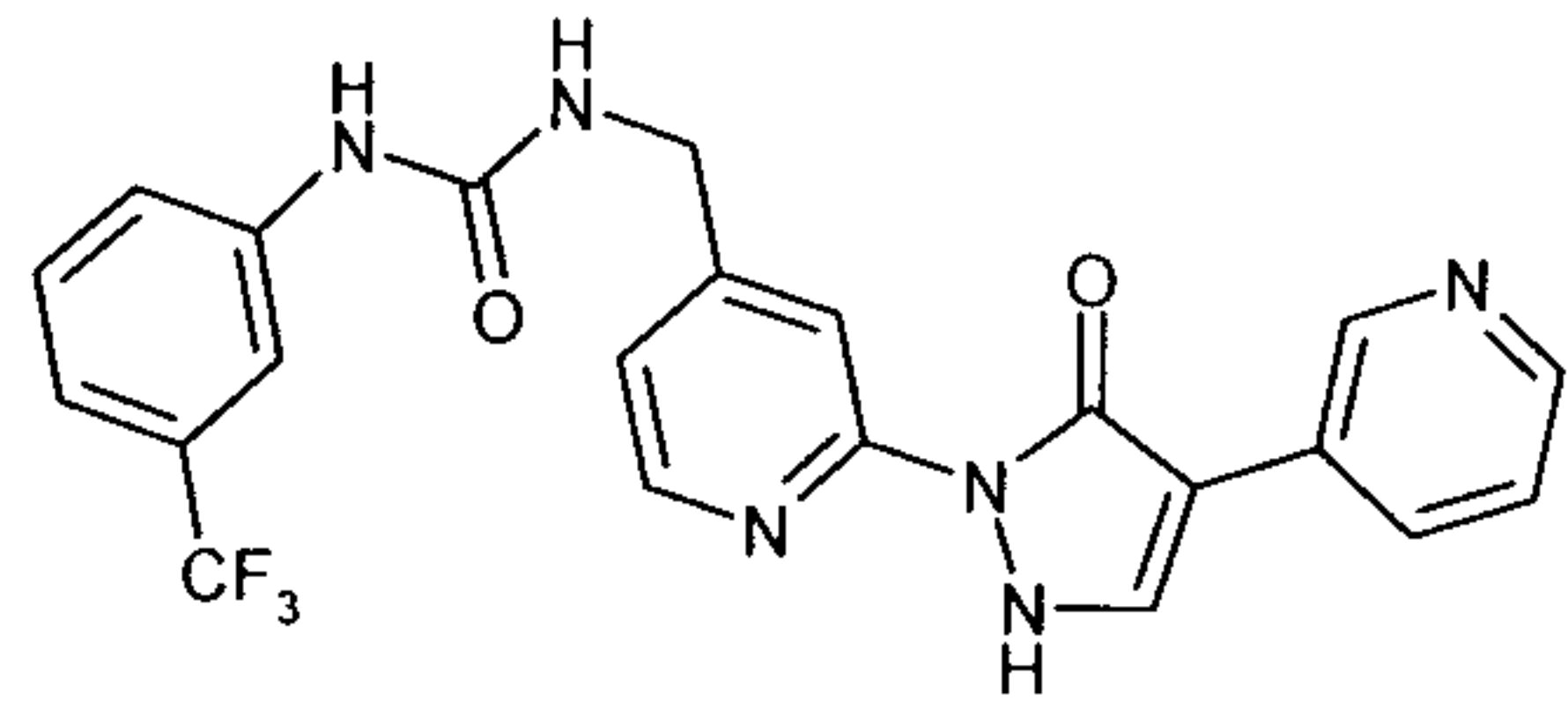
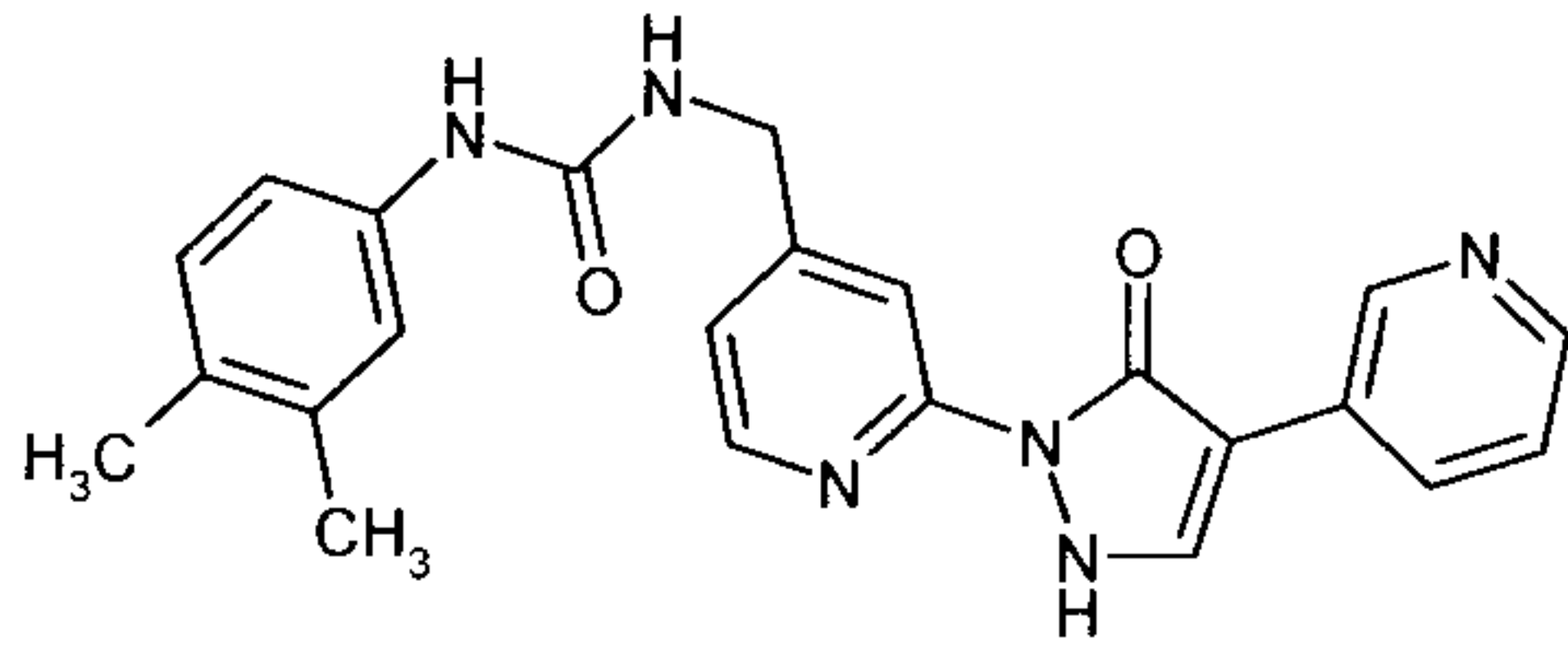
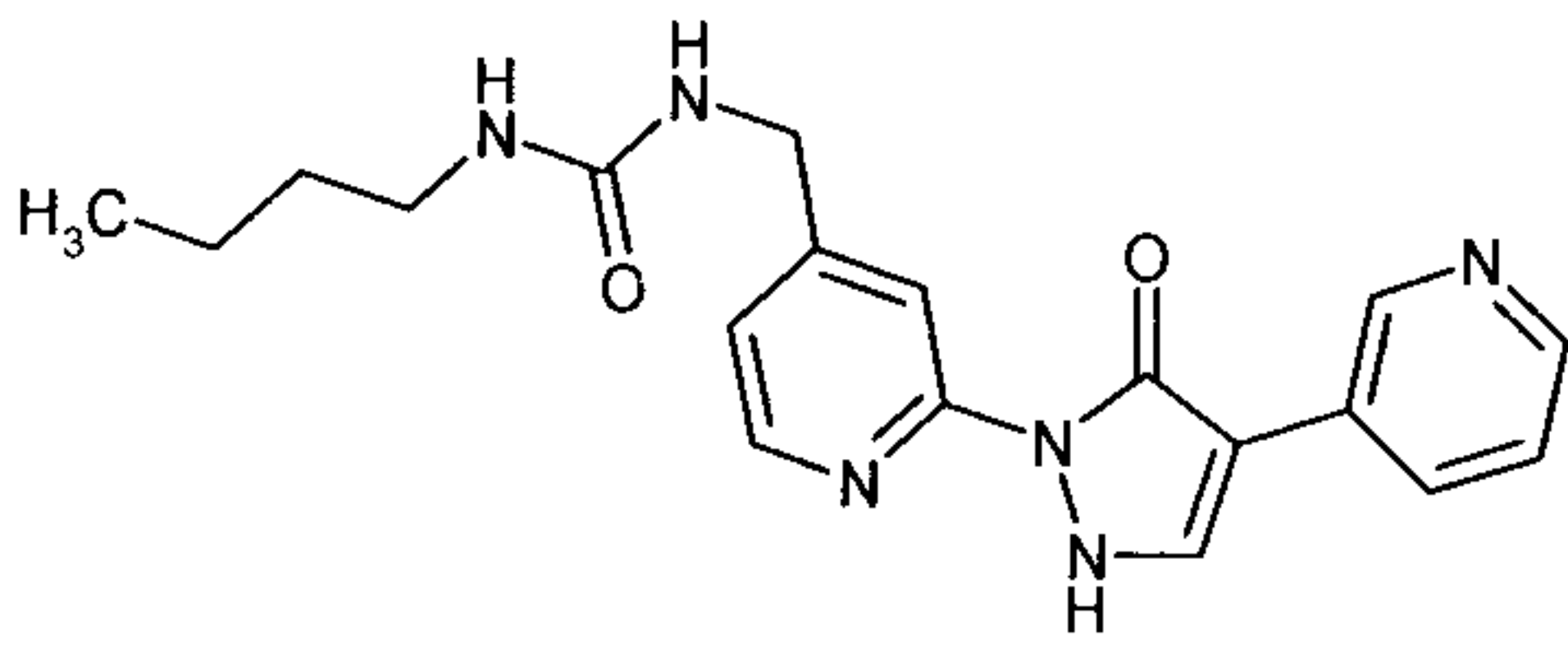
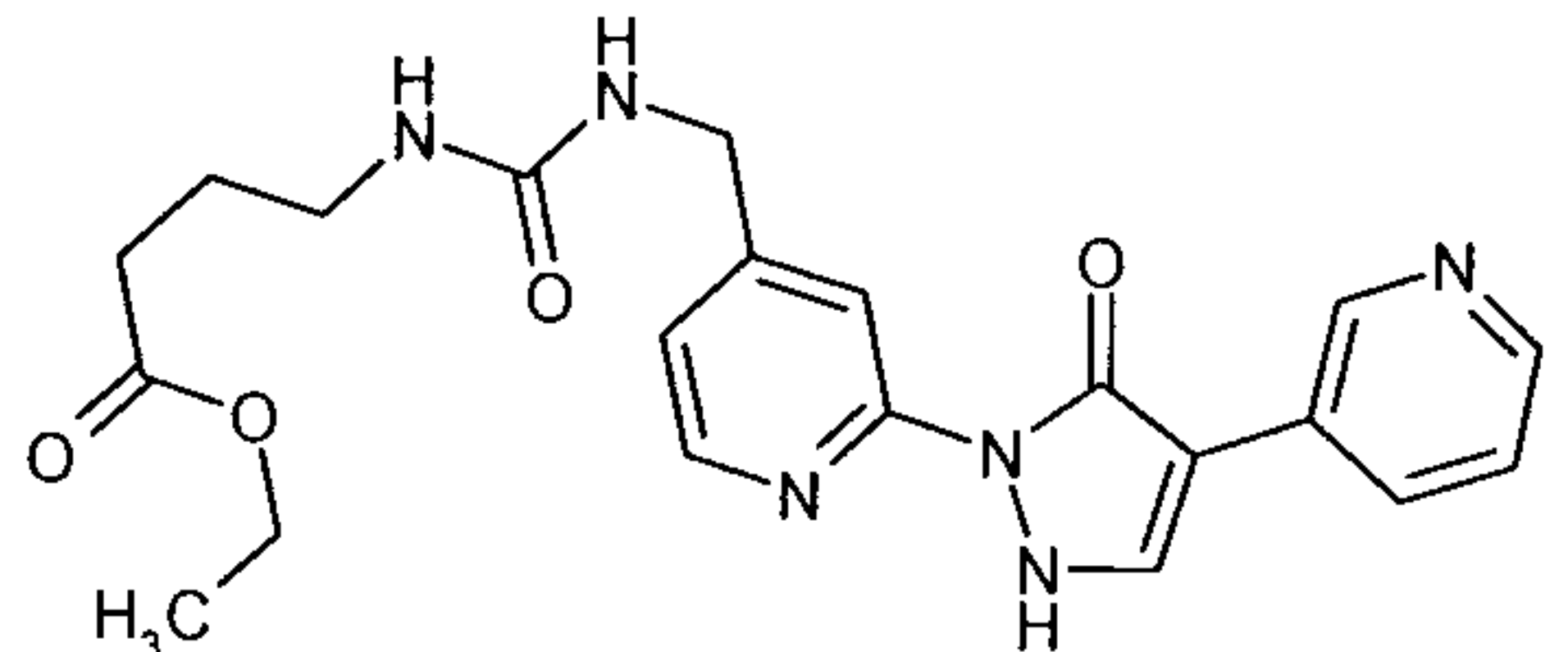
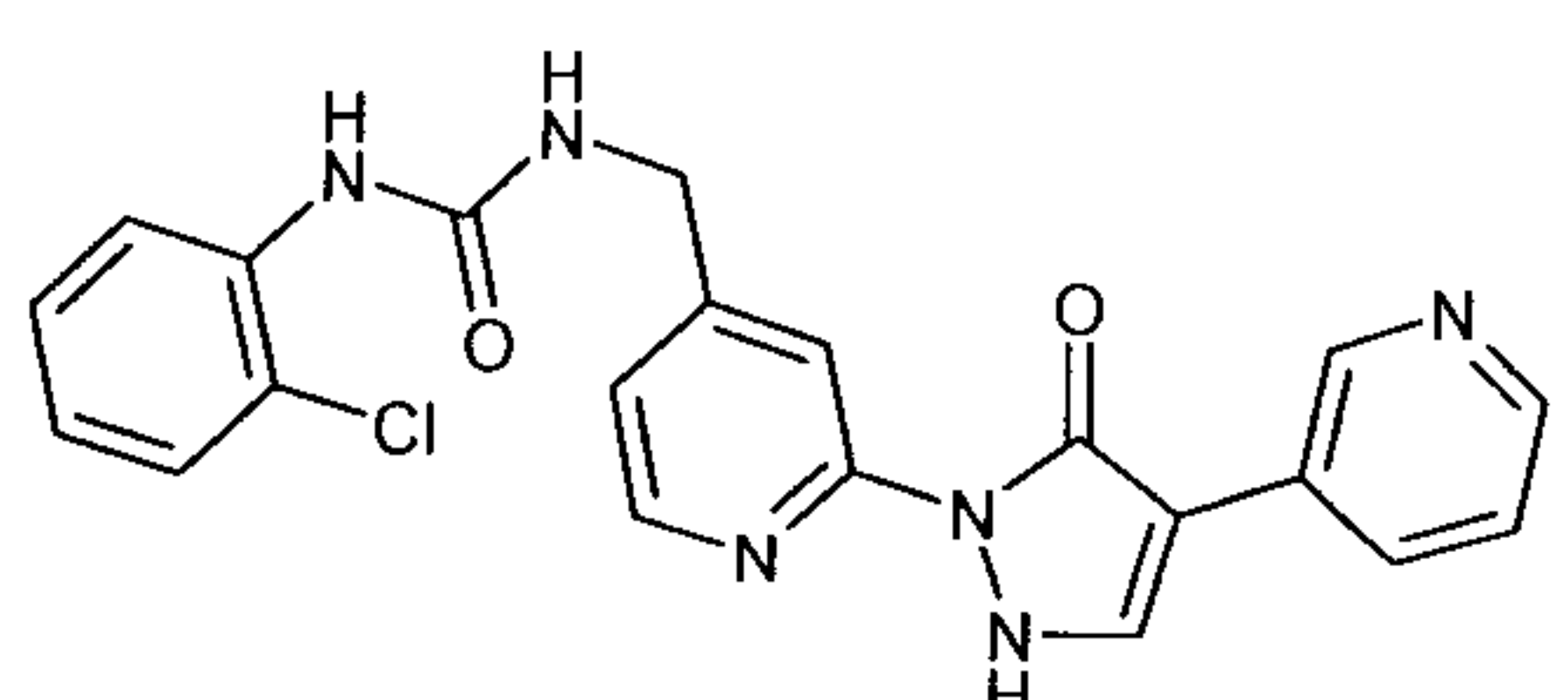
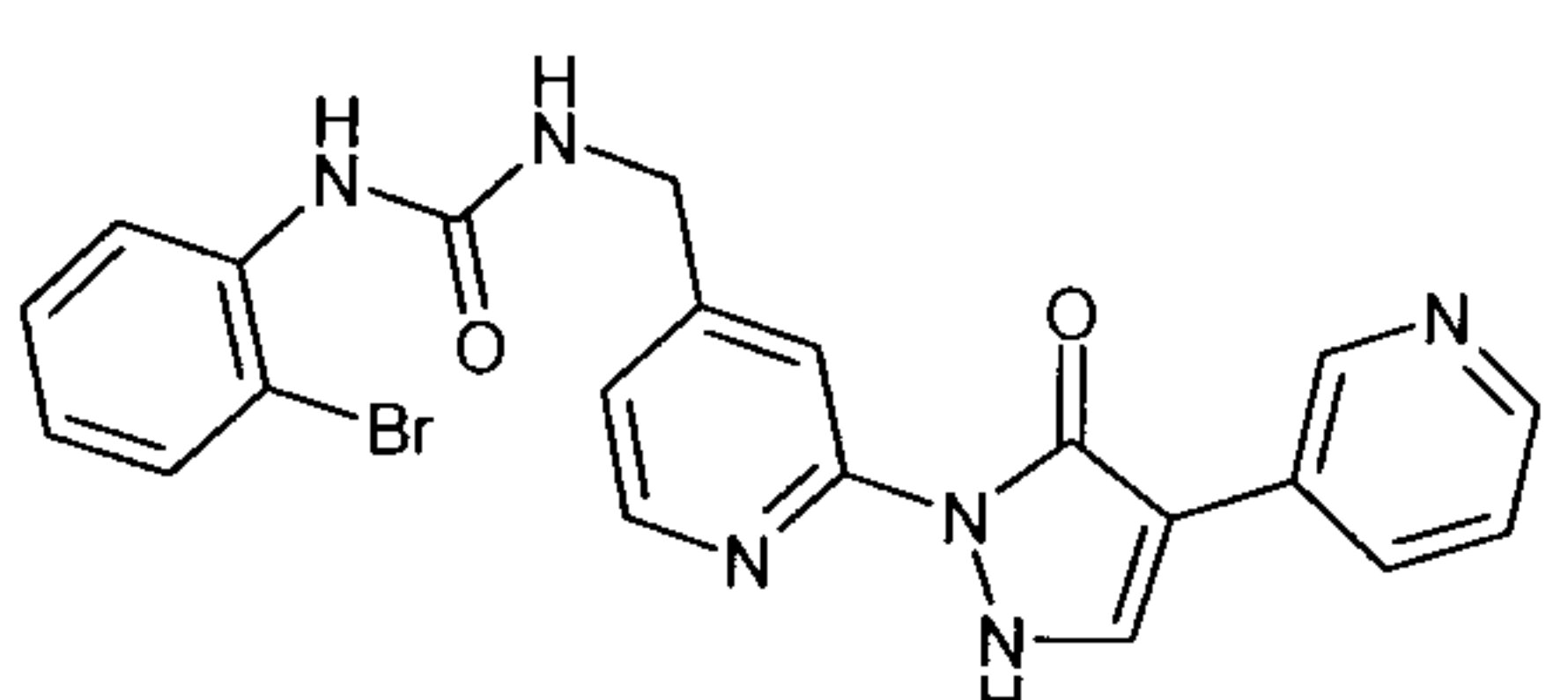
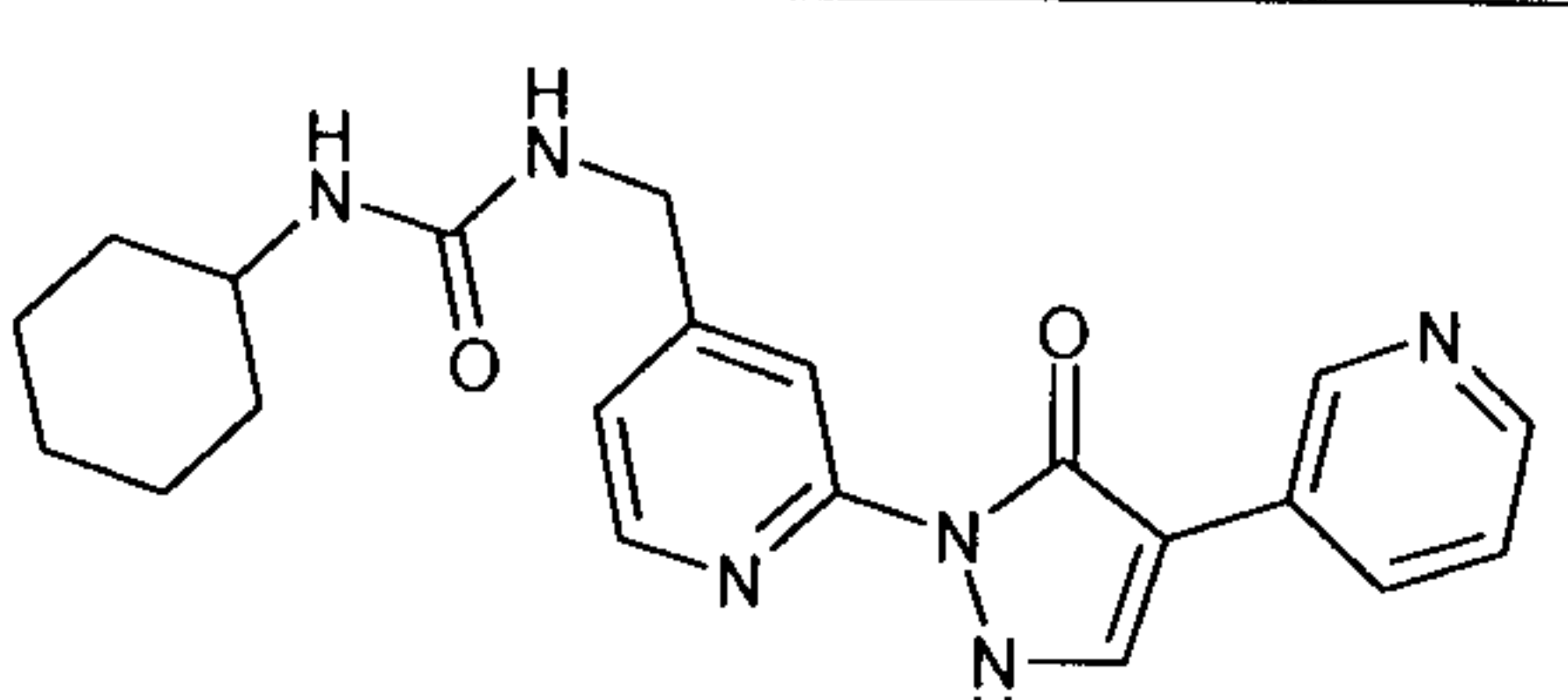
Table 1

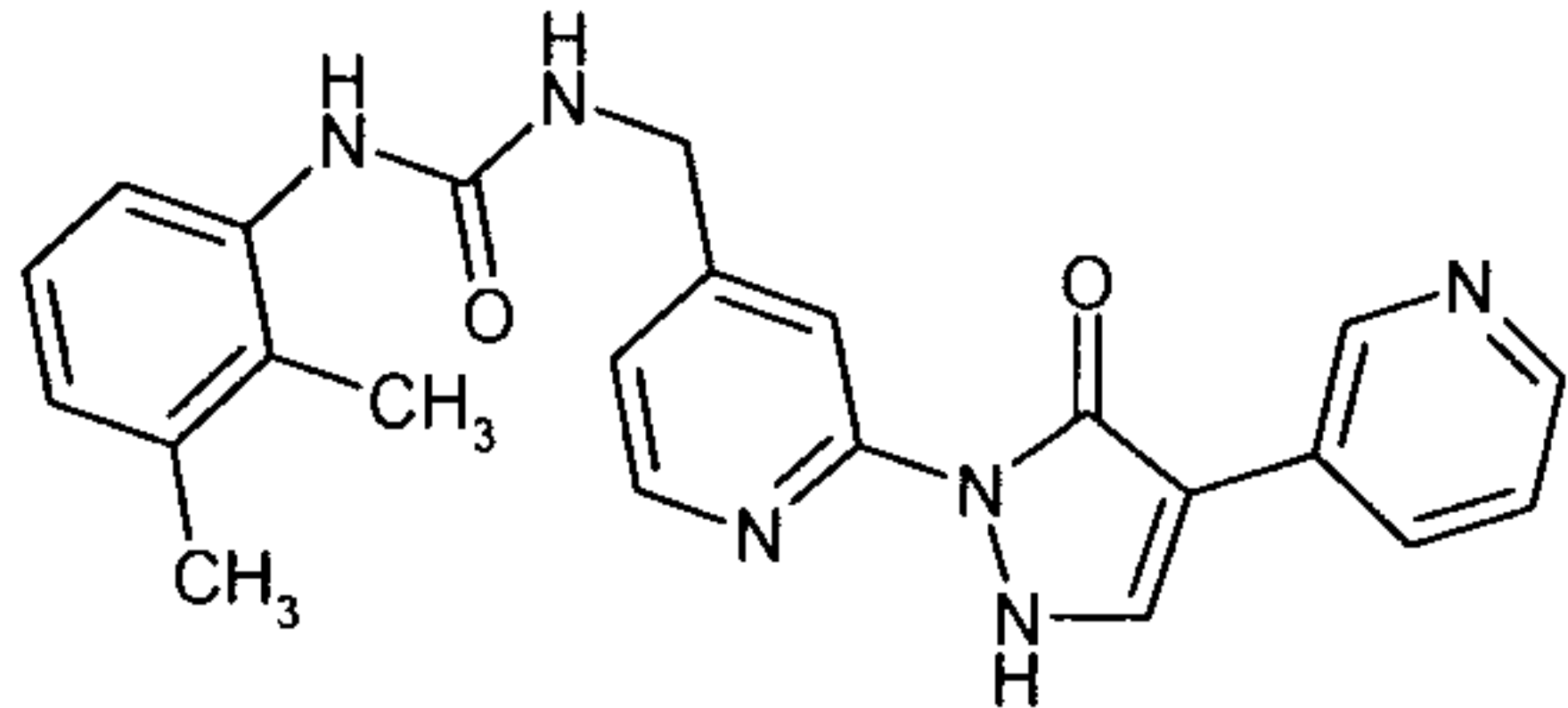
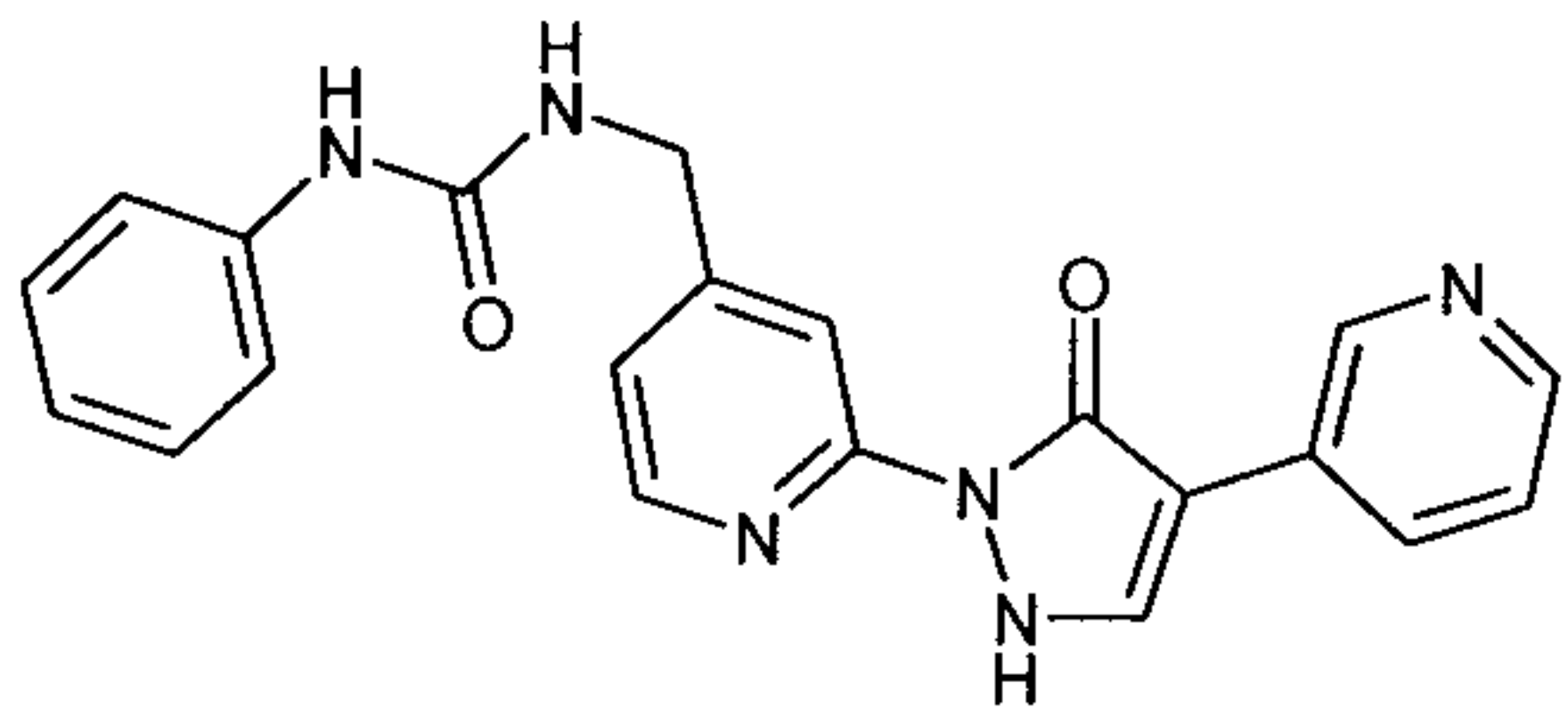
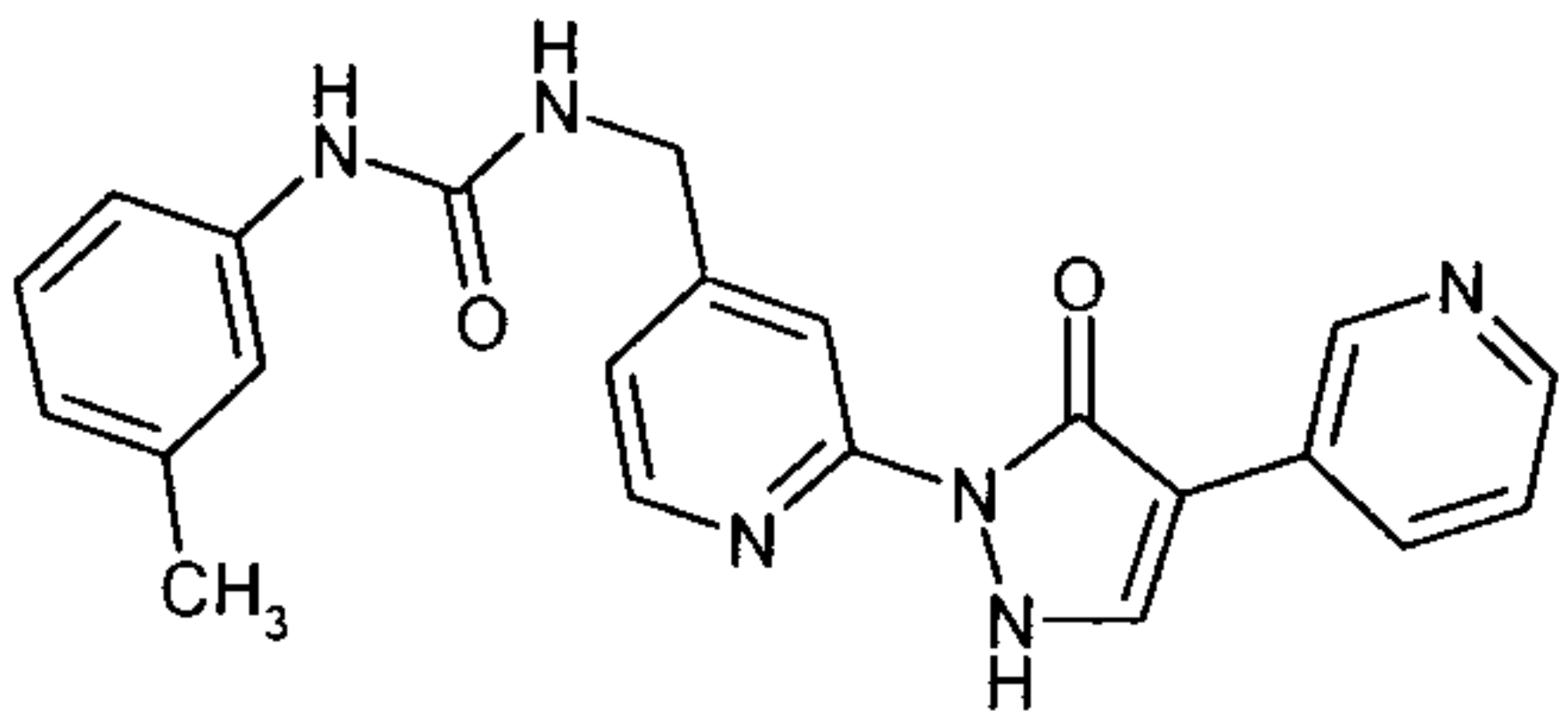
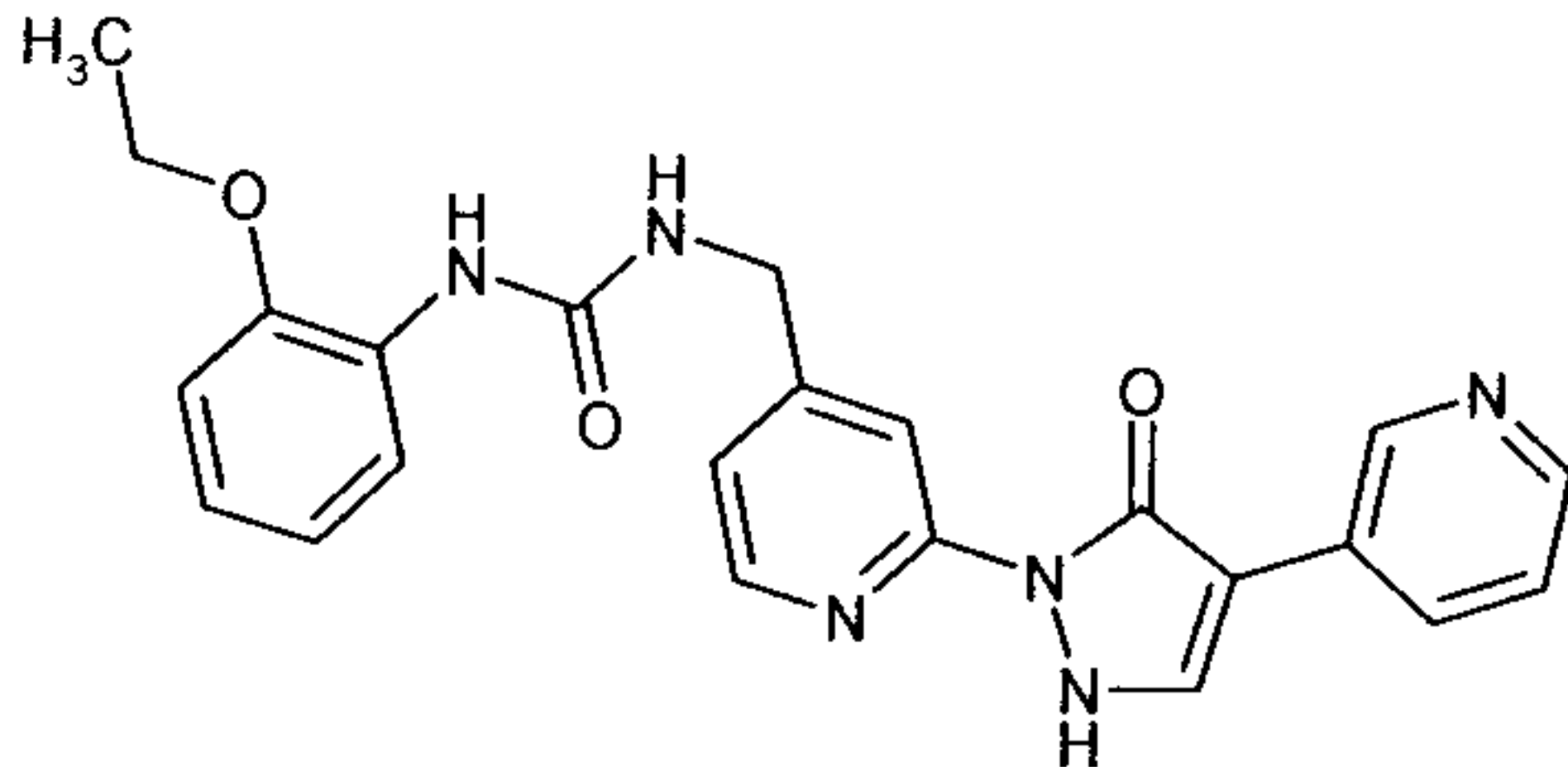
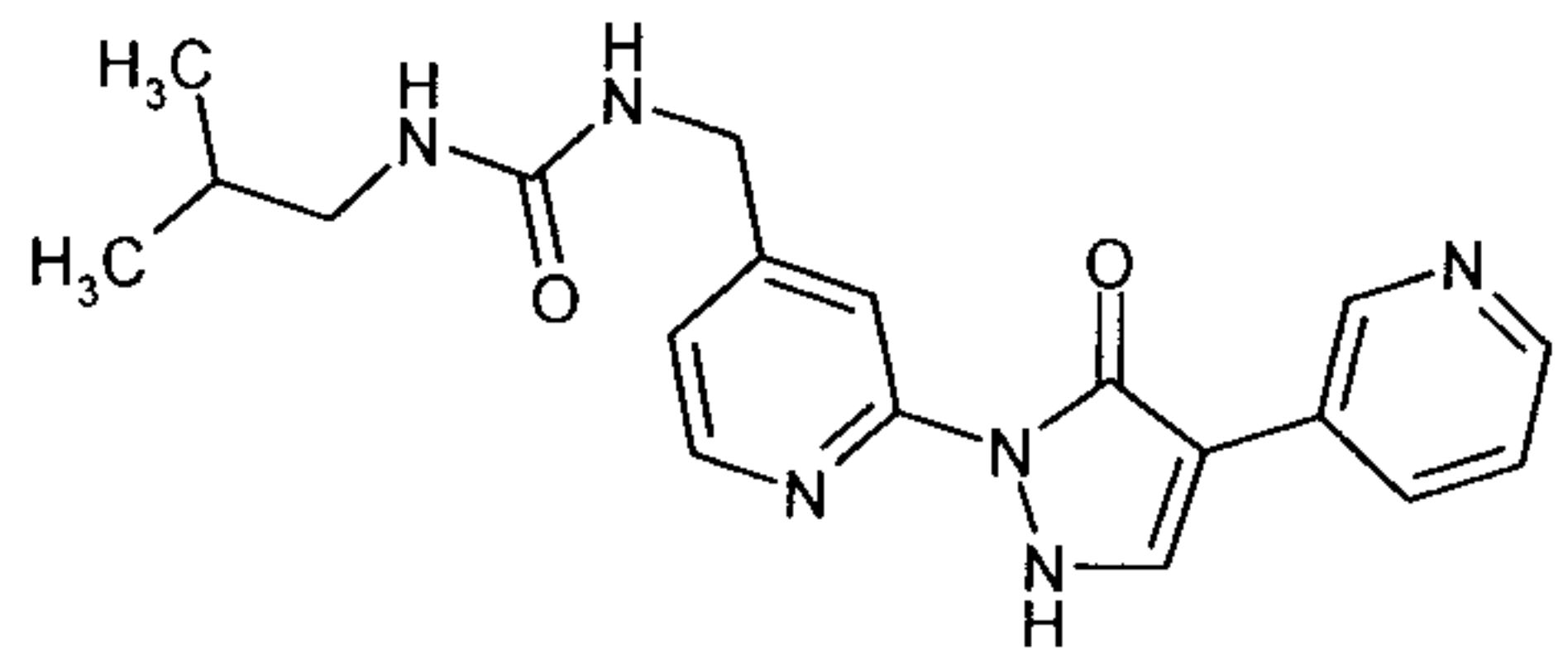
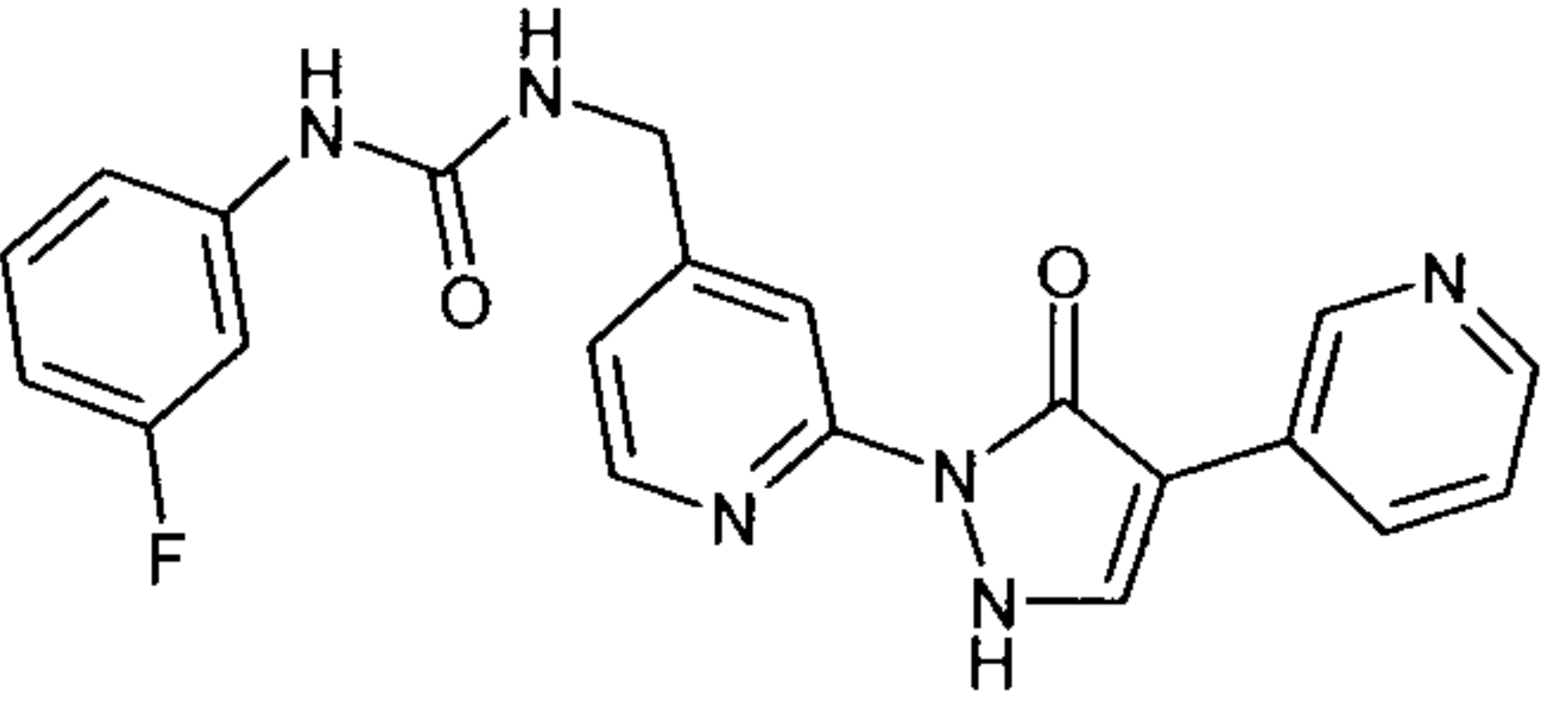
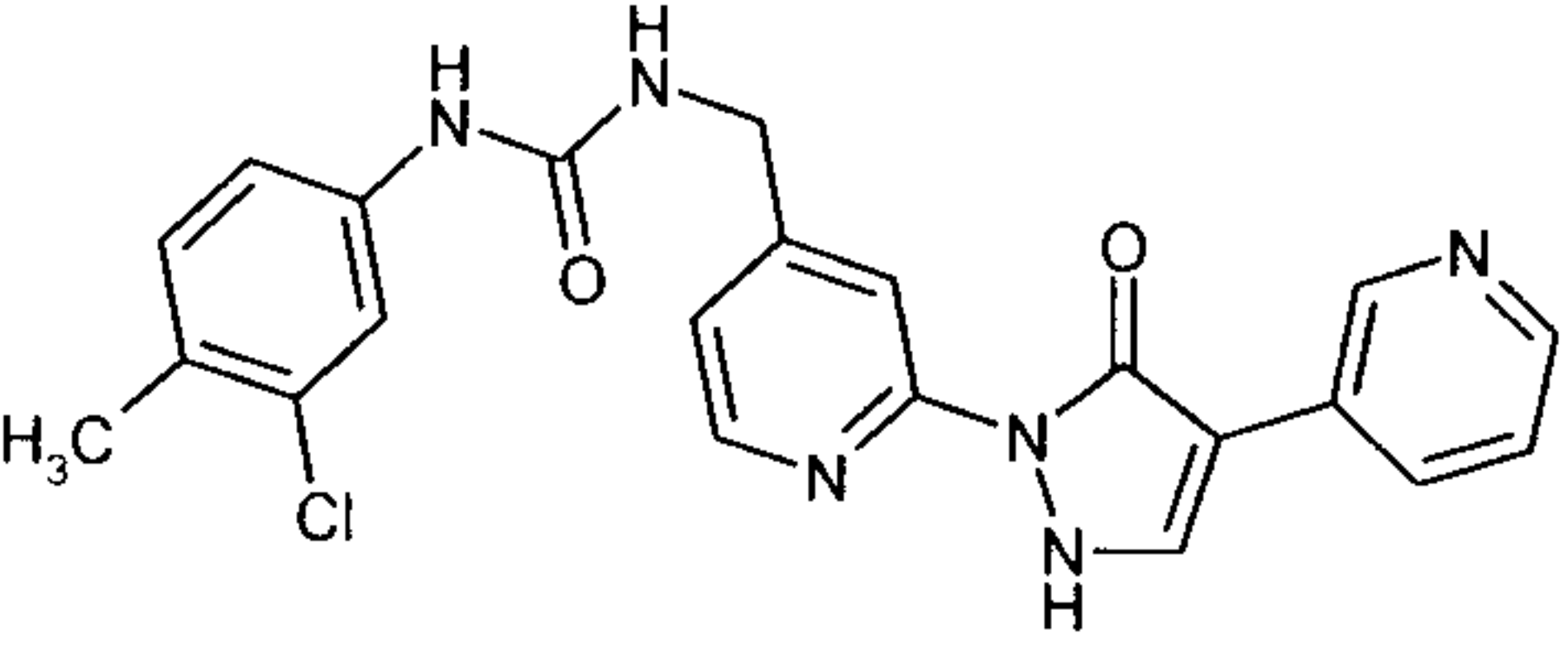
Example No.	Structure	Yield (% of theory)	MS (ESI): $[M+H]^+$; LC-MS: R_t (Method 8)
26		9%	$m/z = 425$; 1.32 min
27		7%	$m/z = 415$; 1.31 min
28		11%	$m/z = 401$; 1.28 min

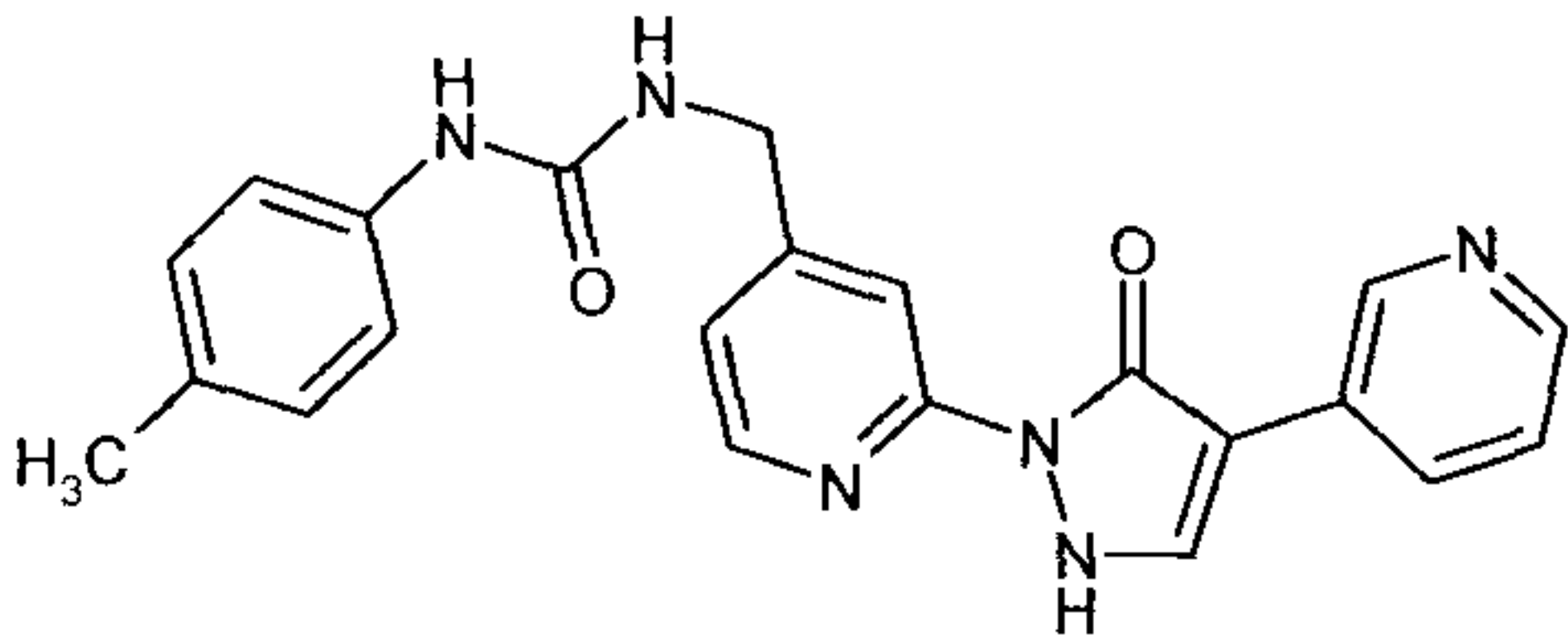
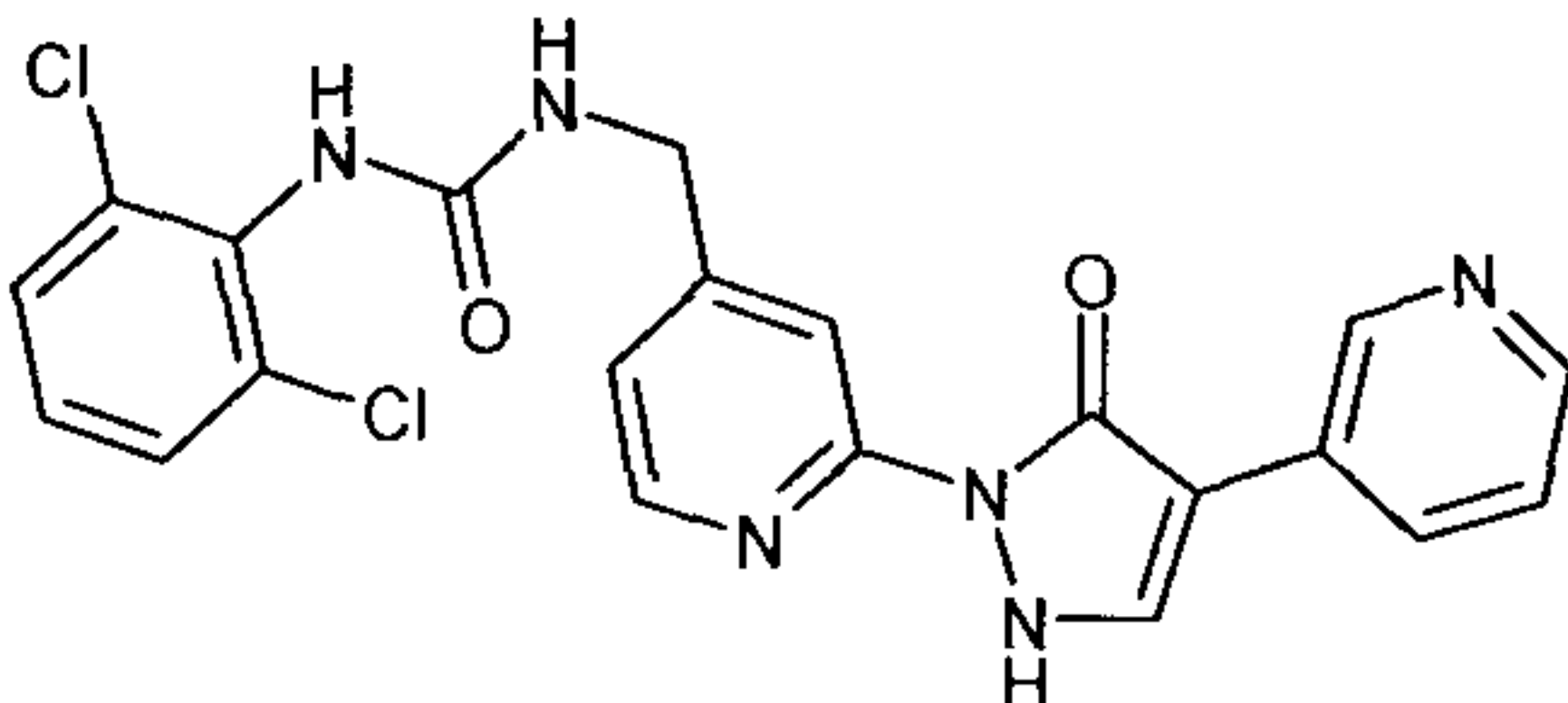
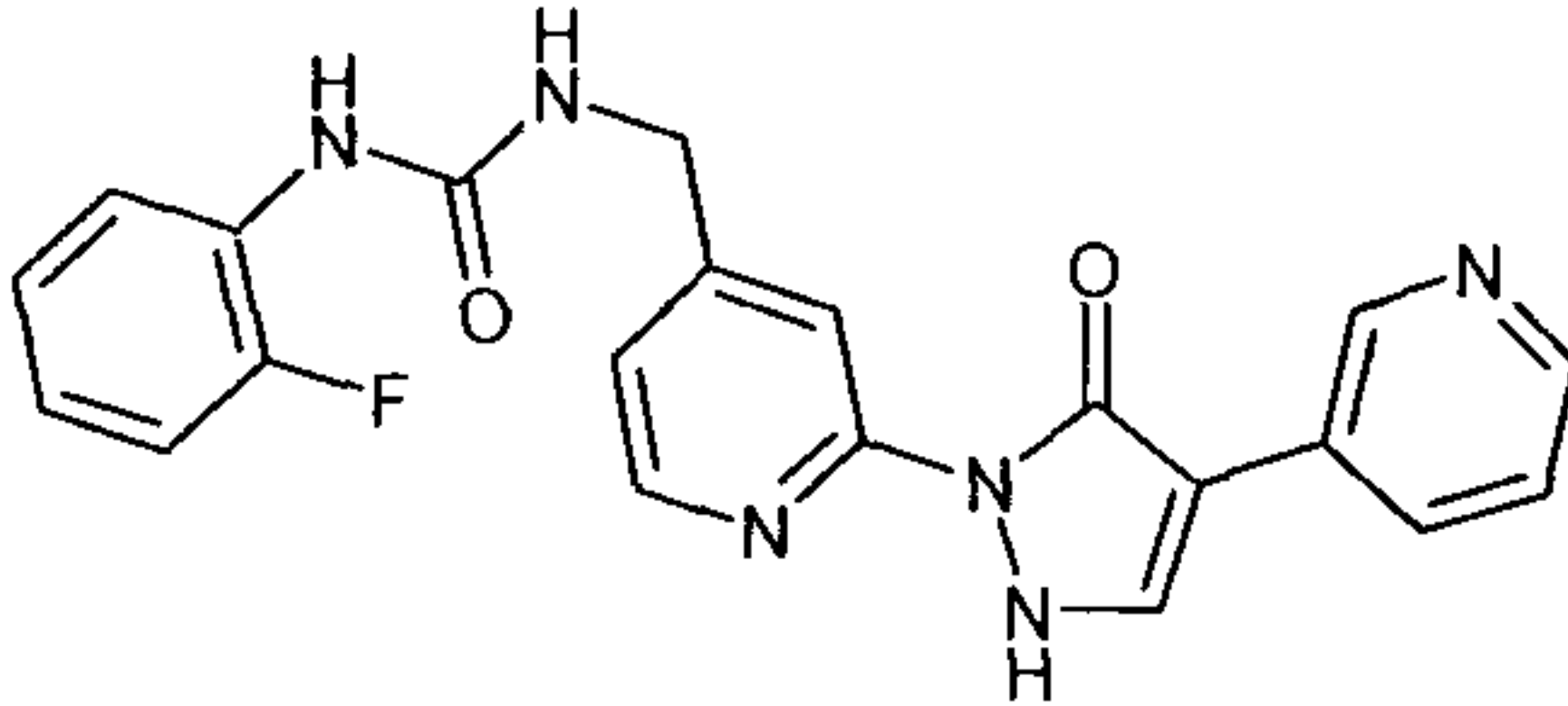
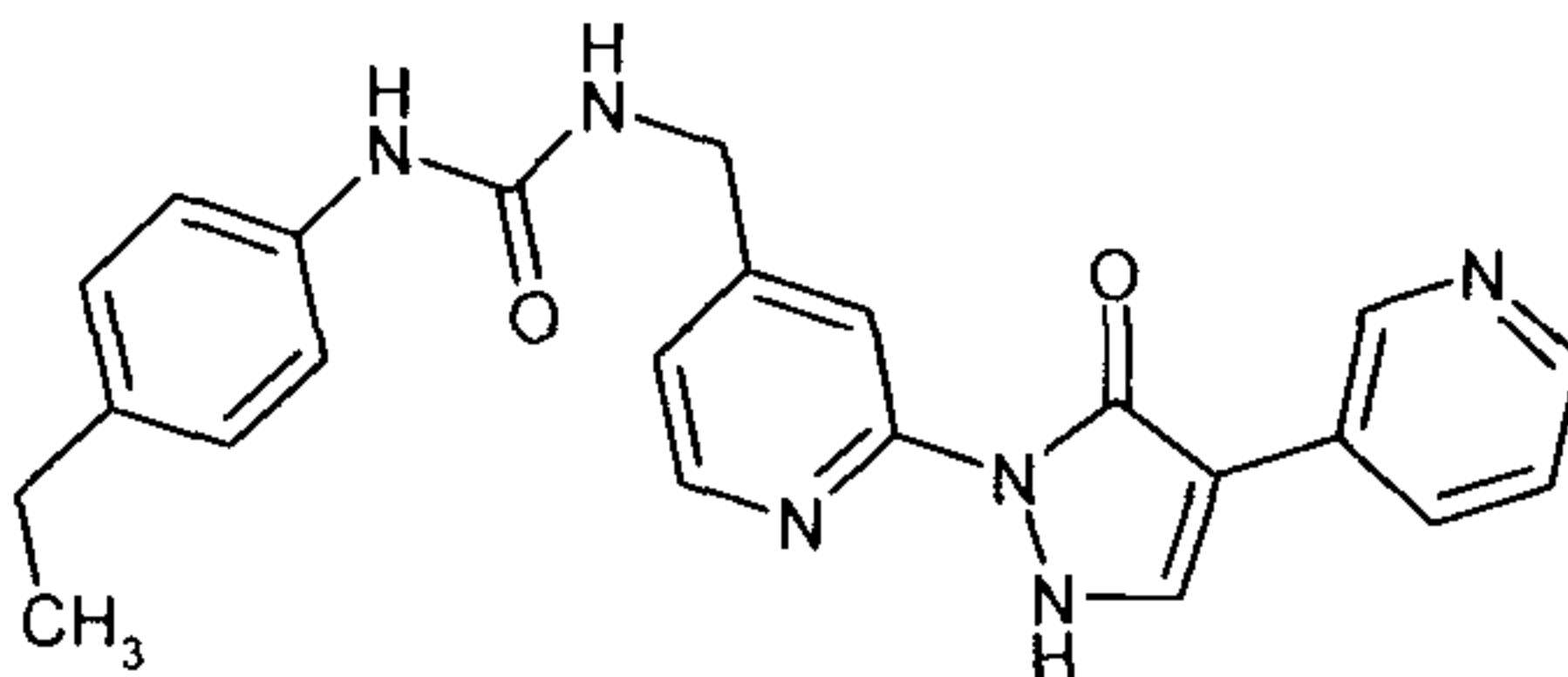
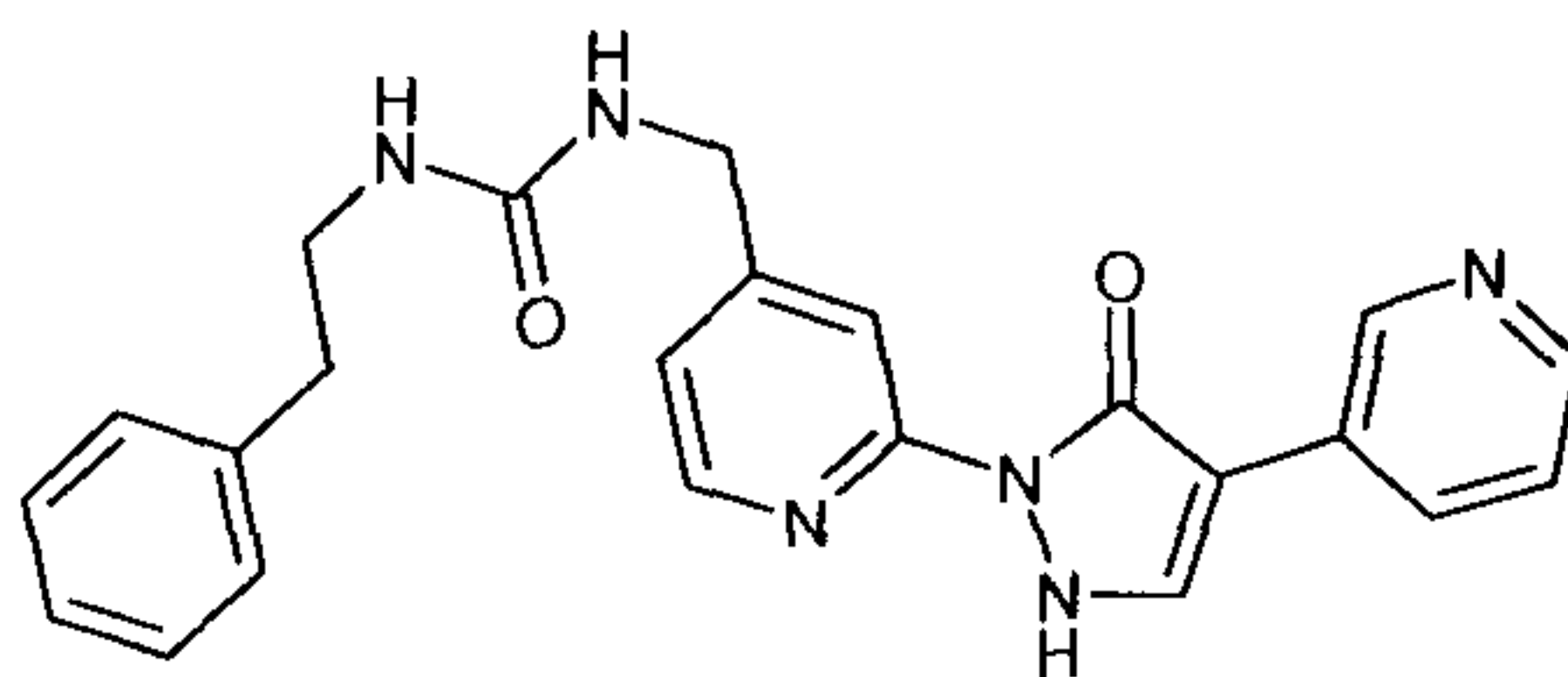
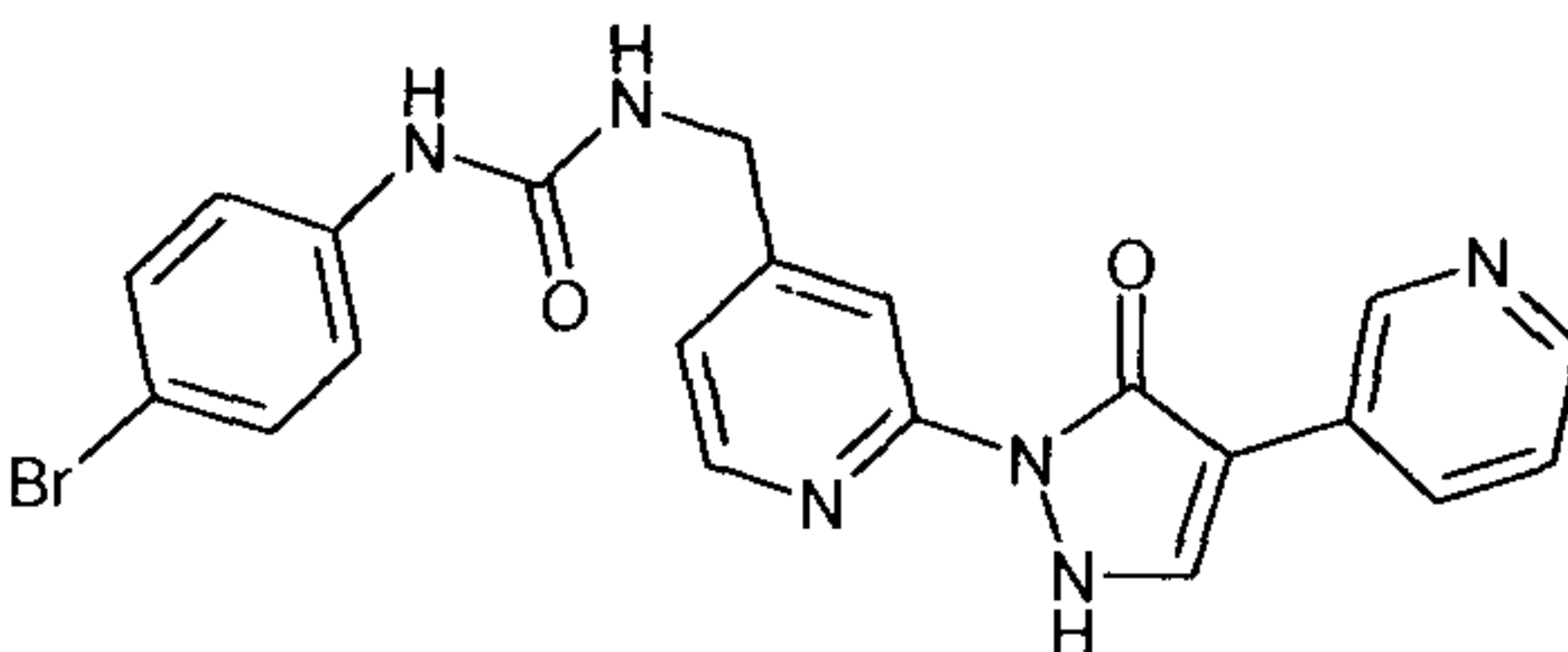
Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 8)
29		10%	m/z = 423; 1.20 min
30		8%	m/z = 401; 1.25 min
31		13%	m/z = 456; 1.57 min
32		18%	m/z = 415; 1.30 min
33		17%	m/z = 441; 1.38 min
34		15%	m/z = 455; 1.52 min
35		10%	m/z = 447; 1.31 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 8)
36		16%	m/z = 415; 1.30 min
37		7%	m/z = 429; 1.37 min
38		18%	m/z = 465; 1.44 min
39		11%	m/z = 417; 1.33 min
40		8%	m/z = 415; 1.36 min
41		14%	m/z = 431; 1.34 min
42		15%	m/z = 381; 1.31 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 8)
43		11%	m/z = 439; 1.33 min
44		14%	m/z = 457; 1.51 min
45		14%	m/z = 455; 1.52 min
46		10%	m/z = 447; 1.33 min
47		20%	m/z = 455; 1.47 min
48		4%	m/z = 407; 1.22 min
49		15%	m/z = 415; 1.35 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 8)
50		15%	m/z = 455; 1.48 min
51		17%	m/z = 415; 1.42 min
52		3%	m/z = 367; 1.21 min
53		13%	m/z = 425; 1.19 min
54		16%	m/z = 421; 1.36 min
55		12%	m/z = 465; 1.37 min
56		8%	m/z = 393; 1.29 min

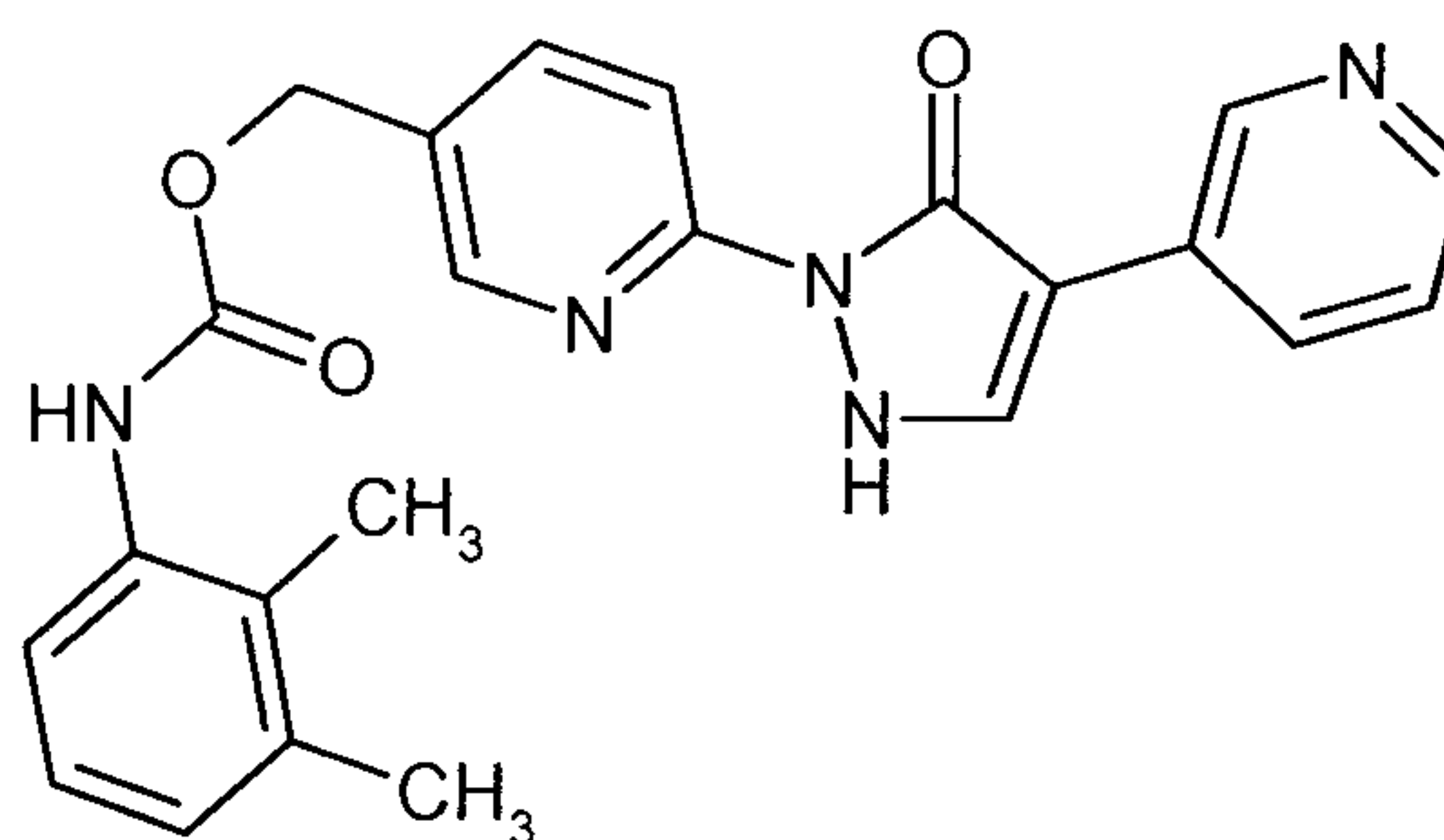
Example No.	Structure	Yield (% of theory)	MS (ESI): $[M+H]^+$; LC-MS: R_t (Method 8)
57		10%	$m/z = 415$; 1.35 min
58		15%	$m/z = 387$; 1.28 min
59		19%	$m/z = 401$; 1.35 min
60		17%	$m/z = 431$; 1.40 min
61		14%	$m/z = 367$; 1.20 min
62		10%	$m/z = 405$; 1.33 min
63		26%	$m/z = 435$; 1.49 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 8)
64		22%	m/z = 401; 1.35 min
65		8%	m/z = 455; 1.28 min
66		12%	m/z = 405; 1.31 min
67		6%	m/z = 415; 1.44 min
68		13%	m/z = 415; 1.30 min
69		7%	m/z = 465; 1.44 min

Example 70

[6-(5-Oxo-4-pyridin-3-yl-2,5-dihydro-1H-pyrazol-1-yl)pyridin-3-yl]methyl (2,3-dimethylphenyl)-carbamate

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2.7 g (10 mmol) of 2-[5-(hydroxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3*H*-pyrazol-3-one [for the preparation, see WO 2006/114213] are dissolved in 60 ml of 1,2-dichloroethane and provided as a stock solution.

- 5 15 mg (0.1 mmol) of 1-isocyanato-2,3-dimethylbenzene are initially charged, and 600 μ l (0.1 mmol) of the above stock solution and 26 mg (0.2 mmol) of *N,N*-diisopropylethylamine (Hünig base) are added. The reaction mixture is stirred at RT for 16 h. For work-up, the solvent is removed under reduced pressure, the residue is taken up in DMSO and filtered and the filtrate is purified directly by preparative LC-MS (Method 9). The product fractions are concentrated under
- 10 reduced pressure, and the residue is dried.

Yield: 0.6 mg (2% of theory)

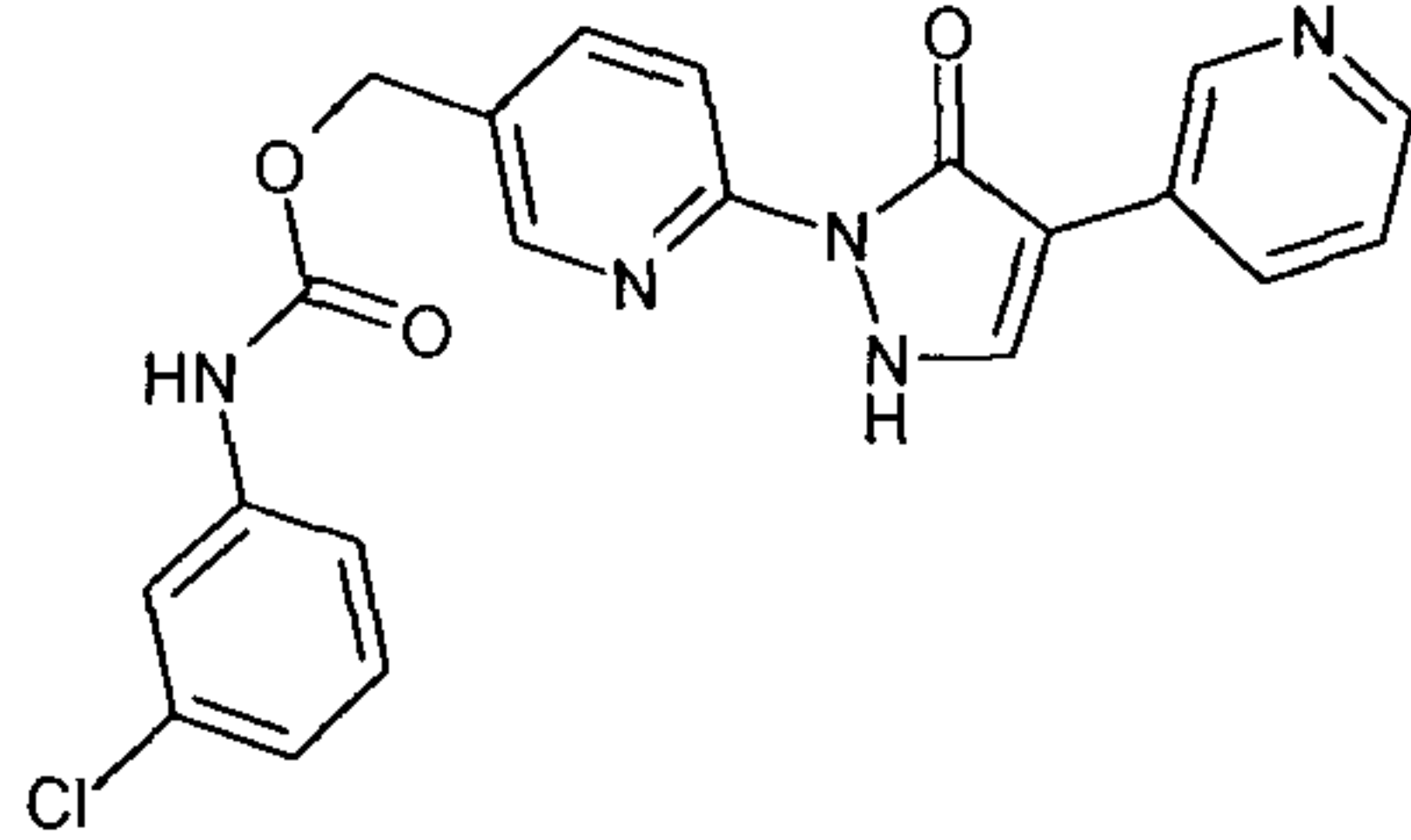
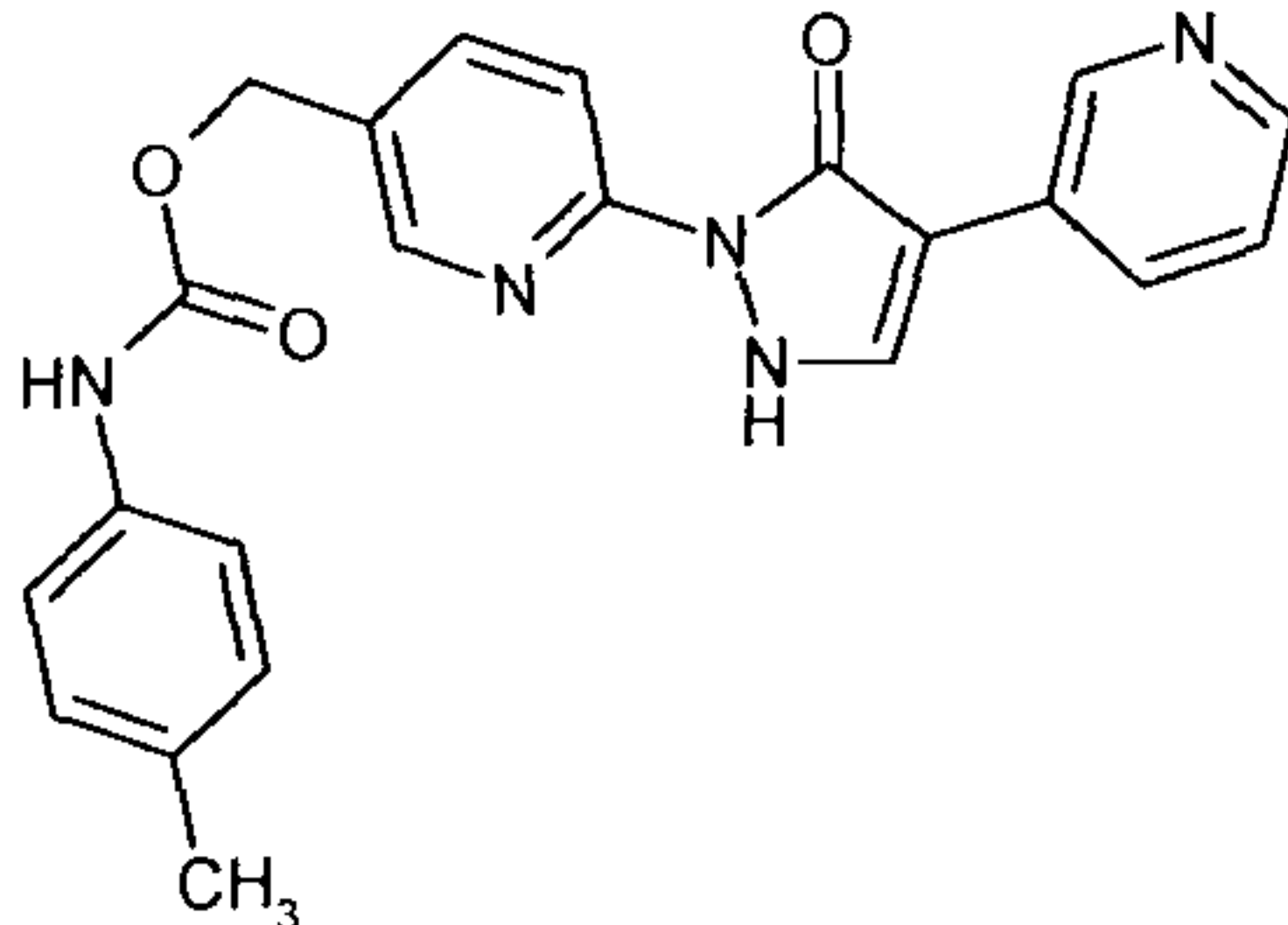
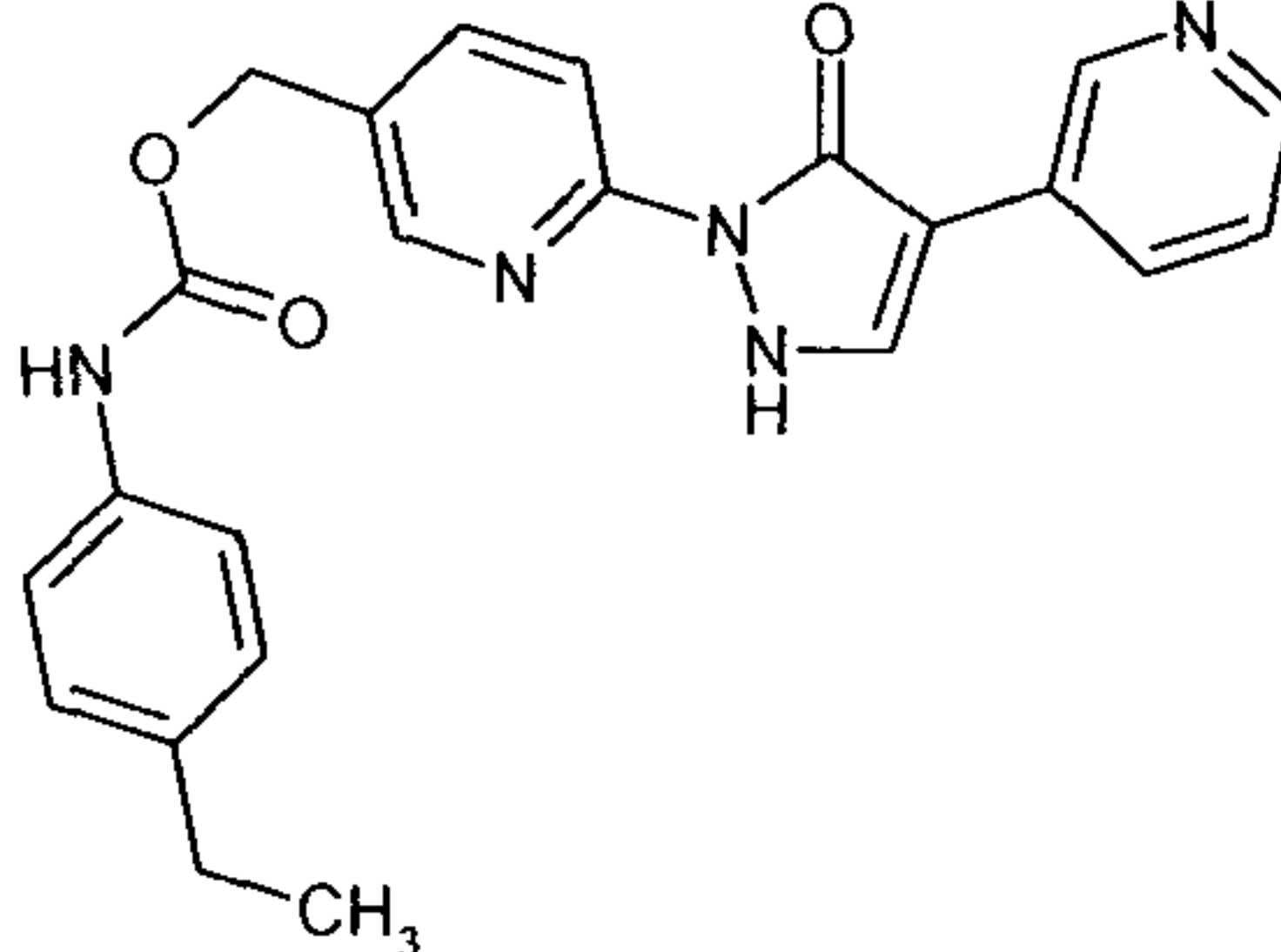
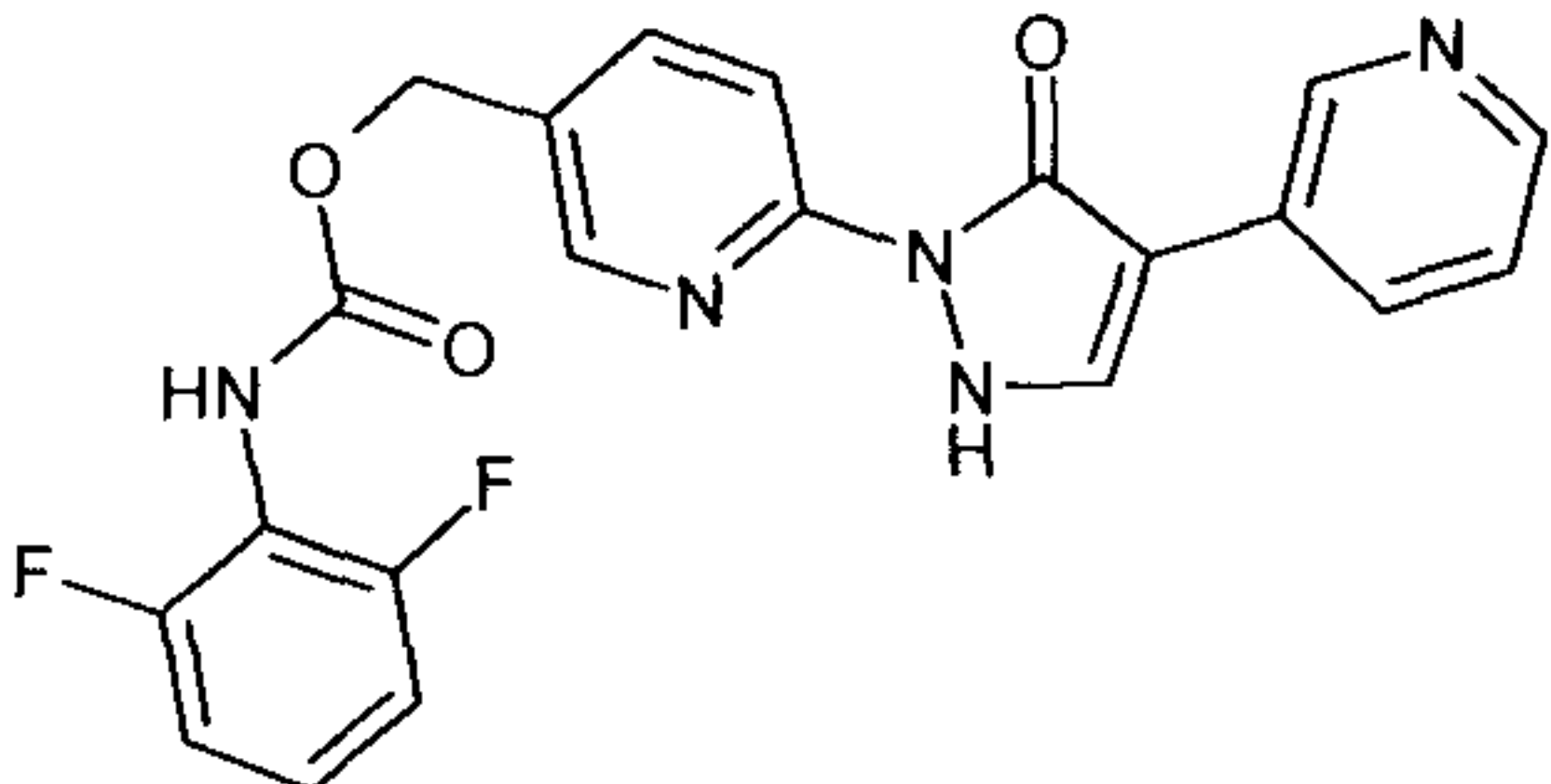
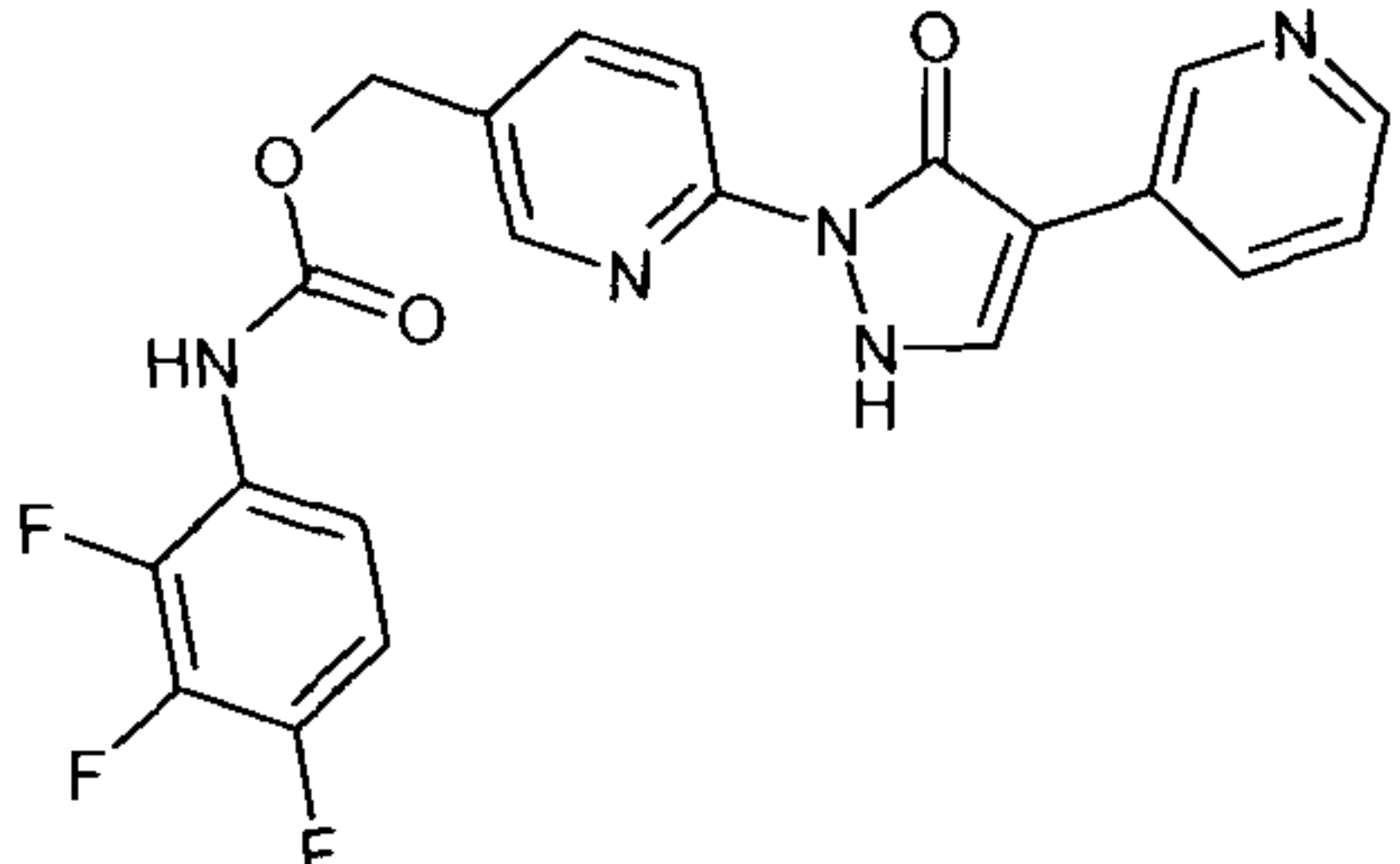
LC-MS (Method 9): $R_t = 1.58$ min; MS (ESIpos): $m/z = 416$ $[M+H]^+$.

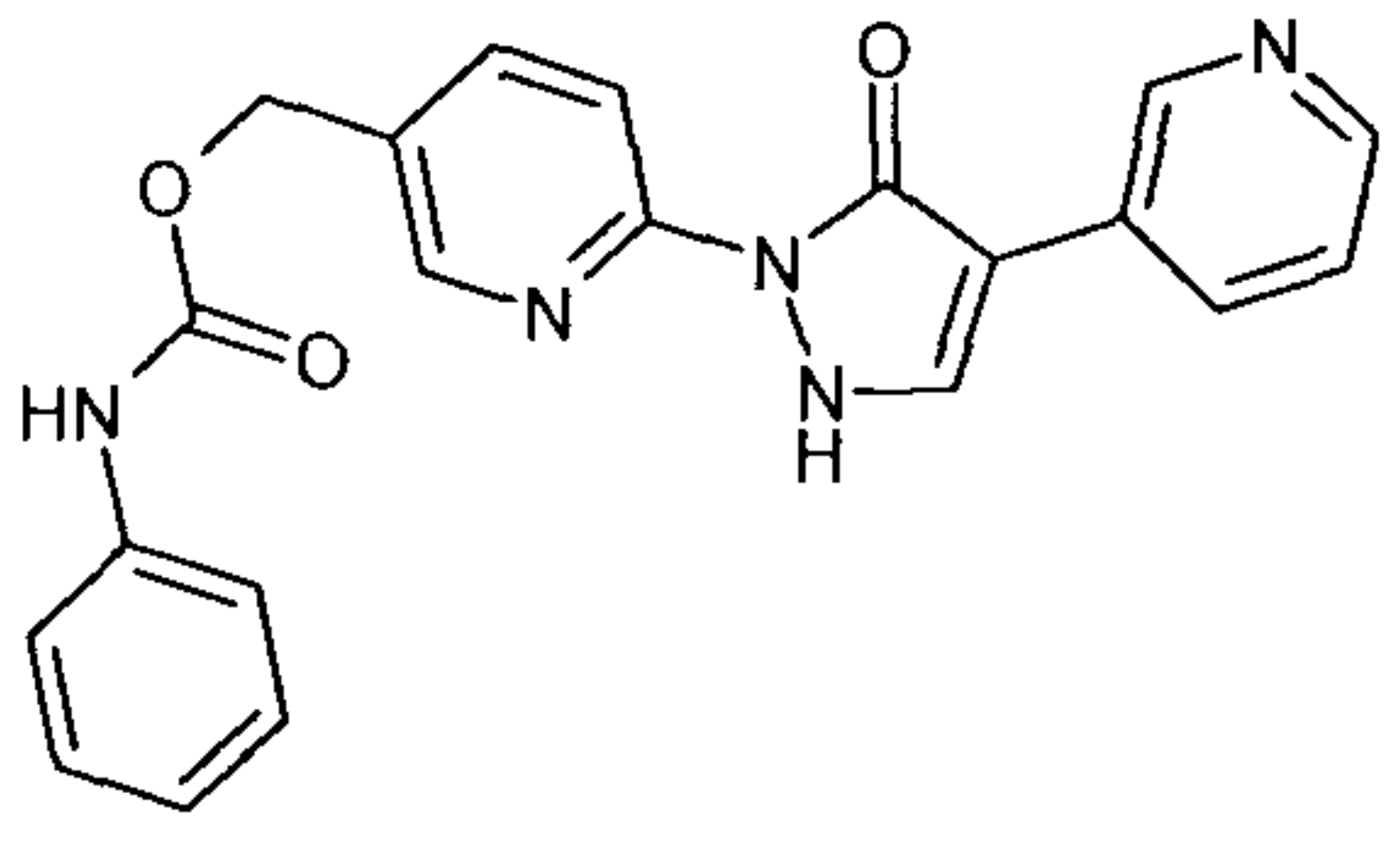
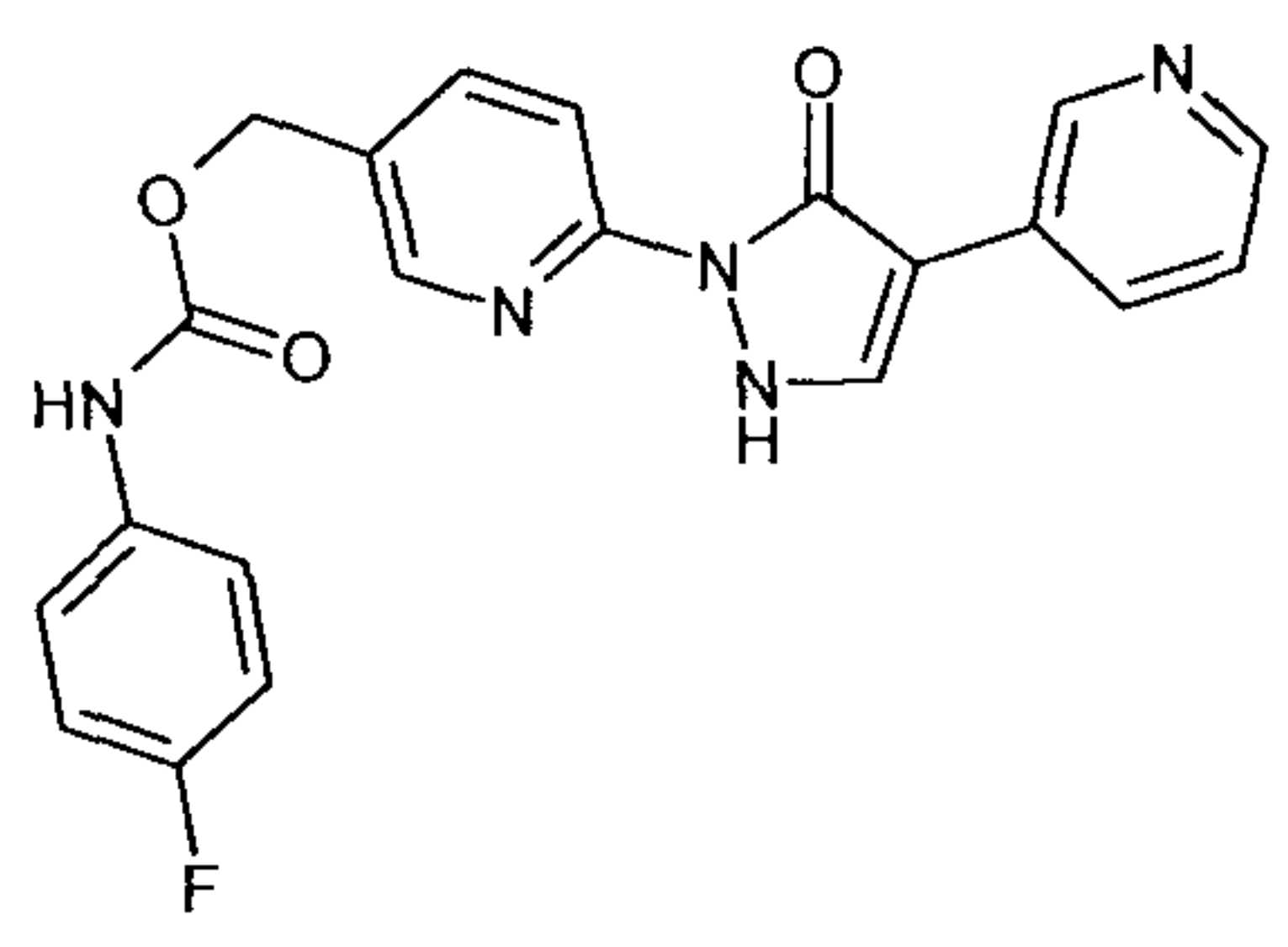
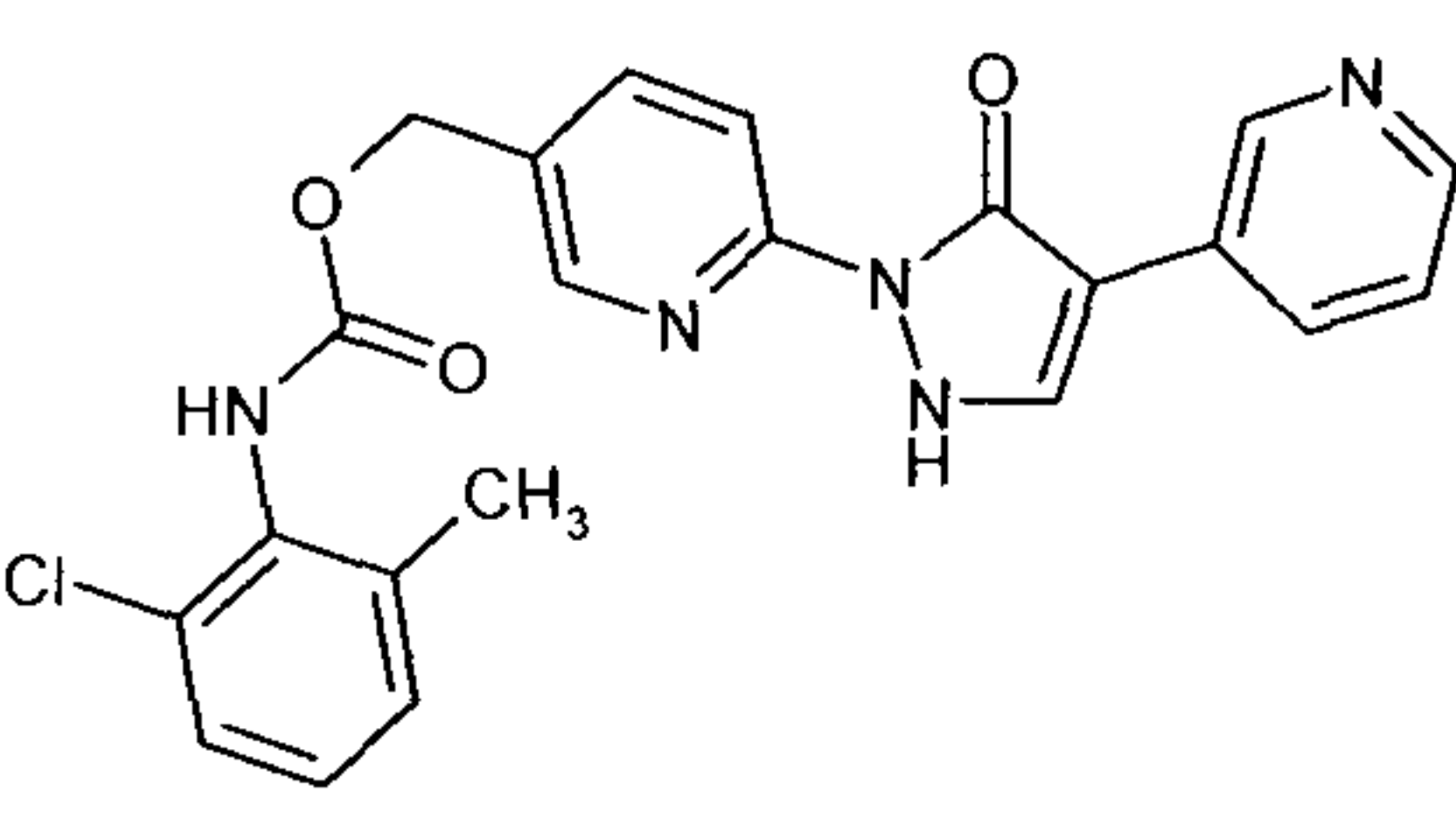
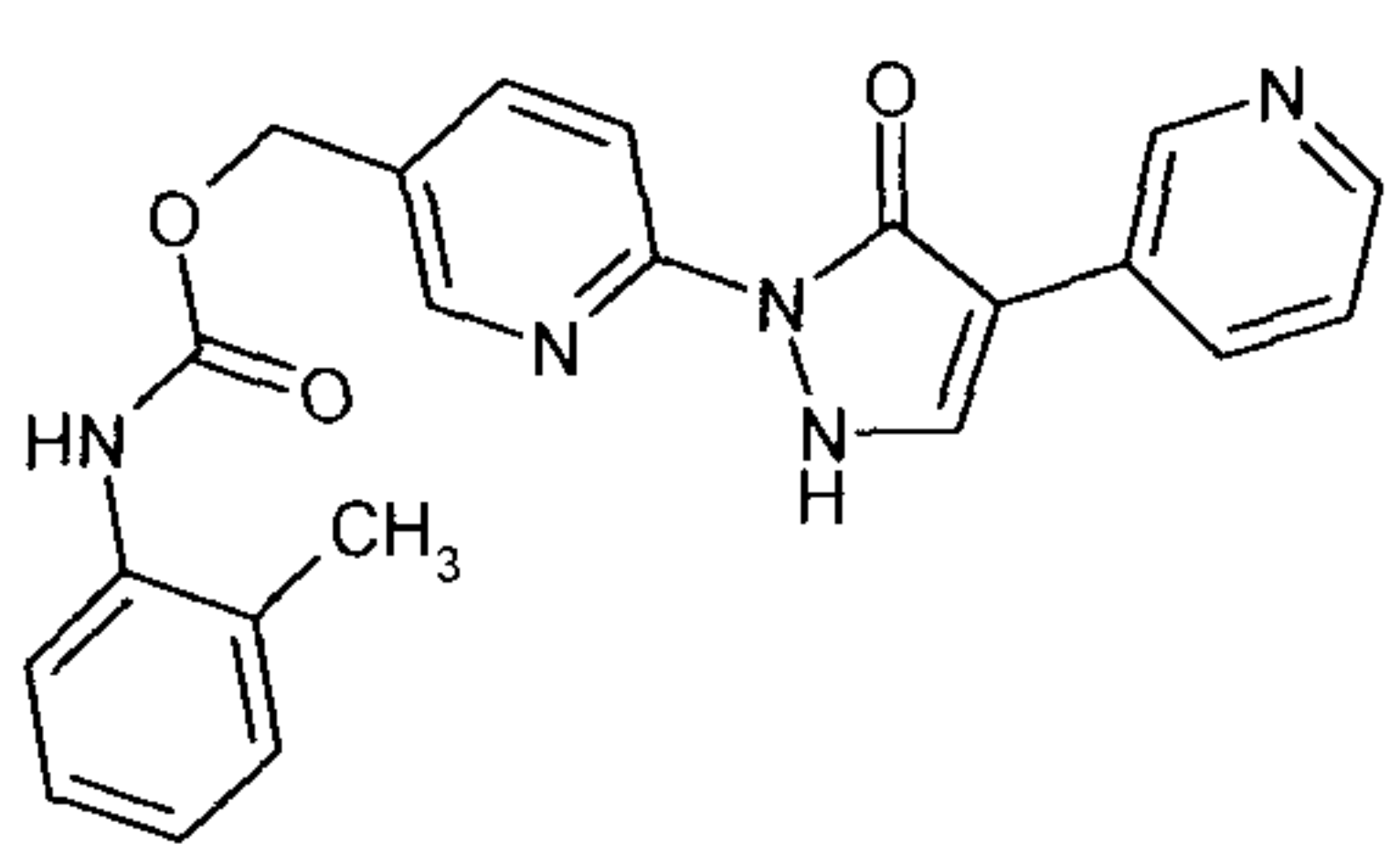
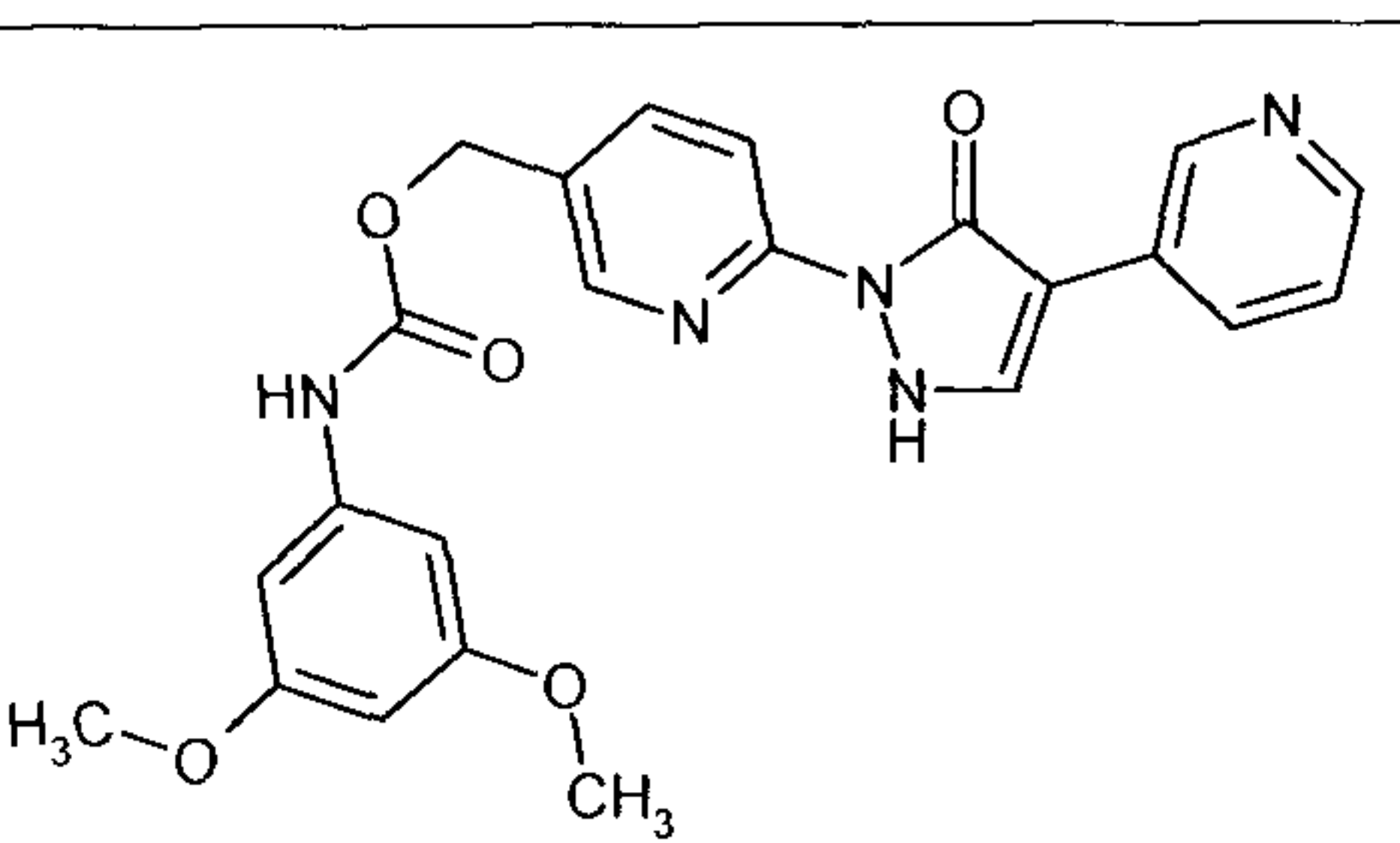
The compounds listed in Table 2 are prepared analogously to the procedure of Example 70 from 0.1 mmol of 2-[5-(hydroxymethyl)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3*H*-pyrazol-3-one and

15 0.1 mmol of the appropriate isocyanate:

Table 2

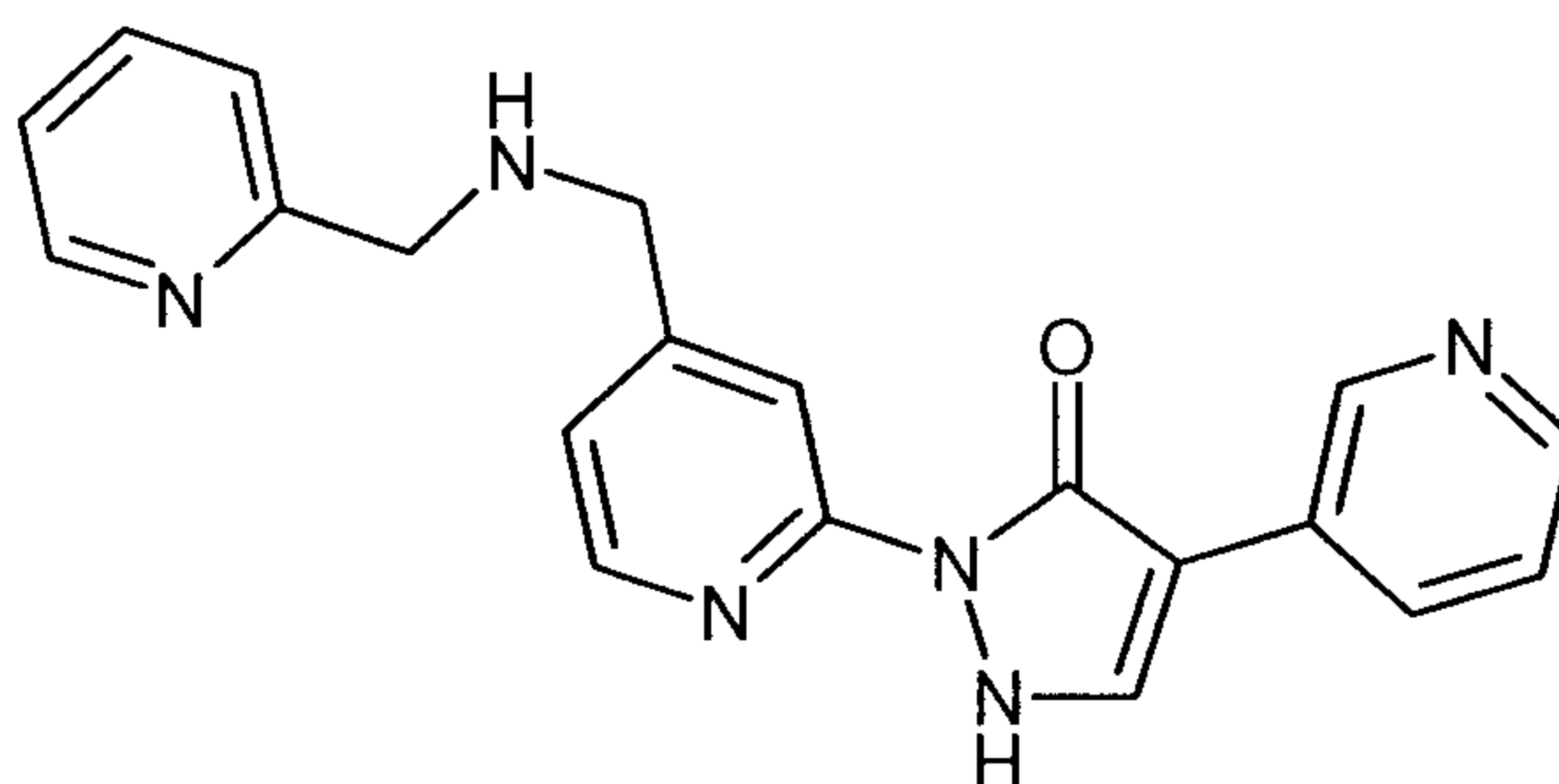
Example No.	Structure	Yield (% of theory)	MS (ESI): $[M+H]^+$; LC-MS: R_t (Method 9)
71		4%	$m/z = 406$; 1.55 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 9)
72		2%	m/z = 422; 1.63 min
73		1%	m/z = 402; 1.57 min
74		3%	m/z = 416; 1.67 min
75		2%	m/z = 424; 1.44 min
76		2%	m/z = 442; 1.58 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 9)
77		2%	m/z = 388; 1.48 min
78		4%	m/z = 406; 1.52 min
79		2%	m/z = 436; 1.53 min
80		1%	m/z = 402; 1.51 min
81		2%	m/z = 448; 1.55 min

Example 82

4-Pyridin-3-yl-2-(4-{[(pyridin-2-ylmethyl)amino]methyl}pyridin-2-yl)-1,2-dihydro-3H-pyrazol-3-one



2.7 g (10 mmol) of the compound from Example 4A are dissolved in 60 ml of ethanol and provided as a stock solution.

11 mg (0.1 mmol) of pyridine-2-carbaldehyde are initially charged, and 600 μ l (0.1 mmol) of the
5 above stock solution and 26 mg (0.2 mmol) of *N,N*-diisopropylethylamine (Hünig base) are added. The reaction mixture is stirred at RT for 16 h, 4 mg (0.1 mmol) of sodium borohydride are then added and the mixture is shaken at RT for a further 3 h. For work-up, the mixture is added to 100 μ l of water, the solvent is removed under reduced pressure and the residue is dissolved in DMSO. After filtration, the filtrate is purified by preparative LC-MS (Method 9). The product fractions are
10 concentrated under reduced pressure, and the residue is dried.

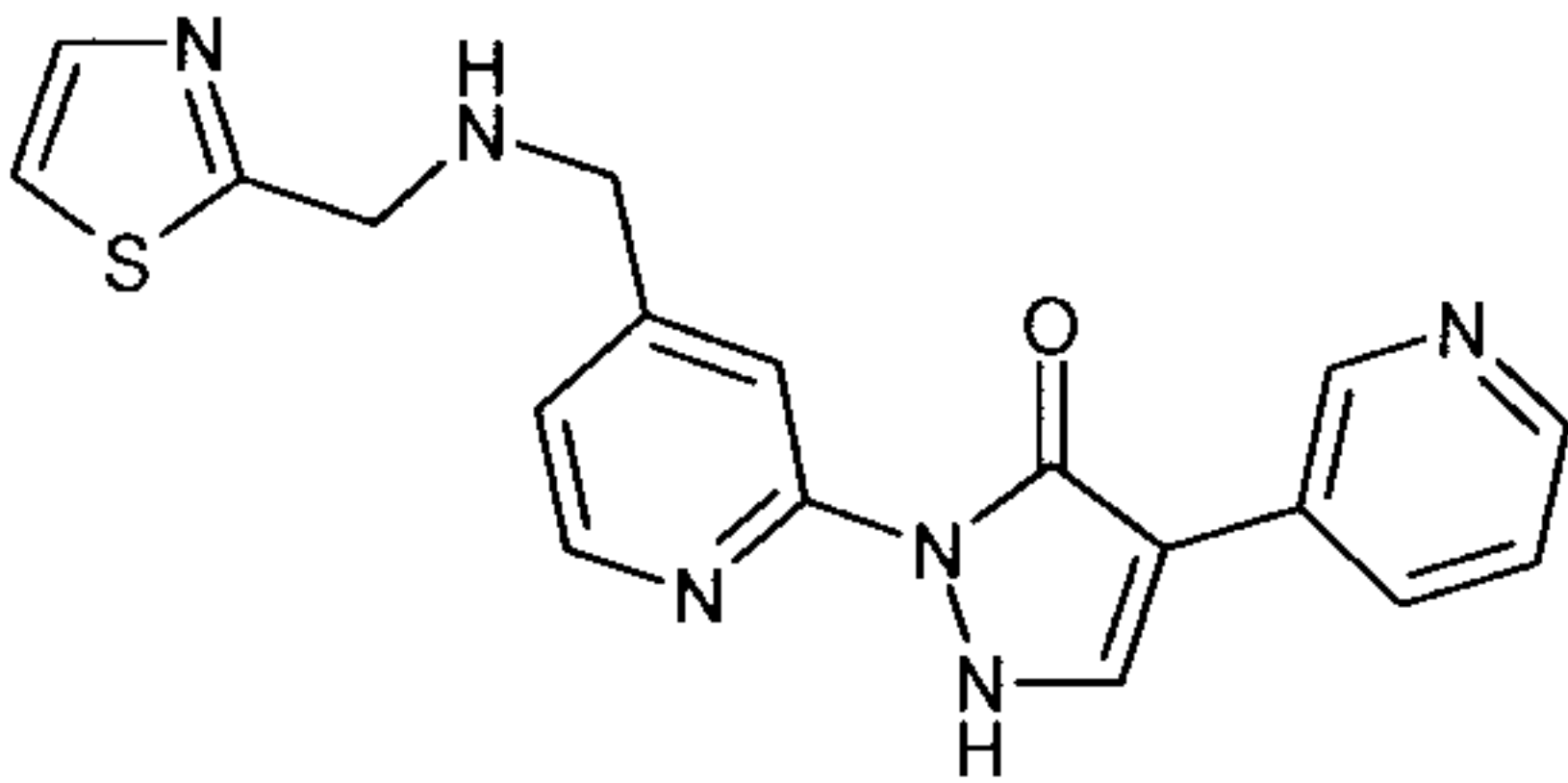
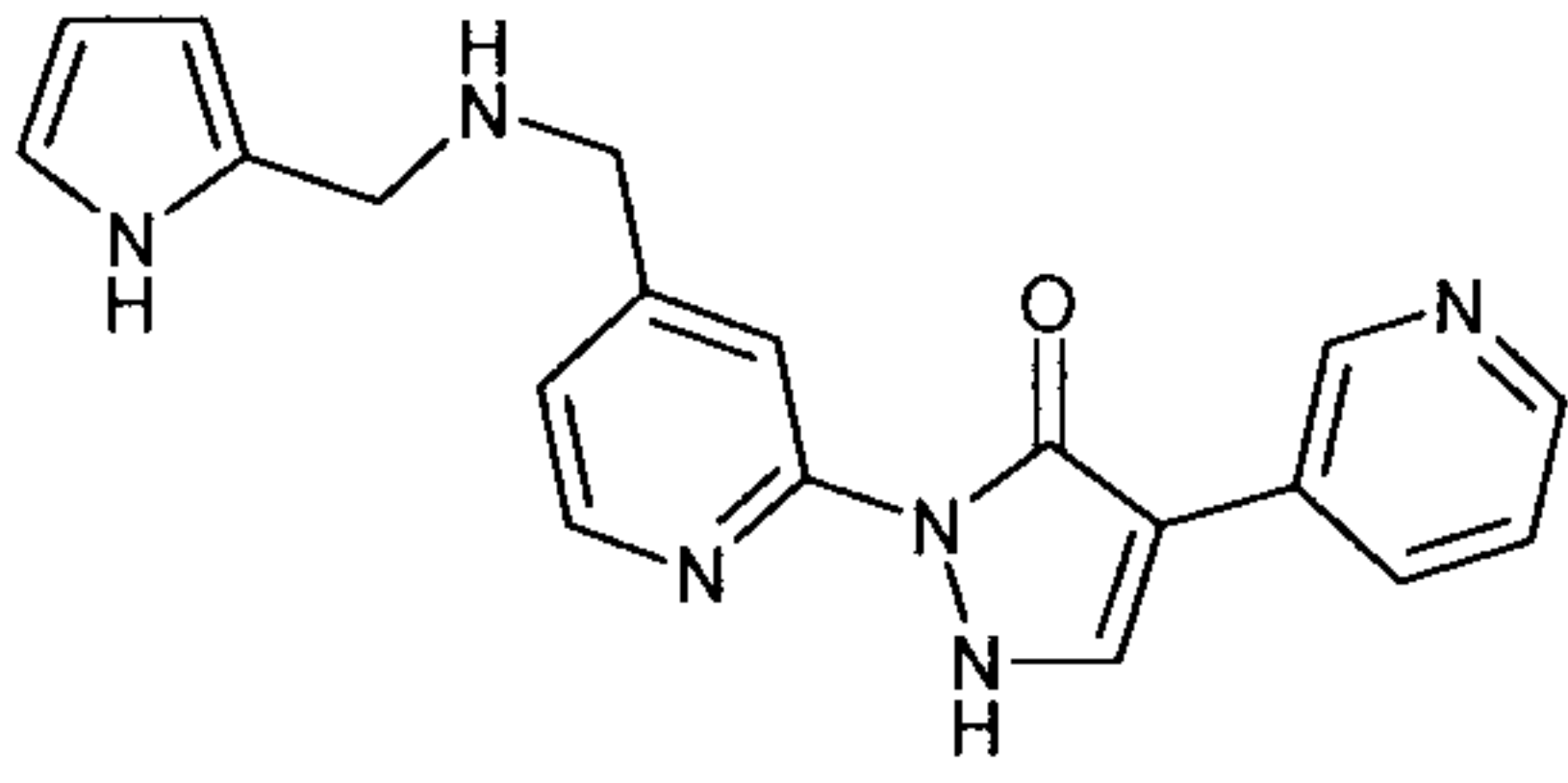
Yield: 0.7 mg (2% of theory)

LC-MS (Method 9): R_t = 1.56 min; MS (ESIpos): m/z = 358 $[M+H]^+$.

The compounds listed in Table 3 are prepared analogously to the procedure of Example 82 from 0.1 mmol of the compound from Example 4A and 0.1 mmol of the appropriate aldehyde:

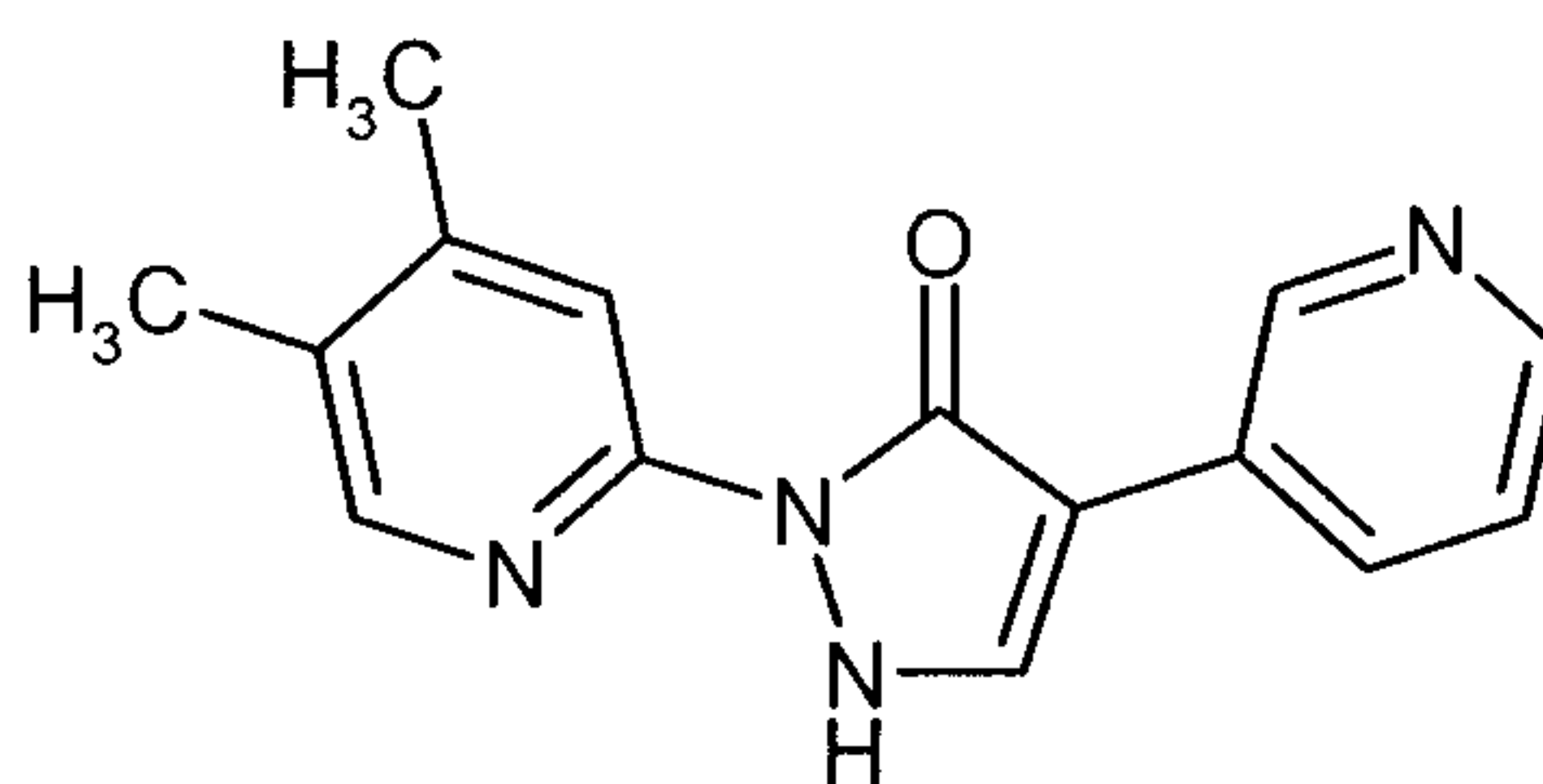
15 Table 3

Example No.	Structure	Yield (% of theory)	MS (ESI): $[M+H]^+$; LC-MS: R_t (Method 9)
83		2%	m/z = 386; 1.31 min

Example No.	Structure	Yield (% of theory)	MS (ESI): [M+H] ⁺ ; LC-MS: R _t (Method 9)
84		2%	m/z = 364; 1.59 min
85		4%	m/z = 347; 1.36 min

Example 86

2-(4,5-Dimethylpyridin-2-yl)-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one



- 5 220 mg (1.0 mmol) of the compound from Example 2A are initially charged in 5 ml of ethanol. 137 mg (1.0 mmol) of the compound from Example 21A and 38 mg (0.2 mmol) of p-toluenesulfonic acid are added, and the mixture is stirred under reflux for 16 h. The mixture is then allowed to cool to RT, and the solid formed is filtered off, washed with *tert*-butyl methyl ether and dried under high vacuum. This gives 28 mg of the title compound. The mother liquor is put aside
- 10 and used for preparing the hydrochloride (see Example 87).

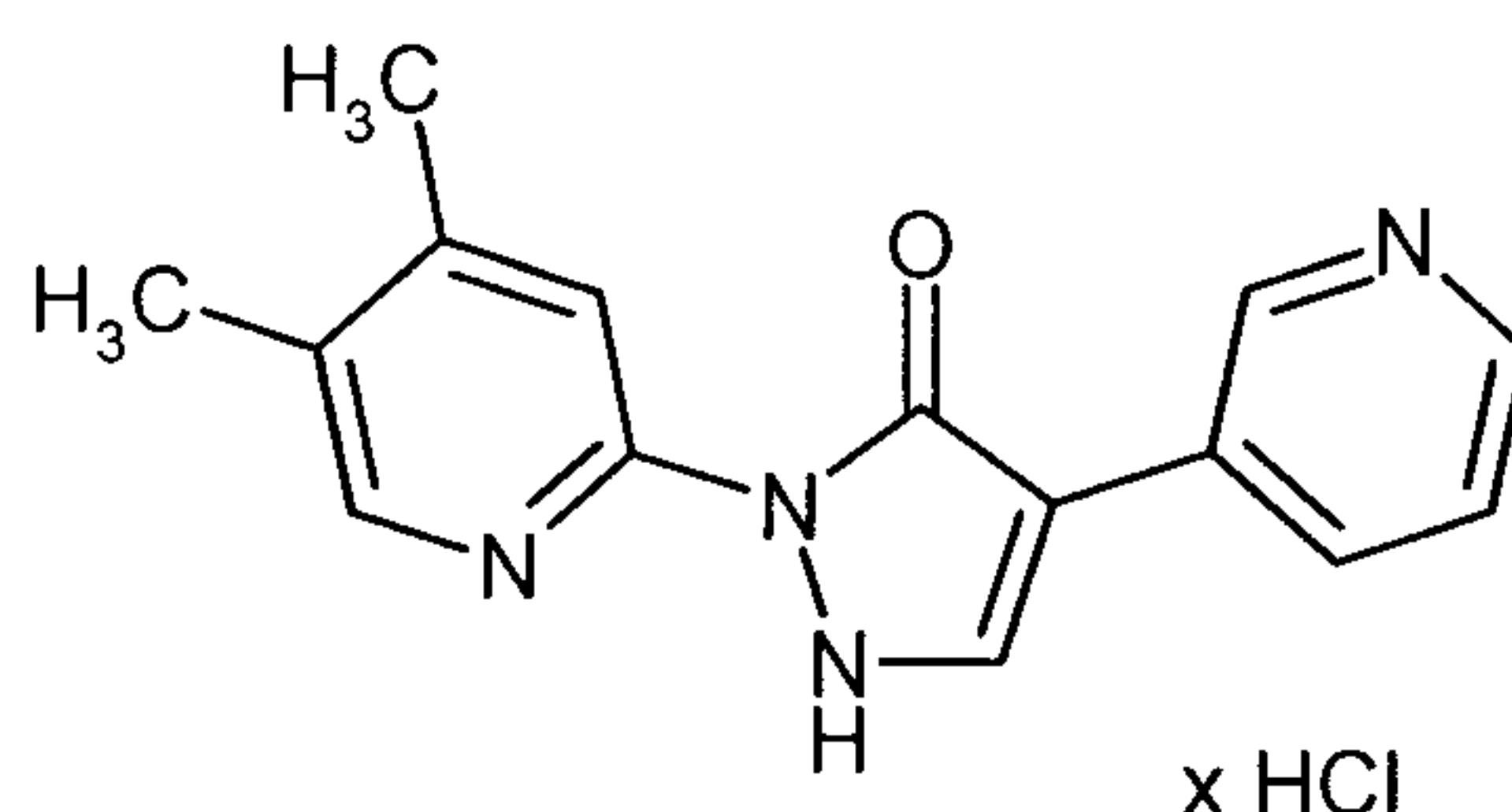
Yield: 28 mg (11% of theory)

LC-MS (Method 6): R_t = 1.10 min; MS (ESIpos): m/z = 267 [M+H]⁺;

¹H-NMR (400 MHz, DMSO-d₆): δ = 9.05 (s, 1H), 8.37-8.28 (m, 2H), 8.24-8.15 (m, 2H), 8.09-7.95 (s, 1H), 7.36 (dd, 1H), 2.36 (s, 3H), 2.25 (s, 3H).

Example 87

2-(4,5-Dimethylpyridin-2-yl)-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one hydrochloride



The mother liquor obtained during the preparation of Example 86 (see above) is concentrated on a rotary evaporator, and the residue is purified by preparative HPLC (RP18-column; mobile phase: acetonitrile/water-gradient with addition of 0.1% TFA to the water). The residue obtained after the concentration of the product fractions is triturated with 5 ml of a 4 N solution of hydrogen chloride in dioxane for 30 min. The solid is filtered off, washed twice with *tert*-butyl methyl ether and dried under high vacuum.

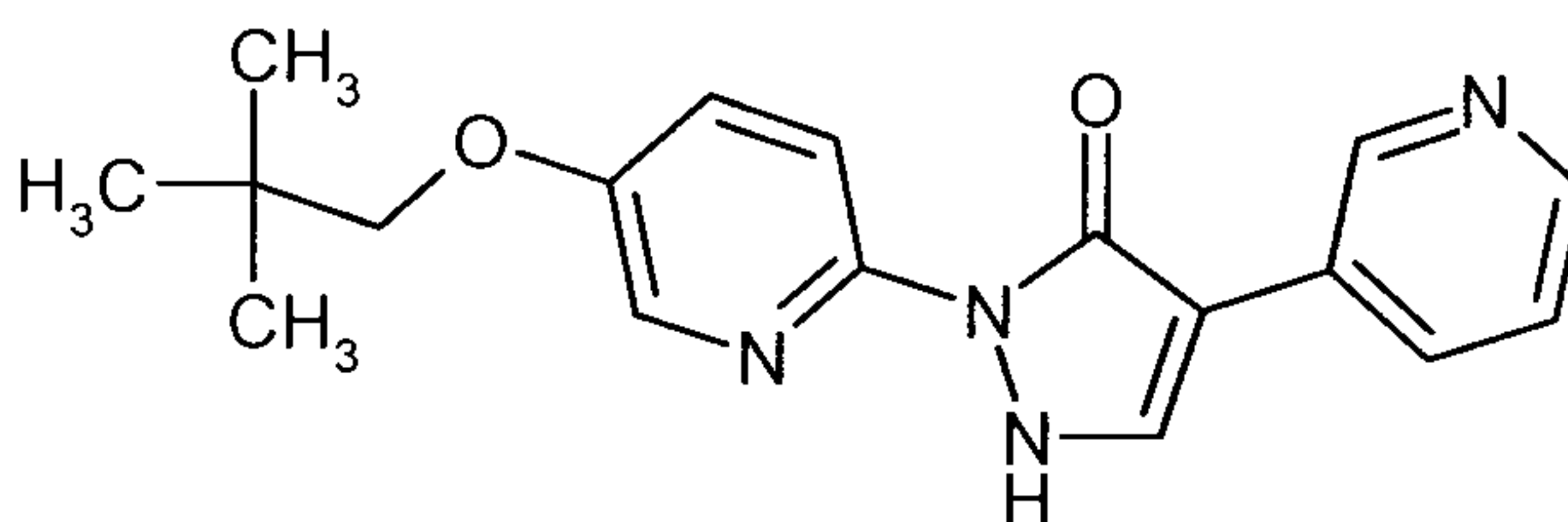
Yield: 100 mg (33% of theory, based on 1.0 mmol of the compound from Example 21A)

LC-MS (Method 6): $R_t = 1.12$ min; MS (ESIpos): $m/z = 267$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 9.32$ (s, 1H), 8.94 (d, 1H), 8.61 (s, 1H), 8.57 (d, 1H), 8.23 (s, 1H), 8.21 (s, 1H), 8.00 (dd, 1H), 2.41 (s, 3H), 2.28 (s, 3H).

Example 88

2-[5-(2,2-Dimethylpropoxy)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one



220 mg (1.0 mmol) of the compound from Example 2A are initially charged in 5 ml of ethanol. 260 mg (purity 75%, 1.0 mmol) of the compound from Example 19A and 38 mg (0.2 mmol) of *p*-toluenesulfonic acid are added, and the mixture is stirred under reflux for 16 h. The mixture is then allowed to cool to RT, and the solid formed is filtered off, washed with *tert*-butyl methyl ether and dried under high vacuum. This gives 37 mg of the title compound. The mother liquor is put aside and used for preparing the hydrochloride (see Example 89).

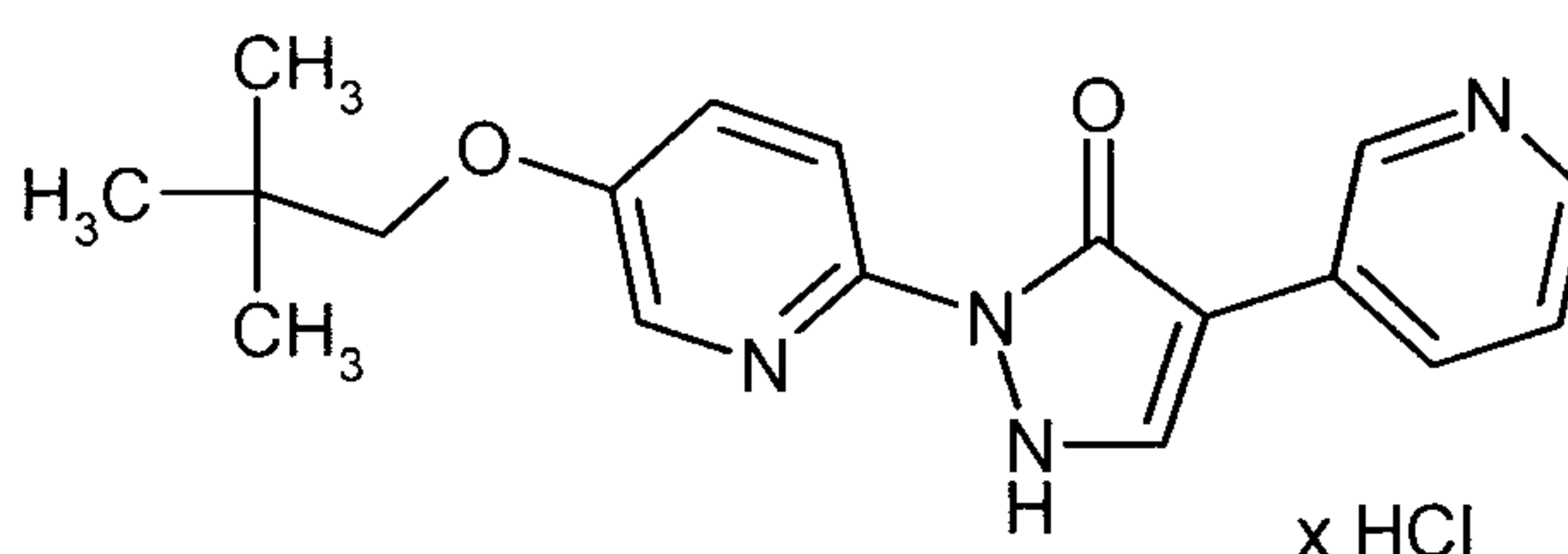
Yield: 37 mg (11% of theory)

LC-MS (Method 5): $R_t = 1.05$ min; MS (ESIpos): $m/z = 325$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.08$ (s, 1H), 8.45-8.35 (m, 2H), 8.32-8.15 (m, 3H), 7.70 (dd, 1H), 7.37 (dd, 1H), 3.76 (s, 2H), 1.01 (s, 9H).

5 **Example 89**

2-[5-(2,2-Dimethylpropoxy)pyridin-2-yl]-4-pyridin-3-yl-1,2-dihydro-3H-pyrazol-3-one
hydrochloride



10 The mother liquor obtained during the preparation of Example 88 (see above) is concentrated on a rotary evaporator, and the residue is purified by preparative HPLC (RP18-column; mobile phase: acetonitrile/water-gradient with addition of 0.1% TFA to the water). The residue obtained after the concentration of the product fractions is triturated with 5 ml of a 4 N solution of hydrogen chloride in dioxane for 30 min. The solid is filtered off, washed twice with *tert*-butyl methyl ether and dried under high vacuum.

15 Yield: 160 mg (44% of theory, based on 1.0 mmol of the compound from Example 19A)

LC-MS (Method 2): $R_t = 1.52$ min; MS (ESIpos): $m/z = 325$ $[M+H]^+$;

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): $\delta = 9.39$ (s, 1H), 8.96 (d, 1H), 8.74 (s, 1H), 8.64 (d, 1H), 8.30 (d, 1H), 8.21 (d, 1H), 8.00 (dd, 1H), 7.70 (dd, 1H), 3.78 (s, 2H), 1.01 (s, 9H).

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B. Evaluation of the pharmacological activity

The pharmacological properties of the compounds according to the invention can be demonstrated in the following assays:

Abbreviations:

DMEM Dulbecco's modified Eagle medium

FCS fetal calf serum

TMB 3,3',5,5'-tetramethylbenzidine

Tris tris(hydroxymethyl)aminomethane

5

1. **In vitro tests for determination of the activity and selectivity of HIF prolyl 4-hydroxylase inhibitors**

1.a) **Inhibition of the activity of HIF prolyl hydroxylase:**

Hydroxylated HIF bonds specifically to the von Hippel-Lindau protein-elongin B-elongin C complex (VBC complex). This interaction occurs only if HIF is hydroxylated on a conserved prolyl radical. It is the basis for the biochemical determination of HIF prolyl hydroxylase activity. The test is carried out as described [Oehme F., Jonghaus W., Narouz-Ott L., Huetter J., Flamme I., *Anal. Biochem.* 330 (1), 74-80 (2004)]:

A clear 96-well microtiter plate coated with NeutrAvidin HBC (Pierce) is incubated with blocker casein for 30 minutes. The plate is then washed three times with 200 µl each time of wash buffer (50 mM Tris, pH 7.5, 100 mM NaCl, 10 % (v/v) blocker casein, 0.05 % (v/v) TweenTM 20) per well. The peptide biotin-DLDLEMLAPYIPMDDDFQL (Eurogentec, 4102 Seraing, Belgium) is added in a concentration of 400 nM in 100 µl wash buffer. This peptide serves as a substrate for the prolyl hydroxylation and is bonded to the microtiter plate. After incubation for 60 minutes, the plate is washed three times with wash buffer, incubated with 1 mM biotin in blocker casein for 30 minutes and then washed again three times with wash buffer.

To carry out the prolyl hydroxylase reaction, the peptide substrate bonded to the plate is incubated with a cell lysate containing prolyl hydroxylase for 1 to 60 minutes. The reaction takes place in 100 µl reaction buffer (20 mM Tris, pH 7.5, 5 mM KCl, 1.5 mM MgCl₂, 1 µM - 1 mM 2-oxoglutarate, 10 µM FeSO₄, 2 mM ascorbate) at room temperature. The reaction mixture

25

moreover contains various concentrations of the prolyl hydroxylase inhibitor to be tested. The test substance is preferably, but not exclusively, employed at concentrations of between 1 nM and 100 μ M. The reaction is stopped by washing the plate three times with wash buffer.

For quantitative determination of the prolyl hydroxylation, a fusion protein which contains both
5 thioredoxin from *E. coli* and the VBC complex in 80 μ l bonding buffer (50 mM Tris, pH 7.5, 120 mM NaCl) is added. After 15 minutes, 10 μ l of a solution of polyclonal anti-thioredoxin antibodies from rabbit in bonding buffer are added. After a further 30 minutes, 10 μ l of a solution of anti-rabbit immunoglobulin coupled to horseradish peroxidase in bonding buffer are added. After
10 incubation at room temperature for 30 minutes, the plate is washed three times with wash buffer in order to remove non-bonded VBC complex and antibodies. To determine the amount of bonded VBC complex, the plate is incubated with TMB for 15 minutes. The color reaction is ended by addition of 100 μ l 1 M sulfuric acid. The amount of bonded VBC complex is determined by measurement of the optical density at 450 nm. It is proportional to the amount of hydroxylated proline in the peptide substrate.

15 Alternatively, a VBC complex coupled to europium (Perkin Elmer) can be used for detection of the prolyl hydroxylation. In this case, the amount of bonded VBC complex is determined by the fluorescence with respect to time. The use of VBC complex labeled with [³⁵S]-methionine is moreover possible. For this, the radioactively labeled VBC complex can be prepared by *in vitro* transcription-translation in reticulocyte lysate.

20 The embodiment examples inhibit the activity of HIF prolyl hydroxylase in this test with an IC₅₀ value of ≤ 30 μ M. Representative IC₅₀ values for the embodiment examples are reproduced in the following Table 1:

Table 1

Example No.	IC ₅₀ [μ M]
5	6.3
8	5.2
10	0.26
18	0.91
22	3.24
65	0.9

Example No.	IC ₅₀ [μM]
80	1.6
89	3.7

1.b) Cellular, functional *in vitro* test:

The activity of the compounds according to the invention is quantified with the aid of a recombinant cell line. The cell is originally derived from a human lung carcinoma cell line (A549, ATCC: American Type Culture Collection, Manassas, VA 20108, USA). The test cell line is transfected in a stable manner with a vector which contains the reporter gene of *Photinus pyralis* luciferase (called luciferase in the following) under the control of an artificial minimal promoter. The minimal promoter comprises two hypoxia-responsible elements upstream of a TATA box [Oehme F., Ellinghaus P., Kolkhof P., Smith T.J., Ramakrishnan S., Hütter J., Schramm M., Flamme I., *Biochem. Biophys. Res. Commun.* **296** (2), 343-9 (2002)]. Under the effect of hypoxia (for example culturing in the presence of 1% oxygen for 24 hours) or under the action of non-selective dioxygenase inhibitors (for example desferroxamine in a concentration of 100 μM, cobalt chloride in a concentration of 100 μM or N-oxalylglycine diethyl ester in a concentration of 1 mM), the test cell line produces luciferase, which can be detected and quantified with the aid of suitable bioluminescence reagents (for example Steady-Glo® Luciferase Assay System, Promega Corporation, Madison, WI 53711, USA) and a suitable luminometer.

Test procedure: On the day before the test, the cells are plated out in an exactly calculated amount of culture medium (DMEM, 10% FCS, 2 mM glutamine) in 384- or 1536-well microtiter plates and kept in a cell incubator (96% atmospheric humidity, 5% v/v CO₂, 37°C). On the test day, the test substances are added to the culture medium in graduated concentrations. No test substance is added to the cells in batches serving as negative controls. As a positive control for determination of the sensitivity of the cell to inhibitors, desferroxamine for example is added in a final concentration of 100 μM. Six to 24 hours after transfer of the test substances into the wells of the microtiter plates, the resulting light signal is measured in the luminometer. A dose/effect relationship is plotted with the aid of the measurement values, which serves as the basis for determining the half-maximum active concentration (called the EC₅₀ value).

1.c) Cellular, functional *in vitro* test of modification of the gene expression:

To investigate the modification of the expression of specific mRNAs in human cell lines after treatment with test substances, the following cell lines are cultured on 6- or 24-well plates: human

hepatoma cells (HUH, JCRB Cell Bank, Japan), human embryonal kidney fibroblasts (HEK/293, ATCC, Manassas, VA 20108, USA), human cervical carcinoma cells (HeLa, ATCC, Manassas, VA 20108, USA), human umbilical vein endothelial cells (HUVEC, Cambrex, East Rutherford, New Jersey 07073, USA). 24 hours after addition of the test substances, the cells are washed with
5 phosphate-buffered saline and the total RNA is obtained from them using a suitable method (for example Trizol[®] reagent, Invitrogen GmbH, 76131 Karlsruhe, Germany).

For a typical analysis experiment, 1 µg each of the total RNA obtained in this way is digested with DNase I and translated into a complementary DNA (cDNA) using a suitable reverse transcriptase reaction (ImProm-II Reverse Transcription System, Promega Corporation, Madison, WI 53711,
10 USA). 2.5% of the cDNA batch obtained in this way is used in each case for the polymerase chain reaction. The expression level of the mRNA of the genes to be investigated is investigated by means of the *real time quantitative polymerase chain reaction* [TaqMan-PCR; Heid C.A., Stevens J., Livak K.J., Williams P.M., *Genome Res.* 6 (10), 986-94 (1996)] using an ABI Prism 7700 sequence detection instrument (Applied Biosystems, Inc.). The primer-probe combinations used
15 here are generated by means of Primer Express 1.5 Software (Applied Biosystems, Inc.). Specifically, the mRNAs of erythropoietin, carboanhydrase IX, lactate dehydrogenase A and vascular endothelial cell growth factor are investigated.

Substances according to the present invention lead to a significant dose-dependent increase in the mRNA of hypoxia-induced genes in cells of human origin.

20 2. **In vivo tests for detection of the action in the cardiovascular system**

2.a) **In vivo test of modification of gene expression:**

The test compounds dissolved in suitable solvents are administered to mice or rats either orally by stomach tube administration, intraperitoneally or intravenously. Typical dosages are 0.1, 0.5, 1, 5, 10, 20, 50, 100 and 300 mg substance per kg of body weight and administration. Control animals
25 receive only solvent. 4, 8 or 24 hours after administration of the test substance the animals are sacrificed with an overdose of isoflurane and a subsequent fracture of the neck and the organs to be investigated are removed. Parts of the organs are shock-frozen in liquid nitrogen. Total RNA is obtained from the organ parts as described under B.1.a) and this is translated into a cDNA. The expression level of the mRNA of the genes to be investigated is investigated by means of the *real*
30 *time quantitative polymerase chain reaction* [TaqMan-PCR; Heid C.A., Stevens J., Livak K.J., Williams P.M., *Genome Res.* 6 (10), 986-94 (1996)] using an ABI Prism 7700 sequence detection instrument (Applied Biosystems, Inc.).

Substances according to the present invention lead to a significant dose-dependent increase in the mRNA of erythropoietin in the kidney after oral or parenteral administration compared with the placebo control.

2.b) Determination of the erythropoietin level in serum:

5 The test substance in a suitable solvent is administered to mice or rats either intraperitoneally or orally once or twice daily. Typical dosages are 0.1, 0.5, 1, 5, 10, 20, 50, 100 and 300 mg substance per kg of body weight and administration. Placebo control animals receive only solvent. Before the administration and four hours after the last administration of substance, 50 µl of blood are taken from the animals from the retroorbital venous plexus or the tail vein under short narcosis. The
10 blood is rendered uncoagulable by addition of lithium heparin. The blood plasma is obtained by centrifugation. The content of erythropoietin in the blood plasma is determined with the aid of an erythropoietin-ELISA (Quantikine® mouse Epo Immunoassay, R&D Systems, Inc., Minneapolis, USA) in accordance with the manufacturer's instructions. The measurement values are converted into pg/ml with the aid of a reference measurement recorded for mouse erythropoietin.

15 Substances according to the present invention lead to a significant dose-dependent increase in the plasma erythropoietin after oral and parenteral administration compared with the starting value and the placebo control.

2.c) Determination of the cell composition of peripheral blood:

The test substance in a suitable solvent is administered to mice or rats either intraperitoneally or orally once or twice daily for several days. Typical dosages are for example 0.1, 0.5, 1, 5, 10, 20,
20 50, 100 and 300 mg substance per kg of body weight and administration. Control animals receive only solvent. At the end of the study, blood is taken from the animals from the venous plexus of the corner of the eye or the tail vein under short narcosis and is rendered uncoagulable by addition of sodium citrate. The concentrations of erythrocytes, leukocytes and thrombocytes are determined
25 in the blood samples in a suitable electronic measuring apparatus. The concentration of the reticulocytes is determined by microscope screening of in each case 1000 erythrocytes with the aid of blood smears stained with a stain solution suitable for this purpose (KABE Labortechnik, Nümbrecht). For determination of the hematocrit, blood is taken from the retroorbital venous plexus by means of a hematocrit capillary and the hematocrit value is read off manually after
30 centrifugation of the capillary in a centrifuge suitable for this purpose.

Substances according to the present invention lead to a significant dose-dependent increase in the hematocrit, the erythrocyte count and the reticulocytes after oral and parenteral administration

compared with the starting value and the placebo control.

C. Embodiment examples for pharmaceutical compositions

The compounds according to the invention can be converted into pharmaceutical formulations as follows.

Tablet:

5 **Composition:**

100 mg of the compound according to the invention, 50 mg lactose (monohydrate), 50 mg maize starch (native), 10 mg polyvinylpyrrolidone (PVP 25) (BASF, Ludwigshafen, Germany) and 2 mg magnesium stearate.

Tablet weight 212 mg. Diameter 8 mm, radius of curvature 12 mm.

10 **Preparation:**

The mixture of compound according to the invention, lactose and starch is granulated with a 5% strength solution (w/w) of the PVP in water. After drying, the granules are mixed with the magnesium stearate for 5 minutes. This mixture is pressed with a conventional tablet press (for tablet format see above). A pressing force of 15 kN is used as the recommended value for the
15 pressing.

Suspension for oral administration:

Composition:

1000 mg of the compound according to the invention, 1000 mg ethanol (96%), 400 mg Rhodigel® (xanthan gum from FMC, Pennsylvania, USA) and 99 g water.

20 10 ml of oral suspension correspond to an individual dose of 100 mg of the compound according to the invention.

Preparation:

The Rhodigel is suspended in ethanol and the compound according to the invention is added to the suspension. The water is added with stirring. The mixture is stirred for approx. 6 h until swelling
25 of the Rhodigel has ended.

Solution for oral administration:

Composition:

500 mg of the compound according to the invention, 2.5 g polysorbate and 97 g polyethylene glycol 400. 20 g of oral solution correspond to an individual dose of 100 mg of the compound
5 according to the invention.

Preparation:

The compound according to the invention is suspended in a mixture of polyethylene glycol and polysorbate, while stirring. The stirring operation is continued until dissolution of the compound according to the invention is complete.

10 **i.v. Solution:**

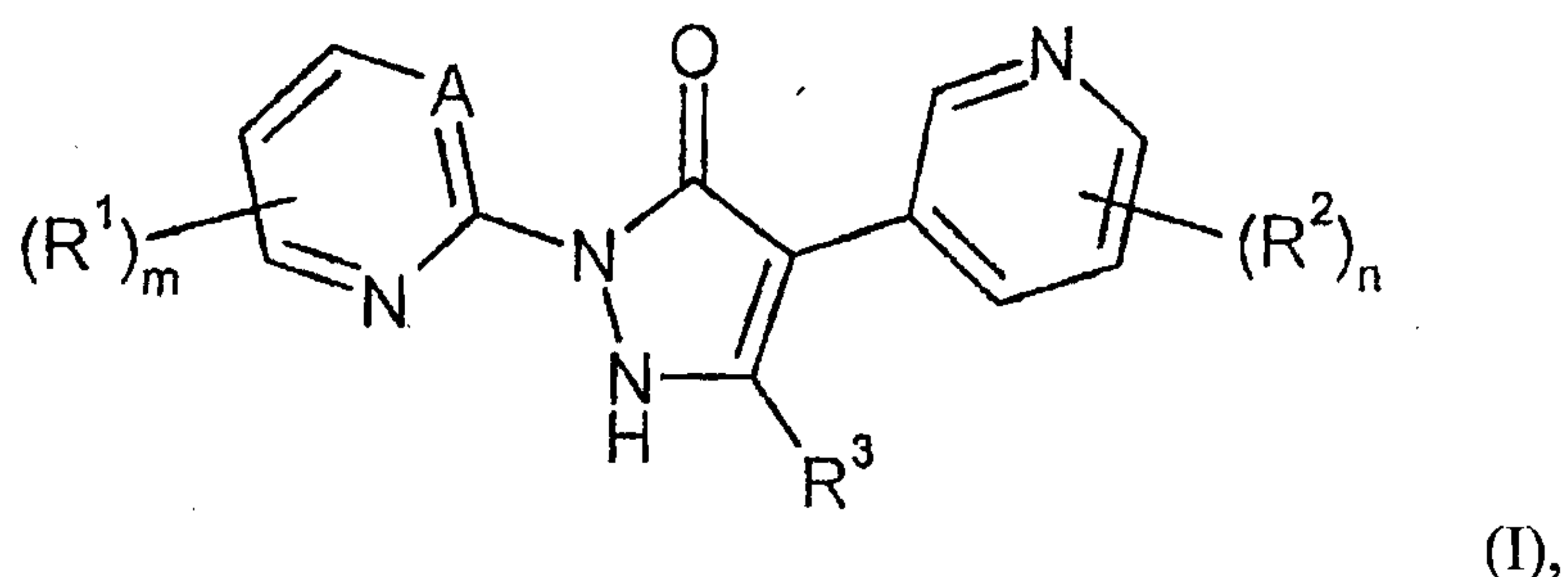
The compound according to the invention is dissolved in a concentration below the saturation solubility in a physiologically acceptable solvent (for example isotonic saline solution, glucose solution 5% and/or PEG 400 solution 30%). The solution is subjected to sterile filtration and is transferred into sterile and pyrogen-free injection containers.

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CLAIMS:

1. A compound of the formula (I)



in which

- 5 A represents CH,

R^1 represents a substituent selected from the group consisting of (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹ and -NR²⁵R²⁶ in which

- 10 (i) (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of (C₁-C₆)-alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and
15 -NR²⁵R²⁶,

- where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered
20 heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

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(ii) $R^6, R^9, R^{12}, R^{14}, R^{16}, R^{19}, R^{23}$ and R^{25} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) $R^7, R^{10}, R^{11}, R^{13}, R^{15}, R^{17}, R^{18}$ and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R^6 and R^7, R^9 and R^{10}, R^{11} and R^{12}, R^{13} and R^{14}, R^{15} and R^{16}, R^{16} and R^{17}, R^{18} and R^{19} and also R^{25} and R^{26} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen,

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cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of -O-C(=O)-NR^{9A}R^{10A},
 5 -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A} and
 -NR^{25A}R^{26A} in which

(i) R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A} and R^{25A} independently of one another represent
 (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl,
 hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-
 10 alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another
 represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano,
 trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-
 alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

15 and/or in which

(iii) R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A},
 R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which
 they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or
 disubstituted by identical or different substituents from the group consisting of halogen,
 20 cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo,
 amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-
 alkoxycarbonyl,

m represents the number 1,

n represents the number 0 or 1

25 and

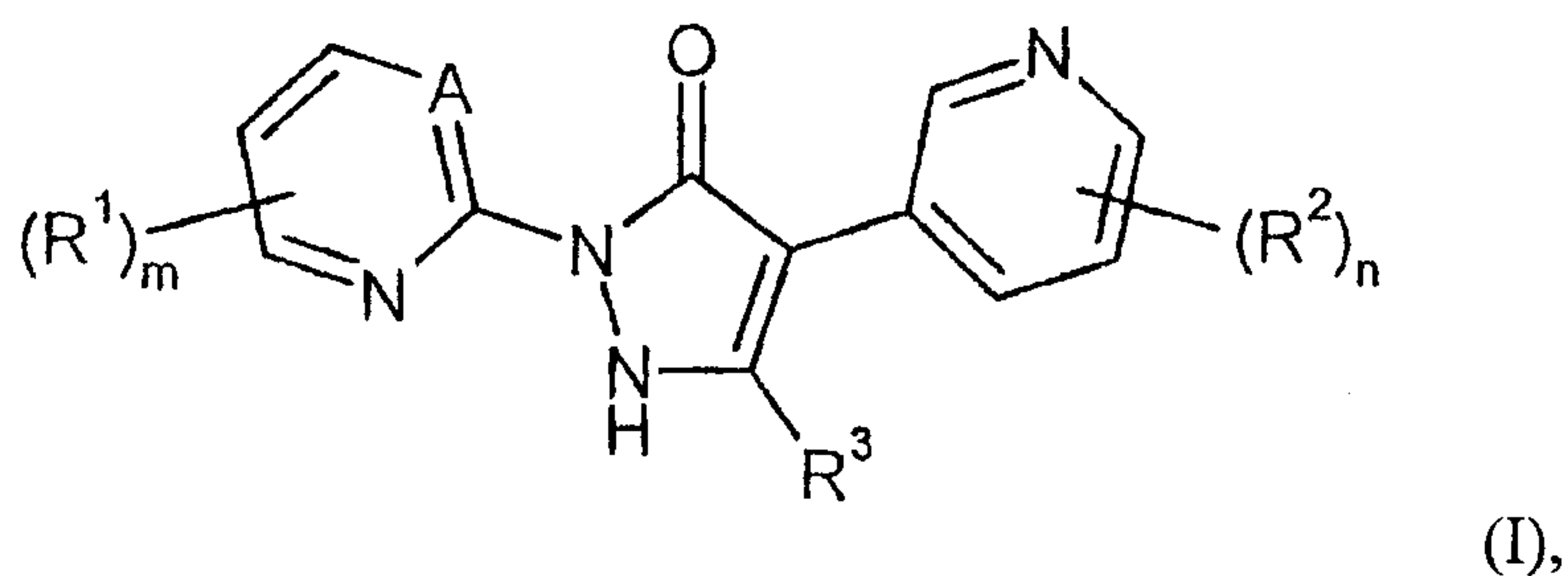
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R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

2. A compound of the formula (I)



5 in which

A represents CH,

R^1 represents a substituent selected from the group consisting of (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl, 5- or 6-membered heteroaryl, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹ and -NR²⁵R²⁶

10 in which

(i) (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl for their part may in each case be mono- to trisubstituted by identical or different radicals selected from the group consisting of (C₁-C₆)-alkyl, halogen, cyano, oxo, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶,

where the last-mentioned alkyl radical for its part may be substituted up to three times by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-

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alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

(ii) R⁶, R⁹, R¹², R¹⁴, R¹⁶, R¹⁹, R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl,

5 (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, 10 hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, 15 (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different 20 substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, 25 R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they

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are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, nitro, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, trifluoromethoxy, amino, hydroxycarbonyl and -C(=O)-NH-R^{7A} in which

(C₁-C₆)-alkyl and (C₁-C₆)-alkoxy for their part may be substituted by hydroxyl

and

R^{7A} represents hydrogen or (C₁-C₄)-alkyl,

m represents the number 1,

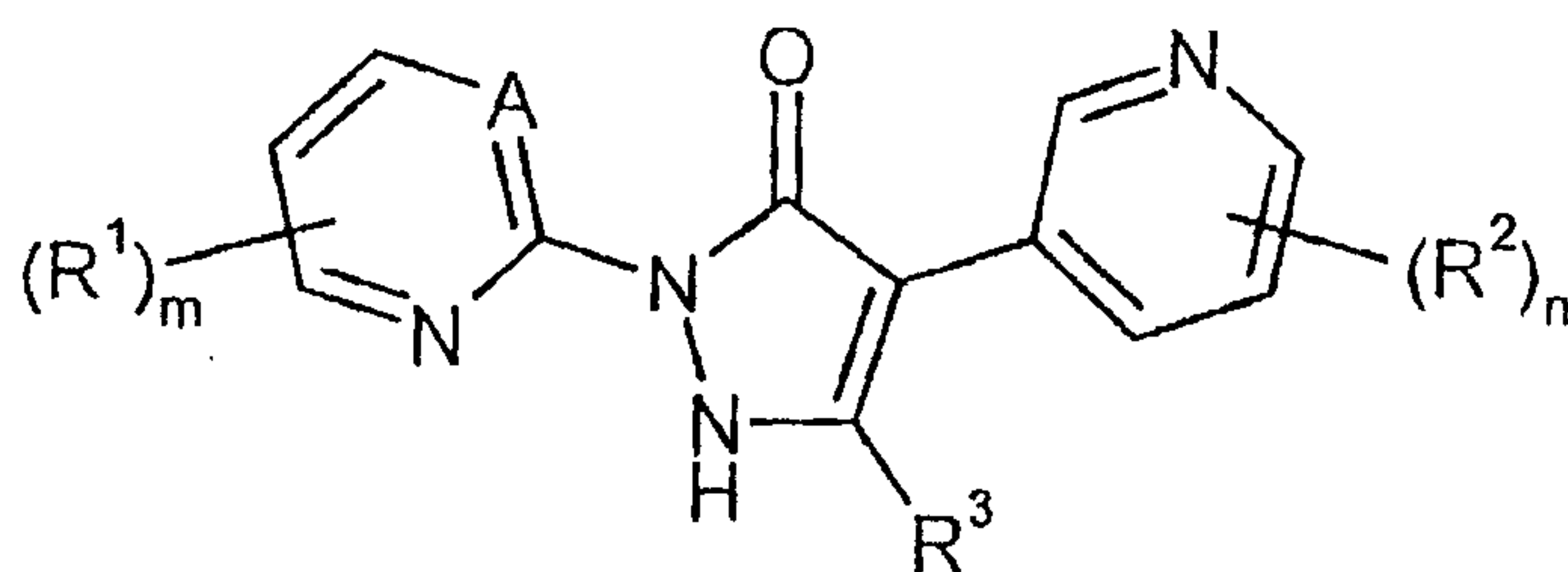
n represents the number 0 or 1

and

R³ represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

3. A compound of the formula (I)



(I),

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in which

A represents CH,

R¹ represents a substituent selected from the group consisting of (C₁-C₆)-alkyl, trifluoromethyl, halogen, cyano, nitro, hydroxyl, (C₁-C₆)-alkoxy, amino, hydroxycarbonyl,

5 (C₁-C₆)-alkoxycarbonyl and -C(=O)-NH-R⁷ in which

(C₁-C₆)-alkyl for its part may be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino or a group of the formula -NH-C(=O)-R¹², -NH-C(=O)-NH-R¹⁶ or -NH-SO₂-R¹⁹ in which

10 R¹², R¹⁶ and R¹⁹ each represent (C₁-C₆)-alkyl which may be substituted by hydroxyl or (C₁-C₄)-alkoxy,

and

R⁷ represents hydrogen or (C₁-C₆)-alkyl which may be substituted by hydroxyl or (C₁-C₄)-alkoxy,

R² represents a substituent selected from the group consisting of -O-C(=O)-NR^{9A}R^{10A},
15 -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A} and -NR^{25A}R^{26A} in which

(i) R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-
20 alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

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and/or in which

(iii) R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or
 5 disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

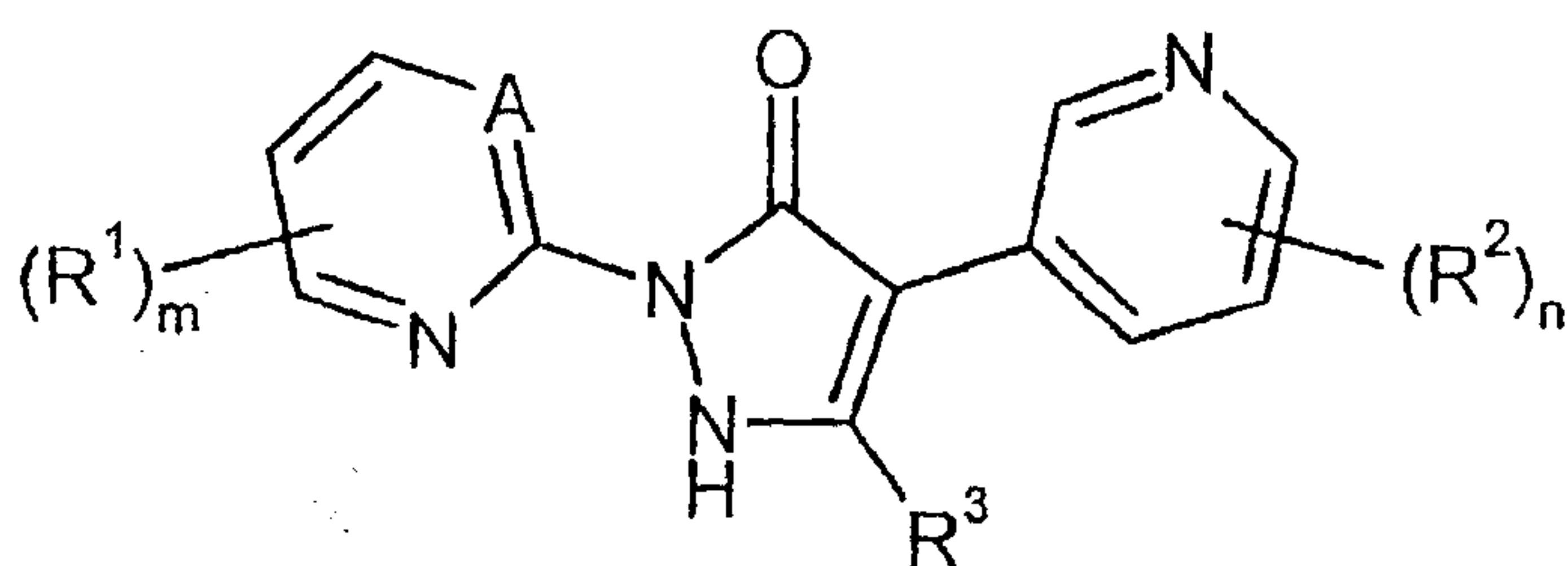
10 n represents the number 1

and

 R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

4. A compound of the formula (I)



15

(I),

in which

A represents CH,

 R^1 represents (C₁-C₆)-alkyl which

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(i) is mono- or disubstituted by identical or different radicals from the group consisting of halogen, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -R¹¹-(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and
 5 -NR²⁵R²⁶

and additionally may be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino or (C₁-C₄)-acylamino,

or

(ii) is disubstituted by identical or different radicals from the group consisting
 10 of hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and (C₁-C₄)-acylamino

in which

(a) the abovementioned cycloalkyl and heterocycloalkyl radicals for their part may in each case be substituted up to three times by identical or different substituents selected
 15 from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

(b) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen
 20 and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

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(c) R^6 , R^9 and R^{14} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(d) R^{12} , R^{16} and R^{19} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, amino, mono-(C₁-C₄)-alkylamino,

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di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(e) R²³ and R²⁵ independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl
 5 and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino,
 10 hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl is mono- to trisubstituted by identical or different radicals selected from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-
 15 alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and/or in which

(f) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to
 20 trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-
 25 alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl,

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-C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which

(i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R^{6A} and R^{7A}, R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A}, R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

n represents the number 0 or 1

and

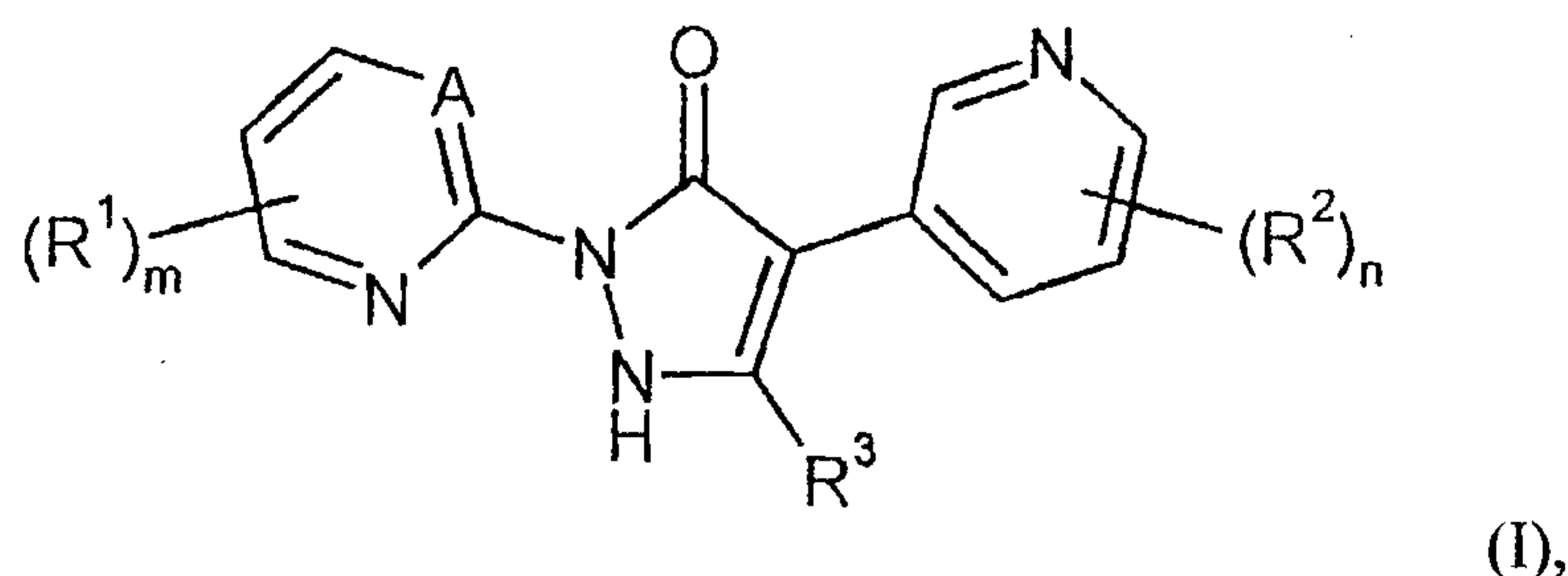
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R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

5. A compound of the formula (I)



5 in which

A represents CH,

R^1 represents (C_1-C_6) -alkoxy which is mono- or disubstituted by identical or different radicals selected from the group consisting of halogen, cyano, trifluoromethyl, (C_3-C_6) -cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxyl, amino, hydroxycarbonyl, aminocarbonyl, $-C(=O)-$
 10 NR^6R^7 , $-O-C(=O)-NR^9R^{10}$, $-NR^{11}-C(=O)-R^{12}$, $-NR^{13}-C(=O)-OR^{14}$, $-NR^{15}-C(=O)-NR^{16}R^{17}$,
 $-NR^{18}-SO_2-R^{19}$, $-OR^{23}$ and $-NR^{25}R^{26}$ in which

(i) (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino,
 15 hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,

(ii) R^6 , R^9 , R^{12} , R^{14} , R^{16} , R^{19} , R^{23} and R^{25} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C_1-C_6) -alkyl, (C_3-C_6) -cycloalkyl and 4- to 6-membered heterocycloalkyl, where

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(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) R⁷, R¹⁰, R¹¹, R¹³, R¹⁵, R¹⁷, R¹⁸ and R²⁶ independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₆)-alkyl,

where (C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷, R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

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R^2 represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which

5 (i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, 10 trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono- 15 (C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

(iv) R^{6A} and R^{7A}, R^{9A} and R^{10A}, R^{11A} and R^{12A}, R^{13A} and R^{14A}, R^{15A} and R^{16A}, R^{16A} and R^{17A}, R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which 20 may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

25 n represents the number 0 or 1

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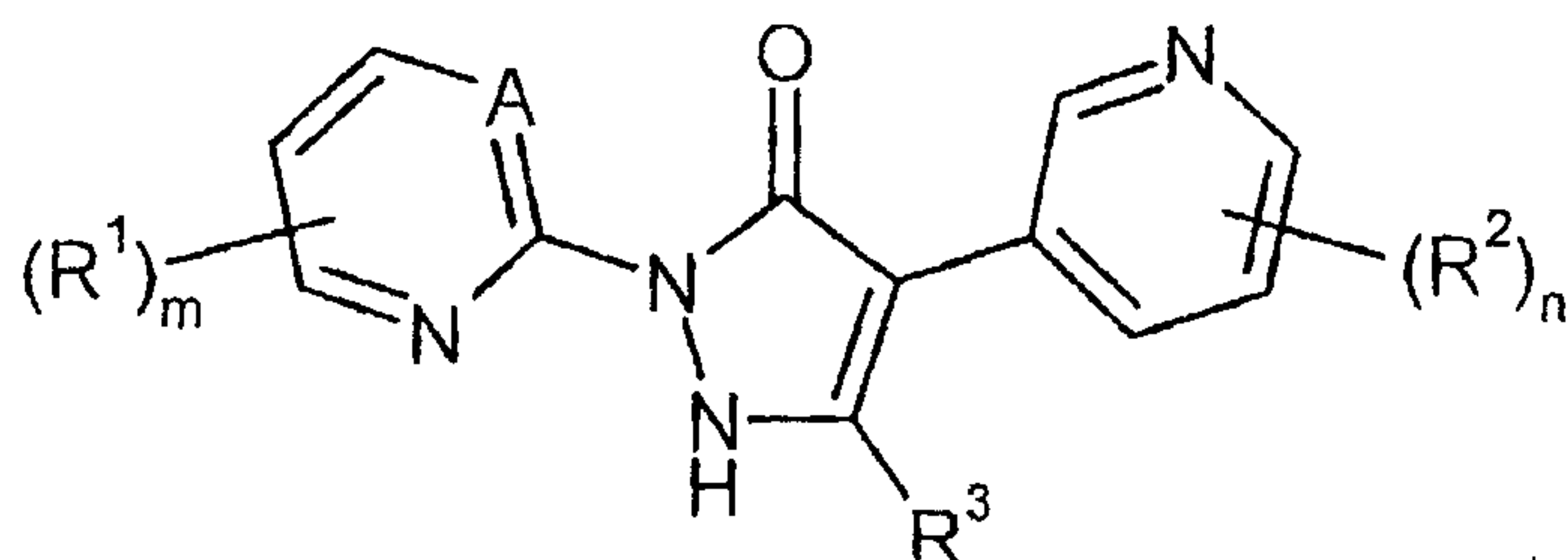
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and

 R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

6. A compound of the formula (I)



(I),

in which

A represents CH,

 R^1 represents the group $-C(=O)-NR^6R^7$

in which

10 (i) R^6 represents (C_3-C_6) -cycloalkyl or 4- to 6-membered heterocycloalkyl which may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, trifluoromethoxy, oxo, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino, hydroxycarbonyl and (C_1-C_4) -alkoxycarbonyl,

15 or

represents (C_1-C_6) -alkyl which

(a) is mono- or disubstituted by identical or different radicals selected from the group consisting of halogen, cyano, trifluoromethyl, amino, mono- (C_1-C_4) -alkylamino,

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di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl

and may additionally be substituted by hydroxyl or (C₁-C₄)-alkoxy,

or

5 (b) is disubstituted by hydroxyl and/or (C₁-C₄)-alkoxy,

and

R⁷ represents hydrogen,

or in which

10 (ii) R⁶ represents (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, 15 hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, 20 (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl

and

R⁷ represents (C₁-C₆)-alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxyl,

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trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

or in which

(iii) R⁶ and R⁷ together with the nitrogen atom to which they are attached form
 5 a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

R² represents a substituent selected from the group consisting of halogen, cyano, (C₁-C₆)-
 10 alkyl, trifluoromethyl, hydroxyl, trifluoromethoxy, amino, hydroxycarbonyl, aminocarbonyl, -C(=O)-NR^{6A}R^{7A}, -O-C(=O)-NR^{9A}R^{10A}, -NR^{11A}-C(=O)-R^{12A}, -NR^{13A}-C(=O)-OR^{14A}, -NR^{15A}-C(=O)-NR^{16A}R^{17A}, -NR^{18A}-SO₂-R^{19A}, -OR^{23A} and -NR^{25A}R^{26A} in which

(i) (C₁-C₆)-alkyl may be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-
 15 alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(ii) R^{6A}, R^{9A}, R^{12A}, R^{14A}, R^{16A}, R^{19A}, R^{23A} and R^{25A} independently of one another represent (C₁-C₆)-alkyl which may in each case be substituted by halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

(iii) R^{7A}, R^{10A}, R^{11A}, R^{13A}, R^{15A}, R^{17A}, R^{18A} and R^{26A} independently of one another represent hydrogen or (C₁-C₆)-alkyl which may in each case be substituted by
 20 halogen, cyano, trifluoromethyl, hydroxyl, trifluoromethoxy, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl or (C₁-C₄)-alkoxycarbonyl,

and/or in which

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(iv) R^{6A} and R^{7A} , R^{9A} and R^{10A} , R^{11A} and R^{12A} , R^{13A} and R^{14A} , R^{15A} and R^{16A} , R^{16A} and R^{17A} , R^{18A} and R^{19A} and also R^{25A} and R^{26A} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- or disubstituted by identical or different substituents from the group consisting of halogen, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, trifluoromethoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl and (C₁-C₄)-alkoxycarbonyl,

m represents the number 1,

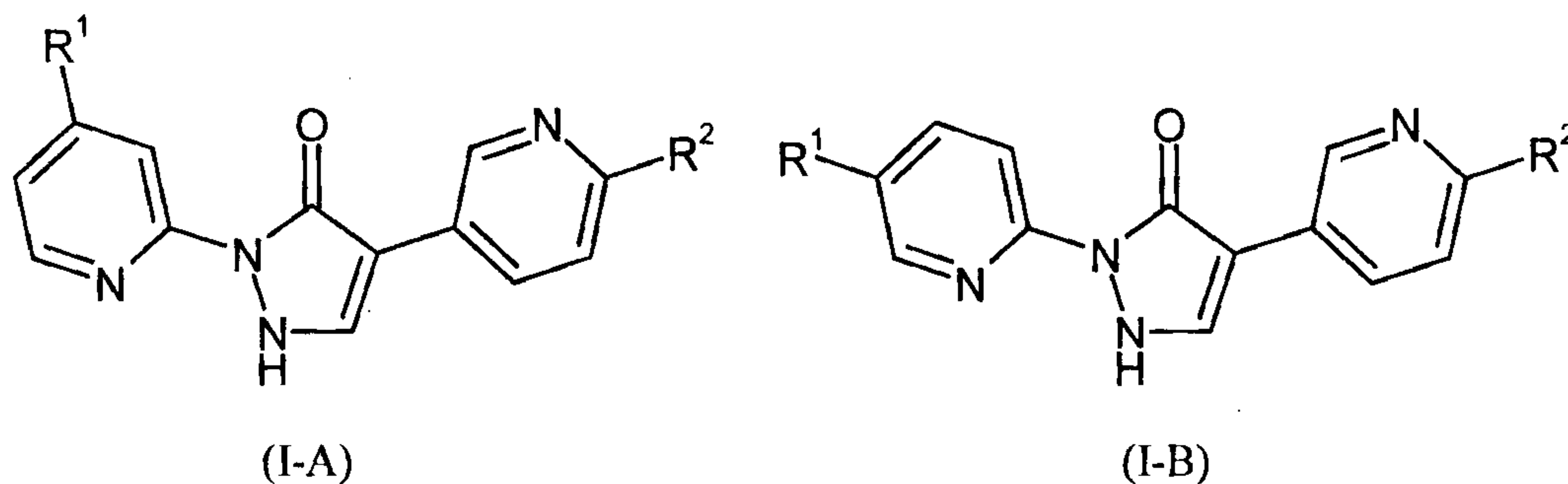
n represents the number 0 or 1

10 and

R^3 represents hydrogen,

or a salt, solvate or solvate of the salt thereof.

7. The compound as claimed in claim 2 of the formula (I-A) or (I-B)



15 in which

R^1 represents 4- to 6-membered heterocycloalkyl, phenyl or 5- or 6-membered heteroaryl which may in each case be mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, bromine, cyano, (C₁-C₄)-alkyl, hydroxyl, amino, hydroxycarbonyl, -OR²³ and -NR²⁵R²⁶ in which

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(C₁-C₄)-alkyl for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl and 5- or 6-membered heteroaryl,

R²³ and R²⁵ independently of one another for each individual occurrence represent (C₁-C₄)-alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and

R²⁶ for each individual occurrence represents hydrogen or (C₁-C₄)-alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and

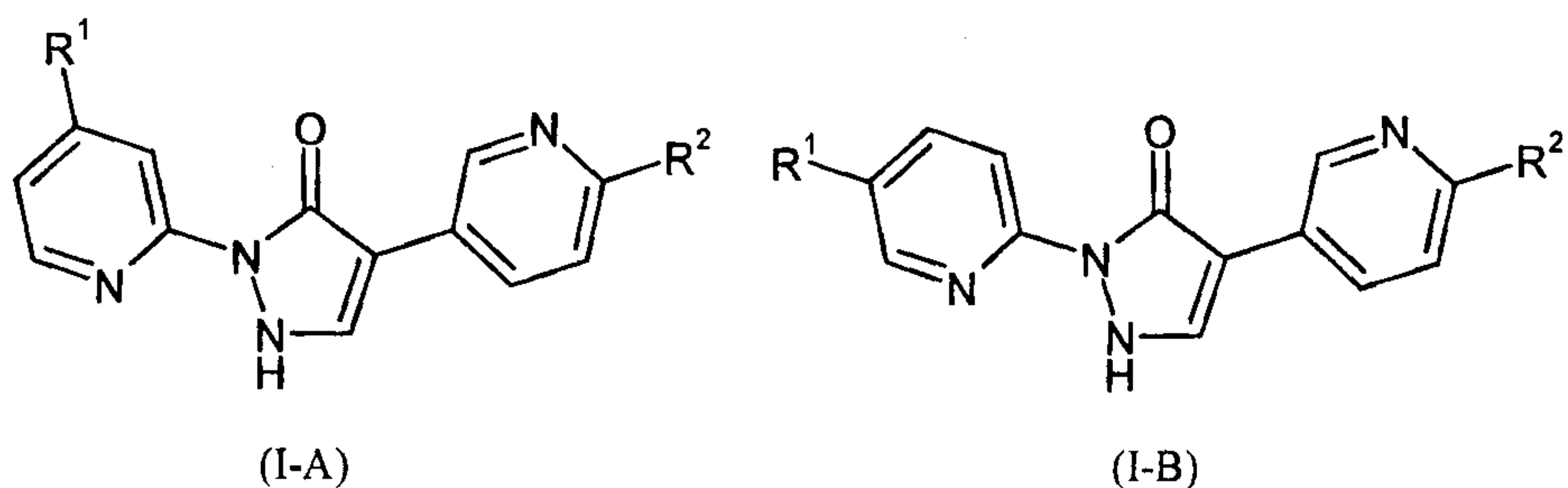
R² represents hydrogen, fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl,

or a salt, solvate or solvate of the salt thereof.

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8. The compound as claimed in claim 4 of the formula (I-A) or (I-B)



in which

R¹ represents (C₁-C₆)-alkyl which

5 (i) is mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxycarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶

and may additionally be substituted by hydroxyl, (C₁-C₄)-alkoxy, amino,
10 mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino or (C₁-C₄)-acylamino,

or

(ii) is disubstituted by identical or different radicals selected from the group consisting of hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and (C₁-C₄)-acylamino

15 in which

(a) the above-mentioned cycloalkyl and heterocycloalkyl radicals for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and
20 hydroxycarbonyl,

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(b) R^7 , R^{10} , R^{11} , R^{13} , R^{15} , R^{17} , R^{18} and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₄)-alkyl,

where (C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

(c) R^6 , R^9 and R^{14} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(d) R^{12} , R^{16} and R^{19} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl,

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(C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl is mono- to trisubstituted by identical or different radicals
 5 selected from the group consisting of fluorine, chlorine, cyano, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(e) R²³ and R²⁵ independently of one another for each individual occurrence
 represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl
 10 and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in
 each case be substituted up to three times by identical or different substituents selected from
 the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl,
 (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and
 15 hydroxycarbonyl

and

(C₁-C₄)-alkyl is mono- to trisubstituted by identical or different radicals
 selected from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy,
 amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-
 20 cycloalkyl and 4- to 6-membered heterocycloalkyl,

and/or in which

(f) R⁶ and R⁷, R⁹ and R¹⁰, R¹¹ and R¹², R¹³ and R¹⁴, R¹⁵ and R¹⁶, R¹⁶ and R¹⁷,
 R¹⁸ and R¹⁹ and also R²⁵ and R²⁶ in each case as a pair together with the atoms to which they
 are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to
 25 trisubstituted by identical or different substituents from the group consisting of fluorine,

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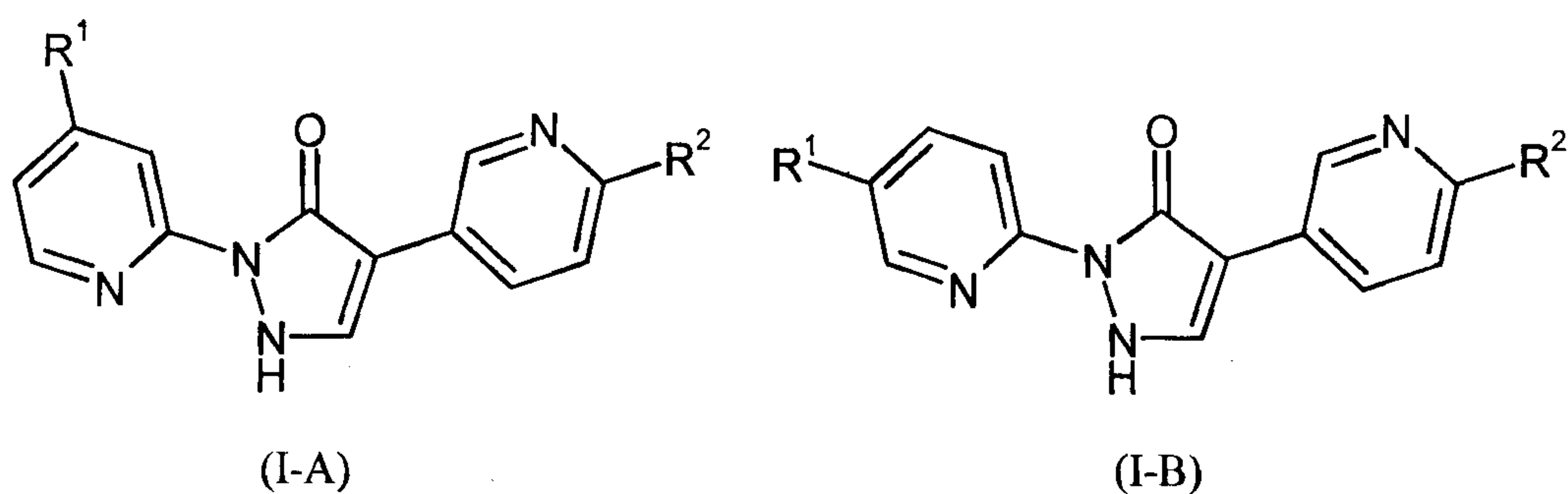
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chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and

R² represents hydrogen, fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl, or a salt, solvate or solvate of the salt thereof.

9. The compound as claimed in claim 5 of the formula (I-A) or (I-B)



in which

10 R¹ represents (C₁-C₆)-alkoxy which is mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl, (C₃-C₆)-cycloalkyl, 4- to 6-membered heterocycloalkyl, hydroxyl, amino, hydroxycarbonyl, -C(=O)-NR⁶R⁷, -O-C(=O)-NR⁹R¹⁰, -NR¹¹-C(=O)-R¹², -NR¹³-C(=O)-OR¹⁴, -NR¹⁵-C(=O)-NR¹⁶R¹⁷, -NR¹⁸-SO₂-R¹⁹, -OR²³ and -NR²⁵R²⁶ in which

15 (i) (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

(ii) $R^6, R^9, R^{12}, R^{14}, R^{16}, R^{19}, R^{23}$ and R^{25} independently of one another for each individual occurrence represent a radical selected from the group consisting of (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

(iii) $R^7, R^{10}, R^{11}, R^{13}, R^{15}, R^{17}, R^{18}$ and R^{26} independently of one another for each individual occurrence represent a radical selected from the group consisting of hydrogen and (C₁-C₄)-alkyl,

where (C₁-C₄)-alkyl may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and/or in which

(iv) R^6 and R^7, R^9 and R^{10}, R^{11} and R^{12}, R^{13} and R^{14}, R^{15} and R^{16}, R^{16} and R^{17}, R^{18} and R^{19} and also R^{25} and R^{26} in each case as a pair together with the atoms to which they are attached may form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine,

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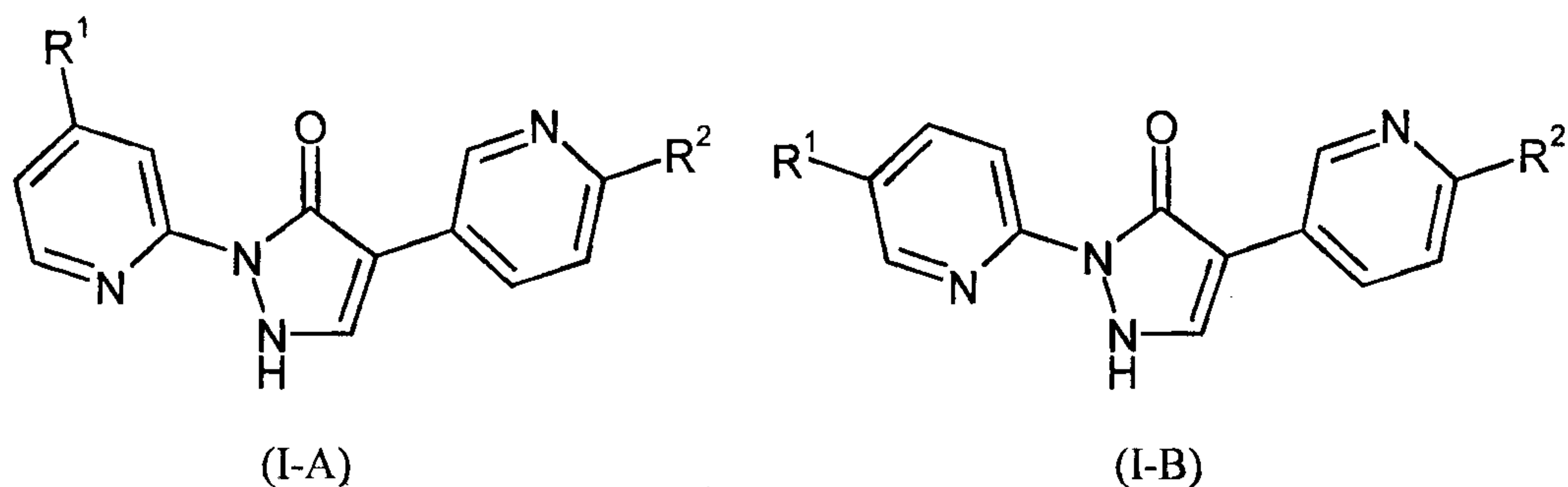
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chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

and

R² represents hydrogen, fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxymethyl, (C₁-C₄)-alkoxy, trifluoromethoxy, amino or hydroxycarbonyl, or a salt, solvate or solvate of the salt thereof.

10. The compound as claimed in claim 6 of the formula (I-A) or (I-B)



in which

10 R¹ represents the group -C(=O)-NR⁶R⁷

in which

(i) R⁶ represents (C₃-C₆)-cycloalkyl or 4- to 6-membered heterocycloalkyl which may in each case be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl,

or

represents (C₁-C₆)-alkyl which

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(a) is mono- or disubstituted by identical or different radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl

5 and may additionally be substituted by hydroxyl or (C₁-C₄)-alkoxy,
or

(b) is disubstituted by hydroxyl and/or (C₁-C₄)-alkoxy,
and

R⁷ represents hydrogen,

10 or in which

(ii) R⁶ represents (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or 4- to 6-membered heterocycloalkyl, where

(C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl for their part may in each case be substituted up to three times by identical or different substituents selected from
15 the group consisting of fluorine, chlorine, cyano, (C₁-C₄)-alkyl, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, oxo, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino and hydroxycarbonyl

and

(C₁-C₆)-alkyl may be mono- to trisubstituted by identical or different
20 substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C₁-C₄)-alkoxy, amino, mono-(C₁-C₄)-alkylamino, di-(C₁-C₄)-alkylamino, hydroxycarbonyl, (C₃-C₆)-cycloalkyl and 4- to 6-membered heterocycloalkyl,

and

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R^7 represents (C_1-C_4) -alkyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, hydroxyl, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -alkylamino and hydroxycarbonyl,

5 or in which

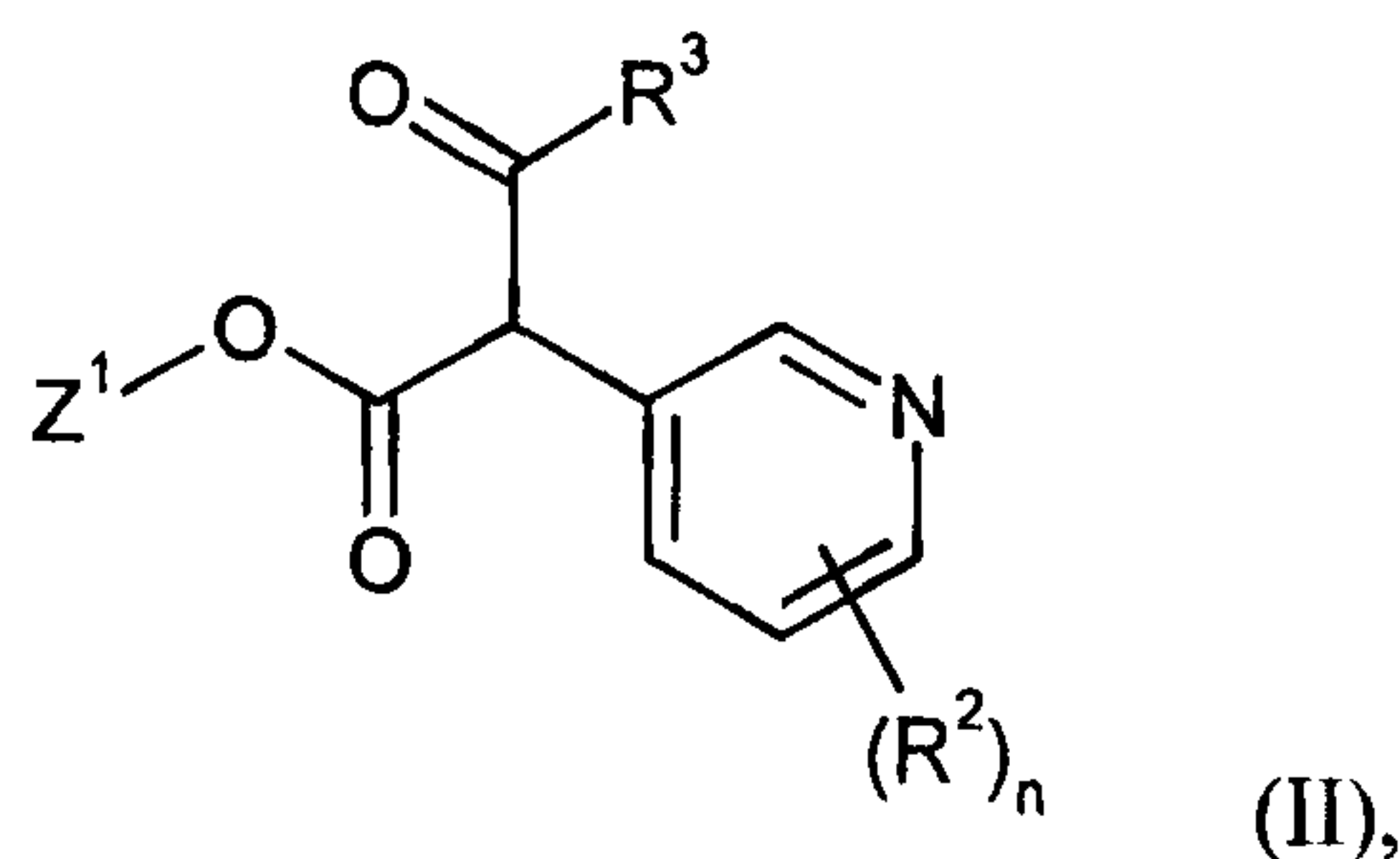
(iii) R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycloalkyl ring which may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxyl, (C_1-C_4) -alkoxy, amino, mono- (C_1-C_4) -alkylamino, di- (C_1-C_4) -
10 alkylamino and hydroxycarbonyl,

and

R^2 represents hydrogen, fluorine, chlorine, cyano, (C_1-C_4) -alkyl, trifluoromethyl, hydroxymethyl, (C_1-C_4) -alkoxy, trifluoromethoxy, amino or hydroxycarbonyl, or a salt, solvate or solvate of the salt thereof.

15 11. A process for the preparation of a compound of the formula (I) as defined in any one of claims 1 to 10, comprising:

reacting a compound of the formula (II)



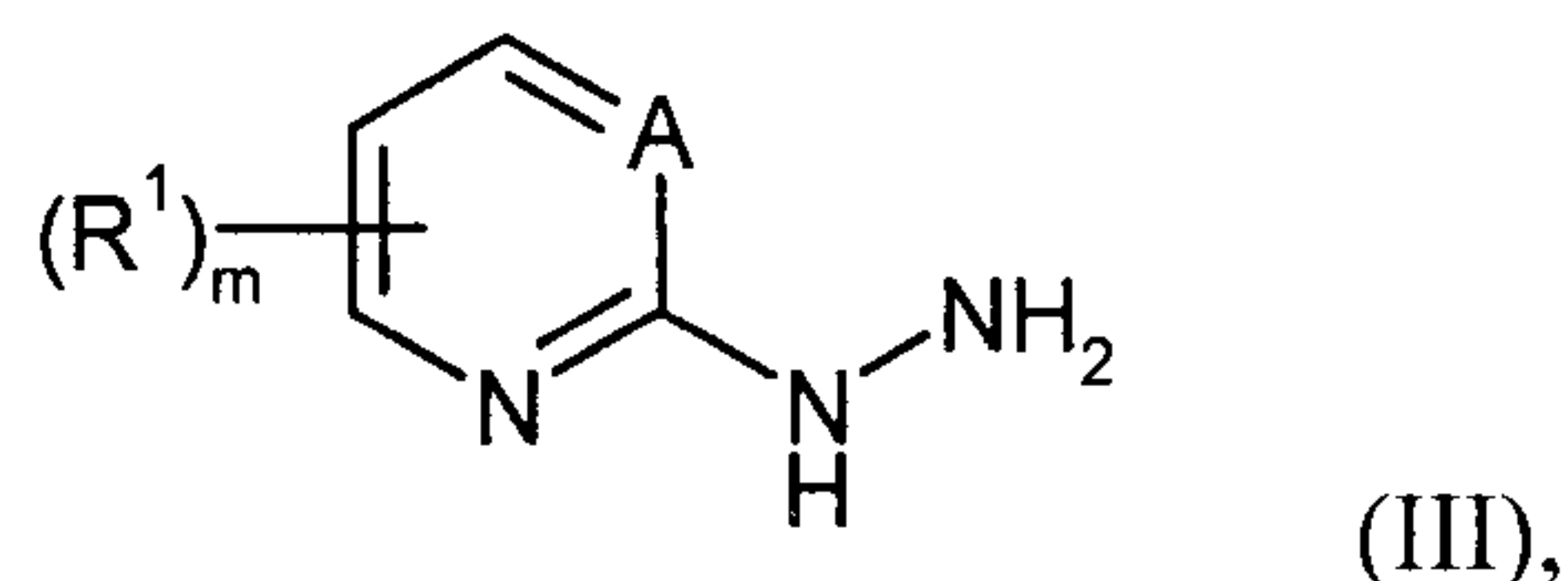
in which R^2 , R^3 and n have the meanings given in any one of claims 1 to 10 and

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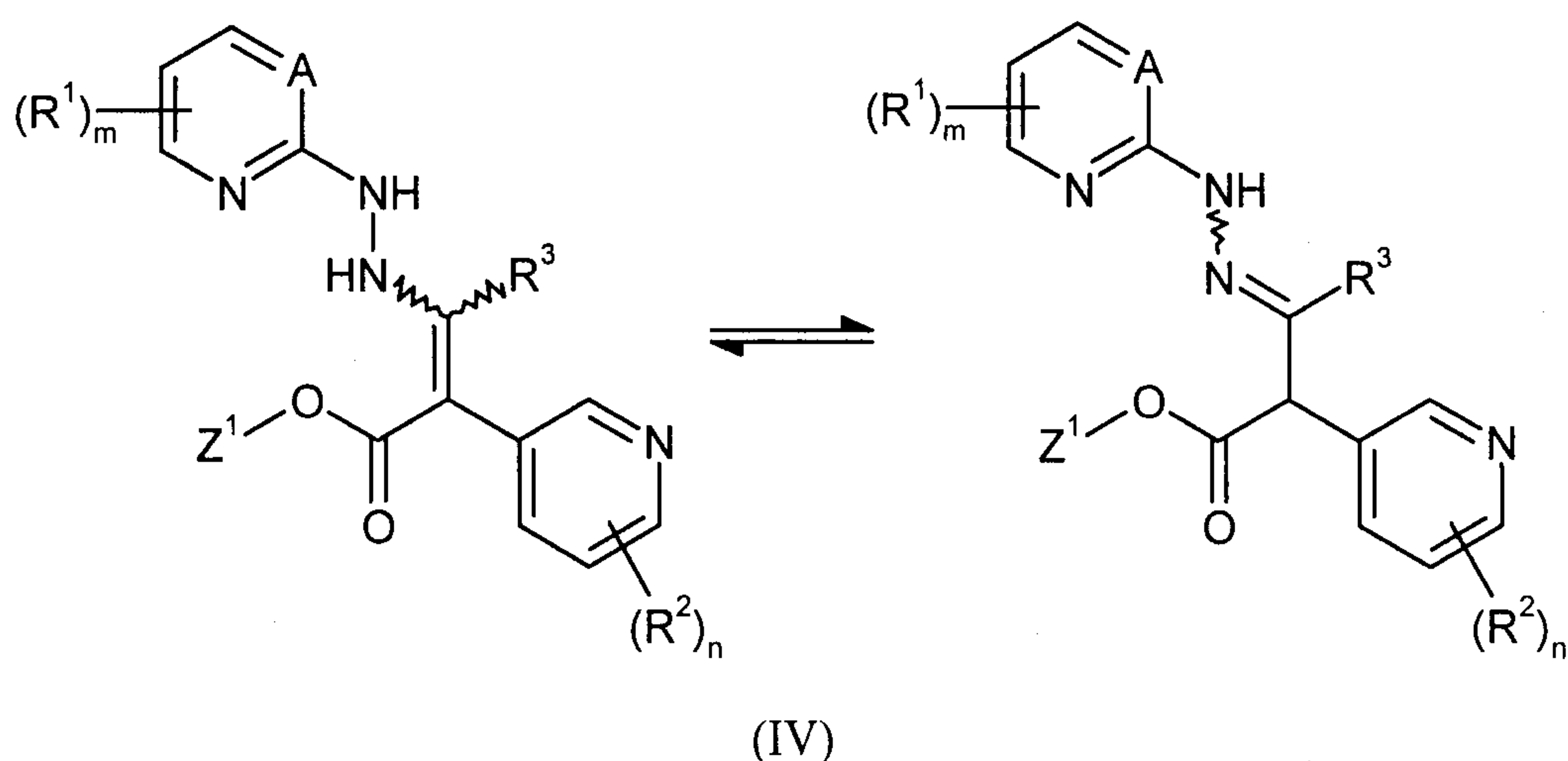
Z^1 represents methyl or ethyl,

in an inert solvent, if appropriate in the presence of an acid, with a compound of the formula (III)



5 in which A, R^1 and m have the meanings given in any one of claims 1 to 10,

to give a compound of the formula (IV)



in which Z^1 , A, R^1 , R^2 , R^3 , m and n have the meanings given above,

10 which, already under these reaction conditions or in a subsequent reaction step under the influence of a base, cyclize to give a compound of the formula (I); and

converting the compound of the formula (I), if appropriate with the appropriate (i) solvents and/or (ii) bases or acids, into its solvate, salt and/or solvate of the salt.

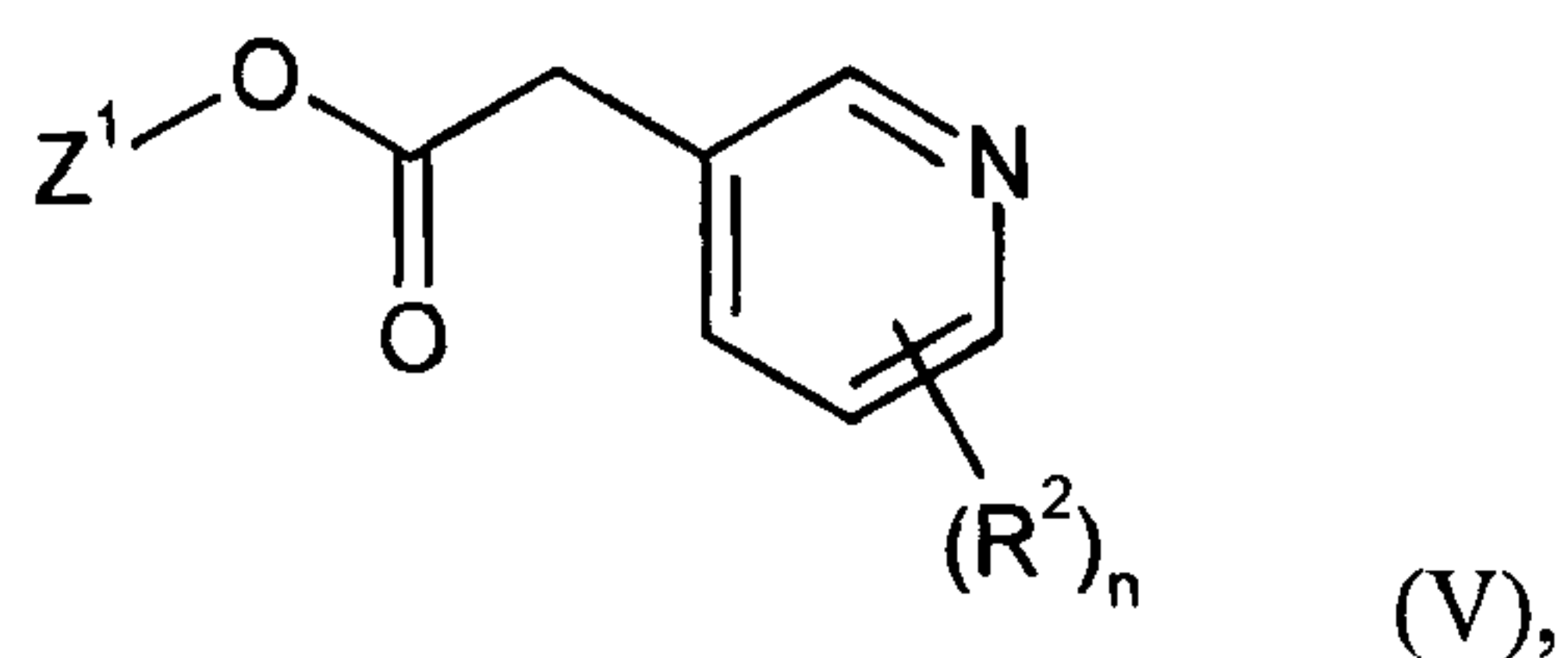
12. A process for the preparation of a compound of the formula (I) as defined in

15 any one of claims 1 to 10 in which R^3 represents hydrogen, comprising:

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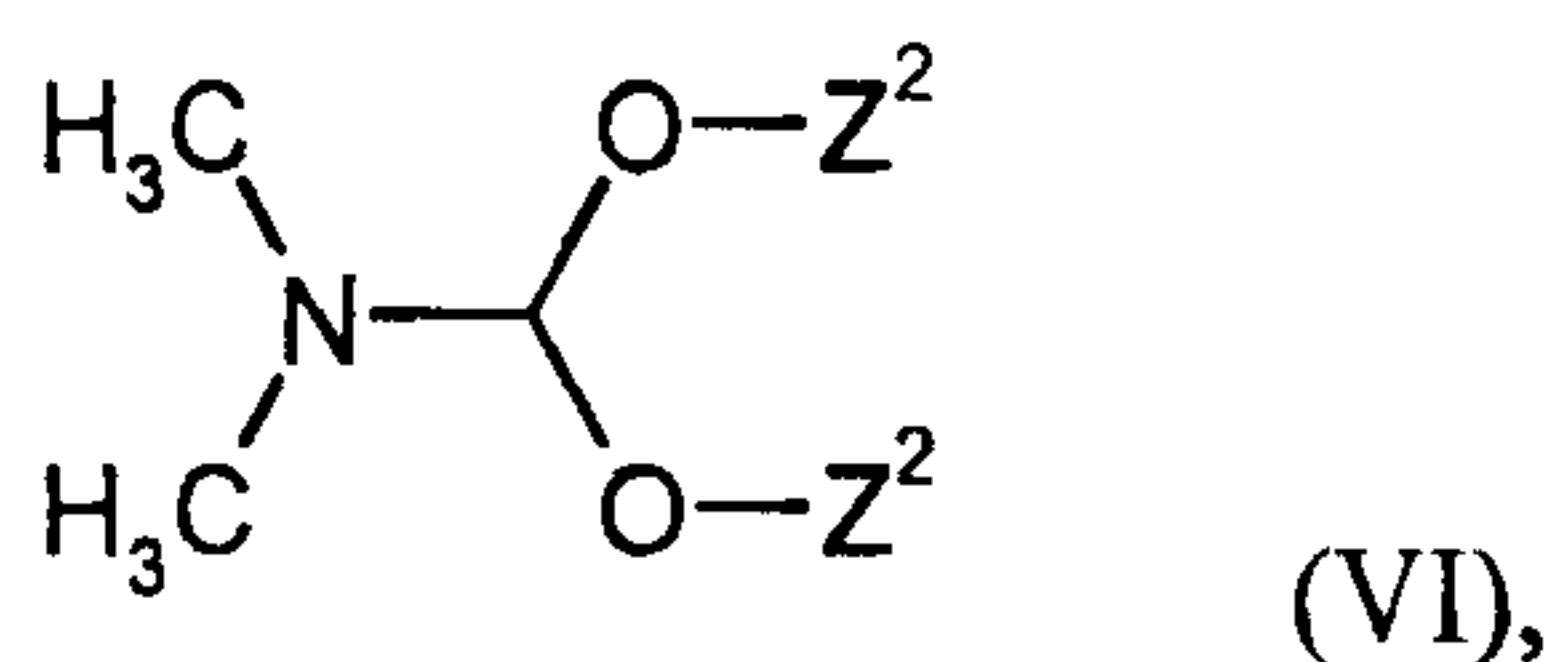
initially condensing a compound of the formula (V)



in which R^2 and n have the meanings given in any one of claims 1 to 10 and

Z^1 represents methyl or ethyl,

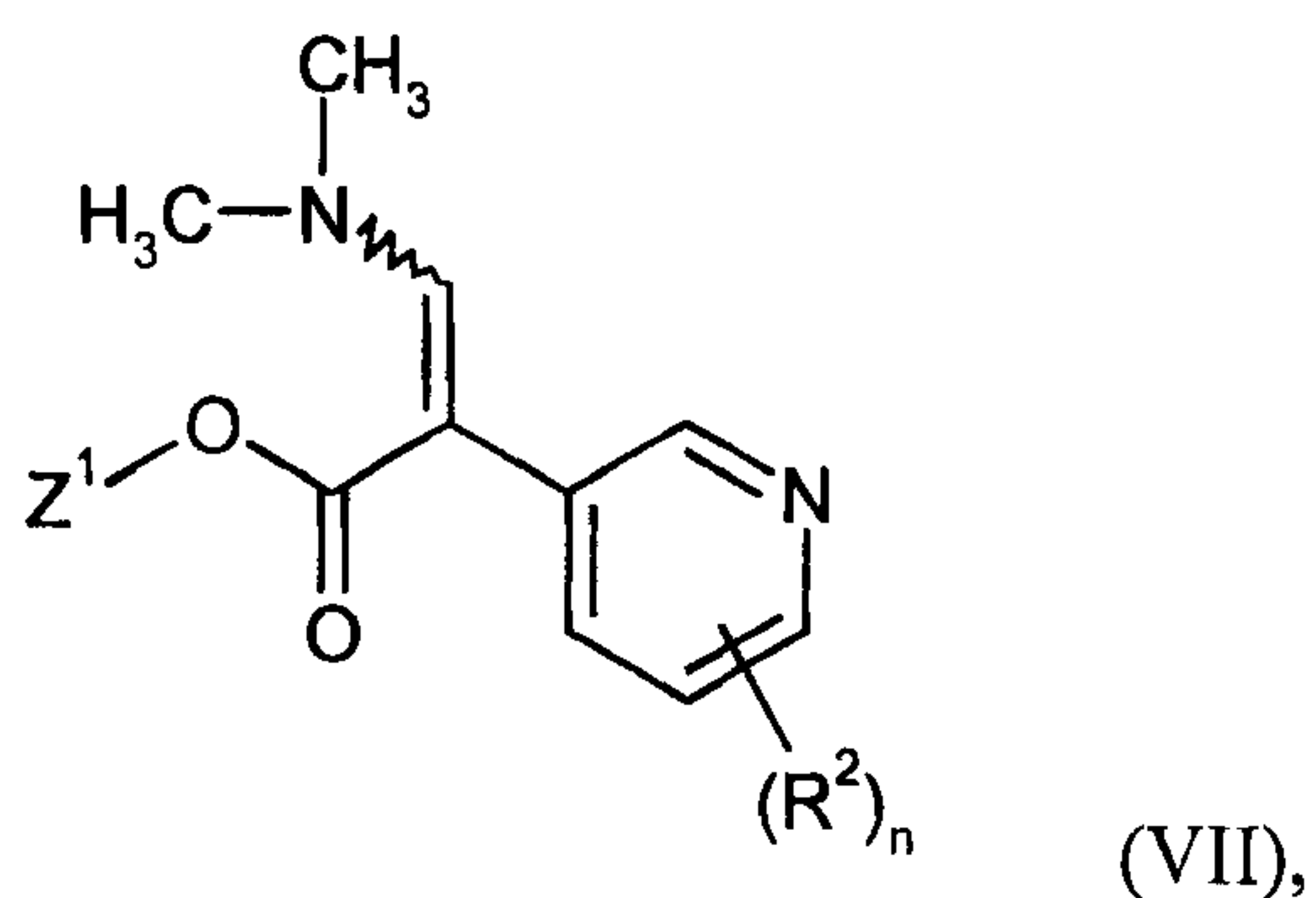
5 with a compound of the formula (VI)



in which

Z^2 represents methyl or ethyl,

to give a compound of the formula (VII)



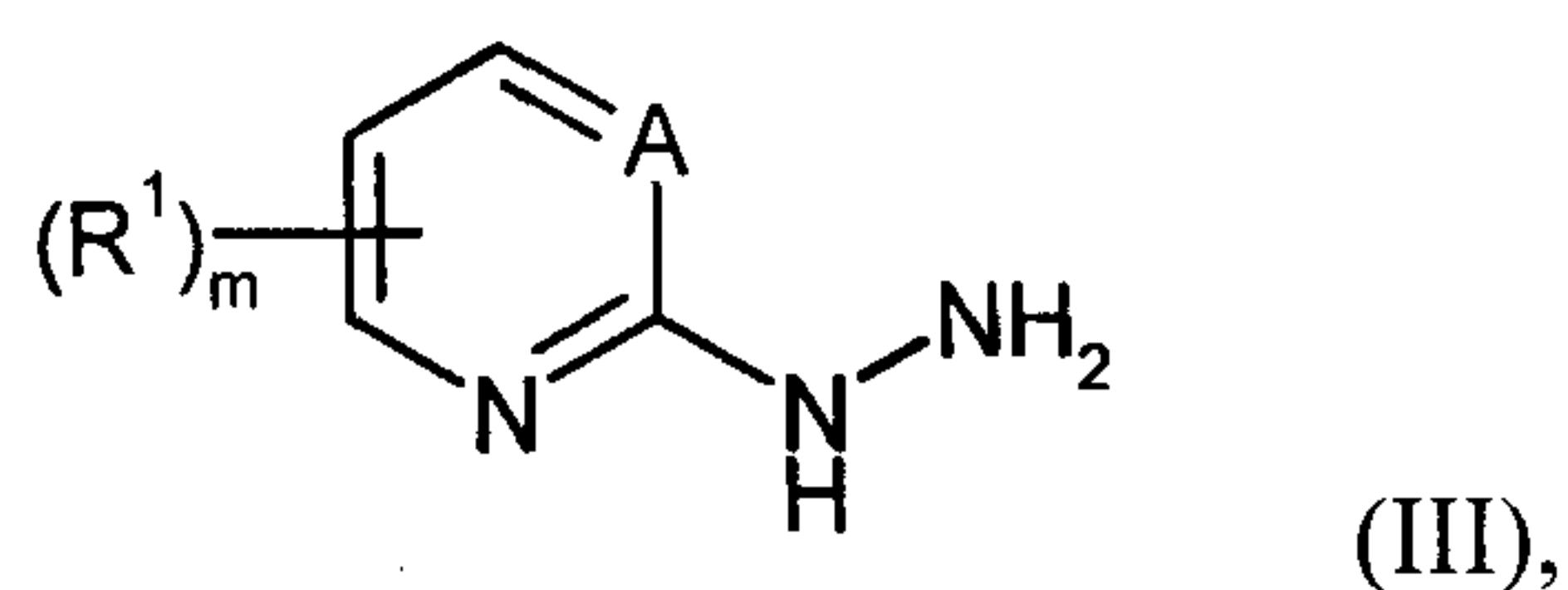
10

in which Z^1 , R^2 and n have the meanings given above;

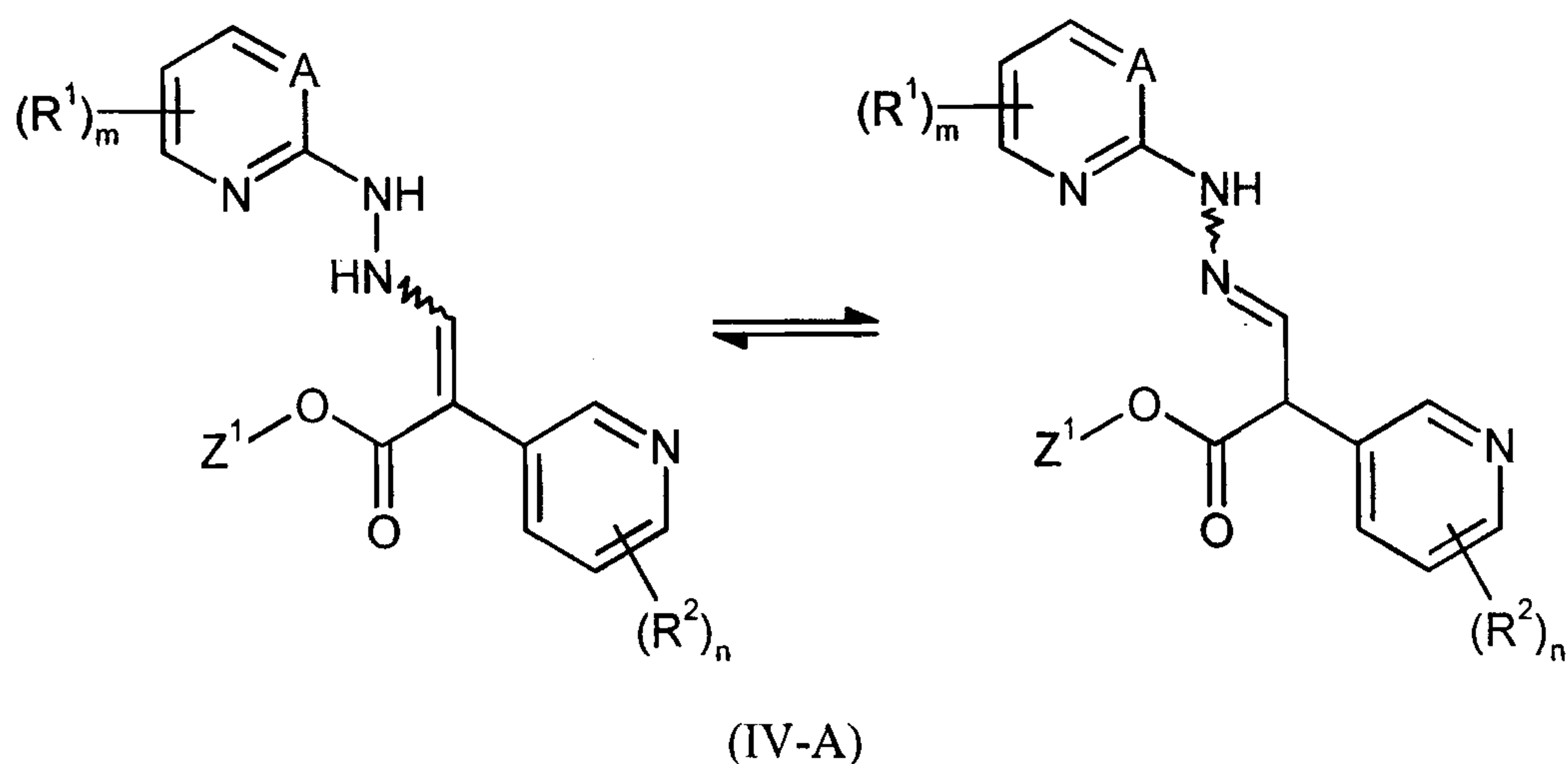
and then reacting in the presence of an acid with a compound of the formula (III)

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in which A, R¹ and m have the meanings given in any one of claims 1 to 10,
to give a compound of the formula (IV-A)



in which Z¹, A, R¹, R², m and n have the meanings given above,

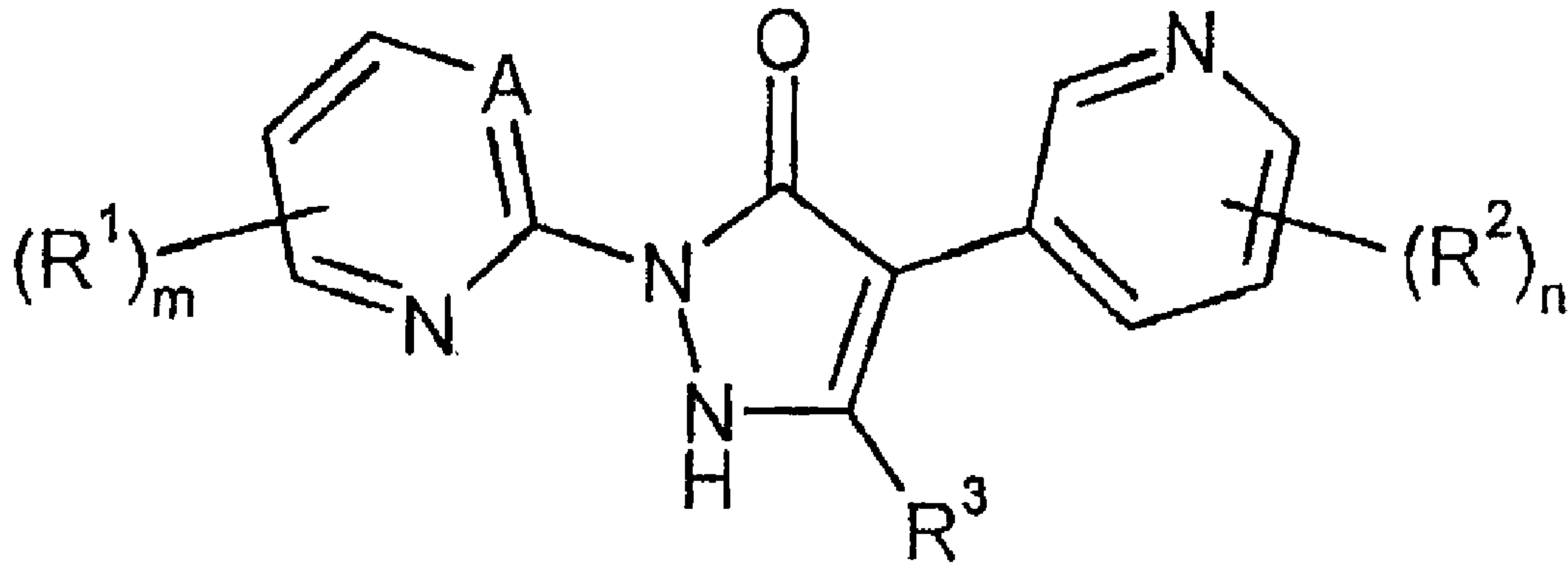
which, already under these reaction conditions or in a subsequent reaction step under the influence of a base, cyclize to give the compound of the formula (I) in which R³ represents hydrogen.

- 10 13. Use of a compound as defined in any one of claims 1 to 10, or a pharmaceutically acceptable salt, solvate or solvate of the salt thereof, for the preparation of a medicament for treatment and/or prophylaxis of a cardiovascular disease, cardiac insufficiency, anemia, a chronic kidney disease or renal insufficiency.
14. A medicament comprising a compound as defined in any one of claims 1 to 10,
- 15 or a pharmaceutically acceptable salt, solvate or solvate of the salt thereof, in combination with an inert, non-toxic, pharmaceutically suitable auxiliary.

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15. A medicament comprising a compound as defined in any one of claims 1 to 10, or a pharmaceutically acceptable salt, solvate or solvate of the salt thereof, in combination with one or more further compounds chosen from the group consisting of ACE inhibitors, angiotensin II receptor antagonists, beta receptor blockers, calcium antagonists, PDE inhibitors, mineralocorticoid receptor antagonists, diuretics, aspirin, iron supplements, vitamin B12 and folic acid supplements, statins, digitalis (digoxin) derivatives, tumor chemotherapeutics and antibiotics.
16. The medicament as claimed in claim 14 or 15 for treatment and/or prophylaxis of a cardiovascular disease, cardiac insufficiency, anemia, a chronic kidney disease or renal insufficiency.
17. Use of a compound as defined in any one of claims 1 to 10, or a pharmaceutically acceptable salt, solvate or solvate of the salt thereof, for treatment and/or prophylaxis of a cardiovascular disease, cardiac insufficiency, anemia, a chronic kidney disease or renal insufficiency in a human or animal.



(I)