1,3-Dipolar Cycloadditions to (5*Z*)-1-Acyl-5-(cyanomethylidene)-imidazolidine-2,4-diones: Synthesis and Transformations of Spirohydantoin Derivatives

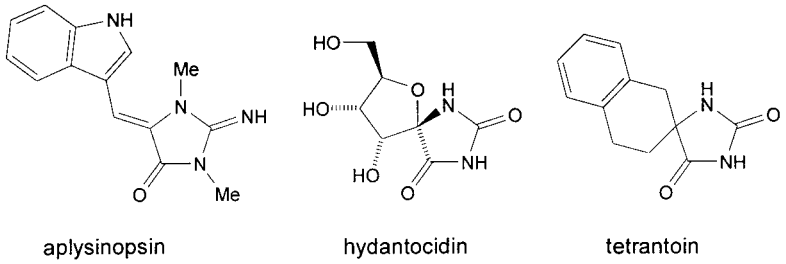
by **Uroš Grošelj**[a]), **Aleš Drobnič**[a]), **Simon Rečnik**[a]), **Jurij Svete**[a])*, **Branko Stanovnik**[a])*, **Amalija Golobič**[a]), **Nina Lah**[a]), **Ivan Leban**[a]), **Anton Meden**[a]), and **Simona Golič-Grdadolnik**[b])

[a]) Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, SI-1000 Ljubljana

[b]) National Institute of Chemistry, Hajdrihova 19, SI-1000 Ljubljana

Cycloadditions of various 1,3-dipoles to (5*Z*)-1-acyl-5-(cyanomethylidene)-3-methylimidazolidine-2,4-diones **8** or **9**, prepared in 3 steps from hydantoin (**1**) (*Schemes 1* and *2*), were studied. In all cases, reactions proceeded regio- and stereoselectively. The type of product depended on the 1,3-dipole and/or dipolarophile employed as well as on reaction conditions. Thus, with stable dipoles under neutral conditions, spirohydantoin derivatives **12**–**16** were obtained (*Scheme 2*), while under basic or acidic conditions, pyrazole- or isoxazole-5-carboxamides **18** and **23**–**26** and carboxylate **27** were formed *via* aromatization of the newly formed dihydroazole ring, followed by the simultaneous cleavage of the hydantoin ring (*Schemes 3–5*).

Introduction. – There are several examples of naturally occurring and synthetic hydantoin (= imidazolidine-2,4-dione) derivatives exhibiting various biological activities, such as antitumor [1][2], antiarrhythmic [3], anticonvulsant [4], and herbicidal [5] activity, inhibition of glycogen phosphorylase [6] and aldose reductase [7], and neurotransmission [8] effects. Examples of such compounds are aplysinopsin [1][8][9], hydantocidin and its analogs [5–7], and tetrantoin [4] (*Fig. 1*).



aplysinopsin hydantocidin tetrantoin

Fig. 1. *Hydantoin derivatives exhibiting biological activities.*

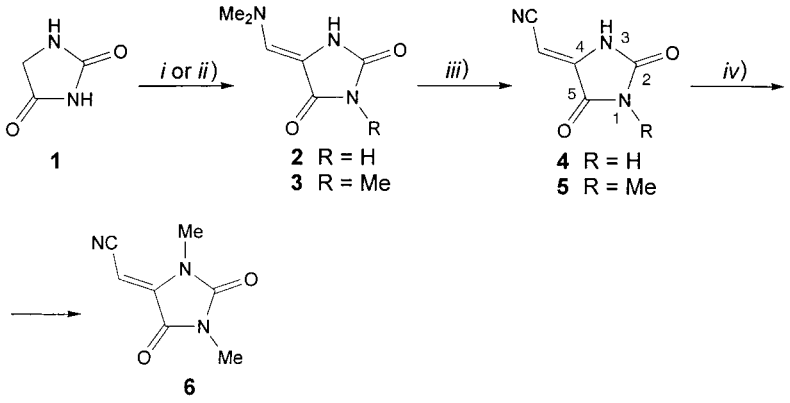
On the other hand, 2-substituted alkyl 3-(dimethylamino)prop-2-enoates, 2-substituted alkyl 3-cyanoprop-2-enoates, and their cyclic analogs are easily available and proved to be efficient reagents for the preparation of various heterocyclic systems [10]. In this connection, 2-substituted alkyl 3-cyanoprop-2-enoates and their chiral cyclic analogs were employed as dipolarophiles in 1,3-dipolar cycloaddition reactions leading to pyrazoles, isoxazoles, and their fused and spiro analogs [11][12]. Recently, we reported a simple and stereoselective synthesis of aplysinopsin analogs, which

employs 3-(dimethylamino)-2-(vinylamino)prop-2-enoate and 5-[(dimethylamino)-methylidene]hydantoin derivatives as the key intermediates [13]. As an extension of our work in this field towards the synthesis of spirohydantoins, we report the preparation of (5*Z*)-1-acetyl-5-(cyanomethylidene)-3-methylimidazolidine- 2,4-dione (**8**) and (5*Z*)-1-benzoyl-5-(cyanomethylidene)-3-methylimidazolidine-2,4-dione (**9**) and their transformations with various 1,3-dipoles.

Results and Discussion. – The starting compounds (5*Z*)-5-(dimethylamino)methylidene]imidazolidine-2,4-dione (**2**) and (5*Z*)-5-(dimethylamino)methylidene]-3-methylimidazolidine-2,4-dione (**3**) were prepared from hydantoin (**1**) according to the procedures described previously [13] (*Scheme 1*). Treatment of compounds **2** or **3** with KCN in AcOH at room temperature gave the corresponding (2*Z*)-2-(2,5-dioxoimidazolidin-4-ylidene)acetonitrile (**4**) and (2*Z*)-2-(1-methyl-2,5-dioxoimidazolidin-4-ylidene)acetonitrile (**5**) in 70% yield. The (*Z*)-configuration of the exocyclic C=C bond in compound **5** was established by X-ray analysis (see *Fig. 2*). Treatment of imidazolidinylideneacetonitriles **4** or **5** with excess CH_2N_2 (**7**) furnished, in both cases, the same product, (2*Z*)-2-(1,3-dimethyl-2,5-dioxoimidazolidin-4-ylidene)acetonitrile (**6**) in quantitative yield.

Since no cycloadduct was formed upon reaction of **4** or **5** with excess CH_2N_2 (**7**), compound **5** was transformed into its 1-acetyl and 1-benzoyl derivatives **8** and **9**, respectively, to increase the dipolarophilicity of the exocyclic C=C bond. These 1-acyl derivatives **8** and **9** were then treated with the following 1,3-dipoles: CH_2N_2 (**7**), the azomethine imine (1*Z*)-5,5-dimethyl-3-oxo-1-[(2,4,6-trimethoxyphenyl)methylidene]-pyrazolidin-1-ium-2-ide (**10**), and 2,4,6-trimethoxybenzonitrile *N*-oxide (**11a**). In all cases, compounds **8** and **9** underwent regioselective 1,3-dipolar cycloaddition reactions to give the corresponding spirocyclic adducts. Thus, reaction of **8** and **9** with excess CH_2N_2 (**7**) afforded *rel*-(4*R*,5*R*)-6-acetyl-8-methyl-7,9-dioxo-1,2,6,8-tetraazaspiro[4.4]-non-1-ene-4-carbonitrile (**12**) and its 6-benzoyl analog **13** in 66 and 74% yield,

Scheme 1



i) *t*-BuOCH(NMe_2)$_2$, MeCN, reflux, **1** → **2**. *ii*) $Me_2NCH(OMe)_2$, MeCN, reflux, **1** → **3**. *iii*) KCN, AcOH, r.t. *iv*) CH_2N_2 (**7**), Et_2O, −10° – r.t.

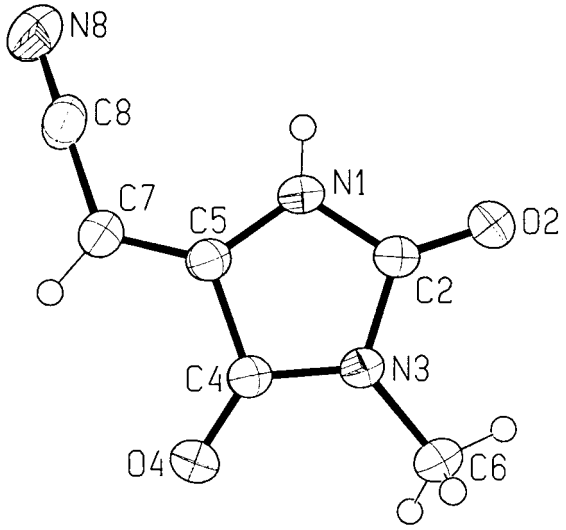


Fig. 2. *ORTEP View of the asymmetric unit of compound* **5** *with labelling* (arbitrary) *of non-H-atoms.* Ellipsoids are at 50% probability level.

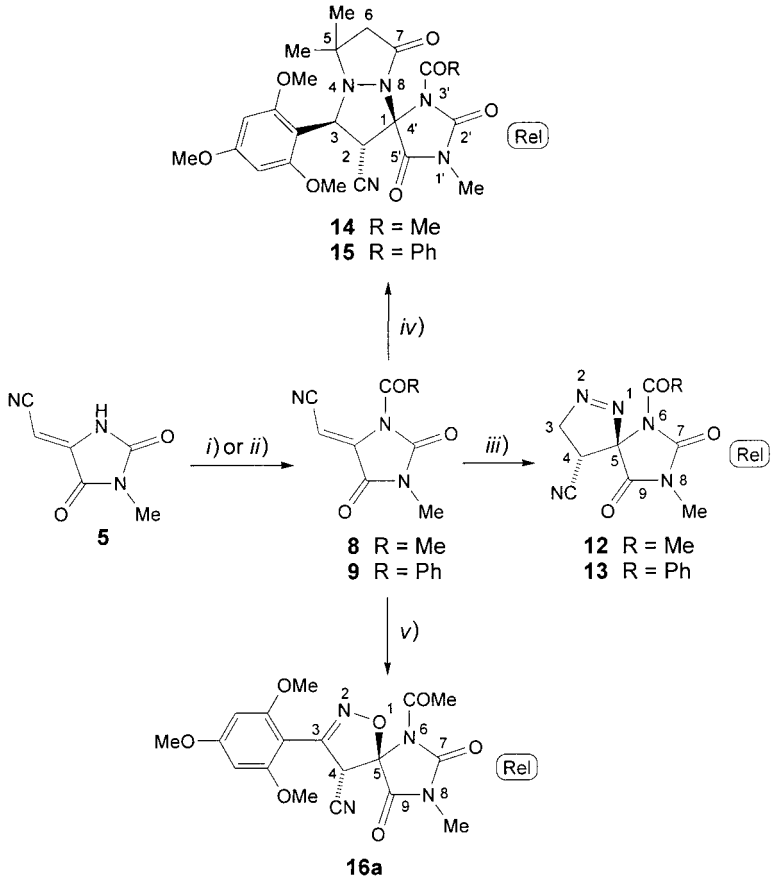
respectively. Similarly, 1,3-dipolar cycloaddition of azomethine imine **10** to dipolarophiles **8** and **9** took place upon microwave irradiation in refluxing 1,4-dioxane to give the corresponding *rel*-(1*R*,2*R*,3*S*)-3′-acyl-1′,5,5-trimethyl-2′,5′,7-trioxo-3-(2,4,6-trimethoxyphenyl)spiro[1*H*,5*H*]pyrazolo[1,2-*a*]pyrazole-1,4′-imidazolidine]-2-carbonitrile **14** and **15**, respectively, in moderate yields. Finally, treatment of the dipolarophile **8** with 2,4,6-trimethoxybenzonitrile *N*-oxide (**11a**) in $CHCl_3$ under reflux gave *rel*-(4*R*,5*S*)-6-acetyl-8-methyl-7,9-dioxo-3-(2,4,6-trimethoxyphenyl)-1-oxa-2,6,8-triazaspiro[4.4]non-2-ene-4-carbonitrile (**16a**) in 73% yield (*Scheme 2*).

The relative configuration around the C(2)–C(3) single bond in cycloadduct **14** was established by NMR. The coupling constant (J(H–C(2), H–C(3)) = 10¼Hz) was not in good agreement with the reported values for related di- and perhydropyrazoles (J = 3–10 Hz for *cis*-configuration; J = 10–14 Hz for *trans*-configuration) [14]. Since no NOE effect was observed between H–C(2) and H–C(3), we supposed that these two protons were *trans*-oriented. In the ^{1}H-NMR spectrum of compound **14**, the MeO groups of the 2,4,6-trimethoxyphenyl substituent were nonequivalent (3*s*, each 3 H). The distances between H–C(2) and H–C(3) and the corresponding nearest *ortho*-MeO groups of the aryl residue were determined by NOESY technique. The results (d(H–C(2)···MeO) = d(H–C(3)···MeO) = 0.32 nm) were in agreement with the proposed configuration (*Fig. 3*).

Furthermore, the structures of **12**, **14** and **16a** were confirmed by X-ray diffraction (*Figs. 4–6*).

On the other hand, reaction of 1-benzoyl derivative **9** with 2,4,6-trimethoxybenzonitrile *N*-oxide (**11a**) and 2,4,6-trimethylbenzonitrile *N*-oxide (**11b**) in $CHCl_3$ under reflux furnished the corresponding *N*-[(benzoylamino)carbonyl]isoxazol-5-carboxamides **18a**,**b** (*Scheme 3*). Analogously, the *N*-[(acylamino)carbonyl]-1*H*-pyrazol-5-

Scheme 2



i) Ac_2O, pyridine, r.t., **5** → **8**. *ii*) PhCOCl, pyridine, r.t., **5** → **9**. *iii*) CH_2N_2 (**7**), Et_2O, $CHCl_3$, $-10°$ – r.t. *iv*) (1*Z*)-5,5-dimethyl-3-oxo-1-[(2,4,6-trimethoxyphenyl)methylidene]pyrazolidin-1-ium-2-ide (**10**), 1,4-dioxane, microwave (1000 W), reflux. *v*) 2,4,6-$(MeO)_3C_6H_2C{\equiv}N^+{-}O^-$ (**11a**), $CHCl_3$, reflux.

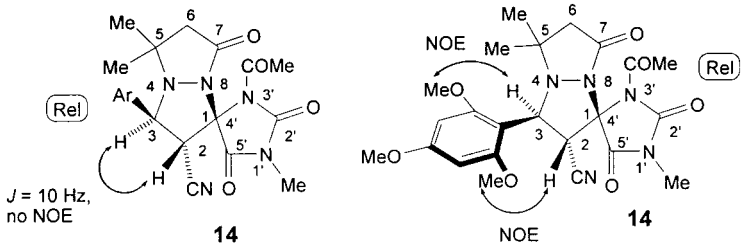


Fig. 3. *Configuration of* **14**

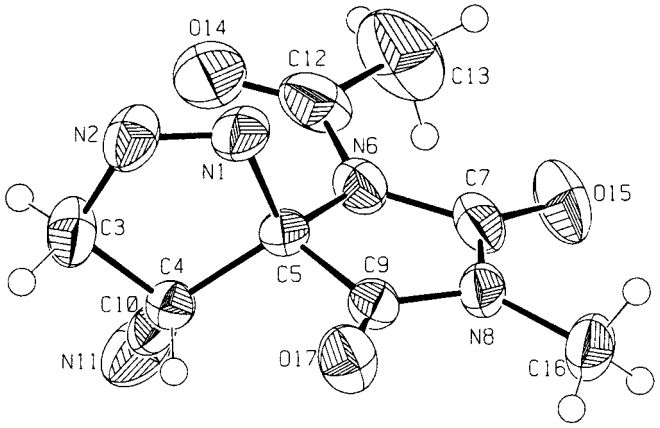


Fig. 4. *ORTEP View of the asymmetric unit of compound* **12** *with labelling* (arbitrary) *of non-H-atoms.* Ellipsoids are at 50% probability level.

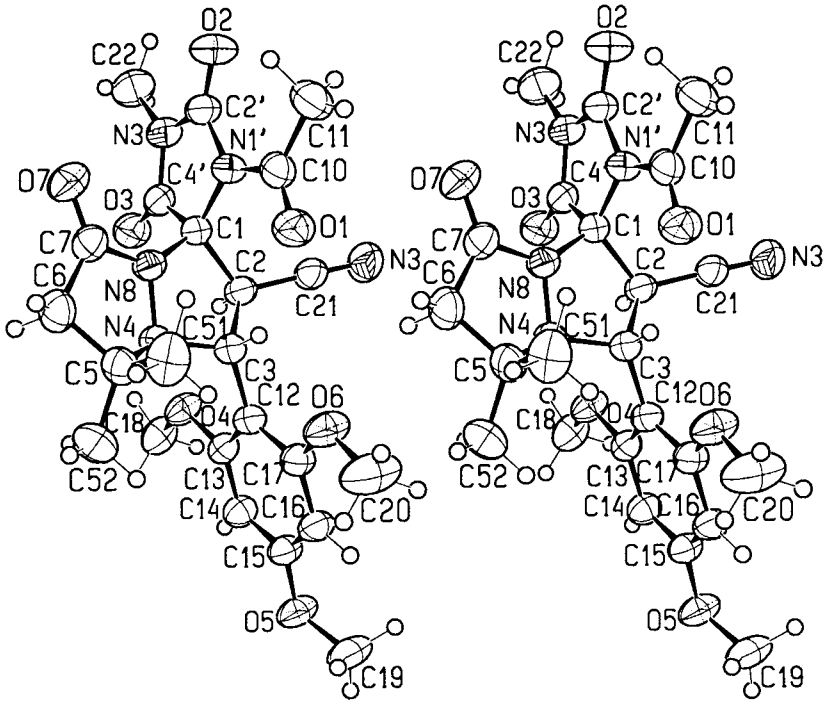


Fig. 5. *ORTEP Stereoview of the asymmetric unit of compound* **14** *with labelling* (arbitrary) *of non-H-atoms.* Ellipsoids are at 50% probability level.

carboxamides **23a** and **24a** were obtained upon treatment of dipolarophiles **8** and **9** with 4-chloro-*N*-phenylbenzonitrile imine (**20a**), formed *in situ* from 4-chloro-*N*-phenylbenzenecarbohydrazonoyl chloride (**19a**) and Ag_2O, in CH_2Cl_2 at room temperature.

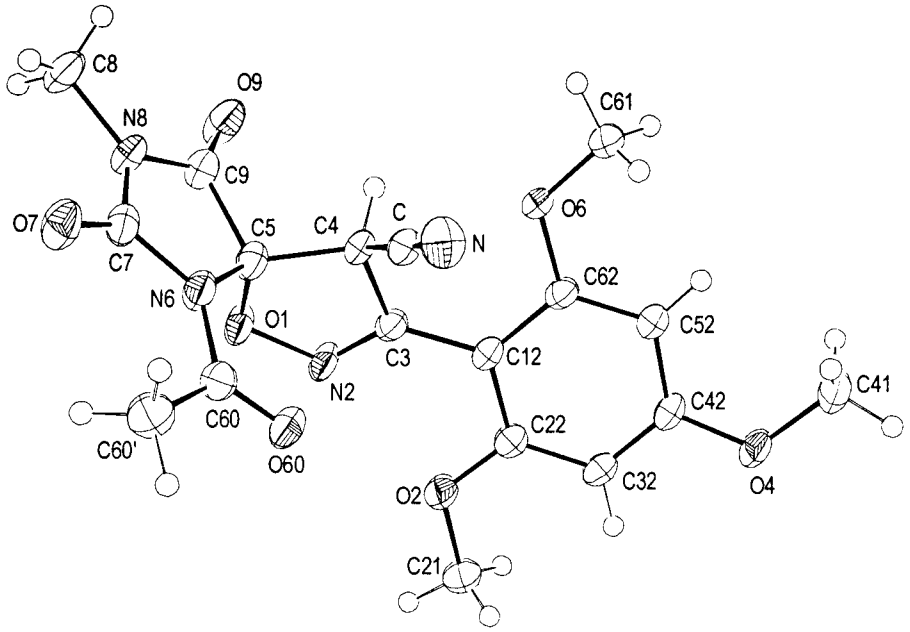


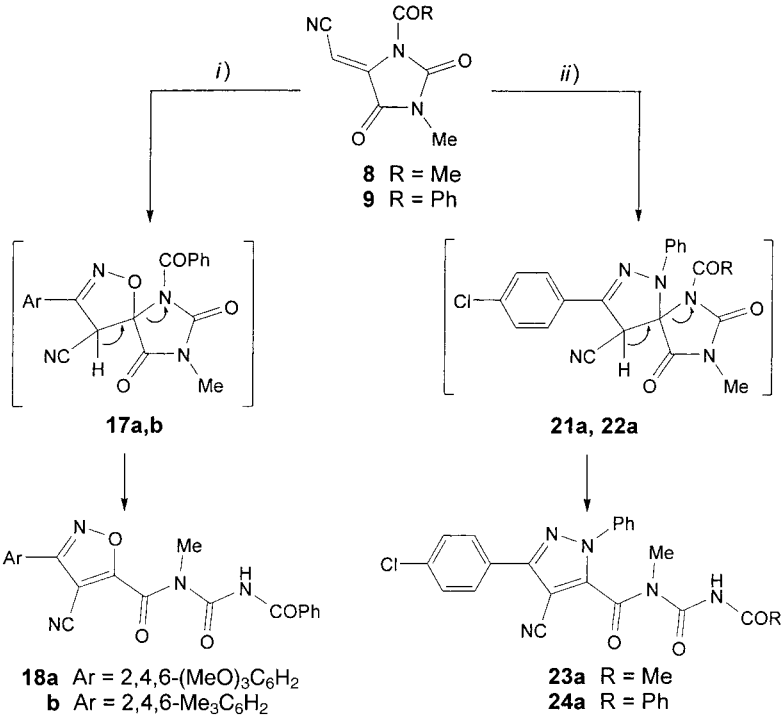
Fig. 6. *ORTEP View of the asymmetric unit of compound* **16a** *with labelling* (arbitrary) *of non-H-atoms.* Ellipsoids are at 50% probability level.

The structure of compound **18b** was determined by X-ray-analysis (*Fig. 7*). According to our previous results in the acyclic 2-(acylamino)-3-cyanoprop-2-enoate series, formation of the *N*-[(acylamino)carbonyl]carboxamides **18a**,**b**, **23a**, and **24a** could be rationalized by initial formation of primary spiro cycloadducts **17a**,**b**, **21a**, and **22a**, respectively, followed by isomerization leading to opening of the hydantoin ring and aromatization of the isoxazoline or pyrazoline rings [11].

However, when the reactions of **8** with benzenecarbohydrazonoyl chlorides **19a**,**b** were carried out in the presence of Et_3N in CH_2Cl_2 under reflux or in the presence of Ag_2O in MeCN under reflux, the carboxamides **25a**,**b** were obtained (*Scheme 4*). Presumably also in this case, spiro compounds **21a**,**b** were formed first, followed by isomerization to the *N*-[(acetylamino)carbonyl]carboxamides **23a**,**b** as intermediates, from which, under slightly more drastic conditions, MeCONCO was eliminated to give pyrazole-5-carboxamides **25a**,**b**. This reaction sequence was supported by independent experiments, where **23a** and **18b** were treated with Et_3N in refluxing CH_2Cl_2 to give the carboxamides **25a** and **26b**, respectively (*Scheme 4*).

Heating compound **8** with nitrile oxides **11a**–**c** in $CHCl_3$ followed by purification of the crude mixture by column chromatography (CC; silica gel, $CHCl_3$/MeOH 100:1) afforded the corresponding methyl 3-aryl-4-cyanoisoxazole-3-carboxylates **27a**–**c** (*Scheme 5*). Apparently, silica-gel-catalyzed methanolysis took place during chromatographic purification with the MeOH-containing eluent. To establish which possible intermediates could be involved in the reaction mechanism, additional experiments were carried out. First, passing the spiro compound **16a** through a silica-gel-filled

Scheme 3



i) 2,4,6-$(MeO)_3C_6H_2{\equiv}N^+{-}O^-$ (**11a**) or 2,4,6-$Me_3C_6H_2C{\equiv}N^+{-}O^-$ (**11b**), $CHCl_3$, reflux. *ii*) 4-$ClC_6H_4C(Cl){=}$NNHPh (**19a**), Ag_2O, CH_2Cl_2, r.t.

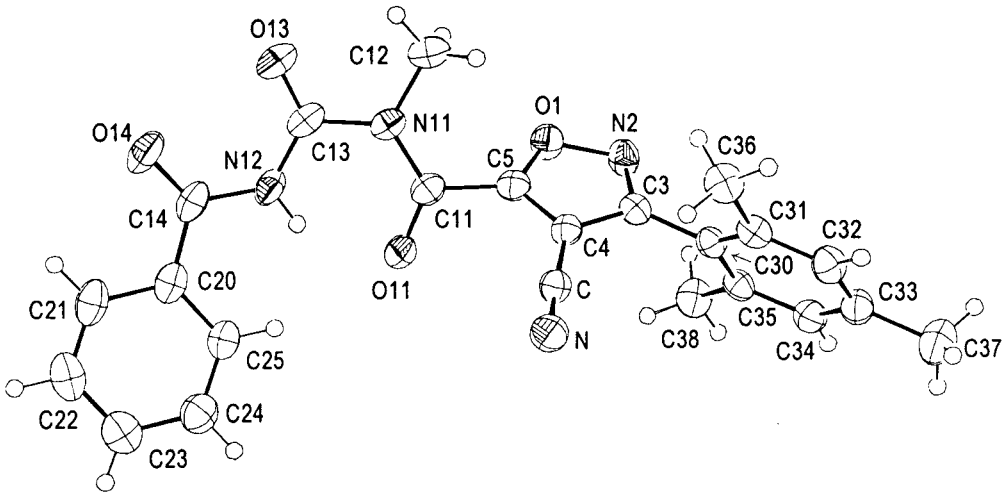
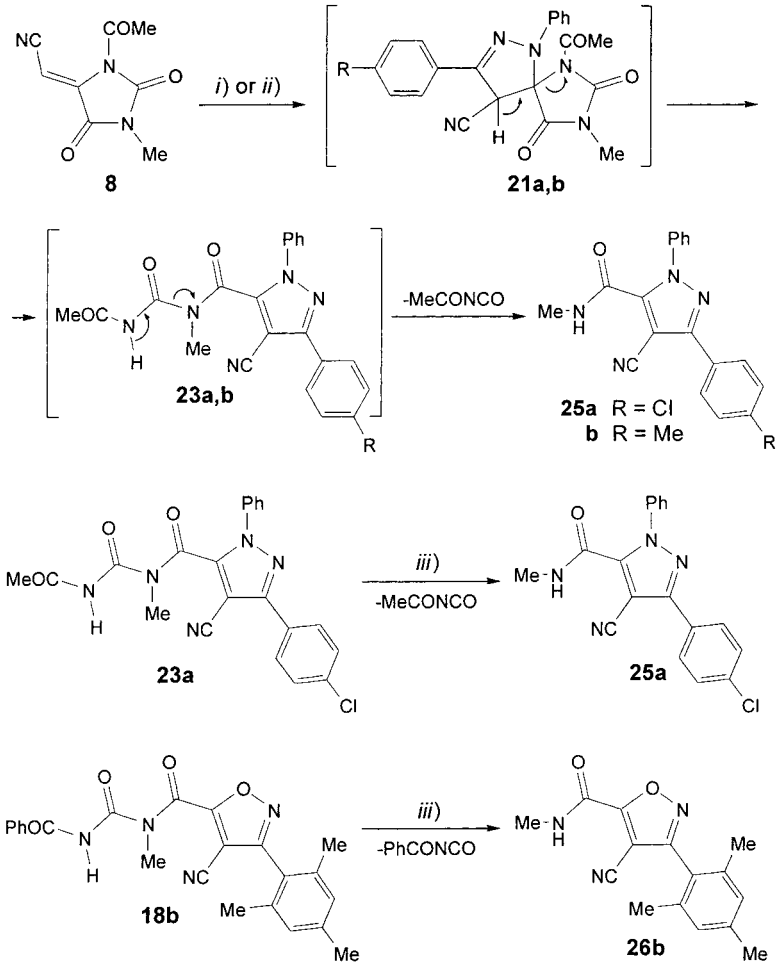


Fig. 7. *ORTEP View of the asymmetric unit of compound* **18b** *with labelling* (arbitrary) *of non-H-atoms.* Ellipsoids are at 50% probability level.

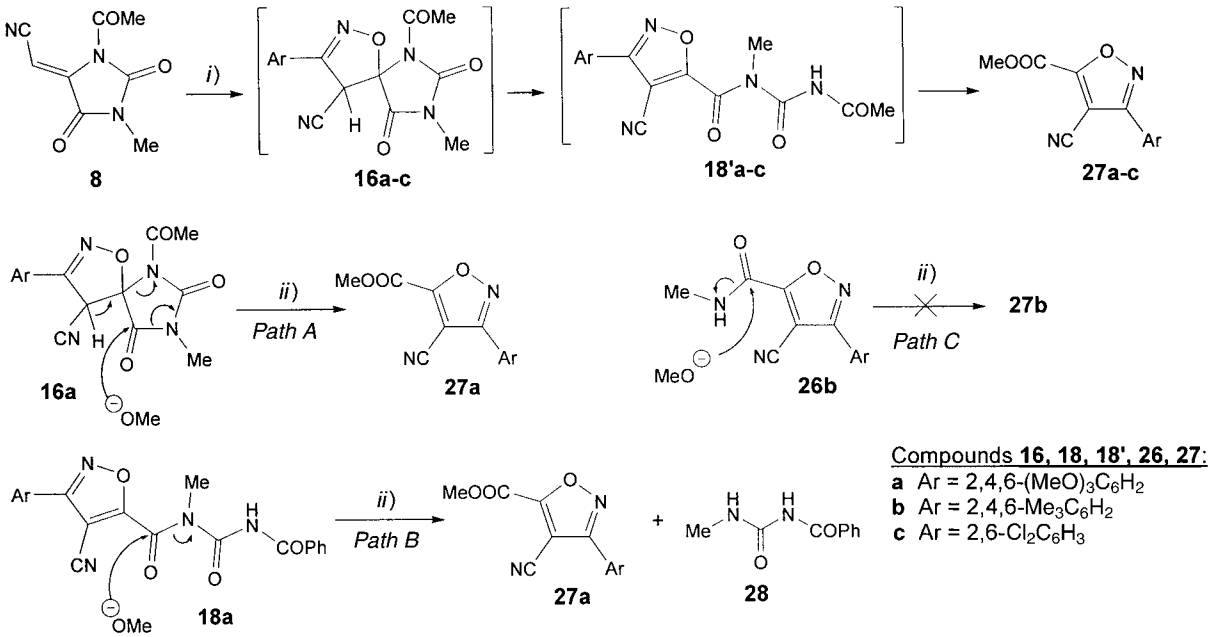
Scheme 4



i) 4-$ClC_6H_4C(Cl)$=NNHPh (**19a**) or 4-$MeC_6H_4C(Cl)$=NNHPh (**19b**), Et_3N, CH_2Cl_2, reflux (*G.P. A*). *ii*) **19a**, Ag_2O, MeCN, reflux (*G.P. B*). *iii*) Et_3N, CH_2Cl_2, reflux (*G.P. C*).

column with $CHCl_3$/MeOH as eluent furnished isoxazole-5-carboxylate **27a** (*Scheme 5*, *Path A*). Then, under the same conditions, isoxazole-5-carboxylate **27a** and benzamide **28** were obtained from *N*-[(benzoylamino)carbonyl]carboxamide **18a** (*Path B*). On the other hand, isoxazole-5-carboxamide **26b** was not transformed into methyl isoxazole-5-carboxylate **27b** upon passing through a silica-gel-filled column with $CHCl_3$/MeOH as eluent (*Path C*). These experiments might indicate that the formation of methyl isoxazole-5-carboxylates **27** proceeds *via* spiro compounds **16** and/or *N*-[(acylamino)-carbonyl]carboxamides **18** followed by silica-gel-catalyzed transacylation into **27** (*Paths A* and *B*, resp.), although isoxazole-5-carboxamides **26** (*Path C*) still cannot be excluded as possible intermediates.

Scheme 5



i) 2,4,6-$(MeO)_3C_6H_2C{\equiv}N^+{-}O^-$ (**11a**), 2,4,6-$Me_3C_6H_2C{\equiv}N^+{-}O^-$ (**11b**), or 2,6-$Cl_2C_6H_3C{\equiv}N^+{-}O^-$ (**11c**), $CHCl_3$, reflux, then CC ($CHCl_3$/MeOH 100 :1) (*G.P. A*). *ii*) CC ($CHCl_3$/MeOH 100 :1) (*G.P. B*).

Conclusion. – The (5*Z*)-1-acyl-5-(cyanomethylidene)imidazolidine-2,4-diones **8** and **9** are easily available precursors for the preparation of various spirohydantoin derivatives **12**–**16** by 1,3-dipolar cycloadditions to various 1,3-dipoles under mild and/or neutral conditions. However, reactions of **8** and **9** with nitrile oxides and nitrile imines under more drastic conditions, such as upon heating or in the presence of a base or an acid, furnished 3-aryl-4-cyanoisoxazole- or 3-aryl-4-cyano-1*H*-pyrazole-5-carboxylic acid derivatives **18** and **23**–**27**. According to experimental evidence, these reactions might proceed *via* isomerization of the initially formed spirohydantoins **16**, **17**, and **21** into *N*-[(acylamino)carbonyl]carboxamides **18**, **23**, and **24**, followed by transformation into substituted isoxazole- or 1*H*-pyrazole-5-carboxylic acid derivatives **25**–**27**. The relative ease of isomerization of spirohydantoins to the *N*-[(acylamino)carbonyl]-carboxamides could be explained by the tendency for aromatization of the newly formed dihydroisoxazole or dihydro-1*H*-pyrazole ring (see, *e.g.*, *Scheme 3*) which is achieved by elimination of the amide moiety resulting in opening of the hydantoin ring.

Experimental Part

General. (5*Z*)-5-[(Dimethylamino)methylidene]imidazolidine-2,4-dione (**2**), (5*Z*)-5-[(dimethylamino)-methylidene]-3-methylimidazolidine-2,4-dione (**3**) [13], CH_2N_2 (**7**) [15], (1*Z*)-5,5-dimethyl-3-oxo-1-[(2,4,6-trimethoxyphenyl)methylidene)]pyrazolidin-1-ium-2-ide (**10**) [16], 2,4,6-trimethoxybenzonitrile *N*-oxide (**11a**), 2,4,6-trimethylbenzonitrile *N*-oxide (**11b**), 2,6-dichlorobenzonitrile *N*-oxide (**11c**) [17], 4-chloro-*N*-phenylbenzenecarbohydrazonoyl chloride (**19a**), and 4-methyl-*N*-phenylbenzenecarbohydrazonoyl chloride (**19b**) [18] were prepared according to the published procedures. All starting materials were commercially available (in most cases from *Fluka*) and purified by standard techniques. Column chromatography (CC): silica gel *60* (0.04–0.063 mm, *Fluka*). TLC: alu foils coated with silica gel *60 F 254* (0.2 mm, *Merck*). Microwave irradiation: *Milestone LAVIS-1000* laboratory microwave oven with a reflux condenser. M.p.: *Kofler* micro hot stage. IR: *Perkin-Elmer Spectrum-BX-FTIR* and *Perkin-Elmer 1310* spectrometers; KBr pellets; in cm^{-1}. ^1H- (300 MHz) and ^{13}C-NMR (75.5 MHz): *Bruker Avance-DPX 300* spectrometer; δ in ppm rel. to Me_4Si as internal standard (=0 ppm), *J* in Hz. MS: in *m*/*z*. Elemental analyses: *Perkin-Elmer CHN Analyser 2400*. MS: *Autospeck Q (VG-Analytical)* spectrometer.

(2Z)-2-(2,5-Dioxoimidazolidin-4-ylidene)acetonitrile (**4**). A soln. of KCN (0.358 g, 5.5 mmol) in a soln. of **2** (0.775 g, 5 mmol) in AcOH (10 ml) was left at r.t. for 2 days. Volatile components were evaporated, and the residue was purified by CC (AcOEt/hexane 1:1): **4** (0.481 g, 70%). M.p. 194–196°. IR: 2210 (C≡N), 1770, 1700 (C=O). ^1H-NMR ((D_6)DMSO): 5.43 (*s*, CHCN); 11.66 (br. *s*, NH). ^{13}C-NMR ((D_6)DMSO): 73.09; 116.6; 146.0; 155.5; 163.9. Anal. calc. for $C_5H_3N_3O_2$ (137.10): C 43.80, H 2.21, N 30.65; found: C 43.68, H 2.06, N 50.51.

(2Z)-2-(1-Methyl-2,5-dioxoimidazolidin-4-ylidene)acetonitrile (**5**). A soln. of KCN (0.715 g, 11 mmol) in a soln. of **3** (1.690 g, 10 mmol) in AcOH (20 ml) was left at r.t. for 2 days. Volatile components were evaporated, the residue was dissolved in H_2O (20 ml), the soln. left at r.t. for 24 h, and the precipitate collected by filtration: **5** (1.056 g, 70%). M.p. 186–188°. IR: 2200 (C≡N), 1780, 1730 (C=O). ^1H-NMR ((D_6)DMSO): 2.91 (*s*, Me–N(1)); 5.57 (*s*, CHCN); 11.91 (br. *s*, H–N(3)). ^{13}C-NMR ((D_6)DMSO): 25.2; 74.1; 116.4; 145.0; 155.2; 162.7. Anal. calc. for $C_6H_5N_3O_2$ (151.12): C 47.69, H 3.33, N 27.81; found: C 47.33, H 3.20, N 27.54.

(2Z)-2-(1,3-Dimethyl-2,5-dioxoimidazolidin-4-ylidene)acetonitrile (**6**). A cold soln. (0–5°) of diazomethane (**7**) in Et_2O (*ca.* 0.2M, 15 ml, *ca.* 3 mmol) was added to a soln. of **4** or **5** (1 mmol) in THF (10 ml) at –10°, and the soln. was left at –10° for 12 h. Volatile components were left to evaporate in a ventilated hood to give **6** (0.166 g, 99%). M.p. 108–110°. IR: 2200 (C≡N), 1710, 1760 (C=O). ^1H-NMR ((D_6)DMSO): 2.95 (*s*, Me–N(1)); 3.35 (*s*, Me – N(3)); 5.67 (*s*, CHCN). ^{13}C-NMR ((D_6)DMSO): 25.9; 28.4; 73.9; 116.8; 144.2; 155.2; 162.2. Anal. calc. for $C_7H_7N_3O_2$ (165.15): C 50.91, H 4.27, N 25.44; found: C 50.53, H 4.43, N 25.48.

(5Z)-1-Acetyl-5-(cyanomethylidene)-3-methylimidazolidine-2,4-dione (**8**). Ac_2O (3.6 ml, 36 mmol) was added to a soln. of **4** (1.812 g, 12 mmol) in anh. pyridine (5 ml), and the soln. was left at r.t. for 2 h. The mixture was poured into a mixture of ice (20 ml), H_2O (20 ml), and AcOH (5 ml), and the precipitate was collected by filtration to give **8** (1.657 g, 72%). M.p. 124–126°. IR: 2200 (C≡N), 1780, 1700 (C=O). ^1H-NMR ((D_6)DMSO):

2.58 (*s*, MeCO); 3.00 (*s*, Me–N(3)); 6.20 (*s*, CHCN). Anal. calc. for $C_8H_7N_3O_3$ (193.16): C 49.74, H 3.65, N 21.75; found: C 49.67, H 3.45, N 21.40.

(5Z)-1-Benzoyl-5-(cyanomethylidene)-3-methylimidazolidine-2,4-dione (**9**). As described for **8**, with PhCOCl (0.35 ml, 3 mmol), **5** (0.507 g, 3 mmol), and pyridine (1 ml) for 3.5 h. Workup with ice (5 ml), H_2O (5 ml), and AcOH (1 ml). The precipitate was washed with EtOH (5 ml): **9** (0.265 g, 35%). M.p. 159–160°. IR: 2220 (C≡N), 1790, 1720 (C=O). ^{1}H-NMR ((D$_6$)DMSO): 2.96 (*s*, Me–N(3)); 6.27 (*s*, CHCN); 7.55–7.60 (*m*, 2 arom. H); 7.72–7.78 (*m*, 1 arom. H); 7.95–7.98 (*m*, 2 arom. H). Anal. calc. for $C_{13}H_9N_3O_3$ (255.23): C 61.18, H 3.55, N 16.46; found: C 60.91, H 3.58, N 16.05.

rel-*(4*R*,5*R*)-6-Acetyl-8-methyl-7,9-dioxo-1,2,6,8-tetraazaspiro[4.4]non-1-ene-4-carbonitrile* (**12**). A soln. of diazomethane (**7**) in Et_2O (*ca.* 0.4M, 10 ml, *ca.* 4 mmol) was added to a soln. of **8** (0.193 g, 1 mmol) in CH_2Cl_2 (7 ml). After 12 h at r.t., heptane was added slowly with stirring until the soln. became slightly turbid. The more volatile components (mostly Et_2O and CH_2Cl_2) were left to evaporate in a well-ventilated hood to 1/2 of the initial volume (*ca.* 10 ml). The precipitate was filtered off and washed with Et_2O: **12** (0.145 g, 66%). M.p. 143–145°. IR: 2230 (C≡N), 1710, 1790 (C=O). ^{1}H-NMR ((D$_6$)DMSO): 2.54 (*s*, MeCO); 3.07 (*s*, Me–N(8)); 3.65 (*dd*, *J* = 6.8, 9.5, H–C(4)); 5.12 (*dd*, *J* = 6.8, 18.8, 1 H–C(3)); 5.48 (*dd*, *J* = 9.8, 18.8, 1 H–C(3)). ^{13}C-NMR ((D$_6$)DMSO): 25.5; 26.7; 27.9; 84.2; 103.5; 117.2; 153.6; 166.5; 169.5. Anal. calc. for $C_9H_9N_5O_3$ (235.20): C 45.96, H 3.86, N 29.78; found: C 45.70, H 3.65, N 29.60.

rel-*(4*R*,5*R*)-6-Benzoyl-8-methyl-7,9-dioxo-1,2,6,8-tetraazaspiro[4.4]non-1-ene-4-carbonitrile* (**13**). A soln. of diazomethane (**7**) in Et_2O (*ca.* 0.5M, 16 ml, *ca.* 8 mmol) was added to a soln. of **9** (0.255 g, 1 mmol) in $CHCl_3$ (10 ml), and the solution was left at r.t. for 12 h. The precipitate was filtered off and washed with Et_2O: **13** (0.220 g, 74%). M.p. 180–182°. IR: 2240 (C≡N), 1800, 1730–1680 (C=O). ^{1}H-NMR ((D$_6$)DMSO): 3.05 (*s*, Me–N(8)); 3.85 (*dd*, *J* = 6.8, 9.4, H–C(4)); 5.23 (*dd*, *J* = 6.8, 18.8, 1 H–C(3)); 5.54 (*dd*, *J* = 9.8, 18.8, 1 H–C(3)); 7.47–7.52 (*m*, 2 arom. H); 7.60–7.65 (*m*, 1 arom. H); 7.67–7.69 (*m*, 2 arom. H). ^{13}C-NMR ((D$_6$)DMSO): 26.8; 27.4; 84.4; 104.3; 117.0; 128.7; 129.5; 133.4; 134.2; 152.8; 166.5; 168.6. Anal. calc. for $C_{14}H_{11}N_5O_3$ (297.27): C 56.56, H 3.73, N 23.56; found: C 56.70, H 3.73, N 23.64.

Cycloadducts **14** and **15**: *General Procedure.* A mixture of dipolarophile **8** or **9** (0.5 mmol), azomethine imine **10** (0.322 g, 1.1 mmol), and anh. 1,4-dioxane (15 ml) was irradiated under reflux in a laboratory microwave oven (*P* = 1000 W, pulse width 0.1 s) for 1.5–2.5 h. Volatile components were evaporated, and the residue was purified by CC. Nonpolar impurities were eluted with AcOEt/hexane 2:1 followed by elution of the product with AcOEt: spiro compounds **14** and **15**, resp.

rel-*(1*R*,2*R*,3*S*)-3′-Acetyl-1′,5,5-trimethyl-2′,5′,7-trioxo-3-(2,4,6-trimethoxyphenyl)spiro[1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-1,4′-imidazolidine]-2-carbonitrile* (**14**). From **8** (1.5 h): 0.320 g (66%). M.p. 259–262° ($CHCl_3$/hexane). IR: 2250 (C≡N), 1800, 1730, 1680 (C=O). ^{1}H-NMR ($CDCl_3$): 0.87, 1.38 (2*s*, 1:1, 2 Me–C(5)); 2.30 (*d*, *J* = 16.2, 1 H–C(6)); 2.68 (*s*, MeCO); 2.71 (*d*, *J* = 16.2, 1 H–C(6)); 3.19 (*s*, Me–N(1′)); 3.83, 3.89, 3.92 (3*s*, 1:1:1, 3 MeO); 5.42 (*d*, *J* = 10.0, H–C(2)); 5.73 (*d*, *J* = 10.0, H–C(3)); 6.16 (*s*, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 20.7; 25.8; 25.9; 26.3; 42.7; 50.7; 53.2; 55.4; 56.1; 56.5; 61.5; 72.3; 91.2; 92.4; 101.3; 114.8; 152.6; 160.5; 161.7; 162.4; 163.9; 167.1; 169.3. Anal. calc. for $C_{23}H_{27}N_5O_7$ (485.49): C 56.90, H 5.61, N 14.43; found: C 56.92, H 5.64, N 14.25.

rel-*(1*R*,2*R*,3*S*)-3′-Benzoyl-1′,5,5-trimethyl-2′,5′,7-trioxo-3-(2,4,6-trimethoxyphenyl)spiro[1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-1,4′-imidazolidine]-2-carbonitrile* (**15**). From **9** (2.5 h): 0.224 g (41%). M.p. 210–212° ($CHCl_3$/hexane). IR: 2250 (C≡N), 1810, 1740, 1710 (C=O). ^{1}H-NMR ($CDCl_3$): 0.88, 1.35 (2*s*, 1:1, Me–C(5)); 2.33 (*d*, *J* = 16.2, 1 H–C(6)); 2.77 (*d*, *J* = 16.2, 1 H–C(6)); 3.17 (*s*, Me–N(1′)); 3.84, 3.90, 3.94 (3*s*, 1:1:1, 3 MeO); 5.51 (*d*, *J* = 10.2, H–C(2)); 5.82 (*d*, *J* = 10.2, H–C(3)); 6.17 (*s*, 2 arom. H); 7.42–7.47 (*m*, 2 arom. H); 7.52–7.58 (*m*, 1 arom. H); 7.72–7.75 (*m*, 2 arom. H). Anal. calc. for $C_{28}H_{29}N_5O_7$ (547.56): C 61.42, H 5.34, N 12.79; found: C 61.62, H 5.42, N 13.08.

rel-*(4*R*,5*S*)-6-Acetyl-8-methyl-7,9-dioxo-3-(2,4,6-trimethoxyphenyl)-1-oxa-2,6,8-triazaspiro[4.4]non-2-ene-4-carbonitrile* (**16a**). A mixture of **8** (0.147 g, 0.76 mmol), nitrile oxide **11a** (0.159 g, 0.76 mmol), and $CHCl_3$ (5 ml) was refluxed for 4 h. The mixture was evaporated to 1/2 of the initial volume, and heptane (*ca.* 2 ml) was added slowly with stirring until the soln. became slightly turbid. Crystallization was induced by scratching, and the precipitate was filtered off: **16a** (0.082 g, 20%). M.p. 176–178° (heptane/$CHCl_3$). IR: 2230 (C≡N), 1810, 1740 (C=O). ^{1}H-NMR ($CDCl_3$): 2.62 (*s*, MeCO); 3.21 (*s*, Me–N(8)); 3.86, 3.91 (2*s*, 1:2, 3 MeO); 5.55 (*s*, H–C(4)); 6.21 (*s*, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 25.5; 26.0; 48.4; 55.6; 56.5; 91.6; 92.0; 96.2; 112.1; 147.1; 152.0; 160.8; 164.1; 167.0; 168.5. Anal. calc. for $C_{18}H_{18}N_4O_7$ (402.36): C 53.73, H 4.51, N 13.92; found: C 53.47, H 4.59, N 13.72.

N-*[(Benzoylamino)carbonyl]isoxazole-5-carboxamides* **18a**,**b**: *General Procedure.* A mixture of **9** (0.255 g, 1 mmol), nitrile oxide **11a**,**b** (1 mmol), and $CHCl_3$ (10 ml) was refluxed for 3–4 h. Volatile components were

partially evaporated to 1/2 of the initial volume (*ca.* 5 ml) and heptane was added slowly until an oil separated; the oil crystallized upon scratching. The precipitate was filtered off: carboxamides **18a**,**b**.

N-*[(Benzoylamino)carbonyl]-4-cyano*-N-*methyl-3-(2,4,6-trimethoxyphenyl)isoxazole-5-carboxamide* (**18a**). From **11a** (4 h): 0.305 g (66%). M.p. 147–150° (AcOEt/hexane). IR: 3206 (NH), 2248 (C≡N), 1773, 1655 (C=O). ^{1}H-NMR ($CDCl_3$): 3.61 (*s*, MeN); 3.84, 3.89 (2*s*, 2:1, 3 MeO); 6.23 (*s*, 2 arom. H); 7.51–7.56 (*m*, 2 arom. H); 7.60–7.66 (*m*, 1 arom. H); 7.96–7.99 (*m*, 2 arom. H); 12.22 (*s*, NH). ^{13}C-NMR ($CDCl_3$): 33.6; 56.0; 56.4; 91.4; 95.1; 102.3; 110.0; 128.2; 129.5; 132.9; 133.9; 149.2; 158.7; 160.0; 160.4; 164.7; 164.8; 166.0. Anal. calc. for $C_{23}H_{20}N_4O_7$ (464.43): C 59.48, H 4.34, N 12.06; found: C 59.70, H 4.04, N 11.83.

N-*[(Benzoylamino)carbonyl]-4-cyano*-N-*methyl-3-(2,4,6-trimethylphenyl)isoxazole-5-carboxamide* (**18b**). From **11b** (3 h): 0.259 g (62%). M.p. 145–181° (AcOEt/hexane). IR: 3201 (NH), 2250 (C≡N), 1780, 1760 (C=O). ^{1}H-NMR ($CDCl_3$): 2.15, 2.34 (2*s*, 2:1, 3 arom. Me); 3.62 (*s*, MeN); 7.00 (*s*, 2 arom. H); 7.50–7.55 (*m*, 2 arom. H); 7.60–7.63 (*m*, 1 arom. H); 7.95–7.97 (*m*, 2 arom. H); 12.05 (*s*, NH). Anal. calc. for $C_{23}H_{20}N_4O_4$ (416.43): C 66.34, H 4.84, N 13.45; found: C 66.52, H 4.73, N 13.26.

*1*H-*Pyrazole-5-carboxamides* **23a** and **24a**: *General Procedure.* Ag_2O (0.281 g, 1.21 mmol) was added to a soln. of **8** or **9** (1 mmol) and hydrazonoyl chloride **19a** (0.265 g, 1 mmol) in CH_2Cl_2 (11 ml), and the mixture was stirred at r.t. for 1–3 h. After filtration and evaporation, the residue was purified by CC: carboxamides **23a** and **24a**, resp.

N-*[(Acetylamino)carbonyl]-3-(4-chlorophenyl)-4-cyano*-N-*methyl-1-phenyl-1*H-*pyrazole-5-carboxamide* (**23a**). From **8** (1 h; CC (Et_2O)): 0.359 g (85%). M.p. 167–170° (CH_2Cl_2/hexane). IR: 3272 (N–H), 2236 (C≡N), 1748, 1713, 1662 (C=O). ^{1}H-NMR ($CDCl_3$): 2.45 (*s*, MeCO); 3.17 (*s*, MeN); 7.47–7.57 (*m*, 7 arom. H); 7.99–8.03 (*m*, 2 arom. H); 10.78 (*s*, NH). ^{13}C-NMR ($CDCl_3$): 26.1; 33.6; 91.9; 112.6; 123.8; 128.1; 128.5; 129.8; 130.5; 130.6; 136.9; 138.2; 142.0; 150.5; 152.9; 163.2; 171.7. EI-MS: 421 (M^+). Anal. calc. for $C_{21}H_{16}ClN_5O_3$ (421.84): C 59.79, H 3.82, N 16.60; found: C 59.69, H 3.72, N 16.23.

N-*[(Benzoylamino)carbonyl]-3-(4-chlorophenyl)-4-cyano-1-phenyl-1*H-*pyrazole-5-carboxamide* (**24a**). From **9** (3 h; CC (CH_2Cl_2/petroleum ether/Et_2O 10:2:1)): 0.394 g (81%). M.p. 143–145° (CH_2Cl_2/hexane). IR: 3207 (N–H), 2236 (C≡N), 1780, 1657 (C=O). ^{1}H–NMR ($CDCl_3$): 3.17 (*s*, MeN); 7.48–7.66 (*m*, 10 arom. H); 7.95–8.05 (*m*, 4 arom. H); 12.17 (*s*, NH). ^{13}C-NMR ($CDCl_3$): 33.6; 92.2; 112.5, 123.5; 128.1; 128.3; 128.5; 129.5; 129.8; 130.7, 130.7; 132.93; 133.9; 136.9; 138.1; 141.8; 148.9; 153.1; 164.2; 164.7. Anal. calc. for $C_{26}H_{16}ClN_5O_3$ (483.91): C 64.53, H 3.75, N 14.47; found: C 64.55, H 3.60, N 14.08.

*1*H-*Pyrazole-5-carboxamides* **25a**,**b**. *General Procedure A* (*G.P. A*). Et_3N (0.05 ml, 0.36 mmol) was added to a soln. of **8** (0.038 g, 0.2 mmol) and hydrazonoyl chloride **19a**,**b** (0.2 mmol) in CH_2Cl_2 (4 ml), and the mixture was refluxed for 3–4 h. Volatile components were evaporated, and the residue was purified by CC (Et_2O) and crystallization from *i*-Pr_2O/$CHCl_3$: carboxamides **25a**,**b**.

General Procedure B (*G.P. B*). Ag_2O (0.213 g, 0.92 mmol) was added to a soln. of **8** (0.089 g, 0.46 mmol) and hydrazonoyl chloride **19a** (0.122 g, 0.46 mmol) in MeCN (7 ml), and the mixture was refluxed for 3 h. The mixture was then cooled and filtered, the filtrate evaporated, and the residue purified by CC (Et_2O): carboxamide **25a**.

General Procedure C (*G.P. C*). Et_3N (0.14 ml, 1.4 mmol) was added to a soln. of **23a** (0.084 g, 0.2 mmol) in CH_2Cl_2 (5 ml), and the mixture was refluxed for 3 h. Volatile components were evaporated, and the residue was purified by CC (Et_2O): carboxamide **25a**.

3-(4-Chlorophenyl)-4-cyano-N-*methyl-1-phenyl-1*H-*pyrazole-5-carboxamide* (**25a**). From **19a** and Et_3N (3 h, *G.P. A*). 0.026 g (40%): From **19a** and Ag_2O (*G.P. B*). 0.109 g (70%). From **23a** and Et_3N (*G.P. C*): 0.050 g (74%). M.p. 218–221° ($CHCl_3$/*i*-Pr_2O). IR: 3290 (N–H), 2240 (C≡N), 1660 (C=O). ^{1}H-NMR ((D_6)DMSO): 2.79 (*d*, J = 4.9, MeN); 7.51–7.59 (*m*, 5 arom. H); 7.64–7.69 (*m*, 2 arom. H); 7.95–7.99 (*m*, 2 arom. H); 9.17 (*q*, J = 4.9, NH). ^{13}C-NMR ((D_6)DMSO): 27.1; 91.4; 114.0; 124.5; 129.1; 129.3; 130.2; 130.3; 130.4; 135.6; 138.9; 145.6; 151.5; 158.5. Anal. calc. for $C_{18}H_{13}ClN_4O$ (336.77): C 64.19, H 3.89, N 16.64; found: C 64.51, H 3.69, N 16.40.

4-Cyano-N-*methyl-3-(4-methylphenyl)-1-phenyl-1*H-*pyrazole-5-carboxamide* (**25b**). From **9** and Et_3N (4 h, *G.P. A*): 0.017 g (27%). M.p. 207–211° ($CHCl_3$/*i*-Pr_2O). IR: 3260 (N–H), 2230 (C≡N), 1650 (C=O). ^{1}H-NMR ((D_6)DMSO): 2.39 (*s*, 1 arom. Me); 2.79 (*d*, J = 4.9, MeN); 7.38–7.40 (*m*, 2 arom. H); 7.52–7.58 (*m*, 5 arom. H); 7.83–7.86 (*m*, 2 arom. H); 9.15 (*q*, J = 4.9, NH). Anal. calc. for $C_{19}H_{16}N_4O$ (316.36): C 72.13, H 5.10, N 17.71; found: C 72.13, H 5.07, N 17.67.

4-Cyano-N-*methyl-3-(2,4,6-trimethylphenyl)isoxazole-5-carboxamide* (**26b**) *Solvate with Heptane 3:1.* Et_3N (0.1 ml, 0.71 mmol) was added to a soln. of **18b** (0.060 g, 0.144 mmol) in CH_2Cl_2 (3 ml), and the mixture was heated under reflux for 2 h. Volatile components were evaporated, and the residue was purified by CC (AcOEt/petroleum ether 1:3). The product was crystallized from CH_2Cl_2/heptane: 3 **26b**·C_7H_{16} (0.033 g, 76%). M.p.

127–129°. IR: 3356 (NH), 2251 (C≡N), 1671 (C=O). ^{1}H-NMR ($CDCl_3$): 0.88 (br. *t*, 2 Me of heptane); 1.27 (br., 5 CH_2 of heptane); 2.14, 2.34 (2*s*, 2:1, 3 arom. Me); 3.11 (*d*, *J* = 5.3, MeN); 6.62 (*br. s*, NH); 6.98 (*s*, 2 arom. H). ^{13}C-NMR ($CDCl_3$) **26b**: 20.3; 21.6; 26.9; 97.7; 109.6; 121.4; 129.3; 137.6; 141.2; 154.5; 164.4; 167.4; heptane: 14.5; 23.1; 26.9; 29.4; 32.3. Anal. calc. for $C_{52}H_{61}N_9O_6$ (908.10): C 68.78, H 6.77, N 13.88; found: C 69.22, H 6.48, N 13.69. HR-MS: 269.117770 $C_{15}H_{15}N_3O_2^+$; calc. 269.117050.

Methyl Isoxazole-5-carboxylates **27a–c** *and Benzamide* **28**. *General Procedure* (*G.P. A*). A mixture of **8** (0.193 g, 1 mmol) and nitrile oxide **11a–c** (1 mmol) in $CHCl_3$ (15 ml) was stirred at r.t. or reflux for 3 h or 3 days. Volatile components were evaporated, and the residue was purified by CC ($CHCl_3$/MeOH 100:1). The product was dissolved in petroleum ether (*ca.* 20 ml), and the soln. was left at −15° for 12 h. The precipitate was filtered off: methyl isoxazole-5-carboxylates **27a–c**.

General Procedure (*G.P. B*). Compound **16a** (0.113 g, 0.28 mmol) or **18a** (0.066 g, 0.14 mmol) was passed through a silica gel filled column with $CHCl_3$/MeOH 100:1 as eluent. Fractions containing the products **27a** and **28** were combined and evaporated *in vacuo*. Each residue was dissolved in hexane (*ca.* 10 ml), and the soln. was left at −15° for 12 h. Each precipitate was filtered off: methyl isoxazole-5-carboxylate **27a** and benzamide **28**, resp.

Methyl 4-Cyano-3-(2,4,6-trimethoxyphenyl)isoxazole-5-carboxylate (**27a**). From **11a** (reflux, 5 h; *G.P. A*): 0.181 g (57%). From **16a** (*G.P. B*): 0.062 g (69%). From **18a** (*G.P. B*): 0.040 g (88%). M.p. 149–151° (petroleum ether). IR: 2250 (C≡N), 1740 (C=O). ^{1}H-NMR ($CDCl_3$): 3.82, 3.87 (2*s*, 2:1 3 arom. Me); 4.07 (*s*, MeOOC–C(5)); 6.21 (*s*, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 54.0; 55.9; 56.3; 91.2; 95.8; 101.0; 110.2; 155.7; 158.8; 160.0; 163.3; 164.5. Anal. calc. for $C_{15}H_{14}N_2O_6$ (318.28): C 56.60, H 4.43, N 8.80; found: C 56.92, H 4.48, N 8.62.

Methyl 4-Cyano-3-(2,4,6-trimethylphenyl)isoxazole-5-carboxylate (**27b**). From **11b** (reflux, 3 h; *G.P. A*): 0.216 g (80%). M.p. 76–77° (petroleum ether). IR: 2250 (C≡N), 1740 (C=O). ^{1}H-NMR ($CDCl_3$): 2.14, 2.34 (2*s*, 2:1, 3 arom. Me); 4.11 (s, MeOOC–C(5)); 6.98 (*s*, 2 arom. H). Anal. calc. for $C_{15}H_{14}N_2O_3$ (270.28): C 66.66, H 5.22, N 10.36; found: C 66.97, H 5.28, N 10.37.

Methyl 4-Cyano-3-(2,6-dichlorophenyl)isoxazole-5-carboxylate (**27c**). From **11c** (r.t., 3 days; *G.P. A*): 0.133 g (45%). M.p. 89–91° (petroleum ether). IR: 2250 (C≡N), 1730 (C=O). ^{1}H-NMR ($CDCl_3$): 4.12 (*s*, MeOOC); 7.44–7.53 (*m*, 3 arom. H). Anal. calc. for $C_{12}H_6Cl_2N_2O_3$ (297.09): C 48.51, H 2.04, N 9.43; found: C 48.73, H 2.02, N 9.17.

N-*[(Methylamino)carbonyl]benzamide* (**28**). From **18a** (*G.P. B*): 0.022 g (86%). M.p. 164–169° ([19]: m.p. 170–171°). IR: 3332 (NH), 1702, 11678 (C=O). ^{1}H-NMR ($CDCl_3$): 2.96 (*d*, *J* = 4.9, Me); 7.47–7.52 (*m*, 2 arom. H); 7.57–7.63 (*m*, 1 arom. H); 7.90–7.94 (*m*, 2 arom. H); 8.59 (br. *s*, MeN*H*); 8.97 (*s*, CONH).

X-Ray Crystal-Structure Analyses for Compounds **5**, **12**, **14**, **16a**, *and* **18b**. Diffraction data for compounds **5** and **12** were collected on an *Enraf-Nonius-CAD4* and for **14**, **16a**, and **18b** on a *Nonius Kappa CCD* diffractometer. Graphite monochromated MoK_α radiation was used in all cases. For **5** and **12** intensities of reflections were corrected for *Lorentz*-polarization effects, and decay with the Xtal3.4 [20] program package. Data for **14**, **16a**, and **18b** were processed with the DENZO [21] program. Due to low values of the linear absorption coefficients for all five compounds, no absorption correction was applied. Structures were solved by direct methods: **5**, **12**, and **14** with the SIR97 [22] and **16a** and **18b** with the SHELX-97 [23] program. For the structures of **5**, **12**, and **14**, we employed full-matrix least-squares refinement on *F* magnitudes with anisotropic displacement factors for all non-H-atoms using Xtal3.4 [20]. The positions of H-atoms of **5** and **12** were obtained from the difference *Fourier* map. Most of the H-atoms of **14** were also located by means of difference *Fourier* map, the remaining were calculated by means of expected geometry. The parameters of H-atoms of compounds **5** and **14** were not refined in the final refinement, while those of compound **12** were refined isotropically with restrained C–H bonds. In the final cycle of the refinement, we used 936, 1957, and 3387 reflections, and 100, 181, and 317 parameters for **5**, **12**, and **14**, respectively. The number of restraints for **12** was 29. Structures **16a** and **18b** were refined by full-matrix least-squares on F^2 with SHELX-97 [23]. Non-H-atoms were refined anisotropically; H-atoms were placed at ideal positions with the displacement parameters taken as 1.2 times (aromatic) and 1.5 times (methyl) of their parent atoms. The resulting crystal data and details concerning data collection and refinement for all five compounds are given in the *Table*. The crystallographic data for compounds **5**, **12**, **14**, **16a**, and **18b** have also been deposited with the *Cambridge Crystallographic Data Center* as supplementary material with the deposition numbers CCDC 162165, CCDC 162166, CCDC 162167, CCDC 162168, and CCDC 162169, resp. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

The asymmetric units of compounds **5**, **12**, **14**, **16a**, and **18b** are presented in *Figs. 2* and *4–7*, resp. *Figs. 2*, *4*, and *5* were prepared with the aid of ORTEP-II [24] and *Figs. 6* and *7* with ORTEP-III [25]. In the structure of compound **5**, the molecules are nearly planar. They are connected *via* intermolecular NH···O H-bonds: the

Table 1. *Crystal Data, Data Collection, and Structure Refinement for Compounds* **5**, **12**, **14**, **16a**, and **18b**

	5	**12**	**14**	**16a**	**18**
Formula	$C_6H_5N_3O_2$	$C_9H_9N_5O_3$	$C_{23}H_{27}N_5O_7$	$C_{18}H_{18}N_4O_7$	$C_{23}H_{20}N_4O_4$
M_r	151.14	235.2	485.5	402.36	416.43
Crystal system	orthorhombic	monoclinic	triclinic	monoclinic	monoclinic
Space group	$P2_12_12_1$, No. 19	$P2_1/n$, No. 14	P-1, No. 2	$P2_1/n$, No. 14	$P2_1/c$, No. 14
a [Å]	5.934(1)	5.5300(6)	8.3590(2)	14.0062(3)	15.2342(3)
b [Å]	6.223(1)	13.549(1)	10.4270(2)	9.3111(2)	7.21270(10)
c [Å]	18.073(1)	14.600(1)	15.2693(4)	14.9528(3)	19.2387(5)
α [°]	90.00	90.00	72.5466(11)	90.00	90.00
β [°]	90.00	95.788(7)	84.4195(10)	111.1870(10)	105.2210(7)
γ [°]	90.00	90.00	70.6496(12)	90.00	90.00
V [Å^3]	667.39(16)	1088.34(16)	1197.87(5)	1826.02(7)	2039.79(7)
Z	4	4	2	4	4
ρ [Mg m^{-3}]	1.504	1.435	1.346	1.464	1.356
μ [mm^{-1}]	0.117	0.112	0.101	0.115	0.095
T [K]	293(1)	293(1)	150(1)	200(1)	150(1)
Diffractometer	*Enraf Nonius CAD4*	*Enraf Nonius CAD4*	*Nonius Kappa CCD*	*Nonius Kappa CCD*	*Nonius Kappa CCD*
θ_{max} [°]	28.0	28.0	27.5	25.0	27.5
Total refl.	6483	6299	9643	5871	16357
Independent refl.	972	2617	5494	3142	4662
Observed refl.	884	1960	3387	2710	3091
Threshold criterion	$I_{net} > 2.5\sigma(I_{net})$	$I_{net} > 2.5\sigma(I_{net})$	$F^2 > 2.0\sigma(F^2)$	$F^2 > 2.0\sigma(F^2)$	$F^2 > 2.0\sigma(F^2)$
Final R and R_w	0.032, 0.033	0.048, 0.031	0.047, 0.053	0.036, 0.088	0.0532, 0.1393
$(\Delta/\sigma)_{max}$	0.0004	0.024	0.0002	0.0001	0.048
R_{int}	0.013	0.014	0.030	0.0181	0.0558
$\Delta\rho_{max}$, $\Delta\rho_{min}$ [e Å^{-3}]	0.187, −0.176	0.245, −0.321	0.507, −0.555	0.350, −0.167	0.316, −0.273

N(1)..O(4) contact distance is 2.876(2) Å and N(1)–H···O(4) angle is 176.8(1)°. The configuration about the C(5)=C(7) bond is *Z*. Molecules of **12**, **14**, and **16a** are chiral, but the corresponding solid-state compounds are racemates. The molecules of **18b** are twisted about the C(3)–C(30) and C(5)–C(11) bonds. An intramolecular contact of the N–H···O type with the N(12)..O(11) contact distance of 2.596(1) Å is present in these molecules. Bond lengths and angles of all five compounds are within expected ranges and in agreement with the values reported for related structures [26].

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