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Nitroimidazoles XVII. Nucleophilic Amination or Ring Transformation in Reactions of 1-Aryl-4-nitroimidazoles with 4-Amino-1,2,4-triazole or Hydroxylamine

Jerzy Suwiński* and Krzysztof Świerczek

Institute of Organic Chemistry and Technology
Silesian Technical University, 44-100 Gliwice, Poland

Tadeusz Głowiak

Institute of Chemistry, University of Wrocław
50-383 Wrocław, Poland

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Abstract: 1-aryl-4-nitroimidazoles under action of 4-amino-1,2,4-triazole in the presence of MeONa in DMSO undergo a vicarious nucleophilic substitution of hydrogen to give 5-amino-1-aryl-4-nitroimidazoles. If reacted with hydroxylamine in the presence of KOH or MeONa in methanol (but not in DMSO) 1-aryl-4-nitroimidazoles undergo a transformation to 4-acylamino-2-aryl-1-oxy-2H-1,2,3-triazoles but do not yield amination products.

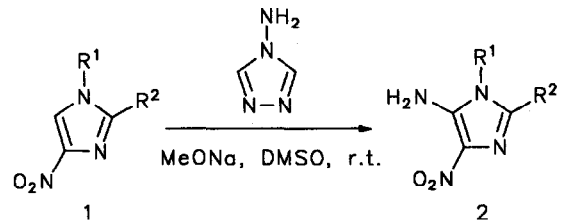
Recently, we have reported great differences in behavior of 2-methyl-4-nitro-1-phenylimidazole towards nucleophilic aminating reagents, hydroxylamine and 4-amino-1,2,4-triazole. This work is a continuation of our earlier communication[1].

In spite of rapid progress in the chemistry of nitroimidazoles during last thirty years[2], initiated by the isolation of a natural nitroimidazole-based antibiotic-azomycine[3] and followed by the discovery of a wide spectrum of biological activity of other nitroimidazoles[4], the state of knowledge on 1-aryl-4-nitroimidazoles is far from satisfactory . A short time ago, the only known compounds of this type were 4-nitro-1-phenylimidazoles containing nitro groups in the para and ortho positions of a benzene ring. These derivatives can be obtained by arylation of 4(5)-nitroimidazoles with the corresponding halogenonitrobenzenes[5].Recently, we have described a very convenient method for preparing a number of 1-aryl-4-nitroimidazoles from 1,4-dinitroimidazoles and aniline or its derivatives substituted in the benzene ring both with electron donor groups and some electron acceptor groups[6,7].Some heteroaromatic aminocompounds[8] can also be used in place of anilines. We have found that 1-aryl-4-nitroimidazoles are formed from 1,4-dinitroimidazoles and primary amines as a result of a transformation of the imidazole ring initiated by nucleophilic attack of the amine on carbon 5 in the imidazole derivative[9]. We have also found that 4-nitro-1-phenylimidazole can be obtained in a similar ANRORC reaction from 4-nitro-1-(p-toluenesulfonyl)imidazole and aniline[10].

The availability of 1-aryl-4-nitroimidazoles and the expected transformation of the imidazole ring by nucleophilic attack on these compounds have encouraged us to undertake systematic studies on reactions of 1-aryl-4-nitroimidazoles with electron donors. This work is the first in a series. It contains the results of our

studies on the reactions of some 1-aryl-4-nitroimidazoles with known nucleophilic aminating reagents such as 4-amino-1,2,4-triazole[11] and hydroxylamine[12] in the presence of strong bases.

From the reaction mixtures resulting from treatment of compound **1a-b** and **1i** (scheme 1) with 4-amino-



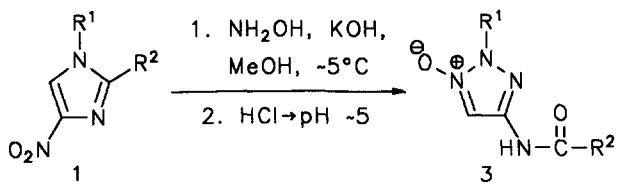
1 2

	R^1	R^2		Yield(%)
1a	phenyl	Me	**2a**	45
1b	4-methoxyphenyl	Me	**2b**	72
1c	3-chlorophenyl	Me	**2c**	0
1i	phenyl	H	**2i**	30

Scheme 1

1,2,4-triazole in the presence of MeONa in DMSO only the corresponding 5-amino-1-aryl-4-nitroimidazoles **2a-b** and **2i** were separated with moderate yields. Under similar conditions, compound **1c** was decomposed to products which were very soluble in water (in contrast to the very poorly soluble compounds **2**). The yields of **2** depend on the presence of substituents both in benzene and imidazole rings. Electron donating substituents in these rings seem to promote the amination reaction. This was rather unexpected in such a vicarious nucleophilic substitution of hydrogen in nitro aromatic compounds[13] ie. amination with 4-amino-1,2,4-triazole. It can be, however, explained by slower rates of competitive degradation reactions of the imidazole ring.

When allowed to react with hydroxylamine hydrochloride in methanol in the presence of excess KOH 1-aryl-4-nitroimidazoles **1a-k** (scheme 2) yielded no trace of amine derivatives of type **2**. The latter can be



1 3

	R^1	R^2		Yield(%)
1a	phenyl	Me	**3a**	56
1b	4-methoxyphenyl	Me	**3b**	52
1c	3-chlorophenyl	Me	**3c**	61
1d	3-methylphenyl	Me	**3d**	61
1e	4-nitrophenyl	Me	**3e**	~5
1f	4-(diethylamino)phenyl	Me	**3f**	0
1g	2-pirydyl	Me	**3g**	53
1h	3-pirydyl	Me	**3h**	57
1i	phenyl	H	**3i**	8
1j	4-methoxyphenyl	H	**3j**	6.5
1k	3-chlorophenyl	H	**3k**	33
1l	4-nitrophenyl	Cl	**3l**	0

Scheme 2

easily recognized by their colour and lack of solubility in reaction medium.Thus, 1-aryl-4-nitroimidazoles differ completely in behavior from 1-methyl-4-nitroimidazoles which react with hydroxylamine in alkaline alcoholic solution to give 5-amino-4-nitroimidazoles[14] in moderate yields.

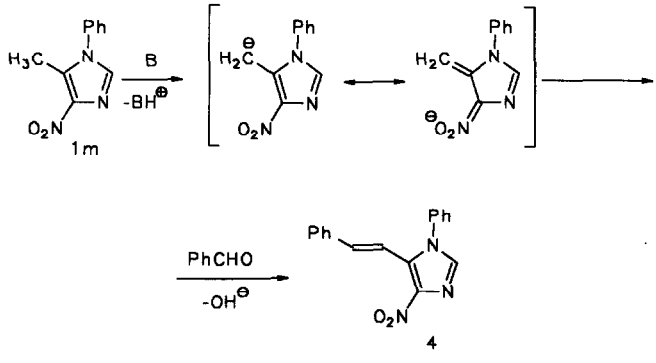
The solutions obtained after reaction of 1-aryl-4-nitroimidazoles with hydroxylamine were acidified to precipitate the reaction products. They were the products of imidazole ring transformation, isomeric with compounds of type **2**, namely,4-acylamino-2-aryl-1-oxy-2H-1,2,3-triazoles **3a-e** and **3g-k**. The reactions conditions were not optimised but yields ranged from 52 to 61%, except for compounds **1e** and **1f** containing very strongly electron donating (Et_2N) or withdrawing (NO_2) substituents in para position of a benzene ring. In these cases, the reaction either did not proceed at all or only with difficulty. Unidentified products were formed.

Replacement of 1-aryl-2-methyl-4-nitroimidazoles by derivatives **1i-k** containing a hydrogen atom instead of a methyl group in a position 2 resulted in a considerable drop in yields of transformation products **3i-k** and a remarkable difference in yields depending on a nature of substituent in a benzene ring. For example, 3'-chlorophenyl derivative **1k** produced **3k** with a yield four times greater than that of **3j** from the 4'-methoxy derivative **1j**.

Neither the transformation product **3l** nor possibly other derivatives of 1,2,3-triazole were obtained from 2-chloro-4-nitro-1-(4'-nitrophenyl)imidazole **1l** and hydroxylamine.

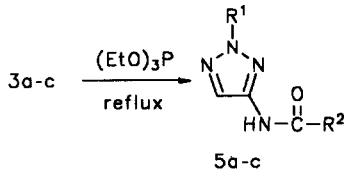
The reaction of **1a** with hydroxylamine was also carried out in anhydrous methanol in the presence of MeONa in great excess. This did not affect the yield of **3a** but the use of MeONa in quantity sufficient only to convert hydroxylamine hydrochloride to a free base resulted in the recovery of unchanged **1a**. This may indicate that a hydroxylammonium anion participates in reaction or a succesive step in the reaction is catalyzed by strong bases. The reaction of **1a** with hydroxylamine in methanol-KOH solution carried out in presence of p-anisidyne used in 10 times excess yielded only **3a**, the methoxy derivative **3b** was not detected in the post reaction mixture. This suggests an intramolecular character of the ring transformation reactions. It was also found that 5-amino-1-aryl-4-nitroimidazoles do not undergo a transformation into 4-acylamino-2-aryl-1-oxy-2H-1,2,3-triazoles on reaction with hydroxylamine. Therefore, compounds **2** are not intermediates in the formation of **3** from **1**. It should be noted that the attempts to synthesize **3a** from **1a** and hydroxylamine in DMSO in the presence of MeONa have failed. No formation of amination product **2a** was observed, only degradation products soluble in water were formed.

The reaction of 5-methyl-4-nitro-1-phenylimidazole **1m** with hydroxylamine and NaOMe gave an intractable mixture. It is possible that complications arise in this case due to deprotonation to give highly reactive carboanion.The formation of the latter was indirectly confirmed by a base catalyzed condensation of **1m** with benzaldehyde to 4-nitro-1-phenyl-5-styrylimidazole **4** (scheme 3).



Scheme 3

The structure of the products was examined by elementary analysis and spectroscopic determinations (MS, ^1H and ^{13}C NMR, IR, UV). The structure of **3a** was additionally proved by its reduction with boiling triethyl phosphite to a known 4-acetylamino-1-phenyl-2H-1,2,3-triazole **5a**[15]. Similarly, reduction of **3b-c** gave the corresponding triazoles **5b-c** with high yields (scheme 4). ^1H and ^{13}C NMR spectra of compounds **3a-c** and **5a-c** show some differences that can be used to determine the position of N-oxide group in products **3**. The C^5 - H



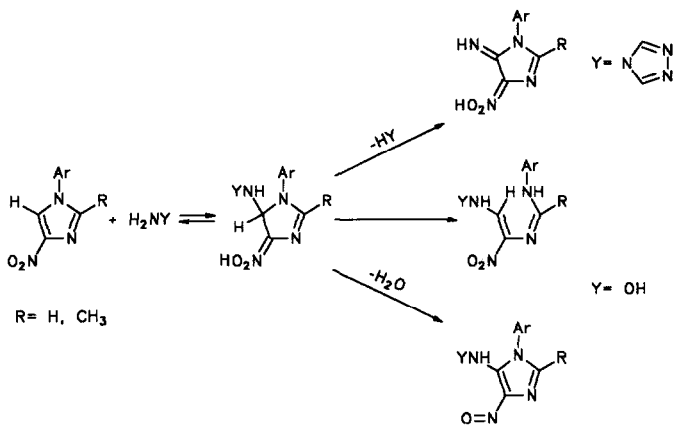
Scheme 4

proton signal in **5** is shifted towards lower field by approx. 0.2 ppm, whereas the C^5 carbon signal in the ^{13}C spectra is shifted by approx. 17 ppm. This suggests that the N-oxide group in compound **3** is present in the vicinity of the C-H group. Also, the fragmentation of **3a** based on HRMS data (scheme 5) is in agreement with the proposed structure. Finally, the structure of **3a** was confirmed by X-ray analysis (figure).

Crystallographic data are collected in table 1. The lengths of bonds and angles between them are presented in tables 2 and 3.

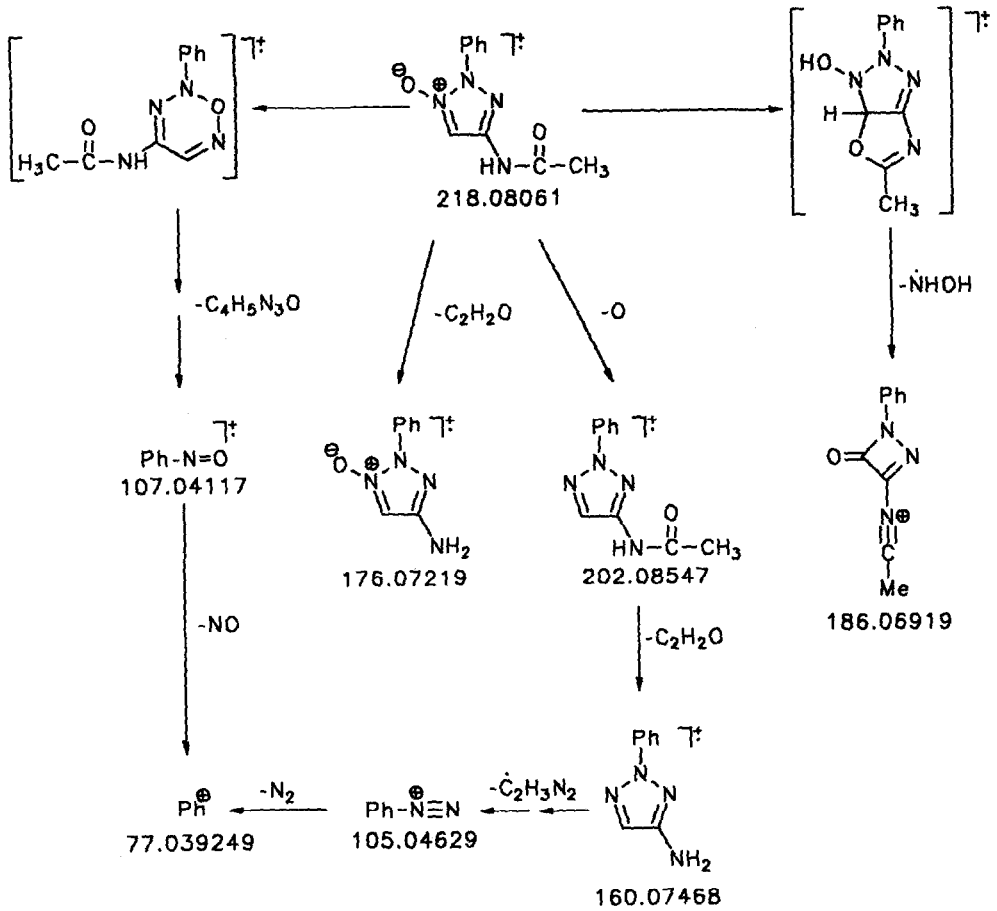
Comparision of the ^1H and ^{13}C NMR and UV spectra of **3a** and the remaining transformation products indicates that all the compounds **3** have the same 4-acylamino-2-aryl-1-oxy-2H-1,2,3-triazole structure. These compounds are acidic and dissolve in hydroxide solutions. The amide proton signal in the ^1H NMR spectra of these compounds is considerably shifted towards low field in comparison with signals of other N-substituted amides.

The mechanisms of amination of 1-aryl-4-nitroimidazoles with 4-amino-1,2,4-triazole and their transformation under action of hydroxylamine in the presence of bases have not been unequivocably established. The our submitted proposed mechanisms are mostly speculative, but based on literature data concerning a behavior of similar compounds[9,10,16,18]. It seems likely that in both cases the reaction commences with nitrogen deprotonation in aminating reagent (4-amino-1,2,4-triazole or hydroxylamine) and attack of the produced N-anion on position 5 of the 1-aryl-4-nitroimidazole. This results in the formation of a σ-adduct stabilized with nitro group present in a position 4 (scheme 6). A possible alternative nucleophilic attack on a carbon atom in

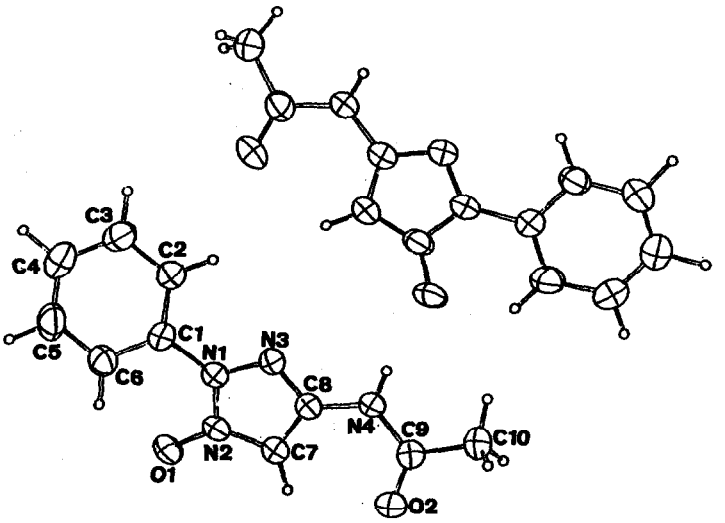


Scheme 6

position 2 is probably a cause of reduced yields of type **2** and **3** products from 1-aryl-4-nitroimidazoles having no methyl group in a position 2 of imidazole ring. Further reactions of σ-adduct are dependent on both the nucleofugicity of the substituent at the nitrogen atom of the aminating reagent and possible stabilization of an anion at a nitrogen 1 of imidazole ring. For simplification, the schemes 6 and 7 show neither the equilibria between inert molecules and relevant anions nor tautomerism.The importance of the substituent at N^1 is indicated by at least a different behavior of 1-aryl- and 1-methyl-4-nitroimidazole[14] in the presence of hydroxylamine and also an easy opening of imidazole ring in 1,4-dinitro-[9] and 1-(p-toluenesulfonyl)- 4-nitroimidazoles[10] under the



Scheme 5
Main fragmentation routes of compound **3a**



Figure

Table 1

Physical properties and parameters for data collection and refinement of compound **3a**

Formula	$C_{10}H_{10}N_4O_2$
Crystall dimensions	0.10x0.20x0.25 mm^3
Mol. wt.	218.22
Crystal system	Triclinic
Space group	$P\bar{1}$
a	8.720(2) Å
b	10.979(3) Å
c	11.272(3) Å
α	89.44(3)°
β	75.80(3)°
γ	84.29(3)°
V	1040.9(5) Å^3
Z	4
D_{cal}	1.392 g/cm^3
F (000)	456
$\mu(CuK_\alpha)$	8.59 cm^{-1}
Number of measured reflections	3028
Number of observed reflections	2491 [I>3σ(I)]
Number of variables	369
Agreement factors	
R	0.037
R_w	0.034
$w=1/\sigma^2(F)$	

Table 2

Bond Lengths (Å) in Compound **3a**

Bond	Length	Bond	Length
O(1)-N(2)	1.288(2)	C(1)-C(2)	1.379(3)
O(2)-C(9)	1.215(3)	C(1)-C(6)	1.389(3)
N(1)-N(2)	1.367(3)	C(2)-C(3)	1.381(4)
N(1)-N(3)	1.347(3)	C(3)-C(4)	1.385(4)
N(1)-C(1)	1.425(3)	C(4)-C(5)	1.380(4)
N(2)-C(7)	1.337(3)	C(5)-C(6)	1.387(4)
N(3)-C(8)	1.329(3)	C(7)-C(8)	1.387(3)
N(4)-C(8)	1.381(3)	C(9)-C(10)	1.495(4)
N(4)-C(9)	1.369(3)		

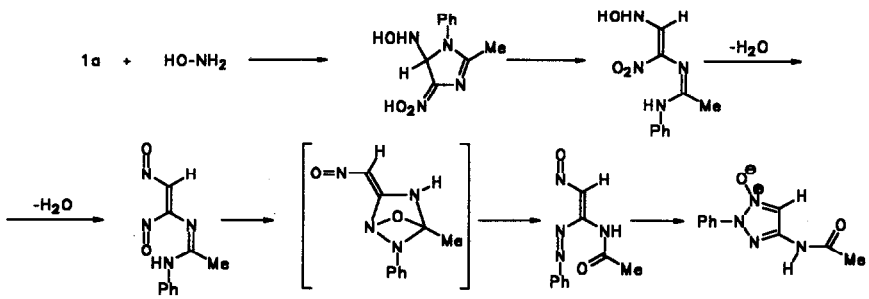
Table 3

Bond Angles (deg.) in Compound **3a**

Atoms	Bond	Atoms	Bond
C(1)-C(2)-C(3)	118.7(2)	N(1)-N(2)-C(7)	107.3(2)
C(2)-C(3)-C(4)	120.7(3)	O(1)-N(2)-C(7)	130.8(2)
C(3)-C(4)-C(5)	119.9(3)	N(2)-C(7)-C(8)	105.5(2)
C(4)-C(5)-C(6)	120.3(3)	C(7)-C(8)-N(3)	118.8(2)
C(5)-C(6)-C(1)	118.7(2)	C(7)-C(8)-N(4)	129.5(2)
C(6)-C(1)-C(2)	121.6(2)	C(8)-N(3)-N(1)	104.4(2)
C(6)-C(1)-N(1)	118.0(2)	C(8)-N(4)-C(9)	124.1(2)
C(2)-C(1)-N(1)	120.4(2)	N(4)-C(8)-N(3)	118.8(2)
C(1)-N(1)-N(2)	124.6(2)	N(4)-C(9)-O(2)	121.6(2)
C(1)-N(1)-N(3)	124.1(2)	N(4)-C(9)-C(10)	115.4(2)
N(2)-N(1)-N(3)	111.1(2)	O(2)-C(9)-C(10)	123.0(3)
N(1)-N(2)-O(1)	121.9(2)		

influence of the amines. Greater nucleofugicity of the 1,2,4-triazolium anion (pK_a triazole approx. 10) than that of hydroxyl anion (pK_a water approx. 15.5) may influence considerably a course of reaction by enhancing the amination with 4-amino-1,2,4-triazole. Examples of the reduction of the nitro group to a nitroso group in vicarious nucleophilic substitution of hydrogen[13], including amination with hydroxylamine[17], are also known. A few of 4-nitrosoimidazoles described (prepared by other methods) undergo a ring transformation[18] under influence of nucleophilic reagents.

Several alternative schemes for the transformation of 1-aryl-4-nitroimidazoles into 4-acetylamino-2-aryl-1-oxy-2H-1,2,3-triazoles under influence of hydroxylamine in strongly basic medium have been considered (however, it can not be excluded that products ere finally formed by acidification of a reaction mixture). Our proposal (scheme 7) involves a N^1- C^5 bond cleavage in an adduct **6** followed by an intramolecular disproportionation of hydroxylamine and nitro groups to yield a dinitrosocompound (being in an equilibrium with the furoxane derivative). In result of an intramolecular cycloaddition of NO to CN bond a bicyclic system is formed. Rings opening and recyclization yield in formation of **3**. This proposal seems to be in agreement with all our observations. In the literature[16], one can find analogies to most of reaction steps covered by this concept.



Scheme 7

EXPERIMENTAL:

The melting points were determined in open tubes. TLC was performed on plates with silica gel 60 F_{254}, developed with benzene-ethyl acetate (1:5) and observed under UV light. UV-VIS spectra were recorded on a Specord M40 spectrophotometer in methanol solution. ^1H and ^{13}C NMR on a Tesla BS-587 (80 and 20 MHz) spectrometer in DMSO-d_6 with TMS as the internal standard. Mass spectra were recorded on LKB-2091 or LKB-9000A instrument. Accurate mass measurements were carried out using a Finnigan 8200 spectrometer.

Crystal structure determination:

The diffraction data were collected with CuK_α radiation (=1.54178 Å) on a Syntex $P2_1$ four-circle diffractometer with graphite monochromator. The lattice parameters were obtained from the least-squares refinement of 25 reflections ($24.0° < 2\theta < 30.0°$). All diffraction data were collected at a room temperature (298 K) by the θ-2θ scanning technique to $2\theta_{max}=120.0°$. The collected crystallographic data and refinement procedure are given in table 3. Lorenz and polarization corrections were applied. Absorption corrections were not necessary. The structure was determined by a direct method and refined by a full-matrix least-squares technique. The non-hydrogen atoms were determined with anisotropic thermal parameters. The positions of all hydrogen atoms were determined with isotropic thermal parameters.

Preparation of 1-aryl-4-nitroimidazoles:

The method used for preparation of compound **1a-d**, **1f** and **1i-k** is described in Salwińska and Suwiński's work[6], and that of compounds **1g-h** in Suwiński and Szczepankiewicz's paper[8]. The compound **1e** was prepared by heating a sodium salt of 2-methyl-4(5)-nitroimidazole and 4-fluoronitrobenzene in DMF[5]. M.p. 188-188.5°C (lit.[5] 185-187°C).

2-Chloro-4-nitro-1-(4'-nitrophenyl)imidazole (1l): 2.5g (17 mmol) 2-chloro-4(5)-nitroimidazole was dissolved in MeONa solution prepared by dissolving 0.39g (17 mmol) sodium in 30 cm^3 methanol. Methanol excess was removed under reduced pressure. The prepared imidazolium salt and 2.4g (17 mmol) 4-fluoronitrobenzene were heated to boiling in 20 cm^3 DMF for 45 minutes. After cooling, the post-reaction mixture was poured into 200 cm^3 water with precipitation of a yellow sediment. After its filtering off, rinsing with water and drying crude product **1l** (2.3g , 50% theoretical yield) was obtained. Its crystallization from a DMF-methanol mixture yielded bright yellow plates m.p. 197.5 - 198°C. Found: C, 40.15; H, 1.80; N, 20.96. $C_9H_5N_4O_4Cl$ requires: C, 40.24; H, 1.86; N, 20.87. UV: λ_{max}=291 nm,ε_{max}=14100. ^{1}H NMR: 7.8-8.5 (m, 4H), 8.91 (s, 1H).

Amination of 1-aryl-4-nitroimidazoles:

5-Amino-2-methyl-4-nitro-1-phenylimidazole (2a) : a suspension of MeONa (2.8g, 52 mmol) in 30 cm^3 DMSO* was poured into a solution of **1a** (1g, 4.9 mmol) and 4-amino-1,2,4-triazole (2g, 24 mmol) in 10 cm^3 DMSO agitated at a room temperature. The prepared red suspension was stirred for 2 hours and then poured into 200 cm^3 saturated NH_4Cl solution. The precipitated sediment was filtered off, rinsed with water and dried. Crude **2a** (0.48g, 45% theoretical yield) was obtained. Its crystallization from a DMF-ethanol mixture yielded yellow crystals m.p. 260-263°C (with decomposition). Found C, 54.74; H, 4.67; N, 25.76. $C_{10}H_{10}N_4O_2$ requires: C, 55.04; H, 4.62; N, 25.68. UV: λ_{max}=365 nm,ε_{max}=15700. ^{1}H NMR: 1.97 (s, 3H), 7.25 (broad s, 2H), 7.4-7.6 (m, 5H). MS: 218 (M^+, 81), 202 (5), 186 (6), 172 (2), 171 (3), 170 (4), 160 (8), 159 (6), 158 (4), 146 (12), 145 (4), 144 (15), 143 (9), 129 (7), 119 (50), 118 (86), 103(7), 91(6), 83(7), 78(9), 77(100).

5-Amino-1-(4'-methoxyphenyl)-2-methyl-4-nitroimidazole (2b): following the procedure as described for **2a**, crude **2b** (0.93g, 72% theoretical yield) was obtained from **1b** (1.2g, 5.2 mmol). Its crystallization from DMF-ethanol mixture yielded yellow crystals m.p. about 250 °C (with decomposition). Found: C, 53.09; H, 4.88; N, 22.62. $C_{11}H_{12}N_4O_3$ requires: C, 53.22; H, 4.87; N, 22.57. UV: λ_{max}= 365 nm, ε_{max}=15400. ^{1}H NMR: 1.96 (s, 3H), 3.81 (s, 3H), 7.0-7.5 (m, 6H) including 7.20 (broad). MS: 248 (M^+, 100), 232 (4), 202 (2), 200 (4), 176 (41), 175 (9), 174 (11), 173 (6), 172 (7), 160 (19), 159 (35), 149 (76), 148 (93), 147 (7), 134 (7), 133 (17), 108 (6), 107 (15).

5-Amino-4-nitro-1-phenylimidazole (2i): following the procedure as described for **2a**,crude **2i** (0.32g, 30% theoretical yield) was obtained from **1i** (1g, 5.3 mmol). After its crystallization from a DMF-ethanol mixture, yellow crystals m.p. about 250°C (with decomposition) were obtained. Found: C, 52.62; H, 4.00; N, 27.48. $C_9H_8N_4O_2$ requires: C, 52.94; H, 3.95; N, 27.44. UV:λ_{max}=361 nm, ε_{max}=13400. MS: 204 (M^+, 100), 188 (4), 158 (4), 156 (4), 144 (4), 131 (6), 119 (37), 105 (5), 104 (55), 103 (4), 78 (7), 77 (82).

Ring transformation in 1-aryl-4-nitroimidazoles:

4-Acetylamino-1-oxy-2-phenyl-2H-1,2,3-triazole (3a): a solution of KOH (5g, 89 mmol) in 15 cm^3 methanol was added dropwise to a suspension of **1a** (1g, 4.9 mmol) and hydroxylammonium chloride (2.5g, 36 mmol) in 35 cm^3 methanol agitated at a temperature below 5°C. Then, the mixture was acidified with conc. HCl to pH about 5. Most methanol was removed from the preparated mixture under reduced pressure and 30 cm^3 water was added. Crude **3a** (0.61g, 56% theoretical yield) was filtered off and then crystallized from a water-methanol mixture obtaining glossy needles m.p. 183°C. Found: C, 55.02; H, 5.24; N, 25.40; M^+, 218.08061. $C_{10}H_{10}N_4O_2$ requires: C, 55.04; H, 4.62; N, 25.68; M^+, 218.08037. UV: λ_{max}=285 nm, ε_{max}=10400. IR (KBr): 3260, 3170, 2920, 2810, 2780, 1680, 1560, 1520, 1260 cm^{-1}. ^{1}H NMR (DMSO-d_6, 80 MHz): 2.08 (s, 3H), 7.4-7.8 (m, 5H), 7.90 (s, 1H), 11.08 (broad s, 1H). ^{13}C NMR (DMSO-d_6, 20 MHz): 22.7 (q, 1C), 109.8 (d, 1C), 122.6 (d, 2C), 128.3 (d, 1C), 128.6 (d, 2C), 133.9 (s, 1C), 141.3 (s, 1C), 167.7 (s, 1C). MS m/z: 218 (M^+, 44), 202 (4), 186 (12), 176 (58), 161 (5), 160 (10), 159 (7), 158 (6), 133 (5),117 (7), 107 (17), 105 (21), 91 (14), 77 (100), 71 (16), 65 (5), 64 (4), 51 (17), 43 (74), 30 (2), 28 (5), 15 (4). HRMS (m/z, formula, Δ ppm): 218.08061, $C_{10}H_{10}N_4O_2$, 1.1; 202.08547, $C_{10}H_{10}N_4O$, ~0; 186.06919, $C_{10}H_8N_3O$, 13.2; 176.07219, $C_8H_8N_4O$, 13.5; 160.07468, $C_8H_8N_4$, 1.3; 107.04117, C_6H_5NO, 37.9; 105.04629, $C_6H_5N_2$, 9.7; 91.044763, C_6H_5N, 20.8; 77.039249, C_6H_5, 1.6; 71.024709, $C_2H_3N_2O$, 2.4.

* DMSO produced by REACHIM (USSR)

4-Acetylamino-2-(4'-methoxyphenyl)-1-oxy-2H-1,2,3-triazole (3b): following the procedure as described for **3a** (except, this the reaction mixture was agitated for 4 hours after addition of KOH), crude **3b** (0.66g, 52% theoretical yield) was obtained from **1b** (1.2g, 5.2 mmol). The crude product was crystallized from a water-methanol mixture yielding bright green needles m.p. 183-183.5°C. Found: C, 53.15; H, 4.79; N, 22.67. $C_{11}H_{12}N_4O_3$ requires: C, 53.22; H, 4.87; N, 22.57. UV: λ_{max}= 289 nm, ε_{max}=12200. ^{1}H NMR: 2.07 (s, 3H), 3.80 (s, 3H), 7.0-7.7 (m, 4H), 7.84 (s, 1H), 11.03 (broad s, 1H). ^{13}C NMR: 22.7, 55.3, 108.6, 113.8, 124.9, 141.0, 158.9, 167.7. MS: 248 (M^+, 25), 232 (1), 216 (15), 206 (25), 191 (11), 190 (5), 189 (13), 163 (3), 162 (5), 147 (18), 111 (33), 113 (36), 122 (22), 121 (30), 108 (11), 107 (100).

4-Acetylamino-2-(3'-chlorophenyl)-1-oxy-2H-1,2,3-triazole (3c): a solution of KOH (50g, 890 mmol) in 100 cm^3 methanol was added dropwise to a suspension of **1c** (11.9g, 50 mmol) and hydroxylammonium chloride (25g, 360 mmol) in 150 cm^3 methanol agitated at a temperature kept below 5°C. After KOH dropping, stirring was continued at this temperature for 2 hours. Then, the mixture was acidified with about 40 cm^3 concentrated HCl to pH about 5. After cooling, the sediment was filtered off, rinsed with water and dried yielding mixture of products (10.3g). It was then crystallized from a DMF-acetone mixture obtaining unidentified very sparingly soluble substance (2.5g) and **3c** (7.7g, 61% theoretical yield) in a form of white needles m.p. 238.5-239°C. Found: C, 47.15; H, 3.52; N, 22.23. $C_{10}H_9N_4O_2Cl$ requires: C, 47.54; H, 3.59 ; N, 22.18. UV: λ_{max}= 292 nm, ε_{max}=11500. ^{1}H NMR: 2.08 (s, 3H), 7.4-7.9 (m, 4H), 7.94 (s, 1H), 11.11 (broad s, 1H). ^{13}C NMR: 22.7, 109.4, 120.6, 121.7, 127.9, 130.3, 132.7, 134.8, 141.6, 167.7. MS: 252 (M^+, 11), 236 (1), 220 (5), 210 (33), 195 (6), 194 (8), 193 (6), 166 (5), 151 (4), 141 (21), 139 (19), 125 (9), 112 (13), 111 (100).

4-Acetylamino-2-(3'-methylphenyl)-1-oxy-2H-1,2,3-triazole (3d): following the procedure as described for **3a** (except, a reaction mixture was agitated for 4 hours after addition of KOH), crude **3d** (0.72g, 61% theoretical yield) was obtained from **1d** (1.1g, 5.1 mmol). The crude product was crystallized from a water-methanol mixture yielding glossy crystals m.p. 197-198°C. Found: C, 56.51; H, 5.22; N, 24.16. $C_{11}H_{12}N_4O_2$ requires: C, 56.89; H, 5.21; N, 24.12. UV: λ_{max}= 284 nm, ε_{max}=10300. ^{1}H NMR: 2.07 (s, 3H), 2.37 (s, 3H), 7.2-7.7 (m, 4H), 7.87 (s, 1H), 11.03 (broad s, 1H). ^{13}C NMR: 20.8, 22.7, 109.0, 119.7, 122.7, 122.9, 128.4, 128.9, 133.2, 138.2, 141.2, 167.7. MS: 232 (M^+, 13), 216 (1), 200 (5), 190 (14), 175 (3), 174 (4), 173 (9), 146 (3), 131 (5), 121 (13), 119 (12), 105 (5), 92 (11), 91 (100).

4-Acetylamino-2-(4'-nitrophenyl)-1-oxy-2H-1,2,3-triazole (3e): a solution of KOH (5g, 89 mmol) in 15 cm^3 methanol was added to a suspension of **1e** (1.24g, 5 mmol) and hydroxylammonium chloride (2,5g, 36 mmol) in 35 cm^3 methanol agitated at a temperature kept below 10°C. After KOH dropping, stirring was continued for one hour at a room temperature. Then, the mixture was acidified with about 6 cm^3 concentrated HCl to pH about 5. After cooling, the sediment was filtered off, rinsed with water and dried yielding mixture of products (1.13g). Unidentified, very sparingly soluble substance (0.09g, m.p.>360°C) was separated by extraction with boiling DMF. A fraction soluble in DMF consisted two compounds (TLC). Yellow small needles **3e** (0.06g, 4.6 % theoretical yield) were separated by crystallization several times from DMF. We were not able to separate a second component from the soluble fraction.M.p. 261-265°C (with decomposition). Found: C, 45.47; H, 3.36; N, 26.53. $C_{10}H_9N_5O_4$ requires: C, 45.63; H, 3.45; N, 26.61. UV: λ_{max}= 327 nm, ε_{max}=13300. ^{1}H NMR: 2.09 (s, 3H), 8.03 (s, 1H), 8.1-8.5 (m, 4H), 11.21 (broad s, 1H). ^{13}C NMR: 22.7, 110.1, 121.4, 124.3, 138.5, 142.2, 145.3, 167.9. MS: 263 (M^+, 22), 231 (12), 221 (95), 206 (5), 205 (6), 204 (5), 178 (3), 177 (4), 175 (28), 152 (29), 150 (27), 136 (8), 123 (29), 122 (100).

4-Acetylamino-1-oxy-2-(2'-pyridyl)-2H-1,2,3-triazole (3g): following the procedure as described for **3a** (except, keeping a temperature below 10°C when KOH was dropped in and continued by agitation of reaction mixture for one hour at a room temperature), crude **3g** (0.53g, 53% theoretical yield) was obtained from **1g** (0.94g, 4.6 mmol). The crude product was crystallized from methanol yielding white crystals m.p. 218-221°C. Found: C, 49.04; H, 4.05; N, 32.12. $C_9H_9N_5O_2$ requires: C, 49.31; H, 4.14; N, 31.95. UV: λ_{max}= nm, ε_{max}=. ^{1}H NMR: 2.08 (s, 3H), 7.4-7.6 (m, 1H), 7.8-8.2 (m, 3H) including 7.94 (s), 8.5-8.7 (m, 1H), 11.18 (broad s, 1H). MS: 219 (M^+, 5), 203 (0.4), 177 (2), 161 (3), 134 (100), 108 (4), 92 (2), 79 (42), 78 (50).

4-Acetylamino-1-oxy-2-(3'-pyridyl)-2H-1,2,3-triazole (3h) : following the procedure as described for **3a**

(except, after KOH dropping in, a reaction mixture was agitated for 2 hours), crude **3h** (0.61g, 57% theoretical yield) was obtained from **1h** (1g, 4.9 mmol). The crude product was crystallized from DMF yielding glossy needles m.p. 262-265°C (with decomposition). Found: C, 49.24; H, 4.10; N, 32.10. $C_9H_9N_5O_2$ requires: C, 49.31; H, 4.14; N, 31.95. UV: λ_{max}=295 nm, ε_{max}=11200. ^{1}H NMR: 2.08 (s, 3H), 7.4-7.7 (m, 1H), 7.96 (s, 1H),8.1-8.3 (m, 1H), 8.5-8.7 (m, 1H), 8.8-9.0 (m, 1H), 11.13 (broad s, 1H). MS: 219 (M^+, 17), 203 (0.7), 187 (12), 177 (53), 162 (1), 161 (5), 160 (3), 147 (39), 134 (5), 133 (1), 108 (12), 106 (7), 92 (12), 79 (52), 78 (100).

4-Formylamino-1-oxy-2-phenyl-2H-1,2,3-triazole (3i): following the procedure as described for **3c**, crude **3i** (0.8g, 8% theoretical yield) was obtained from **1i** (9.45g, 50 mmol). The crude product was crystallized from methanol yielding glossy crystals m.p. 211°C (with decomposition). Found: C, 52.69; H, 3.89; N, 27.57. $C_9H_8N_4O_2$ requires: C, 52.94; H, 3.95; N, 27.44.. UV: λ_{max}=283 nm, ε_{max}=10500. ^{1}H NMR: 7.4-7.9 (m, 5H), 7.96 (s, 1H), 8.29 (d, 1.2 Hz, 1H), 11.18 (broad s, 1H). ^{13}C NMR: 109.1, 122.7, 128.4, 128.5, 133.8, 140.1, 158.9. MS: 204 (M^+, 16`), 188 (0.4), 187 (0.8), 176 (10), 172 (2), 161 (2), 160 (1), 159 (2), 146 (1), 133 (1), 132 (2), 117 (3), 107 (8), 105 (9), 92 (4), 91 (16), 78 (9), 77 (100).

4-Formylamino-2-(4'-methoxyphenyl)-1-oxy-2H-1,2,3-triazole (3j): following the procedure as described for **3c** (except, agitation of a reaction mixture for 24 hours to increase gradually a temperature to 15°C after KOH dropping in), crude **3j** (0.75g, 6.5% theoretical yield) was obtained from **1j** (10.95g, 50 mmol). The crude product was crystallized from methanol yielding glossy crystals m.p. 195.5-196.5°C). Found: C, 50.98; H, 4.31; N, 23.95. $C_{10}H_{10}N_4O_3$ requires: C, 51.28; H, 4.30; N, 23.92.. UV: λ_{max}=290 nm, ε_{max}=11100. ^{1}H NMR: 3.80 (s, 3H), 7.0-7.8 (m, 4H), 7.91 (s, 1H), 8.28 (d, 1.4 Hz, 1H), 11.24 (broad s, 1H). ^{13}C NMR: 55.3, 108.7, 113.8, 125.1, 126.6, 139.5, 158.8, 158.9. MS: 234 (M^+, 51), 218 (3), 217 (4), 206 (28), 202 (8), 191 (23), 190 (5), 189 (14), 176 (4),163 (3), 162 (8), 147 (34), 137 (38), 135 (37), 134 (17), 122 (32), 121 (61), 108 (12), 107 (100).

2-(3'-chlorophenyl)-4-formylamino-1-oxy-2H-1,2,3-triazole (3k): following the procedure as described for **3c** (except, agitation for 1.5 hour after KOH dropping in), crude **3k** (3.9g, 33% theoretical yield) was obtained from **1k** (11.2g, 50 mmol). The crude product was crystallized from a DMF-acetone mixture yielding white crystals m.p. 250°C (with decomposition).. Found: C, 45.03; H, 2.85; N, 23.56. $C_9H_7N_4O_2Cl$ requires: C, 45.30; H, 2.96; N, 23.48.. UV: λ_{max}=288 nm, ε_{max}=11000. ^{1}H NMR: 7.5-7.8 (m, 4H), 8.00 (s, 1H), 8.30 (s, 1H), 11.35 (broad s, 1H). MS: 238 (M^+, 11), 222 (2), 221 (1), 210 (8), 206 (2), 195 (3), 194 (3), 193 (4), 180 (2), 167 (2), 166 (3), 151 (2), 141 (13), 139 (9), 125 (14), 112 (9), 111 (100).

Reduction of 4-acetylamino-2-aryl-1-oxy-2H-1,2,3-triazoles:

4-Acetylamino-2-phenyl-2H-1,2,3-triazole (5a): 3a (1.1g, 5 mmol) and triethyl phosphite (4.2 cm^3, 4g, 24 mmol) were heated up to a mild boiling under nitrogen for 4 hours. After cooling, the reaction mixture was poured into 50 cm^3 water. The precipitated sediment was rinsed with water and dried yielding crude **5a** (0.89g, 88% theoretical yield). The crude product was crystallized from a water-methanol mixture obtaining white needles m.p. 169-170°C (lit.[15]: 166°). Found: C, 58.96; H, 5.04; N, 27.87. $C_{10}H_{10}N_4O$ requires: C, 59.40; H, 4.98; N, 27.71.. UV: λ_{max}=282 nm, ε_{max}=22900. ^{1}H NMR: 2.08 (s, 3H), 7.3-7.9 (m, 5H), 8.13 (s, 1H), 11.03 (broad s, 1H). ^{13}C NMR: 22.9, 117.7, 127.1, 129.6, 139.2, 146.2, 168.3. MS: 202 (M^+, 33), 161 (9), 160 (100), 133 (12), 105 (5), 92 (3), 91 (30), 77 (40).

4-Acetylamino-2-(4'-methoxyphenyl)-2H-1,2,3-triazole (5b): Following the procedure as described for **5a** crude **5b** (0.39g, 69% theoretical yield) was obtained from **3b** (0.6g, 2.4 mmol) and triethyl phosphite (2.1 cm^3, 2g, 12 mmol). The crude product was crystallized from a water-methanol mixture obtaining white crystals m.p. 180-181.5°C. Found: C, 56.33; H, 5.24; N, 23.95. $C_{11}H_{12}N_4O_2$ requires: C, 56.89; H, 5.21; N, 24.12.. UV: λ_{max}=290 nm, ε_{max}=23400. ^{1}H NMR: 2.06 (s, 3H), 3.76 (s, 3H), 6.9-7.8 (m, 4H), 8.04 (s, 1H), 10.94 (broad s, 1H). ^{13}C NMR: 22.8, 55.4, 114.7, 119.2, 126.2, 132.8, 145.7, 158.3, 168.4. MS: 232 (M^+, 48), 191 (10), 190 (100), 175 (29), 135 (8), 122 (26), 121 (93), 107 (28).

4-Acetylamino-2-(3'-chlorophenyl)-2H-1,2,3-triazole (5c): Following the procedure asdescribed for **5a** (3 cm^3 DMF was additionally used as a solvent) crude **5c** (1.2g, 99% theoretical yield) was obtained from **3c** (1.3g, 5.1

mmol) . The crude product was crystallized from a DMF-methanol mixture obtaining white crystals m.p. 198-202°C. Found: C, 49.63; H, 3.69; N, 23.39. $C_{10}H_9N_4OCl$ requires: C, 50.75; H, 3.83; N, 23.67. UV: λ_{max}=288 nm, ε_{max}=19900. ^{1}H NMR: 2.09 (s, 3H), 7.3-7.9 (m, 4H), 8.17 (s, 1H), 11.12 (broad s, 1H).

Condensation of 5-methyl-4-nitro-1-phenylimidazole with benzaldehyde:

4-Nitro-1-phenyl-5-styryloimidazole (4): 1m (0.5g, 2.5 mmol) and benzaldehyde (2 cm^3, 2.1g, 20 mmol) and 0.2 cm^3 piperidine were heated for 3.5 hours at a temperature of 140 to 150°C. The cooled reaction mixture was poured into 30 cm^3 diethyl ether. The precipitate was filtered off and rinsed with diethyl ether yielding crude 4 (0.1g, 14% theoretical yield. The latter was crystallized from methanol and obtained needles m.p. 197-199.5°C. Found: C, 69.90; H, 4.49; N, 14.37. $C_{17}H_{13}N_3O_2$ requires: C, 70.11; H, 4.46; N, 14.43. UV: λ_{max1}=272 nm, ε_{max1}=21100; λ_{max2}=361 nm, ε_{max2}=13000. ^{1}H NMR: 6.54 (d, 16.8 Hz, 1H), 7.27 (s, 5H), 7.31 (d, 16.8 Hz, 1H), 7.56 (s, 5H), 8.06 (s, 1H).

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REFERENCES:

1. Suwiński, J.; Świerczek, K.; Głowiak, T. *Tetrahedron Lett.* **1992**, *33*, 7941
2. Nair, M.D.; Nagarajan, K. *Progress in Drug Research* vol. 27, p. 163, (ed. Jucker, E.), Birkhauser Verlag Basel, 1983
3. Nakamura, S. *Pharm. Bull.***1955**, *3*, 379
4. *Nitroimidazoles* (ed. Breccia, A., Cavalleri, B. , Adams, G.E.) NATO Adv. Study Inst., series A, vol. 42, Plenum Press, New York, 1982
5. Klink, R.; Hepding, L. *British patent* 1133408, **1968**, in *Chem. Abstr.* **1968**, *70*, P 47456
6. Salwińska, E.; Suwiński, J. *Polish J. Chem.* **1990**, *64*, 813
7. Suwiński, J.; Szczepankiewicz, W.; Wideł, M. *Archiv Pharm (Weinheim)*,**1992**, *325*, 317
8. Suwiński, J.; Szczepankiewicz, W. *Polish J. Chem.* **1991**, *65*, 515
9. Llempen, H.; Salwińska, E.; Suwiński J.; Szczepankiewicz, W. *Polish J. chem.***1992**, *66*, 943
10. Salwińska, E.; Suwiński, J. *Polish J. Chem.* **1992**, *66*, 1623
11. Katritzky, A.R.; Laurenzo, K.S. *J. Org. Chem.* **1988**, *53*, 3978
12. Angeli, A.; Angelico, F. *Gazz. Chim. Ital.* **1901**, *31*, 27
13. Mąkosza, M. *Usp. Khim.* **1989**, *58*, 1298
14. Sunjić, V.; Fajdiga, T.; Japelj, M.; Rems, P. *J. Heterocyclic Chem.* **1969**, *6*, 53
15. Thiele, Shleussner *Ann.*, **1897**, *295*, 156 in *Beilstein* H XXVI, 135
16. *Comprehensive Heterocyclic Chemistry* (ed. Katritzky, A.R., Rees, C.W.) vol. 5, Pergamon Press, Oxford 1984
17. Nasielski-Hinkens, R.; Fancon F.; Owen, J.P. *Bull. Soc. Chim. Belg* .**1984**, *93*, 953
18. Cavalleri, B.; Bellani, P.; Lancini, G. *J. Heterocyclic Chem.* **1973**, *10*, 357