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Mendeleev Commun., 1993, **3**(**5**), 213–214

Mendeleev Communications

Reaction of 6-Nitro-1,2,4-triazolo[1,5-*a*]pyrimidines with Benzylamine: an Unusual Synthesis of 1-Hydroxyimidazoles

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Heating of 5-methyl-6-nitro-7-(*p*-*N*,*N*-dimethylaminophenyl)-1,2,4-triazolo[1,5-*a*]pyrimidines with benzylamine in ethanol or DMF leads to 1-hydroxy-2-phenyl-4-methyl-5-benzylimino(*p*-*N*,*N*-dimethylaminophenyl)methylidinoimidazole.

Intramolecular condensations of nitroarenes containing *ortho*-substituents find useful applications in the synthesis of a variety of heterocycles.[1] Under severe conditions base-catalysed cyclization of *N*-benzyl-*o*-nitroanilines leads to the formation of benzimidazole *N*-oxides.[2] A similar reaction for *ortho*-substituted nitroazines has been reported. Thus, 5-nitro-6-amino-substituted uracils afforded 7-hydroxyxanthene derivatives.[3] We have found that the formation of heterocyclic systems *via* the above-mentioned condensation is possible by interaction of nitroheteroarenes with benzylamine without preliminary attachment of the benzylamino fragment of the *ortho*-position. Moreover, the presence of substituents on the *ortho*-positions does not hinder the reaction.

On heating derivatives of 5-methyl-6-nitro-7-(*p*-*N*,*N*-dimethylaminophenyl)-1,2,4-triazolo[1,5-*a*]pyrimidine **1**[4] with an excess of benzylamine in ethanol or DMF, 1-hydroxy-2-phenyl-4-methyl-5-benzylimino(*p*-*N*,*N*-dimethylaminophenyl)methyli-dinoimidazole **2** was obtained, Scheme 1.†

An X-ray structural analysis of compound **2** (Fig. 1) showed that the characteristic feature of this molecule is the *cis* configuration of the aryl and benzyl groups with respect to the imine bond C(4)–N(3) stabilized by the intramolecular hydrogen bond O(1)-H ··· N(3) [O(1) ··· N(3) 2.53 Å]. The fragment formed by the atoms O(1)N(1)C(3)C(4)N(3) is almost planar and forms an angle of 4.5 ° with the plane of the five-membered heterocycle; with the plane of the aryl C(5)–C(10) and phenyl C(14)–C(19) groups this angle is 105.9 ° and 77.5 °, respectively. Torsion of the phenyl group–C(21)–C(26) around the C(1)–C(21) bond–is not large (9.1 °). The torsional angle C(4)N(3)C(13)C(14) is −114.8 °.

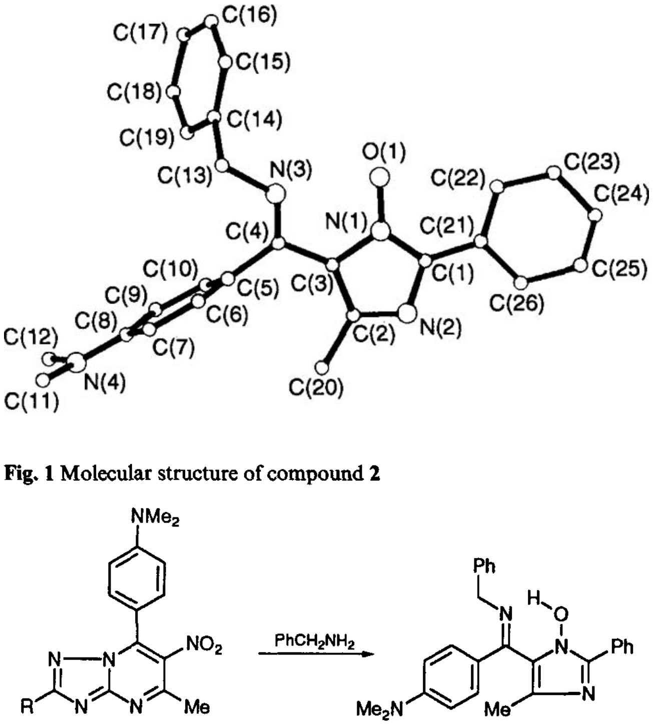
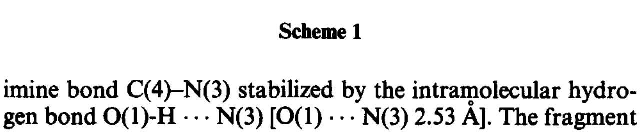


Fig. 1 Molecular structure of compound **2**



1a R = H
b R = CF$_3$

2

Scheme 1

The nature of substituents R in the azole ring greatly influences the course of the reaction: refluxing the reagents in

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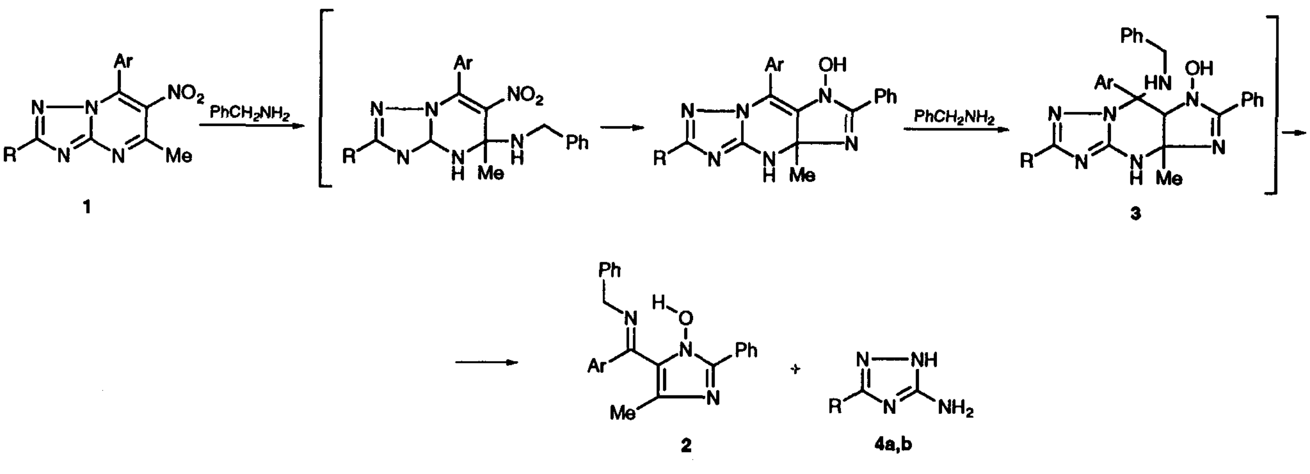
† *Experimental procedure and selected spectroscopic data* for 1-hydroxy-2-phenyl-4-methyl-5-benzylimino(*p*-*N*,*N*-dimethylaminophenyl)-methylidinoimidazole **2**: a solution of 2-trifluoromethyl-5-methyl-6-nitro-7-(*p*-*N*,*N*-dimethylaminophenyl)-1,2,4-triazolo[1,5-*a*]pyrimidine **1b** (0.73 g, 2 mmol) and benzylamine (4.5 ml, 40 mmol) in ethanol (400 ml) was refluxed for 4 h, then ethanol and benzylamine were evaporated under reduced pressure. The residue was dissolved in acetone (20 ml) and the solution was cooled to −15 °C to yield yellow crystals which were isolated and recrystallizd from ethanol (0.87 g, 31%), m.p. 197–199 °C.

^{1}H NMR ([^{2}H$_6$]DMSO) δ 1.62 (s, 3H, Me), 3.04 [s, 6H, NMe$_2$], 4.61 (s, 2H, NCH$_2$), 6.88 (d, 2H 3,5-H in Ar), 7.20–7.58 (m, 10H, 2 × Ph), 8.42–8.50 (m, 2H, 2,6-H in Ar); MS *m*/*z* 410 (M$^+$, 18%), 393 (100), 248 (12), 105 (17) 104 (12), 91 (79) 77 (20), 65 (14); IR, ν/cm^{-1} 3460, 2910–2800, 1600, 1480, 1370, 1130, 680.

Crystal data for **2**: $C_{26}H_{26}N_4 \cdot H_2O$, triclinic, space group *P*1, $a = 12.057(1)$ Å, $b = 9.694(1)$ Å, $c = 10.970(1)$ Å, $\alpha = 85.96(1)°$, $\beta = 62.84\,(1)°$, $\gamma = 82.76(1)°$, $V = 1131.6(3)$ Å^3, $Z = 2$. Experimental data were measured on a Syntex PI diffractometer (λMoK$_\alpha$, graphite monochromator θ-2θ scan, $3 < 2\theta < 47°$). The structure was solved by a direct method and refined by full-matrix least-squares in the anisotropic approximation to $R = 0.121$ ($R_w = 0.122$) for 1400 independent reflections with $F^2 > 3\alpha$. Tables of bond lengths, bond angles and atomic coordinates have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Notice to Authors, *Mendeleev Commun.*, 1993, issue 1.



Scheme 2

DMF or DMSO is absolutely necessary to convert the compound **1a** (R = H) into **2**, whereas introduction of a strong electron withdrawing substituent (**1b**; R = CF_3) into the azole ring allows one to carry out the reaction in ethanol.

One plausible mechanism of the reaction involves the following sequence: the addition of benzylamine at the C-5 position of nitrotriazolopyrimidine **1** and reductive condensation of the added benzylamine fragment with the nitro group followed by the addition of one more benzylamine molecule at the C-7 position. Destruction of the pyrimidine ring in the proposed intermediates **3** should result in the formation of 1-hydroxyimidazoles **2** and aminotriazoles **4a,b**, Scheme 2. Attempts to isolate the compounds **4** have failed, however such cleavage of the pyrimidine ring appears to be a characteristic feature of the partially-hydrogenated nitrotriazolopyrimidine system.[5] Indeed, the related diadducts derived from the addition of nucleophiles at the C-5 and C-7 positions of 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidines have always transformed into amino-1,2,4-triazoles.[6,7] The discovery of this unusual transformation seems to be even more interesting because of the absence of a general approach to the synthesis of imidazole systems.

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Received: Moscow, 25th February 1993
Cambridge, 1st April 1993; Com. 3/01158E