3*H*-1,3,4-Benzotriazepines from (*N*-Arylbenzimidoyl)-5-dimethylaminotetrazoles: 1,7- *vs.* 1,5-Cyclisation of Extended Dipolar Nitrile Imines

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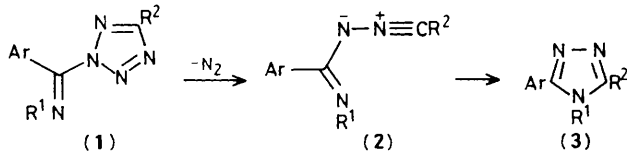
Thermolysis of both 1- and 2-*N*-arylbenzimidoyl-5-dimethylaminotetrazoles [(**7**) or (**8**)] generates nitrile imines (**9**), which cyclise to yield either 1,2,4-triazoles (**10**) or 3*H*-1,3,4-benzotriazepines (**12**), depending on the nature of the *N*-aryl group and on conditions.

The formation of five-membered rings by 6π-electrocyclisation of 1,5-dipoles is an important principle in heterocyclic chemistry.[1] A classical example of such a reaction is the synthesis of 1,2,4-triazoles (**3**) by heating imidoyl chlorides with tetrazoles in pyridine, reported by Huisgen, Sauer, and Seidel.[2] The authors proposed that 2-imidoyltetrazoles (**1**) are formed initially; loss of nitrogen generates the imino-nitrile imines (**2**), which undergo ring-closure (Scheme 1). We have found that in the case of certain dimethylamino-nitrile imines (**2**; R^1 = Ar, R^2 = NMe_2) the 1,5-electrocyclisation is suppressed in favour of a 1,7-cyclisation at the *N*-aryl group.

Two series of 1- and 2-*N*-arylbenzimidoyl-5-dimethylamino-tetrazoles were prepared. The 1-imidoyltetrazoles were obtained as follows: treatment of the secondary amides (**4**) with dimethylcyanamide in the presence of phosphorus oxychloride, followed by perchloric acid, gave 1-chloro-1-dimethylamino-2,4-diazabuta-1,3-dienylium salts (**5**),[3] which reacted with aqueous sodium azide to yield the azido-perchlorates (**6**). The latter lost the elements of perchloric acid by the action of sodium hydroxide to form the 1-imidoyltetrazoles (**7**); addition of perchloric acid regenerated the azides (**6**) (Scheme 2). Thus, 2',6'-dimethylbenzanilide (**4a**) gave the perchlorate (**5a**) (60%), m.p. 196.5—198 °C,† and thence the azide (**6a**) (91%), m.p. 117 °C (decomp.),† $\nu_{max.}$ 3260 (NH) and 2140 (N_3) cm^{-1}, and the tetrazole (**7a**) (97%), m.p. 118.5 °C (decomp.),† $\nu_{max.}$ 1635 cm^{-1}. The structure of (**7a**) was confirmed by *X*-ray analysis.‡ The geometry of the five-membered ring resembles that of other tetrazoles;[4] thus, the ring is planar within experimental error and the N(2)–N(3) linkage has predominantly double-bond character. The salts (**5b**), m.p. 189—191 °C,† and (**5c**), m.p. 201—202 °C,† similarly afforded the 1-imidoyltetrazoles (**7b**), m.p. 120 °C (decomp.),† and (**7c**), m.p. 130 °C (decomp.),† respectively, in almost quantitative yields.

The 2-imidoyltetrazoles (**8a—f**), m.p. (decomp.) 89, 124, 134, 124, 157, and 106 °C,† respectively, were obtained in 80—90% yields by treating 5-dimethylaminotetrazole[5] with the appropriate imidoyl chloride in ice-cold pyridine. 5-Dimethylamino-1-(*N*-2,6-dimethylphenylbenzimidoyl)tetrazole (**7a**) decomposed in boiling xylene to give the 1,2,4-triazole (**10a**) (29%), m.p. 171—172 °C;† this compound was produced in 85% yield when the isomer (**8a**) was heated. We

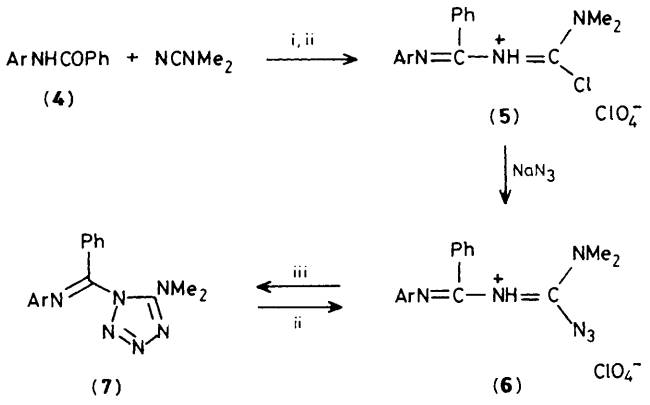


R^1 = Ar or Me, R^2 = Ar or Pr^i

Scheme 1

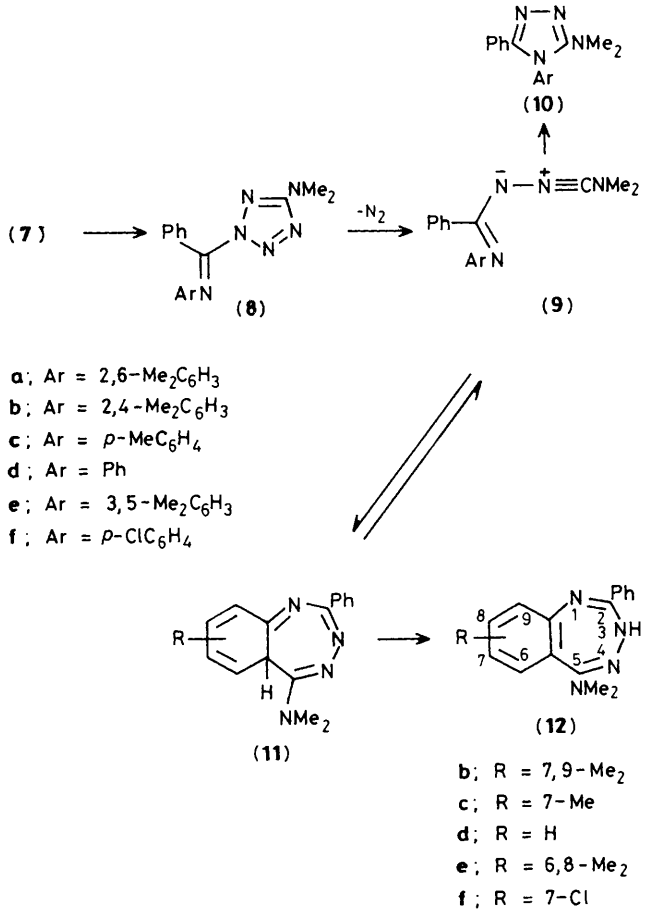
† Satisfactory analytical and spectroscopic data were obtained.

‡ *Crystal data:* (**7a**), $C_{18}H_{20}N_6$, monoclinic, space group $P2_1/c$, a = 9.785(1), b = 7.701(1), c = 23.847(3) Å, β = 100.31(1)°, U = 1768.0(4) Å^3, Z = 4, D_x = 1.203 Mg m^{-3}, λ(Cu-K_α) = 1.54178 Å, μ = 5.29 mm^{-1}, F(000) = 680, T = 293(1) K, R = 0.060 for 3091 independent reflections. (**12b**), $C_{18}H_{20}N_4$, monoclinic, $P2_1/c$, a = 11.592(1), b = 14.781(2), c = 9.497(1) Å, β = 98.32(1)°, U = 1610.1(3) Å^3, Z = 4, D_x = 1.206 Mg m^{-3}, λ(Cu-K_α) = 1.54178 Å, μ = 5.03 mm^{-1}, F(000) = 624, T = 293(1) K, R = 0.056 for 2703 independent reflections. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.



a; Ar = 2,6-$Me_2C_6H_3$
b; Ar = 2,4-$Me_2C_6H_3$
c; Ar = p-MeC_6H_4

Scheme 2. i, $POCl_3$; ii, $HClO_4$; iii, NaOH.



Scheme 3

suggest that the former reaction proceeds by an initial [1,5] shift of the imidoyl group (**7a**) → (**8a**) (see Scheme 3).

The thermolysis of the tetrazole (**7b**) or its isomer (**8b**) took a different course. Both gave a yellow product (30 and 68% yield, respectively), m.p. 170—171 °C,† which was evidently not a triazole since its i.r. spectrum showed NH absorption at 3300 cm^{-1}. This indicated that substitution in one of the aryl groups had occurred. The ^1H n.m.r. spectrum showed the

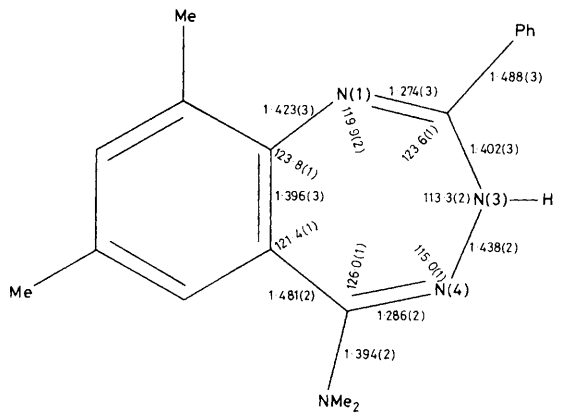
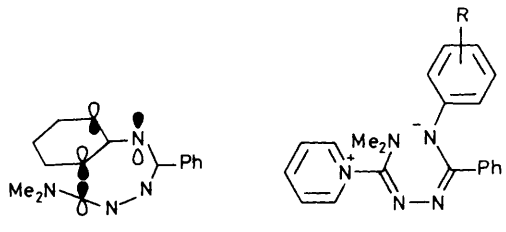


Figure 1. Bond lengths and angles for the seven-membered ring of the benzotriazepine (**12b**).



presence of a phenyl group [δ 7.45 (m, 3H) and 7.96 (m, 2H)] and of a 1,2,3,5-tetrasubstituted benzene ring [δ 7.09 (br s, H) and 7.16 (br s, H)]. The compound was considered to contain a seven-membered ring; the 3*H*-1,3,4-benzotriazepine structure (**12b**) was established by *X*-ray crystallography‡ (see Figure 1).

The seven-membered ring in the compound is severely puckered into a double sofa conformation with hinges at N(1)–C(5) and C(2)–N(4); the displacements of C(2), N(3), and N(4) out of the least-squares plane through the remaining four ring atoms are −0.738(3), −1.481(3), and −0.662(3) Å, respectively. The endocyclic bond lengths indicate double bonds between N(1)–C(2) and N(4)–C(5). In the crystal, the hydrogen atom at N(3) is hydrogen-bonded to N(1) in a symmetry-related molecule; the N · · · N distance is 3.096(3) Å.

The formation of benzotriazepines from (*N*-arylbenzimidoyl)-5-dimethylaminotetrazoles was found to be general: the *p*-tolyl compounds (**7c**) and (**8c**) both gave 7-methyl-5-dimethylamino-2-phenyl-3*H*-1,3,4-benzotriazepine (**12c**), m.p. 235 °C (decomp.),† in 30 and 85% yield, respectively, and thermolysis of compounds (**8d—f**) neat or in boiling xylene produced the pale-yellow benzotriazepines (**12d—f**), respectively, m.p. (decomp.) 230, 178.5, and 209 °C,† in 42—73% yields. The benzotriazepines are the first fully unsaturated members of this class without substituents on nitrogen.[6]

The benzotriazepine (**12c**) was also obtained (86%) by heating compound (**8c**) in nitrobenzene and in 46% yield by warming a mixture of 5-dimethylaminotetrazole and *N*-*p*-tolylbenzimidoyl chloride in 2,4,6-collidine. However, when the latter reaction was conducted in hot pyridine the triazole (**10c**) (21%), m.p. 174—175 °C,† was isolated, together with a small amount of the benzotriazepine (**12c**) (<5%). Treatment of 5-dimethylaminotetrazole with *N*-*p*-chlorophenylbenzimidoyl chloride in hot pyridine similarly gave the triazole (**10f**) (50%), m.p. 207—208.5 °C;† no benzotriazepine was detected.

The formation of the benzotriazepines from the nitrile imines (**9**) is a new example of a dipolar 1,7-electrocyclisation at a benzene ring. Padwa *et al.*[7] reported that 3*H*-2-benzazepines are produced from styryl-nitrile ylides and Sharp and his co-workers[8] have extensively investigated the formation of 3*H*-1,2-benzodiazepines from β-aryl-α,β-unsaturated diazoalkanes. Robertson and Sharp have pointed out[9] that the helical conformation required for antarafacial 8π-electrocyclisation is easily attained. In the present case, this is the preferred mode of reaction [*cf.* (**13**)] of the nitrile imines (**9**) in neutral non-polar and polar solvents and in the presence of the sterically hindered base 2,4,6-collidine. The primary products (**11**) rearrange to the benzotriazepines (**12**) by a [1,5] shift of hydrogen. When this is precluded by the presence of two *ortho*-substituents, as in (**9a**), the ring-closure is diverted to give the triazole (**10a**). A possible rationale for the formation of triazoles in the presence of pyridine is the intermediacy of adducts (**14**), formed by attack of the base at the terminal carbon atom of the nitrile imines. The geometry of these adducts favours 1,5-cyclisation.

Received, 22nd August 1986; Com. 1207

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