STUDIES IN CYCLOADDITION REACTIONS : SYNTHESIS OF NOVEL 1,3-DIARYL-1H,9H-TETRAZOLO[1,2-a]BENZOTRIAZOLES

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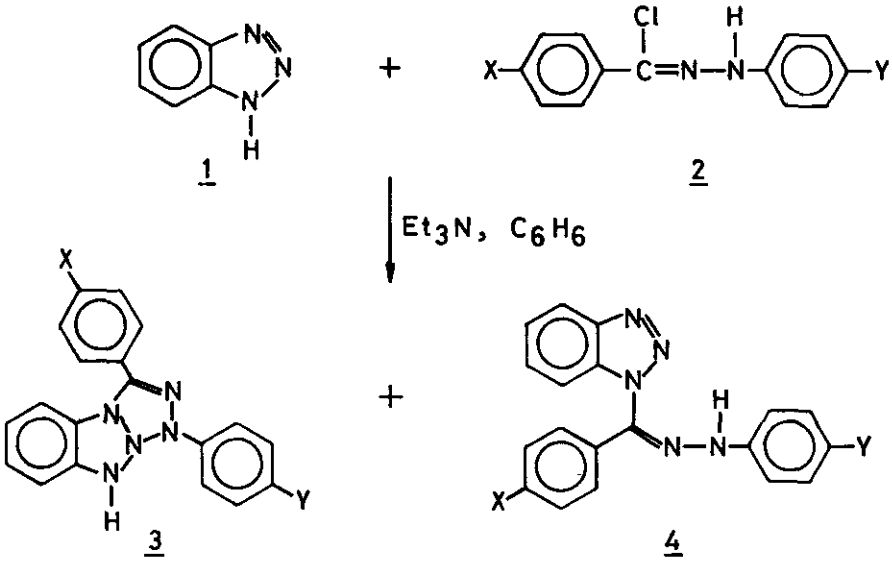
Abstract - 1,3-Diphenyl derivatives of the new heterocyclic system 1H,9H-tetrazolo[1,2-a]benzotriazole have been prepared by the 1,3-dipolar cycloaddition reaction of nitrileimines to benzotriazole. 1-(N-phenylbenzhydrazidoyl)-benzotriazoles are also formed simultaneously in the reaction and have been found to be stable and not convertible into the respective tetrazolobenzotriazoles. The tetrazolobenzotriazoles do not decompose into the benzhydrazidoyl benzotriazoles. Methylation of benzotriazole inhibits the addition of the dipole.

Nitrileimines generated *in situ* from hydrazidoyl chlorides have been shown to bring about 1,3-dipolar cycloaddition reaction with a wide variety of heterocyclic systems[1,2]. Pursuing our interest in the synthesis of tetrazoles of potential physiological activity[3] we applied to benzotriazoles 1 this cycloaddition reaction of nitrileimines (from 2) and obtained for the first time, 1,3-diphenyl derivatives of the new system, 1H,9H-tetrazolo[1,2-a]benzotriazole 3 (Scheme).

The structure of the products were established on the basis of spectral data summarized in the table. Cycloadducts corresponding to 3a-e show -NH and C = N frequencies in the ir spectra, while the benzhydrazidoyl benzotriazoles 4a-e show, in addition to the above, N = N frequencies. Loss of N_2 from the molecular ion of 4a and the corresponding products is predominant in the mass spectra of 4a-e, thus giving evidence for the postulated structures. Another significant differentiation is that the cycloadducts 3a-e produce fragments corresponding to $(Y\text{-}C_6H_6N)^+$ at m/e 91, 105, 136, 91 and 91 respectively and that the benzhydrazidoyl benzotriazoles produce fragments corresponding to $(Y\text{-}C_6H_6NH)^+$ at m/e 92, 106, 137, 92 and 92 respectively.

Scheme



1 + 2 → 3 + 4

a: X = Y = H c: X = H, Y = NO_2 e: X = NO_2, Y = H

b: X = H, Y = CH_3 d: X = CH_3, Y = H

Regarding the mechanism of the reaction, the following experimental observations have to be taken into consideration: (i) there is no nucleophilic displacement reaction between benzotriazole and the hydrazidoyl halide even after refluxing for 3 h, (ii) instantaneous reaction sets in on addition of triethylamine with the simultaneous formation of 3 & 4, (iii) products 3 & 4 have been found to be not interconvertible showing that they are not intermediates in the formation of each other and that they are formed simultaneously from the dipole generated in the reaction, (iv) methyl substitution on the benzotriazole inhibits the addition of the dipole; only the dimer of the dipole was isolated from the reaction, (v) acyl substitution on the benzotriazole enhances the reaction, and (vi) effect of substituents in the 5 & 6 positions of benzotriazole and solvent effects influence the reaction.

Prima facie, the reaction appears to be one of nucleophilic addition of benzotriazole to the nitrileimines to produce 4, with simultaneous 1,3-dipolar cycloaddition of nitrileimines to benzotriazole to produce 3. Since the cycloaddition process is symmetry allowed, generally a concerted mechanism[4] is accepted, but the feasibility of a biradical mechanism[5] cannot be ruled out. Details of this discussion will be reported elsewhere.

Table. Melting points, yield and spectral data of the products

product[a]	Mp (°C)	Yield (%)	MS (70 eV m/e (M^+ and other major fragments)	IR (KBr) (cm^{-1})	^1H-NMR[b] (δ)
3a	175	25	313, 194 91	3245 (NH), 1595 (C=N)	7.2-7.9 (m, 14H) 10.6 (s, NH)
3b	144	15	327, 208, 105	3250 (NH), 1610 (C=N)	2.35 (m, 3H), 7.1-8 (m, 13H), 10.5(s, NH)
3c	196	20	358, 239, 136	3195 (NH), 1585 (C=N) 1525, 1330 (NO_2)	6.7-7.7 (m, 13H), 10.5 (s, NH)
3d	145	20	327, 208, 91	3240 (NH), 1585 (C=N)	2.35 (s, 3H), 7-8.1 (m, 13H), 10.5 (s, NH)
3e	199	23	358, 239, 91	3200 (NH), 1590 (C=N) 1525, 1330 (NO_2)	6.8-7.9 (m, 13H) 10.5 (s, NH)
4a	194	45	313, 285, 194, 92	3280 (NH), 1602 (C=N) 1568 (N=N)	7.3-8.0 (m, 14H) 8.65 (s, NH)
4b	165	60	327, 299, 208, 106	3220 (NH), 1610 (C=N) 1570 (N=N)	2.35 (s, 3H), 7-8.1 (m, 13H), 8.6 (s, NH)
4c	236	67	358, 330, 239, 137	3240 (NH), 1595 (C=N) 1525, 1330 (NO_2), 1560 (N=N)	6.6-7.5 (m, 13H) 8.6 (s, NH)
4d	180	45	327, 299 208, 92	3260 (NH), 1595 (C=N) 1575 (N=N)	2.32 (s, 3H), 6.9-8.1 (m, 13H), 8.5 (s, NH)
4e	240	50	358, 330, 239, 92	3240 (NH), 1595 (C=N) 1525, 1330 (NO_2), 1570 (N=N)	6.7-7.6 (m, 13H) 8.6 (s, NH)

[a] All the products gave satisfactory elemental analyses.

[b] Solutions in $CDCl_3$ containing tetramethyl silane as internal standard.

EXPERIMENTAL

A typical experimental procedure for the reaction is described as follows: A mixture of 1.19 g (10 m.mol) of benzotriazole[6] 1, 2.30 g (10 m.mol) of N-phenylbenzhydrazidoyl chloride[7] 2 and 3 ml of triethylamine in 30 ml of dry benzene are refluxed for 3 h by which time the reaction is completed (followed by TLC). After filtering off the fluorescent triethylamine hydrochloride salt, while hot, it was left overnight. 1.4 g (45%) of an yellow crystalline mass of the 1-(N-phenylbenzhydrazidoyl)-benzotriazole 4a was obtained, which is filtered and the filtrate after evaporation was passed over a silica gel (60-120 mesh) column and eluted with a 4:1 mixture of benzene and petroleum ether (60-80°C), to give 0.80 g (25%) of 1,3-diphenyl-1H,9H-tetrazolo[1,2-a]benzotriazole 3a.

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