STUDIES IN CYCLOADDITION REACTIONS: A NOVEL SYNTHESIS OF 1H,9H-1,2,4-TRIAZOLO-[4,3-a]BENZIMIDAZOLES FROM 1-ACYLBENZIMIDAZOLES AND HYDRAZIDOYL CHLORIDE

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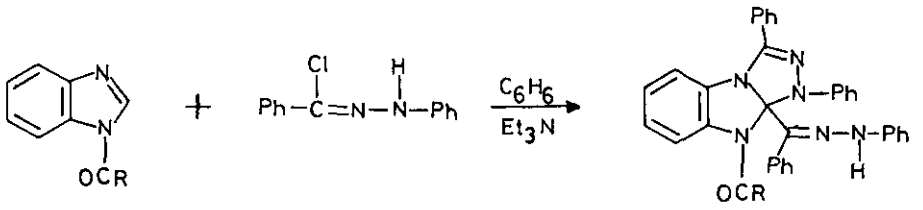
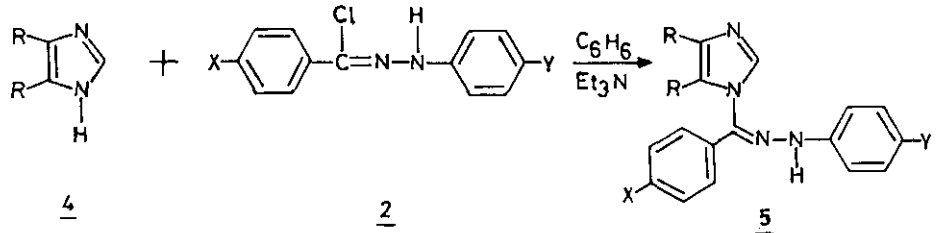
Abstract— 1-Acylbenzimidazoles undergo 1,3-dipolar cycloaddition with nitrileimine to produce derivatives of the 1H,9H-1,2,4-triazolo[4,3-a]benzimidazole system, followed by a rapid in situ substitution at 9a-position by the benzhydrazidoyl moiety. Substituted imidazoles and benzimidazole give 1-benzhydrazidoyl substituted products.

Continuing our work[1] on the cycloaddition of nitrileimines to azoles, we report the results of reactions carried out with imidazoles, benzimidazole, 1-alkylbenzimidazoles and 1-acylbenzimidazoles. Interestingly in the case of 1-acylbenzimidazoles, cycloaddition products have been isolated (Scheme 1). Imidazoles and benzimidazole produce 1-benzhydrazidoyl substituted products (Scheme 2).



1 2 3

Scheme-1



4 2 5

Scheme-2

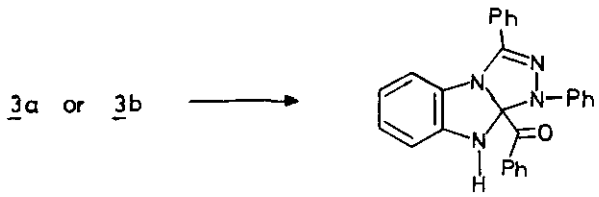
The structure of cycloadduct 3 has been established as 1,3-diphenyl 9-acyl-1H,9H-1,2,4-triazolo[4,3-a] benzimidazole in which a second molecule of the dipole has been incorporated in position 9a. This is the first time to our knowledge that this triazolobenzimidazole system has been synthesized by a single step process from 1-acylbenzimidazole as shown in Scheme 1. Earlier this system was prepared by Elnagdi et al[2] from 2-aminobenzimidazole and C-acetyl-N-phenylhydrazidoyl chloride. In another report[3] this system was prepared through a series of four steps starting from 2-acetamino-N-benzylidene aniline.

Product 3a (R=CH_3) crystallises out from the reaction mixture as the major product. 3b (R=Ph) is isolated by column chromatography (Silica gel, 60-120 mesh; ethyl acetate:benzene = 4:1, v/v). Product 5 is isolated by crystallisation. Table 1 summarises the details of products 3 and 5, their mps and yields.

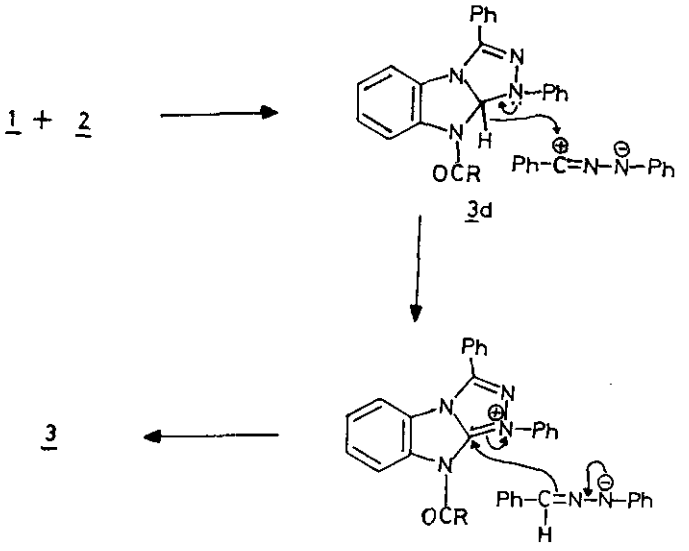
Table 1

Compound No.	Description				mp (°C)	Yield (%)
	R	R'	X	Y		
3a	CH_3	-	-	-	175	55
3b	Ph	-	-	-	160	45
5a	H	H	H	H	194	45
5b	H	H	NO_2	H	247	47
5c	H	H	CH_3	H	195	46
5b	H	H	H	NO_2	243	50
5e	H	H	H	CH_3	193	49
5f	Ph	Ph	H	H	210	51
5g	Ph	Ph	NO_2	H	155	53
5h	Ph	Ph	CH_3	H	212	53
5i	Ph	Ph	H	NO_2	159	55
5j	Ph	Ph	H	CH_3	210	56
5k	-CH=CH-CH=CH-		H	H	235	52
5l	-CH=CH-CH=CH-		NO_2	H	260	56
5m	-CH=CH-CH=CH-		CH_3	H	238	53
5n	-CH=CH-CH=CH-		H	NO_2	265	49
5o	-CH=CH-CH=CH-		H	CH_3	232	47

The structure of the product 5 of the Scheme 2 is established by hydrolysis to the known benzoyl derivatives[4] of 4. The loss of HCN from the molecular ion characteristic of imidazoles has been found in the mass spectra of 5. In the ^{1}H NMR (DMSO-d_6) of the products 5, the signal for 2-proton appears at δ 8.3 the same as for the 2-proton in imidazole 4. All the products gave satisfactory analyses. Attempts to cyclise 5 into the corresponding cycloaddition products with reagents such as NaH, polyphosphoric acid etc., have not been successful. The structure of the cycloadduct 3 is established from the ^{13}C-NMR,IR and the structure of hydrolysis products. ^{13}C-NMR of 3a (R=CH_3) in DMSO-d_6 shows the presence of two sp^3 carbons at δ 56 and 26, out of which the signal at δ 26 shows a splitting into a quartet in the off resonance spectrum while the other signal remains unsplit. This observation is in consonance with the methyl carbon and the quaternary 9a-carbon respectively. A similar observation in respect of 9a-carbon in the ^{13}C-NMR of product 3b (R=Ph) has been made. The carbonyl stretching frequency in 3a is at 1695 cm^{-1} and in 3b at 1675 cm^{-1}. On hydrolysis by 1:1 phosphoric acid and acetic acid mixture, 3a and 3b gave 3c. That the same product 3c is formed from both 3a and 3b on hydrolysis is established by TLC, mixed mp and superimposable IR. The molecular ion and the fragments in the mass spectra of the two products are identical.



It is observed that the product 3 is formed so rapidly that the isolation of its precursor (3d in Scheme-3) i.e., the product without the hydrazidoyl group in position 9a, has not been accomplished. This may be anticipated, if mode of formation of 3 suggested in Scheme 3 is operative. A hydride transfer from 9a-position of 3d to the dipole, followed by a rapid nucleophilic addition of the hydride acceptor to the 9a-position is feasible as benzimidazolines with a hydrogen at the 2-position are known to be good hydride transfer agents[5]. In 3d, the 9a hydrogen behaves like the 2-H of benzimidazoline. This leads us to consider that H-C(NR_2)$_3$ system should be an efficient hydride donor and work in this direction is in progress to confirm the above mechanism.



Scheme-3

ACKNOWLEDGEMENTS

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