

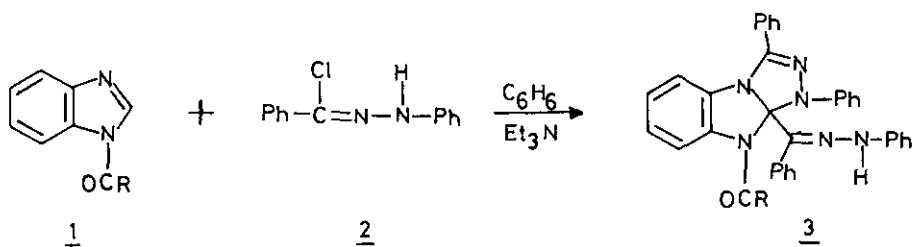
STUDIES IN CYCLOADDITION REACTIONS: A NOVEL SYNTHESIS OF 1H,9H-1,2,4-TRIAZOLO-[4,3-a]BENZIMIDAZOLES FROM 1-ACYLBENZIMIDAZOLES AND HYDRAZIDOYL CHLORIDE

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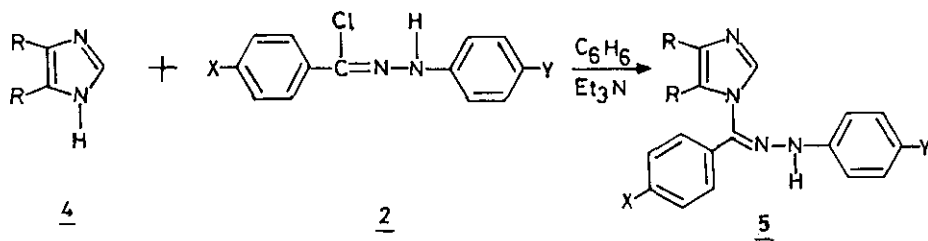
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Abstract— 1-Acylbenzimidazoles undergo 1,3-dipolar cycloaddition with nitrileimine to produce derivatives of the 1H,9H-1,2,4-triazolo[4,3-a]benzimidazole system, followed by a rapid *in situ* substitution at 9a-position by the benzhydrazidoyl moiety.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

Continuing our work¹ 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).



Scheme-1



Scheme-2

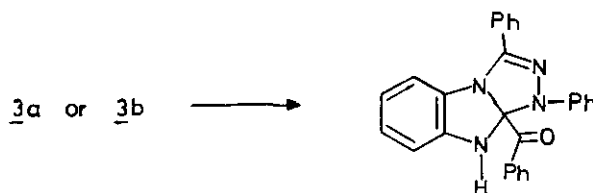
The structure of cycloadduct 3 has been established as 1,3-diphenyl 9-acyl-1H,9H-1,2,4-triazolo[4,3-a]benzimidazole in which a second molecule of the dipole has been incorporated in position 9a. This is the first time to our knowledge that this triazolobenzimidazole system has been synthesized by a single 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 report³ this system was prepared through a series of four steps starting from 2-acetamino-N-benzylidene aniline.

Product 3a (R=CH₃) 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.

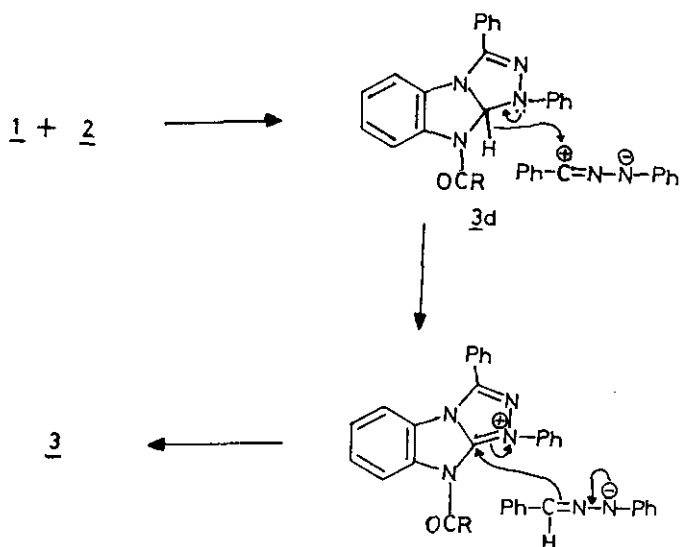
Table 1

Compound No.	Description				mp (°C)	Yield (%)
	R	R'	X	Y		
<u>3a</u>	CH ₃	-	-	-	175	55
<u>3b</u>	Ph	-	-	-	160	45
<u>5a</u>	H	H	H	H	194	45
<u>5b</u>	H	H	NO ₂	H	247	47
<u>5c</u>	H	H	CH ₃	H	195	46
<u>5d</u>	H	H	H	NO ₂	243	50
<u>5e</u>	H	H	H	CH ₃	193	49
<u>5f</u>	Ph	Ph	H	H	210	51
<u>5g</u>	Ph	Ph	NO ₂	H	155	53
<u>5h</u>	Ph	Ph	CH ₃	H	212	53
<u>5i</u>	Ph	Ph	H	NO ₂	159	55
<u>5j</u>	Ph	Ph	H	CH ₃	210	56
<u>5k</u>	-CH=CH-CH=CH-		H	H	235	52
<u>5l</u>	-CH=CH-CH=CH-		NO ₂	H	260	56
<u>5m</u>	-CH=CH-CH=CH-		CH ₃	H	238	53
<u>5n</u>	-CH=CH-CH=CH-		H	NO ₂	265	49
<u>5o</u>	-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 derivatives⁴ of 4. The loss of HCN from the molecular ion characteristic of imidazoles has been found in the mass spectra of 5. In the ¹H NMR (DMSO-d₆) 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 ¹³C-NMR, IR and the structure of hydrolysis products. ¹³C-NMR of 3a (R=CH₃) in DMSO-d₆ shows the presence of two sp³ 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 ¹³C-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 agents⁵. In 3d, the 9a hydrogen behaves like the 2-H of benzimidazoline. This leads us to consider that H-C(NR₂)₃ system should be an efficient hydride donor and work in this direction is in progress to confirm the above mechanism.



Scheme-3

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