The Reaction of Dimethyl Acetylenedicarboxylate with Acetylguanidine and Guanidine

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Summary The products from the reaction of dimethyl acetylenedicarboxylate with acetylguanidine and guanidine, originally formulated as the pyrimidines (IIa) and (IIb), have been shown to the imidazoline derivatives (IIIa) and (IIIb).

RECENTLY Keana and his co-workers described a synthesis of 3,4,5,8,9,10-hexahydro-2-acetamido-9-methoxycarbonylquinazolin-4-one (I) by the Diels–Alder reaction of methyl 2-acetamido-6(1*H*)-oxo-4-pyrimidinecarboxylate (IIa) with butadiene.[1] The pyrimidine (IIa) was prepared by condensation of dimethyl acetylenedicarboxylate (DMAD) with acetylguanidine or guanidine (followed by acetylation of IIb). Both condensation reactions were based on the synthesis of (IIc) from diethyl acetylenedicarboxylate (DEAD) and guanidine described by Ruhemann and Stapleton.[2] A suggestion by Sasaki *et al.*[3] that the DEAD–guanidine product was imidazoline (IIIc) rather than pyrimidine (IIc) led us to suspect that pyrimidines (IIa) and (IIb) prepared by Keana[1] were, in fact, isomeric imidazolines (IIIa) and (IIIb). This would require the butadiene adduct to be re-formulated as spiro-compound (IV).

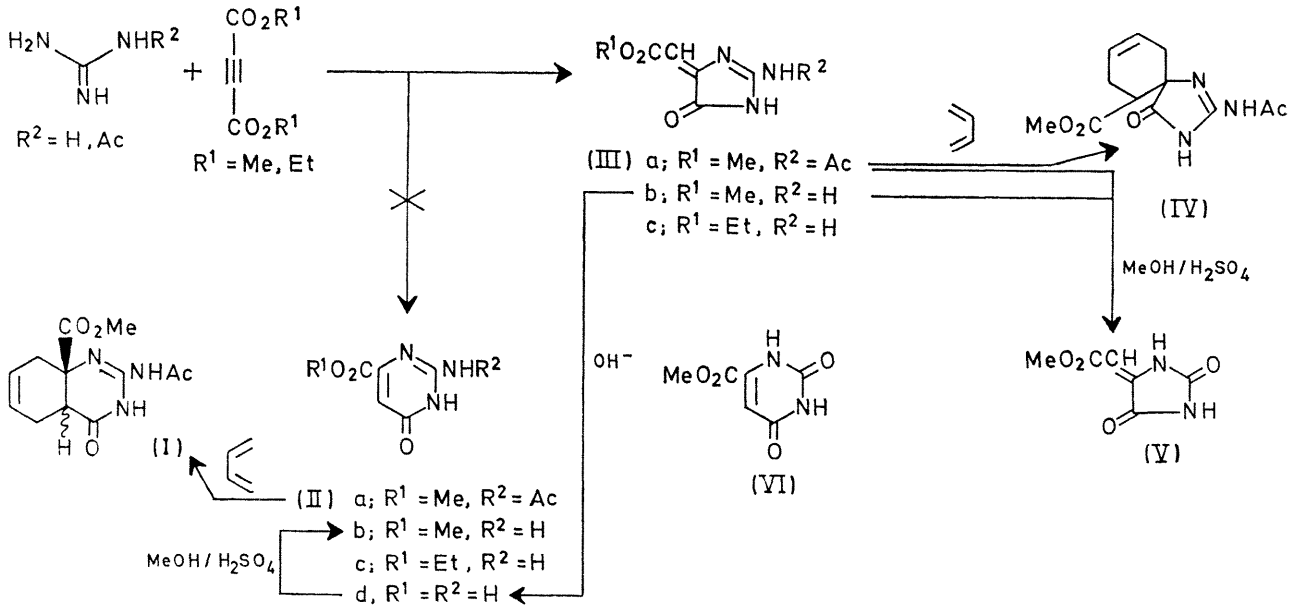
The formation of 2-amino-6(1*H*)-oxo-4-pyrimidinecarboxylic acid (IId)[4,5] by hydrolysis of the DMAD–guanidine product in 1N-NaOH did not dispel our suspicions since 2-amino-5-oxo-$\Delta^{4,\alpha}$-2-imidazolineacetic acid derivatives are known to rearrange to 2-amino-6(1*H*)-oxo-4-pyrimidinecarboxylic acids under such conditions.[6,7]

Material identical with authentic methyl 2-amino-6(1*H*)-oxo-4-pyrimidinecarboxylate (IIb)[5] was prepared from (IId) for comparison with the DMAD–guanidine product. The two compounds were shown to be different but isomeric, confirming the fact that rearrangement had accompanied hydrolysis in the formation of (IId) from the DMAD condensation product. Predictably the DMAD–acetylguanidine product was isomeric with (IIa), the acetyl derivative of (IIb).[8]

	λ_{max} (nm) *in* 95% *EtOH*	
	pH 7	pH 1
(VI)	285 (ϵ7100)	283 (7100)
(IIb)	317 (6400)	284 (4400)
		[shoulder at 318 (2800)]
(V)	238 (7800)	233 (8700)
	295 (13,700)	295 (15,000)
(IIIb)	270 (16,000)	241 (8700)
	315 (8500)	295 (15,000)

Additional evidence favouring imidazoline structures (IIIa) and (IIIb) for the DMAD condensation products was provided by the formation of methyl 2,5-dioxo-$\Delta^{4,\alpha}$-imidazoleacetate (V)[9,10] in good yield, when either compound was subjected to the esterification conditions (boiling MeOH–H_2SO_4) used in the preparation of (IIb).[5]

The similarity between the u.v. spectrum of (IIb) in acid solution and the neutral and acid spectra of methyl orotate (VI)[11] (Table) can readily be explained by the



structural relationship between these two pyrimidines. The analogous similarity between the acid spectrum of the DMAD–guanidine product and the neutral and acid spectra of (V) thus provides further support for imidazoline structures (IIIa) and (IIIb) for the DMAD condensation products.

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[5] (IIb), m.p. 288–291°, was obtained by esterification of (IId) in hot methanolic sulphuric acid as described by G. D. Daves, jun., F. Baiocchi, R. K. Robins, and C. C. Cheng, *J. Org. Chem.*, 1961, **26**, 2755. These workers record a m.p. of 293—294° for (IIb) (*c.f.*, >345° for the DMAD–guanidine product).[1]

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[8] (IIa), m.p. 196—201° was prepared by treatment of (IIb) with boiling acetic anhydride. Physical data supported structure (IIa). The acetylated DMAD–guanidine product had m.p. 278°.[1]

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