

A NOVEL SYNTHESIS OF γ -TRIAZOLO[4,5-d]PYRIMIDINES

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Treatment of 6-azido-1,3-dimethyluracil with alkyl halides in dimethylformamide containing potassium carbonate gave the corresponding 1-alkyl-4,6-dimethyl- γ -triazolo[4,5-d]-pyrimidine-5,7(4H,6H)-diones via 4,6-dimethyl- γ -triazolo[4,5-d]pyrimidine-5,7(4H,6H)-dione.

In recent years considerable interest has been devoted on the derivatives of γ -triazolo[4,5-d]pyrimidine as potential purine antagonists,¹ and several synthetic routes to this ring system have been developed.² We now report a novel synthesis of 1-alkyl-4,6-dimethyl- γ -triazolo[4,5-d]pyrimidine-5,7(4H,6H)-diones (IIa-f) from 6-azido-1,3-dimethyluracil (I).³

Refluxing (I) (0.001 mol) with alkyl halides (0.001 mol) in dimethylformamide (3 ml) containing potassium carbonate (0.001 mol) for 1 hr afforded the corresponding 1-alkyl-4,6-dimethyl- γ -triazolo[4,5-d]pyrimidine-5,7(4H,6H)-diones (IIa-f). An intermediate of these reactions is 4,6-dimethyl- γ -triazolo[4,5-d]pyrimidine-5,7(4H,6H)-dione (IIg),⁴ which was obtained by treatment of (I) with di-

methylformamide containing potassium carbonate under the same conditions^{5,6} (Table). The formation of (IIg) involves the intramolecular cyclization of a vinyl azide⁷ to a triazole. Numerous examples have been reported on the cyclization of imidoyl azides to tetrazoles and of thiocarbonyl azides to thiatriazoles,⁸ however, only one paper has hitherto been recorded on the conversion of a vinyl azide to a triazole.⁹



Table Formation of γ -Triazolo[4,5-d]pyrimidine Derivatives

Alkyl halide	Product	R	$\lambda_{\max}^{\text{H}_2\text{O}}$ nm (log ϵ)	Mp ($^{\circ}\text{C}$) (Recrystn. solvent)	Yield (%)
MeI	IIa	Me	230sh(3.64) 280(3.94) ^a	202-203 ^c (EtOH)	77
EtI	IIb	Et	230sh(3.71) 277(4.07)	83-84 (EtOH)	56
<i>n</i> -PrI	IIc	<i>n</i> -Pr	230sh(3.63) 278(4.49)	78-79 (EtOH)	26
EtOOCCH ₂ Cl	IIId	EtOOCCH ₂	235sh(3.67) 280(4.07)	164-166 ^d (MeOH)	21
CH ₂ =CH-CH ₂ Br	IIe	CH ₂ =CH-CH ₂	306(3.80)	183-184 (MeOH-H ₂ O)	24
Ph-CH ₂ Cl	IIIf	Ph-CH ₂	240sh(3.74) 280(4.10)	119-120 (EtOH)	38
None	IIg	H	230sh(3.83) 268(3.98)	259-260 ^e (H ₂ O)	30

a) Lit.⁴ 230sh(3.56), 280(3.74). b) Lit.⁴ 230sh(3.62), 269(3.93).
 c) Lit.⁴ mp 223-224^o. d) Lit. mp 157-159^o: D.S. Bariana, J. Med. Chem., 1971, 14, 543. e) Lit. mp 260^o.

REFERENCES AND NOTES

- 1 For example, the antitumor activity of γ -triazolo[4,5-d]pyrimidines has been reviewed by R.K. Robins: J. Med. Chem., 1964, 7, 186.
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- 3 W. Pfleiderer and K.-H. Schündehütte, Liebigs Ann. Chem., 1958, 612, 158.
- 4 G. Nübel and W. Pfleiderer, Chem. Ber., 1965, 98, 1060.
- 5 Compounds (IIa-g) were isolated by evaporation of the reaction mixtures, followed by addition of 5% hydrochloric acid, and subsequent extraction with chloroform. Satisfactory analytical and spectral data were obtained for all products.
- 6 Compound (IIg) could not be obtained by refluxing (I) with dimethylformamide alone for 1 hr.
- 7 The starting material (I) possesses a vinyl azide structure.
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