A New Synthesis of Purines

By FUMIO YONEDA,* SHIGURU MATSUMOTO, and MASATSUGU HIGUCHI
(*Faculty of Pharmaceutical Sciences, Kumamoto University, Oe-honmachi, Kumamoto* 862, *Japan*)

Summary Treatment of 6-aminopyrimidines with 4-phenyl-1,2,4-triazoline-3,5-dione gave the Michael-type adducts, 6-amino-5-(4-phenylurazol-1-yl)pyrimidines; fusion of these adducts with several aryl aldehydes gave the corresponding 8-arylpurines.

WE report a new synthetic route to purine derivatives, in which 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD)[1] is effective as a nitrogen source for N-7 of the purine ring system.

PTAD has been found to react readily with 6-aminopyrimidines unsubstituted in position 5, in dioxan at room temperature, to give excellent yields of the Michael-type adducts, 6-amino-5-(4-phenylurazol-1-yl)pyrimidines. 6-Amino-1,3-dimethyl-5-(4-phenylurazol-1-yl)uracil (I), m.p. 241°, 6-amino-1-methyl-5-(4-phenylurazol-1-yl)uracil (II), m.p. 244°, and 6-amino-4-hydroxy-2-phenyl-5-(4-phenylurazol-1-yl)pyrimidine (III), m.p. > 330°, were prepared.

Fusion of (I) with an excess of benzaldehyde (*ca.* 2 equiv.) at 180° for 1 h, followed by dilution with ethanol, gave 8-phenyltheophylline (IV) in good yield. Similarly heating (I) with several aryl aldehydes gave the respective 8-aryltheophyllines. This reaction is also applicable to other adducts to give the corresponding 8-arylpurine derivatives (Table).†

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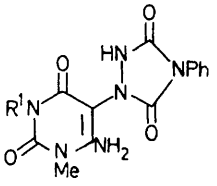
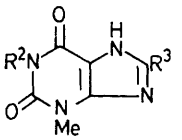
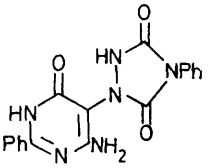


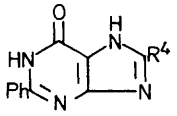
(I) R^1 = Me
(II) R^1 = H



(IV) R^2 = Me, R^3 = Ph
(V) R^2 = Me, R^3 = *p*-ClC_6H_4
(VI) R^2 = Me, R^3 = 3,4-$Cl_2C_6H_3$
(VII) R^2 = Me, R^3 = *p*-$MeOC_6H_4$
(VIII) R^2 = Me, R^3 = *p*-$(Me)_2NC_6H_4$
(IX) R^2 = H, R^3 = Ph
(X) R^2 = H, R^3 = *p*-ClC_6H_4
(XI) R^2 = H, R^3 = 3,4-$Cl_2C_6H_3$



(III)



(XII) R^4 = Ph
(XIII) R^4 = *p*-ClC_6H_4
(XIV) R^4 = 3,4-$Cl_2C_6H_3$

TABLE

Purine formation by reaction of 6-amino-5-(4-phenylurazol-1-yl)pyrimidines (Michael-type adducts) and aryl aldehydes

Michael-type adduct	Aldehyde	Reaction temp/°C	Time/h	Product	Yield[a]/%
(I)	Benzaldehyde	180	1	(IV)	70
(I)	*p*-Chlorobenzaldehyde	180	1·5	(V)	76
(I)	3,4-Dichlorobenzaldehyde	180	0·5	(VI)	82
(I)	*p*-Anisaldehyde	180	1	(VII)	72
(I)	*p*-Dimethylaminobenzaldehyde	140	3	(VIII)	35
(II)	Benzaldehyde	230	3	(IX)	68
(II)	*p*-Chlorobenzaldehyde	230	1	(X)	75
(II)	3,4-Dichlorobenzaldehyde	230	1	(XI)	78
(III)	Benzaldehyde	250	1·5	(XII)	69
(III)	*p*-Chlorobenzaldehyde	250	1	(XIII)	70
(III)	3,4-Dichlorobenzaldehyde	250	1	(XIV)	75

[a] None of these compounds melted below 330°. All compounds were recrystallized from dimethylformamide or ethanol.

† Satisfactory analytical and spectral date were obtained for all products.

[1] R. Stolle, *Ber.*, 1912, **45**, 273.