

## New Synthesis of Purines by the Reaction of Diethyl Azodicarboxylate with 6-Alkylaminouracils

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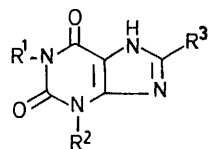
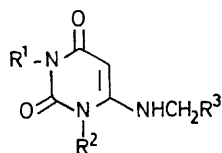
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*Summary* Treatment of 6-alkylamino-uracils with excess of diethyl azodicarboxylate gave the respective xanthine derivatives; reaction of 6-amino-5-(1,2-diethoxycarbonylhydrazino)-1,3-dimethyluracil with aryl aldehydes also gave the corresponding xanthine derivatives.

WE report a new synthesis of purines in which diethyl azodicarboxylate (DAD) acts as a dehydrogenation reagent as well as a nitrogen source for the direct cyclization of 6-*N*-benzyl- and 6-*N*-alkyl-aminouracils.

Fusion of compound (I)<sup>1</sup> with 3 equiv. of DAD at 170—

180° for 2 h, followed by dilution with ethanol gave a good yield of 8-phenyltheophylline (VI).<sup>1</sup> The reaction is equally applicable to other alkylamino-uracils<sup>1</sup> to give the corresponding xanthenes<sup>1</sup> (see Table 1).



(I) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = Ph

(II) R<sup>1</sup> = Me, R<sup>2</sup> = H, R<sup>3</sup> = Ph

(III) R<sup>1</sup> = H, R<sup>2</sup> = Me, R<sup>3</sup> = Ph

(IV) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = Et

(V) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = Pr<sup>n</sup>

(VI) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = Ph

(VII) R<sup>1</sup> = Me, R<sup>2</sup> = H, R<sup>3</sup> = Ph

(VIII) R<sup>1</sup> = H, R<sup>2</sup> = Me, R<sup>3</sup> = Ph

(IX) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = Et

(X) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = Pr<sup>n</sup>

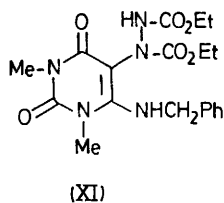
(XIV) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = *p*-ClC<sub>6</sub>H<sub>4</sub>

(XV) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = *p*-MeOC<sub>6</sub>H<sub>4</sub>

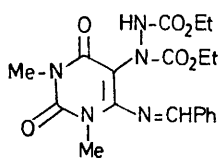
(XVI) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>

(XVII) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>

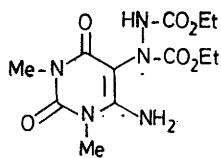
(XVIII) R<sup>1</sup> = R<sup>2</sup> = Me, R<sup>3</sup> = 3,4-CH<sub>2</sub>O<sub>2</sub>-C<sub>6</sub>H<sub>3</sub>



(XI)



(XII)



(XIII)

Treatment of (I) with 1 equiv. of DAD under the same conditions gave the Michael-type adduct (XI), m.p. 156°, † which did not form the desired purine upon thermolysis

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

<sup>1</sup> H. Goldner, G. Dietz, and E. Carstens, *Annalen*, 1966, **691**, 142.

<sup>2</sup> E. C. Taylor and F. Sowinski, *J. Amer. Chem. Soc.*, 1968, **90**, 1374.

TABLE 1

Purine formation by reaction of 6-*N*-benzyl- and 6-*N*-alkyl-aminouracils with DAD for 2 h [3h for (V)]

Starting material	Temp/°C	Product	Yield/%
(I)	180	(VI)	71
(II)	180	(VII)	68
(III)	180	(VIII)	83
(IV)	190	(IX)	50
(V)	200	(X)	30

under any conditions. However, treatment of (XI) with further DAD at 170–180° gave 8-phenyltheophylline as expected, although in less satisfactory yield (*ca.* 40%). DAD probably abstracted two hydrogen atoms from (XI) to give the uracil (XII), which cyclized immediately to a purine.

TABLE 2

Purine formation by reaction of compound (XIII) with aryl aldehydes

Aryl aldehyde	Product	Yield / %
Benzaldehyde <sup>a</sup> .. ..	(VI)	72
<i>p</i> -Chlorobenzaldehyde <sup>a</sup> .. ..	(XIV)	78
<i>p</i> -Anisaldehyde <sup>a</sup> .. ..	(XV)	65
<i>p</i> -Nitrobenzaldehyde <sup>b</sup> .. ..	(XVI)	61
3,4-Dichlorobenzaldehyde <sup>c</sup> .. ..	(XVII)	81
Piperonal <sup>a</sup> .. ..	(XVIII)	73

<sup>a</sup> 170 °C for 4 h. <sup>b</sup> 180 °C for 5 h. <sup>c</sup> 180 °C for 3.5 h.

To confirm this, we have examined the condensation of the uracil (XIII)<sup>2</sup> with aryl aldehydes, which should presumably give intermediates of type (XII). Thus heating (XIII) with several aryl aldehydes at 170–180° for *ca.* 4 h, followed by dilution with ethanol caused the separation of the corresponding purines, although the intermediate (XII) was not detected (see Table 2).

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