New Synthesis of Purines from the Reaction of 6-Amino-1,3-dimethyl-5-nitrosouracil with Benzylidenetriphenylphosphoranes

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Summary Treatment of 6-amino-1,3-dimethyl-5-nitrosouracil with benzylidenetriphenylphosphoranes affords the corresponding theophylline derivatives.

RECENTLY, 4-amino-5-nitrosopyrimidines have received considerable attention as versatile synthetic intermediates in purine synthesis.[1] We report a new, convenient synthesis of purines by treatment of 6-amino-1,3-dimethyl-5-nitrosouracil (I) with benzyl halides and Ph_3P in the presence of a base.

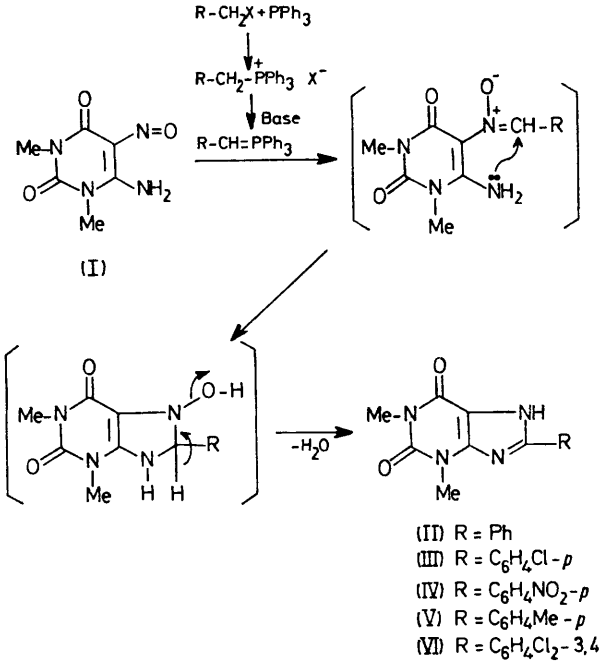
To a boiling suspension of (I) (0·001 mol), benzyl bromide (1·5 equiv.), and Ph_3P in tetrahydrofuran, aqueous NaOH (5%, 0·5 ml) was added and the mixture was heated at reflux for 30 min. The resulting solution was evaporated *in vacuo*, and the residue was washed with ethanol to give a good yield of 8-phenyltheophylline (II) (Scheme).[2] Other substituted benzyl halides provided the corresponding theophyllines (see Table).†

TABLE

Benzyl halide	Product[a]	Yield/%
Benzyl bromide	(II)	75
p-Chlorobenzyl chloride	(III)	59
p-Nitrobenzyl chloride	(IV)	50
p-Methylbenzyl chloride	(V)	57
3,4-Dichlorobenzyl chloride ..	(VI)	48

[a] None of the products melted below 300 °C.

This new purine synthesis is best rationalized by assuming the initial formation of a pyrimidine nitrone‡ by a type of Wittig reaction between the nitroso-group of (I) and the benzylidenetriphenylphosphoranes, followed by intramolecular cyclization and dehydration. The formation of benzylidenetriphenylphosphoranes (Wittig reagents) seems reasonable, since no reaction was observed in the absence of the base or Ph_3P.



SCHEME

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

‡ The reaction of fluorenylidenetriphenylphosphorane with nitrosobenzene has been reported to give fluorenone anil possibly through the initial formation of the corresponding nitrone (A. W. Johnson, *J. Org. Chem.*, 1963, **28**, 252).

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[2] H. Goldner, G. Dietz, and E. Carstens, *Annalen*, 1966, **691**, 142.