(Na_2SO_4), and concentrated. The product was separated by preparative vpc[11] to yield 10 mg (33%) of spiro[4.5]decane-1,6-dione as a clear oil: bp 238–241° dec; ir ($CHCl_3$) 1732 (cyclopentanone C=O), 1698 cm^{-1} (cyclohexanone C=O); mass spectrum (70 eV) *m/e* (rel intensity) 166 (38, M^+), 148 (14), 138 (35), 137 (20), 121 (21), 111 (100), 110 (90), 95 (34), 91 (27), 67 (52), 55 (74), 44 (95), 41 (67).

Preparation of 2-Cyclopentylidenecyclopentan-1-one Oxide (5).—A solution of 2.84 g (85% pure, 0.0140 mol) of *m*-chloroperbenzoic acid in 60 ml of chloroform was added slowly to an ice-cold solution of 2.00 g (13.3 mmol) of 2-cyclopentylidenecyclopentan-1-one (**4**)[12] in 20 ml of chloroform. This mixture was stirred at 3° for 18 hr. The reaction mixture was then filtered, washed with $NaHCO_3$ solution and brine until neutral, dried (Na_2SO_4), and concentrated. The residue was chromatographed on 50 g of silica gel (activity IV, 27.8 × 2.3 cm), with 9:1 hexane–ethyl acetate. The product obtained (1.04 g, 47%) crystallized from hexane to give holohedral plates of 2-cyclopentylidenecyclopenten-1-one oxide (**5**): mp 38–40°; uv max (EtOH) 307 nm (ε 43); ir ($CHCl_3$) 1743 (cyclopentanone C=O), 1160, 960 cm^{-1}; nmr ($CDCl_3$) δ 2.6–1.4 (m); mass spectrum (70 eV) *m/e* (rel intensity) 166 (50, M^+), 148 (40), 138 (55), 125 (21), 110 (100), 109 (32), 96 (34), 95 (75), 91 (44), 67 (80), 66 (40), 55 (65), 44 (48), 41 (64).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.27; H, 8.54.

Preparation of Spiro[4.5]decane-1,6-dione (3).—A solution of 132 mg of 2-cyclopentylidenecyclopentan-1-one oxide (**5**) in 110 ml of acetone was stirred with a stream of nitrogen and irradiated with a 450-W Hanovia lamp through a Pyrex filter. The reaction was stopped after 90 min. The acetone solution was concentrated and preparative vpc[13] was used to collect 6 mg of an unidentified oil, **6**,[14] 15 mg of reactant, and 40 mg (30%) of spiro[4.5]decane-1,6-dione (**3**) as a clear oil: bp 238–240° dec; uv max (EtOH) 287 nm (ε 126); ir ($CHCl_3$) 1732 (cyclopentanone C=O) and 1698 cm^{-1} (cyclohexanone C=O); nmr ($CDCl_3$) δ 2.9–1.1 (m); mass spectrum (70 eV) *m/e* (rel intensity) 166 (62, M^+), 148 (19), 138 (33), 137 (25), 121 (19), 111 (100), 110 (91), 95 (50), 91 (28), 67 (55), 55 (67), 44 (100), 41 (66).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.25; H, 8.74.

The spiro[4.5]decane-1,6-dione was shown to be identical (boiling point, ir, mass spectrum) with the diketone **3**, previously prepared by ozonolysis of the spiro[4.5]undecene **2**. Nmr spectra indicate that **3** and **6** are the only products. The low yield of **3** obtained is due to preparative vpc. Similar results were obtained when **5** was photolyzed in benzene, hexane, ether, and methanol.

Quenching Studies with 2-Cyclopentylidenecyclopentan-1-one Oxide (5).—In a typical experiment approximately 0.010 g of **5** was weighed into a 5-ml volumetric flask. The sample was dissolved in benzene, and 0.5-ml aliquots were placed in 7-mm Pyrex test tubes. Quenchers were added to prepare the following solutions: 0.01, 0.1, and 2.0 *M* piperylene; 0.01 and 0.1 *M* naphthalene; and 2 *M* biphenyl. The test tubes were degassed with nitrogen and irradiated on a merry-go-round with a 450-W Hanovia lamp. The resulting solutions were analyzed by vpc.[11]

Sensitization Studies with 2-Cyclopentylidenecyclopentan-1-one Oxide (5).—The same procedure was used as in the quenching studies, except that the solutions were prepared so that the sensitizer absorbed over 90% of the light at 313.0 nm. The following solutions were used: 0.0615 *M* acetophenone, 0.0324 *M* benzophenone, 0.258 *M* benzaldehyde, and acetone (neat).

Registry No.—**3**, 36803-48-2; **5**, 36803-49-3.

Acknowledgment.—We acknowledge partial support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and Mr. Kuhlman of Wyeth Laboratories for the mass spectra.

(11) The column (6 ft × 0.25 in.) used was packed with 20% Carbowax 20M on 60–80 mesh Chromosorb P.

(12) O. Wallach, *Ber.*, **29**, 2955 (1896).

(13) The column (4 ft × 0.25 in.) used was packed with 20% Carbowax 20M on 60–80 mesh Chromosorb WAW DMCS.

(14) This product is currently under investigation.

Studies in Purine Chemistry. XVI. A One-Step Synthesis of 7-Aryltheophyllines[1,2]

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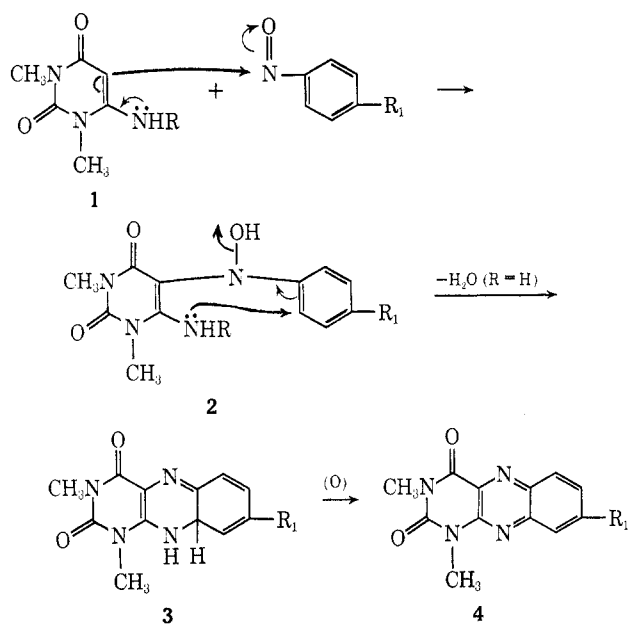
Some time ago we described a new route to 1,3-dimethylalloxazines which involves the condensation of 1,3-dimethyl-6-aminouracil (**1**, R = H) with nitrosobenzenes in the presence of acetic anhydride.[4] A reasonable intermediate in this condensation is the hydroxylamine **2**; the intramolecular dehydrative-cyclization step (**2** to **3**) is presumably facilitated by prior acetylation of the hydroxylamine. Dehydrogenation with excess nitrosobenzene then gives **4**. It appeared that the use of a 6-alkylamino derivative of **1** (R = alkyl) would prevent the final aromatization step (**3** to **4**) and lead to a synthesis of 1,3-dimethyl-5-acetyl-10-alkylleucoflavins.



1 2 3 4

We have found, however, that the reaction of 1,3-dimethyl-6-methylaminouracil (**1**, R = CH_3) with nitrosobenzene in the presence of acetic anhydride gave 7-phenyltheophylline (**8**, R_1 = H; Ar = C_6H_5).[5] Analogous reactions were observed with 1,3-dimethyl-6-ethylaminouracil (**1**, R = C_2H_5) and with 1,3-dimethyl-6-benzylaminouracil (**1**, R = $CH_2C_6H_5$) in condensations with nitrosobenzene and with *p*-chloronitrosobenzene; in all cases, the α-C atom of the 6-alkylamino group becomes the 8-carbon atom of the

(1) Part XV: E. C. Taylor, G. P. Beardsley, and Y. Maki, *J. Org. Chem.*, **36**, 3211 (1971).

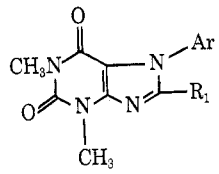
(2) This investigation was supported by the U. S. Army Medical Research and Development Command (Contract No. DA-49-193-MD-2777) and is Contribution No. 1089 in the Army research program on malaria.

(3) Kumamoto University, Kumamoto, Japan.

(4) E. C. Taylor, F. Sowinski, T. Yee, and F. Yoneda, *J. Amer. Chem. Soc.*, **89**, 3369 (1967).

(5) H. Dolman, J. van der Goot, G. H. Mos, and H. D. Moed, *Recl. Trav. Chim. Pays-Bas*, **83**, 1215 (1964), have reported the preparation of this compound by arylation of theophylline with *p*-chloronitrobenzene, followed by reduction and reductive diazotization. This is the only 7-aryltheophylline previously reported.

TABLE I
7-ARYLTHEOPHYLLINES[c]

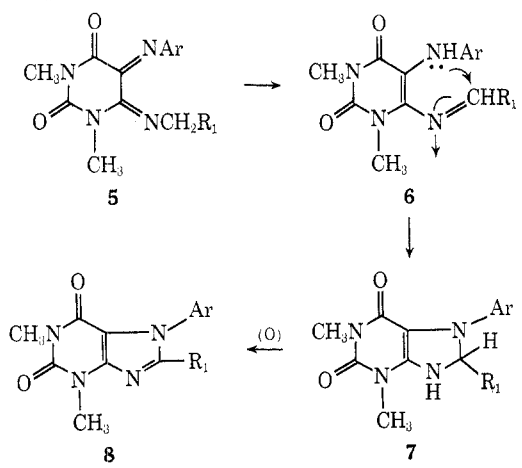


Registry no.	R_1	Ar	Yield, %	Recrystn solvent	Mp, °C[a]
960-61-2	H	C_6H_5	31	Ethanol	195.5[b]
36748-65-9	H	*p*-ClC_6H_4	48	1-Propanol	245.2
36748-66-0	CH_3	C_6H_5	38	Methanol	235.0
36748-67-1	CH_3	*p*-ClC_6H_4	40	Methanol	250.5
36748-68-2	C_6H_5	C_6H_5	48	Ethanol	221.3
36748-69-3	C_6H_5	*p*-ClC_6H_4	70	1-Propanol	267.6

[a] All melting points are corrected and were determined on a Mettler FP-1 apparatus. [b] Lit. mp 193–194.5° (ref 5). [c] Satisfactory analytical values (±0.3% in C, H, N) were reported for all compounds in the table: Ed.

final 7-aryltheophylline.[6] Results are summarized in Table I.

We suggest that this new purine synthesis involves the intermediacy of a 5-hydroxylamino derivative (**2**, R = CH_3, C_2H_5, $CH_2C_6H_5$) which suffers dehydration in the acetic anhydride medium to give the diimine **5**. Prototropic rearrangement would then give the monoimine **6**, which is ideally disposed for intramolecular cyclization to **7**. Subsequent dehydrogenation by excess arylnitroso compound would then lead to the 7-aryltheophylline **8** and an arylhydroxylamine. Since



azoxybenzene (and 4,4′-dichloroazoxybenzene) were also isolated from reactions involving nitrosobenzene and *p*-chloronitrosobenzene, respectively, a further reaction of the hydroxylamine with unreacted arylnitroso compound must occur, indicating the ultimate participation of 3 mol of the latter. Utilization of this stoichiometry significantly improved the yields of the 7-aryltheophyllines.

Experimental Section

7-Aryltheophyllines. General Procedure.—A solution of 0.01 mol of the 1,3-dimethyl-6-alkylaminouracil[7] and 0.03 mol of nitrosobenzene (or *p*-chloronitrosobenzene) in 30 ml of acetic anhydride was heated under gentle reflux for 30 min and poured into 500 ml of water, and the resulting solution was neutralized with aqueous ammonia[8] and allowed to stand overnight at room temperature. The yellow solid which had separated was collected by filtration, washed well with ether to remove coprecipitated azoxybenzene (or 4,4′-dichloroazoxybenzene), and recrystallized as specified in Table I.

(6) For other purine syntheses in which the α-C atom of a 6-alkylamino substituent becomes C-8 in the final product, see, for example, (a) W. Pfleiderer and H.-U. Blank, *Angew. Chem., Int. Ed. Engl.*, **5**, 666 (1966); (b) H. Goldner, G. Dietz, and E. Carstens, *Justus Liebigs Ann. Chem.*, **691**, 142 (1966).

(7) 1,3-Dimethyl-6-methylaminouracil and 1,3-dimethyl-6-ethylaminouracil: W. Pfleiderer and K.-H. Schundehutte, *Justus Liebigs Ann. Chem.*, **612**, 158 (1958). 1,3-Dimethyl-6-benzylaminouracil: H. Bredereck, H. Herlinger, and W. Resemann, *Chem. Ber.*, **93**, 236 (1960).

(8) In the condensation of 1,3-dimethyl-6-methylaminouracil with nitrosobenzene there was no precipitate at this stage; the alkaline solution was extracted with ether and the ether extracts were evaporated to a small volume and cooled to give 7-phenyltheophylline.

Synthesis of Myosmine and Nornicotine, Using an Acyl Carbanion Equivalent as an Intermediate[1a]

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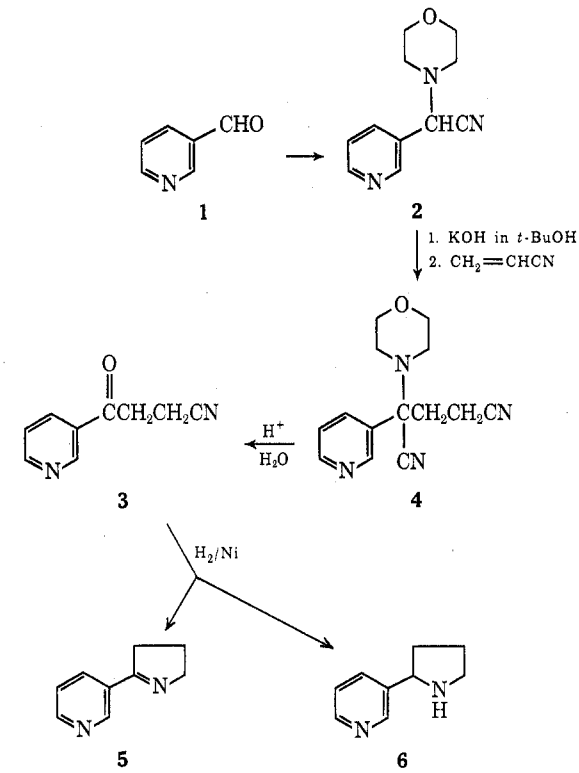
Myosmine (**5**) has been isolated from tobacco smoke and is a minor component of the alkaloids of *Nicotiana tabacum*.[2] It has been synthesized by several methods[3] and on reduction affords nornicotine (**6**).



For our studies on the metabolism of the tobacco alkaloids we required a synthesis of these alkaloids

(1) (a) This investigation was supported by Research Grant GM-13246 from the National Institutes of Health; (b) Contribution No. 122 from this laboratory.

(2) R. L. Stedman, *Chem. Rev.*, **68**, 153 (1968).

(3) (a) E. Späth and L. Mamoli, *Ber.*, **69**, 757 (1936); (b) C. F. Woodward, A. Eisner, and P. G. Haines, *J. Amer. Chem. Soc.*, **66**, 911 (1944); (c) M. L. Stein and A. Burger, *ibid.*, **79**, 154 (1957); (d) R. V. Stevens, M. C. Ellis, and M. P. Wentland, *ibid.*, **90**, 5576 (1968); (e) B. P. Mundy, B. R. Larsen, L. F. McKenzie, and G. Braden, *J. Org. Chem.*, **37**, 1635 (1972).