methoxybenzyl bromide (IX). The crude quaternary salt formed by reaction of the benzyl bromide (IX) with picolinaldehyde was cyclized by refluxing it for nine hours in hydrochloric acid solution. Since ether cleavage occurred during the long heating, the product was 7-bromo-8-hydroxyacridizinium bromide (V. Z = Br) rather than the corresponding methyl ether. This material was identical in melting point and infrared spectrum with that obtained by direct bromination of 8-hydroxyacridizinium bromide.

The chlorination of 8-methoxyacridizinium chloride[5] (IV) was carried out in dimethylformamide using sulfuryl chloride as the chlorinating agent. The monochlorination product, isolated in 60% yield as the picrate, was demonstrated to be 7-chloro-8-methoxyacridizinium picrate by synthesis from 2-chloro-3-methoxytoluene (VIII). The procedure used was analogous to that used in the synthesis of the 7-bromo-8-hydroxyacridizinium ion (V) except that the cyclization time was limited to three hours so that the 7-chloro-8-methoxyacridizinium ion (VI) was obtained with a minimum amount of ether cleavage.

### Experimental

All melting points were taken on the Fisher Johns hot stage and are uncorrected. Except as noted, all analyses were by the Galbraith Laboratories, Knoxville, Tenn.

**7-Bromo-8-hydroxyacridizinium Salts (V). (a) By Direct Bromination.**—A solution containing 0.45 g. of 8-hydroxyacridizinium bromide[5] in 150 ml. of acetic acid was refluxed for 20 min. with 0.2 ml. of bromine. When the mixture cooled a yellow product was obtained, m.p. 280–295°. Recrystallization from ethanol afforded yellow needles of the **bromide**, m.p. 291–296°, yield, 0.39 g. (68%).

The **picrate**, m.p. 231–233° formed as long needles from ethanol.

**(b) From 2-bromo-3-methoxytoluene (VII).**—In a flask containing 4.5 g. of 2-bromo-3-methoxytoluene,[6] 3.91 g. of N-bromosuccinimide, and 50 ml. of dry carbon tetrachloride, 0.5 g. of dibenzoyl peroxide was added, and the resulting suspension refluxed for 1 hr. The solid was removed by filtration, and the filtrate concentrated under reduced pressure. A small quantity of benzene was added and removed under reduced pressure. The residual oil (5.33 g.), which consisted chiefly of 2-bromo-3-methoxybenzyl bromide, was dissolved in 20 ml. of methanol and refluxed for 3 hr. with 2.03 g. of picolinaldehyde. The solvent was evaporated under reduced pressure and the residual oil washed with ether. The ether was decanted and the oil taken up in 20 ml. of concentrated hydrochloric acid and the solution refluxed for 9 hr. Removal of the acid under vacuum and recrystallization of the residue from ethanol afforded 2.51 g. (39%) of the **bromide**, m.p. 293–296°. The preparations of the bromide obtained by methods a and b were shown to be identical by mixture melting point determinations and comparison of infrared spectra.

*Anal.* Calcd. for $C_{13}H_9Br_2NO \cdot H_2O$: C, 41.80; H, 2.95; N, 3.76. Found[7]: C, 42.12; H, 2.96; N, 3.94.

The **picrate** formed as needles from ethanol, m.p. 231–233°. By means of mixture melting point determinations and comparison of infrared spectra, it was shown that this picrate is identical with that obtained by procedure a.

*Anal.* Calcd. for $C_{19}H_{11}BrN_4O_8$: C, 45.34; H, 2.20; N, 11.14. Found: C, 45.45; H, 2.79; N, 11.52.

**7-Chloro-8-methoxyacridizinium Picrate (VI). (a) By Chlorination.**—To a solution containing 0.7 g. (0.0028 mole) of 8-methoxyacridizinium chloride in 15 ml. of dry dimethylformamide, in a flask protected by drying tubes, 0.4 g. (0.003 mole), of sulfuryl chloride was added and the solution was warmed for 20 min., after which an additional 0.1 g. of sulfuryl chloride was added, and heating continued for 0.5 hr. longer. After vacuum evaporation of the dimethylformamide the residue was converted to the picrate and crystallized from ethanol as very small yellow needles, m.p. 215–216°, yield 0.81 g. (60%).

(7) Analysis by Dr. Ing. A. Schoeller, Kronach, Germany.

**(b) From 2-Chloro-3-methoxytoluene (VIII).**—The bromination of 2-chloro-3-methoxytoluene[8] (1.85 g.) was carried out as in the case of the 2-bromo analog (VII). The crude 2-chloro-3-methoxybenzyl bromide (X) was allowed to react with 0.96 g. of picolinaldehyde in refluxing methanol. The crude quaternary salt was cyclized by refluxing it for 3 hr. in 20 ml. of concentrated hydrochloric acid. The crude salt was converted to the **picrate** for purification, m.p. 215–216°. This material was identical in melting point and infrared spectrum with the picrate obtained from the product of the chlorination reaction.

*Anal.* Calcd. for $C_{20}H_{13}ClN_4O_8$: C, 50.80; H, 2.77; N, 11.85. Found: C, 50.49; H, 2.51; N, 11.57.

(8) G. P. Gibson, *J. Chem. Soc.*, **123**, 1269 (1923).

## The Preparation of N,N-Dimethyl- and N,N-Diethylenamines from Ketones

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Recent interest in enamine chemistry[1] prompts the reporting of a simple but useful modification of the Mannich–Davidsen[2] procedure for the preparation from ketones of N,N-dimethyl- and N,N-diethylenamines which previously could not be synthesized readily. The modification involves substituting granular calcium chloride for the normally employed potassium carbonate or calcium oxide to serve as catalyst and dehydrating agent. Although Mannich and Davidsen[2] report the formation of aminals which thermally decompose to the enamine in the reaction of cyclohexanone with piperidine, no evidence for such precursors has been observed in this work. Examination of the ether solution by infrared spectroscopy revealed the presence of the enamine double bond (1640 $cm.^{-1}$) prior to distillative work up. The enamines tabulated were prepared by the general procedure, given in detail for N,N-dimethylamino-1-cyclohexene, of treating the appropriate ketone with either dimethyl- or diethylamine. These enamines were found stable to storage at room temperature in the absence of moisture and oxygen. (See Table I, p. 1398.)

### Experimental

**Materials.**—Commercially available cyclopentanone, cyclohexanone, dimethylamine, diethylamine, anhydrous diethyl ether, and anhydrous 12-mesh calcium chloride were used without further purification.

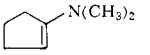
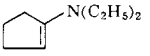
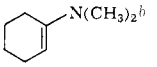
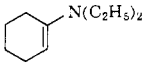
**Dimethylamino-1-cyclohexene.**—To a solution of dimethylamine (150 g., 3.4 moles) in anhydrous diethyl ether (400 ml.) was added cyclohexanone (196 g., 2 moles) and 12-mesh calcium chloride (150 g.). The mixture was vigorously stirred at room temperature under a nitrogen atmosphere for 64 hr. The slurry was filtered, and the residue washed with diethyl ether (200 ml.). Evaporation of the ether and fractionation of the residue afforded the desired enamine (108.3 g., 0.87 mole) as a colorless liquid, b.p. 81° (35 mm.). Ninety-four and a half grams (0.97 mole) of cyclohexanone was recovered.

(1) See, for example, the Abstracts from the 140th National Meeting of the American Chemical Society, Chicago, Ill., September 3–8, 1961, "Symposium on Enamine Chemistry," pp. 44Q–46Q, 53Q–56Q.

(2) C. Mannich and H. Davidsen, *Chem. Ber.*, **69**, 2106 (1936).

TABLE I

N,N-DIMETHYL- AND N,N-DIETHYLENAMINES

| Enamine | Conv.,[a] % | Yield,[a] % | B.p., °C. (mm.) | $n^{25}D$ | Anal. Calcd. | Anal. Found |
|---|---|---|---|---|---|---|
|  | 56 | 87 | 85–86 (104) | 1.4801 | C, 75.62<br>H, 11.76<br>N, 12.59 | 75.85<br>12.10<br>12.89 |
|  | 65 | 63 | 99–101 (60) | 1.4777 | C, 77.63<br>H, 12.31<br>N, 10.06 | 77.81<br>12.19<br>9.66 |
|  [b] | 52 | 83 | 81 (35) | 1.4851 | C, 76.74<br>H, 12.08<br>N, 11.18 | 76.54<br>12.18<br>11.29 |
|  | 35 | 51 | 64 (6) | 1.4820 | C, 78.36<br>H, 12.50<br>N, 9.14 | 78.28<br>12.42<br>8.86 |

[a] Based on ketone used. [b] R. A. Benkeser, R. F. Lambert, P. W. Ryan, and D. G. Stoffey, *J. Am. Chem. Soc.*, **80**, 6573 (1958) report this enamine but fail to give either a synthetic procedure or physical constants.

## Pteridine Chemistry. IX. 2-Amino-4-hydroxy-6(and 7)-phenylpteridines

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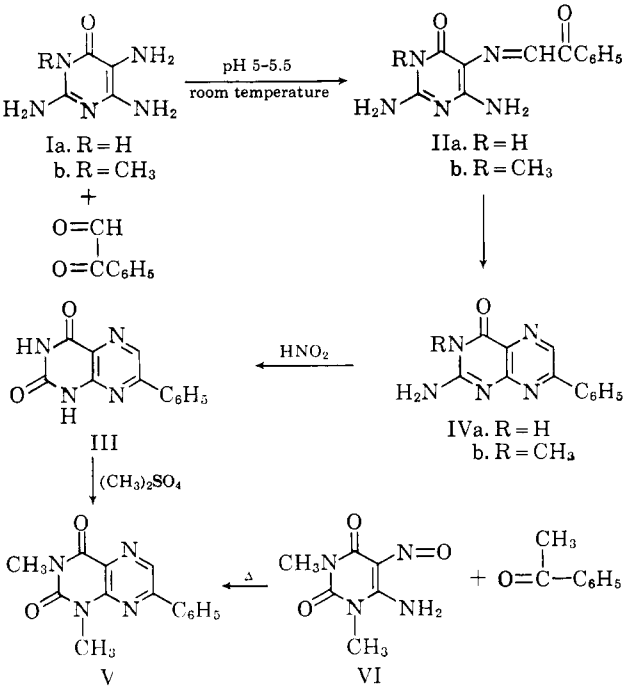
The isomeric 2-amino-4-hydroxy-6(and 7)-phenylpteridines (VIIa and IVa) and their 3-methyl derivatives were considered to be useful compounds for a continuation of the study of the methylation of 2-amino-4-hydroxypteridines.[1] However, the published reports by two groups of investigators on the synthesis of VIIa and/or IVa do not agree on the nature of the products obtained.

In 1952, King and Spensley[2] reported that the reaction between 2,4,5-triamino-6-hydroxypyrimidine (Ia) and phenylglyoxal or $\alpha$-nitroacetophenone gave the 7-phenyl derivative IVa, while Ia and $\alpha,\alpha$-dichloroacetophenone gave the 6-phenyl derivative VIIa. In 1956, Dick, Wood, and Logan[3] re-examined the same three reactions and claimed that in each case the product was the 6-phenyl derivative VIIa. In connection with the use of phenylglyoxal in the above reaction, it should be noted that the reaction between 4,5-diaminopyrimidines and ketoaldehydes has been reported many times in the literature. Under weakly acidic conditions similar to those used by King and Spensley,[2] the primary product has almost invariably been a 7-substituted pteridine.[4,5] The 6-substituted derivatives have been prepared only in special systems containing either strong acid[5] or aldehyde binding agents such as hydrazine or sodium bisulfite.[4] Therefore, it was our opinion that King and Spensley were correct with respect to the phenylglyoxal reaction. This was verified as outlined.

2,4,5-Triamino-6-hydroxypyrimidine (Ia) was condensed with phenylglyoxal hydrate in a weakly acidic water–ethanol solution at room temperature.[2] An ultraviolet absorption spectrum of the initial product indicated that it was primarily the anil IIa. When this product was dissolved in 2.5 *N* sodium hydroxide, ring closure occurred to give a pteridine which was 2-amino-4-hydroxy-7-phenylpteridine (IVa) contaminated with a small amount of 6-phenyl isomer as shown by paper chromatography and ultraviolet absorption spectra (see p. 1399). The impurity was successfully removed by crystallization. The structure of IVa was proved by its conversion to 2,4-dihydroxy-7-phenylpteridine (III)[3] followed by methylation to produce 1,3-dimethyl-7-phenyl-2,4(1*H*,3*H*)-pteridinedione (V). The latter compound V was then synthesized unequivocally as described by Dick, Wood, and Logan[3] from 6-amino-1,3-dimethyl-5-nitroso-2,4-(1*H*,3*H*)-pyrimidinedione (VI) and acetophenone. The two products were identical as shown by infrared and ultraviolet absorption spectra and mixture melting point.




A synthesis of the isomeric 6-phenyl derivative VIIa was discovered during an attempt to utilize directly commercially available phenylglyoxal diethyl acetal. 2,4,5-Triamino-6 hydroxypyrimidine (Ia) was con-

(1) R. B. Angier and W. V. Curran, *J. Org. Chem.*, **27**, 892 (1962).
(2) F. E. King and P. C. Spensley, *J. Chem. Soc.*, 2144 (1952).
(3) G. P. G. Dick, H. C. S. Wood, and W. R. Logan, *ibid.*, 2131 (1956).
(4) A. Albert, *Quart. Rev.*, **6**, 227, 228 (1952).
(5) W. R. Boon, *J. Chem. Soc.*, 2146 (1957).