butanol solution, prepared as described previously. Catalytic hydrogenation of one portion showed absorption of 0.039 mole of hydrogen, indicating that each aliquot contained not more than 2.7 g. of 1-pyrroline.

3-Methylpyrrolidylpyrroles.—A mixture of 1.2 g. of 3-methylpyrrole, b.p. 143°, prepared by the method of Lancaster and VanderWerf,[25] and 50 ml. of pyrroline–butanol solution was refluxed for 24 hours. Vacuum distilling and then four vacuum sublimations of the residue gave 0.73 g. (33%) of a mixture of 3-methylpyrrolidylpyrrole, m.p. 85–97°. The picrate formed from methanolic solution was a deep red oil which could not be made to crystallize.

Anal. Calcd. for $C_9H_{14}N_2$: C, 72.0; H, 9.4; N, 18.7; mol. wt., 150. Found: C, 72.0; H, 9.5; N, 18.6; mol. wt., 153.

2-Methylpyrrolidylpyrroles.—A mixture of 6.8 g. of 2-methylpyrrole, b.p. 148°, and 50 ml. of pyrroline–butanol solution was refluxed for 22 hours. The low-boiling materials were boiled off at 0.5 mm. up to a temperature of 100°. This left 4.5 g. (79%) of a viscous yellow oil which could not be made to crystallize. The picrate, formed in methanolic solution, melted at 159.0–161.0°.

Anal. Calcd. for $C_{15}H_{17}N_5O_7$: C, 47.5; H, 4.5; N, 18.5. Found: C, 47.4; H, 4.6; N, 18.4.

2,5-Dimethyl-3-(2-pyrrolidyl)-pyrrole.—A mixture of 17 g. of 2,5-dimethylpyrrole, b.p. 63–65° at 19 mm., and 50 ml. of pyrroline butanol solution was refluxed for 17 hours. Vacuum distilling up to 50° at 0.25 mm. pressure left 3.2 g. of a viscous yellow residue. Vacuum sublimation gave 2.5 g. (40%) of 2,5-dimethyl-3-pyrrolidylpyrrole, a clear waxy solid. Crystallization from ethyl acetate gave 0.5 g. of white crystals, probably 2,5-dimethyl-3-(2-pyrrolidyl)-pyrrole.

Anal. Calcd. for $C_{10}H_{16}N_2$: C, 73.1; H, 9.8; N, 17.1; mol. wt., 164. Found: C, 73.2; H, 9.8; N, 16.9; mol. wt., 154.

3-(2-Pyrrolidyl)-indole.—A mixture of 2 g. of indole, 50 ml. of butanol–pyrrolidine and 5 ml. of pyrrolidine was refluxed for 30 hours. Vacuum drying and then vacuum sublimation of the residue and crystallization from ethyl acetate gave 1.2 g. (32%) of white crystals, probably 3-(2-pyrrolidyl)-indole, m.p. 135–140°. Recrystallization from ethyl acetate raised the melting point to 145.8–146.6°.

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.4; H, 7.6; N, 15.0; mol. wt., 186. Found: C, 77.4; H, 7.6; N, 15.3; mol. wt., 183.

Attempted condensations of 1-pyrroline with 1-methylpyrrole and with carbazole gave only recovered starting materials.

Reaction of α-Tripiperideine with Pyrrole.—A mixture of 0.50 g. of pure α-tripiperideine, m.p. 61–63°, prepared by the method of Schöpf and Oechler,[14] and 10 g. of pyrrole was refluxed for 24 hours. Vacuum drying and then vacuum sublimation, gave 0.66 g. (74%) of a piperidylpyrrole, m.p. 87.5–90.5°.

Anal. Calcd. for $C_9H_{14}N_2$: C, 72.0; H, 9.4; N, 18.7; mol. wt., 150. Found: C, 72.0; H, 9.5; N, 18.9; mol. wt., 152.

LAWRENCE, KANSAS

[CONTRIBUTION FROM THE MOORE LABORATORY OF CHEMISTRY, AMHERST COLLEGE]

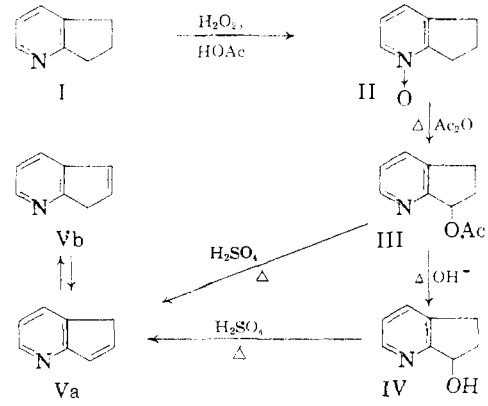
The Preparation of 1,5-Pyrindine[1]

BY MICHAEL M. ROBISON[2]

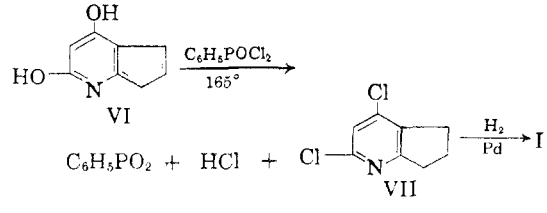
RECEIVED JULY 9, 1958

1,5-Pyrindine has been synthesized by treatment of 7-hydroxy-6,7-dihydro-1,5-pyrindine or its acetate ester with hot, concentrated sulfuric acid. The ester was prepared by treatment of 6,7-dihydro-1,5-pyrindine-N-oxide with acetic anhydride. Sodium bisulfite may be added to the rather unstable pyrindine in a manner apparently analogous to its addition to 2-vinylpyridine. Other chemical and physical properties of the unsaturated compound are described.

Although "pyrindane" (6,7-dihydro-1,5-pyrindine, I) and derivatives have been known for some time, no unsubstituted pyrindine has been prepared.[3] Perhaps the most purposeful approach to the synthesis of the unsaturated compound was that of Prelog and Szpilfogel[4] who attempted to dehydrogenate pyrindane. Dehydrogenation could not be effected either with palladium–charcoal at 350° or with selenium at 400°; in both cases starting material was recovered. Since the desired double bond could not be produced by this method, an alternative approach employed in this Laboratory involved the introduction of a functional group in the five-membered ring whose subsequent elimination resulted in unsaturation. This end was attained by rearrangement of pyrindane-N-oxide (II) on treatment with acetic anhydride.[5]



The requisite pyrindane was obtained *via* 2,4-dihydroxy-6,7-dihydro-1,5-pyrindine (VI) and the 2,4-dichloro derivative VII,[4] the former being



(1) This investigation was supported in part by a research grant, number C-2574, from the National Cancer Institute of the National Institutes of Health, Public Health Service.

(2) CIBA Pharmaceutical Products, Inc., Summit, N. J.

(3) R. C. Elderfield and E. T. Losin in Elderfield's "Heterocyclic Compounds," John Wiley and Sons, Inc., New York, N. Y., Vol. 3, 1952, p. 342.

(4) V. Prelog and S. Szpilfogel, *Helv. Chim. Acta*, **28**, 1684 (1945).

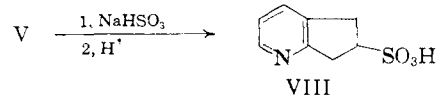
(5) *Cf.* G. Kobayashi and S. Furukawa, *Pharm. Bull. Japan*, **1**, 347 (1953); V. Boekelheide and W. J. Linn, THIS JOURNAL, **76**, 1286 (1954), and O. H. Bullitt and J. T. Maynard, *ibid.*, **76**, 1370 (1954), for analogous rearrangements with alkylpyridines.

synthesized by the method of Schroeder and Rigby.[6] Chlorodehydroxylation of VI was effected by the use of phenylphosphonic dichloride, a reagent which has been found[7] to be superior to the conventional phosphorus oxychloride for many transformations of this type, since reactions with the former, high-boiling substance may be run in an open vessel and on a large scale. Palladium-on-charcoal also was found to be more efficacious than Raney nickel[4] for the hydrogenolysis of VII, since in our hands reduction with the latter catalyst did not proceed to completion. The pyrindane was converted to the N-oxide in 94% yield on reaction with acetic acid–hydrogen peroxide by conventional methods. Treatment of II with acetic anhydride at 100° allowed isolation of 7-acetoxy-6,7-dihydro-1,5-pyrindine (III) in 77% yield. The ester could be converted directly to pyrindine in a yield exceeding 78% by treatment with concentrated sulfuric acid at 125°, or, alternatively, it could be saponified quantitatively to yield the corresponding, crystalline 7-hydroxy derivative IV. Dehydration of the latter with sulfuric acid under the conditions employed with III produced an 88% yield of the olefin.

Since 6,7-dihydro-2,5-pyrindine is known[8] and since rearrangement of 4-alkylpyridine-N-oxides also results in substitution at the alkyl group,[5] there is no apparent reason why 2,5-pyrindine could not also be prepared by this method.

Although the pyrindine apparently possesses marked stability in strongly acid medium, judging by the outcome of the dehydration reaction, the free base itself is quite unstable, like indene and 2-vinylpyridine. Even on storage under nitrogen at −20° in the presence of hydroquinone the material becomes dark red-brown in a few days, and on exposure to air at room temperature it darkens appreciably in a matter of hours.

The product was characterized by analysis, by its ultraviolet and infrared spectra and by its reaction with one mole of hydrogen to regenerate pyrindane. Further evidence for its structure was obtained from its reaction with sodium bisulfite to yield, presumably, 6,7-dihydro-1,5-pyrindine-6-sulfonic acid (VIII) by a conjugate addition similar to that which has been found to take place with 2-vinylpyridine.[9] A similar attempt to effect the uncatalyzed addition of piperidine[9]



VIII

was unsuccessful, starting material being recovered. The acid-catalyzed addition[10] was not investigated, however.

It seems very improbable that the olefin exists solely as 1,5-pyrindine (Va), or its isomer, 1,7-pyrindine (Vb). Rather, it is likely that the material is a mixture of labile, tautomeric forms. The conjugate addition merely indicates that the substance can react as the $\Delta^{6,7}$-compound, and ultraviolet measurements do not permit a decision between the two possible isomers. The ultraviolet spectrum (Fig. 1) is, however, consistent with the

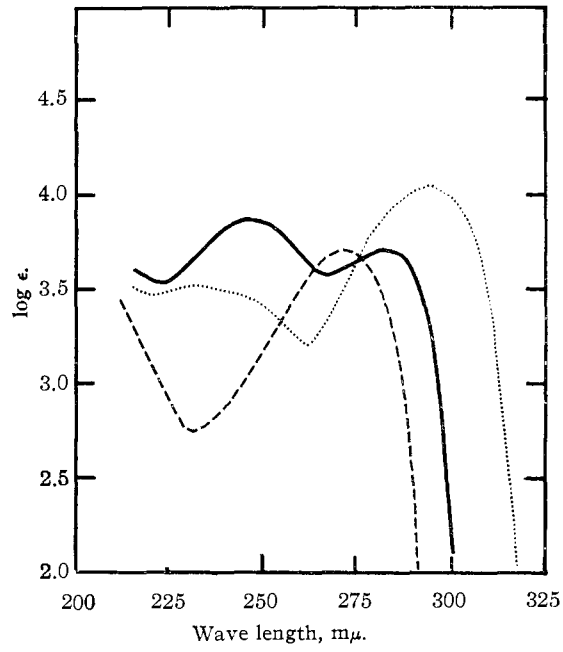


Fig. 1.—Spectra of: - - - - -, 6,7-dihydro-1,5-pyrindine in ethanol (from ref. 4); 1,5-pyrindine: ——, in cyclohexane; . . . . . , in 0.1 *N* HCl.

pyrindine structure, being related to the spectrum of pyrindane as the 2-vinylpyridine spectrum is to that of 2-picoline. It was expected on the basis of the proposed structure that the pyrindine would be colorless. Surprisingly, it was found that even after repeated distillation at pressures as low as 10^{-4} mm. the pure substance is orange. The orange color, which could not be removed by chromatography on alumina, is apparently not due to decomposition, for the colors of the first high-vacuum distillation fractions were not different from those of the residues. Further, it was noted that the orange color of a freshly-distilled sample vanishes strikingly on dilution of the compound with 2-3 volumes of an organic solvent. This visual evidence was confirmed by the absorption spectrum of the material. It was found that a 10^{-4} *M* solution of the substance in cyclohexane is completely transparent above about 305 mμ. It was further noted that the pure material can be frozen in Dry Ice to a solid which has a marked orange tinge initially, but which becomes essentially white on standing. The nature of the orange color of the liquid was not determined.

Because of an impending change of location we do not plan to continue the investigation of pyrindine.

Experimental[11,12]

6,7-Dihydro-1,5-pyrindine (I).—2,4-Dichloro-6,7-dihydro-1,5-pyrindine[7] (9.4 g.) was added to a solution of 7 g. of potassium hydroxide in 250 ml. of 95% ethanol and the solu-

(6) H. E. Schroeder and G. W. Rigby, THIS JOURNAL, **71**, 2205 (1949).
(7) M. M. Robison, *ibid.*, **80**, 5481 (1958).
(8) V. Prelog and O. Metzler, *Helv. Chim. Acta*, **29**, 1170 (1946).
(9) W. E. Doering and R. A. N. Weil, THIS JOURNAL, **69**, 2461 (1947).
(10) H. E. Reich and R. Levine, *ibid.*, **77**, 4913 (1955).
(11) Analyses by Drs. Weiler and Strauss, Oxford, England.
(12) Melting points are corrected, boiling points uncorrected.

tion was shaken with approximately 0.2–0.3 g. of 5% palladium-on-charcoal under hydrogen at 3 atmospheres pressure. During this initial treatment, typically, very little hydrogen was absorbed. After shaking for about 1 hour, approximately 0.5 g. of fresh catalyst was added and hydrogenation was resumed; nearly the theoretical quantity of hydrogen was then absorbed within a few hours. Four such runs were combined after filtration and acidified with phosphoric acid. The ethanol was distilled and steam was passed through the residue to remove a small quantity of weakly-basic material, which presumably included unchanged dichloro compound. When the distillate was clear the residue was made strongly alkaline and the pyrindane was steam distilled and extracted into ether. Evaporation of the dried extracts and distillation afforded 20.4 g. (86%) of colorless pyrindane, b.p. 84–87° (13 mm.), $n^{25}D$ 1.5421.[13]

6,7-Dihydro-1,5-pyridine-N-oxide (II).—A mixture of 15.47 g. of pyrindane, 78 ml. of glacial acetic acid and 13 ml. of 30% hydrogen peroxide was heated at 70–75° for 12 hours, 10.4 ml. more hydrogen peroxide being added after 3 hours. The reaction mixture was worked up by distillation of excess volatile reactants *in vacuo*, treatment of the residue with potassium carbonate and extraction of the product into chloroform, by the procedure used for the preparation of isoquinoline-N-oxide.[14] From the chloroform solution the crude oxide was obtained by evaporation and washing with low-boiling petroleum ether. The tan solid, m.p. 119–124°, weighed 16.48 g. (94%). From the petroleum ether unchanged starting material (3%) was recovered on evaporation. The N-oxide was purified for analysis by sublimation at 110° (0.1 mm.) and recrystallization from ethyl acetate as large, white leaves, m.p. 123.5–125°.

Anal. Calcd. for C_8H_9NO: C, 71.09; H, 6.71. Found: C, 70.86; H, 6.77.

It was subsequently found that alumina chromatography is superior to sublimation for decolorization of large batches of the oxide. A saturated solution of 22 g. of the colored material in acetone was filtered through a 3 × 11 cm. column of alumina[15] and elution was completed with more acetone. The recovery of snow-white solid was over 98%.

7-Acetoxy-6,7-dihydro-1,5-pyridine (III).—Water (1.4 ml., 0.08 mole) was allowed to react with 160 ml. of acetic anhydride[16] and 21.80 g. of the oxide was dissolved in the mixture by swirling. The pink solution was kept at room temperature for 1 hour, then warmed carefully to about 80°, at which point an exothermic reaction took place and occasional cooling was necessary to keep the temperature below 95°. When the temperature fell spontaneously the red-brown liquid was heated in a boiling water-bath for 2.5 hours. Evaporation of the acetic anhydride *in vacuo* and distillation of the residue afforded 21.95 g. (77%) of yellow oil, b.p. 92–96° (0.3 mm.), $n^{21}D$ 1.5285. Two more distillations produced a colorless analytical sample b.p. 94° (0.3 mm.), $n^{26.5}D$ 1.5260. The ultraviolet spectrum of the ester exhibited a maximum at 269 mμ (log ε 3.62) and a minimum at 229 mμ (log ε 2.76). Infrared absorption bands (carbon tetrachloride solution) were found at 1735 and 1240 cm.$^{-1}$ (ester function) and at 1580 cm.$^{-1}$ (ring vibrations).

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26. Found: C, 67.42; H, 6.19.

7-Hydroxy-6,7-dihydro-1,5-pyridine (IV).—A mixture of 1.31 g. of the acetate, 0.4 g. of sodium hydroxide and 3.6 ml. of water was heated on the steam-bath in a nitrogen atmosphere for 15 minutes. The dark solution was cooled, excess potassium carbonate was added and the oil was extracted into chloroform. Evaporation of the dried extracts after filtration through a pad of Darco afforded 1.00 g. (100%) of a light-violet solid, m.p. 84–86.5°. The analytical sample, m.p. 84.5–86°, was prepared by recrystallization from cyclohexane (Darco) and sublimation of the resulting stout, white needles at 80° (0.3 mm.).

Anal. Calcd. for C_8H_9NO: C, 71.09; H, 6.71. Found: C, 71.19, 71.15; H, 6.70, 6.69.

The ultraviolet spectrum was very similar to that of the ester, indicating that substitution had taken place in the 7-position, rather than in the pyridine ring. The absorption maximum was observed at 270.5 mμ (log ε 3.62) and the minimum at 226 mμ (log ε 2.43).

When the saponification was run on a larger scale, it was necessary to extend the heating period and to agitate the mixture to ensure complete reaction.

Pyrindine (V).—Ten milliliters of concentrated sulfuric acid was added in portions with stirring to 7.43 g. of the hydroxypyrindane; a thermometer was immersed in the mixture. During the addition the temperature rose to about 110°. The solution then was heated at 120–130° for 1 hour, during which period it became orange-brown. After cooling, the liquid was poured onto 80 g. of ice, and 44 g. of 50% sodium hydroxide solution was added with cooling. A trace of diphenylamine or hydroquinone was added at once and the water layer was saturated with sodium carbonate before extracting the brown oil into ether. The extract was dried over potassium carbonate and evaporated, and the residual oil was distilled in a stream of dry, oxygen-free nitrogen. The product was obtained as an orange liquid of strong, pyridine-like odor, b.p. 79–82° (8 mm.), yield 5.67 g. (88%). In the first attempt to prepare an analytical sample, the product was redistilled twice under nitrogen, b.p. 82° (8 mm.), $n^{26}D$ 1.5808, d^{24}_4 1.070. Although the orange liquid was sent in an evacuated ampoule, the color was brown when it was received by the analyst and carbon and nitrogen analyses were about 1% low. A somewhat more satisfactory sample finally was prepared in a high-vacuum system. After preliminary distillation as above, the final distillations were carried out at 10^{-4} mm. pressure and the ampoule was sealed without exposure to air. The orange color of this sample did not change while in transit. The substance (pure liquid film) exhibited strong infrared bands at 1380, 1400, 1570 and 1580 cm.$^{-1}$ and a weak shoulder at 1620 cm.$^{-1}$.

Anal. Calcd. for C_8H_7N: C, 82.01; H, 6.03; N, 11.96. Found: C, 81.63; H, 6.23; N, 12.4.

A paper chromatogram of the substance in butanol–acetic acid–water (60:15:25) revealed only one spot at R_f 0.73 on spraying with iodoplatinic acid. When 0.1 g. of the material was adsorbed on 10 g. of alumina[15] and eluted with benzene, some decomposition products were left at the top of the column. The eluted pyrindine was isolated by extraction into dilute hydrochloric acid, basification, extraction into ether and distillation *in vacuo*. The very small quantity of distilled material was still clearly orange.

The direct preparation from the ester was carried out by precisely the same procedure as used for the alcohol. From 8.86 g. of III there was obtained 4.59 g. (78%) of V, b.p. 89–91° (13 mm.), $n^{20}D$ 1.5810. Since a small quantity was spilled in the single preparation by this method, the actual yield is probably comparable to that in the dehydration.

Pyrindine Picrate.—A picrate was formed from equimolar quantities of the amine and picric acid in methanol and was recrystallized from the same solvent. The analytical sample was obtained in the form of yellow needles having a faint chartreuse cast, m.p. 181.5–184° dec.

Anal. Calcd. for $C_8H_7N \cdot C_6H_3N_3O_7$: C, 48.56; H, 2.91. Found: C, 48.82; H, 2.93.

Hydrogenation of Pyrindine.—One millimole of the amine was dissolved in 10 ml. of 95% ethanol and stirred with approximately 50 mg. of pre-reduced Adams catalyst in a hydrogen atmosphere. The compound reacted rapidly with precisely 100% of the theoretical volume of hydrogen. After separation of the catalyst, 6,7-dihydro-1,5-pyrindine picrate was formed in 86% yield by addition of ethanolic picric acid. This product melted at 177.5–180° *without* decomposition, both alone and on admixture with an authentic sample.[17]

6,7-Dihydro-1,5-pyrindine-6-sulfonic Acid (VIII).—Two millimoles of pyrindine was suspended in 1 ml. of water and 1 ml. of saturated sodium bisulfite solution was added.

(13) Prelog and Szpilfogel (ref. 4), who purified the base through the picrate, report b.p. 90° (11 mm.), $n^{20}D$ 1.54446.

(14) M. M. Robison and B. L. Robison, *J. Org. Chem.*, **21**, 1337 (1956).

(15) Fisher 80–200 mesh adsorption alumina was used.

(16) E. Ochiai and Y. Kawazoe, *Pharm. Bull. Japan*, **5**, 606 (1957), have noted that a trace of water is necessary in the rearrangement of isoquinoline-N-oxide. Use of the anhydrous oxide and pure acetic anhydride leads predominantly to tar formation; *cf.* ref. 14.

(17) Prelog (ref. 4) reported m.p. 181–182°. Although the melting points of the picrates of the reduced and unreduced compounds are almost identical, they are readily distinguishable in that the pyrindine derivative decomposes vigorously with gas evolution and blackening, while the dihydro derivative may be melted and remelted without appreciable chemical change.

The amine soon dissolved with evolution of some heat. The mixture was allowed to stand 10 minutes, excess concentrated hydrochloric acid was added and the solution was evaporated to dryness *in vacuo*. Concentrated hydrochloric acid was added to the residue and sodium chloride was separated by filtration, after which the filtrate again was evaporated to yield a yellow oil. Water was added and the solution was placed in a vacuum desiccator over potassium hydroxide. The resulting sticky, brown glass was transformed to a tan solid on warming with 95% ethanol. Recrystallization from the same solvent produced white microcrystals which had no definite melting point but which charred gradually over the range 240–300°. The yield of recrystallized solid was 214 mg. (54%).

Anal. Calcd. for $C_8H_9NSO_3$: C, 48.23; H, 4.55. Found: C, 47.94; H, 4.58.

Attempted Addition of Piperidine to V.—When 1.7 g. of piperidine was added to 1.17 g. of pyrindine, the color darkened. After a 4-hour reflux period, the piperidine was removed from the dark; tarry mixture under reduced pressure and the residue was distilled *in vacuo*. The recovery of unchanged starting material, b.p. 82–86° (16 mm.), $n^{24}D$ 1.5800, was 0.72 g. (62%). An appreciable, tarry residue remained. The distillate was converted to pyrindine picrate, m.p. 181–182.5° dec., both alone and on admixture with authentic material.

Absorption Spectra.—Ultraviolet spectra were measured with a Beckman model DU quartz spectrophotometer from cyclohexane solutions at 10^{-4} *M* concentration, except where otherwise specified. Infrared spectra were measured either with a Baird spectrophotometer or a Perkin–Elmer instrument by Dr. S. M. Nagy and associates at the Microchemical Laboratory, Massachusetts Institute of Technology, and by Dr. Louis A. Carpino, Department of Chemistry, University of Massachusetts.

AMHERST, MASS.

[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Synthesis and Some Stereochemical Aspects of Carbon-methylated Piperazine Quaternary Salts and Related Compounds

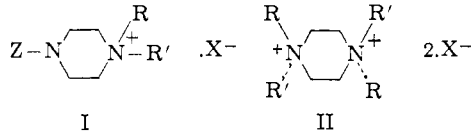
BY M. HARFENIST AND E. MAGNIEN

RECEIVED JUNE 6, 1958

A number of piperazine quaternary salts, most of which had methyl groups on the ring carbons, were made for anthelmintic testing. Procedures for the separation of the stereoisomeric forms of the monoquaternary salts III–V allowed the preparation of each of the stereoisomeric bis-quaternary salts VI, and the absolute identification of the racemic isomer VIb. The highest melting stereoisomer, VIa, had an excellent therapeutic index against *Syphacia obvelata* in the mouse.

The high activity against the mouse pinworm *Syphacia obvelata* of some of the piperazine monoquaternary salts previously reported[1] (I, Z = H, COOR, $CONR_2$, NO) led us to prepare a variety of related quaternaries. These include some monoquaternary salts like I, Z = $COOC_2H_5$ but with one or two ring carbons methylated, some like I but with Z = alkyl, and a number of piperazine bis-quaternaries, both with and without ring carbons methylated. Most of such compounds are tabulated below and require no further comment. However, it is necessary to consider certain facets of the stereochemistry of the bis-quaternary salts.

Only one isomer was isolated for each of the bis-quaternaries II; no attempt to obtain the other possible isomer was made. It can be assumed on the basis of earlier X-ray diffraction measurements[2] that, as would be anticipated, the isomers reported here are the (presumably less soluble) *trans* alkylated isomers shown.



I II

Because of the high therapeutic index (of the least soluble, highest melting isomer) of the 1,4-2,5-*trans*-tetramethyl-1,4-bis-dodecylpiperazinium salt VIa (see flow chart) against *S. obvelata* in the mouse, a more thorough study of its stereoisomers was made. It is apparent that VI exists as two *meso* forms VIa and VIc and one racemic pair (VIb and its enantiomer). It proved possible to isolate only the highest melting form directly in appreciable yield from the quaternization of N,N′-bis-dodecyl-2,5-*trans*-dimethylpiperazine with two moles of methyl iodide. A yield of about 40% of analytically pure material of constant melting point was obtained. This is shown below to be one of the *meso* forms.

It was necessary to prepare the other isomers of VI by the more selective process illustrated in the flow chart.

The separation of the two possible isomers of compound III was accomplished by crystallization of the bulk of the higher melting IIIa, and chromatography of the remaining material. Mixtures of IIIa and IIIb were obtained with either dodecylation, followed by methylation with methyl iodide to III as shown in the flow sheet, or by methylation of 1-carbethoxy-2,5-*trans*-dimethylpiperazine by the Clarke–Eschweiler method, and then quaternization with dodecyl iodide. The latter procedure appeared to give somewhat more of the lower melting IIIb, but dehydrohalogenation of the dodecyl iodide made a quantitative study difficult. In view of the vast body of literature on quaternization in which only one of a possible pair of stereoisomers is obtained by one order of alkylation–quaternization, and the epimer alone by reversing the order of addition of the two alkyl groups,[3] further study of this reaction is contemplated.

Decarbethoxylation of each isomer of III to the corresponding secondary amine IV with constant boiling aqueous hydrochloric acid was followed by dodecylation to the tertiary amines V. Treatment of the resulting isomers of V with methyl

(1) M. Harfenist, THIS JOURNAL, **79**, 2211 (1957).

(2) W. E. Hanby and H. N. Rydon, *J. Chem. Soc.*, 833 (1945).

(3) For a discussion of some factors influencing this specificity and many references, see G. Fodor, *Bull. soc. chim., France*, 1032 (1956); G. Fodor, *et al.*, *J. Chem. Soc.*, 1411 (1956), 3504 (1955); *cf.* also K. Zeile and W. Schulz, *Helv. Chim. Acta*, **88**, 1078 (1955).