Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.7; H, 7.94. Found: C, 66.8; H, 7.95.

β-Carboxy-γ-(*trans*-1-decalyl)-spirobutyrolactone (IX).—β-Carbethoxy-β-(*trans*-1-Δ¹-octahydronaphthyl)-propionic acid (2 g.) was refluxed with a mixture of glacial acetic acid (15 ml.) and concentrated hydrochloric acid (15 ml.) for 30 min. After cooling, the mixture was diluted, and the resulting semi-solid was isolated and crystallized from benzene–petroleum ether (b.p. 60–80°) as colorless prisms, m.p. 181–182° (0.7 g.).

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.7; H, 7.94. Found: C, 66.6; H, 7.96.

3-Carbethoxy-Δ⁸-octahydro-4,5-benzindan-1-one (X).—The half-ester VII (14 g.) in acetic anhydride (200 ml.) was refluxed with anhydrous zinc chloride (2 g.) in glacial acetic acid (100 ml.) for 5 hr. under nitrogen. Acetic acid and anhydride were removed *in vacuo* and the residue poured into water which was made alkaline with sodium carbonate. A dried ethereal extract on evaporation gave an almost colorless viscous oil, b.p. 163–165° (0.5 mm.) (8.9 g.), $n^{20}D$ 1.5190.

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.28; H, 8.39. Found: C, 72.9; H, 8.32.

The semicarbazone crystallized from ethanol; m.p. 222–223°. *Anal.* Calcd. for $C_{17}H_{25}O_3N_3$: C, 63.95; H, 7.84; N, 13.17. Found: C, 64.1; H, 7.96; N, 13.13.

The 2,4-dinitrophenylhydrazone, m.p. 199–200°, crystallized from ethanol–ethyl acetate as red prisms. *Anal.* Calcd. for $C_{22}H_{26}O_6N_4$: N, 12.67. Found: N, 12.99.

Δ⁸-Octahydro-4,5-benzindan-1-one (XI).[8]—A mixture of the keto ester X (5.2 g.) and concentrated hydrochloric acid (80 ml.) was refluxed for one hour. The reaction mixture, after dilution with equal volume of water, was ether-extracted. The ethereal solution was washed with sodium carbonate solution, water then dried. There resulted on distillation Δ⁸-octahydro-4,5-benzindan-1-one (XI), as colorless oil, b.p. 104–105° (0.2 mm.), $n^{20}D$ 1.5370 (yield 3 g.). The 2,4-dinitrophenylhydrazone, m.p. 203–204°, crystallized from ethanol–xylene as dark red plates.

Anal. Calcd. for $C_{19}H_{22}O_4N_4$: C, 61.62; H, 5.94; N, 15.13. Found: C, 61.49; H, 6.09; N, 14.73.

Decahydro-4,5-benzindan-1-one (XII).[8]—The unsaturated ketone XI (4 g.) was dissolved in ethanol (40 ml.) and hydrogenated at a 10% palladium–barium sulfate catalyst (1 g.) at atmospheric temperature and pressure. The uptake ceased when one mole had been absorbed. There resulted, after removal of the catalyst and solvent, a viscous oil which solidified under light petroleum (b.p. 40–60°) to give decahydro-4,5-benzindan-1-one (XII) as colorless prisms, m.p. 57.5–59° (yield 3.2 g.).

The 2,4-dinitrophenylhydrazone crystallized from ethanol–xylene in orange plates, m.p. 213–214° (lit.[8] gave a lower m.p. 204–205° from acetic acid).

Anal. Calcd. for $C_{19}H_{24}O_4N_4$: C, 61.3; H, 6.5; N, 15.1. Found: C, 61.2; H, 6.4; N, 15.0.

Acknowledgment.—The author wishes to thank Professor W. H. Linnell of the School of Pharmacy for his interest and advice in the execution of part of this research.

LONDON, ENGLAND
CAIRO, EGYPT

[COMMUNICATION NO. 1855 FROM THE KODAK RESEARCH LABORATORIES]

The Preparation of Some Vinylpiperidines

BY H. L. COHEN AND L. M. MINSK

RECEIVED OCTOBER 9, 1956

The preparation of 2- and 4-vinylpiperidines and their N-methyl derivatives is reported. None of the compounds could be homopolymerized by the usual methods.

Introduction

It has been reported by Heidrich[1] that 1-methyl-2-vinylpiperidine polymerizes on distillation or on standing for several months at room temperature. Since it is known that allylic amines, to which the 2-vinylpiperidines are formally similar, do not homopolymerize readily, it appeared of interest to prepare some of the vinylpiperidines and study their polymerization tendencies.

The preparation of 2-vinylpiperidine by the dehydration of 2-(2-hydroxyethyl)-piperidine, using a concentrated sulfuric acid–glacial acetic acid mixture at 165°, was reported by Ladenburg.[2] This compound was said to form a readily crystallizable picrate, although no details on the preparation or properties of this derivative were given. Dehydration, using concentrated hydrochloric acid at 165°, of 1-methyl-2-(2-hydroxyethyl)-piperidine was reported by Heidrich[1] to give 1-methyl-2-vinylpiperidine. No reports on the preparation of 4-vinylpiperidine or its N-methyl derivative could be found.

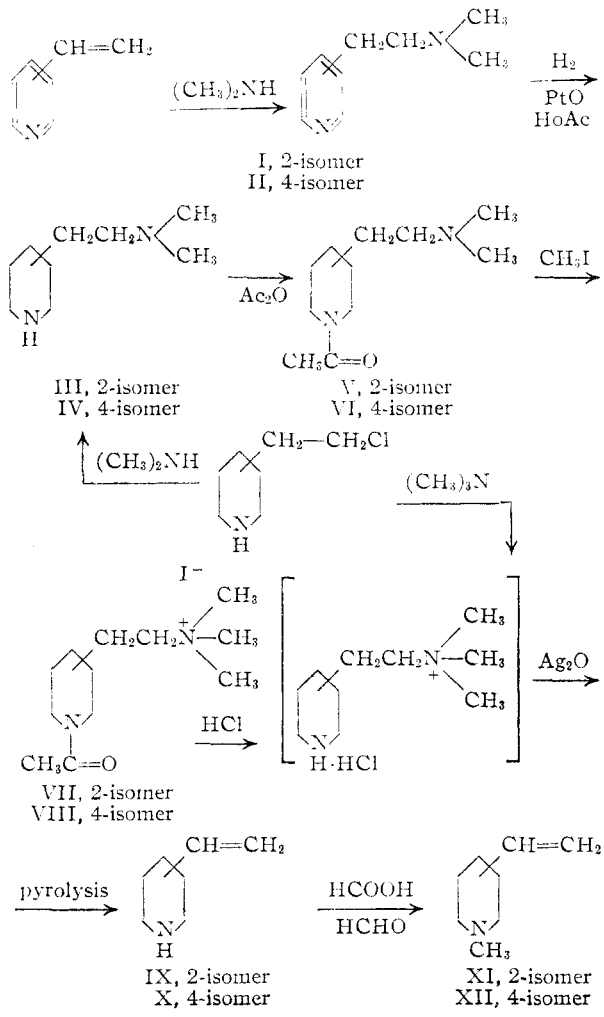
Attempts to dehydrate 2-(2-hydroxyethyl)-piperidine in these Laboratories, with Ladenburg's procedure, gave inconsistent results. At best, only a small yield (1 to 3%) of 2-vinylpiperidine was obtained. The major portion of the product consisted of material of unknown structure with a much higher boiling point than the starting material. It was only slightly soluble in ether and miscible with water. The fact that treatment with picric acid gave an oil from which only a small amount of crystalline material could be isolated would seem to indicate that this high-boiling material was not homogeneous. Dehydration of (2-hydroxyethyl)-piperidine in an alumina-packed column at various temperatures in the 375–425° range gave only small yields of basic material from which no pure vinylpiperidine could be isolated.

Since the yields in the dehydration studies were not encouraging, a synthetic sequence based on the pyrolysis of 2-(2-piperidinoethyl)-trimethylammonium hydroxide was tried (structures I–XII in the diagram). Addition of dimethylamine to 2-vinylpyridine in a steel bomb at 150° gave 2-(2-dimethylaminoethyl)-pyridine (I) in good yield.[3] Hydrogenation of this compound over Raney nickel at high pressure was not successful since

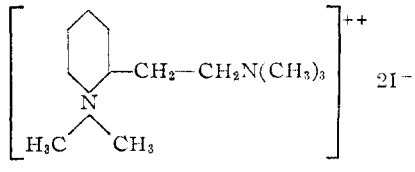
(1) M. Heidrich, *Ber.*, **34**, 1889 (1901).
(2) A. Ladenburg, *ibid.*, **22**, 2583 (1889).

(3) (a) Preparation of 2-(2-dimethylaminoethyl)-pyridine has been reported by H. E. Reich and R. Levine, THIS JOURNAL, **77**, 4913 (1955); (b) preparation of 4-(2-dimethylaminoethyl)-pyridine has been reported by A. J. Matuszko and A. Taurins, *Can. J. Chem.*, **32**, 538 (1954).

temperatures high enough to effect reduction caused reversal of the pyridoethylation reaction.[4] Hydrogenation in acetic acid solution over platinum oxide, on the other hand, proceeded smoothly at 60° and at 3 atm. pressure, giving a good yield of 2-(2-dimethylaminoethyl)-piperidine (III). This compound was also prepared by the reaction between 2-(2-chloroethyl)-piperidine hydrochloride and dimethylamine in a steel bomb at 125°.



Quaternization of III with a molar equivalent of methyl iodide was then attempted in the hope that addition would be limited to the tertiary amino group. It was found, however, that the heterocyclic nitrogen was attacked preferentially, a 25% yield of the diquaternary compound being the only product isolated.



(4) This result probably explains why W. E. Doering and R. A. N. Weil, THIS JOURNAL, **69**, 2461 (1947), obtained such a small yield from the reaction between 2-vinylpyridine and diethylamine. The temperature of their reaction (165°) would cause dissociation of the addition product.

The 2-(2-dimethylaminoethyl)-piperidine was therefore acetylated with acetic anhydride. This product reacted readily with methyl iodide to give a good yield of the quaternary iodo compound, VII. Conversion of this derivative to the quaternary hydroxide by using silver oxide, followed by pyrolysis, however, did not give the expected vinylpiperidine. Instead, some 2-(2-dimethylaminoethyl)-piperidine was recovered, together with other high-boiling material whose structure has not, as yet, been elucidated. Treatment of VII with concentrated sodium hydroxide, according to the procedure used by Woodward and Doering[5] for the preparation of homomeroquinine, gave a similar result.

The N-acetyl quaternary iodide was, therefore, hydrolyzed by refluxing with 6 *N* hydrochloric acid, and the amine, without isolation, was then subjected to the Hofmann elimination reaction, giving a moderate yield of the desired 2-vinylpiperidine (IX). Treatment of the 2-vinylpiperidine with a formaldehyde–formic acid mixture gave 1-methyl-2-vinylpiperidine (XI).

In an alternate synthesis, 2-(2-chloroethyl)-piperidine was heated with an excess of trimethylamine to 125° in a steel bomb. Following removal of excess trimethylamine, the residue, without purification, was subjected to the silver oxide pyrolysis procedure, giving a moderate yield of 2-vinylpiperidine. The respective 4-vinylpiperidines were obtained in an analogous manner.

Polymerization studies of these four compounds (IX, X, XI, XII) were not encouraging. Attempts to catalyze the polymerization by benzoyl peroxide, azobisisobutyronitrile, boron trifluoride, sulfuric acid and the persulfate–bisulfite oxidation–reduction system gave no isolable polymer. Contrary to Heidrich's results, N-methyl-2-vinylpiperidine could not be polymerized, even on heating for 6 hours at 165–175°. Since the properties of Heidrich's polymers are not given, this discrepancy in results cannot be explained. Irradiation of samples sealed in quartz with ultraviolet radiation caused separation of solid material in some cases. However, the supernatant liquids were not viscous and the solid materials were insoluble in fairly concentrated acetic acid, indicating that extensive decomposition had taken place.

Experimental

2-(2-Dimethylaminoethyl)-pyridine (I).—Commercial 2-vinylpyridine (Reilly Tar and Chemical Co.) was distilled, and the fraction boiling at 56–57° at 10 mm. was collected. A mixture of 65 g. (0.62 mole) of purified 2-vinylpyridine, 1 g. of hydroquinone, and 100 g. of anhydrous dimethylamine was heated in a steel bomb to 140–150° for 18 hours. After cooling, the contents were distilled, and the fraction boiling between 93–97° at 15 mm. was collected. This was redistilled through a 3-ft. glass helix-packed column with a variable take-off, giving 63 g. (68%) of a fraction boiling at 104–105° at 20 mm.

Anal. Calcd. for $C_9H_{14}N_2$: C, 71.93; H, 9.39; N, 18.65. Found: C, 72.0; H, 9.2; N, 18.6.

Monopicrate, m.p. 84.5–85.0° (from benzene–ether). Calcd. for $C_{15}H_{17}N_5O_7$: C, 47.49; H, 4.52; N, 18.46. Found: C, 47.5; H, 4.85; N, 18.45.

Dipicrate, m.p. 184–185° (from dioxane). Calcd. for

(5) R. B. Woodward and W. E. Doering, *ibid.*, **67**, 860 (1945).

$C_{21}H_{20}N_8O_{14}$: C, 41.45; H, 3.31; N, 18.42. Found: C, 41.75; H, 3.65; N, 18.45.

4-(2-Dimethylaminoethyl)-pyridine (II).—Prepared from distilled 4-vinylpyridine by the procedure described above, b.p. 108–109.5° at 14 mm., yield 77 g. (83%).

Anal. Calcd. for $C_9H_{14}N_2$: C, 71.93; H, 9.31; N, 18.65. Found: C, 72.15; H, 9.15; N, 18.5.

Monopicrate, m.p. 105.5–106.0° (from ethanol). Calcd. for $C_{15}H_{17}N_5O_7$: C, 47.9; H, 4.52; N, 18.46. Found: C, 47.7; H, 4.7; N, 18.55.

Dipicrate, m.p. 159–160° (from dioxane). Calcd. for $C_{21}H_{20}N_8O_{14}$: C, 41.45; H, 3.31; N, 18.46. Found: C, 41.6; H, 3.55; N, 18.7.

Attempted Reduction of 4-(2-Dimethylaminoethyl)-pyridine.—A mixture of 75 g. of 4-(2-dimethylaminoethyl)-pyridine, 150 ml. of dioxane and 15 g. of Raney nickel in a stainless-steel bomb was shaken with hydrogen at 200 atm. pressure as the temperature was slowly increased. At 160°, a small amount of hydrogen was absorbed, amounting to about 0.05 mole. Absorption then appeared to stop and did not resume, even though the temperature was raised to 180°. After keeping at 175° for 12 hours, the mixture was cooled, filtered and distilled. A yield of 60 g. of 4-vinylpyridine, b.p. 55–60°, was obtained. Picrate, m.p. 175–176°; mixed m.p. with authentic material 175–176°.

Preparation of 4-(2-Dimethylaminoethyl)-piperidine (IV).—A mixture of 18 g. (0.12 mole) of 4-(2-dimethylaminoethyl)-pyridine, 150 ml. of glacial acetic acid and 1.0 g. of Adams catalyst (smaller quantities resulted in incomplete reduction) was shaken on a Parr machine at 60° for 3 hours, by which time the theoretical amount of hydrogen had been absorbed. The mixture was filtered, and then evaporated to dryness on a steam-bath under vacuum. The residue, dissolved in 50 ml. of water, was made alkaline by the careful addition of 40 ml. of 50% sodium hydroxide solution, the temperature being kept below 20° by cooling in an ice-bath. After some additional water had been added to dissolve the precipitated sodium acetate, the two-phase system was extracted twice with 50-ml. portions of ether. The extracts were dried over anhydrous potassium carbonate, filtered, and distilled, giving 12.1 g. (66%) of material boiling between 103 and 107° at 17 mm. A fraction, b.p. 103–104°, was submitted for analysis.

Calcd. for $C_9H_{20}N_2$: C, 69.17; H, 12.90; N, 17.93. Found: C, 68.8; H, 13.15; N, 17.55.

Dipicrate, m.p. 188–189° (from alcohol). Calcd. for $C_{21}H_{26}N_8O_{14}$: C, 41.04; H, 4.27; N, 18.24. Found: C, 40.9; H, 4.4; N, 18.6.

Preparation of 2-(2-Dimethylaminoethyl)-piperidine (III) (Method A).—The reduction of 18 g. of 2-(2-dimethylaminoethyl)-pyridine in acetic acid solution by the procedure just described gave 14 g. (70%) of 2-(2-dimethylaminoethyl)-piperidine, b.p. 80–81° at 9 mm.

Anal. Calcd. for $C_9H_{20}N_2$: C, 69.17; H, 12.9; N, 17.93. Found: C, 69.5; H, 13.1; N, 18.3.

Dipicrate, m.p. 175.0–175.5° (from dioxane). Calcd. for $C_{21}H_{20}N_8O_{14}$: C, 41.04; H, 4.27; N, 18.24. Found: C, 41.2; H, 4.6; N, 18.0.

2-(2-Dimethylaminoethyl)-piperidine (Method B).—A mixture of 18.3 g. (0.1 mole) of 2-(2-chloroethyl)-piperidine hydrochloride, 22.5 g. (0.5 mole) of anhydrous dimethylamine and 60 ml. of anhydrous ethanol was heated in a stainless-steel bomb to 120–130° for 12 hours, then cooled.

After the precipitated methylamine hydrochloride was filtered, the solvent was evaporated on a steam-bath under vacuum. The residue, dissolved in 25 ml. of water, was treated with 20 ml. of 50% sodium hydroxide in small portions, the temperature being kept below 10°. The oil which separated was extracted with ether. The combined extracts were dried over potassium carbonate, filtered, and distilled, giving 8.4 g. (54%) of product, b.p. 81–82°. Dipicrate, m.p. 175–175.5°; mixed m.p. with dipicrate from method A, 175.0–175.5°.

Preparation of 1-Acetyl-2-(2-dimethylaminoethyl)-piperidine (V).—A solution of 145 g. (1.4 moles) of acetic anhydride in 350 ml. of ether was added dropwise over a period of one-half hour to a solution of 109 g. (0.7 mole) of 2-(2-dimethylaminoethyl)-piperidine in 1.0 liter of ether. After the solution had been refluxed for an additional hour, the condenser was removed, allowing the ether to evaporate. To the residue was added an equal volume of water, followed by enough anhydrous potassium carbonate to cause separation into two phases. The amine, which was insoluble in ether, was extracted with dioxane. The combined extracts were dried over potassium carbonate, filtered, and distilled, and the fraction boiling at 91–92° at 0.1 mm. was collected; yield 100 g. (72%).

Anal. Calcd. for $C_{11}H_{22}N_2O$: C, 66.61; H, 11.18; N, 14.13. Found: C, 66.4; H, 11.2; N, 14.3.

Picrate, m.p. 162–163° (from alcohol). Calcd. for $C_{17}H_{25}N_5O_8$: C, 47.77; H, 5.90; N, 16.39. Found: C, 47.8; H, 5.95; N, 16.1.

Preparation of 1-Acetyl-4-(2-dimethylaminoethyl)-piperidine (VI).—This compound was obtained in an 85% yield from 4-(2-dimethylaminoethyl)-piperidine by the method just described, b.p. 131.5–131.7° at 1.0 mm.

Anal. Calcd. for $C_{11}H_{22}N_2O$: C, 66.61; H, 11.18; N, 14.13. Found: C, 66.1; H, 11.45; N, 14.1.

Picrate, m.p. 114–116° (from alcohol). Calcd. for $C_{17}H_{25}N_5O_8$: C, 47.77; H, 5.90; N, 16.39. Found: C, 48.1; H, 6.1; N, 16.45.

Preparation of 2-[2-(1-Acetopiperidyl)]-ethyltrimethylammonium Iodide (VII).—A solution of 142 g. (1.0 mole) of methyl iodide in 350 ml. of acetone was added slowly, with swirling, to a solution of 100 g. (0.5 mole) of 1-acetyl-2-(2-dimethylaminoethyl)-piperidine in 500 ml. of acetone while the mixture was being cooled under a water tap. After standing overnight, the precipitate was filtered and dried; yield 175 g. (100%).

Recrystallization of 2.0 g. of this material from 100 ml. of boiling alcohol gave 1.5 g. (75%) of material which did not melt below 250°. It was not hygroscopic.

Anal. Calcd. for $C_{12}H_{25}N_2I$: C, 42.35; H, 7.41; N, 8.24; I, 37.30. Found: C, 42.3; H, 7.5; N, 7.8; I, 37.6.

Preparation of 2-[4-(1-Acetopiperidyl)]-ethyltrimethylammonium Iodide (VIII).—Prepared in 95% yield from 1-acetyl-4-(2-dimethylaminoethyl)-piperidine by the method just described, this quaternary salt was deliquescent. Recrystallization from alcohol gave an analytical sample.

Anal. Calcd. for $C_{12}H_{25}N_2I$: C, 42.35; H, 7.41; N, 8.25; I, 37.30. Found: C, 42.45; H, 7.55; N, 8.2; I, 37.3.

Preparation of 2-Vinylpiperidine (IX) (Method A).—A solution of 68 g. (0.2 mole) of 2-[2-(1-acetopiperidyl)]-ethyltrimethylammonium iodide and 250 ml. of concentrated hydrochloric acid in 250 ml. of water was heated under reflux for 72 hours. The mixture turned orange, and some iodine condensed on the condenser surface. The excess solvent was removed under vacuum on a steam-bath, leaving 75 g. of an orange, very viscous sirup which could not be caused to crystallize. It was dissolved in 100 ml. of water and treated with a suspension of freshly prepared silver oxide from 120 g. of silver nitrate in 750 ml. of water. The mixture was stirred for an additional hour, and then filtered.

The filtrate was then distilled to dryness. The first 750 ml. of distillate was neutral and was therefore discarded. The remainder of the distillate was saturated with potassium carbonate, causing separation of an oil. The phases were separated, and the aqueous phase was extracted three times with 50-ml. portions of ether. The combined ether extracts were dried over potassium carbonate, filtered, and distilled, giving 12.1 g. (55%) of colorless liquid, b.p. 139–144°, and 5.2 g. (16% recovery) of a fraction, b.p. 83–84° at 10 mm.

The fraction boiling at 139–144° was carefully refractionated, giving 11.0 g., b.p. 141–142° at atm. pressure; 68.0–69.0° at 58 mm.; 54° at 25 mm.; 47° at 17 mm.; $n^{25}D$ 1.4639.

Anal. Calcd. for $C_7H_{13}N$: C, 75.67; H, 11.78; N, 12.60. Found: C, 75.75; H, 11.85; N, 12.7.

Picrate, m.p. 142.5–143.5° (from benzene, then alcohol). Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.88; H, 4.74; N, 16.47. Found: C, 45.8; H, 4.8; N, 16.6.

The higher-boiling liquid was converted to its dipicrate, m.p. 172.5–174°, mixed melting point with authentic 2-(2-dimethylaminoethyl)-piperidine picrate, 173–174°.

Method B.—2-(2-Chloroethyl)-piperidine hydrochloride, m.p. 148–150°, was prepared by the method of Norton and collaborators.[6]

(6) T. R. Norton, R. A. Seibert, A. A. Benson and F. W. Bergstrom, THIS JOURNAL, **68**, 1572 (1946).

A mixture of 27 g. (0.15 mole) of 2-(2-chloroethyl)-piperidine hydrochloride, 50 g. (0.84 mole) of anhydrous trimethylamine, and 100 ml. of absolute methanol was heated in a steel bomb at 125° for 12 hours. After the bomb was opened, the excess trimethylamine and methanol were removed by heating on a steam-bath under vacuum. The resulting yellow viscous sirup was insoluble in ether and acetone and very soluble in alcohol. It was dissolved in 50 ml. of water and stirred for one hour with freshly precipitated silver oxide made from 100 g. of silver nitrate. The silver salts were filtered, and the filtrate was distilled to dryness. The portion of the distillate which was alkaline was saturated with potassium carbonate, extracted with ether, and the combined ether extracts were dried over potassium carbonate. After removal of the ether, distillation gave 3.4 g. (20%) of 2-vinylpiperidine, boiling at 138–142°. The picrate melted at 143–144° and showed no depression on mixing with the picrate obtained by using method A.

4-Vinylpiperidine (X) (Method A).—4-Vinylpiperidine was prepared from 2-[4-(1-acetopiperidyl)]-ethyltrimethylammonium iodide in the manner described; yield of 4-vinylpiperidine, 45%, b.p. 75.5–76.1° at 54 mm.; 54.5–55° at 18 mm.; n_D^{25} 1.4674.

Anal. Calcd. for $C_7H_{13}N$: C, 75.63; H, 11.78; N, 12.60. Found: C, 76.0; H, 11.8; N, 12.8.

Picrate, m.p. 136.5–137.5° (from ethanol). Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.88; H, 4.74; N, 16.47. Found: C, 45.9; H, 4.9; N, 16.6.

There was also isolated 4-(2-dimethylaminoethyl)-piperidine, b.p. 99–103° at 18 mm., representing a 27% recovery of this material. The melting point of picrate was 187–189°; mixed m.p. with known sample, 188–189°.

Method B.—4-(2-Chloroethyl)-piperidine was obtained in a 75% yield from 4-(2-hydroxyethyl)-piperidine by the method described for 2-(2-chloroethyl)-piperidine. It melted at 149–150°.

Anal. Calcd. for $C_7H_{15}NCl$: C, 45.76; H, 8.22; N, 7.61; Cl, 38.52. Found: C, 45.9; H, 8.3; N, 7.8; Cl, 38.5.

This was converted in 35% yield to 4-vinylpiperidine by the method already described for IX; melting point of the picrate, 135–137°, undepressed admixture with a sample prepared by method A.

Preparation of N-Methyl-2-vinylpiperidine (XI).—A mixture of 22.2 g. (0.2 mole) of 2-vinylpiperidine, 26 g. (0.5 mole) of 90% formic acid and 26 g. of 37% formaldehyde solution was heated 8 hours on a steam-bath. After the solution was cooled, 40 ml. of 6 *N* hydrochloric acid was added. The excess acid was then removed by heating on a steam-bath under vacuum. The residue was treated carefully with 20 ml. of 50% sodium hydroxide and cooled with ice to keep the temperature below 30°. The mixture was then extracted with ether, and the combined ether extracts were dried over potassium carbonate, and distilled. There was obtained 14 g. of material, b.p. 59–59.6° at 40 mm.

Anal. Calcd. for $C_8H_{15}N$: C, 76.73; H, 12.09; N, 11.19. Found: C, 76.9; H, 11.9; N, 11.3.

Heating at 160–170° for 6 hours in a sealed tube caused no change in the compound. Picrate, m.p. 150–151° (from alcohol). Calcd. for $C_{14}H_{18}N_4O_7$: C, 47.45; H, 5.12; N, 15.82. Found: C, 47.6; H, 4.7; N, 16.1.

Preparation of N-Methyl-4-vinylpiperidine (XII).—This was prepared in 60% yield from 4-vinylpiperidine by the method described for XI; b.p. 62–62.2° at 40 mm.

Anal. Calcd. for $C_8H_{15}N$: C, 76.73; H, 12.09; N, 11.19. Found: C, 76.6; H, 12.2; N, 11.25.

Picrate, m.p. 143–144° (from alcohol). Calcd. for $C_{14}H_{18}N_4O_7$: C, 47.45; H, 5.12; N, 15.82. Found: C, 47.3; H, 5.0; N, 15.9.

ROCHESTER 4, NEW YORK

COMMUNICATIONS TO THE EDITOR

RAPID DEUTERIUM EXCHANGE IN THIAZOLIUM SALTS[1]

Sir:

In the course of work on a model system for thiamine action we have been led to investigate the stability of an anion at C-2 of thiazolium salts (I). Such a species is formally analogous to a cyanide ion, in that both are anions on a carbon atom which is multiply bonded to nitrogen,[2] and (I) might be expected to catalyze benzoin condensation and similar reactions in the same fashion as does cyanide ion. This is of special interest since thiazolium salts are known to be catalysts for the benzoin condensation,[3] and since thiamine, a thiazolium salt, is involved in biological catalysis of reactions formally analogous to the benzoin condensation.

It was decided that deuterium exchange would be the best way to demonstrate whether such an anion is indeed stable, since deuterium exchange at C-2 could only occur, under mild conditions, through the formation of (I), electrophilic attack by a deuteron on the positively charged thiazolium ring being of course quite improbable. It has been found that thiazolium salts do indeed exchange at C-2 with deuterium oxide very readily, and that *this occurs in the absence of any basic catalyst.*

3,4-Dimethylthiazolium bromide (II) incorporates one atom of deuterium (found,[4] 1.1 atoms) on standing in D_2O at room temperature for 20 hours, and then vacuum drying. Similarly 3-benzyl-4-methylthiazolium bromide incorporates 1.2 atoms of deuterium under these conditions. Both compounds show a strong C–D stretching band[5] in the infrared (KBr pellet) at 4.5μ. The high intensity compared to that in a synthetic sample of 3-benzyl(α-d_2)-4-methylthiazolium bromide suggests that the deuterium is not located on a saturated carbon, and this is supported by the

(1) This is part II of the series "The Mechanism of Thiamine Action"; for part I see R. Breslow, *Chemistry and Industry*, R 28 (1956).

(2) A related species apparently is formed during the decarboxylation of pyridine-2-carboxylic acid (B. R. Brown and D. Ll. Hammick, *J. Chem. Soc.*, 659 (1949)).

(3) T. Ugai, S. Tanaka and S. Dokawa, *J. Pharm. Soc. Japan*, **63**, 269 (1943).

(4) The author wishes to acknowledge the assistance of Miss Laura Ponticorvo with these analyses, which were done by combustion and mass-spectral analysis after conversion of water to hydrogen gas.

(5) See, for instance, R. N. Jones and C. Sandorfy in A. Weissberger "Techniques of Organic Chemistry," Vol. IX, Interscience Publishers, New York, N. Y., 1956, Chap. IV.