Amination Reactions of *cis*-1,4-Dichloro-2-butene

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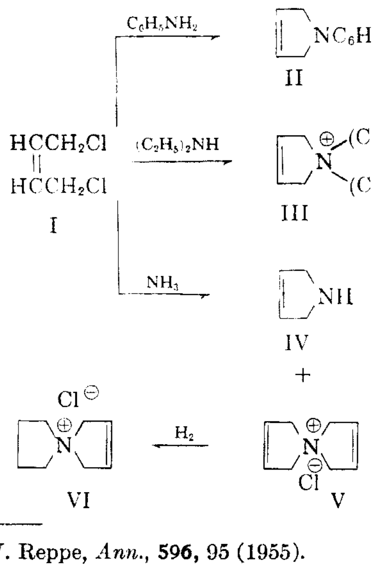
Ammonia and amines with *cis*-1,4-dichloro-2-butene produce cyclic products in contrast to their reactions with *trans*-1,4-dichloro-2-butene, which yield diamines or polyamines of high molecular weight. Although 3-pyrroline may be obtained from ammonia, the more readily obtainable product is a spiro compound formed by reaction of two moles of the dichloride with one mole of ammonia.

cis-1,4-Dichloro-2-butene, I, reacts with ammonia and with amines to yield cyclic products. Thus, with the primary amine aniline, *N*-phenyl-3-pyrroline, II, is formed, and with the secondary amine diethylamine, *N*,*N*-diethyl-3-pyrrolinium chloride, III, is formed and was isolated as its picrate. Secondary amines exemplified by pyrrolidine and morpholine have been reported[1] to yield noncyclic *N*,*N*,*N'*,*N'*-tetrasubstituted 2-butene-1,4-diamines when treated with the *cis* dichloride. Reaction of the dichloride with ammonia yields the expected 3-pyrroline, IV, in small amounts and the unexpected spiro compound 5-azaspiro[4.4]nona-2,7-dienium chloride, V, in larger quantities. The structure of the spiro compound was established by catalytic hydrogenation to the known[2] 5-azaspiro[4.4]nonanium chloride, VI. Identity was established also by comparison with an authentic sample prepared from pyrrolidine and 1,4-dichlorobutane. The unexpected formation of a spiro compound is analogous to the formation of 5-azaspiro[4.4]nonanium bromide from the reaction of ammonia with 1,4-dibromobutane.[3]



This general behavior of the *cis* dichloride may be contrasted with the *trans*, which with secondary amines readily gives good yields of *N*,*N*,*N'*,*N'*-tetraalkyl-2-butene-1,4-diamines and with primary amines or ammonia gives largely products of very high molecular weight.[4]

A preparation of *cis*-1,4-dichloro-2-butene from *cis*-2-butene-1,4-diol[5] utilizing thionyl chloride as a chlorinating agent is described. The picrate of 5-azaspiro[4.4]nonanium chloride is also described.

EXPERIMENTAL

The melting points of the spiro compounds were taken on a Kofler Melting Point Apparatus and are corrected. All others were taken in an oil bath and are also corrected. The analyses were performed by Carl Tiedke's Laboratory of Microchemistry in Teaneck, N. J., Geller Laboratories of Bardonia, N. Y., and Alfred Bernhardt of Muhlhein/Ruhr, Germany.

cis-1,4-Dichloro-2-butene (I). Thionyl chloride, 208 g. (1.74 moles), was added dropwise, over about 3 hr., to a cooled (below 10°), stirred mixture of 54 g. (0.61 mole) of *cis*-2-butene-1,4-diol and 1 ml. of pyridine. The mixture was allowed to stand overnight at room temperature and distilled through a 20-cm. Vigreux column under water pump vacuum. The fraction boiling at 83–85° (80 mm.) amounted to 43 g. (56%) of *cis*-1,4-dichloro-2-butene. Reported b.p. 22.5° (3 mm.) and 152.5° (758 mm.).[6] This compound was also obtained in essentially the same yield when an excess of pyridine was used, and in 43% yield from the diol, phosphorus trichloride, and pyridine.[6]

1-Phenyl-3-pyrroline (II). A solution of 62.5 g. (0.5 mole) of *cis*-1,4-dichloro-2-butene in 40 ml. of anhydrous benzene was added slowly and with cooling to a solution of 279 g. (3 moles) of aniline in 300 ml. of benzene. The mixture was allowed to stand for several days until there was no further precipitation. The aniline hydrochloride precipitate, after drying, weighed 122.6 g. (95%). The filtrate was distilled at atmospheric pressure to remove the benzene and then at 5 mm. to remove the aniline. The still-pot residue yielded, after recrystallization from methanol, 44.4 g. (61%) of 1-phenyl-3-pyrroline, m.p. 101–102° (reported[7] m.p. 101–102°).

1,1-Diethylpyrrolinium chloride (III *as picrate*). A solution of 62.5 g. (0.5 mole) of *cis*-1,4-dichloro-2-butene in 40 ml. of anhydrous benzene was added slowly, with cooling, to 219.4 g. (3 moles) of diethylamine in 375 ml. of anhydrous benzene. The mixture was allowed to stand at room temperature for several days with periodic filtering until no more precipitate formed. The combined hygroscopic precipitates were dissolved in a small amount of water, cooled, and treated with a saturated solution of sodium hydroxide. Three layers were obtained: diethylamine, a yellow-orange oil, and the aqueous layer. When the diethylamine layer was

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(1) W. Reppe, *Ann.*, **596**, 95 (1955).

(2) F. F. Blicke and E. B. Hotelling, *J. Am. Chem. Soc.*, **76**, 5099 (1954).

(3) J. v. Braun, *Ber.*, **70**, 979 (1937).

(4) L. H. Amundsen, R. H. Mayor, L. S. Pitts, and L. A. Melentacchi, *J. Am. Chem. Soc.*, **73**, 2118 (1951).

(5) This chemical was graciously provided by the General Aniline and Film Co., Inc., of Easton, Pa. Before it became commercially available, some was made in this laboratory by the hydrogenation over Raney nickel of 2-butyne-1,4-diol, obtained from the General Aniline and Film Co. [A. W. Johnson, *J. Chem. Soc.*, 1014 (1946)].

(6) K. Mislow and H. M. Hellman, *J. Am. Chem. Soc.*, **73**, 244 (1951).

(7) A. Arbuzov, *Doklady Akad. Nauk S.S.S.R.*, **63**, 531 (1948); *Chem. Abstr.*, **43**, 5403 (1949).

distilled, no other product was detected. The yellow oil (42 g., 52%) was presumed to be 1,1-diethylpyrrolinium chloride, and this was confirmed by conversion to a *picrate* that melted at 247–248° after recrystallization from ethanol.

Anal. Calcd. for $C_{14}H_{18}N_4O_7$: C, 47.45; H, 5.12; N, 15.81. Found: C, 47.28; H, 5.19; N, 15.71.

3-Pyrroline (IV). *cis*-1,4-Dichloro-2-butene (62.5 g., 0.5 mole) dissolved in 150 ml. of ethanol was added slowly and with cooling to 667 ml. (10 moles) of 28% aqueous ammonia. Enough additional ethanol was added to produce one phase. After the mixture had been standing at room temperature for 3 days, air was passed through it to remove the excess ammonia. The mixture was neutralized with concd. hydrochloric acid, with cooling, and evaporated to dryness under vacuum. The solid was dissolved in the minimum amount of water, which was then made strongly basic with sodium hydroxide and extracted with ether. The extract was washed with saturated aqueous sodium chloride, dried over potassium hydroxide, and distilled to yield 4.8 g. (14%) of 3-pyrroline boiling at 91° (reported[8] b.p. 90–91°). A *picrate* was prepared which melted at 155.6–157° (reported[9] m.p. 156°).

5-Azaspiro[4.4]nona-2,7-dienium chloride (V). Freshly distilled *cis*-1,4-dichloro-2-butene (30 g., 0.24 mole) was added to 100 ml. of absolute ethanol which had previously been saturated with anhydrous ammonia at 25°. After about 30 min., a white precipitate began to form. After 36 hr. at 5°, the ammonium chloride (14 g., 73%) was filtered. The filtrate was shaken for 1 hr. with 25 g. of Amberlite IRA-400 (basic form, dried overnight with Drierite under vacuum) to transform the remaining ammonium chloride to ammonia. The resin was filtered and the solvent was removed *in vacuo* at 40° to give 15.2 g. of a semicrystalline, yellow material. This material was triturated with four successive portions of dry acetone and filtered to yield 13.6 g. (72%) of slightly yellow,[10] slightly hygroscopic product, m.p. 259–260°. A portion was decolorized by recrystallization from absolute ethanol (dissolved warm and cooled in Dry Ice-acetone) and dried over phosphorus pentoxide under vacuum at 80°, m.p. 260–261°.

Anal. Calcd. for $C_8H_{12}ClN$: C, 60.99; H, 7.67; Cl, 22.55; N, 8.88. Found: C, 60.90; H, 7.77; Cl, 22.61; N, 8.97.

A *picrate* was prepared in ethanol and recrystallized from the same solvent, m.p. 218–219°.

Anal. Calcd. for $C_{14}H_{14}N_4O_7$: C, 48.00; H, 4.03; N, 16.00. Found: C, 48.26; H, 4.11; N, 16.07.

A *styphnate* was prepared in absolute ethanol and recrystallized from the same solvent, m.p. 140.5–141°.

Anal. Calcd. for $C_{14}H_{14}N_4O_8$: C, 45.90; H, 3.85; N, 15.30. Found: C, 45.87; H, 3.97; N, 15.50.

5-Azaspiro[4.4]nonanium chloride (VI). Pyrrolidine and 1,4-dichlorobutane were condensed in the presence of sodium hydroxide by the general procedure of Blicke and Hotelling[2] to give a low yield (8%) of hygroscopic product, m.p. 289–295°[11] (reported[2] m.p. 277–279°). The *chloroaurate*[2] melted at 254–256° (reported[2] m.p. 254–256°). A *picrate* was prepared in absolute ethanol and recrystallized from the same solvent, m.p. 263–264°.

Anal. Calcd. for $C_{14}H_{18}N_4O_7$: C, 47.45; H, 5.12; N, 15.81. Found: C, 47.63; H, 5.19; N, 15.76.

Reduction of 5-azaspiro[4.4]nona-2,7-dienium chloride (V). A mixture of 3 g. of 5-azaspiro[4.4]nona-2,7-dienium chloride, 0.25 g. of 5% palladium on charcoal and 75 ml. of absolute ethanol was hydrogenated at 33 p.s.i. Hydrogenation was complete in about 11 min.; after filtration, the solvent was removed under reduced pressure. After the addition of 100 ml. of dry benzene, the crystalline product was filtered in the absence of air and dried at 80° under reduced pressure; yield 2.4 g. (79%) of 5-azaspiro[4.4]nonanium chloride; m.p. 286–289°.[11] The *picrate* melted at 264–265° and the *chloroaurate* melted at 256–262°. In each case, mixture melting points with the synthetic specimens described above were undepressed.

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[8] G. L. Ciamician and M. Dennstedt, *Ber.*, **15**, 1831 (1882).

[9] F. Anderlini, *Ber.*, **22**, 2512 (1889).

[10] The amount of color varied directly with the time elapsing between distillation and use of the dichloride.

[11] The extreme hygroscopic nature of this substance causes its melting point to depend upon how it is taken. This sample was baked on a Kofler block at 250° before the measurement was taken.

Heterocyclic Compounds from Dinitriles[1]

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As part of a general study on the preparation of heterocyclic nitrogen compounds form nitriles[2–5] in cold concentrated sulfuric acid, a logical extension of this reaction was pursued which led to α,ω-bis(heterocyclyl)alkanes, I, Ia. The addition of 2,5-dimethyl-2,5-hexanediol, 2-methyl-2,4-pentanediol, and 4-mercapto-2-methyl-2-butanol to a cold solution of a dinitrile in concentrated sulfuric acid yielded *N*-heterocyclic bases of the type, II, III, and IV, respectively. This reaction is considered to occur in a manner completely analogous to that which affords the corresponding monocyclic derivatives.[5]

The ring closure may be limited to the formation of a monocyclic product by utilizing equimolar quantities of the dinitrile and the alcohol derivative. Under the conditions of the reaction, no appreciable hydrolysis of the remaining nitrile group occurs. This fact was demonstrated when 2-methyl-2,4-pentanediol was added to an excess of succinonitrile in sulfuric acid. When the reaction mixture was quenched in ice and water and subsequently neutralized, only the 2-(2-cyanoethyl)dihydro-1,3-oxazine (V) was isolated and no amide (VI) was found to be present. There was obtained, however, a considerable quantity of succinamide derived from the excess succinonitrile employed in the reaction. This reaction was previously performed in connection with another study and details are given elsewhere.[4] This behavior has been

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[1] This investigation was supported by funds granted by the United States Public Health Service, National Institutes of Health (RG-6248).

[2] A. I. Meyers and J. J. Ritter, *J. Org. Chem.*, **23**, 1918 (1958).

[3] A. I. Meyers, *J. Org. Chem.*, **24**, 1233 (1959).

[4] A. I. Meyers, *J. Org. Chem.*, **25**, 145 (1960).

[5] A. I. Meyers, *J. Org. Chem.*, **25**, 1147 (1960).