earlier.[4,12,13] The physical properties of previously unreported free bases are given in Table II.

4-(4-Biphenylyl)-2-methyloxazole.—Acetamide (7.72 g.) and *p*-phenylphenacyl bromide (35.7 g.) were melted together and heated for 4 hours at 165°. The acetamide was removed from the reaction mixture with water, and the remaining solid was dried and extracted with boiling ethanol. The ethanol solution was taken to dryness, and the solid was triturated with boiling hexane. The product from the hexane was recrystallized twice to give 0.34 g.

4-[5-Phenyl-2-(1,3,4-oxadiazolyl)]-pyridine.—To a solution of 4.1 ml. of benzoyl chloride in pyridine was added 5.1 g. of isonicotinoyl hydrazide. The solution was heated for five minutes on a water-bath, cooled and poured into water. The solid was filtered off, dried (7 g.) and recrystallized from water to give **1-benzoyl-2-isonicotinoylhydrazine**, m.p. 232–234°. *Anal.* Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.77; H, 4.80; N, 17.62.

A solution of 4.9 g. of the hydrazine in 25 ml. of phosphorus oxychloride was refluxed for five hours. The excess phosphorous oxychloride was removed, and the residue was poured into water. The water was taken to *p*H 6 and the solid was filtered off, dried and recrystallized to give 2.8 g.

4-(5-Phenyl-2-oxazolyl)-pyridine N-Oxide.—A mixture of 1 g. of 4-(5-phenyl-2-oxazolyl)-pyridine, 15 ml. of glacial acetic acid and 1.5 ml. of 30% hydrogen peroxide was heated on a water-bath for seven hours. The reaction mixture was taken to dryness and the residue was washed with ether. Recrystallization from acetone gave 0.46 g.

The ultraviolet absorption spectra were taken with a Beckman model DK-1 recording spectrophotometer. The solutions were of 95% ethanol and the concentrations were *ca.* 2.5×10^{-5} mole/l. The infrared absorption spectra of these compounds may be found in the Sadtler Standard Spectra.[14]

Acknowledgments.—The authors wish to express their appreciation to Dr. J. E. Furchner for making available the results of the hypotensive testing, and to Dr. G. H. Daub for valuable discussion. Mrs. R. Lier determined a number of the ultraviolet spectra.

(12) V. N. Kerr, F. N. Hayes, D. G. Ott and E. Hansbury, *J. Org. Chem.*, in press.

(13) V. N. Kerr, F. N. Hayes, D. G. Ott, R. Lier and E. Hansbury, *J. Org. Chem.*, in press.

(14) Samuel P. Sadtler and Son, Inc., Research Laboratories, Philadelphia 2, Pa.

LOS ALAMOS, N. MEX.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BRIGHAM YOUNG UNIVERSITY]

Quinoxalines. I. Preparation and Stereochemistry of Decahydroquinoxalines

BY H. SMITH BROADBENT, EVAN L. ALLRED,[1] LYNN PENDLETON[1] AND CHARLES W. WHITTLE[1]

RECEIVED MAY 26, 1959

The first authentic synthesis of *cis*-decahydroquinoxaline (XI) (m.p. 56–58°) is herein described. It was obtained in high yield by the hydrogenation of quinoxaline (X), or tetrahydroquinoxaline, over 5% rhodium-on-alumina catalyst at 100° and 136 atm. or over freshly prepared Raney nickel W-6 under similar conditions. Evidence is presented supporting the stereochemical assignment and demonstrating that previously reported preparations of decahydroquinoxaline have yielded either tetrahydroquinoxaline (VII), *trans*-decahydroquinoxaline (VIII) or mixtures of the *cis* and *trans* forms.

Decahydroquinoxaline should exist in two geometrically isomeric forms, *cis*- XI and *trans*- VIII depending on the manner of fusion of the cyclohexane and piperazine rings. The presence of the hetero atoms further introduces the possibility of molecular dissymmetry, the *cis* form being *meso* and the *trans* form the racemic (D,L) compound or mixture. Conformational variations involving boat or chair rings and equatorial or axial N–H bonds are also possible.

In the first reported preparation of a decahydroquinoxaline, Mousseron and Combes[2] treated cyclohexene oxide (IV) with 2-aminoethanol followed by chlorination and ammonolytic ring closure. Neither yields nor physical constants were given for the decahydroquinoxaline. An N,N′-dinitroso derivative melting with decomposition at 160° was mentioned. This has now been shown to be N,N′-dinitrosotetrahydroquinoxaline.

Later Beck, Hamlin and Weston[3] prepared a decahydroquinoxaline, m.p. 150–151° (24%), by the action of ethylenediamine on cyclohexene oxide followed by catalytic dehydrative ring closure. Its hydrochloride melted at 365° dec. Neither group discussed the problem of stereoisomerism.

We have now succeeded in the complete hydrogenation of either quinoxaline (X) or of tetrahydroquinoxaline (VII) directly to decahydroquinoxaline by the use of the proper catalytic system, *viz.*, either freshly prepared Raney W-6[4] or 5% rhodium-on-alumina[5] (preferably the latter) at 100° and 136 atm., to give virtually quantitative yields of pure material XII melting at 56–58°. The reaction, however, is extremely sensitive to poisoning of the catalyst. The N,N′-dinitroso derivative was also prepared, m.p. 87–89°.

In view of the known stereochemistry of epoxide ring openings, catalytic hydrogenations and symmetry-physical property considerations, we tentatively assigned the *trans* configuration to the high melting product of Beck, *et al.*, and the *cis* configuration to the low melting, more soluble product we had obtained by hydrogenation. Later work has confirmed this assignment.

Subsequently, Christie, Rohde and Shultz[6] reported the hydrogenation of tetrahydroquinoxalinium ion (VII) in ethanolic hydrogen chloride using platinum oxide at 60° and 50–80 p.s.i.g. Despite a reported crude yield of 90% crude dihydrochloride, the final yield of product melting

(1) Abstracted from the M.S. Thesis, of E. L. A. (1955), C. W. W. (1956) and L. P. (1958).

(2) M. Mousseron and G. Combes, *Bull. soc. chim. France*, 82 (1947).

(3) K. M. Beck, K. E. Hamlin and A. W. Weston, THIS JOURNAL, **74**, 605 (1952).

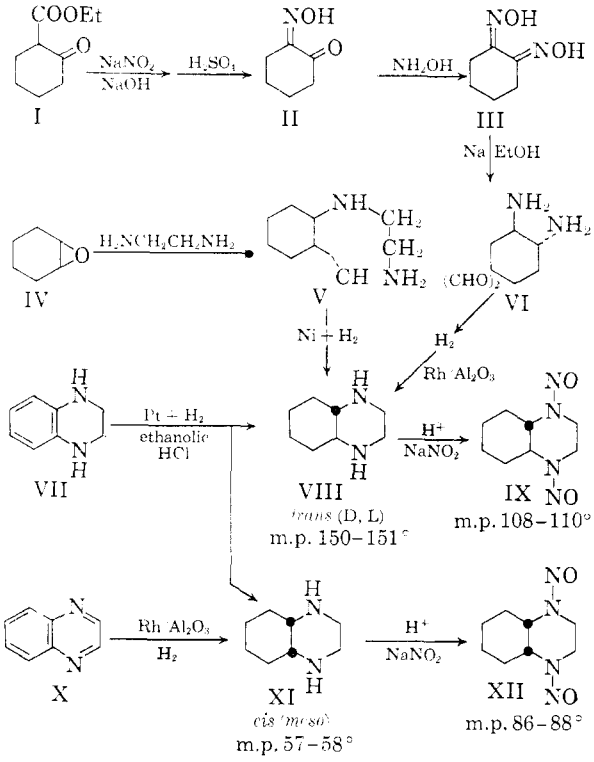
(4) H. R. Billica and H. Adkins, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 176.

(5) Baker and Co., Inc., "Engelhard Industries News-Letter," January, 1950.

(6) W. Christie, W. Rohde and H. P. Shultz, *J. Org. Chem.*, **21**, 243 (1956).

at 152.5–153° (from petroleum ether) was astonishingly low (12.8%). The N,N′-dinitroso derivative IX melted at 110–111°. Because of the method of preparation they provisionally assigned to their product (and that of Beck, *et al.*, which had the same properties) the *cis* configuration. Since Mousseron's substance gave a different dinitroso derivative, it was assumed to be *trans*.

A vigorous investigation, which had been underway in our own laboratories to establish the configuration of the decahydroquinoxalines conclusively, was now directed also toward an elucidation of the apparent discrepancies between the reported data and our own. The results are given.



The work of Shultz, *et al.*,[6] and of Beck, *et al.*,[3] was carefully repeated and confirmed; however, prior to final purification the decahydroquinoxaline prepared according to the former method melted over a considerable range, 57–132°. This substance was separated by chromatography on a neutral alumina (Woelm, activity grade 1) column by adsorption from ethyl ether followed by elution with alcohol-free chloroform into substantial proportions of both the low and the high melting forms of decahydroquinoxaline. A similar procedure revealed the presence of only a trace of the high melting isomer in the decahydroquinoxaline prepared by our own method together with spectrophotometric traces of tetrahydroquinoxaline accompanying the predominant low melting form of decahydroquinoxaline. The identity of all fractions was confirmed by analysis and ultraviolet spectra. By analogy it would appear that the product of Beck and co-workers, which was not chromatographically examined, was predominantly the high melting form accompanied perhaps by small amount of the low melting form. Experiments on test mixtures of both forms together demonstrated that recrystallization from petroleum ether results in the rapid isolation of the pure high melting form only, in explanation of the work of Shultz and co-workers.

The technique of gas partition chromatography likewise made possible a partial separation of the crude decahydroquinoxalines into the low and high melting forms at 208° on a 10-ft. silicone column. The two fractions collected melted at 55–63 and 140–145°, respectively. These were further identified by analysis and derivatives. Carbowax and diglycerol columns would not effect separation.

An authentic specimen of N,N′-dinitrosotetrahydroquinoxaline was prepared and found to be identical in behavior with that reported by Mousseron as the N,N′-dinitrosodecahydroquinoxaline. Further the dinitroso derivative of the product of Beck, *et al.*, was prepared. A mixed melting point determination confirmed its identity with that obtained by Shultz, *et al.*

Two logical approaches were available for making the correct configurational assignments for the two isomers: *trans*-decahydroquinoxaline, being a racemate of D- and L- forms could be resolved into its optical antipodes or either isomer could by synthesized by a stereospecific route. The former approach utilizing seven different derivatives, the mono-*d*-tartrate, the di-*d*-tartranilate, the mono-*l*-malate, the di-*d*-10-camphorsulfonate, the mono-*d*-camphorate, the mono-*l*-5-pyrrolidone-2-carboxylate and the 1,4-bis(-*l*-menthoxyacetyl), was tried and proved unfruitful in our hands.

The latter approach was successful and the identity of the high melting isomer of decahydroquinoxaline as the racemic *trans* form VIII was unequivocally established by its synthesis from *trans*-1,2-cyclohexanediamine[7,8] (VI) prepared from ethyl 2-oxocyclohexanecarboxylate (I) as indicated on the equation diagram. The *trans*-cyclohexanediamine was condensed first with aq. glyoxal, yielding a highly labile hexahydroquinoxaline intermediate which could not be isolated but which was hydrogenated directly giving a 20% yield of pure vacuum sublimed *trans*-decahydroquinoxaline, m.p. 147–148°. Although considerable tar was formed no evidence of the low melting *cis* isomer could be detected.

Dehydrogenation of *cis*-decahydroquinoxaline to tetrahydroquinoxaline was accomplished in refluxing *p*-cymene under a slow stream of nitrogen in the presence of 5% rhodium–alumina. Similar treatment of *trans*-decahydroquinoxaline caused no dehydrogenation. Moreover, during these investigations the curious fact was discovered that *cis*-decahydroqunoxaline was dehydrogenated to tetrahydroquinoxaline merely on dissolving it in phenyl ether at 60°, diluting with ethyl ether, extracting with acid and basifying. Other solvents such as chloroform, ethyl ether, benzene or isoöctane showed no such property under similar conditions. *trans*-Decahydroquinoxaline showed no such behavior.

(7) F. M. Jaeger and J. A. van Dijk, *Proc. Akad. Sci. Amsterdam*, **39**, 384 (1936).

(8) F. M. Jaeger and L. Bijkerk, *ibid.*, **40**, 12 (1937).

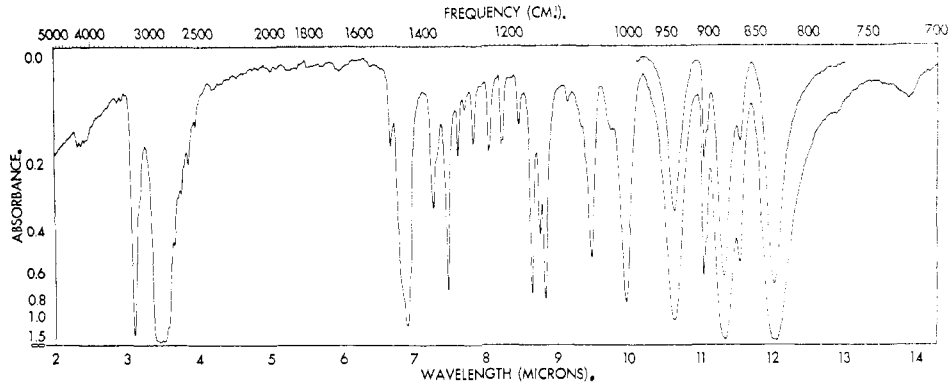


Fig. 1.—Infrared spectrum of *trans*-decahydroquinoxaline (Nujol mull).

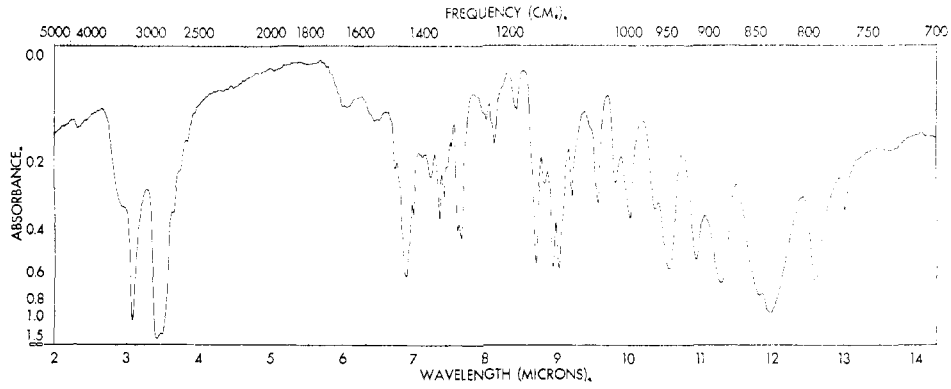


Fig. 2.—Infrared spectrum of *cis*-decahydroquinoxaline (Nujol mull).

This study was greatly complicated by the fact that the low melting *cis* form very avidly absorbs carbon dioxide from the air changing melting point from 56–58 to 58–128°. The *trans* form absorbs carbon dioxide very slowly and, if carefully purified, not at all. Careful controls established that the melting point change of the *cis* form was due entirely to this carbon dioxide formation and not to oxidation which might be suspected in view of its very facile dehydrogenation (*cf.* above).

Ultraviolet spectra of chromatographically purified *cis*- and *trans*-decahydroquinoxalines in isooctane showed only continuously rising absorption in the short wave length end of the spectrum with no maxima down to the limit of the instrument (*ca.* 210 mμ with carefully cleaned optics), thus indicating the absence of unsaturation. The presence of tetrahydroquinoxaline could readily be detected in the ultraviolet spectra of the decahydroquinoxalines not especially purified.

The infrared spectra of both *cis*- and *deca*-hydroquinoxaline represented in Fig. 1 and 2 show good N–H stretching bands at 3.1 μ and demonstrate the absence of N=C and C=C groups. While it is not possible at present to differentiate the two isomers on the basis of infrared data alone, their spectra are consistent with the structure proposed. Differing spectra in chloroform and especially water solutions (not shown) demonstrate that the two forms differ molecularly in the manner of ring fusion and not merely in conformation or in crystalline form.

Quantitative measurements of basicity for both stereoisomers of decahydroquinoxaline Table I, show their similarity, although the *cis* form is somewhat more basic for the 0 to +1 transition.

TABLE I

Compound	Solvent	pK_a's
Cis	H_2O	9.85, 5.33
	66% aq. DMF	9.62, 5.3
Trans	H_2O	9.66, 5.33
	66% aq. DMF	9.37, 5.3

Experimental[9]

Quinoxaline (X).—The procedure of Cavagnol and Wiselogle[10] was followed in detail. Yields were 80–90%, m.p. 29–30°, b.p. 105–110° (11–12 mm.). The procedure of Jones and McLaughlin,[11] although more convenient, yielded a product which in our hands was very difficult to hydrogenate beyond the tetrahydro stage. This may be due to trace impurities which poison the catalyst.

Tetrahydroquinoxaline (VII) was occasionally prepared according to the procedures of Cavagnol and Wiselogle[11] or Shultz, *et al.*,[6] in yields, 85–95%, m.p. 96–98°, b.p. 124–127°, 60 μ. In most cases, however, the method of Morley[12] was employed. This method is inexpensive and convenient, but since particular attention to detail is required for success, the following well-proven procedure is given. A mixture of 48 g. (0.44 mole) of a good grade catechol (catechol from some sources did not work as well as others; Eastman Kodak Co. practical grade was satisfactory) and 40 ml. (0.49 mole) of ethylenediamine monohy-

(9) All melting points were taken on a Fischer–Johns apparatus. All melting and boiling points are uncorrected. Pressure reactions were conducted in standard Parr and Aminco equipment. Elemental analyses were performed by Weiler and Strauss, 164 Banbury Rd., Oxford, England.

(10) J. C. Cavagnol and F. Y. Wiselogle, THIS JOURNAL, **69**, 796 (1947).

(11) R. G. Jones and K. C. McLaughlin, *Org. Syntheses*, **30**, 89 (1952).

(12) J. S. Morley, *J. Chem. Soc.*, 4005 (1952).

drate was heated at 200–210° in a glass liner in a high pressure rocking autoclave at 200–220° for 15–60 hours. It is essential that the reaction mass not come in contact with metal which appears to catalyze a reaction resulting only in tars. Poor yields will also result if insufficient reaction time is employed. The reaction mass was melted into water and the suspension extracted with three 75-ml. portions of benzene. The benzene solution was washed twice with 250 ml. of 5% sodium hydroxide and twice with water. After the benzene solution had been dried over anhy. sodium sulfate, filtered and reduced in volume, the product was precipitated with Skellysolve B. Recrystallization gave 29 g. (50%), m.p. 93–95°. The N,N'-dinitroso derivative was prepared by the addition of a cold aq. solution of 2.33 g. (0.033 mole) of sodium nitrite to a cold solution of 2 g. (0.014 mole) of tetrahydroquinoxaline in 13 ml. of dilute hydrochloric acid. The precipitate was recrystallized from absolute ethanol, m.p. 157–164° (dec.), 70% yield; λ_{max} 220 mμ (ε 10,020), 254 mμ (ε 1298), 311 mμ (ε 1324).

cis-**Decahydroquinoxaline (XI) (Rhodium Catalyst).**—Thirteen grams (0.1 mole) of quinoxaline (tetrahydroquinoxaline was frequently similarly used), 1 g. of 5% rhodium-on-alumina catalyst[5] and 30 ml. of absolute ethanol were placed in a glass liner and agitated in a stainless steel rocking bomb at 100° under 136 atm. hydrogen until the theoretical pressure drop had occurred (usually 4–6 hours). (This reaction is extraordinarily sensitive to "poisoning." Unless the apparatus is scrupulously clean reduction of the hetero ring only will occur, which happens much more easily than reduction of the homo ring.) After the catalyst was filtered off, the solvent was removed under reduced pressure and the residue distilled yielding 13 g. (93%) of white product boiling at 85–87° (0.25 mm.), m.p. 56–58°.

Anal. Calcd. for $C_8H_{16}N_2$: C, 68.52; H, 11.50; mol. wt., 140.2. Found: C, 68.45; H, 11.52; mol. wt., 145 (titration).

The dihydrochloride was prepared by precipitation from ether solution with anhy. hydrogen chloride; m.p. after recrystallization from abs. ethanol, 293–300° dec.

Anal. Calcd. for $C_8H_{18}N_2Cl_2$: C, 45.08; H, 8.51. Found: C, 45.75; H, 8.37.

The dipicrate precipitated from ethanol and recrystallized from ethanol–acetone melted at 275° dec.

Anal. Calcd. for $C_{20}H_{22}O_{14}N_8$: C, 40.18; H, 3.71. Found: C, 40.16; H, 3.75.

The N,N'-diacetyl derivative was prepared by refluxing with acetic anhydride, drowning, and recrystallizing from Skellysolve D; white crystals, m.p. 144–146°.

Anal. Calcd. for $C_{12}H_{20}O_2N_2$: C, 64.22; H, 8.98. Found: C, 64.18; H, 9.32.

The N,N'-dinitroso derivative XII was prepared by the dropwise addition of cold satd. aq. sodium nitrite to a cold solution of the amine in dil. hydrochloric acid. The precipitate was recrystallized from ethanol–water giving a yellow solid, m.p. 86–88°.

Anal. Calcd. for $C_8H_{14}O_2H_4$: C, 48.47; H, 7.16; N, 28.26. Found: C, 48.90; H, 6.78; N, 27.8.

Other Catalysts in the Preparation of *cis*-Decahydroquinoxaline.—A solution of 18.5 g. (0.142 mole) of tetrahydroquinoxaline in 60 ml. of abs. ethanol was shaken overnight at 93°, 130 atm. hydrogen, with *ca.* 6 g. of fresh Raney nickel W-6 catalyst.[4] After filtration and distillation, 14.8 g. (74%) of white platelets was obtained, m.p. 57–58°.

Common catalysts such as platinum dioxide in ethanol or Raney nickel W-2 caused only hydrogenolysis and then only under drastic conditions. Rhodium-on-alumina with acetic acid solutions of tetrahydroquinoxaline yielded only tars.

trans-**Decahydroquinoxaline (VIII) (A).**—The procedure of Beck, *et al.*,[3] was followed essentially except that by extending the reaction time to 2 hr. and with careful recrystallization from ethanol–Skellysolve B the yield could be materially increased; m.p. 150–151° (40–45%); lit.[3] m.p. 150–151° (25%).

The dinitroso derivative IX was prepared in the same manner as for *cis*-decahydroquinoxaline, m.p. 108–110°.

The diacetyl derivative prepared as for *cis*-decahydroquinoxaline melted at 93.5–94.5°.

Anal. Calcd. for $C_{12}H_{20}O_2N_2$: C, 64.22; H, 8.98. Found: C, 64.18; H, 9.32.

(B).—The procedure of Shultz and co-workers[6] was followed in detail. The crude product melted at 57–132°. After repeated recrystallizations from Skellysolve B, 0.2 g. (1%) of *trans*-decahydroquinoxaline was obtained melting at 146–148° (reported[6] 12.5%, m.p. 152.5–153°).

A dinitroso derivative prepared as described above from the high melting fraction melted at 107–108° (reported[6] 110–111°).

A dinitroso derivative prepared from a low melting fraction (57–69°) obtained from the crude hydrogenation mixture melted at 85.5–87°.

Mixed Melting Points.—Mixed melting points on the N,N'-dinitroso derivatives of the decahydroquinoxalines obtained by the various methods established the identity of the high melting fraction obtained by Shultz method with the product obtained by Beck, *et al.*, and the identity of the low melting fraction isolated by us from the crude material obtained by Shultz method with the decahydroquinoxaline obtained by us in essentially quantitative yield by hydrogenating quinoxaline over rhodium-on-alumina.

Chromatographic Separations.—Five to ten ml. of a saturated ethereal solution of decahydroquinoxaline prepared by the hydrogenation of quinoxaline over rhodium-on-alumina was poured on the top of a 1 × 20 cm. column of neutral alumina (Woelm), activity grade 1, and eluted with chloroform previously rendered alcohol-free by distillation from calcium shavings. Ninety-seven 1-ml. fractions of the eluate were collected, evaporated to dryness, and the residues examined. The *trans* form was eluted first, the *cis* form much later. Quantitative estimates showed that <5% of the material was of the high (*trans*) melting form, the balance being the low (*cis*) melting form.

A like separation was performed on the crude decahydroquinoxaline prepared by the method of Shultz and co-workers.[6] The results showed considerably more material proportionally in the high melting (*trans*) fraction and considerably less, although a very substantial amount, in the low melting (*cis*) fraction.

In both separations both the high and low melting fractions were characterized by analyses, dinitroso derivatives, and by ultraviolet spectra which, incidentally, showed traces of tetrahydroquinoxaline accompanying the last fractions of the low melting (*cis*) form.

Dehydrogenation of *cis*-Decahydroquinoxaline.—Two grams of *cis*-decahydroquinoxaline dissolved in 25 ml. of *p*-cymene was refluxed with 0.5 g. of 5% rhodium-on-alumina for 2.5 hours under a slow stream of nitrogen. On filtering and cooling, tetrahydroquinoxaline, m.p. 95–96° (80%), was obtained.

A similar procedure failed to dehydrogenate *trans*-decahydroquinoxaline.

A sample of *cis*-decahydroquinoxaline was dissolved in phenyl ether warmed to 60° for 5 minutes, cooled, and extracted with dil. hydrochloric acid. On basifying the extracts, tetrahydroquinoxaline, m.p. 96–97°, was obtained. Water, benzene, toluene or isoöctane solutions had no such effect. *trans*-Decahydroquinoxaline was not affected by phenyl ether under these conditions.

Attempted Aerial Oxidation of *cis*-Decahydroquinoxaline.—A 0.0714 *M* solution of pure *cis*-decahydroquinoxaline in spectrograde isoöctane was prepared and poured through a calcium oxide column directly into a closed system to remove carbonate. While maintaining the solution at 62–67°, carbon dioxide-free oxygen was bubbled through. At intervals over a 23-hr. period, samples were withdrawn and ultraviolet spectra run. No trace of oxidation to unsaturated products could be detected in the spectra. Evaporation of the solution recovered the *cis*-decahydroquinoxaline unchanged.

Preparation of *trans*-1,2-Diaminocyclohexane (VI).[7,8]—A mixture of 40 g. (0.24 mole) of ethyl 2-ketocyclohexanecarboxylate,[13] 16.2 g. (0.24 ml.) of sodium nitrite and 456 g. (0.49 mole) of 6% potassium hydroxide solution was shaken in a sealed bottle for 48 hr., then slowly poured into 120 ml. of cold (5–15°) 30% sulfuric acid. The resulting mixture was extracted for 3 days with ether in a liquid–liquid extractor. The extract was evaporated leaving 21.5 g. (72%) of a viscous, tan oil assumed to be isonitrosocyclohexanone. This material was so labile that it could not be

(13) H. R. Snyder, L. A. Brooks and S. H. Shapiro, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 531.

distilled without decomposition even at 50 μ pressure. The yields in subsequent runs, 34, 64, 46, 31, 62, 94 and 74%, varied unaccountably. Jaeger and van Dijk,[7] who gave almost no experimental detail, did not give a yield for this preparation, but did state that the product was an uncrystallizable oil. Other workers[14] have reported their inability to repeat this preparation.

The crude 2-isonitrosocyclohexanone was transformed into 1,2-cyclohexanedionedioxime in yields varying from 22 to 58% by treatment with equivalent amounts of hydroxylamine hydrochloride and sodium methoxide in methanol. After recrystallization from methanol–water it melted at 190–195°

In a typical run 10 g. (0.07 mole) of the dioxime in 560 ml. of boiling absolute ethanol was reduced by the addition of 70 g. of sodium. After cooling and diluting with water the product was steam distilled into hydrochloric acid solution. After concentration under reduced pressure the 1,2-cyclohexanediamine dihydrochloride crystallized (54% yield).

The dihydrochloride was converted to the free amine by dissolving in excess sodium hydroxide solution, extracting with ether, drying over sodium metal and distilling. The product boiled at 79–81° (15 mm.) (82%), reported[7] b.p. 79–81° (15 mm.). Over-all yields based on the starting ethyl 2-ketocyclohexanecarboxylate varied from 0–20%. The free amine absorbed carbon dioxide and water with great avidity.

The configuration of the product as *trans*-1,2-cyclohexanediamine has been established by resolution with *d*-tartaric acid.[8]

Preparation of *trans*-Decahydroquinoxaline from *trans*-1,2-Cyclohexanediamine.—To 0.9 g. (0.008 mole) of the diamine was added 1.5 g. of 30% aq. glyoxal (0.008 mole). After standing 5 min., 10 ml. of absolute ethanol and 0.4 g. of 5% rhodium-on-alumina catalyst were added and the reaction mixture hydrogenated for 4 hr. at 200° and 102 p.s.i. After filtration, evaporation to dryness and vacuum sublimation, 0.25 g. (20%) of authentic *trans*-decahydroquinoxaline, m.p. 147–148°, was obtained. No low melting isomer was obtained. Tar accounted for the balance of the material. The dinitroso derivative and mixed melting point comparisons further identified the product.

Acknowledgments.—This investigation was generously supported by grants from the Eli Lilly Co., 1954–1958, and by a fellowship to L. P. from the Linde Division, Union Carbide Corporation. Especial thanks are due to Dr. Reuben G. Jones, Director of Organic Research, Lilly, for his good offices and to Dr. Harold Boaz, Physicochemical Department, Lilly, for the data on infrared spectra and pK_a's.

PROVO, UTAH

(14) E. G. Rauh, G. F. Smith, C. V. Banks and H. Diehl, *J. Org. Chem.*, **10**, 199 (1945).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, HARVARD UNIVERSITY]

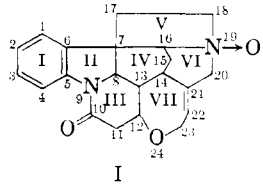
18-Oxostrychnine

BY PAUL J. SCHEUER[1,2]

RECEIVED FEBRUARY 23, 1959

Oxostrychnine, a neutral by-product in the isomerization of strychnine-N-oxide to pseudostrychnine, is shown to be the 18-oxo compound.

The transformation of cyclic tertiary amines to corresponding lactams has frequently been observed in the course of structural studies on alkaloids, particularly among those of the garrya group.[3] An analogous lactam was first observed in the strychnine series by Brehm[4] as a by-product in the isomerization of strychnine-N-oxide (I) to pseudostrychnine (II). In addition to pseudostrychnine, a neutral substance, m.p. 332–334°, of the empirical



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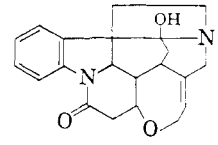

II

composition $C_{21}H_{20}N_2O_3$ was isolated. Brehm, who named the neutral substance oxostrychnine, obtained pseudo- and oxostrychnine in a yield ratio of 80:20 when catalytic amounts of dichromate were used to effect the decomposition of the N-oxide. It was later found that when equimolar quantities of dichromate are utilized, the two compounds are produced in an approximately equal ratio.

Beside the likely C-16 position which becomes hydroxylated in pseudostrychnine, the two most probable positions for the new oxygen atom in oxostrychnine are C-18 or C-20. That the strychnine skeleton had indeed remained intact during the changes leading to the formation of the oxo compound—thus eliminating the C-16 position from further consideration—was shown by the conversion of oxostrychnine to dihydroöxostrychnine, m.p. 321–324°, by means of catalytic hydrogenation and by further transformation of the dihydro derivative with lithium aluminum hydride to the known dihydrostrychnidine, m.p. 212–215°.

A priori it might be argued that the most likely point of attachment of the new oxygen atom in oxostrychnine is at the allylic position, C-20. It may be noted, however, that the formation of the major reaction product, pseudostrychnine (II), involves placement of a new oxygen atom at the non-allylic C-16. Furthermore, spectral data indicated strongly that the 18-oxo structure is correct. In addition to the infrared band at *ca.* 6 μ (5.97 μ in potassium bromide, 6.03 μ in Nujol), which is also present in strychnine and is assigned to the >N^a–CO–grouping, oxostrychnine exhibited a second lactam band at *ca.* 5.87 μ (5.82 μ in

(1) University of Hawaii, Honolulu 14, Hawaii. From the Ph.D. Thesis of P. J. S., Harvard, 1950.

(2) A summary of results of this work was published by H. L. Holmes in R. H. F. Manske and H. L. Holmes, eds., "The Alkaloids," Vol. 2, Academic Press, Inc., New York, N. Y., 1952, pp. 522–524.

(3) K. Wiesner and Z. Valenta in L. Zechmeister, ed., "Fortschritte der Chemie Organischer Naturstoffe," Vol. 16, Springer, Vienna, 1958, p. 26 ff.

(4) W. J. Brehm, Ph.D. Thesis, Harvard, 1948.