covered from the reaction filtrate in 75% yield, m.p. 116–118°.

In another experiment one molar equivalent of phenylmagnesium bromide was added to an ether–benzene solution containing 2.0 g. of the *cis* isomer to give an immediate heavy precipitate. To this solution was then added 2.0 g. of the *trans* isomer and the mixture stirred at 20° for one hour. Decomposition of the precipitated complex produced 1.55 g. of the *trans* isomer, m.p. 74–76°, and 1.9 g. of the *cis* isomer, m.p. 117–118°, was recovered from the filtrate.

A mixture of the *cis*- and *trans*-1-cyclohexyl-2-phenyl-3-*p*-toluylethylenimines[1] (0.01 mole each) on treatment with 0.011 mole of *p*-tolylmagnesium bromide gave a yellow precipitate which decomposed to regenerate a 20% yield of the *trans* ketone, m.p. 89–90°. From the filtrate 95% of the unchanged *cis*-ethylene imine ketone, m.p. 110–112°, was recovered.

Competitive Addition of Phenyllithium.—An apparatus was constructed so that the phenyllithium could be prepared in ether solution under nitrogen,[15] a portion removed and titrated[16] and other portions transferred to measuring burets and then added to reaction flasks without opening the system to the air.

A mixture of *cis*- and *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine (3.0 g., 0.0092 mole of each) dissolved in 50% ether–benzene was cooled to 0° and treated dropwise with stirring over a period of one hour with 31 ml. (0.0092 mole) of the phenyllithium solution. The reaction mixture was stirred an additional hour at room temperature and decomposed with iced ammonium chloride. Careful fractional recrystallizations from benzene and petroleum ether mixtures separated 2.2 g. of XIVA, m.p. 115–117° from 2.1 g. of unchanged *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine. A mixture of this sample of XIVA with XIB showed m.p. 95–108°.

In a similar manner a mixture (3.0 g. each) of *cis*- and *trans*-1-benzyl-2-phenyl-3-benzoylethylenimine[1] resulted in 2.0 g. of the known[4] *cis*-1-benzyl-2-phenyl-3-(diphenylhydroxymethyl)-ethylenimine (XVI), m.p. 134–136°; a mixed m.p. with an authentic sample showed no depression. From the reaction mixture 2.3 g. of the *cis* ketone was recovered.

A mixture of 2.0 g. each of the *cis* and *trans* forms of 1-cyclohexyl-2-phenyl-3-benzoylethylenimine gave 0.60 g. of carbinol IX and a trace of carbinol X. From the reaction mixture filtrate was also recovered 0.82 g. of the unchanged *trans* ketone.

Oxidation of Ethylene Imine Carbinols.—Oxidation[4] of VA and VIA gave phenyl *p*-tolyl ketone in both cases.

MINNEAPOLIS, MINN. RECEIVED JULY 17, 1950

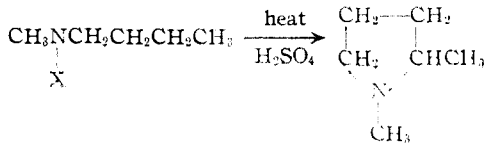
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

Preparation of Quinuclidines[1]

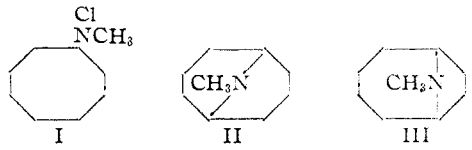
BY S. WAWZONEK, M. F. NELSON JR., AND P. J. THELEN

N-Bromo- and N-chloro-4-alkylpiperidines are converted into quinuclidines by irradiating first with ultraviolet light in 85% sulfuric acid at temperatures ranging from 0 to 23° and then treating with alkali. Comparable yields are obtained with both the bromoamine and the chloroamine. Evidence is presented that the β-bromoalkylpiperidine is an intermediate in the reaction.

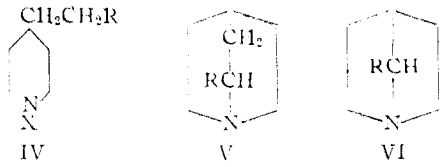
N-Haloalkylamines are converted in sulfuric acid by heat into substituted pyrrolidines.[2]



N-Halocycloalkylamines when treated in a similar manner, differ in their behavior and give bicyclic compounds which vary in the size of the rings formed. N-Chloro-N-methylcycloheptylamine, for example, behaves normally and gives tropane which involves a pyrrolidine ring.[3] N-Chloro-N-methylcycloöctylamine (I) behaves differently because of steric factors and gives N-methylgranatanine (II) in which two piperidine rings are present rather than the substituted pyrrolidine, 9-azabicyclo[4,2,1]nonane[4] (III)



The present paper reports a new variation in this ring closure with N-halo-4-alkylpiperidines (IV) which gives quinuclidines (V) rather than 1-azabicyclo[2,2,1]heptane (VI).



The ring closure was carried out in 85% sulfuric acid with both the N-chloro- and the N-bromoamines. Best yields were obtained if the solution was irradiated with ultraviolet light at room temperature or lower for twenty-four hours. A summary of the results obtained is given in Table I.

The results indicate that comparable yields are obtained with both the bromoamines and the chloroamines in all cases except one. N-Bromo-4-*n*-propylpiperidine gives a better yield than the corresponding chloro compound. The behavior of the N-bromo compounds is opposite to that observed when cyclization is brought about by heat[2b] and is probably due to the milder cyclization conditions used.

The quinuclidines were isolated in the customary manner by treating the sulfuric acid solution with excess alkali, steam distilling and removing the secondary amines as benzenesulfonamides. When the irradiated sulfuric acid solution of N-bromo-4-ethylpiperidine (IX) was adjusted quickly to *p*H 9 with dilute alkali and then warmed to 40°, the solution became acidic (*p*H 5). This phenomenon

(1) Abstracted in part from the Ph.D. thesis (1948) of P. J. Thelen and the Ph.D. thesis (1949) of M. F. Nelson, Jr. Presented before the Division of Organic Chemistry at the Chicago meeting of the American Chemical Society, September, 1950.

(2) (a) E. C. Britton, U. S. Patent 1,607,605; *C. A.*, **21**, 249 (1927); (b) G. H. Coleman and G. E. Goheen, THIS JOURNAL, **60**, 730 (1938); (c) G. H. Coleman, G. Nichols and T. F. Martens, *Org. Syn.*, **25**, 14 (1945).

(3) G. H. Coleman and J. J. Carnes, *Proc. Iowa Acad. Sci.*, **49**, 288 (1942) (abstract).

(4) S. Wawzonek and P. J. Thelen, THIS JOURNAL, **72**, 2118 (1950).

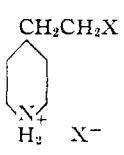
TABLE I

CYCLIZATION OF N-HALOALKYLPIPERIDINES IN SULFURIC ACID

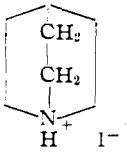
-Piperidine	Reaction temperature, °C.	Yield of picrate of quinuclidines, %
N-Chloro-4-ethyl	0–5	19.2
N-Chloro-4-ethyl	23	21.3
N-Chloro-4-ethyl	120[a]	7.0
N-Bromo-4-ethyl	0–5[b]	19.8
N-Bromo-4-ethyl	23[b]	20.2
N-Chloro-4-*n*-propyl	23	8.2
N-Bromo-4-*n*-propyl	23	20.4
N-Bromo-4-*n*-propyl	50	1.0
N-Chloro-4-*n*-butyl	23	2.0
N-Bromo-4-*n*-butyl	23	1.0
N-Chloro-2-methyl-4-ethyl	0–5[c]	1.3
N-Bromo-2-methyl-4-ethyl	23	2.2
N-Chloro-3-methyl-4-ethyl	23	22.6
N-Bromo-3-methyl-4-ethyl	23	27.4
N-Chloro-2,6-dimethyl-4-ethyl	0–8	Trace

[a] Solution was heated for 30 minutes and was not irradiated. [b] Irradiation of bromoamine (5.0 g.) was carried out in the presence of bromine (1.0 g.). [c] Chlorine gas was bubbled through the reaction mixture during the irradiation.

could be repeated several times before the solution would remain constant at *p*H 9. This behavior resembles that observed in the cyclization of 4-(β-iodoethyl)-piperidine hydroiodide (VII) (X = I) to quinuclidine hydroiodide (VIII) in dilute alkali[5]



VII

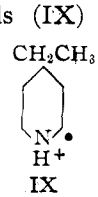


VIII

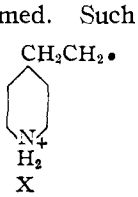
and is an indication that 4-(β-bromoethyl)-piperidine is produced in the irradiation of N-bromo-4-ethylpiperidine in sulfuric acid solution. The former (VII) (X = Br) is then cyclized by the alkaline treatment into quinuclidine. This behavior is in agreement with the free radical mechanism previously proposed[4] for this reaction.

Further evidence for the 4-(β-bromoethyl)-piperidine is the very small yield (2.6%) of quinuclidine obtained from a typical irradiated solution neutralized with potassium carbonate and then treated with an excess of piperidine.

The other products formed in this cyclization, 4-ethylpiperidine (50%) and the alkali insoluble-non-volatile material (24%), are probably formed by disproportionation reactions of the two intermediate free radicals (IX) (X) formed. Such reactions



IX



X

apparently are favored by α-substituents in the piperidine since very poor yields of the corresponding quinuclidine were obtained from N-halo-2-methyl-4-ethylpiperidine and N-chloro-2,6-dimethyl-4-ethylpiperidine.

Quinuclidine was identified by comparison with a sample prepared from 4-(β-iodoethyl)-piperidine.[5] The substituted quinuclidines were characterized as picrates. These derivatives had similar melting points to those reported in the literature.

Experimental[6]

All the cyclizations listed were carried out according to the procedure given for quinuclidine.

Quinuclidine.—4-Ethylpiperidine[7] (5 g.) in carbon tetrachloride (100 ml.) at 0–5° was treated with sodium hypochlorite (20%) or sodium hypobromite solution (15%) chilled to 0–5° for three minutes. The aqueous layer was discarded and the procedure repeated with an additional 50 ml. of chilled hypohalite solution. The resulting carbon tetrachloride solution was separated and dried for one hour over anhydrous potassium carbonate in a flask immersed in an ice-bath. Titration using potassium iodide and sodium thiosulfate indicated 78% conversion to the N-bromoamine. The resulting cold solution of haloamine was extracted by shaking with two 50-ml. portions of cold (0–5°) 85% sulfuric acid and the acid extracts were combined, and placed in a 250-ml. Berzelius beaker. The solution was then irradiated with ultraviolet light for 20 hours at 0–5° with slow mechanical stirring. After completion of the irradiation the mixture was added to 1000 ml. of ice-water, made strongly alkaline with 40% sodium hydroxide solution and steam distilled into 100 ml. of 6 *N* hydrochloric acid until the distillate coming over was no longer basic to litmus. The alkali insoluble non-volatile residue remaining in the flask weighed 1.2 g. The hydrochloric acid solution was concentrated to 100 ml., cooled and shaken with benzenesulfonyl chloride (6 g.) and 40% sodium hydroxide solution (30 ml.). The resulting alkaline solution was made acid to litmus with 6 *N* hydrochloric acid, cooled and extracted with two 100-ml. portions of ether to separate the N-benzenesulfonyl derivative of 4-ethylpiperidine (8.1 g.). The acid layer was made strongly basic with 40% sodium hydroxide and steam distilled until the distillate no longer came over basic to litmus.

The picrate of quinuclidine as precipitated from the distillate by adding a cold saturated alcohol solution of picric acid until the resulting mixture had a *p*H 6.0–6.5 to nitrazine paper. More picrate could be obtained by concentrating the mother liquor to one third its original volume and cooling. The combined crystals (4.1 g.) were purified by crystallizing twice from a 50-50 mixture of methanol and ligroin (60–70°); m.p. 274–275°. Prelog[8] reports a melting point of 275–276° for this derivative. A mixture with a sample prepared from 4-β-hydroxypiperidine[5] melted at the same point.

The hydrochloride of quinuclidine was prepared by treating the distillate from the Hinsberg separation with hydrochloric acid and evaporating. It melted at 364–365° after two crystallizations from absolute ethanol. Brown and Eldred[9] report 369–374° as the melting point of this derivative.

Quinuclidine was obtained by treating the hydrochloride with alkali and distilling the resulting oil from sodium. It melted at 156° (sealed tube) and did not lower the melting point of a sample made from β-hydroxyethylpiperidine.[5]

The use of either 95% or 100% sulfuric acid in the cyclization of the N-haloamine did not materially affect the yield of quinuclidine.

Mechanism of the Ring Closure.—4-Ethylpyridine (5 g.) was converted into the N-bromoamine and irradiated in the usual manner. The resulting solution was diluted with enough ice-water to make 600 ml. of solution and then divided into two equal parts. One portion when treated in the customary fashion gave a 20.3% yield of quinuclidine. To the second portion 5 ml. of Grammercy indicator was added and the solution adjusted to *p*H 9 with 2 *N* sodium hydroxide and then heated to 40°. The solution

(5) J. Meisenheimer, *Ann.*, **420**, 190 (1920).

(6) Melting points and boiling points are not corrected.

(7) S. Wawzonek, M. F. Nelson, Jr. and P. J. Thelen, unpublished work.

(8) V. Prelog and Cerkovnikow, *Ann.*, **525**, 292 (1936).

(9) H. C. Brown and N. R. Eldred, THIS JOURNAL, **71**, 445 (1949).

rapidly changed to *p*H of 5.0 and was again made alkaline. The solution again turned acidic on heating and continued to do so until the solution had so been treated four times with alkali. The resulting solution gave a 19.5% yield of quinuclidine picrate.

A typical diluted irradiated solution when carefully neutralized to *p*H 7 with potassium carbonate and then treated with piperidine (10 g.) gave upon working up in the customary manner a 2.6% yield of quinuclidine picrate.

2-Methylquinuclidine.—Ring closure was carried out on N-bromo- and N-chloro-4-*n*-propylpiperidine in a manner similar to that used in the preparation of quinuclidine. The picrate after two recrystallizations from ethanol and two from a 50-50 mixture of ligroin (60–70°) and acetone melted at 282–283° with decomposition. Prelog[8] reports 286° as the melting point for this derivative.

Ring closure of either N-bromo- or N-chloro-2-methyl-4-ethylpiperidine gave a maximum of 2% yield of 2-methylquinuclidine. The picrate from this sample after three crystallizations from acetone-ligroin (60–70°) melted at 285°. A mixture with the picrate of the sample obtained from N-halo-4-*n*-propylamine melted with no depression.

2-Ethylquinuclidine.—This compound was prepared by the ring closure of N-bromo and N-chloro-4-*n*-butylpiperidine. The picrate, after three recrystallizations from acetone–ligroin (60–70°) melted at 172° with decomposition. Prelog[8] reports a melting point of 170–171° for this derivative.

3-Methylquinuclidine.—This amine was prepared by ring closures of N-bromo- and N-chloro-3-methyl-4-ethylpiperidine. The picrate after three recrystallizations from acetone–ligroin melted at 229–230°. Prelog[8] reports a melting point of 227° for this compound.

Ring Closure of N-Chloro-2,6-dimethyl-4-ethylpiperidine.—Ring closure of N-chloro-2,6-dimethyl-4-ethylpiperidine gave only a trace of a tertiary amine picrate.

IOWA CITY, IOWA RECEIVED DECEMBER 15, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Compounds with Boron at the Bridgehead—A Study of the Steric Consequences of Planar Boron[1]

BY HERBERT C. BROWN AND EDWARD A. FLETCHER[2]

2-Ethyl-2-(hydroxymethyl)-1,3-propanediol[3] reacts with boric acid to lose the calculated quantity of water, forming the ester. The product is polymeric. The monomer is not formed from the polymer at 270° and 10^{-3} mm. It is concluded that the strain involved in accommodating the planar boron atom at the cage bridgehead (IV) must be exceedingly large. In the product each trimethylolpropane molecule must be combined with two or three different boron atoms—a relatively strain free polymer results. Triethanolamine reacts with boric acid to produce a monomeric ester, a volatile solid (VII or VIII). The product reacts with methyl iodide; the reaction follows second order kinetics, but is much slower than the corresponding reactions of simple tertiary amines. The energy of activation is 18.5 kcal. for triethanolamine borate *versus* 13.0 for triethanolamine itself. The product reacts with strong acids only at a slow, measurable rate. It is concluded from these experiments that the lone pair of the nitrogen atom cannot be free and the product must, therefore, have the "triptych" structure (VIII).

Introduction

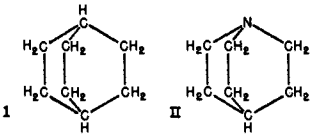
The stereochemistry of tetrahedral carbon, planar platinum and pyramidal nitrogen has been intensively investigated. The stereochemistry of planar boron, on the other hand, has received little attention. Yet there are ample indications that the planar trigonal configuration must lead to an unusual stereochemistry of considerable interest.

Thus certain major differences in the chemistry of substituted amines, R_3N, and borines, R_3B, may have their basis in the differences in configuration. For example, triisopropylamine has not yet been prepared although triisopropylboron is easily synthesized.[4] The preparation of di-*t*-butylamine has been reported but once,[5] and the synthesis involves a difficult procedure; yet tri-*t*-butylboron is easily synthesized and is highly stable.[4] It is, of course, dangerous to draw firm conclusions from evidence of this kind. Nevertheless, the differences are so great as to suggest that they cannot be the result of the minor differences in the covalent radii of boron and nitrogen. The differences are more plausibly attributed to the differences in configuration. Apparently the planar configuration of boron accommodates large bulky groups far more readily than does the pyramidal configuration of nitrogen.

To obtain information as to the steric consequences of planar trigonal atoms, we have undertaken a number of studies of the stereochemistry of tricovalent boron. The present paper is concerned with compounds containing boron at the bridgehead.

Polymeric Trimethylolpropane Borate

Bicyclic ("cage") compounds containing normally tetrahedral atoms, such as carbon and nitrogen, at the bridgehead are well known. Bicyclo-(2.2.2)-octane (I) and quinuclidine (II) are easily prepared and highly stable, suggesting that the structures contain relatively strainless rings and the usual bond angles.[6]



The synthesis of related "cage" compounds containing boron at the bridgehead (III, IV) would presumably involve a distortion of the boron angles from their preferred 120° value to the approxi-

(1) Studies in Stereochemistry. XVIII. This paper was presented in part before the Division of Physical and Inorganic Chemistry at the 117th Meeting of the American Chemical Society in Detroit, Michigan, April 17, 1950.

(2) E. I. du Pont de Nemours and Company Fellow at Purdue University, 1949–1950.

(3) We shall, for convenience, refer hereafter to this substance by its common name, trimethylolpropane.

(4) E. Krause and P. Nobbe, *Ber.*, **64B**, 2112 (1931); H. C. Brown, THIS JOURNAL, **67**, 378 (1945).

(5) F. Klages, G. Nober, F. Kircher and M. Bock, *Ann.*, **547**, 1 (1941).

(6) K. Alder, G. Stein, F. v. Buddenbrock, W. Eckardt, W. Frercks and S. Schneider, *Ann.*, **514**, 1 (1934); J. Meisenheimer, J. Neresheimer and W. Schneider, *ibid.*, **420**, 190 (1920).