Hence an unequivocal choice between mechanisms 6 or 7 and 10 is not presently possible.[43]

The finding of carboxyl group catalysis which increases the rate 200-fold over that due to hydronium ion at pH 3–4 is of possible biochemical significance in the mechanism of action of sulfatases. Moreover, the gross mechanistic features are similar to those exhibited by salicyl phosphate; thus the analogy to phosphate ester chemistry may continue. Kaiser, *et al.*,[44,45] have recently reported the unusual alkaline lability of cyclic five-membered sulfates, whose behavior appears to closely resemble the cyclic phosphates. Investigations aimed at elucidating the actual mechanism of salicyl sulfate hydrolysis and the nature of catalytic effects by metal ions are currently in progress.[46]

Acknowledgment. This investigation was supported by Public Health Service Research Grant GM 13306-01.

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[43] It may be argued that the similarity in activation parameters for k_{H^+} and k_0 are indicative of mechanistic continuity and, therefore, that the carboxyl serves as in 6 to stabilize either electrostatically or *via* hydrogen bonding a reactive zwitterionic species. This should be viewed only as a working hypothesis.

[44] E. T. Kaiser, I. R. Katz, and T. F. Wulfers, *J. Am. Chem. Soc.*, 87, 3781 (1963).

[45] O. R. Zaborsky and E. T. Kaiser, *ibid.*, 88, 3084 (1966).

[46] F. Huege, unpublished work.

Elimination Reactions. VI. Rearrangement and Elimination Reaction of Benzylcyclopropyldimethylammonium Bromide[1]

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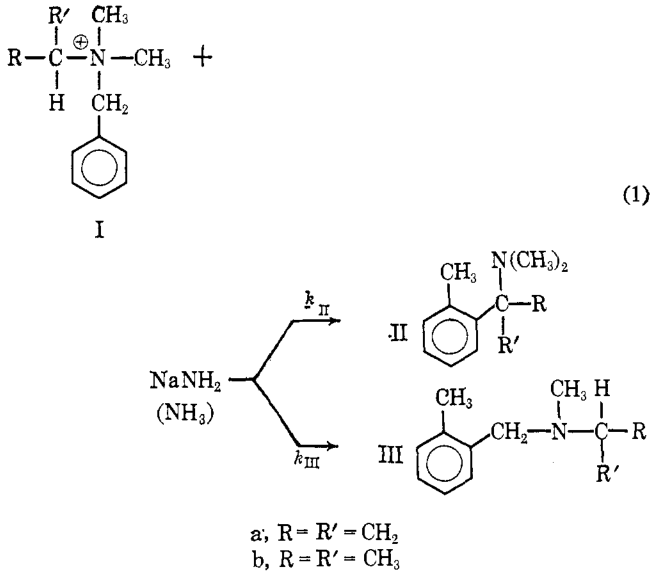
Abstract: Benzylcyclopropyldimethylammonium bromide was treated with sodium amide in liquid ammonia to learn more of the effect of the cyclopropane ring on the course of the Sommelet–Hauser rearrangement. Rearrangement to α-(N-methyl-N-cyclopropylamino)-*o*-xylene was accompanied by an unexpected elimination reaction which gave cyclopropene and benzyldimethylamine. An explanation for the formation of only one of the two possible Sommelet–Hauser products is suggested and some factors affecting the ease of elimination in this system are discussed.

Treatment of an alkylbenzyldimethylammonium halide (I) with sodium or potassium amide in liquid ammonia leads to the *ortho* substitution or Sommelet–Hauser rearrangement,[3] diagram 1. As shown in diagram 1, *ortho* substitution may occur *via* two pathways which lead to isomers II and III. When R is an alkyl group and R′ = H, the reaction gives mainly isomer III ($k_{\mathrm{II}}/k_{\mathrm{III}}$ = 0.28).[4] However, when R is an unsaturated moiety, *e.g.*, R = phenyl or vinyl and R′ = H, then isomer II is produced almost exclusively.[4]



(1)

An interesting contrast exists between the saturated cases where R′ = H, R = isopropyl in I and R′ = H, R = cyclopropyl. In the latter example, isomer II predominates ($k_{\mathrm{II}}/k_{\mathrm{III}}$ = 4.0) whereas, in the former, isomer III is favored ($k_{\mathrm{II}}/k_{\mathrm{III}}$ = 0.2).[3,4]

To learn more of the effect of the small ring on the course of the Sommelet–Hauser rearrangement, we prepared benzylcyclopropyldimethylammonium bromide (Ia) and subjected it to sodium amide in liquid ammonia. The results from similar treatment of benzyldimethylisopropylammonium bromide (Ib) were available from an earlier study.[3]

Results

Exposure of bromide Ia to sodium amide in liquid ammonia for 3 hr produced two amines which were separated by fractional distillation. According to evidence presented below, the less volatile amine, isolated in 40% yield, is α-(N-methyl-N-cyclopropylamino)-*o*-xylene (IIIa). Combustion analyses and boiling point established the formula as $C_{12}H_{17}N$. In the

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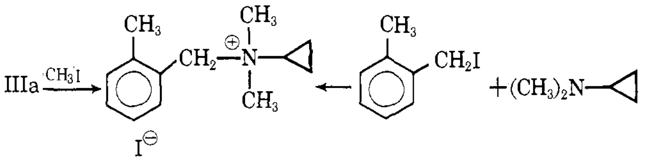
[1] Presented in part at the 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965.

[2] North Carolina State University, Raleigh, N. C. 27607.

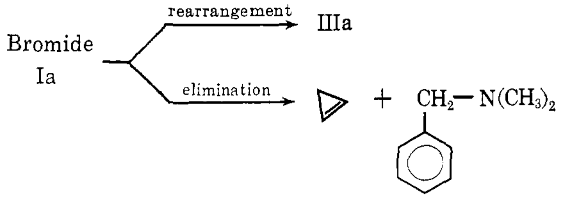
[3] F. N. Jones and C. R. Hauser, *J. Org. Chem.*, 27, 1542 (1962).

[4] C. L. Bumgardner, *J. Am. Chem. Soc.*, 85, 73 (1963).

nmr spectrum (ppm), signals were observed at 7.1 (aryl), at 3.6 (methylene), at 2.3 and 2.2 (C-methyl and N-methyl), and at 0.4 (cyclopropyl) with intensity ratios consistent with structure IIIa. The infrared spectrum (cm^{-1}) contained bands at 740 (*ortho*-disubstituted benzene), 1020, and 3150 (cyclopropane). Gas phase chromatography over several columns indicated homogeneity. Finally, the methiodide prepared by treating amine IIIa with methyl iodide and that formed by allowing α-iodo-*o*-xylene to react with cyclopropyldimethylamine were found to be identical.



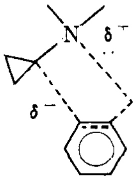
The physical constants and infrared spectrum of the more volatile amine (20% yield) sufficed for its identification as benzyldimethylamine. Isolation of this amine suggested that an elimination reaction giving cyclopropene was competing with the Sommelet rearrangement. This possibility was investigated in another experiment in which a sample of the evolved gases was fractionated on a vacuum line and the components were analyzed by mass spectrometry. Cyclopropene and ammonia were observed.



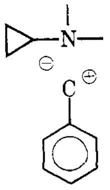
Discussion

Jones and Hauser[3] observed that reaction of quaternary salt Ib gives both isomers IIb and IIIb. The k_{II}/k_{III} ratio, 0.14, is lower than that observed for I when R = *n*-alkyl and R′ = H, so that branching at the α-carbon atom has a retarding effect on k_{II}. It is tempting to attribute this to a decrease in acidity of the α-hydrogen which must be removed before II can be formed. In the reaction of Ia, however, isomer IIa is not observed even though the α-hydrogen attached to the small ring in Ia should be more acidic than the methyl α-hydrogen atoms.[5]

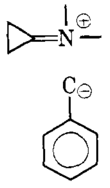
An explanation to account for k_{II} being very low in the reaction of Ia is suggested by a comparison of structures IV, V, and VI which represent possible transition states standing between Ia and IIa. Structure IV pictures a highly synchronized transition state where charge neutralization is proceeding uniformly. Structure V is a state involving charge separation, the positive charge concentrated on the benzyl carbon atom and negative charge on the small ring. Finally, structure VI shows positive charge on the nitrogen atom and negative charge at the benzyl carbon atom. Structures IV (a spiro arrangement) and VI (a methylene cyclopropane) obviously require introduction of some strain and therefore might represent enough energy to account for the exclusive production of amine IIIa.[6] Interestingly, structure VI is reminiscent of *intermediates* which have been proposed for certain Wittig[7] and Stevens[8] rearrangements. A structure analogous to VI, intermediate VII, may be invoked to account for reactions of benzylphenyldimethylammonium halide in the presence of strong base. This quaternary salt not only undergoes rearrangement[9] but yields a trace of toluene as well.[10] Interception by a proton source of the benzyl carbanion in intermediate VII could give rise to toluene.[11]



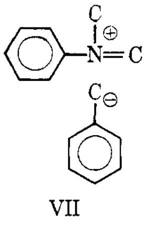
IV



V



VI



VII

How bulk differences between the isopropyl and cyclopropyl groups may affect the k_{II}/k_{III} ratios in the reactions of Ia and Ib is not known, however, so such factors, which could provide an alternative explanation, cannot be dismissed.

The fact that elimination to give cyclopropene is able to compete with rearrangement of Ia is remarkable. Synthesis of cyclopropene *via* the Hofmann route involves high-temperature (325°) pyrolysis of cyclopropyltrimethylammonium hydroxide, a reaction which must be carried out in a carefully prepared platinized asbestos flask.[12a,b,c] Bromide Ia and sodium amide, however, generate cyclopropene at −33°, conditions which

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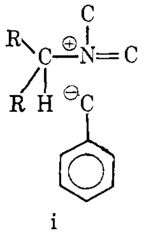
[5] H. E. Zimmerman and B. S. Thyagarajan, *J. Am. Chem. Soc.*, **82**, 2505 (1960).

[6] As a referee pointed out, changing from an isopropyl to a cyclopropyl group may also increase k_{III}. This is suggested by consideration of structure i ($R = CH_3$ and $R = CH_2$) analogous to VI and VII.



i

[7] P. T. Lansbury and V. A. Pattison, *J. Am. Chem. Soc.*, **84**, 4295 (1962). In a number of cases, particularly those involving secondary and tertiary alkyl benzyl ethers, a free-radical rather than a carbanion pathway is indicated: P. T. Lansbury and J. D. Sidler, *Tetrahedron Letters*, 691 (1965); P. T. Lansbury, V. A. Pattison, J. D. Sidler, and J. B. Bieber, to be published. We are indebted to Professor Lansbury for the opportunity to view his manuscript prior to its publication.

[8] E. F. Jenny and J. Druey, *Angew. Chem. Intern. Ed. Engl.*, **1**, 155 (1962); E. F. Jenny and K. Schenker, paper presented at the Winter Assembly of the Swiss Chemical Society, Feb 20, 1965; *Angew. Chem. Intern. Ed. Engl.*, **4**, 441 (1965).

[9] G. C. Jones, W. Q. Beard, and C. R. Hauser, *J. Org. Chem.*, **28**, 199 (1963).

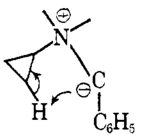
[10] Unpublished observations from our laboratory.

[11] A homolytic cleavage initiated by one electron transfer to the quaternary salt is also a possibility.

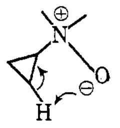
[12] (a) M. J. Schlatter, *J. Am. Chem. Soc.*, **63**, 1733 (1941); (b) K. B. Wiberg and W. J. Bartley, *ibid.*, **82**, 6375 (1960). (c) Cyclopropene also may be prepared (10% yield) from allyl chloride and sodium amide: G. L. Closs and K. D. Krantz, *J. Org. Chem.*, **31**, 638 (1966).

might prove useful for preparing cyclopropene derivatives.

A factor which may promote elimination from bromide Ia is the near 0° dihedral angle in the cyclopropyl ring between carbon–hydrogen bonds *cis* to the carbon–nitrogen bond.[13] This situation is favorable, as shown in structure VIII for $\alpha'\beta$ (*cis*) elimination of benzyldimethylamine, a process common to a number of



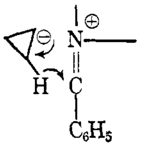
VIII



IX

benzyltrialkylammonium halides on treatment with sodium amide.[14] However, thermal decomposition of amine oxide IX, which might be expected to proceed similarly,[15] does not yield cyclopropene.[12b]

As an alternative to the highly concerted transition state VIII, structure X may be considered as the transition state (or perhaps an intermediate) in the elimination reaction of bromide Ia. Structure X possesses a conjugated double bond, concentrates negative charge in an orbital rich in s character, and is not as strained as VIII where the cyclopropene double bond is more highly developed.[16]



X

Experimental Section[17]

Cyclopropyldimethylamine. Cyclopropylamine (Aldrich Chemical Co.) was treated with formic acid and formaldehyde in the manner described for methylation of cyclopropylcarbinylamine.[4] From 11.4 g of cyclopropylamine was obtained 6.63 g (39%) of cyclopropyldimethylamine, bp 58–62°. An analytical sample distilled through a spinning-band column had $n^{25}\text{D}$ 1.3976.

Anal. Calcd for $C_5H_{11}N$: N, 16.5. Found: N, 16.7.

The nmr and infrared spectra showed that the ring was still intact.

Benzylcyclopropyldimethylammonium Bromide. A solution of 5.22 g of cyclopropyldimethylamine and 10.5 g of benzyl bromide in 100 ml of dry benzene was heated under reflux for 15 hr. Filtration of the cooled mixture yielded 13.7 g (87%) of benzylcyclopropyldimethylammonium bromide, mp 168–170°.

Anal. Calcd for $C_{12}H_{18}NBr$: C, 56.25; H, 7.03; N, 5.47. Found: C, 56.30; H, 7.18; N, 5.42.

Reaction of Benzylcyclopropyldimethylammonium Bromide with Sodium Amide. To 100 ml of liquid ammonia containing 0.076 mole of sodium amide was added over a 15-min period 13.0 g of benzylcyclopropyldimethylammonium bromide. The mixture was stirred for 4 hr; then 6.0 g of ammonium chloride was added. Ether (50 ml) was introduced dropwise, the Dry Ice condenser was replaced by a water condenser, and the ammonia was allowed to evaporate overnight. Water was then added the resulting; layers were separated. The ether solution was extracted several times with 10% hydrochloric acid solution. The combined acid extracts were made strongly alkaline with 10% sodium hydroxide solution, and the oil which separated was extracted with ether. The ether extract was washed with water and dried over magnesium sulfate. Distillation through a spinning-band column yielded 1.30 g of benzyldimethylamine, bp 77–78° (32 mm), $n^{20}\text{D}$ 1.4999, identified by its infrared spectrum, and 3.43 g of α-(N-methyl-N-cyclopropylamino)-*o*-xylene, bp 80–84° (5 mm), $n^{26}\text{D}$ 1.5090–1.5096.

Anal. Calcd for $C_{12}H_{17}N$: C, 82.28; H, 9.71; N, 8.00. Found: C, 82.28; H, 9.81; N, 8.01.

The salient features of the infrared and nmr spectra appear in the Results section.

In a similar experiment a trap cooled in Dry Ice–acetone was attached to the exit end of the Dry Ice–acetone reflux condenser. At the end of the reaction, mass spectrometry indicated that the trap contained ammonia and cyclopropene.

N-(*o*-Methylbenzyl)-N-cyclopropyl-N,N-dimethylammonium Iodide. a. To 4.61 g of α-iodo-*o*-xylene[4] in 25 ml of anhydrous ether was added 1.70 g of cyclopropyldimethylamine. The mixture was placed in a refrigerator for 2 days. Filtration then yielded 4.55 g (72%) of N-(*o*-methylbenzyl)-N-cyclopropyl-N,N-dimethylammonium iodide, mp 110–113°. Recrystallization from absolute ethanol raised the melting point to 115–118°.

Anal. Calcd for $C_{13}H_{20}NI$: C, 49.22; H, 6.36; N, 4.41. Found: C, 49.04; H, 6.44; N, 4.13.

b. Treatment of α-(N-methyl-N-cyclopropylamino)-*o*-xylene with methyl iodide in ether resulted in a methiodide which had the same melting point and infrared spectrum as that described in a. A mixture melting point was not depressed.

Anal. Calcd for $C_{13}H_{20}NI$: N, 4.41. Found: N, 4.34.

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(13) O. Hassel and J. H. Viervoll, *Acta Chem. Scand.*, **1**, 149 (1947).

(14) C. L. Bumgardner, *J. Org. Chem.*, **27**, 1035 (1962).

(15) A. C. Cope and C. L. Bumgardner, *J. Am. Chem. Soc.*, **79**, 4729 (1957).

(16) An α-elimination pathway constitutes another possibility: V. Franzen and G. Wittig, *Angew. Chem.*, **72**, 417 (1960).

(17) Boiling points and melting points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Infracord spectrophotometer with a sodium chloride prism. Nuclear magnetic resonance spectra were obtained with either a Varian Associates, Model V-3000-B, high-resolution spectrometer using a 40-Mc probe or a Varian Associates A-60 spectrometer. A-60 spectra ($DCCl_3$ solutions, probe temperature 38°) were measured using TMS as internal standard; 40-Mc spectra (probe temperature 30°) were measured from external TMS. Mass spectra were determined with a C.E.C. Type 21-620 mass spectrometer.