[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Reactions of Methiodides of Certain *exo*-Methylenecyclohexadieneamines with Sodium Amide. Relation to *ortho* Substitution Rearrangement[1]

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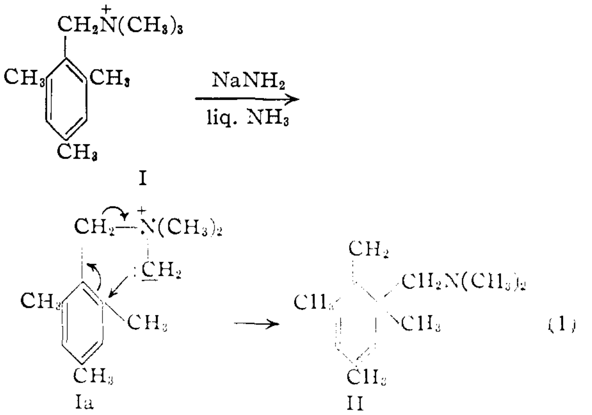
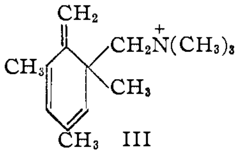
The *exo*-methylenecyclohexadieneamine obtained from the rearrangement of the 2,4,6-trimethylbenzyltrimethylammonium ion by means of sodium amide in liquid ammonia was converted to another *exo*-methyleneamine by further treatment of its methiodide with this reagent. Like the former *exo*-methyleneamine, the latter alicyclic product underwent thermal isomerization to a β-arylethylamine, and an acid-induced decomposition to form an aromatic hydrocarbon. The mechanism for the conversion of the first *exo*-methyleneamine to the second is presented. Still further rearrangements are considered.

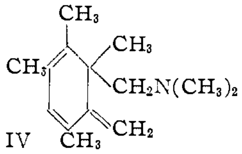
It has been shown[2] recently that quaternary ammonium ion I undergoes with sodium amide in liquid ammonia the first phase of the *ortho* substitution rearrangement to form *exo*-methyleneamine II. The mechanism probably involves an S$_N$1′ type of displacement within intermediate carbanion Ia (eq. 1).



It has now been found that the methiodide of *exo*-methyleneamine II, the cation of which is quaternary ammonium ion III, is converted by sodium amide in liquid ammonia to another *exo*-methyleneamine (IV) in 79% yield.

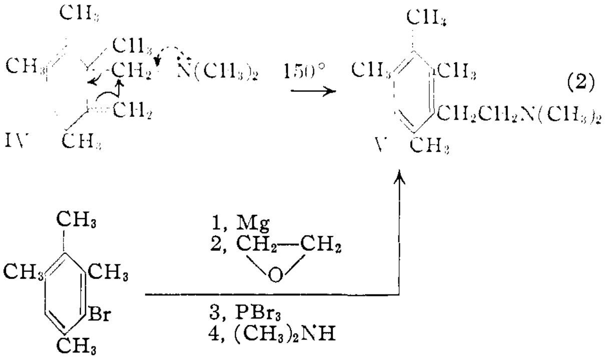


III

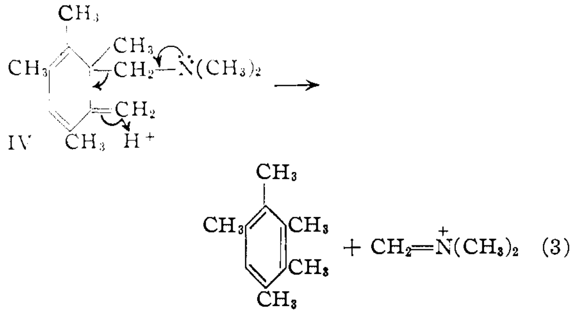


IV

The structure of this product was established by its ultraviolet absorption spectrum and by certain of its reactions. Thus, similar to II,[2] *exo*-methyleneamine IV underwent thermal isomerization at 150° to form β-isodurylethyldimethylamine (V, 55%), the structure of which was established by an independent synthesis from 2-bromoisodurene and ethylene oxide (eq. 2).

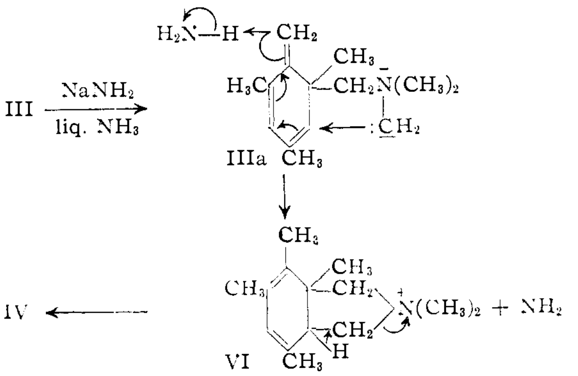


Also, similar to II,[2] *exo*-methyleneamine IV reacted rapidly with dilute hydrochloric acid to form pentamethylbenzene and presumably dimethylmethyleneiminium ion which underwent alkaline hydrolysis to give formaldehyde and dimethylamine (eq. 3).



The mechanism of formation of exo-methyleneamine IV from quaternary ammonium ion III appears to involve the conversion of intermediate carbanion IIIa to an intermediate cyclic quaternary ammonium ion VI which undergoes β-elimination as represented in Scheme A.

SCHEME A



In agreement with this mechanism, the yield of IV from III was equally as good (78–79%) with one equivalent of sodium amide as with three equivalents of this base, even though the amide ion ef-

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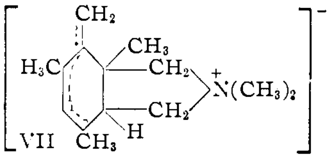
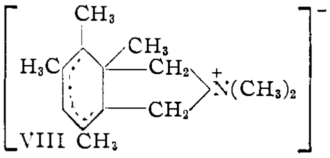
(1) Supported by the National Science Foundation.

(2) C. R. Hauser and D. N. Van Eenam, THIS JOURNAL, **79**, 5512 (1957).

fects two of the steps in the process (see Scheme A). This was anticipated, since an equivalent of the amide ion is generated as by-product in the conversion of intermediate carbanion IIIa to intermediate quaternary ion VI.

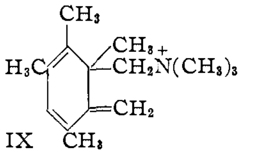
However, Scheme A is probably over simplified since it does not account for the deep coloration (red-purple)[3] that accompanies the over-all conversion of III to IV. Apparently intermediate carbanions are formed in addition to carbanion IIIa. Such a carbanion might be VII or possibly VIII,[4] each of which would have three resonance structures. The former carbanion would be the intermediate between IIIa and VI, and the latter, the intermediate between VI and IV. Of course, two isomers in addition to VI might arise as intermediate carbanion VII acquires a proton from the medium (ammonia).

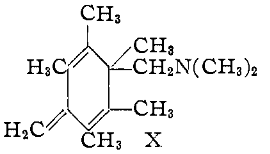

VII


VIII

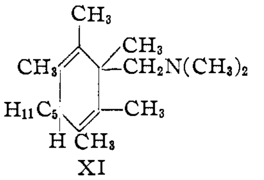
These results show that, although quaternary ion III has an unsubstituted "*ortho*" position, the normal *ortho* substitution rearrangement does not occur. Presumably this is because there is no double bond across which such an SNi′ type of displacement could operate (see Ia).

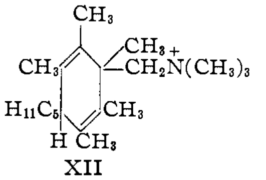
It was of interest to study the further reaction of the methiodide of *exo*-methyleneamine IV with sodium amide in liquid ammonia, since molecular models indicated the possibility of introducing an *exo*-methylene group across the ring to the *para* position in a manner analogous to that represented in Scheme A. This methiodide IX produced a deep coloration (like methiodide III) to form an alicyclic amine analyzing for X (73%). The quinoid-type structure of X may be indicated by its ultraviolet absorption spectrum (λ_{max} 256 mμ, log ε 3.3).


IX


X

However, attempts to rearomatize the ring of the product employing reactions that have been found characteristic of *exo*-methyleneamines II and IV were unsuccessful. Thus, it failed to undergo thermal isomerization at 150,[5] and it produced a polymer with dilute hydrochloric acid[6] instead of the expected hexamethylbenzene. On the other hand, the alicyclic amine reacted with bromine to eliminate dimethylmethyleneiminium bromide (as observed with *exo*-methyleneamine II)[2] although the expected aromatic product evidently was not formed. More significantly, the alicyclic amine reacted with butyllithium in ether accompanied by coloration (as observed with *exo*-methyleneamine II) to give an alicyclic amine analyzing for XI (91%) which was converted by methyl iodide to a methiodide analyzing for XII (94%). Reaction of the latter product with potassium amide in liquid ammonia caused the expected[7] elimination of the carbanion of tetramethylammonium iodide which was isolated as tetramethylammonium picrate (72%), but, instead of the anticipated[7] *n*-amylpentamethylbenzene, a non-aromatic hydrocarbon was obtained. The latter hydrocarbon readily absorbed bromine under conditions that failed with hexamethylbenzene.


XI


XII

In view of these results structures X, XI and XII are to be considered only working models. Somewhere in this series of reactions other alicyclic rings might have been formed.

Experimental[8]

***exo*-Methylenecyclohexadieneamine Methiodide III.**—*exo*-Methyleneamine II, b.p. 50–51° at 0.4 mm., n^{25}_{D} 1.5111, was prepared as described previously[2] in 70% yield by the rearrangement of 2,4,6-trimethylbenzyltrimethylammonium chloride (I) with sodium amide in liquid ammonia. The product has an ultraviolet absorption maximum occurring at 313 mμ (3.8), calcd.[9] 313 mμ.

Conversion of this alicyclic amine II into *exo*-methylenecyclohexadieneamine methiodide III was effected[2] in 99% yield by the action of methyl iodide on II in acetonitrile solution. After crystallization from acetonitrile–ether and drying *in vacuo*, this salt[10] melted with decomposition at 153–154°.

Rearrangement of III to 6-Methylene-1,2,3,5-tetramethyl-1-dimethylaminomethylcyclohexadiene-2,4 (IV).—To a rapidly stirred suspension of 0.33 mole of sodium amide in 500 ml. of liquid ammonia contained in a 1-l. three-necked flask equipped with condenser and sealed stirrer was added over 5 minutes 36.0 g. (0.11 mole) of finely powdered *exo*-methyleneamine methiodide III. The violet-colored reaction mixture was stirred for 30 minutes, and 13.4 g. (0.25 mole) of ammonium chloride was added (color faded) to

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[3] No such deep coloration is observed in the conversion of quaternary ion I to *exo*-methyleneamine II; see ref. 2.

[4] Since the two steps in most base-catalyzed β-eliminations are simultaneous, carbanion VIII might not be an intermediate.

[5] Thermal isomerization of the type shown by *exo*-methyleneamine IV (equation 2) might not occur with structure X because *para* groups would be involved.

[6] This acidic decomposition was accompanied by a deep violet coloration which indicates the intermediate formation of a carbonium ion similar to that observed by Shriner and Geipel (THIS JOURNAL, **79**, 227 (1957)) in the reaction of an *exo*-methylene hydrocarbon with acid.

[7] See C. R. Hauser and D. N. Van Eenam, *ibid.*, **79**, 6277 (1957).

[8] Melting and boiling points are uncorrected. Microanalyses are by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Ultraviolet absorption spectra were measured in 95% ethanol solution using a Warren Spectracord Model 3000 automatic-recording spectrophotometer.

[9] For calculations of absorption maxima by Woodward's rules, see L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Third ed., Reinhold Publishing Corp., New York, N. Y., 1949, pp. 185–188.

[10] This methiodide, which gradually darkened and partially decomposed on exposure to air, was used immediately for further reaction.

destroy the excess amide. Reagent grade ether (600 ml.) was added dropwise while the liquid ammonia was evaporated on the steam-bath. As soon as the ether began to reflux in the cold condenser the reaction mixture was cooled, filtered, and the solvent carefully distilled on the steam-bath, the last traces being removed *in vacuo* at 35°. The residual oil was distilled[11] through a 40-cm. Podbielniak type column to afford, after a trace of forerun (apparently pentamethylbenzene, m.p. 51–52°), 16.9 g. (79%) of *exo*-methyleneamine IV, b.p. 61–61.5° at 0.4 mm., $n^{25}\text{D}$ 1.5232.

Anal. Calcd. for $C_{14}H_{23}N$: C, 81.89; H, 11.29; N, 6.82. Found: C, 82.02; H, 11.27; N, 6.73; ultraviolet absorption spectrum, calcd.[9] λ_{max} 318 mμ; found λ_{max} 321 mμ (3.9).

Also there was obtained from the above distillation 1.9 g. (9%) of the thermal isomerization product, aromatic amine V, b.p. 88.5–89° at 0.45 mm., and 2.0 g. (9%) of polymeric residue.

When the reaction was repeated employing 0.11 mole each of sodium amide and *exo*-methyleneamine methiodide III in 500 ml. of liquid ammonia, there was obtained 16.8 g. (78%) of *exo*-methyleneamine IV, b.p. 61–61.5° at 0.4 mm., $n^{25}\text{D}$ 1.5231; 1.9 g. (9%) of aromatic amine V, b.p. 89–90° at 0.4 mm.; and 2.2 g. (9%) of undistillable residue.

Thermal Isomerization of IV to Form β-Isodurylethyldimethylamine (V).—A 16.8-g. (0.082 mole) sample of *exo*-methyleneamine IV, b.p. 61–61.5° at 0.4 mm., was heated in a flask immersed in a Woods metal bath at 150° (electrically controlled) for one hour. The orange product was distilled *in vacuo* to give 9.2 g. (55%) of colorless β-isodurylethyldimethylamine (V), b.p. 88.5–89° at 0.45 mm., $n^{25}\text{D}$ 1.5162.

Anal. Calcd. for $C_{14}H_{23}N$: C, 81.89; H, 11.29; N, 6.82. Found: C, 81.96; H, 11.37; N, 6.87.

The picrate, recrystallized three times from 95% ethanol, melted at 179.5–180°.

Anal. Calcd. for $C_{20}H_{26}N_4O_7$: C, 55.29; H, 6.03; N, 12.90. Found: C, 55.47; H, 5.95; N, 13.01.

Independent Synthesis of β-Isodurylethyldimethylamine (V).—This aromatic tertiary amine was prepared in three steps by adaptations of the method described previously[2] for the synthesis of β-mesitylethyldimethylamine.

The Grignard reagent, prepared *via* the entrainment method from 0.21 mole of 2-bromoisodurene, 0.21 mole of ethyl bromide and 0.43 g. atom of magnesium turnings, was converted to β-isodurylethanol in 62% yield by the addition of 0.86 mole of ethylene oxide. The pale yellow product distilled *in vacuo* at 132–133° at 3 mm., and solidified on standing, m.p. 41–42°.

A solution of 0.133 mole of this alcohol in benzene was converted by an equivalent of phosphorus tribromide to β-isodurylethyl bromide (52%, undistilled) which was treated with a 20-fold excess of anhydrous dimethylamine in absolute methanol solution (in an amber colored bottle in the dark) for one month. There was obtained 9.5 g. (67%, 22% over-all) of β-isodurylethyldimethylamine (V), b.p. 90–90.5° at 0.5 mm., $n^{25}\text{D}$ 1.5162; picrate m.p. 178.5–179.5°. A mixed melting point with the picrate of the tertiary amine obtained by the thermal isomerization of *exo*-methyleneamine IV was the same.

Reaction of *exo*-Methyleneamine IV with Hydrochloric Acid to Form Pentamethylbenzene.—To crude *exo*-methyleneamine IV, obtained from the rearrangement of 0.05 mole of *exo*-methylenamine methiodide III with 0.15 mole of sodium amide, was added all at once with stirring 125 ml. of cold 6 *N* hydrochloric acid. The amine dissolved immediately with slight warming, and the resulting solution became turbid within several seconds. After standing for 5 minutes (when crystals had risen to the surface), the mixture was extracted with ether. The ethereal extract was washed with water, dried and the solvent removed. There was obtained, after one crystallization from methanol (cooled to −78°), 5.1 g. (71%) of pentamethylbenzene, m.p. 51–52°; this melting point was not lowered on admixture with an authentic sample of pentamethylbenzene, m.p. 52–53°. Based on the 78% yield of pure IV from III (see above), this represents a 91% conversion of IV to pentamethylbenzene.

When the aqueous acidified layer (containing dimethylmethyleneiminium chloride) was made alkaline with sodium hydroxide solution, strong fumes of formaldehyde and dimethylamine were detected.[2]

Reaction of Methiodide IX with Sodium Amide.—This methiodide,[10] m.p. 188–189° dec., was prepared in 98% yield from *exo*-methyleneamine IV and methyl iodide in acetonitrile.

To a stirred suspension of 0.31 mole of sodium amide in 800 ml. of liquid ammonia was added rapidly 53.5 g. (0.154 mole) of finely powdered methiodide IX essentially as described for *exo*-methyleneamine methiodide III. After stirring for 1 hour (color changed from vivid red to deep purple), the reaction mixture was decomposed with ammonium chloride (color faded) and the ammonia replaced by reagent grade ether. The resulting suspension[12] was filtered, the solvent carefully evaporated *in vacuo* from the filtrate, and the residual oil (which had a camphoric odor) distilled to give 24.7 g. (73%) of a product analyzing for X, b.p. 70–71° at 0.4 mm., $n^{25}\text{D}$ 1.5103, leaving 10.4 g. of polymeric material.

Anal. Calcd. for $C_{15}H_{25}N$: C, 82.13; H, 11.49; N, 6.38. Found: C, 81.85; H, 11.48; N, 6.39; ultraviolet absorption spectrum, found λ_{max} 256 mμ (3.9).

This product was converted in acetonitrile solution to its methiodide X in 98% yield. After two crystallizations from acetonitrile–ether the salt melted with decomposition at 220–220.5° (prior darkening at 218°).

Anal. Calcd. for $C_{16}H_{28}NI$: C, 53.18; H, 7.81; N, 3.84. Found: C, 53.28; H, 7.72; N, 3.81.

Reaction of Product X with Bromine.—To a stirred, ice-cooled solution of 5.5 g. (0.025 mole) of product X in 50 ml. of dry carbon tetrachloride was added dropwise over 10 minutes a solution of 4.3 g. (0.027 mole) of anhydrous bromine in 50 ml. of carbon tetrachloride, essentially as described[2] for the bromination of *exo*-methyleneamine II. As the bromine color was discharged a cream colored precipitate of dimethylmethyleneiminium bromide appeared. After continued stirring for 30 minutes, the resulting reaction mixture was triturated with 50 ml. of water (precipitate readily dissolved) and the layers separated.

The aqueous layer, which smelled strongly of formaldehyde, was shaken with 3.5 g. (0.026 mole) of phenyl isothiocyanate to precipitate N,N-dimethylphenylthiourea. This derivative, after crystallization from a minimum of refluxing ethanol, was obtained in 74% yield, m.p. and mixed m.p. 134–135° (reported[13] m.p. 135°).

The pale yellow carbon tetrachloride layer was washed with water, dried, and the solvent evaporated. This afforded 5.6 g. of a gummy, dark colored residue which could not be crystallized, but which was shown to contain bromine by undergoing quaternary ammonium salt formation with trimethylamine. The bromide had a camphoric odor.

Reaction of Product X with Butyllithium.—To a cooled (0°), stirred solution of butyllithium (prepared from 0.23 g. atom of lithium and 0.10 mole of *n*-butyl bromide in 150 ml. of ether) was added rapidly 16.4 g. (0.075 mole) of product X in 100 ml. of ether, essentially as described[2] for the butylation of *exo*-methyleneamine II. After several seconds the solution became yellow colored, and this coloration increased in intensity up to 15 minutes. Water was now cautiously added to hydrolyze the reaction mixture (color faded after the addition of about 2 ml. of this reagent), the ethereal layer washed with water, dried and the solvent removed. There was obtained, after a trace of forerun consisting of recovered X, 18.9 g. (91%) of a product[14] analyzing for XI, b.p. 89–90° at 0.15 mm., $n^{25}\text{D}$ 1.4915.

Anal. Calcd. for $C_{19}H_{35}N$: C, 82.24; H, 12.71; N, 5.05. Found: C, 82.25; H, 12.63; N, 5.04.

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(11) In the corresponding isolation of *exo*-methyleneamine II, steam distillation was desirable in removing the product from polymeric material (see ref. 2, note 26). However, in the present case the low polymer content in the crude reaction mixture rendered steam distillation unnecessary.

(12) This suspension of mixed salts contained some unreacted methiodide IV which was recovered (see ref. 2, note 25) and twice more treated with excess sodium amide in liquid ammonia, the three fractions of product being combined.

(13) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Fourth ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 288.

(14) An ultraviolet absorption spectrum gave no well-defined absorption maximum.

Conversion of this amine to its methiodide XII was effected in 94% yield with methyl iodide in acetonitrile. After two crystallizations from acetonitrile–ether the quaternary ammonium iodide melted with decomposition at 237–239°.

Anal. Calcd. for $C_{20}H_{38}NI$: C, 57.26; H, 9.13; N, 3.34. Found: C, 57.00; H, 9.02; N, 3.47.

Reaction of Methiodide XII with Potassium Amide.—To a stirred solution of 0.10 mole of potassium amide in 300 ml. of liquid ammonia was added rapidly 18.1 g. (0.043 mole) of methiodide XII essentially as described for the reaction of *n*-amylcyclohexadieneamine methiodides with potassium amide.[7] The resulting deep red reaction mixture was stirred for 1 hour, the ammonia replaced by ether, and the mixture hydrolyzed by the cautious addition of 50 ml. of water. The aqueous and ethereal layers were separated, the latter being washed with water, dried over magnesium sulfate, filtered, and the solvent evaporated. Distillation *in vacuo* afforded 4.2 g. (45%) of a non-aromatic hydrocarbon,[14] b.p. 76–77° at 0.15 mm., n^{25}_{D} 1.5023, leaving a dark-colored, viscous residue of 4.4 g.

Anal. Calcd. for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 87.62; H, 12.35.

The aqueous alkaline layer containing tetramethylammonium hydroxide was neutralized with hydrochloric acid, followed by the addition of 12 g. (0.05 mole) of picric acid. The resulting suspension was heated to boiling (solution attained), then cooled to 0°, and the precipitated quaternary ammonium salt collected on a funnel. After recrystallization from a minimum of boiling water there was obtained 9.4 g. (72%) of tetramethylammonium picrate, m.p. 310–312° (reported[15] m.p. 312–313°). A mixed melting point with an authentic sample of tetramethylammonium picrate, m.p. 313–314°, was not depressed.

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[15] W. Lossen, *Ann.*, **181**, 364 (1876).

DURHAM, NORTH CAROLINA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

The Rearrangement of Cyclohexene Oxides with Magnesium Bromide Etherate[1-3]

BY SAIYID M. NAQVI, JEROME P. HORWITZ AND ROBERT FILLER

RECEIVED APRIL 1, 1957

Cyclohexene oxide, 1-methylcyclohexene oxide and 1-ethylcyclohexene oxide rearrange in the presence of magnesium bromide etherate at 0 and 60°. At 0°, cyclohexene oxide is converted to *trans*-2-bromocyclohexanol, whereas at 60° a mixture of *trans*-2-bromocyclohexanol and cyclopentanecarboxaldehyde is isolated. At 0°, 1-methylcyclohexene oxide rearranges to 1-methylcyclopentanecarboxaldehyde, while at 60° a mixture of 2-methylcyclohexanone and methylcyclopentyl ketone is obtained. 1-Ethylcyclohexene oxide rearranges predominantly to 1-ethylcyclopentanecarboxaldehyde at 0° and to 2-ethylcyclohexanone at 60°. Mechanisms for the formation of products are proposed and the results are also rationalized in terms of conformational analysis.

Several studies involving the rearrangement of cyclopentene and cyclohexene halohydrins and epoxides have been carried out. Bartlett[4-6] and his co-workers demonstrated that in both the 5- and 6-membered ring systems, the *trans*-1,2-chlorohydrins formed epoxides on treatment with alkali, whereas the *cis* isomers gave rearranged products. Thus, *trans*-2-chloro-1-methyl-1-cyclohexanol gave the epoxide, while the *cis* compound rearranged to methyl cyclopentyl ketone. When the *cis* isomer was heated to 200°, 2-methylcyclohexanone and a small amount of the ring-contracted ketone were obtained.

Tiffeneau, Tchoubar and Le Tellier[7] reported that *trans*-2-chloro-1-alkyl-1-cyclohexanols, after reaction with ethylmagnesium bromide, formed the corresponding alkyl cyclopentyl ketone. Under the same conditions, the *cis* analog gave the uncontracted rearranged product, the 2-alkylcyclohexanone.

Geissman and Akawie[8] studied the *cis*- and *trans*-2-chloro-1-indanols and proposed two general mechanisms to explain the course of these rearrangements.

Bedos[9] reported that cyclohexene oxide rearranged in the presence of magnesium bromide etherate at an elevated temperature to cyclopentanecarboxyaldehyde. Tiffeneau[10] found that cyclohexene oxide was converted to *trans*-2-bromocyclohexanol at 0°, whereas at a higher temperature, cyclopentanecarboxaldehyde was obtained. Similarly, he reported that 1-methylcyclohexene oxide formed the two isomeric *trans*-bromohydrins when the reaction was carried out at 0°. The stable isomer rearranged at a higher temperature to methyl cyclopentyl ketone while the unstable one was converted to a mixture of 2-methylcyclohexanone and 1-methylcyclopentanecarboxaldehyde. Unfortunately, both Bedos and Tiffeneau reported meager experimental data, both with regard to reaction conditions and to the separation and identification of the products. In some cases, they did not prove the structures of their products and did not offer stereochemical interpretations of the observed results. The primary purpose of our investigation was to shed additional light on the mechanism of this rearrangement.

We observed, in agreement with Tiffeneau, that cyclohexene oxide and magnesium bromide etherate at 0° gave only *trans*-2-bromocyclohexanol in over 60% yield. At 60°, however, a mixture of *trans*-2-bromocyclohexanol and cyclopentanecarboxaldehyde, in yields of 49 and 40%, respectively,

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[1] Abstracted from the thesis submitted to the Graduate School of Illinois Institute of Technology by Saiyid M. Naqvi in partial fulfillment of the requirements for the degree of Master of Science.

[2] Presented before the Division of Organic Chemistry at the 130th Meeting of the American Chemical Society, Atlantic City, N. J., September, 1956.

[3] This work was supported by a grant from the Research Corporation.

[4] P. D. Bartlett and R. H. Rosenwald, THIS JOURNAL, **56**, 1990 (1934).

[5] P. D. Bartlett and R. V. White, *ibid.*, **56**, 2785 (1934).

[6] P. D. Bartlett, *ibid.*, **57**, 224 (1935).

[7] M. Tiffeneau, B. Tchoubar and S. Le Tellier, *Compt. rend.*, **216**, 856 (1943).

[8] T. A. Geissman and R. I. Akawie, THIS JOURNAL, **73**, 1993 (1951).

[9] P. Bedos, *Compt. rend.*, **189**, 255 (1929).

[10] M. Tiffeneau and B. Tchoubar, *ibid.*, **207**, 918–919 (1938).