presence of ferric chloride. A mixture of 13.2 g. (0.05 mole) of *o*-xylylene bromide and 170 ml. of benzene was treated with 6.0 g. (0.037 mole) of ferric chloride in the same manner as above. The products isolated were as follows: 6.6 g. (79 mole %) of diphenylmethane, b.p. 133–135° (13 mm.), and 3.8 g. (30 mole %) of *o*-dibenzylbenzene.

The reaction of o-xylylene bromide with benzene in the presence of stannic chloride. Similar treatment of 13.2 g. (0.05 mole) of *o*-xylylene bromide and 80 ml. of benzene with 11.9 g. (0.1 mole) of stannic chloride gave 1.5 g. (18 mole %) of diphenylmethane, besides 5.2 g. of *o*-xylylene bromide which was recovered unchanged.

KYÔTO, JAPAN

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Ring Opening in Benzocyclobutene Derivatives. I. The Reaction of *trans*-1,2-Diiodobenzocyclobutene with Dimethylamine[1]

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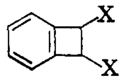
Treatment of *trans*-1,2-diiodobenzocyclobutene with dimethylamine leads to the formation of α,α,α′-trisdimethylamino-*o*-xylene and a small amount of α-dimethylamino-*o*-tolualdehyde. The formation of these products is rationalized by postulating an opening of the four-membered ring initiated by nucleophilic attack of dimethylamine.

Benzocyclobutene and its derivatives have lately become of interest for two reasons: First, these compounds are highly strained due to the presence of a fused benzene and four-membered ring system; second, benzocyclobutene derivatives are possible precursors of benzocyclobutadiene, a compound of great theoretical interest for which some molecular orbital calculations predict a substantial delocalization energy.[3]

Due to the strain inherent in the benzocyclobutene nucleus, the prediction has been made that compounds containing this structural feature might not be capable of existence, or at best be highly reactive.[4] However, a whole series of benzocyclobutene derivatives, including benzocyclobutene itself, have been prepared and have been found to be quite stable.[5–8] Among these stable benzocyclobutene derivatives were the dihalobenzocyclobutenes, 1,2-dibromobenzocyclobutene (I) and 1,2-diiodobenzocyclobutene (II). These dihalides were stable towards boiling alcohol, alcoholic potassium acetate, and maleic anhydride.[5] Catalytic reduction did not rupture the four-membered ring but, instead, produced benzocyclobutene.[7] It was only when dibromide I was heated with bromine at 150° for twelve hours that ring opening occurred to give α,α,α′,α′-tetrabromo-*o*-xylene.[5,9]



I. X = Br
II. X = I

It has recently been found in this laboratory, however, that dihalides I and II undergo a facile ring opening when treated with secondary amines. This reaction was first observed when a mixture of dibromide I and diiodide II was treated with piperidine. Upon heating to 50° a mixture of piperidinium bromide and iodide precipitated and an undistillable red oil was obtained. In the subsequent investigation of this reaction, pure *trans*-diiodide II was used to eliminate the possibility of different reactions from different stereoisomers and to make possible the determination of the amount of amine salt formed. Dimethylamine was employed as the amine in order to make the products readily distillable.

When *trans*-diiodide II was treated with an excess of dimethylamine in an Adkins bomb at 60° for six hours, a mixture of two liquid products was formed along with two equivalents of dimethylammonium iodide. The lower boiling product, formed in 10% yield, was shown to be α-dimethylamino-*o*-tolualdehyde (III); evidence for the structure of this compound is presented below. The major product, formed in 64% yield, was a highly re-

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[1] This paper is based on portions of a thesis submitted by M. W. Hanna to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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[3] J. D. Roberts, A. Streitweiser, Jr., and C. M. Regan, *J. Am. Chem. Soc.*, **74**, 4579 (1952).

[4] W. Baker (The Tilden Lecture, 1944), *J. Chem. Soc.*, **258**, (1945).

[5] M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **79**, 1701 (1957).

[6] M. P. Cava, R. L. Little, and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2257 (1958).

[7] M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2255 (1958).

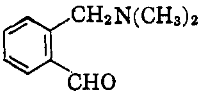
[8] M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **79**, 3606 (1957).

[9] Some other examples of ring opening in benzocyclobutene derivatives have recently been reported. See M. P. Cava and K. Muth, *J. Am. Chem. Soc.*, **82**, 652 (1960).

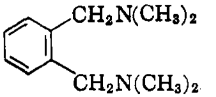
active liquid that began to decompose within fifteen minutes after distillation even though stored under argon. If this highly reactive liquid was reduced immediately after distillation using Raney nickel and dry Skellysolve F, a new amine was formed. This new amine was shown to be α,α-bis-dimethylamino-*o*-xylene (IV) by comparison of its properties with those of an authentic sample prepared by the method of von Braun and Cahn.[10] The infrared spectrum of diamine IV prepared by this method was identical with that of the reduction product. A mixture melting point determination of the two dipicrates showed no depression.

If the highly reactive liquid was treated with dilute acid and then with base, a product different from the starting material was obtained. An infrared spectrum and a mixture melting point determination of its picrate showed that this liquid product was identical with the lower boiling product obtained in the original reaction of diiodide II with dimethylamine; therefore, it was the aminoaldehyde III.

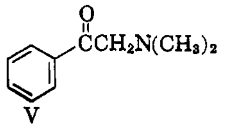
Assignment of structure III to the product resulting from acid treatment of the highly reactive liquid and to the lower boiling product from the original reaction was based on the following evidence: combustion analysis of the pure liquid was consistent with the formula $C_{10}H_{13}NO$; both a picrate and a 2,4-dinitrophenylhydrazone derivative were formed, and the analyses of these derivatives were also consistent with products derived from a compound having the composition $C_{10}H_{13}NO$. Three structures containing a benzene ring and a dimethylamino group attached to a side-chain can be written with this empirical formula. These possibilities are ω-dimethylaminoacetophenone (V) and α-dimethylaminophenylacetaldehyde (VI).



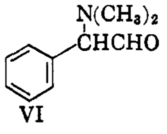
III



IV



V

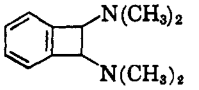


VI

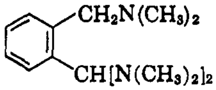
Amino aldehyde III reduced Tollens reagent readily, and its infrared spectrum exhibited a band at 1690 cm.$^{-1}$, indicating the presence of an aromatic aldehyde. Furthermore, *ortho*-disubstitution would be expected in a product derived from diiodide II; and a strong band in the infrared spectrum at 760 cm.$^{-1}$, coupled with the absence of a strong band at 700 cm.$^{-1}$, confirmed this. Only structure III is consistent with all of the above evidence.

Confirmation that dimethylamine was lost in the conversion of the reactive liquid to aminoaldehyde III was obtained by treating the original reactive product with picric acid. After five recrystallizations, analytically pure dimethylamine picrate was obtained whose melting point was not depressed upon admixture with an authentic sample.

On the basis of these reactions there are two possible structures for the major product of the reaction of *trans*-diiodide II with dimethylamine. 1,2 - Bisdimethylaminobenzocyclobutene (VII) would be expected on the basis of the structure of the starting material and that of the reduction product diamine IV; α,α,α'-trisdimethylamino-*o*-xylene (VIII) would be reasonable on the basis of the acid-decomposition product, aminoaldehyde III.



VII



VIII

The correct structure for this product can be decided upon by a consideration of its proton magnetic resonance spectrum. The spectra of both diamine VII and triamine VIII will contain absorptions due to the methyl and aromatic ring hydrogens, but these will appear in the high and the low field portions of the spectra respectively. These absorptions will be neglected in the following discussion since they are common to both compounds. Diamine VII, then, should exhibit only one peak in its proton-resonance spectrum—that due to the two equivalent benzocyclobutenyl protons. Triamine VIII, however, should contain two peaks with approximately a 2:1 ratio of intensities, corresponding to the absorptions of the benzyl and benzylidine hydrogens respectively. The observed spectrum was exactly that expected for triamine VIII, having one absorption at 6.60τ and one at 5.87τ.[11] The absorption at 6.60τ had twice the intensity of the 5.87τ peak and was, therefore, due to the two benzyl hydrogens, while the absorption at 5.87τ was due to the one benzylidine hydrogen. Additional evidence that this was the proper assignment came from the observation that the benzyl protons in benzyldimethylamine have a resonance peak at 6.68τ.[12] Furthermore, in the proton resonance spectrum of bisdimethylaminomethane, the resonance peak due to the methylene protons was shifted to a lower value of the magnetic field with respect to the methyl

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[10] J. von Braun and R. S. Cahn, *Ann.*, **436**, 262 (1924).

[11] For a definition of τ see G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

[12] G. V. D. Tiers, *Characteristic Nuclear Magnetic Resonance "Shielding" Values (Spectral Positions) for Hydrogen in Organic Structures*, Central Research Department, Minnesota Mining and Manufacturing Co., St. Paul, Minn., March 28, 1958, p. 15.

protons by a factor of 0.44τ.[13] This chemical shift can be considered an approximate measure of the effect of adding a second dimethylamino group to a saturated carbon atom. It would be expected, then, that the absorption due to the benzylidine proton in triamine VIII would be shifted to a lower field value by a factor of comparable magnitude. In agreement with this expectation a shift of 0.73τ to a lower value of the applied field was observed. Thus NMR provides conclusive evidence for the assignment of structure VIII to the highly reactive liquid obtained in the reaction of *trans*-diiodide II with dimethylamine.[14]

The occurrence of a ring opening in the reaction of *trans*-diiodide II with dimethylamine was surprising in view of the stability of its four-membered ring toward other reagents. Under the conditions of its formation it must remain in the presence of a large excess of iodide ion at 80° for eight to ten days. Yet, no ring opened product has been reported, and the yield of diiodide II is often as high as 90%. This indicates that diiodide II, like dibromide I, is fairly resistant to ring opening by nucleophilic reagents. Dimethylamine is a more powerful nucleophilic reagent than iodide ion and, in addition, is a fairly strong base. Its action on *trans*-diiodide II could be due therefore to either one or a combination of these properties. Since it is known that dibromide I was converted *via* an elimination-addition mechanism to 5-bromobenzo[a]biphenylene by treatment with potassium *t*-butoxide,[15] it is possible that a *cis* elimination of hydrogen iodide is the first step in the reaction of diiodide II with dimethylamine. To test the reactivity of this diiodide toward a base comparable with dimethylamine, a sample was heated in refluxing triethylamine for twenty-four hours. If elimination is important in this reaction, a compound similar to the above biphenylene derivative should be formed. At the completion of this reaction, however, there was no evidence of formation of triethylammonium iodide, and pure diiodide II was recovered in 85% yield.

It is probable, then, that the nucleophilic character of dimethylamine was responsible for the ring opening in *trans*-diiodide II. A possible reaction sequence is shown in Fig. 1. An attack of a dimethylamine molecule on diiodide II, instead of displacing an iodine atom, produces ring opening resulting in the formation of carbanion IXa. Shift of a proton would then give α-dimethylamino-α,α′-diiodo-*o*-xylene (IXb), and this intermediate would quickly react with the excess dimethylamine to give triamine VIII.

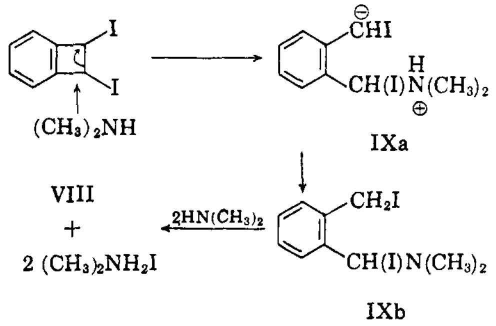

Figure 1

The initial step in this reaction sequence involves the breaking of a carbon-carbon bond and the formation of a carbon-nitrogen bond. A consideration of bond energies indicates that the initial product, carbanion IXa, would have a higher energy than the starting material by a factor of 14 kcal./mole. However, considerable strain is relieved when the benzocyclobutene ring is broken, and this would act to lower the energy of intermediate IX. A rough estimate of the strain energy in the four-membered ring of benzocyclobutene derivatives, using the force constants for the in-plane C—H deformation in benzene and a similar deformation in methane, indicated a minimum strain energy of 20 kcal./mole. Thus, the energy gained by relieving the strain present in diiodide II is enough to make the first step in the above reaction sequence thermodynamically feasible.

If the mechanism described above is correct, then ring opening should occur upon attack by a nucleophilic reagent whenever the bond being formed between the nucleophilic reagent and the carbon atom of the four-membered ring has an energy greater than 60–65 kcal./mole. This postulate is consistent with the observation that diiodide II is stable in the presence of a large excess of iodide ion since the carbon-iodine bond energy in benzyl iodide is only 43 kcal./mole.

EXPERIMENTAL[16]

trans-1,2-Diiodobenzocyclobutene (II) was prepared by the method of Coleman and Jensen,[17] m.p. 62–64° (lit. m.p. 63–64°).

Treatment of trans-1,2-diiodobenzocyclobutene with dimethylamine. Preparation of α-dimethylamino-o-tolualdehyde (III) *and α,α,α′-trisdimethylamino-o-xylene* (VIII). *trans*-1,2-Diiodobenzocyclobutene (17.8 g., 0.05 mole) and anhydrous dimethylamine (22.5 g., 0.5 mole) were placed in a glass-lined Adkins bomb and heated at 50–60° for 6 hr. The bomb was allowed to cool overnight. The yellow oily product was transferred to a 500-ml. Erlenmeyer flask with the aid of

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[13] G. V. D. Tiers, private communication, 1959.

[14] In a previous communication, S. W. Fenton and M. W. Hanna, *J. Org. Chem.*, **24**, 579 (1959), this compound was erroneously reported to be diamine VII.

[15] M. P. Cava and J. F. Stucker, *J. Am. Chem. Soc.*, **79**, 1706 (1957).

[16] Melting points were determined in a silicone oil bath and are uncorrected; infrared spectra were determined on a Perkin-Elmer Model 21 double-beam spectrophotometer; microanalyses were performed at the University of Minnesota by Mrs. Olga Hamerston and Mr. William C. Kuryla.

[17] W. E. Coleman and F. R. Jensen, *J. Org. Chem.*, **23**, 869 (1958).

250 ml. of anhydrous ether. A large quantity of solid formed when the ether was added; this solid was broken up with a stirring rod to release occluded liquid. The solid was separated by filtration and washed with two small portions of anhydrous ether; there remained 16 g. (93% of the amount calculated for 2 equivalents) of white dimethylammonium iodide, m.p. 149–152°.

The solvent was removed from the combined filtrate and washings, and the residue was distilled. Four fractions were collected: (0.88 g.) b.p. 57–62°/0.09 mm., $n_D^{26.8}$ 1.5216; (0.79 g.) b.p. 62–67°/0.09 mm., $n_D^{26.8}$ 1.5152; (0.90 g.) b.p. 67–71°/0.09 mm., $n_D^{26.8}$ 1.5118; (5.76 g.) b.p. 71–74°/0.09 mm., $n_D^{26.8}$ 1.5088. The high boiling fraction, α,α,α'-trisdimethylamino-*o*-xylene, also boiled at 100–102°/2.5 mm.; it always had an index of refraction between 1.5094 and 1.5095 at 25°. The lower boiling fractions were mixtures of α,α,α'-trisdimethylamino-*o*-xylene and α-dimethylamino-*o*-tolualdehyde. The yields of α-dimethylamino-*o*-tolualdehyde and α,α,α'-trisdimethylaminobenzocyclobutene calculated on the basis of the index of refraction of each fraction were 10.4% and 63.3% respectively.

Purification of α-dimethylamino-o-tolualdehyde. The low boiling fractions from several runs of the above reaction were combined and distilled. The fraction boiling at 82–84°/2.5 mm., $n_D^{23.3}$ 1.5352, was collected. Redistillation of 0.84 g. of this material yielded the following three fractions: (0.04 g.) b.p. 77–84°/2.5 mm., n_D^{23} 1.5364; (0.14 g.) b.p. 84–85°/2.5 mm., n_D^{23} 1.5356; (0.46 g.) b.p. 85–86°/2.5 mm., n_D^{23} 1.5349. Fraction 2 was submitted for analysis.

Anal. Calcd. for $C_{10}H_{13}NO$: C, 73.59; H, 8.03. Found: C, 73.65; H, 8.13.

The ultraviolet spectrum (iso-octane) of this compound exhibited maxima at 284 mμ (log ϵ 3.11) and 243 mμ (log ϵ 4.05).

The 2,4-dinitrophenylhydrazone derivative was prepared by treating crude α-dimethylamino-*o*-tolualdehyde (0.20 g.) with 61 ml. of a solution prepared by dissolving 0.4 g. of 2,4-dinitrophenylhydrazine in 25 ml. of concd. hydrochloric acid, adding 25 ml. of water and diluting to 100 ml. with 95% alcohol. A massive orange solid precipitated and was separated by filtration; it melted with decomposition at 272–276°. This material was partially dissolved in 200 ml. of hot water and sodium carbonate was slowly added until the solution was slightly basic. Cooling and filtration yielded a fluffy, dark-red solid, m.p. 171–175°, which after two recrystallizations from aqueous methanol yielded extremely fine fibers, m.p. 174–175°.

Anal. Calcd. for $C_{16}H_{17}N_5O_4$: C, 55.97; H, 4.99; N, 20.40. Found: C, 55.94; H, 4.96; N, 20.34.

The *picrate derivative* was prepared by dissolving crude α-dimethylamino-*o*-tolualdehyde (0.37 g., $n_D^{28.9}$ 1.5208) in 2.5 ml. of ethanol, and adding 5 ml. of a saturated solution of picric acid in 95% ethanol. The mixture was heated on a steam bath until all of the material precipitated by the picric acid had dissolved. Cooling and filtration yielded 0.56 g. of yellow needles, m.p. 129–140°. After five recrystallizations 0.19 g. of material, m.p. 148–149°, was obtained.

Anal. Calcd. for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.11; N, 14.28. Found: C, 49.22; H, 4.19; N, 13.76.

Treatment of triamine VIII *with dilute hydrochloric acid.* A solution of 0.8086 g. of triamine VIII in aqueous alcohol was treated with hydrochloric acid. The solution was made basic with solid potassium hydroxide and was then extracted with two 100-ml. portions of ether. Evaporation of the ether after drying the solution over magnesium sulfate yielded 0.36 g. (64%) of α-dimethylamino-*o*-tolualdehyde. The infrared spectrum of this product was identical in all respects with the spectrum of α-dimethylamino-*o*-tolualdehyde prepared previously. Treatment of this liquid with picric acid produced yellow needles, m.p. 148–150.5°. The melting point of this compound was not depressed upon admixture with α-dimethylamino-*o*-tolualdehyde picrate.

Treatment of triamine VIII *with picric acid.* Triamine VIII (0.90 g.) was dissolved in 10 ml. of 95% ethanol, and 10 ml. of a saturated ethanolic picric acid solution was added. The solution was heated on the steam bath for a few minutes and then was cooled. The yellow precipitate (0.77 g.), m.p. 155–159°, was recrystallized three times from alcohol yielding 0.14 g. of material, m.p. 158.9–161.2°. A mixture of this picrate and dimethylamine picrate melted at 158.7–161.2°.

Anal. Calcd. for $C_8H_{10}N_4O_7$: C, 35.04; H, 3.68; N, 20.43. Found: C, 35.60; H, 3.82; N, 20.57.

Reduction of triamine VIII. Triamine VIII (2.00 g., 0.0085 mole) was placed in a Parr shaker along with 50 ml. of petroleum ether (b.p. 30–60°) and $^1/_8$ teaspoonful of Raney nickel. This mixture was shaken at room temperature overnight under 2 atm. hydrogen pressure. The solution was filtered through Filtercel to remove the nickel and the solvent was distilled. Distillation of the residue yielded 1.28 g. (78%) of α,α'-bisdimethylamino-*o*-xylene, b.p. 80–82°/4.2 mm., n_D^{26} 1.5020–1.5032.

Treatment of a small quantity of this liquid with alcoholic picric acid gave a *picrate*, yellow needles, m.p. 134.8–135.8°.

Anal. Calcd. for $C_{18}H_{23}N_5O_7$: C, 51.30; H, 5.50; N, 16.62. Found: C, 52.07; H, 5.49; N, 16.70.

If a large excess of picric acid was used and the mixture was heated at the reflux temperature for 15 min. on a steam bath, a *dipicrate*, m.p. 190–191°, was formed. Recrystallization of 0.19 g. of this compound yielded 0.11 g. yellow needles, m.p. 192.6–194.1°.

Anal. Calcd. for $C_{24}H_{26}N_8O_{14}$: C, 44.31; H, 4.03; N, 17.23. Found: C, 44.61; H, 4.09; N, 16.93.

The infrared spectrum of the liquid was identical in all respects with that of an authentic sample of α,α'-bisdimethylamino-*o*-xylene. A mixture of two dipicrates melted at 192.6–194.1°.

β-Phenylethyldimethylamine was prepared by the method of Ichi and Wisegarver,[18] b.p. 95–98°/18 mm., n_D^{22} 1.5013 (lit. b.p. 97–98°/22 mm.).

α,α'-Bisdimethylamino-o-xylene was prepared by the method of von Braun and Cahn,[10] b.p. 80–81°/4.3 mm., n_D^{29} 1.5004 (lit. b.p. 105–106°/14 mm.).

Treatment of this liquid with hot alcoholic picric acid yielded a *dipicrate*, m.p. 190–192°. A small portion of this picrate (80 mg.) was recrystallized from alcohol to give 40 mg. of pure product, m.p. 192.8–194.1° (lit.[18] m.p. 187–188°).

Anal. Calcd. for $C_{24}H_{26}N_8O_{14}$: C, 44.31; H, 4.03; N, 17.23. Found: C, 44.25; H, 3.92; N, 17.11.

Treatment of trans-1,2-diiodobenzocyclobutene with triethylamine. Commercial triethylamine was distilled from potassium hydroxide and 25 ml. of amine, b.p. 87–89°, was collected in a 50-ml. round-bottom flask containing a magnetic stirring bar and 3.56 g. (0.01 mole) of *trans*-1,2-diiodobenzocyclobutene. A condenser was attached to the flask and the reaction mixture was stirred at the reflux temperature under an argon atmosphere for 24 hr. After this time most of the triethylamine was removed under reduced pressure and the oily residue was treated with 25 ml. of hot petroleum ether (b.p. 60–68°). A white solid crystallized upon cooling. This solid was separated by filtration yielding 2.42 g. of material, m.p. 61.5–63.5°. A mixture of this solid and authentic *trans*-1,2-diiodobenzocyclobutene melted at 61.5–63.5°. Concentration of the mother liquors produced an additional 0.61 g. of material, m.p. 61.0–63.5°. This brought the total amount of starting material recovered to 84.5%.

Acknowledgment. The authors wish to thank Dr. G. V. D. Tiers of the Minnesota Mining and Manufacturing Co. for his assistance in obtaining and interpreting the proton resonance spectra reported in this paper.

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[18] R. N. Ichi and B. B. Wisegarver, *Org. Syntheses*, Coll. Vol. III, 723 (1955).