Electrophilic Addition of Molecular Bromine to a Stereochemically Defined Cyclopropane

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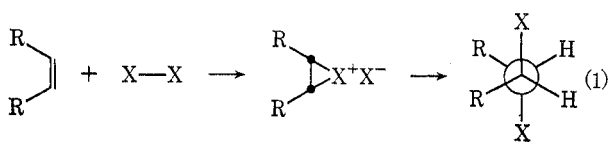
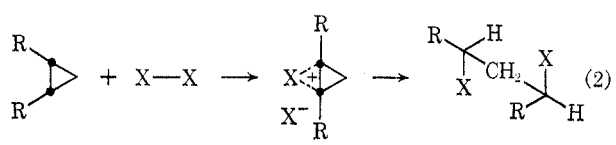
The polar addition of molecular bromine to bicyclo[3.1.0]hexane has been carried out at −30 to −50° in chloroform with the exclusion of light. Addition is predominantly to the internal, more substituted cyclopropane bond. The major products (83%) are *cis*- and *trans*-1,3-dibromocyclohexane and *trans*-1,2-dibromocyclohexane. Minor products have also been studied. The reaction lacks the stereospecificity that characterizes halogen additions to analogous alkenes, such as cyclohexene. These results are discussed primarily in terms of the nonbridged, secondary carbonium ion. There is no evidence that requires a 1,3-bridged bromonium ion.

The mechanisms of halogen additions to alkenes are among the most thoroughly studied in organic chemistry.[2] In contrast, studies of halogen additions to cyclopropane rings have only recently been initiated.[3,4] Stereochemical methods in particular have not been fully utilized in developing the mechanistic foundations for this type of reaction. The work of Deno and Lincoln[3b] identified the important mechanistic pathways but did not include stereochemistry. The halogenation of bicyclo[2.1.0]pentane, as studied by LaLonde,[3a] proceeded by an isomerization pathway that precluded a stereochemical discussion of the initial addition.

Our present approach is to examine halogen additions to cyclopropane rings, with special attention to the stereochemical concomitants. One result from stereochemical studies of additions to alkenes was the suggestion that the reaction proceeds to a symmetrical or unsymmetrical bridged halonium ion intermediate, which may be destroyed by stereochemically well defined pathways (eq 1).[5] By analogous experiments



with cyclopropanes, evidence concerning a possible homobridged pathway (eq 2) may be forthcoming. A

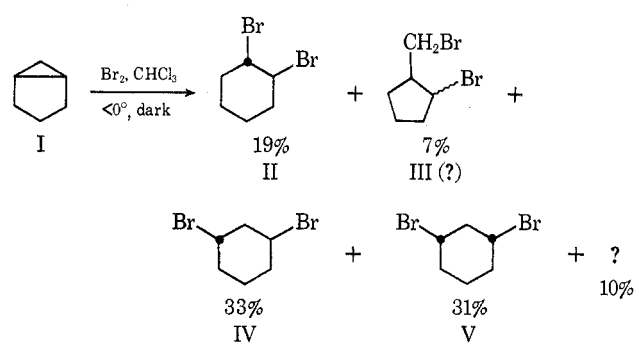


similar bridged structure for protonated cyclopropanes has received considerable attention recently, and acceptance of such intermediates is now widespread.[6] In the present paper, we discuss the reaction of molecular bromine with bicyclo[3.1.0]hexane, a system that may be capable of revealing the stereochemical pathways for electrophilic addition to the three-membered ring.

Results and Discussion

Bicyclo[3.1.0]hexane was allowed to react in chloroform with an equimolar quantity of bromine at −50° in the dark (see Experimental Section). The solvent was removed by vacuum distillation below 0°, and the reaction mixture was examined immediately by vpc. If the mixture was heated to reflux, the product proportions remained constant. Each component was collected by preparative vpc and identified by comparison of its spectral and chromatographic properties with those of authentic material. The three major components (see below) were subjected to the reaction conditions and found to be stable even above 0°. No isomerization could therefore have occurred during solvent removal.

The products and their percentages (the mean of four runs with a standard deviation of about 1.5%) are given below. Compounds II, IV, and V were identi-



fied unequivocally by comparison with the spectra of known materials.[7] Compound III was identified as to formula by its mass spectrum (parent peak triplet at *m/e* 240/242/244). Its nmr spectrum contains a sharp doublet (J = 6 Hz) at δ 3.6, indicative of a $BrCH_2$ group coupled to a methine proton. The structure proof is not, however, complete. Much of the unidentified 10% consists of several shorter retention time materials, possibly alkenes. 1,1-Dibromocyclohexane, *cis*-1,2-dibromocyclohexane, and *trans*-1,4-dibromocyclohexane were synthesized and found not to be in

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(2) For reviews, see (a) G. Heublein, *Z. Chem.*, **9**, 281 (1969); (b) W. R. Dolbier, Jr., *J. Chem. Educ.*, **46**, 342 (1969); (c) R. C. Storr in "Organic Reaction Mechanisms, 1968," B. Capon and C. W. Rees, Ed., Interscience, London, 1969, pp 156–161.

(3) For addition of bromine, see (a) R. T. LaLonde, *J. Amer. Chem. Soc.*, **87**, 4217 (1965); (b) N. C. Deno and D. N. Lincoln, *ibid.*, **88**, 5357 (1966); (c) A. J. Gordon, *J. Chem. Educ.*, **44**, 461 (1967).

(4) For additions of other electrophiles, see among others (a) R. J. Ouellette, A. South, Jr., and D. L. Shaw, *J. Amer. Chem. Soc.*, **87**, 2602 ((1965); (b) R. T. LaLonde, J.-y. Ding, and M. A. Tobias, *ibid.*, **89**, 6651 (1967); (c) H. Hart and R. H. Schlosberg, *ibid.*, **88**, 5030 (1966); **90**, 5189 (1968); (d) V. I. Sokolov, N. B. Rodina, and O. A. Reutov, *J. Org. Chem. USSR*, **3**, 2038 (1967).

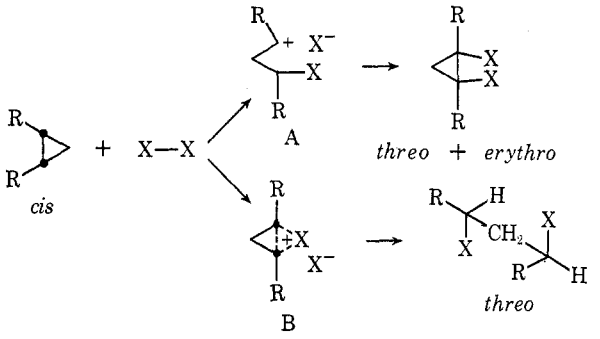
(5) The mechanistic alternatives and refinements have been discussed in ref 2a.

(6) For a review, see C. J. Collins, *Chem. Rev.*, **69**, 543 (1969).

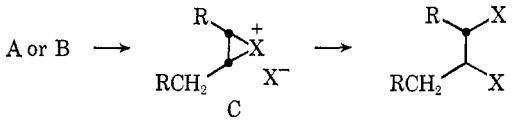
(7) B. Franzus and B. E. Hudson, Jr., *J. Org. Chem.*, **28**, 2238 (1963).

the reaction mixture. One peak amounting to 1% of the mixture was identical in retention time with *cis*-1,4-dibromocyclohexane, but a rigorous identification could not be made.

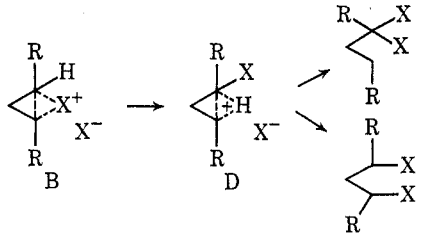
The reactions of cyclopropane rings with electrophiles may be discussed in terms of either nonbridged A or bridged B ions that can yield 1,3 products.[8] The nonbridged pathway should be nonstereospecific, but the opening of the bridged ion B should occur stereospecifically *trans*, *e.g.*, a *cis* starting material should yield a *threo* product, *trans*-1,3-dibromocyclohexane in the present example.



Hydride shifts in either A or B may produce a 1,2-bromine bridge C,[3a] which would be opened stereo-



specifically to a *trans*-1,2 product. Conceivably, the 1,3-bromine bridge could also rearrange to a proton-bridged species[3b] D, which could give 1,1- and 1,3-substituted products.



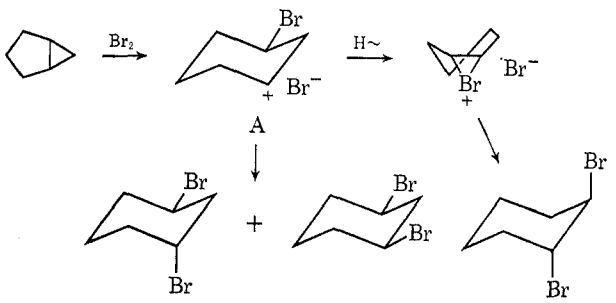
The above discussion of these mechanisms has assumed that bromine addition is favored at the more substituted cyclopropane bond, since higher substitution might better stabilize a partial or full positive charge. Addition to the less substituted bond would yield, by the same set of mechanisms, another series of products, in which the R groups are on adjacent carbon atoms.

It remains to discuss the observed products from bromination of bicyclo[3.1.0]hexane in terms of the above intermediates A–D, in hopes that certain mechanisms may be proved or disproved. Since the three principal products possess six-membered rings, at least 83% of the reaction must occur on the more substituted cyclopropane bond. The small amount of the suspected cyclopentane III may be produced by initial attack on one of the less substituted bonds.

About 19% of the reaction, corresponding to the proportion of *trans*-1,2-dibromocyclohexane (II), must pass through intermediate C [R,R, $(CH_2)_3$; X, Br]. This same intermediate is also proposed for the polar bromination of cyclohexene, in which *trans*-1,2-dibromocyclohexane is produced stereospecifically and exclusively. It is therefore a dead end intermediate in the present reaction. No further rearrangements may proceed from it. Since C can be produced either from A or B, its formation gives no information concerning the initial intermediate.

Because the 1,3-dibromocyclohexanes form almost two-thirds of the reaction mixture, pathways to their formation are more important than in the bicyclo[2.1.0]pentane case,[3a] in which the 1,2 product is formed almost exclusively. The presence of both the *cis*- and the *trans*-1,3-dibromocyclohexane excludes the bridged ion B from being the only intermediate that yields 1,3 products. The nonbridged mechanism A is very appealing, since IV and V are formed in almost equal amounts. A mechanism involving only bridged species demands the improbable necessity that half of B react to form the *trans* compound, and the other half rearrange to D to form the *cis* compound stereospecifically.[9] At present we favor the nonbridged mechanism (Scheme I) since IV and V are produced in similar

SCHEME I



amounts. None of the data presently at hand require the intermediacy of bromine-bridged ions, although such intermediates cannot be entirely rejected. Deno and coworkers[10] have presented evidence that methylcyclopropane forms a nonbridged ion on protonation. Rearrangement of substituted cyclopropanes to secondary carbonium ions on electrophilic attack may in general preclude any stereoselectivity such as is found in the analogous reactions of substituted alkenes.

Experimental Section

Nmr spectra were taken on Varian Models A-60 and T-60 spectrometers and the Bruker 90-MHz HFX-10.[11] Infrared spectra were recorded on Beckman IR-5 and IR-10 spectrophotometers. Mass spectra were obtained from a CEC model 21-104 analytical mass spectrometer. Gas chromatographic experiments were carried out on F & M Model 700 and Varian Aerograph Model 1520B instruments. Analytic and preparative

(8) Two complications are neglected. First, the bridged intermediate could be unsymmetrical. Second, the initial step in either case might be the formation of a charge-transfer complex. The latter situation is much less likely for cyclopropanes than with alkenes. *Cf.* B. C. Menon and R. E. Pincock, *Can. J. Chem.*, **47**, 3327 (1969).

(9) The opening of D should always be stereospecific, with a *cis*-D yielding an *erythro* product, *cis*-1,3-dibromocyclohexane in the present case.

(10) N. C. Deno, D. LaVietes, J. Mockus, and P. C. Scholl, *J. Amer. Chem. Soc.*, **90**, 6460 (1968); N. C. Deno, W. E. Billup, D. LaVietes, P. C. Scholl, and S. Schneider, *ibid.*, **92**, 3700 (1970).

(11) We thank the National Science Foundation for a grant that made the purchase of this instrument possible.

experiments utilized 0.25 in × 6 ft columns containing 10% Carbowax 20M on Chromosorb G, DMCS treated.

Bicyclo[3.1.0]hexane (I) was prepared by the Simmons–Smith reaction on cyclopentene.[12]

trans-**1,2-Dibromocyclohexane** (II) was prepared by the method of Snyder and Brooks.[13]

1-Bromocyclohexene.—The method of Stevens and Valicenti was used to prepare this compound from 2,3-dibromocyclohexene.[14]

1,1-Dibromocyclohexane.—1-Bromocyclohexene (2.0 g) was dissolved in 40 ml of anhydrous ether in a round-bottomed flask equipped with a Dry Ice condenser and a gas-inlet tube. The flask was immersed in an ice bath, 0.1 g of $FeCl_3$ was added, and anhydrous hydrogen bromide was bubbled into the solution for 2 hr. The reaction mixture was washed with four 25-ml portions of water and one 25-ml portion of 10% sodium carbonate, and dried over anhydrous sodium carbonate. 1,1-Dibromocyclohexane (2.1 g) was isolated by distillation [bp 72–81° (7 mm)].[15]

cis-**1,2-Dibromocyclohexane.**—1-Bromocyclohexene (2.5 g) in 250 ml of pentane was irradiated for 1 hr in a Hanovia ultraviolet apparatus, as anhydrous hydrogen bromide was bubbled through the solution. The excess HBr was removed by washing with water and 10% sodium carbonate, and the dried pentane solution was distilled to give 1.7 g of pure *cis*-1,2-dibromocyclohexane [bp 104–105° (9 mm)].[15]

3-Bromocyclohexene was prepared from cyclohexene and N-bromosuccinimide.

1,3-Dibromocyclohexanes (*trans*, IV; *cis*, V).—3-Bromocyclohexene (1.6 g) was placed in a flask containing 6 ml of 48% aqueous hydrobromic acid. The flask was stoppered, heated to 65°, and allowed to stir for 7 hr. From the organic phase, the *cis*- and *trans*-1,3-dibromocyclohexanes were obtained by preparative gas chromatography. Their nmr spectra agreed with those of Franzus and Hudson.[7]

A mixture of *cis*-1,3-, *trans*-1,3-, *cis*-1,4-, and *trans*-1,4-dibromocyclohexane was prepared from the reaction of cyclohexane-1,3-diol with PBr_3 following the method of Franzus and Hudson.[7]

Reaction of Bromine with Bicyclo[3.1.0]hexane.—The brominations were performed in a dark room under red light; the flasks were covered with aluminum foil. Bicyclo[3.1.0]hexane (1.0 g) in 10 ml of chloroform (Baker analyzed reagent grade) and bromine (0.5 g) in 10 ml of chloroform were cooled in separate flasks to −50°. The bromine solution was added slowly to the cyclopropane compounds, and the reaction mixture was then allowed to stand at −30° for about 5 min. The solvent was removed under aspirator pressure below 0°, and the residue was analyzed directly by gas chromatography. The nmr spectrum of the immediate reaction mixture did not change with time.

(12) H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.*, **81**, 4256 (1959).

(13) H. R. Snyder and L. A. Brooks, "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., Wiley, New York, N. Y., 1943, pp 171–172.

(14) C. L. Stevens and J. A. Valicenti, *J. Amer. Chem. Soc.*, **87**, 838 (1965).

(15) H. L. Goering and L. L. Sims, *ibid.*, **77**, 3465 (1955).

Registry No.—Bromine, 7726-95-6; I, 285-58-5.

Alumina-Catalyzed Reactions of Hydroxyarenes and Hydroaromatic Ketones. VI. Mediation of Alcohols in the Reduction Rearrangement of Hexamethylcyclohexadienones[1a]

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At 320° on alumina 2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone (1) in a solvent of methanol, 1-propanol, 2-propanol, or benzene is converted into hexamethylbenzene as the main identified product (24–88 mol %). 2,3,4,4,5,6-Hexamethyl-2,5-cyclohexadienone (in methanol) gives quantitative conversion into hexamethylbenzene under the same conditions. Mechanisms of the reactions are interpreted in terms of surface processes of Meerwein–Ponndorf–Verley reduction and subsequent dienol–benzene rearrangement. Partial demethylation of 1 on the catalyst accounts directly for the formation of by-products (pentamethylbenzene and pentamethylphenol) and indirectly for the occurrence of the main reaction in benzene.

Recently, Ramana and Pillai[2] reported catalysis by sodium-containing alumina of hydrogen-transfer reactions between alcohols (of three of more carbon atoms) and carbonyl compounds in a manner formally similar to the Meerwein–Pondorff–Verley (MPV) reduction and the Oppenauer oxidation. Studies in our laboratory[3–5] with the naphthalene ring system have also shown that methanol plus alumina serve for conversions such as (1) 1-tetralone into 1,2-dihydronaphthalene and (2) 1-oxo-2,2-dimethyl-1,2-dihydronaphthalene and 2-oxo-1,1-dimethyl-1,2-dihydronaphthalene into 1,2-dimethylnaphthalene. It was proposed that reactions 1 and 2 (as well as conversions of naphthols to di- and polymethylnaphthalenes) proceed through a step of the MPV type, whereby hydride transfer occurs from a surface methoxide group to the carbonyl carbon atom to produce a chemisorbed hydronaphthoxide, plus formaldehyde (or other oxidation products).[3–6] In case 1, the transformation is completed by loss of a proton and an oxide ion from the hydronaphthoxide to the alumina surface. In case 2, an attendant process of methyl migration (neopentyl-type rearrangement) is involved.

In further study of reduction–rearrangement such as occurs in case 2 we now report reactions of 2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone (**1**)[7] and its cross-conjugated isomer 2,3,4,4,5,6-hexamethyl-2,5-cyclohexadienone (**2**)[8] with excess alcohol when passed through a bed of Houdry hard alumina (designated catalyst C,[9] containing ~0.4% sodium ion) at 320 and 420°. For **1** at 320° (experiments 1, 3, 4) the major product was hexamethylbenzene (**4**), irrespective of whether methanol, 1-propanol, or 2-propanol was used as the alcohol (see Table I). This result is consistent

(1) (a) This investigation was supported by Research Grant No. CA-5969 from the National Cancer Institute, U. S. Public Health Service. For part V, see ref 5. (b) Research Assistant, 1964–1967.

(2) D. V. Ramana and C. N. Pillai, *Can. J. Chem.*, **47**, 3705 (1969).

(3) J. Shabtai, L. H. Klemm, and D. R. Taylor, *J. Org. Chem.*, **33**, 1489 (1968).

(4) L. H. Klemm, J. Shabtai, and C. E. Klopfenstein, *ibid.*, **35**, 1069 (1970).

(5) J. Shabtai, L. H. Klemm, and D. R. Taylor, *ibid.*, **35**, 1075 (1970).

(6) (a) L. H. Klemm, J. Shabtai, and D. R. Taylor, *ibid.*, **33**, 1480 (1968); (b) *ibid.*, **33**, 1494 (1968).

(7) H. Hart, P. M. Collins, and A. J. Waring, *J. Amer. Chem. Soc.*, **88**, 1005 (1966).

(8) H. Hart and D. W. Swatton, *ibid.*, **89**, 1874 (1967).

(9) This designation for the Houdry alumina catalyst was used in previous papers in this series.[3–6]