Stereochemistry of Vapor Phase Dehalogenation of *meso*- and DL-2,3-Dibromobutane with Zinc[1]

MARSHALL GORDON AND JAMES V. HAY[2]

Department of Chemistry, Murray State University, Murray, Kentucky 42071

Received March 22, 1967

We have observed that the elimination of bromine atoms from the isomeric 2,3-dibromobutanes occurs in a stereospecific manner, giving products expected for a "*trans*" debromination when the bromobutanes in vapor form are passed through a heated column of granular zinc.

Stereospecific elimination of halogens from vicinal dihalides has been reported using iodide ion[3] and metals.[4] An excellent summary of metal-promoted eliminations is given by Banthorpe.[5] Schubert and co-workers[4] obtained principally *trans* debromination products from *meso*- and *dl*-2,3-dibromobutane and *meso*- and *dl*-1,2-dibromo-1,2-dideuterioethane using either magnesium in tetrahydrofuran or zinc in water. Recently, Prince and Bremer have reported *trans* elimination of bromine atoms from the dibromobutanes using sodium selenide in both dimethylformamide and dimethyl sulfoxide.[6]

Using our system for elimination of vicinal halogens, the yield of alkenes increases with increasing temperature, decreasing flow rate, and increasing column length. Quantitative yields of ethylene were obtained from ethylene bromide using a column temperature of 100° and a helium flow rate of 8 ml/min. The dibromobutanes were debrominated at a considerably lower column temperature of 50°. Attempts are being made to ascertain the optimum conditions of flow rate, column temperature, and length for complete stereospecific debromination. *meso*-2,3-Dibromobutane gave *trans*-2-butene (92%) and *cis*-2-butene (8%); *dl*-2,3-dibromobutane gave *cis*-2-butene (89%) and *trans*-2-butene (11%).[7]

We are presently engaged in determining the stereospecificity of elimination of halogens from other vicinal dihalides and to what extent the stereochemistry of these reactions is affected by use of different metals in the dehalogenation column. A kinetic investigation of the reaction and evaluation of Arrhenius parameters should provide insight as to the nature of the metal-catalyzed reaction.

(1) This research was supported by a grant from the Committee of Research and Institutional Studies, Murray State University, Murray, Ky. 42071.

(2) This paper was taken in part from the thesis presented by James V. Hay to the Graduate School of Murray State University in partial fulfillment of the requirements for the degree Master of Science.

(3) S. Winstein, D. Pressman, and W. G. Young, *J. Am. Chem. Soc.*, **61**, 1645 (1939).

(4) W. M. Schubert, B. S. Rabinovitch, N. R. Larson, and V. A. Sims, *J. Am. Chem. Soc.*, **74**, 4590 (1952).

(5) D. V. Banthorpe in "Reaction Mechanisms in Organic Chemistry," Vol. 2, E. D. Hughes, Ed., Elsevier Publishing Co., The Netherlands, 1963, p 136.

(6) M. Prince and B. W. Bremer, *J. Org. Chem.*, **32**, 1655 (1967).

(7) These values represent the averages for ten consecutive runs. After each run the column was repacked with fresh zinc. The compositions of the mixtures of butenes are expected to change as the zinc:zinc bromide ratio changes, *i.e.*, as a given packing is continuously used.

Experimental Section

Preparation of the Dibromobutanes.—Pure *dl*-2,3-dibromobutane was prepared by addition of bromine to *cis*-2-butene (Matheson Co., 99.82% pure) using the method of Young, Dillon, and Lucas.[8] The product was purified by two distillations through a 24-in. stainless steel spinning band column: bp 76–77° (50 mm), $n^{25}D$ 1.5120 (lit.[8] bp 75.6–75.8° (50 mm), $n^{25}D$ 1.5125). *meso*-2,3-Dibromobutane prepared from *trans*-2-butene (Matheson Co., 99.26% pure) was a colorless liquid: bp 73–74° (50 mm), $n^{25}D$ 1.5089 (lit.[8] bp 72.7–72.9° (50 mm), $n^{25}D$ 1.5092).

Debromination of Dibromobutanes.—The apparatus used in this study consisted of the following items in sequence: carrier gas supply and control, "vaporizer" with sampler, oven containing column packed with metal, exit sampler, and flowmeter. Pure helium was used to carry vaporized bromobutanes onto the column and to remove butenes formed by dehalogenation. The vaporizer was constructed of Pyrex glass in such a manner as to permit sampling of the vaporized dibromobutanes prior to their contact with the column. A 10 ft × 0.25 in. column packed with zinc (40 mesh, 99+% pure) was placed in a high mass oven capable of temperature stability to ±0.05°. Samples of the effluent gas from the column were analyzed by glpc. To demonstrate that isomerization of the dibromobutanes did not occur during vaporization, samples of the dibromobutanes were taken from the vaporizer at the beginning and the end of each run and the refractive indices were noted before and after heating; they were identical. Also, authentic samples of *cis*- and *trans*-butenes were passed through the column to determine if the heated column used for debromination could bring about isomerization of the butenes; it did not.

Analysis of Butenes.—Samples of the effluent gas from the column were taken using a syringe and injected into an Aerograph HY-Fi Model 600-D hydrogen flame gas chromatograph equipped with a 20-ft ⅛-in. column packed with silver nitrate in benzyl cyanide (30%) on Chromsorb W connected to a 6-ft ⅛-in. column packed with dimethylsulfolane (30%) on Chromsorb W. Retention times were 7.80 min for *cis* and 4.12 min for *trans* at a temperature of 35° and flow rate 30 ml/min.

Registry No.—*meso*-2,3-Dibromobutane, 5780-13-2; *dl*-2,3-dibromobutane, 14897-69-9; zinc, 7440-66-6.

(8) W. G. Young, R. T. Dillon, and H. J. Lucas, *J. Am. Chem. Soc.*, **51**, 2528 (1929).

The Reactions of Acidic Reagents with Diene–Quinone Adduct Epoxides. II

W. J. MUSLINER, H. S. WILGUS, III, AND J. W. GATES, JR.

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

Received July 5, 1967

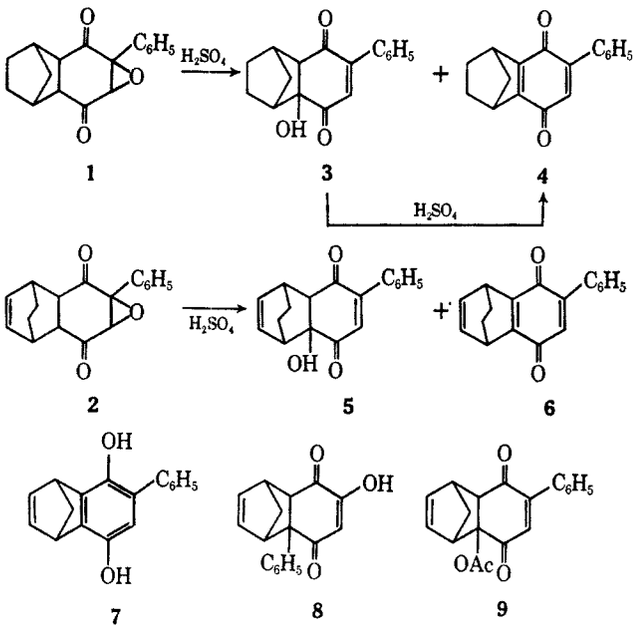
In a previous communication,[1] the reactions of several diene–quinone epoxides with boron trifluoride etherate to afford ring-contracted indanedione derivatives were described. We now report the anomalous reactions of two such epoxides **1** and **2** upon treatment with mineral acid.

Treatment of **1** or **2** with 50% sulfuric acid in dioxane at 80° yielded two products in each case. Quinone **6** was identified by comparison with an authentic sample[2] and a sample of quinone **4** was independently synthesized by oxidation of the product

(1) H. S. Wilgus, III, E. N. Oftedahl, W. J. Musliner, and J. W. Gates, Jr., *J. Org. Chem.*, **32**, 3208 (1967).

(2) R. F. Porter, W. W. Rees, E. Frauenglass, H. S. Wilgus, III, G. H. Nawn, P. P. Chiesa, and J. W. Gates, Jr., *J. Org. Chem.*, **29**, 588 (1964).

SCHEME I



of hydrogenation of 7[2] using procedures reported for similar transformations[2,3] (Scheme I).

Structure **3** for the second product is consistent with the infrared spectrum which shows absorptions at 3500 (–OH) and 1665 cm^{-1} (conj C=O) and with the nmr spectrum ($CDCl_3$) which exhibits one olefinic proton as a singlet at τ 3.12 and one ring-juncture proton as a multiplet at τ 7.50 ppm. That this product is probably an isolable intermediate in the conversion of **1** into **4** was demonstrated by the isolation of **4** in 30% yield when **3** was treated with acid in the same way as **1**.

When, in an attempt to synthesize **3**, cyclopentadiene was added to 2-hydroxy-5-phenyl-*p*-benzoquinone, compound **8** was obtained, as shown by its ultraviolet spectrum. The addition of cyclopentadiene to 2-acetoxy-5-phenyl-*p*-benzoquinone, however, gave adduct **9**.[4] The correctness of structure **3** was demonstrated by catalytic reduction of **9** to afford material identical with the acetylation product of **3**.

The structure of product **5**, the material obtained from epoxide **2**, is based upon analysis and upon spectral data similar to those for **3** as well as upon the analogy between the two reactions.

Experimental Section[5]

2-Phenyl-4a-hydroxy-5,8-methano-4a,5,6,7,8,8a-hexahydro-1,4-naphthoquinone (3).—To a stirred solution of 15 g of epoxide **1** in 200 ml of dioxane at 80° was added 25 ml of 50% sulfuric acid. Stirring was continued for 0.5 hr at 80° and then the solution was poured onto 600 g of ice. The resulting suspension was extracted three times with 100 ml of chloroform and the extract was washed once with water, dried over anhydrous magnesium sulfate, and evaporated. The red oil was taken up to 50 ml of ethanol and chilled to yield 7.6 g of material, mp 143–155° (softens at 120°). This solid, upon recrystallization from 75 ml of ethanol, gave 6.3 g of product **3**, mp 146–155°, which was purified as described below. The filtrates from the original crystallization, upon standing in the cold, deposited reddish crystals, mp 103–105°, 3.3 g (22% yield), identified as **4** by melting point, mixture melting point, and infrared comparison with an authentic sample.

The crude product **3** (6.3 g), mp 146–155°, was purified by stirring for 0.5 hr with 100 ml of ethanol at 40° and filtering at that temperature. The undissolved solid (3.7 g) was pure **3** (42% yield): mp 159–160°, $\lambda_{max}^{C_2H_5OH}$ 305 mμ (log ϵ 3.92).[6]

Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.1; H, 6.0. Found: C, 75.8; H, 6.0.

The filtrate was concentrated to 25 ml and chilled to yield 2.5 g, 16.5% recovery, of unreacted epoxide **1**, mp 118–123°.

Preparation of 2-Phenyl-5,8-methano-5,6,7,8-tetrahydro-1,4-naphthoquinone (4) from 3.—A solution of 2 g of **3** in 26 ml of dioxane at 80° was treated with 3 ml of 50% sulfuric acid and stirred for 0.5 hr at 80°. At the end of this time, the pink solution was poured onto ice and the resulting dispersion extracted with chloroform. After the extract had dried, the extract was evaporated and the residue taken up in 15 ml of hot ethanol and chilled to yield 1.1 g of unreacted **3**, 55% recovery, mp 158–160°. Upon standing, the filtrate deposited 0.6 g, 30% yield, of quinone **4**, mp 101–103°, as shown by melting point, mixture melting point, and infrared spectra.

2-Phenyl-4a-acetoxy-5,8-methano-4a,5,6,7,8,8a-hexahydro-1,4-naphthoquinone from 3.—A solution of 0.5 g of the hydroxy compound **3**, 10 ml of acetic anhydride, and 2 ml of pyridine was heated for 1.5 hr on a steam bath and then poured onto 50 g of ice. After 0.5 hr, the precipitate was collected and crystallized from ethanol to yield 0.4 g: mp 144–145°; ν_{max}^{KBr} 1740, 1685, 1670 cm^{-1}.

Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.5; H, 5.9. Found: C, 73.3; H, 6.2.

2-Acetoxy-5-phenyl-1,4-benzoquinone.—A suspension of 21 g of 2-hydroxy-5-phenyl-1,4-benzoquinone,[7] $\lambda_{max}^{C_2H_5OH}$ 307 mμ (log ϵ 3.98), in 125 ml of acetic anhydride was warmed to 80° on a steam bath and to this suspension 2 ml of pyridine was added, with swirling. After the immediate reaction, the solution was warmed for 5 min on a steam bath and then poured onto 800 g of ice. The resulting slurry was stirred for 30 min and the precipitate collected by filtration. After crystallization from ethanol, the yield of product, mp 108–110°, was 22 g (87%), ν_{max}^{KBr} 1780, 1660 cm^{-1}.

Anal. Calcd for $C_{14}H_{10}O_4$: C, 69.4; H, 4.1. Found: C, 69.1; H, 4.2.

2-Phenyl-4a-acetoxy-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (9).—A benzene solution of 5.5 g of 2-acetoxy-phenyl-1,4-benzoquinone with an excess of cyclopentadiene was refluxed for 18 hr. The solvent was removed *in vacuo* and the product recrystallized first from ligroin and then from ethanol: yield, 4.6 g (66%); mp 119–121°; ν_{max}^{KBr} 1740, 1670 cm^{-1}.

Anal. Calcd for $C_{19}H_{16}O_4$: C, 74.0; H, 5.2. Found: C, 73.6; H, 5.4.

2-Phenyl-4a-acetoxy-5,8-methano-4a,5,6,7,8,8a-hexahydro-1,4-naphthoquinone from 9.—An ethyl acetate solution of 0.5 g of **9** was hydrogenated for 3 min in a Parr shaker with Pd–C as catalyst. After filtration and removal of solvent, the product was recrystallized from ethanol as yellow needles: melting point and mixture melting point with the material obtained from the acetylation of **3**, 142–143°; yield, 0.5 g. The infrared spectra of samples prepared from **3** and **9** were identical.

2-Hydroxy-4a-phenyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (8).—A solution of 4.0 g of 2-phenyl-5-hydroxy-1,4-benzoquinone[7] and 4.5 ml of cyclopentadiene in 50 ml of benzene was heated at reflux for 18 hr and then evaporated to a syrup. This residue was crystallized from ethanol to yield 3.2 g (62%) of product, mp 152–154°. Recrystallization gave material with mp 154–155°; ν_{max}^{KBr} 1650 cm^{-1}; $\lambda_{max}^{C_2H_5OH}$ 281 mμ (log ϵ 4.0).

Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.7; H, 5.3. Found: C, 76.8; H, 5.5.

2-Phenyl-4a-hydroxy-5,8-ethano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (5).—To a solution of 3.5 g of epoxide **2** in 70 ml of dioxane heated to 80°, 8 ml of 50% sulfuric acid was added. The solution was heated on a steam bath for 1.5 hr

(3) H. S. Wilgus, III, E. Frauenglass, P. P. Chiesa, G. H. Nawn, F. J. Evans, and J. W. Gates, Jr., *Can. J. Chem.*, **44**, 603 (1966).

(4) H. D. Hartyler and R. E. Benson, *J. Org. Chem.*, **26**, 3507 (1961); M. F. Ausell, G. C. Calling, B. W. Nash, and D. A. Wilson, *Proc. Chem. Soc.*, 405 (1960).

(5) Infrared spectra were obtained with Baird Models AK-1 or NK-1 or Perkin-Elmer Infracord Model 137 instruments. Nmr spectra were measured with a Varian A-60 spectrometer with TMS as an internal standard (taken as τ 10).

(6) The known[3] cyclopentadiene adduct of phenyl-*p*-benzoquinone exhibits $\lambda_{max}^{C_2H_5OH}$ 305 mμ (log ϵ 3.83).

(7) L. F. Fieser, *J. Am. Chem. Soc.*, **70**, 3165 (1948).

and then poured onto ice. The crude semisolid was treated with 50–100 ml of hot ligroin and filtered. This solution afforded 0.3 g of recovered starting material and 0.5 g of crude quinone **6**, mp 111–115°; the infrared spectrum was identical with that of a known sample. The ligroin-insoluble material was recrystallized first from a large volume of ligroin and then from ethanol–water to afford 0.3 g of pale yellow product **5**: mp 153–155° (sinter 145°); ν_{max}^{KBr} 3420 (-OH) and 1660 cm^{-1} (conj C=O); $\lambda_{max}^{C_2H_5OH}$ 304 mμ (log ε 3.66); one olefinic proton ($CDCl_3$) at τ 3.14 ppm (singlet).

Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.1; H, 5.8. Found: C, 77.5; H, 5.9.

Registry No.—**3**, 14908-33-9; acetate of **3**, 15038-92-3; **5**, 14908-34-0; **8**, 14908-35-1; **9**, 14908-36-2; 2-acetoxy-5-phenyl-1,4-benzoquinone, 14908-37-3.

Constituents of *Brucea sumatrana* Roxb. I. Brusatol[1]

KENG Y. SIM,[2] JAMES J. SIMS, AND T. A. GEISSMAN

Department of Chemistry, University of California, Los Angeles, California 90024

Received August 3, 1967

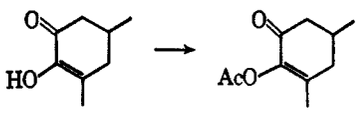
Recent studies on the bitter principles of a number of genera of the family Simaroubaceae have brought to light a group of structurally allied compounds with close chemical and botanical relationships with each other and other constituents of plants of the families Meliaceae and Rutaceae.[3] A number of the simaroubaceous principles are well known in herbal medicine as effective antiamebic agents.[4] A genus of this family that is widely known in Asia for its antidysenteric properties and whose chemical constitution has come under occasional study[5] is *Brucea*, of which *B. sumatrana*, *B. javanica*, *B. antidysenterica*, and *B. amarissima* are known under various local names (ko-sam, ya-tan-tzu, k'u-shen-tzu, lao-ya-tan) as herbal remedies for human amebiasis. Earlier chemical studies[5] resulted in the isolation of a number of crystalline compounds, none of which, however, was well characterized.

We have examined the seeds of *Brucea sumatrana*[6] and have isolated a crystalline compound, brusatol.[7] Brusatol, mp 276–278°, is very bitter, gives a dark green color with ferric chloride, and no color with concentrated sulfuric acid.[8] It could be acetylated to yield a monoacetate and a triacetate, in the first of which the loss of the ferric chloride color reaction and the shift in the ultraviolet absorption spectrum from that characteristic of a diosphenol to one showing the characteristics of an α,β-unsaturated ketone indicated that brusatol was a diosphenol that contained two additional hydroxyl groups and that the diosphenolic hydroxyl group was the first to undergo acylation.

Elementary and functional group analyses of brusatol showed that it has the composition $C_{26}H_{32}O_{11}$ and contains a methoxyl group and what was at first thought to be an acetyl group.[7,9] Early analytical results of acetyl group and methoxyl group determination were not mutually consistent with any molecular formula. The reason for this became clear when brusatol was at length found to be a senecioyl and not an acetyl ester.

The mass spectrum of brusatol showed a weak molecular ion at *m/e* 520, which corresponds to the formula $C_{26}H_{32}O_{11}$, a peak at *m/e* 502 (M − H_2O), and a base peak at *m/e* 55. A peak at *m/e* 83 in brusatol monoacetate corresponds with the fragment $((CH_3)_2C{=}CHCO)^+$, a conclusion that is supported by the observation that in the mass spectrum of dihydrobrusatol are observed peaks at *m/e* values of 57 and 85. These values further suggest that the values *m/e* 55 and 57 are due, respectively, to the ions $((CH_3)_2C{=}CH)^+$ and $((CH_3)CHCH_2)^+$ (or $(CH_3)_3C^+$), formed by the loss of carbon monoxide from the corresponding acylium ions.

The ultraviolet spectrum of brusatol gave a clear indication that a diosphenolic grouping was present. Brusatol has λ_{max} 219 mμ (log ε 4.13) and 279 (3.88) in ethanol and upon addition of alkali the lower wavelength peak remains unaltered while the other shifts to 320 mμ. The brusatol acetates retain the peak at about 220 mμ, but the higher wavelength peak of brusatol is replaced by a shoulder at about 240 mμ (log ε about 4). These observations, along with the nmr spectra, which show the vinylic methyl group but no vinylic hydrogen, are in accord with the presence in brusatol of the grouping **1**, converted by acetylation into **2**.



1 2

The nmr spectra of brusatol (**3**) (measured in pyridine) and its two acetyl derivatives provide information which, along with the assumption that the compound is one of the group of simarolides characteristic of the plant family, define most of the structural features of the molecule. In particular, three-proton singlets at δ 1.90 and 2.11 (in brusatol), the latter of which was initially assigned[7] to an acetyl group, disclosed the presence of the senecioyl grouping, and signals for two protons at δ 4.23 in the monoacetate which appeared at δ 5.32 in the triacetate showed that brusatol contained two secondary hydroxyl groups. A three-proton singlet at δ 3.78 (in the monoacetate) and δ 3.72 (in the triacetate), which disappeared upon alkaline hydrolysis, indicated the presence of a methoxycarbonyl grouping.

(1) Contribution No. 2124 from the Department of Chemistry, U.C.L.A.

(2) University of Singapore; Fulbright Research Scholar, 1967, University of California, Los Angeles.

(3) For a recent review of the literature of studies on simaroubaceous plants, see J. Polonsky, *Planta Med. Suppl.*, 107 (1966).

(4) T. A. Geissman, *Ann. Rev. Pharmacol.*, **4**, 305 (1964).

(5) Y. T. Chang, *Chinese Med. J.*, **69**, 87 (1951).

(6) The seed was procured by S. B. Penick and Co. We are grateful to Mr. Hans R. Schmidt, pharmacognosist, for his efforts in procuring the material and authenticating its identification and in providing us with the crude extracts.

(7) A preliminary account of this work was presented at the colloquium on Phytochemistry and Medicinal Plants of the Pacific Area, Nouméa, New Caledonia, May 1964, and appears in *Bull. Groupe Franc. Argiles*, **144**, 205 (1966).

(8) A characteristic property of a number of the bitter lactones found in the simaroubaceous plants is the intense red to blue colorations that they show when treated with concentrated sulfuric acid.

(9) Brusatol was originally reported[7] to have the composition $C_{25}H_{44}O_{11}$. Mass spectra later provided evidence which made possible the revision to the composition now known to be correct.