rated after 15 hr. reaction time at 25° and recrystallized from benzene, weighed 0.11 g. The crystals, although turning black slowly on heating, melted sharply at 209–210°.

Anal. Calcd. for $C_{13}H_{11}N_3O_4$: C, 57.12; H, 4.03; N, 15.38. Found: C, 56.97; H, 4.39; N, 15.1.

(vi) 5-Bromo-2-nitroanisole (0.33 g.) and azetidine yielded crystals after 30 hr. After a total of 50 hr. the mixture was worked up to yield 0.16 g. of yellow needles melting at 123°. Analysis indicated the compound to be 2,4-bis(N-azetidino)-nitrobenzene.

Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.76; H, 6.48; N, 18.01. Found: C, 62.03; H, 6.65; N, 17.72.

(vii) With 3,4-dinitrobromobenzene (0.25 g.) orange crystals were observed after 60 hr., and after a total of 110 hr. the reaction mixture was worked up to yield 0.12 g. of yellow product with m.p. 122°, unchanged when mixed with the product from vi.

Anal. Found: C, 61.07; H, 6.61; N, 17.53.

The infrared spectra of the products from vi and vii were identical.

(viii) Bromobenzene, *p*-bromochlorobenzene, and 2-bromonaphthalene were recovered from their respective reaction mixtures after 100 days at 50°.

(ix) Reactions involving *m*-bromonitrobenzene and 3,5-dinitrobenzene were similar in behavior. Reaction mixtures reddened rapidly, especially in the case of the dinitro compound. Quenching the reaction in the early stages allowed only the starting material to be isolated in each case, with an amount of intractable material which increased with time. After 100 days the mononitro compound had been converted almost entirely to a brown gummy material which did not dissolve in any common solvent. After 21 days, the dinitro compound had been completely replaced by a black solid with solubility characteristics as unhelpful as in the other case.

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The Brominative Decarboxylation of Bicyclo[2.2.2]octane-1-carboxylic Acid in Halogenated Solvents[1]

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The brominative decarboxylation of bicyclo[2.2.2]octane-1-carboxylic acid in the presence of mercuric oxide in carbon tetrachloride yields appreciable quantities of both 1-chloro- and 1-bromobicyclo[2.2.2]octane. Even in bromotrichloromethane some 1-chlorobicyclo[2.2.2]octane is formed. These results are readily interpreted on the basis of a free radical mechanism. The intermediate 1-bicyclo[2.2.2]octyl free radical is apparently sufficiently reactive to abstract chlorine rather than bromine from bromotrichloromethane. The addition of a mixture of acid and mercuric oxide to excess bromine in bromotrichloromethane provides the desired 1-bromobicyclo[2.2.2]octane free of contamination by the chloride. It was also found that the pure bromide was obtained by reaction in 1,2-dibromoethane. The reaction of the acid and oxide with iodine in carbon tetrachloride yields 1-bicyclo[2.2.2]octyl bicyclo[2.2.2]octane-1-carboxylate and 1-chlorobicyclo[2.2.2]octane.

The Hunsdiecker reaction, the decarboxylation of the silver salt of a carboxylic acid in the presence of molecular halogen, frequently is a valuable method for the introduction of halogens.[3] Recently, Cristol and Firth demonstrated that the use of mercuric oxide with the carboxylic acid possessed considerable advantage obviating the necessity for fully anhydrous conditions.[4] We attempted to apply this reaction for the synthesis of 1-bromobicyclo[2.2.2]octane. However, the adoption of conventional conditions, *i.e.*, the addition of bromine to the mercuric oxide–carboxylic acid mixture in refluxing carbon tetrachloride, yielded a mixture of 1-chloro- and 1-bromobicyclo-[2.2.2]octane. A search of the literature revealed that such side reactions leading to important quantities of impurities had previously been encountered in the Hunsdiecker reaction. For example, Dauben and Tilles observed chlorobenzene among the products of brominative decarboxylation of silver benzoate in carbon tetrachloride.[5] Similarly, Roberts and Chambers noted that chlorine containing substances were formed in the application of the Hunsdiecker reaction to cyclopropane carboxylic acid in tetrachloroethane.[6] Wilder and Winston reported the treatment of the silver salt of apocamphane-1-carboxylic acid with bromine in carbon tetrachloride yielded a mixture of substances which contained both chlorine and bromine.[7] Unfortunately, these workers were unable to characterize the products of the side reactions. The potential utility of the Hunsdiecker reaction in future studies in this laboratory led us to investigate the process in more detail.

Results and Discussion

Under the conditions suggested by Cristol and his students,[4] the addition of bromine to a mixture of red mercuric oxide and bicyclo[2.2.2]octane-1-carboxylic acid in refluxing carbon tetrachloride yielded a waxy solid with a broad melting range. Several sublimations did not significantly improve the melting behavior of the material. Vapor phase chromatography revealed the reaction product was a complex mixture of two major and four lesser components. (The four lesser compounds are discussed in the Experimental.) The two substances formed in high yield comprised more than 80% of the mixture and accounted for 75–85% of the starting bicycloöctane. These compounds were eluted from the column and their melting points and spectra obtained. Comparison with authentic materials revealed them to be the expected 1-bromo- and the unexpected 1-chlorobicyclo[2.2.2]octane. Even more unexpected was the product distribution favoring the chloride (68%) over the bromide (32%).

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(1) Chemistry of the bicyclo[2.2.2]octanes. Part I. This research was supported by a grant, G14211, from the National Science Foundation.

(2) Esso Educational Foundation Fellow, 1961–1962.

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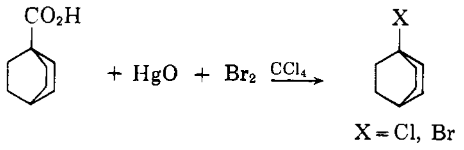

In these experiments, the solvent, carbon tetrachloride, provides the only source of chlorine for the formation of the dominant product, 1-chlorobicyclo[2.2.2]octane. A free radical mechanism, as suggested for the Hunsdiecker reaction[3] and apparently applicable for the Cristol modification, offers the most attractive explanation for the results.

$$RCO_2Br \longrightarrow RCO_2\cdot + Br\cdot$$

$$RCO_2\cdot \longrightarrow R\cdot + CO_2$$

$$R\cdot + Br_2 \longrightarrow RBr + Br\cdot$$

$$R\cdot + Cl_4C \longrightarrow RCl + Cl_3C\cdot$$

Presumably, the hypobromite is decomposed thermally to the intermediate carboxy radical which subsequently loses carbon dioxide to yield, in this case, the reactive 1-bicyclo[2.2.2]octyl radical. This species is apparently capable of abstracting chlorine from carbon tetrachloride even in the presence of bromine. The very high reactivity of the bridgehead radical[8] accounts for the feeble selective properties of this intermediate.

A search was then begun for conditions which would lead to pure 1-bromobicyclo[2.2.2]octane. The competitive reactions of the free radical with bromine and carbon tetrachloride suggested an increase in the bromine to carbon tetrachloride ratio would favor the formation of pure bromide. In the normal addition experiments described above the Br_2/CCl_4 mole ratio was only 2.5×10^{-4}.

A 200-fold increase in the proportion of bromine to about 4×10^{-2} was achieved by the technique of inverse addition,[3] *i.e.*, addition of the red mercuric oxide–carboxylic acid mixture to a refluxing solution of bromine in carbon tetrachloride. The reaction of bicyclo[2.2.2]octane-1-carboxylic acid under these conditions gave an 80% yield of a mixture composed of 66% 1-bromo- and only 34% 1-chlorobicyclo[2.2.2]octane. Thus, the product ratio although still unsatisfactory was considerably improved by the inverse addition technique.

At the suggestion of W. H. Urry, bromotrichloromethane was adopted as a solvent. The ease of abstraction of bromine from this halocarbon is well documented.[9] The brominative decarboxylation of the bicyclic acid was carried out at 75° (for comparison with results in carbon tetrachloride) employing the normal addition procedure. The products were obtained in good yield, but the bromide remained contaminated with 7% of the chloro compound. Inverse addition of the reagents to bromotrichloromethane at 75° provided pure 1-bromobicyclo[2.2.2]octane with less than 0.5% of the 1-chloro derivative. These observations are also best interpreted in terms of the competitive reactions of the non-selective 1-bicyclo[2.2.2]octyl radical, R·.

$$R\cdot + BrCCl_3 \longrightarrow RBr + \cdot CCl_3$$

$$R\cdot + ClCBrCl_2 \longrightarrow RCl + \cdot CBrCl_2$$

$$R\cdot + Br_2 \longrightarrow RBr + \cdot Br$$

The great reactivity of the bridgehead radical is illustrated by its ability to abstract chlorine from bromotrichloromethane.

Careful examination of the chromatograms indicated hexachloroethane was not obtained in either carbon tetrachloride or bromotrichloromethane. However, bromotrichloromethane was formed in significant quantities in the reaction in carbon tetrachloride. The failure of the trichloromethyl radicals to dimerize is rationalized on the basis of a more facile reaction with the available bromine.

$$Cl_3C\cdot + Br_2 \longrightarrow Cl_3CBr + Br\cdot$$

In previous work, the side reactions have been successfully circumvented by the application of Freon[6,10] or petroleum ether[11] as a solvent for the Hunsdiecker reaction of bridgehead radicals. The results of the current study indicate bromotrichloromethane is equally useful. We have also found the brominative decarboxylation of bicyclo[2.2.2]octane-1-carboxylic acid in 1,2-dibromoethane is a fully homogeneous reaction yielding 75–85% of the pure bromide by the normal addition route. This is the most fully satisfactory solvent for effecting the conversion.

Attempts to prepare 1-iodobicyclo[2.2.2]octane employing the normal addition procedure in carbon tetrachloride yielded a mixture of 1-chlorobicyclo[2.2.2]-octane and the Simonini ester, 1-bicyclo[2.2.2]octyl bicyclo[2.2.2]octane-1-carboxylate, in a ratio of 1.0 to 9. No detectable amount of the iodide was formed. The same reaction in cyclohexane produced only the ester in 65% conversion.

In conclusion, the results of this study attest to the dangers of employing chlorocarbon solvents for brominative decarboxylation. Our observations are prejudiced by the remarkable reactivity of the bridgehead radical. However, caution in the choice of solvents appears desirable for other radicals, *e.g.*, primary, of modest reactivity.

Experimental

Materials.—Bicyclo[2.2.2]octane-1-carboxylic acid was prepared by the method of Grob and his associates.[11] The product acid was sublimed three times at 100° at 1 mm. and exhibited a m.p. 140.5–142° (lit.,[11] 140.5–142°). Commercially available reagent grade bromine, iodine, mercuric oxide, and carbon tetrachloride were employed without further purification. Bromotrichloromethane (Matheson, Coleman and Bell) was washed with concentrated sodium hydroxide, dried, and distilled. The fraction boiling between 102–103° was collected and stored in a dark bottle. Dibromoethane and cyclohexane were treated by conventional procedures prior to use.[12] Hexachloroethane, m.p. 186.5–187°, was obtained through the courtesy of N. C. Yang.

General Procedure, Normal Addition.—Bicyclo[2.2.2]octane-1-carboxylic acid (1.0 g., 0.0065 mole) and red mercuric oxide (1.0 g., 0.0046 mole) were placed in a 50-ml. three-neck flask equipped with reflux condenser, addition funnel, and magnetic stirrer. Solvent (20–25 ml.) was added to the solids and the mixture heated to 70–80° while stirring vigorously. A solution

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[10] J. D. Roberts, W. T. Moreland, and W. Frazer, *ibid.*, **75**, 637 (1953).

[11] C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta*, **41**, 1191 (1958).

[12] A. Weissberger, *et al.*, "Technique of Organic Chemistry, Vol. **7**, Organic Solvents," Interscience Publishers, Inc., New York, N. Y., 1955.

of bromine (1.0 g., 0.0062 mole) in the solvent (8–10 ml.) was added slowly through the addition funnel. When the addition was complete, the reaction mixture was heated for an additional hour, then cooled to room temperature and filtered to remove inorganic solids. Residual unreacted acid was extracted into aqueous 5.0 *M* sodium hydroxide. The solution was dried over Drierite and concentrated to about 5 ml. by careful fractionation. The concentrate was examined by vapor phase chromatography. This procedure was used for carbon tetrachloride, bromotrichloromethane, and 1,2-dibromoethane.

The attempted preparations of 1-iodobicyclo[2.2.2]octane followed the same procedure except that iodine (insoluble in these solvents at room temperature) was added as a solid.

General Procedure, Inverse Addition.—For inverse addition, bromine in the appropriate solvent was first placed in the reaction flask. The insolubility of the mercuric oxide–carboxylic acid mixture in carbon tetrachloride or bromotrichloromethane prevented the simple addition of these reagents as a homogeneous phase. However, heating the mixture and rapid shaking made dropwise addition practicable. The reaction mixtures were treated as described for normal addition.

1-Halobicyclo[2.2.2]octanes.—A pure sample of 1-bromobicyclo[2.2.2]octane was prepared by the method of normal addition with 1,2-dibromoethane as solvent. The concentrated solution of the product in the reaction solvent was chromatographed on alumina. The desired bromide was eluted with cyclohexane. The hydrocarbon was evaporated and the residue purified by sublimation at 75° at 2 mm. The yield of purified material was 63%.

Pure samples of these materials were also obtained by preparative vapor phase chromatography. The melting points of 1-chloro- (m.p. 103.5–104.5; lit.,[13] 104–105°) and 1-bromobicyclo-[2.2.2]octane (m.p. 58.5–59.5°; lit.,[13] 64.5–65.5°) were in reasonable agreement and the infrared spectra were identical to those reported for samples prepared from 1-hydroxybicyclo-[2.2.2]octane.[13]

1-Bicyclo[2.2.2]octyl Bicyclo[2.2.2]octane-1-carboxylate.—The ester was prepared by the normal addition procedure with iodine as previously described. A white, waxy solid was isolated in 61% yield. After sublimation at 80° at 2 mm., the material melted sharply at 88.5–89.5° and exhibited a strong absorption at 1740 cm.$^{-1}$ in carbon tetrachloride solution.

Anal.[14] Calcd. for $C_{17}H_{26}O_2$: C, 77.80; H, 9.98. Found: C, 77.89; H, 10.09.

Vapor Phase Chromatography.—Analyses were achieved by examination of the reaction products on 6 ft. × 1/4 in. column of Dow-Corning Hi-Vac grease on firebrick at 90–100° with 80–100 ml. helium min.$^{-1}$. For trapping experiments a 6 ft. × 3/8 in. column was employed. Under these conditions, the reaction solvents were eluted first followed by 1-chlorobicyclo-[2.2.2]octane, hexachloroethane, and 1-bicyclo[2.2.2]octyl bicyclo[2.2.2]octane-1-carboxylate with similar but not identical retention times. 1-Bromobicyclo[2.2.2]octane was considerably separated from these substances.

A typical chromatogram as that obtained for the products of the normal addition of bromine to a mixture of mercuric oxide and the acid in carbon tetrachloride showed a large elution peak for the excess solvent followed by a lesser quantity of bromotrichloromethane. The Simonini ester and hexachloroethane were not observed, but large quantities of 1-chloro- and 1-bromobicyclo [2.2.2]octane were eluted. At long retention times, four additional products representing about 15–20% of the area for the halobicyclo[2.2.2]octanes were detected.

The four products with longer retention times were formed in all experiments involving brominative decarboxylation, regardless of the solvent employed. Only three of these materials could be obtained in quantities sufficient for infrared spectra. No firm assignment of structure can be made. However, the simplicity of the infrared spectra suggested two of these products (liquids) to be similar di- or trihalogenated bicyclo[2.2.2]octanes. The nature of the third substance (a solid) is very uncertain. It exhibited absorptions at frequencies characteristic of the bicyclic nucleus and, in addition, at 1705 and 1720 cm.$^{-1}$ (in carbon tetrachloride solution).

Yields reported for the halobicyclo[2.2.2]octanes were established by the application of *p*-dichlorobenzene as an internal standard.

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[14] Microanalytical data were obtained by W. Saschek.

Configurations of the 1,3-Cycloheptanediols and the 3-Hydroxycycloheptene Oxides

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The *cis* and *trans* forms of 3-hydroxycycloheptene oxide have been reduced separately with lithium aluminum hydride to give in each case a mixture of only one 1,2-glycol and one 1,3-glycol. From the identity of the 1,2-cycloheptanediol in each case, the configurations of both the 3-hydroxycycloheptene oxide and the accompanying 1,3-cycloheptanediol were assigned.

In earlier work two 1,3-cycloheptanediols were isolated from the mixture of glycols obtained by lithium aluminum hydride reduction of a mixture of the isomeric forms of 3-hydroxycycloheptene oxide and were designated as α- and β-1,3-cycloheptanediol.[1] In order to determine the configurations of the two 1,3-glycols, *cis*- and *trans*-3-hydroxycycloheptene oxides were separated and each was reduced. Each isomer yielded only one 1,2-glycol and one 1,3-glycol. Since both *cis*- and *trans*-1,2-cycloheptanediol are well characterized compounds,[2] the configurations of both the 3-hydroxycycloheptene oxide and the accompanying 1,3-cycloheptanediol could be assigned once the 1,2-cycloheptanediol formed in each reduction had been identified.

Analysis of the mixtures of 3-hydroxycycloheptene oxides by gas chromatography showed that the isomers (designated as A and B) were formed in the same ratio (2:1 A:B) on epoxidation of 2-cyclohepten-1-ol with monoperphthalic acid or peracetic acid. It is interesting to note that the epoxidation of 2-cycloöcten-1-ol yields the *trans* isomer[3] and that the epoxidation of 2-cyclohexen-1-ol yields the *cis* isomer.[4] Fractional distillation of the mixture of 3-hydroxycycloheptene oxides separated pure isomer A from isomer B containing 2% of A. Infrared spectra of the isomers were different, and the phenylurethans melted at 129.5–130.0° and 134.0–134.5°, respectively, and had different infrared spectra.

Reduction of isomer A with lithium aluminum hydride yielded a mixture of glycols containing 81%

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