[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF COLORADO, AND CONTRIBUTION NO. 2298 FROM THE GATES AND CRELLIN LABORATORIES OF THE CALIFORNIA INSTITUTE OF TECHNOLOGY]

Bridged Polycyclic Compounds. VII. The Bromination of Quadricyclo[2,2,1,0^{2,6},0^{3,5}]heptane-2,3-dicarboxylic Acid[1,2]

BY STANLEY J. CRISTOL AND ROBERT T. LALONDE

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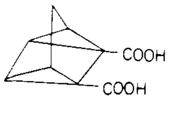
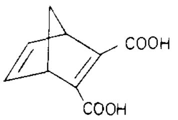
Quadricyclo[2,2,1,0^{2,6},0^{3,5}]heptane-2,3-dicarboxylic acid was brominated in the dark to give *exo*-3-*exo*(or *endo*)-5-dibromotricyclo[2,2,1,0^{2,6}]heptane-2-*endo*-3-dicarboxylic acid. Demonstration of the structure of this dibromodicarboxylic acid was made possible by its conversion to the known γ-lactone of *exo*-3-bromo-*endo*-5-hydroxytricyclo[2,2,1,0^{2,6}]heptane-2,*endo*-3-dicarboxylic acid. The γ-lactone was converted to other known derivatives. The facile solvolysis of the dibromodicarboxylic acid is discussed in terms of its two possible structures.

In previous work[2] it was demonstrated that quadricyclo[2,2,1,0^{2,6}0^{3,5}]heptane - 2,3 - dicarboxylic acid (I) could be obtained in good yield from its valence-bond tautomer bicyclo[2,2,1]heptadiene-2,3-dicarboxylic acid (II). The formation of the quadricyclenedicarboxylic acid, which is the first compound known with this ring system, has promoted a study of the addition of both symmetrical and unsymmetrical reagents to this compound. In this paper we wish to describe the mode of addition of bromine to I.

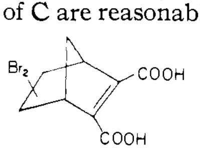


I

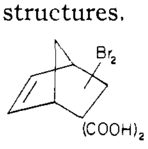


II

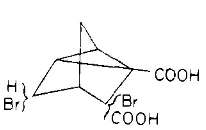
To insure that the bromination of I took place only by an ionic mode of addition, the bromination was carried out in the dark in a mixed solvent of ethyl acetate and carbon tetrachloride. The bromination appeared to be exothermic. A 72% yield of a crude dibromide was obtained. This, when recrystallized, melted at 208°. The dibromide reacted immediately at room temperature with ethanolic silver nitrate, did not react with sodium iodide in acetone, and was soluble in water and in a 5% aqueous solution of sodium bicarbonate. It showed no strong ultraviolet light absorption in the region above 207 mμ and gave a negative potassium permanganate test. These results indicated that this dibromide could not be represented by structures A or B, but that isomers of C are reasonable structures.



A



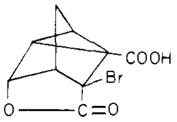
B



C

In the infrared absorption spectrum of the dibromide was found a strong absorption band at 5.80μ. This band is attributable to the carboxylic acid carbonyl absorption.[3] Absence of absorption bands in the region of 6.0-6.40μ[4,5] also indicated that the dibromide did not possess olefinic double bonds. Lack of absorption in the region of 12.3-12.5 μ would suggest[6] that the dibromide did not have the nortricyclene structure (C). However, it will be demonstrated that this inference is incorrect.

The dibromide was observed to react readily in warm water to give a solid melting at 262° which had the empirical formula $C_9H_7BrO_4$. Evidence that this material was a bromolactonic acid was obtained from the infrared spectrum which showed an absorption band at 5.54 μ, an absorption characteristic of strained γ-lactones,[2,7] and an absorption band at 5.89 μ, a band which was assigned to the carboxylic acid carbonyl absorption.[3] This infrared absorption spectrum was identical in every way with the spectrum of an authentic sample of the γ-lactone of *exo*-3-bromo-*endo*-5-hydroxytricyclo[2,2,1,0^{2,6}]heptane-2,*endo*-3-dicarboxylic acid (IV) which is reported to melt at 265°.[8,9] Absent in both spectra was the characteristic nortricyclene absorption in the region of 12.3–12.5 μ.



IV

Treatment of the bromolactonic acid with diazomethane gave the corresponding methyl ester, m.p. 120.5°. The reported melting point of the γ-lactone of *exo*-3-bromo-*endo*-5-hydroxy-2-methoxycarbonyltricyclo[2,2,1,0^{2,6}]heptane-*endo*-3-carboxylic acid (V) is 123°.[8] The infrared spectrum of this ester showed absorption bands at 5.52 μ, an absorption characteristic of a strained γ-lactone, and an absorption at 5.76 μ, an absorption which is within that region characteristic of ester carbonyl absorptions.[11]

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(1) This paper was presented at the Sixteenth International Congress of Pure and Applied Chemistry in Paris, France, in July, 1957.

(2) Previous paper in series: S. J. Cristol and R. L. Snell, THIS JOURNAL, **80**, 1950 (1958).

(3) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 143.

(4) Reference 3, pp. 32–34.

(5) P. R. Schleyer, Abstracts of the 130th Meeting, American Chemical Society, Atlantic City, N. J., September, 1956.

(6) (a) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett and R. Armstrong, THIS JOURNAL, **72**, 3116 (1950); (b) E. R. Lippincott, *ibid.*, **73**, 2001 (1951); (c) C. D. VerNooy and C. S. Rondestvedt, *ibid.*, **77**, 3583 (1955).

(7) (a) J. A. Berson, *ibid.*, **76**, 4975 (1954); (b) P. Wilder, Jr., and A. Winston, *ibid.*, **77**, 5598 (1955).

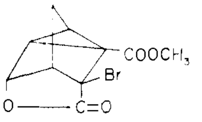
(8) K. Alder and F. Brochhagen, *Ber.*, **87**, 167 (1954).

(9) We have extended the *endo–exo* terminology beyond its original usage in bicyclo[2,2,1]heptane systems[10] to tricyclo[2,2,1,0^{2,6}]heptane systems by referring configurations with respect to the unsubstituted methano bridge. This system will be extendable to nortricyclene derivatives with substituents on all three methano bridges if configurations are always referred to the C_7-carbon atom (same side, *exo*, opposite side, *endo*). It appears to us that use of the terms *endo* and *exo* in these connotations is better than coining new terms, even though the original derivations[10] are not precisely applicable.

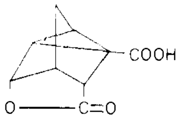
(10) J. Bredt, *J. prakt. Chem.*, **121**, 153 (1929).

(11) L. J. Bellamy, ref. 3, p. 153.

When the bromolactonic acid was hydrogenated according to the method of Alder and Brochhagen,[8] 0.94 mole of hydrogen was absorbed for each mole of bromolactonic acid. The isolated product was the known γ-lactone of *endo*-5-hydroxytricyclo-[2,2,1,$0^{2,6}$]heptane-2,*endo*-3-carboxylic acid,[2,8,12] (VI), m.p. 198°. The identity of the lactonic acid was established by a mixed melting point determination with an authentic sample and a comparison of the infrared spectrum with that of an authentic sample. Thus our bromolactonic acid may also be assigned structure IV.

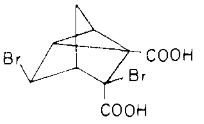


V

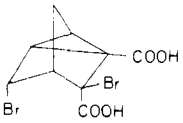


VI

Of the possible dibromides which might result from the addition of bromine to the quadricyclene derivative I only the dibromides shown as structures IIIa or IIIb (C) could be reasonably expected to give the bromolactonic acid IV.



IIIa

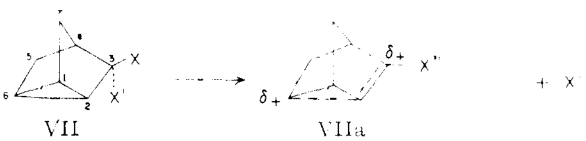


IIIb

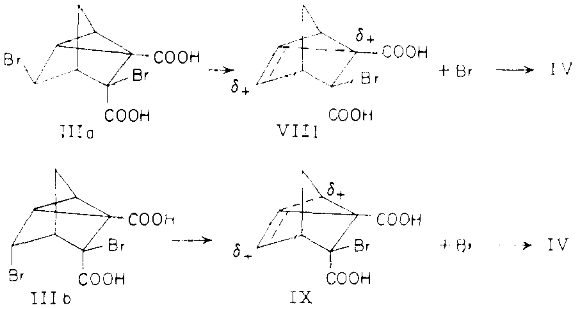
It is interesting to note that the absorption in the region of 12.3-12.5 μ which is presumably characteristic of nortricyclene derivatives,[6] is not found in the three nortricyclene derivatives III, IV and V, which are doubly substituted at C_3 and/or are tetrasubstituted nortricyclenes.[13] At the present time we are unable to state at what stage in substitution on nortricyclenes this absorption disappears, but the trisubstituted lactonic acid VI and various disubstituted derivatives of nortricyclene do show this absorption.

A determination of the pK_a's for *exo*-3,*exo*(or *endo*)-5-dibromotricyclo[2,2,1,$0^{2,6}$]heptane-2,*endo*-3-dicarboxylic acid, IIIa or IIIb, showed that pK_a^1 = 1.9 and pK_a^2 = 5.8. The pK_a^1 undoubtedly represents the facility of the C_3– carboxyl group to ionize since this is an α-bromo substituted acid.[14] Thus, under the reaction conditions by which III is converted to the lactonic acid IV, this C_3-carboxyl group has ionized almost completely. The facile solvolysis of bromide ion and the formation of the bromolactonic acid in aqueous solution may probably be attributed to participation by the C_3-carboxylate ion. On this basis, structure IIIa is to be preferred over structure IIIb since the bromolactonic acid is formed by the attack by the C_3-carboxylate ion on C_5 with inversion, and structure IIIa has the appropriate stereochemistry.

However, carboxylate-ion participation is not the only factor which can be considered for the facile loss of bromide ion. The loss of bromide ion from the dibromide might be also accompanied by carbon participation. The enhanced solvolysis rates of 3-nortricyclyl *p*-bromobenzenesulfonate,[15] chloride, and bromide[16] have been attributed to this effect. Such participation would give rise to the resonance-stabilized intermediate VIIa as shown below. For such participation it is reasonable to believe that the leaving atom, or group, and the participating carbon atoms of the molecule must have a coplanar conformation; *i. e.*, in structure VII, atoms X, C_3, C_2, and C_6 must be coplanar.[17,18] Thus the solvolysis, with carbon participation, of IIIa and subsequent formation of the bromolactonic acid IV would proceed through the intermediate VIII. The solvolysis and subsequent formation of the bromolactonic acid from IIIb would proceed through the intermediate IX.



VII VIIa



IIIa VIII IIIb IX

Of the two intermediates, the formation of IX would be preferred over VIII since the formation of the intermediate VIII would involve the development of a partial positive charge on a carbon atom which is adjacent to a carbonyl carbon atom. Thus only IIIb would be likely to solvolyze with carbon participation and, on the basis that carbon participation is the cause of the rapid loss of bromide ion, structure IIIb would be preferred over IIIa.

Because of the implications involved in the solvolysis of the dibromide and the lack of any other evidence which would indicate the specific orientation of the two bromine atoms in the molecule, we are unable, at this time, to assign a definite structure to this dibromide.

The light-catalyzed bromination of I gave a solid which melted at 183–190°. This crude material was not purified, but an infrared absorption spectrum of this crude material appeared to be identical with the spectrum of *exo*-3,*exo*(or *endo*)-5-dibromo-

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[12] A. Winston and P. Wilder, Jr., THIS JOURNAL, **76**, 3045 (1954).

[13] Quadricyclene-2,3-dicarboxylic acid (I) also may be included in the group of nortricyclene derivatives which do not absorb in the region of 12.3–12.5 μ.

[14] E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, pp. 573–577.

[15] S. Winstein, H. M. Walborsky and K. Schreiber, THIS JOURNAL, **72**, 5795 (1950).

[16] (a) J. D. Roberts, W. Bennett and R. Armstrong, *ibid.*, **72**, 3329 (1950); (b) J. D. Roberts and W. Bennett, *ibid.*, **76**, 4623 (1954).

[17] D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 44 (1956).

[18] S. J. Cristol and R. P. Arganbright, THIS JOURNAL, **79**, 3441 (1957).

tricyclo[2,2,1,$0^{2,6}$]heptane - 2,*endo* - 3 - dicarboxylic acid (III).

Acknowledgments.—The authors are indebted to the Office of Ordnance Research, U. S. Army, for support of this work. S.J.C. is also indebted to the John Simon Guggenheim Memorial Foundation for a fellowship under which this research was initiated. The authors also wish to thank Professor Kurt Alder for his kindness in supplying them with an authentic sample of IV.

Experimental

Bromination of Quadricyclo(2,2,1,$0^{2,6}$,$0^{3,5}$)heptane-2,3-dicarboxylic Acid (I).—To a solution of 0.36 g. (2.0 mmoles) of quadricyclene-2,3-dicarboxylic acid,[2] in 35 ml. of ethyl acetate in a 125-ml. red flask was added 65 ml. of carbon tetrachloride. To this solution was added 0.36 g. (2.26 mmoles) of bromine in 10 ml. of carbon tetrachloride. The contents of the flask were allowed to stand at room temperature for 30 minutes. The bromination was exothermic as evidenced by the slight warming of the reaction flask.

The solvent and excess bromine were removed from the reaction mixture by evaporation in a stream of dry air. The light yellow-colored solid which remained was recrystallized from a mixture of petroleum ether (b.p. 85–100°) and ethyl acetate. One recrystallization gave 0.49 g. (72% yield) of solid melting at 203–206°.[19] Recrystallization from the same mixed solvent raised the melting point to 205–208°. This material was soluble in warm water (200 mg./10 g. of water) and in 5% sodium bicarbonate solution with the evolution of carbon dioxide. The solid (III) did not decolorize a neutral aqueous solution of potassium permanganate, gave a precipitate of silver bromide when ethanolic silver nitrate was added at room temperature and did not react with sodium iodide in acetone at room temperature.

Anal. Calcd. for $C_9H_8Br_2O_4$: C, 31.79; H, 2.37. Found: C, 32.15; H, 2.44.[20]

Conversion of *exo*-3,*exo*(or *endo*)-5-Dibromotricyclo-(2,2,1,$0^{2,6}$)heptane-2,*endo*-3-dicarboxylic Acid (III) to the γ-Lactone of *exo*-3-Bromo-*endo*-5-hydroxytricyclo(2,2,1,$0^{2,6}$)-heptane-2,*endo*-3-dicarboxylic Acid (IV).—A solution of 1.340 g. of III in 250 ml. of water was heated at reflux for one hour. The water was then removed by evaporation in a stream of dry air. The last traces of water were removed *in vacuo*. Recrystallization of the solid residue from a mixture of petroleum ether (b.p. 85–100°) and ethyl acetate gave 228 mg. of solid melting at 255–260°. A second crop, 55 mg. (m.p. 240–250°), was obtained from the recrystallization solvent. A total yield of 28% of the lactone was obtained. Sublimation of the crude IV raised the melting point to 259–262°.[8]

Anal. Calcd. for $C_9H_7BrO_4$: C, 41.73; H, 2.72; Br, 30.85. Found: C, 41.73; H, 2.44; Br, 30.57.

Conversion of the γ-Lactone of *exo*-3-Bromo-*endo*-5-hydroxytricyclo(2,2,1,$0^{2,6}$)heptane-2,*endo*-3-dicarboxylic Acid (IV) to its Methyl Ester V.—The bromolactonic acid (215 mg., 0.827 mmole) was suspended in 80 ml. of anhydrous ether in a 125-ml. flask which was provided with a magnetic stirrer. An ethereal solution of diazomethane was added to the suspension of the bromolactonic acid until the yellow color of diazomethane persisted, and a slight excess of the diazomethane solution was added. Stirring was continued for one hour; during this time the solid completely dissolved. The ether was removed by distillation, and the remaining solid melted at 102–115°. Two recrystallizations of this material from methanol-water raised the melting point to 119.5–120.5°.[8]

Hydrogenation of the γ-Lactone of *exo*-3-Bromo-*endo*-5-hydroxytricyclo(2,2,1,$0^{2,6}$)heptane - 2,*endo* - 3 - dicarboxylic Acid (IV).—In 25 ml. of a 4% aqueous solution of sodium carbonate was dissolved 265 mg. of the bromolactonic acid (1.02 mmoles). This solution was added to a suspension of 1 g. of Raney nickel in 20 ml. of 4% sodium carbonate. The Raney nickel catalyst had been reduced previously. The basic solution of the bromolactonic acid was shaken with catalyst at 23° and under a hydrogen pressure of 620 mm. In 6 hours 940 mmoles of hydrogen was absorbed for each mole of bromolactonic acid.

The catalyst was removed by filtration, and the aqueous sodium carbonate solution was acidified with 20% sulfuric acid. The water was evaporated under a stream of dry air. The last traces of water were removed *in vacuo*. By treating the salt cake which remained with ethyl acetate, the organic material was extracted. The ethyl acetate solution was decolorized with animal charcoal. After removal of the charcoal by filtration, a quantity of petroleum ether (b.p. 85–100°) was added to the ethyl acetate solution. The resulting solution was boiled until the solution became turbid; it was then filtered and cooled. There was obtained 102 mg. of solid, m.p. 150–190°. Recrystallization of this material from a mixture of petroleum ether and ethyl acetate gave a solid melting at 187–195°. A sublimation of this solid raised the melting point to 190–198°. A mixed melting point determination of this material with an authentic sample[8,12,21] of the γ-lactone of *endo*-5-hydrotricyclo-(2,2,1,$0^{2,6}$)heptane-2-*endo*-3-dicarboxylic acid (VI) melted at 196–204°.

The Light-catalyzed Bromination of Quadricyclene-2,3-dicarboxylic Acid (I).—To a suspension of 1.26 g. (7.00 mmoles) of the dicarboxylic acid I in 100 ml. of carbon tetrachloride was added 1.50 g. of bromine (9.39 mmoles) in 10 ml. of carbon tetrachloride. The bromination was carried out in a 125-ml. Vycor flask which was provided with a reflux condenser and a magnetic stirrer. The flask was placed adjacent to an ultraviolet light source (a G. E. AH-4 ultraviolet lamp). The flask and its contents were irradiated for 23 hours. The solid was filtered and dried; 2.27 g. of crude product, m.p. 183–190°, was obtained.

An infrared absorption spectrum of the crude product had a carboxylic acid carbonyl absorption at 5.85 μ. No absorption was found in the region of 6.00–6.40 μ. The spectrum was identical with that of (III).

Acidity Constant Measurements.—A weighed sample of acids III or IV was dissolved in 75 ml. of distilled water, and the solution was titrated with standard alkali using a Beckman *p*H meter to follow the *p*H. The *p*H at the point of three-fourths neutralization of the dibasic acid was taken as the $pK_a{}^2$ for III and had the value 5.8 (uncorrected for ionic strength effects). The $pK_a{}^1$ for III was calculated from values of hydrogen-ion concentration read off the *p*H meter and knowledge of stoichiometric acid concentrations, using the equilibrium constant expression, and had the value 1.9. The pK_a for IV also was calculated in the latter fashion and had the value 3.5.

Infrared absorption spectra were determined with a Perkin–Elmer model 21 spectrophotometer. All of the compounds were run as solids in potassium bromide disks.

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[19] All melting points were taken on a Fisher–Johns melting point apparatus.

[20] Analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

[21] The authentic sample of the γ-lactone VI was prepared by Mr. Robert Snell by treating *exo*-2-bromobicyclo(2,2,1)hept-5-ene-*endo*-2,3-dicarboxylic anhydride with warm water. The authentic sample melted at 206.5–207.5°.