[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

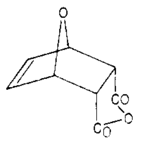
cis-Addition in the Bromination of Bicyclic Olefins. The Structure and Stereochemistry of the Dibromides of *exo-cis*-3,6-Endoxo-Δ^4-tetrahydrophthalic Anhydride and *endo-cis*-3,6-Endomethylene-Δ^4-tetrahydrophthalic Anhydride[1]

BY JEROME A. BERSON AND RONALD SWIDLER

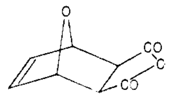
RECEIVED SEPTEMBER 2, 1953

The isomeric dibromides of *exo-cis*-3,6-endoxo-Δ^4-tetrahydrophthalic anhydride are shown to be geometrical isomers of 4,5-dibromo-3,6-endoxohexahydrophthalic anhydride. The configurations of the isomers are shown by optical resolution, the isomer of m.p. 163° being a racemate and therefore *trans*, the isomer of m.p. 331° being a *meso* compound and therefore *cis*. The influence of reaction conditions on the proportions of the isomers and a rationale for the formation of the *cis* isomer are discussed. The structure and stereochemistry of the dibromide, m.p. 206°, obtained on bromination of *endo-cis*-3,6-endomethylene-Δ^4-tetrahydrophthalic anhydride and the mechanism of bromination of *exo-cis* 3,6-endoxotetrahydrophthalic acid and its bearing on the composition of the product mixture are discussed.

Skeletal rearrangement accompanying the action of various addenda upon bicyclic olefins is a common phenomenon.[2] As part of a study of such additions and related processes, we have investigated the bromination of the furan–maleic anhydride adduct, *exo-cis*-3,6-endoxo-Δ^4-tetrahydrophthalic anhydride (Ib).



Ia

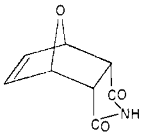


Ib

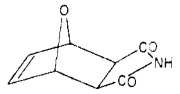
The choice of this substance was prompted by (i) its unique structural features, (ii) the preliminary observation[3] that the bromination yields *two* dibromides, and (iii) the expectation that the stereochemistry and constitution of the products would lend themselves to unequivocal elucidation by classical methods of optical resolution.

Bromination of Ib in methylene chloride gave a mixture of two dibromides (melting at 163° and 331°, respectively) in over 90% yield. Separation of the isomers was easily accomplished since the high-melting product was virtually insoluble in methylene chloride.

Gross Structure of the Dibromides.—Both dibromides were saturated to permanganate and elemental analysis indicated the empirical formula $C_8H_6O_4Br_2$ for each. The presence of anhydride functions in both isomers was demonstrated by hydrolysis to the corresponding dicarboxylic acids, each of which furnished the parent anhydride upon recyclization. In order to demonstrate that drastic structural alteration of the bicyclic system had not occurred during the bromination, both dibromoanhydrides were degraded to the known[4] *exo-cis*-3,6-endoxo-Δ^4-tetrahydrophthalimide (IIb). Chart I summarizes the degradations. This degradation scheme was chosen (in preference to the more obvious one of direct debromination of IIIα and IIIβ to Ib) because of the reported[2d,5] instability of Ib.



IIa



IIb

CHART I

Low-melting series	High-melting series
Dibromoanhydride (IIIα), m.p. 163°	Dibromoanhydride (IIIβ), m.p. 331°
$\downarrow$ NH$_3$	$\downarrow$ NH$_3$
dibromoamidic acid (IVα), m.p. 225°	dibromoamidic acid (IVβ), m.p. >250°
$\downarrow$ SOCl$_2$	$\downarrow$ SOCl$_2$
dibromoimide (Vα), m.p. 221°	dibromoimide (Vβ), m.p. 296°
$\downarrow$ Zn, acetic acid	Zn, acetic acid
exo-unsaturated imide (IIb), m.p. 161° $\leftarrow$	

The conversion of IIIα and IIIβ to IIb establishes that both dibromides possess either the intact endoxocyclohexane skeleton or one which is readily reconverted to it. Although ample precedent exists for considering rearranged structures for either or both of the dibromoanhydrides, the properties of the substances do not permit any such formulation.

(i) The product of a normal Wagner–Meerwein rearrangement would be VIII, by analogy to the ob-

---

(1) Taken in part from the Ph.D. dissertation of Ronald Swidler. A portion of this material was presented at the American Chemical Society Meeting in Los Angeles, Calif., March, 1953 (Abstracts of papers, p. 34M). A preliminary report has been published as a Communication to the Editor, THIS JOURNAL, **75**, 4366 (1953).

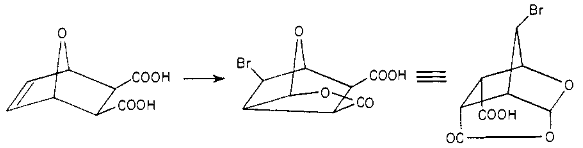
(2) Among the many examples of this behavior may be mentioned: (a) α-pinene → 2,6-dichlorocamphane [O. Aschan, *Ber.*, **61**, 38 (1928); O. Brus, *Compt. rend.*, **180**, 1507 (1925); *cf.* H. Kwart, Abstracts of Papers presented at American Chemical Society Meeting, Atlantic City, N. J., September, 1952, p. 28M]. (b) Santene → π-norisoborneol [O. Aschan, *Ber.*, **40**, 4923 (1907)]. (c) Camphene → isobornyl chloride [H. Meerwein and K. van Emster, *ibid.*, **55**, 2507 (1922)]. (d) *exo-cis*-3,6-Endoxotetrahydrophthalic acid → lactone of 3-hydroxy-4-bromo-5-formylcyclopentanedicarboxylic acid lactol [R. B. Woodward and H. Baer, THIS JOURNAL, **70**, 1161 (1948)]. (e) *exo-cis*-3,6-Endomethylene-Δ^4-tetrahydrophthalic acid → *endo-cis*-3,6-endomethylene-4-hydroxyhexahydrophthalic acid lactone [K. Alder and G. Stein, *Ann.*, **514**, 1 (1934)]. (f) *endo*-Dicyclopentadiene → hydroxydihydro-*exo*-dicyclopentadiene [P. D. Bartlett and A. Schneider, THIS JOURNAL, **68**, 6 (1946)]. (g) Norbornylene → nortricyclyl bromide [J. D. Roberts, E. R. Trumbull, Jr., W. Bennett and R. Armstrong, *ibid.*, **72**, 3116 (1950)]. (h) *exo-cis*-3,6-Endodiphenylvinylidene-Δ^4-tetrahydrophthalic acid → *endo-cis*-3,6-hydroxymethylene-4-hydroxy-5-diphenylvinylhexahydrophthalic acid lactone [K. Alder, F. W. Chambers and W. Trimborn, *Ann.*, **566**, 27 (1950)].

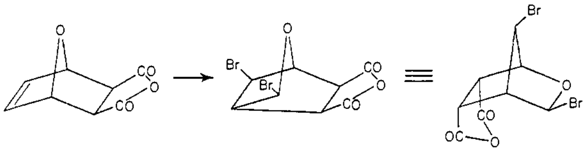
(3) J. A. Berson and R. Swidler, THIS JOURNAL, **75**, 1721 (1953).

(4) H. Kwart and I. Burchuk, *ibid.*, **74**, 3094 (1952).

(5) O. Diels and K. Alder, *Ber.*, **62**, 557 (1929).

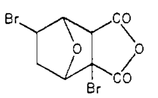
served[2d] formation of VII in the bromination of the *acid* (VI) corresponding to Ib.

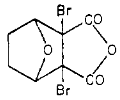

VI VII


Ib VIII

While VIII might be convertible to IIb (*via* a reversal, at some stage of the degradation, of the rearrangement leading to VIII), VIII, as an α-bromoether, should show extraordinarily high reactivity[6] in solvolytic displacement reactions. The observations that derivatives of IIIα and IIIβ survive strenuous solvolytic conditions[7] interdicts the consideration of VIII as a serious structural possibility.

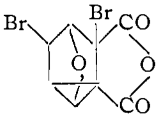
(ii) Rearrangement involving a so-called 2,6-hydrogen shift[8] would lead to IX or X. These structures must be considered unlikely since the forma-


IX


X

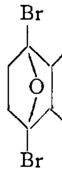
tion of each would involve development of partial positive character adjacent to a carbonyl group during hydride migration. Neither is consistent with the inertness of the bromine atoms of the corresponding esters to solvolytic displacement.[9] Degradation of X to IIb is difficult to rationalize. Also, IX is inconsistent with the structural symmetry of at least one of the dibromides established by the optical resolution results (*vide infra*).

(iii) A rearrangement during bromination analogous to the formation of nortricyclyl bromide from norbornylene[2e] would lead to XI. The stoichiometry of this reaction (leading to $C_8H_4O_4Br_2$) requires *two moles* of bromine per mole of Ib. The observation that IIIα is formed under certain conditions (*vide infra*) in over 90% yield from Ib with *one mole* of bromine eliminates XI as a possible structure for IIIα.


XI

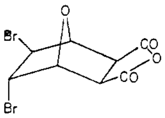
The symmetry of IIIβ (*vide infra*) is also inconsistent with XI.

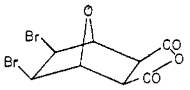
(iv) A bridgehead-halogen structure (XII) would account for the inertness of the bromines to solvolysis,[10] but requires unprecedented and improbable changes for its formation and degradation to IIb.

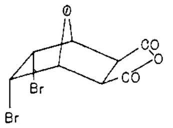

XII

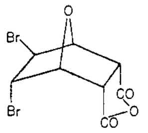
Also XII would not account for the ready release of bromide ion[7] under *bimolecular* displacement conditions.

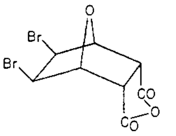
We are led to the conclusion, therefore, that the dibromoanhydrides, IIIα and IIIβ, result structurally from simple saturation of the double bond of Ib and correspond to two of the six theoretically possible stereoisomers (IIIa–IIIf) of 4,5-dibromo-3,6-endoxohexahydrophthalic anhydride.

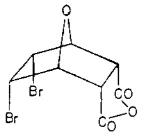

IIIa


IIIb


IIIc


IIId


IIIe


IIIf

Configurations of the Anhydride Functions.—Although Ia, the *endo* isomer of Ib, has never been isolated,[2d] the demonstrable[3] equilibrium between the *endo*- and *exo*-furan–maleic acid adducts leads to the surmise that a similar equilibrium may be set up in solutions of Ib. Bromination of such solutions might therefore lead to a stable dibromide (IIIα or IIIβ) derived from *endo*-anhydride Ia. Although the observation that both IIIα and IIIβ are degraded to an unsaturated imide IIb of known *exo* configuration rather than to the *endo*-imide IIa suggests that the anhydride function of IIIα and IIIβ is *exo*, the reported[4] thermal isomerization of IIa to IIb leaves any definite stereochemical inference ambiguous. It is thus necessary to show that IIa survives the debromination conditions.

Our first attempts to characterize the reportedly[4] unstable IIa met with unexpected difficulties. Thus, bromination of a sample of IIa prepared by the method of Kwart and Burchuk[4] gave a mixture of Vα, m.p. 221°, and a new dibromoimide (Vγ), m.p. 303°. The dibromoimide Vα, already known from the degradation of the dibromoanhydride IIIα, was also formed in high yield by bromination of the *exo*-unsaturated imide IIb. Hydrogenation of the same

---

[6] (a) A. Geuther and H. Laatsch, *Ann.*, **218**, 36 (1883); (b) F. M. Litterscheid, *ibid.*, **330**, 118, 123 (1904); (c) H. R. Henze and J. T. Murchison, THIS JOURNAL, **53**, 4077 (1931).

[7] J. A. Berson and R. Swidler, *ibid.*, **76**, 4057 (1953).

[8] (a) H. Meerwein and F. Montfort, *Ann.*, **435**, 207 (1934); (b) J. D. Roberts and C. C. Lee, THIS JOURNAL, **73**, 5009 (1951); Abstracts of Papers presented at 120th Meeting of the American Chemical Society, New York, N. Y., September 3-7, 1951, p. 24M. (c) W. E. Doering and A. P. Wolf, Abstracts of Papers presented at XIIth International Congress of Pure and Applied Chemistry, New York, N. Y., September 10-13, 1951, p. 437.

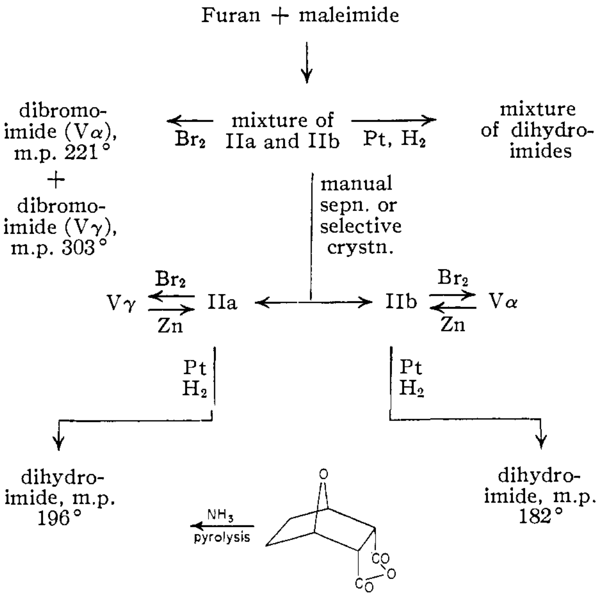
[9] Compare (a) E. D. Hughes, C. K. Ingold and S. Masterman, *J. Chem. Soc.*, 1236 (1937); (b) W. A. Cowdrey, E. D. Hughes and C. K. Ingold, *ibid.*, 1243 (1937).

[10] (a) P. D. Bartlett and L. H. Knox, THIS JOURNAL, **61**, 3184 (1939); (b) P. D. Bartlett and S. G. Cohen, *ibid.*, **62**, 1183 (1940); (c) P. D. Bartlett and E. S. Lewis, *ibid.*, **72**, 1005 (1950); (d) W. von E. Doering and E. Schoenewaldt, *ibid.*, **73**, 2333 (1951).

batch of "*endo*-unsaturated imide" gave a mixture of substances m.p. 130–150°, in contrast to the reported[4] formation of a discrete *endo*-dihydroimide, m.p. 135°. Debromination of the dibromoimide, m.p. 303° ($V\gamma$), gave a sample of IIa (77% yield) which regenerated $V\gamma$ upon bromination (77% yield) and added one mole of hydrogen over platinum to give a *dihydroimide, m.p. 196°*. This material was saturated to permanganate and strongly depressed the melting point of the *exo*-dihydroimide (m.p. 182°) formed from IIb. That the new dihydroimide, m.p. 196°, was indeed *endo-cis*-3,6-endoxohexahydrophthalimide was unequivocally established by its independent synthesis from authentic[11] *endo-cis*-3,6-endoxohexahydrophthalic anhydride *via* the path anhydride → ammonium salt of amidic acid → imide. We deduced, therefore, that our samples of IIa were stereochemically heterogeneous. This was confirmed by isolation of both *endo* IIa and *exo*-IIb material from the crystalline product of the furan–maleimide addition. The separation was facilitated by the observation that the adducts precipitate side by side from ethyl acetate as easily distinguished, characteristic crystals. The *endo* unsaturated imide isolated in this way gave the characteristic dihydro derivative, m.p. 196° upon hydrogenation. It appears, therefore, that, at least in our hands, the addition of furan to maleimide under the conditions reported[4] to yield only IIa (*endo*), yields both IIa and IIb. We are unable to account for the melting point of 135° originally reported[4] for the *endo*-dihydroimide.

The somewhat involved series of changes in the imide series is outlined in Chart II.

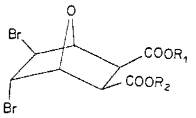
CHART II



The isolation (in 77% yield) of the *endo*-unsaturated imide (IIa) from the debromination of $V\gamma$ under the same conditions used for debromination of $V\alpha$ and $V\beta$ establishes that the *exo*-imide (IIb) is the *proximate* product of the debromination of both $V\alpha$ and $V\beta$. Consequently, there can be little doubt that in both the anhydrides IIIα and IIIβ the anhydride ring is in the *exo*-configuration. Only three structures (IIIa, IIIb, IIIc) need now be considered for IIIα and IIIβ.

Configurations of the Bromines.—*A priori*, we considered that in accord with the generally observed *trans* result of olefin brominations[12] at least one of the dibromides must be IIIa. Of the two remaining structures for the second dibromide, we considered IIIb the more likely on the basis of the general preference for *exo*-addition to bicyclic olefins in a variety of reactions.[13] Also, the exceptionally high melting point of IIIβ, suggesting highly efficient packing in the crystal, seemed reasonable in terms of the unusual W-shape of IIIb. We therefore concluded tentatively that the low-melting dibromoanhydride (IIIα) was probably IIIa and that the high-melting dibromoanhydride (IIIβ) was probably IIIb.

IIIa, a substance with no plane of symmetry, should be separable into enantiomers, while IIIb, although it contains six formally asymmetric centers, is superimposable on its mirror image and is therefore a *meso* compound. The racemic character of IIIa (IIIα) was demonstrated by resolution of the corresponding acid (XIIIa) *via* the quinine salt. The resolution was not carried to completion, but material of high optical activity was obtained. Regeneration of XIIIa from the less-soluble diastereomeric quinine salt after recrystallization afforded (−)XIIIa, $[\alpha]_D$ −77.5°. From the more-soluble fractions was obtained (+)XIIIa, $[\alpha]_D$ +14.1°. It is of interest that the infrared spectra of racemic and optically active XIIIa *in mineral oil mulls* show slight but perceptible differences, as do those of the corresponding racemic and optically active anhydrides (IIIa). These differences are not unexpected, since the racemic materials, which are higher-melting and less soluble than the enantiomers, are undoubtedly true racemates rather than racemic mixtures. However, the spectra of the active and racemic anhydrides in chloroform *solution* are identical, as are those of chloroform solutions of the active and racemic dimethyl esters (XIIIb).



XIIIa, $R_1, R_2 = H$
b, $R_1, R_2 = CH_3$

To demonstrate the *meso* character of IIIβ, we applied the principle of Stoermer and Steinbeck,[14] in which a *meso* substance is rendered asymmetric by structural modification, the derivative is resolved and this optically active substance is rend-

---

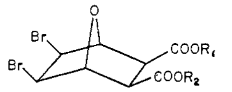
[11] (a) K. Alder and K. H. Backendorf, *Ann.*, **535**, 113 (1938); (b) *cf.* reference 2d for the correct configurational assignment.

[12] I. Roberts and G. E. Kimball, THIS JOURNAL, **59**, 947 (1937), and references cited therein.

[13] (a) K. Alder and G. Stein, *Ann.*, **515**, 185 (1935); **525**, 183 (1936). (b) For an ingenious application of this rule see G. Stork, E. E. van Tamelen, L. J. Friedman and A. W. Burgstahler, THIS JOURNAL, **75**, 384 (1953).

[14] (a) R. Stoermer and H. J. Steinbeck, *Ber.*, **65**, 413 (1932); (b) R. P. Linstead and W. von E. Doering, THIS JOURNAL, **64**, 2003 (1942).

dered symmetrical (and consequently optically inactive) again by suitable alteration. The half-methyl ester (XIVa), prepared from IIIβ and methanol, was partially resolved *via* the quinine salt,



XIVa, R_1, = H; R_2 = CH_3
b, R_1, R_2 = CH_3
c, R_1, R_2 = H

giving (+)XIVa, $[\alpha]_D$ +2.5° and (−)XIVa, $[\alpha]_D$ −3.3°. The infrared spectra of racemic and (−)XIVa were identical. Reaction of (+)XIVa with methanol and a trace of sulfuric acid gave *optically inactive* dimethyl ester XIVb in excellent yield. This substance was identical with dimethyl ester prepared from *meso*-IIIβ and acidulated methanol. The total methylation reaction mixture from the reaction of (−)XIVa with methanol was also optically inactive, indicating that preferential fractionation of optically inactive XIVb from a small quantity of optically active ester had not occurred. Hydrolysis of (+)XIVa yielded optically inactive acid XIVc.

On the basis of the optical resolution results, IIIα is unequivocally IIIa. While the *meso* properties of IIIβ do not eliminate IIIc as a possible structure, expression IIIb[15] is much to be preferred on the basis of the *exo*-addition rule[13] and the mechanistic considerations to be discussed. IIIa, IIIb and their derivatives now form a relatively complete class of new substances to which configurations may be assigned with a high degree of certainty. These are shown in Table I.

TABLE I

CONFIGURATIONS OF THE 4,5-DIBROMO-3,6-ENDOXOHEXAHYDROPHTHALIC ANHYDRIDES AND THEIR DERIVATIVES

		Configuration of bromines	Configuration of carboxyls, etc.
	Low-melting series		
IIIa (IIIα)	Anhydride, m.p. 163°[a]	*trans*	*exo-cis*
XIIIa	Acid, m.p. 163°[a]	*trans*	*exo-cis*
XIIIb	Dimethyl ester, m.p. 116°[a]	*trans*	*exo-cis*
IVα	Amidic acid, m.p. 225°[a]	*trans*	*exo-cis*
Vα	Imide, m.p. 221°[a]	*trans*	*exo-cis*
	High-melting series		
IIIb (IIIβ)	Anhydride, m.p. 331°	*exo-cis*	*exo-cis*
XIVc	Acid, m.p. 331°	*exo-cis*	*exo-cis*
XIVa	Half-methyl ester, m.p. 321°[a]	*exo-cis*	*exo-cis*
XIVb	Dimethyl ester, m.p. 200°	*exo-cis*	*exo-cis*
IVβ	Amidic acid, m.p. >250°[a]	*exo-cis*	*exo-cis*
Vβ	Imide, m.p. 296°	*exo-cis*	*exo-cis*
Vγ	Imide, m.p. 303°	?	*endo-cis*

[a] M.p. of racemate.

The Bromination Mechanism.—The formation, under certain conditions (*vide infra*), of nearly equal amounts of products of *cis*- and *trans*-addition (IIIb and IIIa), in the face of the generally overwhelming preference for *trans*-addition,[12] is an extraordinary result.[18] The anomaly is not resolved by abandoning the usual considerations[12] in favor of a sterically random bromination process. The proximity of the two bromine atoms of IIIb, both of which are constrained in equatorial conformations by the geometrical requirements of the bicyclic system, must produce a large non-bonded interaction strain. Thus, while the methyl groups in *trans*-1,2-dimethylcyclohexane strongly prefer the equatorial–equatorial (e–e) conformation,[22] the bromines in *trans*-1,2-dibromocyclohexane actually have a slight preference for the polar–polar (p–p) conformation,[23] presumably in part because of the minimization of electrostatic repulsions when the bromines are farther apart. These effects must be even greater in the case of IIIb, for while the bromines in (e–e)-*trans*-1,2-dibromocyclohexane are "staggered," the geometry of IIIb (based on the "boat" form of cyclohexane) requires the bromines to be "eclipsed" and consequently closer together. The large difference in non-bonded interaction strain between IIIb and IIIa should be reflected in the respective transition states in the bromination reaction, and consequently IIIa would be expected to predominate heavily in a random attack of bromine on Ib.

In an effort to determine the factors which control the stereochemistry of the bromination, we have investigated the effect of varying conditions upon the yield, product composition and over-all rate. The results are summarized in Table II. Since the dibromides are not interconverted under the reaction conditions (nor indeed in a variety of other reactions), the yield data of Table II represent valid criteria of the relative rates of formation of the isomers.

While the total yield of dibromides remains roughly constant under all the conditions used, the

---

[15] An additional argument against an *endo*-configuration of the anhydride ring in IIIβ is available if an *exo*-configuration for the bromines is accepted. Thus if IIIβ were IIIe, the corresponding free acid would be expected to lactonize readily in alkaline solution since the carboxylate group is in very nearly the best possible steric situation to effect rear-side displacement of bromide ion. Lactonization of the dimethyl ester of the acid of IIIe under solvolytic conditions might also be expected by analogy to the lactonization of the dimethyl ester from the dibromide[16] (m.p. 206°) of *endo-cis*-3,6-endomethylene-Δ^4-tetrahydrophthalic anhydride in methanolic silver nitrate.[17a] The formation of bromolactones as products of the bromination of unsaturated *esters* also has been observed.[17b]

(16) K. Alder and G. Stein, *Ann.*, **504**, 247 (1933).

(17) (a) J. A. Berson and R. Swidler, unpublished observations; (b) R. T. Arnold, M. de Moura Campos and K. L. Lindsay, THIS JOURNAL, **75**, 1044 (1953).

(18) The classical studies of the halogenations of cinnamic acid[19] and the stilbenes[20] demonstrated the frequent occurrence of formal *cis*-additions. However, these results are complicated by the possibility of isomerization of the starting materials or intermediates during the additions.[21] This situation holds in general for acyclic olefins. [See also H. J. Bernstein, A. de Pullin, B. S. Rabinovitch and N. R. Larson, *J. Chem. Phys.*, **20**, 1227 (1952).]

(19) (a) C. Liebermann and H. Finkenbeiner, *Ber.*, **28**, 2235 (1895); (b) R. Fittig and F. Binder, *Ann.*, **195**, 131 (1879); (c) A. Michael, *J. prakt. Chem.*, [2] **52**, 292 (1895); *Ber.*, **34**, 3663 (1901).

(20) (a) T. Zincke, *ibid.*, **10**, 1002 (1877); (b) H. Limpricht and H. Schwanert, *Ann.*, **145**, 336 (1868); **153**, 121 (1870); (c) R. Otto and F. Stoffel, *Ber.*, **30**, 1800 (1897); (d) J. Wislicenus and F. Seeler, *ibid.*, **28**, 2693 (1895); (e) J. Wislicenus and M. Jahrmarkt, *Chem. Zentr.*, **82**, I, 464 (1901); (f) F. Straus, *Ann.*, **342**, 190 (1905).

(21) G. W. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 298.

(22) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

(23) O. Bastiansen and O. Hassel, *Tids. Kjemi, Bergvesen Met.*, **6**, 96 (1946).

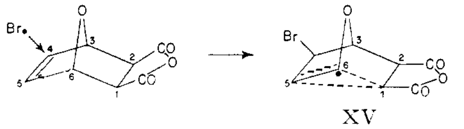
TABLE II

Solvent	Reacn. time,[a] hours	IIIa (*trans*), %	IIIb (*cis*), %
CH_2Cl_2[b]	2.5	60	31
CH_2Cl_2[b]	2.5	63	29
CH_2Cl_2[b,c]	0.25	58	35
CH_2Cl_2[b,c,d]	0.50	55	36
CH_2Cl_2[e]	18	81	9.7
CH_2Cl_2[b,f]	9	61	12.7
Ethyl acetate[b]	2	85	0
Acetic acid[b]	1	91	0

[a] Time required for the color of bromine to be discharged. [b] In diffuse daylight. [c] In a nitrogen atmosphere. [d] Without stirring. [e] In darkness. [f] In an atmosphere of oxygen. The product contained, in addition to IIIa and IIIb, an oil which decolorized permanganate and liberated iodine from potassium iodide.

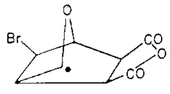
ratio of *cis*- to *trans*-dibromide is remarkably sensitive. The formation of *cis* product (IIIb) is favored by illumination and non-polar solvent and is suppressed by oxygen, polar solvents and the absence of light. These observations strongly suggest that at least a major portion of the *cis*-dibromide is formed *via* a mechanism involving free radicals.[24] While information on the steric outcome of radical brominations is sparse, there are ample grounds for expecting *trans* addition in simple cases. Thus, the radical addition of hydrogen bromide to 1-bromocyclohexene and to 1-methylcyclohexene[25] occurs *trans*, presumably through an intermediate radical in which a bromine atom is midway between the (originally) olefinic carbons. It is clear that a similar radical would be produced in bromine addition to olefins and that completion of the reaction would demand a similar steric result. In our more complicated bicyclic case, this stereo-electronic requirement is reinforced *a fortiori* by the non-bonded interaction strain considerations discussed above.

The occurrence of *cis*-bromination despite these theoretical interdictions implies the operation of some powerful stereoelectronic demand. One explanation for this lies in the possibility of formation of the bridged-radical intermediate XV.[26]



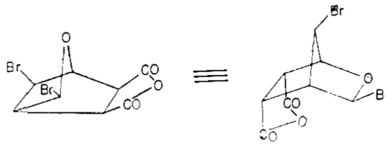
XV

Hypothetically, in the formation of XV, the approach of a bromine atom to the olefin at C_4 would cause the onset of unpairing of the C_4–C_5 π-electrons. The C_1–C_6 bonding electrons are in a favorable situation to become delocalized by interaction with the developing *p*-orbital at C_5 (containing one electron). This interaction would lead directly to the electron-deficient C_1–C_5–C_6 bonding situation represented by XV. Completion of the reaction would presumably require attack of a bromine molecule on XV. It seems reasonable that attack at C_5 or C_6[28] from the side opposite the bridge (*exo*) would be stereoelectronically preferred. Attack at C_5 would lead directly to IIIb. Attack at C_6 would lead to the α-bromoether XVII.[29]



XVI

Ionic rearrangement of XVII to IIIb, catalyzed perhaps by bromine acting as a "Lewis acid"[30] or by a trace of hydrogen bromide,[2c,31] is in direct steric and electronic[32] analogy to the stereospecific change camphene hydrochloride → isobornyl chloride.[2c,27a,31]



XVII

It seems probable that additions to other bicyclic systems may be attended by similar complications and, consequently, that the occurrence of rearranged or sterically abnormal products may be a common feature of such reactions. Two further examples of addition to olefins analogous to Ib illustrate several new effects.

---

[24] The marked increase in *over-all* bromination rate under conditions which favor radical reactions indicates that under these conditions at least part of the *trans*-dibromide may also arise by a radical mechanism.

[25] H. L. Goering, P. I. Abell and B. F. Aycock, THIS JOURNAL, **74**, 3588 (1952).

[26] XV is formulated by analogy to the *cationic* species postulated[27] as intermediates in solvolysis and rearrangement reactions of bicyclic derivatives.

[27] (a) T. P. Nevell, E. de Salas and C. L. Wilson, *J. Chem. Soc.*, 1188 (1939); (b) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, THIS JOURNAL, **74**, 1127 (1952); (c) F. Brown, E. D. Hughes, C. K. Ingold and J. F. Smith, *Nature*, **168**, 65 (1951); (d) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 511-523; (e) P. D. Bartlett in "Organic Chemistry," edited by H. Gilman, John Wiley and Sons, Inc., New York, N. Y., 1953, Vol. III, pp. 66-69.

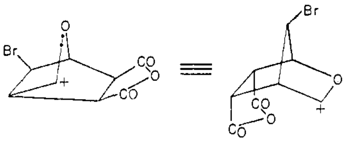
[28] Attack at C_1 would lead to an *unsaturated, monocyclic* dibromide.

[29] Formation of XVII need not involve XV as a discrete species but might instead occur by attack on the rearranged radical XVI. In any case, structural alteration under radical conditions in this type of system has been observed in additions to dehydronorbornylene (S. J. Cristol, private communication).

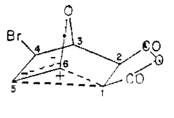
[30] (a) H. A. Benesi and J. H. Hildebrand, THIS JOURNAL, **70**, 2832 (1948); **71**, 2703 (1949); (b) R. S. Mulliken, *ibid.*, **72**, 600 (1950); **74**, 811 (1952); (c) T. M. Cromwell and R. L. Scott, *ibid.*, **72**, 3825 (1950); (d) R. M. Keefer and L. J. Andrews, *ibid.*, **72**, 4677, 5170 (1950); (e) N. W. Blake, H. Winston and J. A. Patterson, *ibid.*, **73**, 4337 (1951); (v) L. J. Andrews and R. M. Keefer, *ibid.*, **74**, 4500 (1952); (g) R. L. Scott, *ibid.*, **75**, 1550 (1953).

[31] P. D. Bartlett and I. Pöckel, *ibid.*, **59**, 820 (1937); **60**, 1585 (1938).

[32] Rearrangement of XVII to IIIb would be facilitated by the bridge oxygen[2d] (through resonance contributions of the type $-\overset{|}{C}=\overset{+}{O}-$) if the mechanism involved a rate-determining ionization to the carbonium ion XVIII. It is, however, not clear that ionization to a bridged-cation species (XIX) would be similarly enhanced. Although the steric requirements of such ions are uncertain, it is conceivable that a significant contribution of a resonance structure involving the bridge oxygen would require an approximation to coplanarity of the atoms C_1, C_5, C_6 and O, a situation difficultly achieved in this bicyclic system.

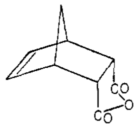


XVIII



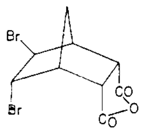
XIX

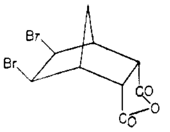
Bromination of *endo-cis*-3,6-Endomethylene-Δ^4-tetrahydrophthalic Anhydride.—Addition of bromine to the cyclopentadiene–maleic anhydride adduct XX in chloroform gives a dibromoanhydride,

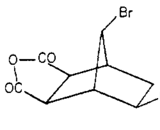

XX

m.p. 206°.[33] The addition seems to be light-catalyzed and gives different results when carried out in polar solvents (*vide infra*).

Craig[33c] has assigned the "normal" *trans* structure XXI to this dibromide. More recently, Kwart and Kaplan[33d] have studied the dipole moment of the substance and have concluded that the observed value is not in accord with XXI but corresponds to that expected of either the *cis*-dibromide XXII or the rearranged dibromide XXIII.

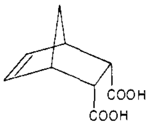

XXI

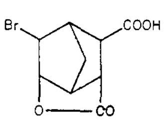

XXII


XXIII

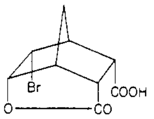
These authors rejected the *cis*-dibromide structure XXII and chose XXIII largely on the grounds that "*cis* vicinal derivatives have never been obtained on addition to bicyclic double bonds with reagents that show a characteristic stepwise pattern to their reaction." This objection is seriously weakened by our observations in the bromination of Ib. Further, it is now possible to show experimentally that both previous assignments of structure to the 206° dibromide are very probably incorrect and that the substance is indeed the *cis*-dibromide XXII.

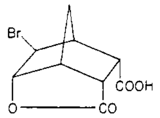
We have investigated the properties of the dicarboxylic acid obtained[33a] on hydrolysis of the 206° anhydride. That this acid is formed from the anhydride without rearrangement was established by the regeneration of the anhydride from the acid and acetic anhydride. Neutralization with alkali of an aqueous solution of the dicarboxylic acid resulted in very rapid release of 0.97 mole of bromide ion and formation of a *bromolactonic acid* identical with that obtained[34a] by brominating *endo-cis*-3,6-endomethylene-Δ^4-tetrahydrophthalic acid (XXIV) in water and assigned[34] structure XXV.

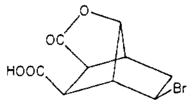

XXIV

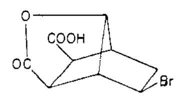

XXV

Since the dicarboxylic acid itself is stable in acid solution,[34a] the only reasonable function attributable to alkali in bringing about the lactonization of the acid is in generating carboxylate ions for intramolecular displacement of bromide. Hence, a rearrangement during the lactonization of the acid seems highly unlikely. It follows that the bromolactonic acid derived from XXI must be XXVI, that from XXII must be XXVII and that from XXIII must be XXVIII (or XXIX).

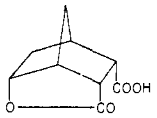

XXVI


XXVII

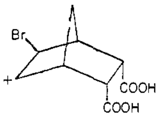

XXVIII


XXIX

While a review of the mass of experimental detail[34] involved in the structure proof of the bromolactonic acid XXV is beyond the space limitations of this paper,[35] the conversion of XXV to the lactonic acid XXX as well as a number of other self-consistent transformations leave no doubt that the structure XXV is essentially[36] correct. Structures XXVIII and XXIX for the bromolactonic acid and consequently structure XXIII for the 206° dibromoanhydride are thus eliminated.


XXX

Two stereoisomers of structure XXV (XXVI and XXVII) have the requisite *endo*-configuration of the lactone and carboxyl groups. The formation of the bromolactonic acid from XXIV can occur (i) by preliminary formation of a dibromoacid followed by elimination of hydrogen bromide or (ii) by formation of a bromonium ion (XXXII or a mechanistic equivalent) followed by lactonization.


XXXII

In case (i), if the bromines of the dibromoacid have the *trans* configuration, the bromolactonic acid must be XXVI, since only the *exo*-bromine is in a favorable position for rear-side displacement by car-

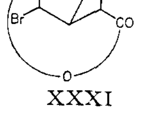
---

[33] (a) K. Alder and G. Stein, *Ann.*, **504**, 247 (1933); (b) reference 2f; (c) D. Craig, THIS JOURNAL, **73**, 4889 (1951); (d) H. Kwart and L. Kaplan, *ibid.*, **75**, 3356 (1953).

[34] (a) K. Alder and G. Stein, *Ann.*, **504**, 216 (1933); (b) **514**, 1 (1934); (c) **525**, 183 (1936); (d) K. Alder and S. Schneider, *ibid.*, **524**, 189 (1936).

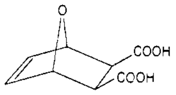
[35] The transformations of XXV and related substances are outlined in detail in "Elsevier's Encyclopedia of Organic Chemistry," edited by E. Josephy and F. Radt, Elsevier Publishing Co., New York, N. Y., 1948, Vol. 12A, p. 981.

[36] It should be pointed out that structure XXXI is not excluded. This point has no bearing on the assignment of structure to the 206° dibromoanhydride.

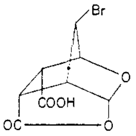

XXXI

boxyl. If the bromines of the dibromoacid have the *cis* configuration, the bromolactonic acid can only be XXVII. In case (ii), by application of the *exo*-addition rule[2d,13] (reinforced in the case of XXIV because of the hindrance provided by the *endo*-carboxyl groups), the bromolactonic acid must be XXVII. Now while the bromolactonic acid is formed in near-quantitative yield by brominating the unsaturated acid XXIV in acid solution, the dibromoacid is stable in acid solution. Therefore, the dibromoacid is not an intermediate in the formation of the bromolactonic acid, and case (ii) applies. The bromolactonic acid is therefore XXVII and the dibromoanhydride is the product of *cis*-bromination, XXII. It will be noted that the only fundamental assumption which is experimentally unsupported in the assignment of structure is that which pertains to the validity of the *exo*-addition rule in this case. Since a number of unequivocally established analogies in closely similar systems exist[12] and since the extension of the rule to the present circumstances is eminently reasonable, the structure XXII for the 206° dibromoanhydride seems highly probable. So far as we are aware, the formation of XXII from XX in 85% yield constitutes the most highly stereospecific case of *cis*-bromination known. We are not yet ready to comment upon the mechanism involved in this reaction, but it is noteworthy that the product composition varies remarkably with solvent. When the addition was carried out in ethyl acetate or in acetic acid, a complex mixture of substances was obtained from which both XXII and a new dibromide (as the methyl ester) were isolated.

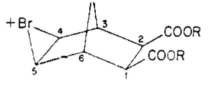
Bromination of *exo-cis*-3,6-Endoxo-Δ^4-tetrahydrophthalic Acid.—Bromination of XXXIII in aqueous solution undoubtedly occurs by a polar mechanism. The product is a mixture of the normal *trans*-dibromoacid XIIIa and the rearranged bromolactonic acid XXXIV in proportions which vary remarkably with the acidity of the medium,[2d,3] the dibromide being formed in small yield in basic solution but in much higher yield in acid solution. These results probably originate in a combination of uniquely synergetic factors. Decomposition of the bromonium ion XXXV may occur (i) by direct attack of bromide ion to give XIIIa, or (ii) by rearrangement to the ion XXXVI followed by lactonization.



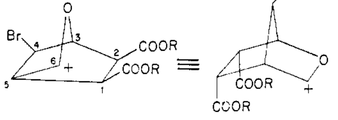
XXXIII



XXXIV



XXXV



XXXVI

In basic solution, process (i) is repressed due to the extra work required to bring bromide ion close to the negatively charged ion XXXV (R = ⊖) compared to that required for approach of bromide ion to the positive species XXXV (R = H). Also, the positive character of the carboxyl carbon atom must oppose the change XXXV → XXXVI because of its inductive effect on the migrating carbon (C_1). This effect is smaller in the anion (XXXV, R = ⊖) than in XXXV (R = H) and consequently, rearrangement becomes more favorable in basic solution. It should be noted, however, that since the carboxyl (or carboxylate) group in XXXV is in very nearly the worst possible position to displace C_1 from C_6 by rear-side attack, little if any kinetic aid to rearrangement is to be anticipated from lactonization.

Experimental[37]

Bromination of *exo-cis*-3,6-Endoxo-Δ^4-tetrahydrophthalic Anhydride.—The solvents for the runs of Table II were: (a) reagent grade ethyl acetate (Baker and Adamson), (b) reagent grade acetic acid (Baker and Adamson), (c) methylene chloride dried over calcium chloride and distilled. For the run in nitrogen atmosphere, the methylene chloride was de-aerated by passing a vigorous stream of nitrogen through a stirred, boiling sample for 15 minutes and then distilling the solvent under nitrogen. The reaction itself was carried out in a system in which the air had been replaced with nitrogen. The runs in diffuse daylight were carried out under ordinary laboratory illumination. For the dark runs, the reagents were mixed and immediately stored in a dark cabinet. The absolute yields of products were reproducible to ±1–3%. A typical run was carried out as follows:

A solution of 10.0 g. of Ib in 300 cc. of methylene chloride was treated under nitrogen with 10.0 g. of bromine (added in one portion). The reagents were thoroughly mixed by stirring. In a few minutes the bromine color had disappeared and a solid precipitate had formed on the walls of the reaction flask. The mixture was filtered and washed with methylene chloride to give 6.85 g. of IIIb, m.p. 331° dec. The dibromide is exceedingly difficultly soluble in most organic solvents. The analytical sample was prepared by recrystallization from a large volume of acetone. It formed glittering rhombohedral tablets.

Anal. Calcd. for $C_8H_6O_4Br_2$: C, 29.48; H, 1.86; Br, 49.04. Found: C, 29.55; H, 1.99; Br, 48.99.

The mother liquor from the bromination was evaporated to dryness to yield 11.5 g. of IIIa, m.p. 158–160°. The properties and analysis of this substance have been reported.[3]

Conversion of Dibromoanhydrides to Dibromoimides. A. Low-Melting Series. Dibromoimide Vα.—A solution of 201.5 g. of IIIa in 1 l. of acetone was added during 40 minutes to 600 cc. of cold concentrated ammonia water while the reaction mixture was kept at 18–20° and stirred vigorously. After an additional 2.5 hours, the precipitated solid was dissolved in 5 l. of water, filtered from a small quantity of insoluble material, and the filtrate made strongly acidic with concentrated hydrochloric acid. The precipitated **amidic acid IVα** was filtered, the filter cake left under suction on the büchner funnel for 12 hours and then dried over potassium hydroxide for several days. The acid (213 g.) melted at 225° with extensive decomposition. A suspension of 180 g. of IVα in 700 cc. of chloroform was treated with 152 cc. of thionyl chloride. The reaction mixture was heated at reflux for six hours, concentrated to a thick paste, poured into 500 cc. of water (caution!) and, after the initial vigorous reaction had subsided, boiled for 30 minutes and chilled in an ice-bath. The dibromoimide was filtered on a sintered glass funnel and dried *in vacuo* over potassium hydroxide for three days. The yield of **dibromoimide Vα** melting at 219–221° was 152 g. (89% over-all from IIIa). Recrystallization from acetone–ethanol (Norit A) gave shimmering, micaceous platelets, m.p. 219–221°.

---

[37] Melting points are uncorrected. The infrared spectra were determined with the Baird Associates recording spectrometer. We are indebted to Mr. M. Robinson of Riker Laboratories, Inc., for the determination of the spectra. The microanalyses were by Messrs. Joseph Pirie and William Schenck of these laboratories and by Dr. Adalbert Elek, Elek Microanalytical Laboratories.

Anal. Calcd. for $C_8H_7O_3NBr_2$: C, 29.56; H, 2.17; N, 4.31. Found: C, 29.72; H, 2.07; N, 4.17.

B. **High-Melting Series. Dibromoimide (Vβ).**—A stirred slurry of 20 g. of finely powdered IIIb in 50 cc. of acetone was treated during ten minutes with 60 cc. of cold concentrated ammonia water. The silvery ammonium salt precipitated. After an additional 15 minutes, enough water was added to dissolve the salt and the reaction mixture was treated as in the preparation of IVα, yielding 21 g. of IVβ. The acid decomposes slowly above 250°. The acid was boiled for six hours with 75 cc. of thionyl chloride and 25 cc. of chloroform and the mixture worked up as in the preparation of Vα, yielding 12.8 g. of Vβ, m.p. 290–293° dec. Recrystallization from acetone gave rectangular plates, m.p. 296° dec. when plunged into a bath at 284°. When heated from room temperature, the compound melted at 280–285° dec.

Anal. Calcd. for $C_8H_7O_3NBr_2$: C, 29.56; H, 2.17; N, 4.31. Found: C, 29.85; H, 2.14; N, 4.28.

IIb. A. **Debromination of Vα.**—A strongly stirred suspension of 110 g. of Vα in 450 cc. of glacial acetic acid was treated with three portions of zinc dust (total, 65 g.) during one hour. The temperature of the reaction mixture rose to 45–50° and the dibromoimide slowly dissolved. After an additional two hours of stirring, the solution was filtered, concentrated *in vacuo* to about half its original volume and treated with 200 cc. of water. Upon cooling the solution, the unsaturated imide separated. By working up the mother liquors, a total of 52 g. of crude IIb was obtained. Recrystallization of this material from water yielded 45 g. of pure imide, m.p. 159–161°, alone or mixed with an authentic sample[4] (reported[4] m.p. 162°). The combined mother liquors were treated with a slight excess of bromine and the resulting solid precipitate recrystallized from ethanol to give 7.8 g. of the dibromoimide Vα, m.p. 219°, alone or mixed with a sample prepared as above. The corrected yield of IIb was thus 88%.

B. **Debromination of Vβ.**—Application of the above procedure to 7 g. of Vβ, 5 g. of zinc and 30 cc. of glacial acetic acid gave 2.7 g. of IIb, m.p. 158–160°, alone or mixed with an authentic sample.[4] Nine-tenths of a gram of Vα was recovered by bromination of the mother liquors. The corrected yield of IIb was thus 87%.

Reaction of Furan with Maleimide. A.—A mixture of 2 g. of maleimide and 5 cc. of furan in 25 cc. of absolute ether was allowed to stand at room temperature for 12 hours. The crystalline precipitate (2.0 g.) melted at 130–132° dec. (reported[4] for the *endo*-adduct, m.p. 131°). As is shown below, this material is a mixture of *endo-* and *exo*-adducts and will be referred to as "the mixed adducts."

B.—A solution of 0.5 g. of maleimide and 1 cc. of furan in 4 cc. of ethyl acetate was allowed to stand overnight at room temperature. The crystalline precipitate (0.7 g.) was examined under a microscope and separated into stout, rhombohedral blocks, alone or mixed with IIb,[4] m.p. 162°, and thick staves, m.p. 127–129°. The lower-melting material could be caused to precipitate preferentially by running the reaction at higher dilution. From a run with 1.0 g. of maleimide, 2 cc. of furan and 20 cc. of ethyl acetate, 0.164 g. of the staves separated. This material melted at 126–128° dec. and was essentially pure *endo*-adduct.

Bromination of the Furan–Maleimide Adducts. A. The "Mixed Adducts." Isolation of Vγ.—A mixture of 0.85 g. of the "mixed adducts" and 0.27 cc. of bromine in 50 cc. of ethyl acetate was allowed to stand for six hours. The precipitate (0.35 g.) melted at 297° dec., after sintering and darkening at 275°. Recrystallization from 80% ethanol gave needles, m.p. 303° dec. A mixed m.p. with the imide Vβ (m.p. 296°) was depressed to 258–264°.

Anal. Calcd. for $C_8H_7O_3NBr_2$: C, 29.56; H, 2.17; N, 4.31. Found: C, 29.63; H, 2.15; N, 4.33.

The ethyl acetate mother liquor was concentrated to a volume of 20 cc. whereupon a second crop (0.65 g., m.p. 205–250°) separated. The residual mother liquor was concentrated to dryness and the resulting oil crystallized from 10 cc. of ethanol to give 0.25 g. of material melting at 204–275°. The ethanol mother liquor was concentrated to a volume of 5 cc. and diluted with 10 cc. of water to yield 0.07 g. of crystals, m.p. 214–219° alone or mixed with Vα.

B. **The *endo*-Adduct (IIa).**—A mixture of 0.083 g. of pure IIa (prepared by debromination of Vγ), 0.030 cc. of bromine and 8 cc. of ethyl acetate was allowed to stand at room temperature overnight. The precipitated solid was washed with 1 cc. of ethyl acetate to give 0.129 g. of Vγ, m.p. 301–303°.

C. **The *exo*-Adduct (IIb).**—A mixture of 1.0 g. of IIb,[4] 0.60 cc. of bromine and 40 cc. of methylene chloride was allowed to stand for 25 minutes at room temperature. The precipitate weighed 1.87 g. and melted at 219–221° alone or mixed with Vα.

Hydrogenation of the Furan–Maleimide Adducts. A. The Mixed Adducts.—A mixture of 0.205 g. of the "mixed adducts" and platinum (from 0.075 g. of platinic oxide) was stirred under hydrogen in 15 cc. of ethyl acetate. After five minutes, 105% of the theoretical quantity of hydrogen had been absorbed whereupon the reaction ceased spontaneously. The catalyst was removed by filtration and the filtrate evaporated to leave a colorless solid, m.p. 130–150°.

B. **The *endo*-Adduct (IIa).**—Hydrogenation of 0.164 g. of IIa (prepared from furan and maleimide in ethyl acetate) over platinum (from 0.070 g. of platinic oxide) in 15 cc. of ethyl acetate ceased after ten minutes with the absorption of 98% of the theoretical amount of gas. The reaction mixture was filtered, concentrated to a volume of 10 cc. and diluted with 3 cc. of Skellysolve B to give 0.104 g. of dihydroimide, m.p. 193–195°. A second crop, 0.046 g., m.p. 183–187°, was also obtained. The melting point of the first crop was not depressed on admixture with a sample of *endo*-dihydroimide prepared by hydrogenation of IIa from the debromination of Vγ nor with a sample prepared by independent synthesis (*vide infra*). The melting point was depressed about 20° on admixture with the *exo*-dihydroimide.[4]

An analytical sample of the *endo*-dihydroimide, recrystallized from ethyl acetate–Skellysolve B, was obtained as white rhombs, m.p. 195–196°.

Anal. Calcd. for $C_8H_9O_3N$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.90; H, 5.59; N, 8.11.

C. **The *exo*-Adduct (IIb).**—Hydrogenation of 0.234 g. of IIb in ethyl acetate over platinum produced the *exo*-dihydroimide. The dihydroimide was obtained after recrystallization from carbon tetrachloride–Skellysolve B as 0.187 g. of bold staves, m.p. 180.5–181.5°, reported[4] m.p. 182°.

Debromination of the *endo*-Dibromoimide (Vγ) to IIa.—A suspension of 1.2 g. of Vγ and 2.0 g. of zinc dust in 10 cc. of glacial acetic acid was agitated for ten minutes. The reaction mixture became warm and the dibromoimide dissolved. After being allowed to stand at room temperature for 90 minutes, the mixture was filtered, the filter cake leached thoroughly with methanol and the combined filtrate and washings evaporated to a small volume. The precipitated solid was washed with ether to yield 0.47 g. of IIa, m.p. 129–131°. The melting point was raised to 130–153° by admixture with the *exo*-adduct IIb. Hydrogenation of a portion of this sample of IIa (0.096 g.) in ethyl acetate over platinum gave the dihydroimide (0.085 g.), m.p. 193–195°.

Synthesis of the *endo*-Dihydroimide from *endo-cis*-3,6-Endoxohexahydrophthalic Anhydride.—Forty-four one-hundredths of a gram of the anhydride[3,11] was treated with 5 cc. of liquid ammonia and the excess ammonia was allowed to evaporate during 30 minutes. The residual white powder was heated in a sublimation pistol to 195° whereupon it melted with the evolution of water and ammonia. After the gas evolution had ceased, the cold finger was filled with ice, the apparatus was connected to vacuum (3–5 mm.) and the residue was sublimed to give 0.336 g. of solid material. The sublimate was recrystallized from water and then from ethyl acetate to give the *endo*-dihydroimide (0.036 g.), m.p. 195–196° alone or mixed with samples prepared as above. A mixed melting point with the *exo*-dihydroimide was depressed to about 140–160°.

Partial Resolution of the *trans*-Dibromoacid XIIIa.—To a hot solution of 48 g. of quinine trihydrate (Merck) in 750 cc. of methanol was added a hot solution of 47.1 g. of XIIIa[3] in 200 cc. of methanol. In a few minutes, a heavy precipitate of tiny platelets separated. The mixture was boiled for 20 minutes and then filtered to yield 80 g. of quinine salt, m.p. 167–170°. The salt was leached for one hour with a mixture of 3200 cc. of isopropyl alcohol and 100 cc. of water, cooled and filtered. The yield of solid m.p. 183–185° was 30 g. This was dissolved in aqueous ammonia and extracted with several portions of chloroform. The aqueous solution was then treated with 40 cc. of concentrated hydrochloric acid whereupon 12.1 g. of acid precipitated. Treatment of the ammoniacal liquor with sodium chloride solution caused separation of the insoluble sodium salt[3] of XIIIa, from which an additional 1.55 g. of XIIIa was regenerated by treatment with 20 cc. of hydrochloric acid. The partially resolved acid was further purified by dissolution in ammonia, precipitation as the sodium salt and regeneration with hydrochloric acid. It was finally recrystallized twice from water to give silky needles melting at 134–135.5°, $[\alpha]_D$ −77.5° (*c* 3.56 in dioxane, *l* 2 dcm.).

Anal. Calcd. for $C_8H_8O_5Br_2$: C, 27.93; H, 2.34. Found: C, 28.04; H, 2.07.

By evaporating the original methanol filtrate from another resolution starting with 15.7 g. of racemic XIIIa and working up the precipitated salt as above, there were obtained 3.1 g. of dextrorotatory XIIIa, $[\alpha]_D$ +14.1° (*c* 9.09 in dioxane, *l* 1 dcm.).

Racemic XIIIa can be separated from (−)XIIIa by crystallization. Thus, three recrystallizations from water of a sample of XIIIa, $[\alpha]_D$ −34.5°, gave XIIIa, $[\alpha]$ −0.5°. The mother liquors were strongly levorotatory.

(−)XIIIb was prepared from (−)XIIIa by boiling for two hours a mixture of 2 g. of partially resolved acid $[\alpha]_D$ −52.9°, in 20 cc. of methanol and 0.5 cc. of fuming sulfuric acid. The reaction mixture was concentrated, diluted with 30 cc. of water, extracted with chloroform and the extract, after being dried over sodium sulfate, was evaporated to dryness. The residue crystallized from carbon tetrachloride–Skellysolve B as 1.15 g. of white needles, $[\alpha]_D$ −44.8° (*c* 6.3 in dioxane, *l* 2 dcm.). Racemic XIIIb is apparently also less soluble than the enantiomers, since evaporation of the mother liquors gave a second crop of ester (0.53 g.), m.p. 82–84°, $[\alpha]_D$ −73.4° (*c* 1.78 in dioxane, *l* 2 dcm.).

(−)IIIa (the anhydride) was prepared by heating 2.8 g. of (−)XIIIa, $[\alpha]_D$ −52.9°, in 10 cc. of acetic anhydride on the steam-bath for 30 minutes. The solution was cooled, filtered and diluted with 20 cc. of carbon tetrachloride and 50 cc. of Skellysolve B, whereupon 2.2 g. of crude anhydride separated. This material, m.p. 129–132°, was recrystallized twice from ethyl acetate–carbon tetrachloride to give (−)IIIa, m.p. 132–137°, $[\alpha]_D$ −59.2° (*c* 1.53 in dioxane, *l* 2 dcm.).

Anal. Calcd. for $C_8H_6O_4Br_2$: C, 29.48; H, 1.86. Found: C, 29.07; H, 1.72.

A sample of (−)IIIa was hydrolyzed in hot water and the solution titrated with standard sodium hydroxide.

Anal. Calcd. for $C_8H_8O_5Br_2$: neut. equiv., 172. Found: neut. equiv., 173 ± 0.5.

That conversion of (−)XIIIa to (−)IIIa occurs without significant racemization was established by the following experiment. A mixture of 0.199 g. of (−)XIIIa, $[\alpha]_D$ −11.8° (*c* 5.32 in dioxane, *l* 2 dcm.), and 1 cc. of acetic anhydride was heated on the steam-bath for 25 minutes. The solvent was completely removed *in vacuo* and the crystalline residue (m.p. 155–157°) made up to a volume of 3.0 cc. in dioxane. This solution showed $[\alpha]_D$ −12.5°. Evaporation of 2.6 cc. of this solution yielded 0.155 g. (95%) of anhydride, (−)IIIa, m.p. 155–157° alone or mixed with racemic IIIa. This was heated with 1 cc. of water on the steam-bath until complete solution occurred (15 minutes) and then for an additional ten minutes. The water was evaporated and the crystalline residue taken up in dioxane, $[\alpha]_D$ −11.6° (*c* 5.43, *l* 2 dcm.).

***meso-cis*-Dibromoacid XIVc.**—The high-melting dibromohydride IIIb was heated with boiling water until solution occurred. The solid which precipitated from the cooled reaction mixture was recrystallized from hot water as exceedingly delicate woolly needles, m.p. 331° dec. The analytical sample was dried at 100° for four hours over phosphorus pentoxide.

Anal. Calcd. for $C_8H_8O_5Br_2$: C, 27.93; H, 2.34. Found: C, 28.18; H, 2.39.

XIVc was converted to IIIb on heating with acetic anhydride on the steam-bath.

***meso-cis*-Dibromodimethyl Ester XIVb.**—A suspension of 2.5 g. of anhydride (IIIb) in 50 cc. of methanol containing 1 cc. of fuming sulfuric acid was boiled for two and one-half hours, concentrated to a volume of 20 cc., diluted with ice-water and the precipitated solid collected at the pump to yield 2.6 g. of XIVb, m.p. 195–198°. Recrystallization from ethyl acetate gave slender rods, m.p. 199–200°.

Anal. Calcd. for $C_{10}H_{12}O_5Br_2$: C, 32.28; H, 3.25. Found: C, 31.92; H, 3.29.

Racemic *cis*-Dibromomonomethyl Ester (XIVa).—A suspension of 10 g. of IIIb in 100 cc. of methanol and 50 cc. of acetone was boiled for seven hours, after which time the appearance of the solid material in the reaction mixture had changed. The solid material was filtered off and a second crop of crystals was obtained by concentrating the filtrate and diluting it with water. The combined crops of crude monomethyl ester were recrystallized from aqueous acetone to give 7.9 g. of product. Recrystallization from methanol gave material melting at 320–321° (with evolution of gas) when heated rapidly from 260°.

Anal. Calcd. for $C_9H_{10}O_5Br_2$: C, 30.19; H, 2.81. Found: C, 30.43; H, 2.92.

Partial Resolution of *cis*-Dibromomonomethyl Ester XIVa.—A hot solution of 16 g. of quinine trihydrate in 200 cc. of acetone was added to a hot solution of 15 g. of XIVa in 400 cc. of acetone. The solution was reduced in volume to 500 cc. by distillation and then allowed to stand overnight in the refrigerator. The precipitated quinine salt, 8.8 g. of spherical aggregates of silky blades, melted at 143–145.5° dec. The acetone mother liquor (A) was preserved. The solid quinine salt was dissolved in a mixture of 200 cc. of acetone and 50 cc. of methanol. This solution was reduced in volume to 75 cc. and cooled overnight in the refrigerator to yield 6.1 g. of salt, m.p. 145–148° dec. The salt was decomposed by trituration with 40 cc. of concentrated hydrochloric acid. The resulting chalky powder was dissolved in 5% potassium carbonate, filtered through a fine fritted glass disc, acidified with concentrated hydrochloric acid and the precipitated acid collected, washed with water until the washings were neutral and dried in air to yield 2.5 g. of (+)XIVa, $[\alpha]_D$ +2.5° (*c* 2.0 in 5% potassium carbonate, *l* 2 dcm.), m.p. 319° dec.

Anal. Calcd. for $C_9H_{10}O_5Br_2$: neut. equiv., 358. Found: neut. equiv., 357.

The acetone mother liquor A deposited a further quantity of solid material after standing a short while. This was removed by filtration and the filtrate was concentrated to a volume of 200 cc. and cooled. The resulting solid was again filtered off, the mother liquor was concentrated to a volume of 100 cc. and treated with 50 cc. of carbon tetrachloride and 50 cc. of Skellysolve B, whereupon a sticky solid separated. This material was filtered off and triturated with 25 cc. of 6 *N* hydrochloric acid to yield a granular precipitate which was washed with water and then dissolved in 25 cc. of 5% potassium carbonate. The alkaline solution was extracted with three 30-cc. portions of chloroform to remove the last traces of quinine, then filtered, acidified with hydrochloric acid and the precipitated acid collected at the pump and dried in air. The yield of (−)XIVa was 2.4 g. After two recrystallizations from 90% methanol, colorless needles melting at 319° dec., $[\alpha]_D$ −3.3° (*c* 4.7 in 10% potassium bicarbonate, *l* 2 dcm.) were obtained.

Anal. Calcd. for $C_9H_{10}O_5Br_2$: C, 30.19; H, 2.81. Found: C, 30.41; H, 3.16.

Methylation of Optically Active XIVa to Optically Inactive XIVb.—A suspension of 0.98 g. of (+)XIVa, $[\alpha]_D$ +2.5°, in 15 cc. of absolute methanol and 7 drops of 30% fuming sulfuric acid was heated at reflux for 2.75 hours. The mixture was distilled to half its original volume and treated with 30 cc. of 5% potassium carbonate. The resulting solid precipitate weighed 0.96 g. (94% of theory) and melted at 196.5–198.5° alone or mixed with a sample of XIVb prepared from IIIb as above. The optical rotation of a pyridine solution of this material (*c* 4.2, *l* 2 dcm.) was too small to detect, the observed α being 0.00° ± 0.01°.

In a similar experiment, esterification of 0.11 g. of (−)-XIVa, $[\alpha]_D$ −3.3°, was carried out with methanolic sulfuric acid. The methanol was removed and the entire residue was taken up in 9.0 cc. of acetonitrile. The observed rotation was −0.02 ± 0.02° (*l* 4 dcm.). The precision of the readings in this case was somewhat less than before due to some darkening of the reaction mixture.

Hydrolysis of (+)XIVa.—A mixture of 0.384 g. of XIVa $[\alpha]_D$ +2.5°, 10 cc. of purified dioxane and 4 cc. of 6 *N* hydrochloric acid was heated at reflux for 82 hours and then allowed to stand at room temperature for ten days. The solid material slowly dissolved. The solvent was removed *in vacuo* and the total residue dissolved in 3.0 cc. of 5% potassium carbonate. The observed rotation of this solution was −0.01 ± 0.02°. Upon acidification of the solution, a solid, m.p. 331°, separated. The m.p. was not depressed on admixture with XIVc.

Action of Alkali on 4,5-Dibromo-*exo-cis*-3,6-endomethylenehexahydrophthalic Acid.—A mixture of 2.1 g. of the acid[34a] and 25 cc. of water was brought to a phenolphthalein end-point with aqueous sodium hydroxide. (A portion of the clear solution immediately gave a positive test for halogen with silver nitrate.) After two hours, a crystalline precipitate appeared. The mixture was acidified with 6 *N* nitric acid, the product was collected at the pump and dried at 100° for 48 hours to give 1.2 g. of the bromolactonic acid XXVII, m.p. 157.5–159°, reported[34a] m.p. 157°. The mother liquors gave 1.13 g. of silver bromide when treated with excess silver nitrate. Alder and co-workers[34a] also report a "bromohydrin," m.p. 116°, which upon drying in the solid state gives the 157° bromolactonic acid. It seems unreasonable to suppose that the 116° material is a bromohydrin since we find it is reformed from the 157° lactone upon simple recrystallization of the latter from water. The low-melting modification is undoubtedly a crystal hydrate.

Conversion of 4,5-dibromo-*exo-cis*-3,6-endomethylenehexahydrophthalic acid to the anhydride XXII was accomplished by heating the dibromoacid with an excess of acetic anhydride at 100° for five minutes. The anhydride had m.p. 205° alone or mixed with a sample of XXII prepared by brominating XX in chloroform.[33]

Bromination of *endo-cis*-3,6-Endomethylene-Δ^4-tetrahydrophthalic Anhydride (XX). A. Ethyl Acetate.—A solution of 122.7 g. of XX in 500 cc. of ethyl acetate was treated with 41 cc. of bromine in 100 cc. of ethyl acetate during one and one-third hours. The temperature of the reaction mixture was kept below 5° and vigorous stirring was used. The clear solution was allowed to come to room temperature whereupon the bromine color faded and a crystalline product separated. This material weighed 55.1 g. and was identified as crude XXII, m.p. 203–205°. The mother liquor was concentrated to a volume of 150 cc. and diluted to 300 cc. with carbon tetrachloride whereupon a further quantity (23.2 g.) of XXII separated, m.p. 192.5–201°.

The residual mother liquor was evaporated to dryness leaving 175 g. of a pale orange glass. Sixty-eight and one-half grams of this material was heated for five hours at reflux with 100 cc. of methanol and 5 cc. of 30% fuming sulfuric acid. After standing an additional fourteen hours at room temperature, the reaction mixture was poured into 250 cc. of cold water, extracted with chloroform and the chloroform extracts washed with potassium bicarbonate and then with water. The chloroform solution was dried with sodium sulfate and evaporated to leave a thick, pale-yellow oil. The oil was distilled through a small Vigreux column to give the following fractions (bath at 220–240°): 1, b.p. 170° (2 mm.), 1.5 g., n^{25}_{D} 1.5205; 2, b.p. 170° (2.5 mm.), 12.1 g., n^{25}_{D} 1.5305; 3, b.p. 170° (2 mm.), 27.1 g., n^{25}_{D} 1.5308; 4, b.p. 171–173.5° (2 mm.), 9.6 g., very viscous oil, n^{25}_{D} 1.5338. Fraction 4 was triturated with cold methanol whereupon a sticky, partially crystalline material separated. Recrystallization from Skellysolve B gave 1.1 g. of colorless needles, m.p. 118–119°.

Anal. Calcd. for $C_{11}H_{14}O_4Br_2$: C, 35.70; H, 3.81. Found: C, 35.78; H, 3.75.

B. Methylene Chloride.—A solution of 12.5 g. of XX in 150 cc. of methylene chloride was treated with 4.5 cc. of bromine. A precipitate appeared after one hour. After 12 hours, the crystalline precipitate was collected to give 20.9 g. of dibromide, m.p. 204–205.5°, reported[33] m.p. 206°.

LOS ANGELES 7, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Structure and Stereochemistry of Bicyclic Derivatives. V.[1] Pyrolysis of *endo-cis*-3,6-Endomethylene-*exo-cis*-4,5-dibromohexahydrophthalic Acid

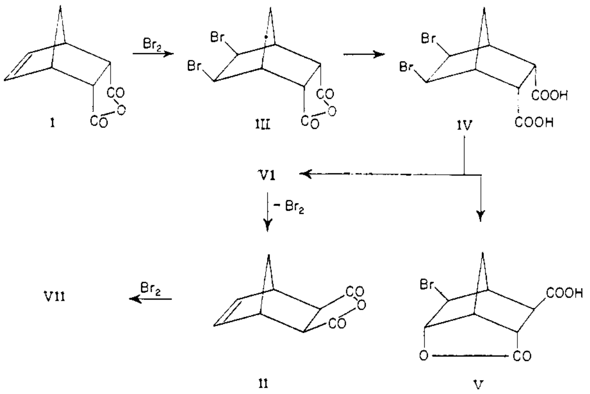
BY JEROME A. BERSON

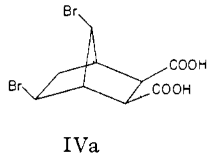
RECEIVED NOVEMBER 27, 1953

The anhydride obtained from the pyrolysis reaction of the title is shown to be a *meso* compound. This finding requires the rejection of the formula proposed by Kwart and Kaplan on the basis of dipole moment studies and confirms the unrearranged "all-*exo*" structure.

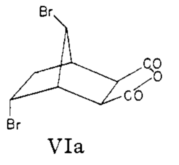
In an investigation of methods of converting the *endo*-cyclopentadiene–maleic anhydride adduct (I) to its *exo*-isomer(II), Alder and Stein[2] discovered that the isomerization could be effected circuitously *via* a sequence involving bromination of I to a dibromide, m.p. 209° (now known to be III[1c,3]), hydrolysis of III to the corresponding dibasic acid IV, pyrolysis of IV at 215° to give a mixture of a bromolactonic acid V and a new dibromoanhydride VI, m.p. 249°, and debromination of VI with zinc to give II. Bromination of II gave not VI but a new dibromoanhydride VII, m.p. 184°.[4] It is the structure of VI with which we are concerned here.

Kwart and Kaplan,[5] on the basis of a study of dipole moments, assigned the structure VIa to the anhydride VI of m.p. 249°. These authors also suggested a mechanism for the formation of VIa by the pyrolysis of the dibasic acid which they believed to be IVa.





IVa



VIa

---

[1] For previous papers in this series see (a) THIS JOURNAL, **75**, 1721 (1953); (b) **75**, 4366 (1953); (c) **76**, 4057 (1954); (d) **76**, 4060 (1954).

[2] (a) K. Alder and G. Stein, *Ann.*, **504**, 247 (1933). (b) The experiments of the German authors have been repeated in detail by P. D. Bartlett and A. Schneider, THIS JOURNAL, **68**, 6 (1946).

[3] *cf.* H. Kwart and L. Kaplan, *ibid.*, **76**, 4072 (1954).

[4] D. Craig, *ibid.*, **73**, 4889 (1951).

[5] H. Kwart and L. Kaplan, *ibid.*, **75**, 3356 (1953).