Evaporating the filtrate *in vacuo* and slurrying the remaining paste with ether gave after filtering and drying 0.595 g (89.9%) of **potassium 1-carbomethoxy-5-nitropentanenitronate**: mp 132–135° dec; neutralization equivalent found, 253 (calcd, 258); ir (Nujol) 1688 ($C{=}O$), 1664 ($C{=}N$), 1555 and 1381 ($NO_2$), and 1255 and 1110 cm$^{-1}$ ($C{=}NO_2^-$); nmr ($D_2O$) δ 4.59 (m, $CH_2NO_2$), 3.73 (s, 3, $OCH_3$), 2.60 (m, 2, $CH_2C{=}NO_2^-$), and 1.75 (m, 4, $CH_2$); uv max ($H_2O$) 294 mμ (log ε 3.94).

**2,6-Dinitrocyclohexanone** (**6**).—Hydrogen chloride was introduced for 1 hr at room temperature into a suspension of disalt **3** (1.437 g, 5.44 mmol) in 200 ml of anhydrous ether. After stirring for an additional 2.5 hr at room temperature, the mixture was filtered and the filtrate was evaporated *in vacuo*. Washing the residue with ether and drying *in vacuo* gave 0.94 g (93.5%) of **2,6-dinitrocyclohexanone** (**6**): mp 100–101° (lit.[5] mp 110.5°); ir (Nujol) 1748 ($C{=}O$) and 1570 and 1379 ($NO_2$); nmr (DMSO-$d_6$) δ 6.10 (m, 2, $CHNO_2$) and 2.3 (m, 6, $CH_2$); nmr ($CH_2Cl_2$)[12] δ 5.25 (m, $CHNO_2$), 12.72 (s, OH), and 2.22 (m, $CH_2$); uv max ($CH_3OH$) 228 mμ (log ε 3.70), 259 (3.63), 321 (3.53), and 422 (4.21).

*Anal.* Calcd for $C_6H_8N_2O_5$: C, 38.30; H, 4.26; N, 14.90. Found: C, 38.56; H, 4.54; N, 14.94.

**2,4-DNP derivative of 6** showed mp 162° dec, ethanol–ethyl acetate; ir (Nujol) 1620 ($C{=}N$) and 1560 and 1553 cm$^{-1}$ ($NO_2$).

*Anal.* Calcd for $C_{12}H_{12}N_6O_8$: C, 39.13; H, 3.26; N, 22.83. Found: C, 39.26; H, 3.20; N, 22.02.

**1,4-Dinitrobutane** (**7**). **A. From Compound 1.**—To a solution of **1** (2.53 g, 10.1 mmol) in 60 ml of water (pH 7.9) was added 85% formic acid (1.105 g, 20.4 mmol) all at once (pH 3.5). After this had stirred for 5 hr at room temperature the pH was 4.3.

Extracting the solution with ether, evaporating the combined extracts *in vacuo*, and recrystallizing the residue from 95% ethanol gave 1.231 g (82.7%) of compound **7**, mp 30–31° (lit.[13] mp 31–32°).

**B. From Compound 2.**—By following a similar procedure as described in part A, 1.374 g (6.48 mmol) of **2** and 0.352 g (6.5 mmol) of 85% formic acid afforded 84.2% **7**.

**1,5-Dinitropentane** (**8**). **A. From Compound 3.**—From 2.64 g (9.98 mmol) of **3** and 1.205 g (20.1 mmol) of glacial acetic acid there was obtained 1.423 g (88.1%) of compound **8**: bp 92–93° (0.01 mm); $n^{20}\mathrm{D}$ 1.4600 (lit.[13] $n^{20}\mathrm{D}$ 1.4601).

**B. From Compound 4.**—Introducing carbon dioxide for 12 hr into 2.208 g (9.8 mmol) of **4** dissolved in water gave 1.442 g (90.5%) of **8**.

**C. From Compound 6.**—From 0.605 g (3.3 mmol) of **6** dissolved in 60 ml of water there was obtained 0.475 g (89.1%) of **8**.

**Methyl 2,5-Dinitropentanoate** (**9**).—To a suspension of compound **1** (3.20 g, 12.8 mmol) in 80 ml of methanol was added glacial acetic acid (3.84 g, 64 mmol). After the mixture refluxed for 12 hr at 65° the resulting solution was concentrated *in vacuo*, the residue was taken up in ether, and the precipitated potassium acetate was filtered off. Concentrating the filtrate *in vacuo* gave 1.76 g (66.7%) of **methyl 2,5-dinitropentanoate**: bp 130–132° (0.28 mm); $n^{20}\mathrm{D}$ 1.4634; ir (Nujol) 1748 ($C{=}O$) and 1575, 1567, and 1374 cm$^{-1}$ ($NO_2$); nmr ($CDCl_3$) δ 5.28 (t with spacing of 6 Hz, 1, $CHNO_2$), 4.52 (m, 2, $CH_2NO_2$), 3.88 (s, 3, $CH_3$), and 2.28 (m, 4, $CH_2$); uv max ($CH_3OH$) 284 mμ (log ε 2.18).

*Anal.* Calcd for $C_6H_{10}N_2O_6$: C, 34.95; H, 4.85; N, 13.60. Found: C, 34.97; H, 4.61; N, 13.69.

Treating **9** (0.485 g, 2.35 mmol) with aqueous potassium hypobromite gave 0.834 g (76.5%) of 1,1,4,4-tetrabromo-1,4-dinitrobutane, mp 99–100° (hexane) (lit.[2] mp 99–100°).

**Methyl 2,6-Dinitrohexanoate** (**10**).—The procedure similar to that described for **9**, except that 2.12 g (8 mmol) of **3** was used, afforded 1.15 g (65.2%) of **methyl 2,6-dinitrohexanoate**: bp 138–140° (0.3 mm); $n^{20}\mathrm{D}$ 1.4630; ir (Nujol) 1770 ($C{=}O$), and 1575, 1558, and 1380 cm$^{-1}$ ($NO_2$); nmr ($CDCl_3$) δ 5.19 (t with spacing of 7 Hz, 1, $CHNO_2$), 4.43 (m, 2, $CH_2NO_2$), 3.86 (s, 3, $CH_3$), and 2.10 (m, 6, $CH_2$); uv max ($CH_3OH$) 268 mμ (log ε 1.96).

*Anal.* Calcd for $C_7H_{12}N_2O_6$: C, 38.18; H, 5.45; N, 12.73. Found: C, 38.46; H, 5.55; N, 12.86.

**Registry No.**—**1,** 12286-73-6; **2,** 26717-79-3; **3,** 12286-74-7; **4,** 26785-71-7; **6,** 26785-72-8; **6,** 2,4-DNP derivative, 26736-24-3; **7,** 4286-49-1; **8,** 6848-84-6; **9,** 26736-27-6; **10,** 26074-70-4; 1-carbomethoxy-5-nitropentanenitronate, 26736-29-8.

**Acknowledgment.**—We are indebted to the Office of Naval Research for the financial support of the work.

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[12] By integration of signal areas it was estimated that in this solvent, **6** was enolized to the extent of 75%.

[13] H. Feuer and G. Leston, *Org. Syn.*, **34**, 37 (1954).

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# The Stereochemistry of Halogenation of Cyclohex-4-ene-1,2-dicarboxylic Acids

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*trans*-Cyclohex-4-ene-1,2-dicarboxylic acid gives on bromination the product of trans-diaxial addition. A product of similar stereochemistry is obtained on reacting the same acid with bromine chloride. The cis diacid yields with bromine chloride a trans-addition product with the bromine cis to the carboxyl group. It is inferred that the cis acid forms a bromomium ion cis to the carboxyl group. A series of halolactones can be prepared from the halogenated compounds. *cis,cis*-3-Phenylcyclohex-4-ene-1,2-dicarboxylic acid, its salt, and mono- and dimethyl ester give direct lactonization on treatment with bromine.

Remote polar substituents exert an influence on the rates[1] and the steric course of electrophilic addition to cyclohexenes.[2] The electrophile enters generally trans to an electron-withdrawing substituent,[2] but a cis epoxidation of the anhydride of I was observed.[3] This was ascribed to the boat conformation of this anhydride[3] or to a complex formation with the peracid,[2] in view of the different steric course of the epoxidation of the ester I.[2]

Halolactonization of cyclohexene-1- and -2-acetic acids gave *cis*-γ-lactones with the halogen trans to the lactone ring.[4] The reason for this stereospecificity could have been a result of a stereospecific halonium ion formation trans to the carboxylate group or simply a consequence of the unreactivity of the cis halonium ion with the carboxylate group in the side chain, due to the strain that would be created by formation of a trans lactone. The *cis*-halonium ion would in this case revert to the olefin, which could then yield a reactive *trans*-halonium ion. Bromination of cyclohex-3-enecarboxylic

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* To whom correspondence should be addressed.

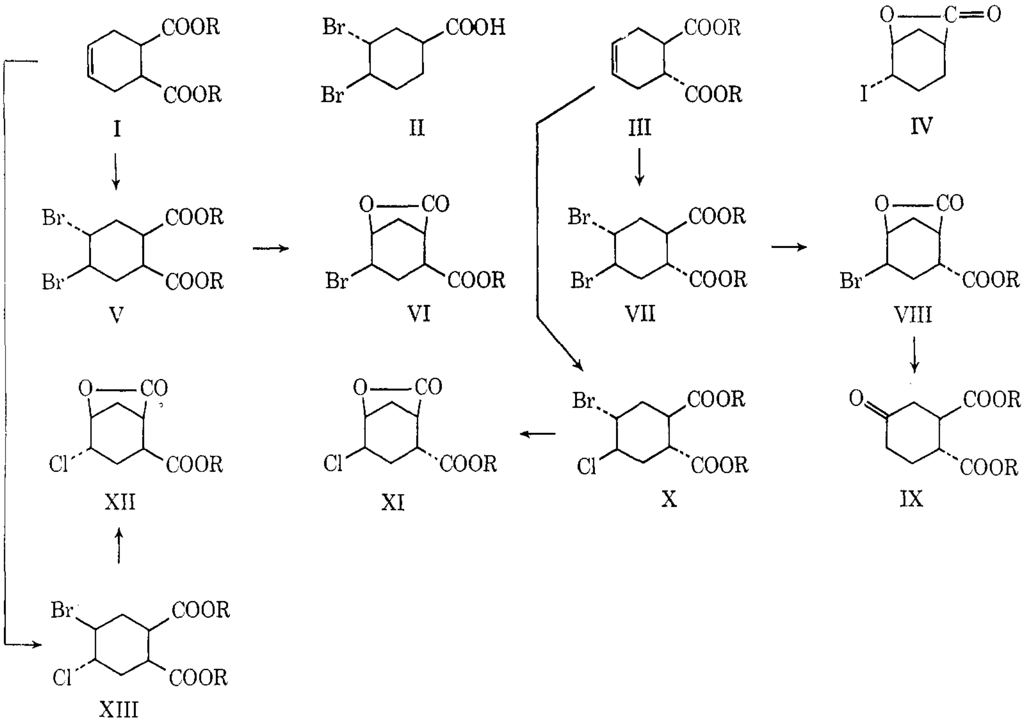
[1] H. Kwart and L. J. Miller, *J. Amer. Chem. Soc.*, **83**, 4552 (1961).

[2] H. B. Henbest, *Proc. Chem. Soc.*, 159 (1963).

[3] A. P. Gray, D. E. Heitmeier, and H. Krauss, *J. Amer. Chem. Soc.*, **84**, 89 (1962).

[4] J. Klein, *ibid.*, **81**, 3611 (1959).

acid gave only one isomer (II) of the possible adducts.[5,6] However, no conclusions can be drawn on the specificity of the bromonium ion formation, since any of these, either cis or trans, would give the same product by trans-diaxial opening[7–10] if the carboxyl maintained an equatorial conformation during the reaction. Symmetric halogens are therefore of no use in solving this problem. We decided, therefore, to study the addition of bromine chloride to *trans*-IIIa and *cis*-cyclohex-4-ene-1,2-dicarboxylic acid (Ia). The dicarboxylic acids were chosen to diminish the number of possible adducts. Addition of bromine chloride to cyclohexenes and steroids was already found to proceed in a trans-diaxial manner[11–13] through a chair-like transition state.[10,11,13,14] A preliminary attempt to react cyclohex-3-enecarboxylic acid with iodine chloride has shown the unsuitability of this reagent for our study, since the obtained chloroiodo adduct[15] gave on treatment with sodium bicarbonate the known[5] iodolactone IV. This compound could be obtained only by a reversal of the chloroiodo compound either to the iodonium ion or to the starting olefin with subsequent trans iodolactonization.



a, R = H
b, R = $CH_3$

The halogenations were carried out also with the methyl esters Ib and IIIb and with the corresponding anhydrides. The structures of the halogenated products obtained from the acids were determined by heating with triethylamine (1 equiv to each carboxyl group) in 1,2-dimethoxyethane (DME). It was assumed that the lactones obtained in this reaction are a product of an intramolecular substitution by the carboxylate of the halogen trans to this group. This assumption seems to be correct, since lactonization in these conditions of Va, obtained[16] by bromination of Ia, gave the same lactone VIa as obtained previously in aqueous base solution.[16]

Bromination of IIIa gave the dibromo derivative VIIa. This compound gave on lactonization the bromolactone VIIIa, characterized by its nmr spectrum[17] and by its reaction with base, that gave the known[18] keto diacid IX. Similarly, the reaction of IIIa with bromine chloride gave a product to which the structure Xa was assigned, since the usual base treatment gave the lactone XIa, characterized by its nmr[17] and ir spectrum. Treatment of IIIb with bromine or bromine chloride gave the esters VIIb and Xb, respectively. It is of interest that no isomers of VII or X were found in the halogenations of III and its esters. It seems that the opening of the bromonium ion, though not the rate-determining step in these reactions,[19–21] is the product determining one. A different isomer in a diaxial reaction could be obtained only when the carboxyls occupy axial positions in the transition state. Such a transition state would develop two diaxial bromine–carboxyl interactions making it of

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(5) R. Creve, A. Heinke, and Ch. Sommer, *Chem. Ber.*, **89**, 1978 (1956).

(6) Another isomer (*ca.* 5%) was also formed. Our unpublished results.

(7) D. H. R. Barton and E. Miller, *J. Amer. Chem. Soc.*, **72**, 1066 (1950).

(8) D. H. R. Barton and W. Rosenfelder, *J. Chem. Soc.*, 1048 (1951).

(9) G. Alt and D. H. R. Barton, *ibid.*, 4284 (1954).

(10) R. L. Eliel and R. S. Haber, *J. Org. Chem.*, **24**, 143 (1959).

(11) D. H. R. Barton, E. Miller, and H. T. Young, *J. Chem. Soc.*, 2598 (1951).

(12) J. G. Ziegler and A. C. Shabica, *J. Amer. Chem. Soc.*, **74**, 4891 (1952).

(13) H. J. Hageman and E. Havinga, *Recl. Trav. Chim. Pays-Bas*, **85**, 1141 (1966).

(14) J. Valls and E. Toromanoff, *Bull. Soc. Chim. Fr.*, 758 (1961).

(15) Our unpublished results.

(16) V. R. Kutcherov, A. L. Shabanov, and A. S. Onishenko, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 844 (1963); A. S. Onishenko, A. L. Shabanov, and V. R. Kucherov, *ibid.*, 852 (1963).

(17) E. Dunkelblum and J. Klein, *Tetrahedron Lett.*, 55 (1968).

(18) P. C. Ayres and R. A. Raphael, *J. Chem. Soc.*, 1779 (1958).

(19) R. E. Buckles, J. L. Miller, and R. J. Thurmaier, *J. Org. Chem.*, **32**, 888 (1967).

(20) R. P. Bell and M. Pring, *J. Chem. Soc. B*, 1119 (1966).

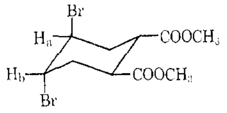
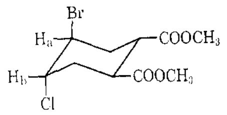
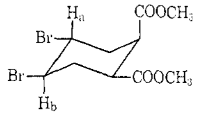
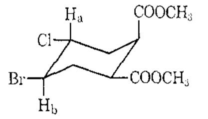
(21) J. H. Rolston and K. Yates, *J. Amer. Chem. Soc.*, **91**, 1483 (1969).

much higher energy relative to that with equatorial carboxyls, although a nonnegligible amount of the conformer with axial carboxyls[22] is present in III.

The reaction of Ia with bromine chloride gave, in good yield, a single diacid contaminated with a small amount of a lactone. Products of similar stereochemistry were obtained in this reaction with the dimethyl ester and anhydride of I, as shown by the interconversion of all these products. Base treatment of the adduct formed from Ia gave, unexpectedly, the chlorolactone XIIa, whose methyl ester XIIb was characterized by nmr.[17] This lactone, *i.e.*, XIIb, was of different stereochemistry from the lactone VIb obtained[16] from the product Va of bromination of Ia. The nmr spectrum in chloroform of the methyl ester of the product of reaction of Ia with bromine chloride was inconclusive but in pyridine and particularly in benzene the hydrogens $\alpha$ to the halogens (Table I) showed coupling constants, proving their diaxial anti conformation[23] and consequently the trans arrangement of the halogens. One of the $\alpha$ protons appeared at 100 MHz in the latter solvent as a septet (degenerate octet) with coupling constants of 12, 8, and 4 Hz ($\tau$ 5.84), and the other ($\tau$ 6.19) as a more involved multiplet with a width of the band similar to that of the first $\alpha$ proton (Figure 1). The structure of the ester is therefore XIIIb and this ester is present predominantly in one conformation, since the other possible conformation has a diaxial bromine–ester interaction. The esters VIIb and Xb are apparently also predominantly in a conformation with equatorial ester groups.

TABLE I

NMR SPECTRA OF HALO ESTERS AT 60 MHz

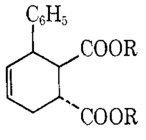
| Ester | In pyridine, $H_a$,$H_b$ | In benzene, $H_a$,$H_b$ |
|---|---|---|
|  | $\tau$ 5.22 (m),<br>$W_{1/2}{}^{a}$ = 8 Hz | $\tau$ 5.90 (m),<br>$W_{1/2}$ = 8 Hz |
|  | $\tau$ 5.40 (m),<br>$W_{1/2}$ = 8 Hz | $\tau$ 6.10 (m),<br>$W_{1/2}$ = 8 Hz |
|  | $\tau$ 5.45 (t, d),<br>$J_1$ = 9 Hz,<br>$J_2$ = 3 Hz | $\tau$ 5.75(t,d), $J_1$ = 8 Hz, $J_2$ = 3 Hz<br>$\tau$ 6.20 (m),<br>$W_{1/2}$ = 18 Hz |
|  | $\tau$ 5.65 (m),<br>$W_{1/2}$ = 22 Hz | $\tau$ 5.90 (t, d),<br>$S_1{}^{b}$ = 8 Hz;<br>$S_2$ = 4 Hz<br>$\tau$ 6.25 (t),<br>$S$ = 7 Hz |

[a] Half-width of the peak. [b] These are separations between the components of the multiplet.

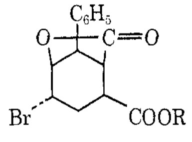
The displacement of the bromine cis to the carboxyls indicates that cyclization to a $\gamma$-lactone by the trans chlorine displacement is very difficult in this system and an ionization of the carbon–bromine bond cis to the carboxyl with subsequent cyclization is a preferred process. This ionization is possibly assisted by the neighboring chlorine. Bromine exerts generally a much more powerful neighboring group assistance than chlorine, but effects due to the greater carbon–chlorine than carbon–bromine bond strength might favor the ionization of the carbon–bromine bond in our system. The possibility that the lactonization occurred on a product of displacement of bromine by triethylamine, where the ammonium group was trans to the carboxyls, cannot be excluded.

The stereochemistry of XIII proves the preferential formation in this system of the bromonium ion cis to the carboxyls. The reason for it is not entirely clear, but it can be assumed that this ion is stabilized by the interaction with the $\pi$ electrons of the axial carboxyl group. This is therefore perhaps a particular case that should not be generalized. Halogenation of the anhydride, the ester, and the acid I proceeds with a similar stereochemistry unlike the epoxidation reaction[2,3] and is possible owing to the lower steric requirements of the halogenating agent relative to the peracid.

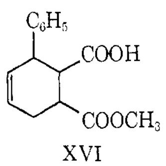
In order to obtain more information on the course of the reaction, we studied the bromination of the phenyl-substituted dicarboxylic acid XIVa in which the position of the axial carboxyl is determined (position 2) by the relative stabilities of the conformers. Bromination of this acid gave directly a bromolactone. The same product was obtained by bromolactonization of the salt of XIVa. Structure XVa was assigned to this compound, since the ester XVb was obtained by bromination of the monoester XVI, formed by treatment of the anhydride of XIVa with methanol. Bromination and a Hunsdiecker reaction of XVI with subsequent dehydrobromination yielded 3-phenylbenzoic acid. The trans disposition of the bromine substituent relative to the lactone ring in XV follows from its nmr spectrum showing the hydrogen $\alpha$ to oxygen at $\tau$ 5.17 as a doublet with a coupling constant[17] of 4 Hz.



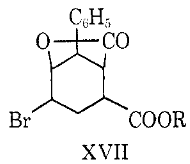
XIV



XV



XVI



XVII

a, R = H
b, R = $CH_3$

It is of interest that bromination of the dimethyl ester XIVb gave directly XVb in fair yield (40%). However, bromination of the anhydride of XIVa yielded a mixture from which an isomeric lactone was isolated in low yield (15%) after hydrolysis and lactonization in basic conditions. Structure XVIIa was assigned to this lactone since its ester (XVIIb) showed in the nmr spectrum a singlet at $\tau$ 4.99 for the hydrogen $\alpha$ to the oxygen and a doublet of doublets at $\tau$ 6.70 for the hy-

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(22) Z. Welwart, *Bull. Soc. Chim. Fr.*, 2203 (1964).

(23) The lower than ordinary coupling constants for an anti arrangement of the protons is due to the halogens: E. I. Snyder, *J. Amer. Chem. Soc.*, **88**, 1155 (1966); R. O. C. Norman and C. B. Thomas, *J. Chem. Soc. B*, 598 (1968); C. A. Kingsbury and W. B. Thornton, *J. Org. Chem.*, **31**, 1000 (1966).

drogen $\alpha$ to bromine with coupling constants of 11 and 6 Hz as expected.[17]

It seems, therefore, that the bromonium ion of XIV is formed trans to the carbonyl groups, differently from that of I, where cis bromonium ion formation was inferred. The reason for this effect is the bulk of the phenyl group in XIV which together with the equatorial carboxyl forces the axial carboxyl group in an "unnatural" conformation[24] with the oxygen pointing inside the ring. Such a conformation hinders sterically the formation of a cis bromonium ion and also stabilizes by a neighboring group effect the charge dispersed on the carbon atoms of the trans bromonium ion. The presence of these effects is supported by the unusual direct lactonization during the bromination of the diester XIVb.

## Experimental Section

Infrared spectra were determined neat, if not stated otherwise, on a Perkin-Elmer 337 spectrophotometer, and nmr spectra on a Varian A 56/60 instrument in $CCl_4$ or $CDCl_3$ using tetramethylsilane as an internal standard. Melting points were not corrected.

*trans*-[25] and *cis*-[26] cyclohex-4-ene-1,2-dicarboxylic acids (IIIa and Ia, respectively), trans[25] and cis anhydrides,[26] and their methyl esters[27] were prepared by known methods.

***cis*-3-Phenylcyclohex-4-ene-*cis*-1,2-dicarboxylic acid (XIVa)** was prepared from the anhydride[28] by dissolution in aqueous sodium hydroxide and subsequent acidification, mp 195–197° (water). Esterification of this acid with diazomethane yielded the dimethyl ester XIVb, mp 61–62° (ethanol), $\nu_{max}$ 1740 cm$^{-1}$ (Nujol). *Anal.* Calcd for $C_{16}H_{18}O_4$: C, 70.1; H, 6.6. Found: C, 69.9; H, 6.7.

**Methyl *cis*-2-carboxy-*cis*-3-phenylcyclohex-4-enecarboxylate (XVI)** was obtained by dissolution of the anhydride[28] of XIVa (20 g) in boiling methanol (150 ml). The precipitate, formed after cooling the solution, was crystallized twice from ethyl acetate giving 11 g melting at 174–175°, $\nu_{max}$ 1740 cm$^{-1}$ (Nujol). *Anal.* Calcd for $C_{15}H_{16}O_4$: C, 69.2; H, 6.2. Found: C, 69.0; H, 6.1.

**Halogenations.**—The substituted cyclohexene (0.05 mol) in dichloromethane (75 ml) was cooled in an ice bath, and an equivalent amount of bromine or bromine chloride, freshly prepared by addition of an equivalent amount of bromine to liquid chlorine[13,29] in dichloromethane (25 ml), was added dropwise with stirring. In the case of the diacids, the reaction was performed on suspensions, due to their low solubility. The solvent was evaporated after the completion of the reaction and the residue was recrystallized.

***trans*-2-Carboxy-*cis*-4-bromo-*trans*-5-chlorocyclohexanecarboxylic acid (Xa)** was obtained from IIIa and bromine chloride in 70% yield, mp 195–196° (water), $\nu_{max}$ 1720 cm$^{-1}$. *Anal.* Calcd for $C_8H_{10}BrClO_4$: C, 33.6; H, 3.5. Found: C, 33.8; H, 3.9.

Dimethyl ester Xb was obtained from IIIb: yield, 90%; mp 72–73° (ethanol); $\nu_{max}$ 1740 cm$^{-1}$. *Anal.* Calcd for $C_{10}H_{14}BrClO_4$: C, 38.2; H, 4.5. Found: C, 38.5; H, 4.5.

***cis*-2-Carboxy-*cis*-4-bromo-*trans*-5-chlorocyclohexanecarboxylic acid (XIIIa)** was obtained in 60% yield from Ia, mp 193–195° (ethyl acetate–hexane), $\nu_{max}$ 1720 cm$^{-1}$. *Anal.* Calcd for $C_8H_{10}BrClO_4$: C, 33.6; H, 3.5. Found: C, 33.8; H, 3.6.

Dimethyl ester XIIIb was prepared from Ib: bp 160–165° (1 mm); yield, 60%; $\nu_{max}$ 1740 cm$^{-1}$. A weak lactone band appears at 1790 cm$^{-1}$. *Anal.* Calcd for $C_{10}H_{14}BrClO_4$: C, 38.2; H, 4.5. Found: C, 39.4; H, 4.1.

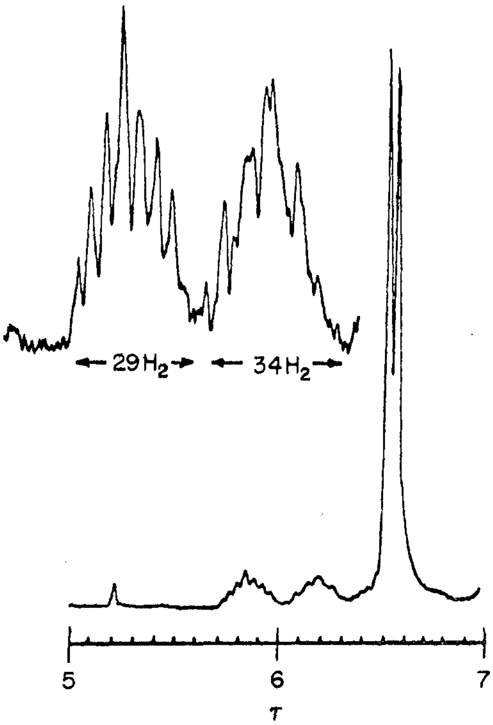

Figure 1.—Nmr spectrum of XIIIb in benzene at 100 MHz.

The anhydride of XIIIa was prepared from the anhydride of Ia in 70% yield: mp 122–123° (benzene–hexane); $\nu_{max}$ 1880, 1800, and 1725 cm$^{-1}$. *Anal.* Calcd for $C_8H_8BrClO_3$: C, 35.9; H, 3.0. Found: C, 35.6; H, 3.2.

***trans*-2-Carboxy-*cis*-4-bromo-*trans*-5-bromocyclohexanecarboxylic acid (VIIa)** was obtained from IIIa and bromine: yield, 85%; mp 184–185° (acetone–water); $\nu_{max}$ 1720 cm$^{-1}$. *Anal.* Calcd for $C_8H_{10}Br_2O_4$: C, 29.1; H, 3.3; Br, 48.5. Found: C, 28.9; H, 3.5; Br, 48.6.

The diester VIIb was obtained in 70% yield from IIIb, mp 75–76° (ethanol), $\nu_{max}$ 1740 cm$^{-1}$. *Anal.* Calcd for $C_{10}H_{14}Br_2O_4$: C, 33.5; H, 3.0. Found: C, 33.5; H, 3.7.

***cis*-2-Carboxy-*cis*-3-phenyl-*cis*-4-hydroxy-*trans*-5-bromocyclohexanecarboxylic acid lactone-(2,4) (XVa)** was obtained in 90% yield by bromination of XIVa, mp 201–202° (ethyl acetate), $\nu_{max}$ 1800 and 1725 cm$^{-1}$. *Anal.* Calcd for $C_{14}H_{13}BrO_4$: C, 51.7; H, 4.0. Found: C, 51.6; H, 4.0.

Esterification of XVa with a diazomethane gave XVb, mp 108–109° (ethanol), $\nu_{max}$ 1800 and 1750 cm$^{-1}$. *Anal.* Calcd for $C_{15}H_{15}BrO_4$: C, 53.1; H, 4.4; Br, 23.6. Found: C, 52.9; H, 4.3; Br, 23.5.

The ester XVb was also obtained in 40% yield from XIVb. Bromination of the anhydride of XIVa (11 g), subsequent treatment with triethylamine in DME, and evaporation of DME under reduced pressure left a residue that was dissolved in DMSO (50 ml) and methyl iodide (15 ml). The mixture was stirred overnight, poured on water, and extracted with dichloromethane. Chromatography on alumina and elution with benzene–chloroform yielded a product that was crystallized from benzene–cyclohexane (2 g), mp 125–126°, $\nu_{max}$ 1790 and 1740 cm$^{-1}$. *Anal.* Calcd for $C_{15}H_{15}BrO_4$: C, 53.1; H, 4.4; Br, 23.6. Found: C, 52.8; H, 4.3; Br, 23.4.

Bromination of the sodium salts of XVI and XIVa was carried out in aqueous solution; 0.02 mol of XVI or XIVa was dissolved in an aqueous solution of 0.02–0.04 mol of NaOH, respectively. To this cooled solution 3.2 g of $Br_2$ in 50 ml of water containing 2.4 g KBr was added dropwise. The reaction mixture was acidified and the precipitate collected. The filtrate was extracted with ether. A 90% yield of XVb was obtained from XVI and a similar yield of XVa from XIVa.

**Lactonization.**—The halogenated acid (3 g) was refluxed for 2 hr in 1,2-dimethoxyethane (50 ml) and 3 ml of $Et_3N$. The reaction mixture was cooled and filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in ethyl acetate, washed rapidly with dilute HCl, and dried and the solvent evaporated.

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***trans,trans,trans*-2-Carboxy-4-hydroxy-5-bromocyclohexanecarboxylic acid lactone-(2,4) (VIIIa)** was obtained in 80% yield from VIIa, mp 129–130° (ethyl acetate), $\nu_{max}$ 1790 and 1720 cm$^{-1}$. Esterification of VIIIa with diazomethane gave VIIIb, mp 89–90° (benzene), $\nu_{max}$ 1790–1740 cm$^{-1}$. *Anal.* Calcd for $C_9H_{11}BrO_4$: C, 41.1; H, 4.2. Found: C, 41.3; H, 4.2.

**Methyl *trans,trans,trans*-2-carboxy-4-hydroxy-5-chlorocyclohexanecarboxylate lactone-(2,4) (XIb)** was prepared in 40% yield from Xa and subsequent esterification with diazomethane, mp 92° (ethanol), $\nu_{max}$ 1800 and 1740 cm$^{-1}$. *Anal.* Calcd for $C_9H_{11}ClO_4$: C, 49.4; H, 5.0; Cl, 16.2. Found: C, 50.0; H, 5.1; Cl, 16.1.

**Methyl *cis*-2-carboxy-*cis*-4-hydroxy-*trans*-5-chlorocyclohexanecarboxylate lactone-(2,4) (XIIb)** was obtained from XIIIa and subsequent esterification with diazomethane, bp 150–155° (0.5 mm), $\nu_{max}$ 1800 and 1740 cm$^{-1}$. *Anal.* Calcd for $C_9H_{11}ClO_4$: C, 49.4; H, 5.0; Cl, 16.2. Found: C, 49.4; H, 5.0; Cl, 16.0.

**Registry No.**—Vb, 26595-97-1; VIIa, 26595-79-9; VIIb, 26595-80-2; VIIIa, 26595-81-3; VIIIb, 19914-90-0; Xa, 26595-83-5; Xb, 26595-84-6; XIb, 26595-85-7; XIIb, 26595-86-8; XIIIa, 26595-87-9; XIIIb, 26595-88-0; XIII anhydride, 26595-89-1; XIVa, 26595-90-4; XIVb, 26595-91-5; XVa, 26595-92-6; XVb, 19914-94-4; XVI, 26595-94-8; XVIIb, 19914-95-5; *trans*-2-carboxy-*cis*-4-chloro-*trans*-5-bromocycohexanecarboxylic acid dimethyl ester (from Table I), 26595-96-0.

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# Solvolysis Studies of Cycloalkylcarbinyl Tosylates. Effect of Adjacent Ring Size on the Rates and Products. Ionization Constant Determinations of Cycloalkanecarboxylic Acids

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First-order titrimetric rate constants, activation parameters, and products were determined for the acetolysis of cycloalkylcarbinyl tosylates of ring size five through twelve. First-order formolysis rate constants were also determined for the series, and trifluoroacetolysis first-order rate constants were determined for cyclohexyl-, cyclononyl-, and cycloundecylcarbinyl tosylates. Ionization constants were measured for the cycloalkanecarboxylic acids of ring size five through twelve. A small rate spread was observed for the series, with the maximum rate being observed for cyclononylcarbinyl tosylate. The observed rate profiles closely parallel the cycloalkane ring strain profile calculated from combustion data. The products (seven- through twelve-membered rings) were mainly 1-methylcycloalkenes, which were shown by deuterium substitution in one case to arise *via* a 1,2-hydride shift. The rate spread was considered to be due to nucleophilic hydrogen participation at the transition state ($k_\Delta$). A smaller contribution of a solvent assisted ($k_s$) pathway also contributed to the total solvolytic rate. Hydrogen participation is proposed as being directly related to relief of ring strain (six- through twelve-membered rings). Inductive contributions of the adjacent ring are also of importance. Cyclopentylcarbinyl tosylate appears to solvolyze *via* a nonclassical ion (carbon participation) to yield ring expanded products.

In the mechanistic analysis of solvolytic reactions of primary substrates it has been proposed that there are competing pathways for displacement of the leaving group. These routes have been designated as $k_\Delta$ (anchimerically assisted ionization) and $k_s$ (anchimerically unassisted ionization) and depend on the solvent and substrate structure.[2,3] The suggestion has been made that the $k_s$ route is the nucleophilic solvent assisted process[4] and we shall adopt this terminology in this manuscript and return to the original definition of Winstein.[3]

These pathways are simultaneous processes and no crossover occurs between them. In solvents of high ionizing power and low nucleophilicity such as trifluoroacetic acid, the $k_\Delta/k_s$ ratios for primary substrates are much higher than in formic acid.[2,5] The solvolyses of primary tosylates have also been performed in fluorosulfuric acid[6,7] and sulfuric acid.[8]

The formation of carbonium ions or ion pairs ($k_c$ route) from primary substrates seems highly unlikely as these cations are perhaps far too unstable to exist in solution.[9-12] A strong nucleophilic solvent bond is indicated in the solvolysis of these substrates proceeding through the $k_s$ route. On the basis of rate, solvent, and isotope effects in the solvolysis of ethyl trifluoromethanesulfonate, it was concluded that substantial bonding to a nucleophilic solvent molecule at the transition state was required even with such a good leaving group as the trifluoromethanesulfonate anion.[13]

On the basis of these pathways ($k_s$ and $k_\Delta$) for primary substrate solvolyses, it has been concluded by Schleyer and coworkers[14] that the presence of any rearranged product in the solvolysis of simple primary systems can be taken as *prima facie* evidence for neighboring group participation.

This picture of competing $k_\Delta$ and $k_s$ routes, with no interconversion between them, has been successfully utilized in the interpretation of the solvolysis

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