Chlorination. I. Physical Evidence for Polar Effects in the Products of the Chlorination of Cyclohexanecarboxylic Acid

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Abstract: As a prelude to the detailed study of the directive influences of the carboxyl group upon both radical and enolic chlorination reactions, the seven monochlorocyclohexanecarboxylic acids (including the previously unreported *cis*-3 and *cis*-4 isomers) and their methyl esters have been synthesized and characterized. Nmr studies of the chloro esters at low temperatures yielded correlations between the chemical shifts of individual protons in cyclohexanecarboxylic acid and in chlorocyclohexane *vs.* predicted reactivity toward attack by an electrophilic radical such as Cl·. Comparison of the $>CHCl$, $>CHCO_2-$, and $-CO_2CH_3$ chemical shifts at low temperature showed that the resonances were dependent (a) upon the conformation (axial or equatorial) of the protons, (b) the distance to the remote polar substituent (Cl or CO_2CH_3), and (c) the *conformation* of the polar substituent. A measure of the additivity of conformational energies ($\Delta G°$) of two polar substituents on a cyclohexane ring was obtained by comparing the observed conformational distribution with values calculated from observed ratios in methyl cyclohexanecarboxylate ($\Delta G°_{-87°} = 1.30 \pm 0.14$ kcal/mole) and chlorocyclohexane ($\Delta G°_{-87°} = -0.67 \pm 0.12$ kcal/mole) in perdeuterioacetone. In general, fair agreement was found for the 1,4- and 1,3-disubstituted systems, but not with the 1,2- or 1,1-systems. Methyl *cis*-2-chlorocyclohexanecarboxylate showed an nmr spectrum which was essentially invariant (equatorial carbomethoxy, axial chloro) over the entire temperature range studied (-87 to $+26°$).

The influence of polar substituents upon chlorination of aliphatic systems has been the subject of a number of investigations.[2,3] In the case of radical chlorination reactions, most of these influences are manifested in the hydrogen-abstraction step and may be summarized in terms of (a) factors affecting the ground-state electron density at the C–H bond being broken, and (b) contributions to the stabilization of the transition state through, *e.g.*, resonance interaction of the incipient radical with the substituent.[4] In general, the first category is of greater importance when a very reactive radical, such as Cl· itself, is the attacking species, since the C–H bond is not broken to a very high degree at the transition state, and the electrophilic nature of the chlorine atom is controlling. The second factor becomes of greater importance as the reactivity of the attacking species is decreased, as in the case of trichloromethanesulfonyl chloride,[5,6] *t*-butyl hypochlorite,[6,7] or solvent-complexed chlorine atoms.[8,9] A convenient way of depicting the contribution of polar effects to the hydrogen-abstraction step may be seen in the contribution of resonance forms II and III to the transition state.[10]

$$\mathrm{R{-}H} + \mathrm{X}\cdot \longrightarrow \underset{\mathrm{I}}{[\mathrm{R{---}H{---}X}\cdot} \longleftrightarrow \underset{\mathrm{II}}{\mathrm{R}^+\,\mathrm{H}\cdot\,\mathrm{X}^-} \longleftrightarrow$$

$$\underset{\mathrm{III}}{\mathrm{R}\cdot\,\mathrm{H}^+\,\mathrm{X}^-]} \longrightarrow \mathrm{R}\cdot + \mathrm{H{-}X} \qquad (1)$$

If the polar substituent happens to be a carboxyl derivative, both polar and resonance stabilization influences on this hydrogen-abstraction step are magnified, and yet another directive influence, the tendency to promote α-chlorination through, *e.g.*, involvement of an enol[11] may manifest itself. Thus a competition between enolic and radical chlorination may be set up.

As a prelude to a study of the directive capabilities of the carboxyl group during the chlorination of aliphatic carboxylic acids under both radical and nonradical conditions,[12] we have isolated and identified the seven monochlorocyclohexanecarboxylic acids and their methyl esters. In addition, the physical properties of the methyl esters have been examined in some detail to see if some correlation of, *e.g.*, the effects of the polar substituents in the molecule with the subsequent chlorination results[12] can be made.[13]

Results

Photochlorination of cyclohexanecarboxylic acid (IVa) gave a mixture of monochloro acids, the direct separation of which by a variety of physical methods was unsuccessful. Fractional distillation gave only partial separation and was complicated by slow release of HCl. Chromatography on silica gel[15] proved to be tedious and unreliable. Conversion of the acid mix-

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[1] To whom correspondence should be addressed.

[2] See, for example, (a) C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York, N. Y., 1957, pp 360–369; (b) A. F. Trotman-Dickenson in "Advances in Free Radical Chemistry," Vol. I, G. H. Williams, Ed., Academic Press, New York, N. Y., 1965, pp 14–16; (c) E. S. Huyser, in ref 2b, pp 95–101.

[3] See also (a) G. A. Russell and P. G. Haffley, *J. Org. Chem.*, **31**, 1869 (1966); (b) H. Singh and J. M. Tedder, *J. Chem. Soc.*, *B*, 612 (1966); (c) J. Rouschaud and A. Bruylants, *Bull. Soc. Chim. Belges*, **76**, 50 (1967), and previous papers in these series pertaining to chlorination.

[4] G. A. Russell, *Tetrahedron*, **8**, 101 (1960).

[5] E. S. Huyser, *J. Am. Chem. Soc.*, **82**, 5246 (1960); E. S. Huyser and B. Giddings, *J. Org. Chem.*, **27**, 3391 (1962).

[6] G. A. Russell and A. Ito, *J. Am. Chem. Soc.*, **85**, 2983 (1963).

[7] C. Walling and B. B. Jacknow, *ibid.*, **82**, 6108 (1960).

[8] (a) G. A. Russell, *ibid.*, **79**, 2977 (1957); **80**, 4987, 5002 (1958); (b) *ibid.*, **80**, 4997 (1958).

[9] C. Walling and M. F. Mayaki, *ibid.*, **81**, 1485 (1959).

[10] G. A. Russell, *Tetrahedron*, **5**, 101 (1959); **8**, 101 (1960); *cf.* F. R. Mayo and C. Walling, *Chem. Rev.*, **46**, 191 (1950). See also discussion by J. Kenner, *Tetrahedron*, **3**, 78 (1958); **8**, 350 (1960); and by J. F. Kochi and D. D. Davis, *Nature*, **202**, 690 (1964).

[11] H. B. Watson, *Chem. Rev.*, **7**, 173 (1930).

[12] Paper II in this series: J. C. Little, A. R. Sexton, Y.-L. C. Tong, and T. E. Zurawic, *J. Am. Chem. Soc.*, **91**, 7098 (1969).

[13] We have learned that a study of the stereochemistry of the hydrogen-abstraction step (eq 1) on acid IVa has been undertaken by Professor C. C. Price and C. Beard of the University of Pennsylvania. Our attention was also directed by Professor Price to a study intended to identify the products of the chlorination of IVa,[14] and we are indebted to him for a copy of Mr. Akune's thesis.

[14] K. Akune, M.S. Thesis, University of Pennsylvania, 1965.

[15] W. A. Nevill, D. S. Frank, and R. D. Trepka, *J. Org. Chem.*, **27**, 422 (1962).

Table I. Nmr Chemical Shifts and Coupling Constants of Methyl Monochlorocyclohexanecarboxylates[a]

Isomer	T_R[b]	$-OCH_3$ (d_6-Acetone)	$-OCH_3$ (CCl_4)[c]	>CHCl (J)[d]	>CHCO$_2$- (J)[d]
Vb, 1-chloro	2.5	−3.761	−3.778		
VIb, *cis*-2	5.0	−3.649[e]	−3.683	−4.79 (*ca.* 3, 3, 3)	−2.84 (10, 5, 3)
VIIb, *trans*-2	3.9	−3.684	−3.702	−4.18 (11, 10.5, 4.1)	−2.58 (11, 11, 4)
VIIIb, *cis*-3	5.5	−3.633	−3.643	−3.99 (11, 11, 4.7, 3.9)	−2.48 (*ca.* 13, 11, 4, 3.5)
IXb, *trans*-3	4.7	−3.635	−3.655	−4.52 (4, 4, 4, 4)	−2.79 (11.5, 11.5, 3.5, 3.5)
Xb, *cis*-4	5.9	−3.641	−3.665	−4.39 (2.4, 3.0)	−2.46 (*ca.* 10, 4)
XIb, *trans*-4	5.0	−3.615	−3.638	−3.98 (*ca.* 10, 4)	−2.39 (*ca.* 11, 4)
IVb (unsubstituted)	1.0	−3.594	−3.615		−2.26 (*ca.* 11, 4)
Chlorocyclohexane				−4.05 (8.6, 3.7)	

[a] Spectra recorded at 100 MHz (Varian HA-100) at 26° as *ca.* 15% solutions in d_6-acetone + TMS. Chemical shifts are shielding (parts per million) relative to internal TMS. In general, coupling constants were determined from low-temperature spectra (*cf.* Table III). [b] Relative retention time at 175° on a 0.25 in. × 10 ft 20% LAC-446 + 2% H_3PO_4 on Chromosorb W-AW column (based on T_R for IVb = 1.0 = *ca.* 4.5 min); F & M 500 instrument, He flow 40 ml/min. [c] These values were observed at 60 MHz (Varian A-60 at 37°) as *ca.* 20% solutions in CCl_4 + TMS. The >CHCl resonances all appeared *ca.* −0.1 ppm from the tabulated values in deuterioacetone. [d] Measured splittings in hertz, which are sufficiently close to the true coupling constants to characterize placement as *trans*-diaxial or *gauche*. [e] 0.25-Hz doublet.

Table II. Physical Properties of Monochlorocyclohexanecarboxylic Acids and Methyl Esters

Isomer	Acids		Methyl esters
	Mp, °C	ν_{max},[a] cm^{-1}	ν_{max},[b] cm^{-1}
V, 1-chloro	60	1718	1748
VI, *cis*-2	98	1718	1750
VII, *trans*-2	85	1718	1750
VIII, *cis*-3	78	1712	1738
IX, *trans*-3	53	1710	1735
X, *cis*-4	112	1711	1738
XI, *trans*-4	159	1708	1740
IV (unsubstituted)	34	1710	1738

[a] 1% in CCl_4. [b] 2% in CCl_4.

ture to the methyl esters eventually gave a monochloro ester fraction which was stable to distillation. Fractionation through an efficient column yielded the pure ester (Vb) of 1-chlorocyclohexanecarboxylic acid (Va); however, the other six monochloro esters could not be separated.[16] Glpc analysis under carefully controlled conditions (see Experimental Section) gave six main peaks, in addition to starting material and small amounts of more highly chlorinated materials, esters and lactones. Photochlorination of the methyl ester IVb gave the same mixture plus an eighth component believed to be the chloromethyl ester XII, and a typical glpc curve of this mixture is shown for reference in Figure 1.

Examination of the ir and nmr spectra of samples trapped from the six glpc peaks having T_R = 2.5 − 5.9 (*cf.* Figure 1) enabled the tentative assignment of structures as the seven monochloro esters Vb–XIb. The peak having T_R = 5.0 (unresolved on any of our columns) proved to be a mixture of VIb and XIb. The assignments were made assuming that the carboxymethyl groups occupied the equatorial configuration in a chair-form ring. Examination of the coupling constants for the >CHCl protons indicated the number and nature of vicinal protons: *trans*-diaxial protons were coupled *ca.* 10–11 Hz while *gauche* couplings of 3–5 Hz were observed. Pertinent data are summarized in Table I.

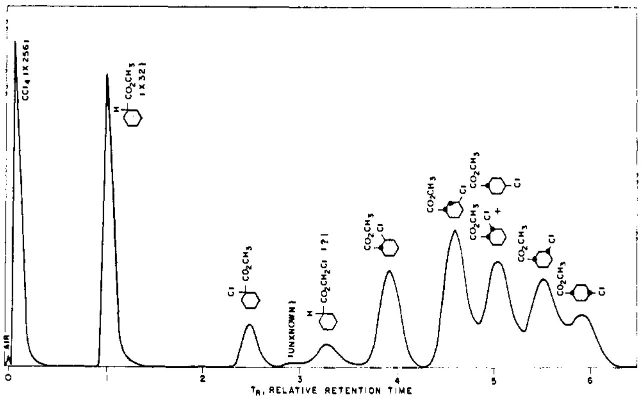

Figure 1. Glpc curve of the products from photochlorination of IVb at 40° in CCl_4. Column: 0.25 in. × 10 ft 20% LAC-446; 2% H_3PO_4 on Chromosorb W-AW.

In general, it was found that >CHCl protons assigned an axial configuration were more shielded than those in an equatorial position, consistent with observations in other systems. The infrared carbonyl absorption frequencies (Table II) generally supported the nmr assignments in that the esters having a chlorine α or β to the carbonyl appeared at lower wavelength than those with the substituent farther removed.

The above assignments were further reinforced by the synthesis of the esters of five of the seven monochlorocyclohexanecarboxylic acids which have been described

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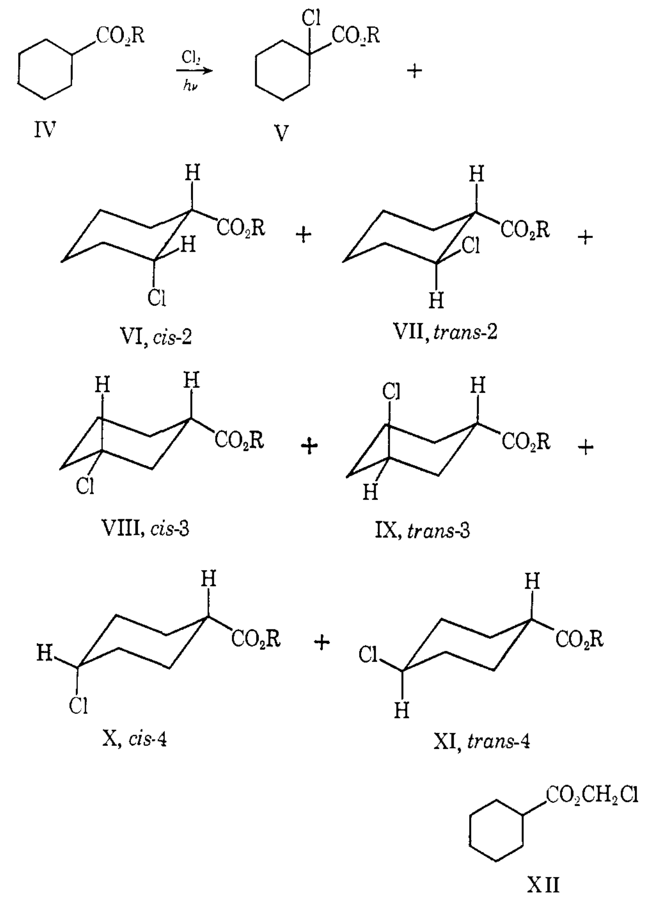
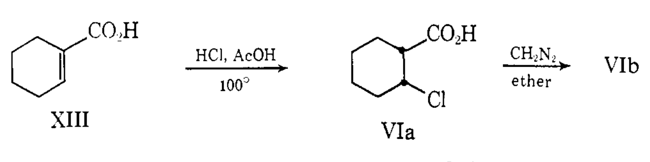
(16) Analysis of a fraction boiling over a one-deg range at 1 mm (through a column rated at 30 plates at 1 atm and total reflux) showed the presence of esters of six acids, the largest component of which was present to the extent of only 35%.



a, R = H
b, R = CH_3

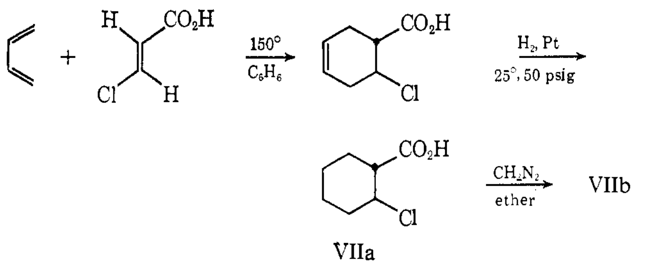
previously.[12,17–20] The 1-chloro acid Va was synthesized by high-temperature Hell–Volhard–Zelinsky (HVZ) chlorination of IVa[12] and yielded derivatives having properties in satisfactory agreement with those reported[17,20,21] for Va derivatives. Esterification with 2,2-dimethoxypropane[22] yielded Vb, the glpc and spectral properties of which agreed perfectly with the material having T_R = 2.5 (Figure 1).

The *cis*-2-chloro acid VIa was synthesized by addition of HCl to 1-cyclohexenecarboxylic acid XIII as described by Vaughan.[18] Treatment with diazomethane yielded the ester VIb, which had T_R = 5.0 (Figure 1)

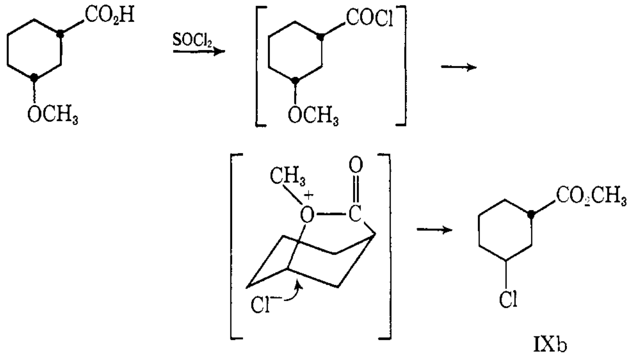


and was eventually shown to be one of the two components represented by this peak (the other was the *trans*-4-chloro ester, XIb, described below).

Reaction of *trans*-3-chloroacrylic acid with butadiene followed by hydrogenation as also described by Vaughan[18] yielded the *trans*-2-chloro acid VIIa, the methyl ester of which was identical with that having T_R = 3.9.



The methyl esters IXb and XIb of *trans*-3- and *trans*-4-chlorocyclohexanecarboxylic acid were prepared from the *cis*-methoxy acids by the method of Noyce and Weingarten.[19] The *trans*-3-chloro ester IXb proved to be



identical with the ester having T_R = 4.7 (Figure 1), and the *trans*-4 isomer comprised the other component at T_R = 5.0 as mentioned above.

Since five of the seven monochloro acids were now available by independent routes, assignment of the other two peaks at T_R = 5.5 and 5.9 to the remaining *cis*-3- (VIIIb) and *cis*-4-chloro ester (Xb) on the basis of their nmr spectra was now done with some assurance. The >CHCl resonance at −6.01 ppm in the spectrum of the ester having T_R = 5.5 (VIIIb) showed coupling with two *trans*-axial protons (J = 11, 11) and two vicinal *gauche* protons (J = 4.7, 3.9), fixing its stereochemistry as axial and hence an equatorial (*cis*-3) chlorine (again assuming equatorial carbomethoxy). Similarly, the >CHCl spectrum of the ester having T_R = 5.9 (Xb) consisted of a triplet (J = 2.4) of triplets (J = 3.0) indicating pairs of magnetically equivalent *gauche* protons and fixing its stereochemistry as equatorial (axial or *cis*-chlorine). The acid VIIIa was prepared by hydrolysis of a glpc-purified sample of VIIb; the *cis*-4-chloro acid Xa was isolated from a mixture resulting from addition of HCl to 3-cyclohexene-1-carboxylic acid and also from a narrow-boiling fraction from the direct chlorination of IVa. The melting points of the free acids are given in Table II.

To complete the structural study of the esters Vb–XIb, their nmr spectra plus those of the unsubstituted ester IVb and chlorocyclohexane were recorded at low temperatures (conformations "frozen" according to the nmr "time scale"). The results are summarized in Table III.

Discussion

Aside from the identification of the products from the chlorination of derivatives of IV and subsequent development of an apparently reliable analytical method

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(17) J. von Braun, F. Jostes, and W. Münch, *Ann.*, **453**, 128 (1927).

(18) W. R. Vaughan, R. L. Craven, R. Q. Little, Jr., and A. C. Schoenthaler, *J. Am. Chem. Soc.*, 77, 1594 (1955).

(19) D. S. Noyce and H. I. Weingarten, *ibid.*, **79**, 3093 (1957).

(20) E. F. Jason and E. K. Fields, U. S. Patent 3,052,716 (1962); Belgian Patent 596,687 (1961); British Patent 966,544 (1964); *Chem. Abstr.*, **61**, 13199*a* (1964).

(21) C. C. Price and M. Schwarcz, *J. Am. Chem. Soc.*, **62**, 2891 (1940).

(22) N. B. Lorette and W. L. Howard, *J. Org. Chem.*, 24, 261 (1959).

Table III. Chemical Shifts of Methyl Chlorocyclohexanecarboxylates at Low Temperatures[a]

Isomer	>CHCl		>$CHCO_2$	OCH_3	
	e	*a*	*a*	*e*	*a*
Vb, 1-chloro				−3.765	−3.824
VIb, *cis*-2	−4.91	(−4.39)	−2.98	−3.661	(*Ca.* −3.68)
VIIb, *trans*-2	N.O.	−4.18	−2.66	−3.684	(*Ca.* −3.70)
VIIIb, *cis*-3	(*Ca.* −4.69)	−4.13	−2.58	−3.634	−3.712[b]
IXb, *trans*-3	−4.77	−4.16	−2.78[c]	−3.632	−3.677
Xb, *cis*-4	−4.67[d]	(*Ca.* −4.09)[d]	−2.43[e]	−3.636[e]	−3.698[e]
XIb, *trans*-4	(−4.65)	−4.07	−2.44	−3.622	−3.668
IVb (unsubstituted)			−2.32[f]	−3.603	−3.651
Chlorocyclohexane	−4.66	−4.00			

[a] Determined from spectra recorded at 100 MHz at −87° (unless noted otherwise) as *ca.* 15% solutions in d_6-acetone + TMS, excepting for Xb and XIb, which were *ca.* 8% solutions. Values given in parentheses are only tentative due to the small population and/or multiplicity of the band: N.O. = not observed. [b] −60°; value for equatorial -OCH_3 at −87° = −3.630 ppm. [c] −70°. [d] −75°; shift for equatorial >CHCl at −87° = −4.68 ppm. [e] −80°. [f] Resonance at −2.74 ppm tentatively assigned to equatorial >$CHCO_2$–.

for further studies[12] (see Experimental Section), some conclusions may possibly be drawn regarding the electron densities of various C–H bonds in the system and their potential contribution during radical reactions *via*, *e.g.*, eq 1. Attempts have previously been made to correlate proton nmr chemical shifts with electron densities in the ground state,[23] and we therefore examined the nmr spectrum of the ester IVb to see if any relationship existed between chemical shift and reactivity. However, the ring protons in IVb could be resolved only into two broad groups near −2.1 and −1.6 ppm. Examination of the >CHCl resonances of the chloro esters VIb–XIb, on the other hand, is a fairly simple matter, allowing one to pinpoint the protons at each position. If the assumption may be made that the effect of the carboxyl on the chemical shifts of these >CHCl protons is a reflection of its effect on the corresponding protons in the unsubstituted acid IVa (or its derivatives), then a potentially very sensitive measure of the magnitude and extent of the polar effect is at hand, providing the chemical shift–electron density arguments[23] are valid.

Attempts to correlate the >CHCl chemical shifts from the room-temperature spectra (Table I) are complicated by the fact that the line positions actually observed represent only an average of the contribution of the axial and equatorial conformers present.[24–26] Since the conformer having hydrogen axial in cyclohexyl chloride is shifted approximately +0.6 ppm (upfield) from that in the equatorial position,[27] it was anticipated that the same chemical shift difference would prevail in the chlorocyclohexanecarboxylic acid system (as was subsequently found). Contribution, therefore, from only a small population having the carbomethoxy group in the axial position would cause a chemical shift change which could well override any polar effect.[28] We therefore undertook to determine the chemical shifts of the individual conformers.

Simple calculations of the chemical shifts of each conformer,[26] using the values observed at room temperature (Table I) and assuming that the published[27,29] $-\Delta G°$ values are additive,[28] gave results which were difficult to rationalize and subsequently proved to be incorrect. The use of "biased"[24,25] or rigid models, such as the *t*-butyl derivatives as suggested by Eliel[30,31] for the simpler systems, was considered and rejected because of the synthetic difficulties involved, and because the validity of the method has recently been challenged by Jensen.[32] The latter investigator showed that in a number of cyclohexyl systems, including the cyclohexyl chlorides, the *t*-butyl group indeed induces a chemical shift of its own, as had been previously cautioned by Eliel.[30b]

We therefore turned to the study of the line positions *via* the low-temperature nmr spectra; the results are summarized in Table III. It was our original intent to extrapolate the observed values to room temperature using the temperature corrections listed by Jensen[32a] for the 4-*t*-butylcyclohexyl chlorides. However, the chloro esters were insufficiently soluble in CS_2 (the solvent used by Jensen) at low temperatures, and the temperature corrections for deuterioacetone proved to be considerably greater than those for CS_2. Thus, the >CHCl resonance for the *cis*-3-chloro ester VIIIb appeared at −3.99 ppm at 26°, while at −87° the axial proton (conformer with equatorial -CO_2CH_3) appeared at −4.13 ppm and the equatorial resonance (axial -CO_2CH_3) was at −4.69 ppm. Since the average or room temperature resonance must lie between the two contributors,[26] the temperature correction for the axial proton (from −87 to +26°) is at least 0.14 ppm in deuterioacetone, contrasting with only 0.022 ppm in CS_2.[32a] Similarly, the *trans*-4 isomer XIb showed resonances at −4.07 ppm (axial H) and −4.65 ppm (equatorial H) at −87°, while the band appeared at −3.98 ppm at room temperature, for a minimum temperature correc-

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(23) See, for example, discussions by (a) J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 26 ff; (b) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 87 ff.

(24) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965.

(25) For an excellent discussion of conformational equilibria in the cyclohexane system, see E. L. Eliel, *Angew. Chem. Intern. Ed. Engl.*, **4**, 761 (1965).

(26) For a description of nmr techniques in conformational equilibria, see N. C. Franklin and H. Feltkamp, *ibid.*, **4**, 774 (1965).

(27) E. L. Eliel and R. J. L. Martin, *J. Am. Chem. Soc.*, **90**, 689 (1968).

(28) Using values recently given by Eliel[27,29] of $-\Delta G°_{25}$ = 0.44 kcal for Cl[27] and 1.27 kcal for CO_2CH_3[29] and assuming that the values are additive, the isomers having the substituents diequatorial (VII, VIII, and XI) should have a 96/4 ratio of equatorial/axial CO_2CH_3 at 25°, while the axial–equatorial substituted isomers (V, VI, IX, and X) should be 77/23 equatorial/axial CO_2CH_3.

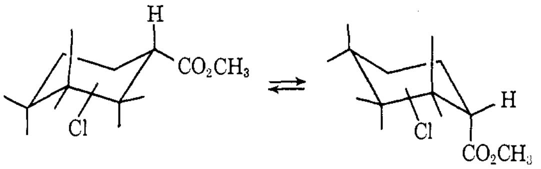
(29) E. L. Eliel and M. C. Reese, *J. Am. Chem. Soc.*, **90**, 1560 (1968).

(30) (a) E. L. Eliel, *Chem. Ind.* (London), 568 (1959); (b) E. L. Eliel, M. H. Gianni, T. H. Williams, and J. B. Stothers, *Tetrahedron Lett.*, 741 (1962).

(31) E. L. Eliel and R. J. L. Martin, *J. Am. Chem. Soc.*, **90**, 682 (1968).

(32) (a) F. R. Jensen and B. H. Beck, *ibid.*, **90**, 3251 (1968); (b) F. R. Jensen, C. H. Bushweller, and B. H. Beck, *ibid.*, **91**, 344 (1969).

Table IV. Comparison of >CHCl Proton Chemical Shifts of Methyl Chlorocyclohexanecarboxylates with Relative Reactivities During Chlorination of Methyl Cyclohexanecarboxylate[a]



>CHCl resonances, equatorial $-CO_2CH_3$ Equat H	>CHCl resonances, equatorial $-CO_2CH_3$ Axial H	Position	>CHCl resonances, axial $-CO_2CH_8$ Equat H	>CHCl resonances, axial $-CO_2CH_8$ Axial H	Relative reactivity, chlorination of IV[b]
−4.91	−4.18	2		−4.39	0.50
−4.77	−4.13	3	*Ca.* −4.69	−4.16	0.91
−4.68	−4.07	4	−4.65	*Ca.* −4.09[c]	1.00
(−4.66	−4.00	Cyclohexyl chloride	−4.66	−4.00)	

[a] Values determined at −87° in perdeuterioacetone. [b] Per hydrogen, photochlorination at 80° in CCl_4 (data from ref 33). [c] At −75°.

tion of 0.09 ppm. These relatively large temperature shifts serve to emphasize one of the many difficulties which must be overcome in studies of conformational equilibria, where one is attempting to measure very small energy differences.

Although the chemical shifts of the individual >CHCl resonances at room temperature were therefore not available from the data at hand, we may still carry out a comparison of the actually observed values for the "frozen" conformations (mostly at −87°). Examination of the data of Table III yields a number of correlations. First of all, the >CHCl resonances still do not showed a definite regularity as presented in the table. However, if we consider that the *conformation* as well as the position of substitution of the carbomethoxy group may influence the chemical shift of these methine protons, a more satisfying correlation appears. Table IV summarizes, for example, these chemical shifts observed when the carbomethoxy is in both the equatorial (dominant) and axial conformations.

As can be seen, the axial conformation of the carbomethoxy seems to affect the axial >CHCl resonances somewhat more than the equatorial, and the equatorial carbomethoxy may have a slightly greater influence on equatorial >CHCl line positions than the axial. As the carbomethoxy becomes more remote, both the axial and the equatorial proton resonances experience a fairly smooth shift toward greater shielding. The unexpected lack of unusual effect of the axial (*syn-*) carbomethoxy on the axial H at the 3 position, as compared with the other 1,3-interactions, is noteworthy.

If the same factors which are affecting the chemical shifts are also operating during free-radical hydrogen-abstraction reactions having polar character at the transition state (*cf.* eq 1), it may be predicted, from this *physical evidence* of the ground-state properties, that there will be a parallel increase in reactivity as the C–H becomes more remote from the carboxyl. We have included in Table IV data showing the relative reactivity of methyl cyclohexanecarboxylate (IVb) toward abstraction by chlorine atoms.[33] Recalling our assumption that the effect of the carboxyl function on the >CHCl protons is a reflection of its effect on the corresponding protons in the unsubstituted material (IVb, in this case), a smooth correlation can be seen between increasing reactivity and increased shielding.

Note that the directive effects of the carbomethoxy may well extend to the 4 position, since in the latter there is still a shift downfield from the unsubstituted compound. This leads to the prediction that the C–H at the 4 position of methyl cyclohexanecarboxylate will be slightly less reactive than that of cyclohexane itself.[34,35]

Similar comparison of the chemical shifts of the $>CHCO_2$ protons at low temperature provides an estimate of the effects of *chlorine* on the C–H chemical shift. If it can now be assumed that the effect of chlorine on the protons in Vb–XIb reflects its influence on the corresponding protons in the unsubstituted system (chlorocyclohexane), we may again compare the results (Table V) with those observed[36] during radical chlorination. Unfortunately, only the chemical shifts of the axial protons could be observed with any degree of confidence: the corresponding conformers having equatorial hydrogens (axial carbomethoxy) were present in too small concentration to be located. However, it has been suggested[13] that the axial hydrogen is the one most likely to undergo abstraction during free-radical attack, so the correlations in Table V may be made with reasonable confidence.

Note once again that the line positions summarized in Table V are sensitive to the conformation of the substituent (chlorine), and two separate series are con-

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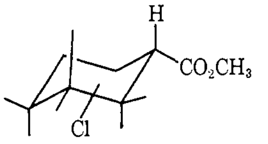
(33) Paper III in this series: J. C. Little, Y.-L. C. Tong, and T. E. Zurawic, in preparation. See ref 2c, p 99, for some preliminary results.

(34) Russell[8] has carried out the competitive chlorination of chlorocyclohexane with cycloheptane and found, by assuming that the cycloheptane hydrogens are 1.11 times as reactive as those in cyclohexane,[8b] that the reactivities are about the same within the limits of the experiments.[35]

(35) We have not taken into account the possible effects of different solvents and temperatures on either the chemical shift of the CH or on the proportion of the axial *vs.* equatorial conformations of the ester group. Since solvent effects on conformational equilibria have indeed been observed in other systems,[25] it is reasonable to assume that they will play a role in this one. It is interesting to note that the differences in chemical shifts of the axial protons with the carbomethoxy in the axial conformation (Table IV, column 5) are the most pronounced. Hence it might be speculated that the preference for axial attack (*cf.* ref 13) might be reduced, particularly in the 2 position, in solvents which favor more of the axial conformation of the ester. We are currently contemplating a further study on the effects of solvents on these conformational equilibria to parallel the solvent effects studies on the radical chlorination.[33]

(36) G. A. Russell, A. Ito, and R. Konaka, *J. Am. Chem. Soc.*, **85**, 2988 (1963).

Table V. Comparison of Axial $>CHCO_2CH_3$ Chemical Shifts[a] of Methyl Chlorocyclohexanecarboxylates with Relative Reactivities During Chlorination of Chlorocyclohexane



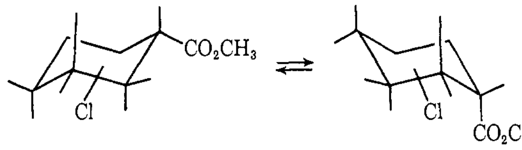
Axial H (equat Cl)	Position	Axial H (axial Cl)	Relative reactivity, chlorination of chlorocyclohexane[b]
−2.66	2	−2.98	0.44
−2.58	3	−2.78[c]	0.79
−2.44	4	−2.43[d]	1.00
(−2.32	IVb	−2.32)	(*ca.* 1.0)[e]

[a] Values determined at −87° in perdeuterioacetone. [b] Per hydrogen, photochlorination at 40° in CCl_4 (data from ref 36). [c] −70°. [d] −80°. [e] The reactivity of the 4 position in chlorocyclohexane has been estimated by competitive chlorination (ref 6) to be about the same as that of cyclohexane (see ref 34).

structed. Again the axial conformation of the substituent has a greater effect on axial protons than does the equatorial. The expected parallel between chemical shift and relative reactivity toward chlorine atom is clearly seen.[36]

To complete the comparison of the effect of the polar substituent on chemical shift, Table VI summarizes the line positions of the carbomethoxy singlet as a function of both the position of chlorine substitution and the conformations of the groups. In this case, the methyl protons were found to be more shielded by 0.03–0.08 ppm when the carbomethoxy was in the *equatorial* position, in contrast to the usual case where axial hydrogen or methyl is at higher field.[37] Also, the influence of the chlorine appeared to be somewhat dependent upon whether it were axial or equatorial, although the differences were not great. The deshielding influence of the chlorine was still evident as far away as the 4 position as evidenced by the 0.02–0.03 ppm deshielding from the unsubstituted ester IVb. The effect of the chlorine is thus transmitted as far away as 7–8 Å, or, alternatively, through *six* σ bonds.[40] Nmr therefore provides a very sensitive means of detecting this effect.

Table VI. $-CO_2CH_3$ Methyl Chemical Shifts of Methyl Chlorocyclohexanecarboxylates at −87° in Perdeuterioacetone



Equatorial $-CO_2CH_3$			Axial $-CO_2CH_3$	
Cl axial	Cl equatorial	Position	Cl axial	Cl equatorial
−3.765		1		−3.824
−3.661	−3.684	2	*Ca.* −3.70	*Ca.* −3.68
−3.632	−3.630	3	−3.712[a]	−3.677
−3.636[b]	−3.622	4	−3.668	−3.698[b]
(−3.603	−3.603	IVb	−3.651	−3.651)

[a] −60°. [b] −80°.

The nature of the transmission of the effects of the polar substituents (carbomethoxy or chloro) to an adjacent or remote hydrogen in these saturated systems bears some consideration. The postulate that the nmr chemical shifts induced by polar substituents is an inductive effect transmitted through the σ bonds[23] has been challenged, *inter alia*, by Zürcher,[41] who maintains that linear electric field effects and, in the case of the carboxyl derivatives, anisotropic magnetic susceptibility,[42] are responsible for the effects observed. These effects, plus interactions with solvent, may well account for the sequences observed, although there are some disturbing regularities in Tables IV–VI which are difficult to rationalize in a straightforward manner using this approach. For example, the smooth shift toward higher field, *regardless of orientation relative to the substituent*, as the proton becomes successively more remote from the substituent, would appear to require a rather unusual and fortuitous combination of anisotropic, dipole, and solvent interactions, whereas incorporation (perhaps in addition to the others) of an inductive effect provides a simple alternative. In the cases where the substituents in question are diaxial, especially the *trans*-1,2-, *cis*-1,3-, *trans*-1,4- progression, should invoke some alternation in the series because of the changes in both internuclear distances and relative orientations.

On the other hand, the preferentially greater influence of the axial substituents on axial protons and equatorial substituents on equatorial proton shifts appear to require the invocation of an explanation other than a purely inductive effect. And of course the magnetic anisotropic effect of the carbonyl on at least those protons in the 2 position cannot be overlooked in view of ample observations in other systems.

Until additional definitive evidence is at hand, therefore, we prefer to conclude that, in view of the apparent correlations of Tables IV and V between chemical shifts and relative reactivities, many of the same factors (of whatever nature) which are the cause of one may well be operating in the other.

Finally, we might make some comment on the question of the additivity of $\Delta G°_x$ values in cyclohexyl systems. There have been a number of studies of systems involving two nonpolar (alkyl) substituents or one nonpolar and one polar substituent,[25,26,37] but little is known about the additivities of two groups having fairly large dipoles, such as the chloro and carbomethoxy groups being considered here.[43] In general,

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(37) Lemieux and coworkers[38] and Lichtenthaler[39] have observed that the methyl singlets of acetylated cyclitols and sugars appear at about 8 Hz higher field when the acetoxy is equatorial. See ref 24, p 398 ff for discussion.

(38) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, 79, 1005 (1957).

(39) (a) F. W. Lichtenthaler and H. O. L. Fischer, *ibid.*, 83, 2005 (1961); (b) F. W. Lichtenthaler, *Chem. Ber.*, 94, 3071 (1961).

(40) Actually, if one were to adapt the theory that the nature of the transmission of these effects from one part of the molecule to another were primarily by means of the σ bonds (see ensuing discussion), the "transmission line" to the 4 position should be considered as two sets of three σ bonds hooked in parallel (each side of the ring).

(41) R. F. Zürcher in "Progress in Nuclear Magnetic Resonance Spectroscopy," Vol. 2, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Ed., Pergamon Press, New York, N. Y., p 205 ff.

(42) See, for example, discussion by D. L. Hooper and R. Kaiser, *Can. J. Chem.*, 43, 2363 (1965).

(43) Professor R. D. Stolow of Tufts University has informed us that he has observed a lack of additivity in 1,4-disubstituted cyclohexyl systems containing, *e.g.*, hydroxy or acyloxy and ketone substituents (*cf.* R. D. Stolow and T. Groom, *Tetrahedron Lett.*, 4069 (1968)). He has also called our attention to similar studies by Professor G. W. Wood

Table VII. Comparison of Calculated and Observed Conformational Energy Differences of Methyl Chlorocyclohexanecarboxylates in Perdeuterioacetone

Isomer	Obsd *e*/*a*,[a] -CO_2CH_3	Obsd $-\Delta G°_{-87°}$, kcal	Calcd $-\Delta G°_{-87°}$, kcal[b]
Vb, 1-chloro	59/41 ± 2	0.13 ± 0.02	0.63 ± 0.26
VIb, *cis*-2	*Ca.* 99/1 ± 1[c]	1.7 ± 0.3	0.63 ± 0.26
VIIb, *trans*-2	*Ca.* 99/1 ± 1	1.7 ± 0.3	1.97 ± 0.26
VIIIb, *cis*-3	94.3/5.7 ± 1.2[d]	1.19 ± 0.10[d]	2.01 ± 0.26[d,e]
IXb, *trans*-3	90/10 ± 1.6	0.81 ± 0.07	0.63 ± 0.26
Xb, *cis*-4	84/16 ± 2	0.61 ± 0.04	0.63 ± 0.26
XIb, *trans*-4	98.2/1.8 ± 0.6	1.48 ± 0.13	1.97 ± 0.26
(IVb, unsubstituted	97.1/2.9	1.30 ± 0.14	)
(chlorocyclohexane	86/14 ± 4[c]	0.67 ± 0.12	)

[a] By area integration of CO_2CH_3 singlets observed at −87°. [b] Assuming that $-\Delta G°_x$ values observed for IVb and chlorocyclohexane are additive. [c] By area integration of >CHCl absorptions. [d] At −60°. [e] Assuming that $\Delta S°_{Cl} = \Delta S°_{CO_2CH_3}$.[47b]

fair additivity agreements have been found with 1,4-systems, less satisfactory agreements are observed in the 1,3-systems, and little found in the 1,2-disubstituted cases.[44] Recent examinations[45] of 1,1-disubstitution (methyl and hydroxyl) indicate that additivity relationships break down here, also.

In order to calculate the $\Delta G°$ values for the model compounds IVb and chlorocyclohexane in acetone and then check the thence-predicted equilibria, the relative populations of the two conformers were needed. Since accurate estimates of the resonances of the individual >CHCl conformers at room temperature could not be obtained with the data at hand, we were unable to employ the method of Eliel[24-26] as modified by Jensen.[32] However, both authors[46] have pointed out that the measurement of peak areas at low temperatures is probably quite reliable, and we have therefore carried out the integrations of the two singlet methyl conformers at these temperatures to evaluate the equilibrium constants and $\Delta G°_x$ values. We have also studied the model compounds IVb and chlorocyclohexane, obtaining the results summarized in Table VII. The $\Delta G°_{-87°}$ values of −1.30 ± 0.14 and −0.67 ± 0.12 kcal/mole, respectively, calculated from the observed ratios of equatorial and axial substituent conformations, may be compared with values of −1.31 ± 0.10 kcal/mole for IVb at −78° and −0.528 ± 0.019 kcal/mole for chlorocyclohexane at −81° in CS_2 + TMS reported by Jensen and coworkers.[32b]

The values observed for IVb and chlorocyclohexane were then used to calculate $\Delta G°_{-87°}$ values for the chloro esters Vb–XIb (column 4 of Table VII). As Table VII shows, agreement is moderately good for the 1,4-disubstituted compounds, fair for the 1,3-isomers,[47a] but quite unsatisfactory for the 1,2- and geminally disubstituted chloro esters, much in line with previous observations in other systems.[44,45] Unexpectedly, both the *cis*-2- and *trans*-2-chloro esters VIb and VIIb were found to be essentially "frozen" at all temperatures with the carboxymethyl in the equatorial conformation. The calculated conformational preference of the carbomethoxy in VIb is 0.63 ± 0.26 kcal/mole if our value of $\Delta G°_{-87°}$ = 0.67 ± 0.12 kcal/mole in acetone is taken for the chlorine. However, the actual preference exceeds this by at least 1 kcal/mole. Clearly, the $\Delta G°$ values failed to be additive in this case, possibly due to a combination of steric effects and dipole repulsion between these two polar substituents.[48]

One further series of data from Table I seems worthy of note. The glpc retention times of each of the *trans* isomers is lower than that of the corresponding *cis*-chloro ester, in complete agreement with previous observations in the case of the dibromo-,[49] dichloro-,[36] bromochloro-,[36] and diacetoxycyclohexanes,[49] as well as the dichloro- and bromochlorocyclopentanes.[6] The relative T_R for *trans*/*cis* is *ca.* 0.8. Moreover, the relative retention times increase as chlorine substitution becomes more remote from the carboxyl, in complete accord with those of similar chlorinated aliphatic esters.[50]

Experimental Section

All melting points are corrected. Infrared spectra were determined by F. L. Beman and his staff of this laboratory, using Perkin-Elmer Models 137-G and 337 Infracord grating spectrometers equipped with Reeder thermocouples. Nmr spectra were determined with A-60 and HA-100 Varian spectrometers using *ca.* 20% solutions in CCl_4 or 15% solutions in perdeuterioacetone and tetramethylsilane as an internal standard. Standard calibration procedures were employed. The spectral data are discussed in the text.

Cyclohexanecarboxylic acid obtained from Monsanto Chemical Co., Eastman Organic Chemicals or by Rh-catalyzed hydrogenation of benzoic acid, was distilled *in vacuo* before use, bp 116° (10 mm). 1-Cyclohexenecarboxylic acid, bp 129° (10 mm), was obtained by base-catalyzed isomerization of 3-cyclohexenecarboxylic acid, bp 119.5° (10 mm), which was obtained in turn from the Diels–Alder reaction of butadiene with acrylic acid. *trans*-3-Chloroacrylic acid was prepared by additon to HCl to propiolic acid.[51]

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and his students: see G. Wood, E. P. Woo, and M. H. Miskow, *Can. J. Chem.*, **49**, 429 (1969), and previous papers. Both groups have attributed stabilization of axial substituents to 1,4-dipolar interactions.

(44) E. L. Eliel, *J. Chem. Educ.*, 37, 126 (1960).

(45) (a) J. J. Uebel and H. W. Goodwin, *J. Org. Chem.*, **33**, 3317 (1968); (b) N. L. Allinger and C. D. Liang, *ibid.*, **33**, 3319 (1968); (c) S. Sicsic and Z. Welvart, *Bull. Soc. Chim. France*, 575 (1967).

(46) (a) A. J. Berlin and F. R. Jensen, *Chem. Ind.* (London), 998 (1960); (b) E. L. Eliel, *Chimia*, 22, 201 (1968).

(47) (a) The existence of some 10% of the *trans*-1,3-diaxial conformer in IXb instead of the <1% calculated from adding $\Delta G°$ values may be due to dipole–dipole attractions as suggested by Stolow and by Wood for the 1,4-disubstituted system (*cf.* ref 43). (b) $\Delta S°$ for the carbomethoxy has been estimated[29] to be *ca.* 0.50 ± 0.11 eu in methanol, and for chlorine, 0.49 eu in *o*-dichlorobenzene (J. Reisse, J. C. Celotti, and G. Chiurdoglu, *Tetrahedron Lett.*, 397 (1965)). Although both values were obtained by methods which have been criticized,[32] the errors introduced by assuming that they are equal in acetone are probably negligible.

(48) C. B. Anderson and D. T. Sepp [*J. Org. Chem.*, **33**, 3272 (1968)] have noticed a similar enhanced conformational preference for the carboxymethyl group in 2-carboxymethylalkyltetrahydropyrans. They have suggested that dipole interactions are responsible.

(49) B. Franzus and B. E. Hudson, Jr., *J. Org. Chem.*, **28**, 2238 (1963).

(50) Chlorobutyric and chlorohexanoic esters: J. C. Little and T. E. Zurawic, unpublished data.

cis-3-Methoxycyclohexanecarboxylic acid, mp 50–51°, and *cis*-4-methoxycyclohexanecarboxylic acid, mp 52–54°, were prepared by Rh-catalyzed hydrogenation of the corresponding anisic acids, obtained from Eastman Organic Chemicals. Phosphorus trichloride was distilled before use.

Glpc Analyses. Crude mixtures of chlorinated IVa were esterified with BF_3–methanol[52] or diazomethane in ether. After an extensive survey of different glpc column packings and conditions, it was found that a polyester column (20% LAC-446 on Chromosorb W-AW) stabilized with 2% H_3PO_4 gave the most reproducible analyses of the methyl esters IV–XIb on our instruments (F & M 500 or 810 equipped with thermal conductivity detectors). Isothermal conditions with column temperatures in the range 150–200° were used, with He flow rates of *ca.* 40 ml/min at 30 psig for a 0.25 in. × 10 ft column. The injection port temperature was maintained at 200–220° and the port was cleaned periodically to avoid pyrolysis of the chloro esters to methyl 1-cyclohexenecarboxylate (T_R = 1.4), depending on the isomers present. In later studies in this series involving quantitative analyses of the chloro esters, the diazomethane technique was found to give a much smaller amount of unesterified acids (T_R = 7.3–9.0), although a number of control studies showed no evidence for fractionation of the products with the BF_3–methanol procedure,[52] if the reflux period were extended to 10–20 min. It was assumed that the area per cent of the glpc curves was proportional to weight per cent present. The glpc peak at T_R = 5.0 due to the mixture of the *cis*-2- and *trans*-4-chloro isomers IX and XIV was analyzed by collecting the material from the glpc eluent and analyzing by 60-mHz nmr using the singlet $-OCH_3$ peaks, which were separated by 2.7 Hz, and were thus readily assayed to within ±5% accuracy.

Preparation of 1-Chlorocyclohexanecarboxylic Acid (Va). Into a mixture of 640 g (5.0 moles) of cyclohexanecarboxylic acid and 5 g of PCl_3 in a 2-l. flask covered with aluminum foil was passed 365 g (5.15 moles) of chlorine at 169–170° over a period of 4.5 hr. After the solution was swept with nitrogen a total of 813 g of the crude product, mp 49–50°, was obtained. Glpc analysis of a methylated sample showed the presence of 6% unreacted IVa, 0.8% of monochloro acids VIa–XIa, 0.4% of materials having retention time higher than those of the monochloro acids, and the balance was Va. The yield of Va was hence 99% at 94% conversion of IVa.

Distillation of the product was complicated by continual slow release of HCl; however, the bulk of the material could be recovered in this fashion, bp 97° (1.5 mm) (lit.[17] bp 138–140° (13 mm)). A sample of the acid recrystallized from hexane as small white granules, mp 60–61° (lit.[20] mp 51–53°).

1-Chlorocyclohexanecarboxamide was prepared according to standard procedures *via* the acid chloride. Recrystallization from water gave purified material, mp 115–116° (lit. mp 110°,[17] 113–114°,[20] and 117–118° [53]).

Methyl 1-Chlorocyclohexanecarboxylate (Vb). Esterification of acid Va with methanol–2,2-dimethoxypropane[22] gave the ester Vb, bp 39–40° (0.3 mm) (lit.[14] bp 72° (6 mm)), n^{25}_{D} 1.4631. Spectral data are given in Tables I–VII. Photochlorination of IVa or IVb was carried out by conventional procedures, with product ratios varying according to conditions used.[12] The free acids were worked up either by direct distillation into narrow fractions followed by conversion to the methyl esters, or, preferably, prior esterification, distillation, and subsequent glpc separation (see text).

***cis*-2-Chlorocyclohexanecarboxylic Acid (VIa).**[18] A mixture of 25.2 g (0.2 mole) of XIII, 36.5 g (1.0 mole) of hydrogen chloride, and 60 g of glacial acetic acid was heated in a glass ampoule to 100° for 20 hr. After the tube was opened, the volatile materials were removed *in vacuo* to yield 31.5 g of crude acids. Glpc analysis showed the presence of 18% of unreacted XIII, 66% VIa, 4% VIIa, 7% IXa, 3% Xa, and 2% XIa. No Va or VIIIa was detected.

The acid mixture was slurried in hexane and filtered to yield the crude VIa. Repeated recrystallization from hexane yielded 8.5 g of pure VIa, mp 96–97° (lit.[18] mp 97.6–98.4°). Treatment of XIII with HCl in acetic acid (same proportions as above) for 40 hr at 105° resulted in isolation of 8.3 g of VIa, mp 95–96°.

Methyl *cis*-2-Chlorocyclohexanecarboxylate (VIb). Treatment of acid VIa with BF_3–methanol[52] gave the ester VIb, bp 105–107° (17 mm). Spectral data are summarized in the tables.

***trans*-2-Chlorocyclohexanecarboxylic Acid (VIIa).** *trans*-6-Chloro-3-cyclohexenecarboxylic acid, prepared from *trans*-3-chloroacrylic acid[46a] and butadiene as described by Vaughan,[18] was reduced with hydrogen in the presence of PtO_2 in acetic acid as outlined[18] to give VIIa, mp 84.5–85° (lit. mp 84.0–85.7°,[18] 84° [54]).

Methyl *trans*-2-Chlorocyclohexanecarboxylate (VIIb). Acid VIIa was esterified with BF_3–methanol[52] to yield the ester VIIb, bp (micro still) *ca.* 100° (15 mm). Spectral data are summarized in the tables.

***cis*-3-Chlorocyclohexanecarboxylic Acid (VIIIa).** A mixture of 50 mg of the methyl chloro ester having glpc T_R of 5.5 (collected using a 0.25 in. × 40 ft column packed with 20% LAC-446 + 2% H_3PO_4 on Chromosorb W-AW), 1 ml of dioxane, and 2 ml of 2 *N* H_2SO_4 was heated to 80–90° for 8 hr, diluted with 2 ml of H_2O, and allowed to stand at room temperature. There was obtained 17 mg of VIIIa as white needles, mp 78°.

Anal. Calcd for $C_7H_{11}ClO$: C, 51.70; H, 6.82; Cl, 21.8. Found: C, 51.40; H, 6.45; Cl, 20.7.

A small sample of the acid VIIIa was reconverted to ester VIIIb with diazomethane. The T_R of this ester was found to be 5.5, and a sample containing the mixture of chloro esters was found to have an enhanced peak height at this retention time when this solution was added to it.

***trans*-3-Chlorocyclohexanecarboxylic Acid (IXa) and Methyl Ester (IXb).** *cis*-3-Methoxycyclohexanecarboxylic acid was refluxed with $SOCl_2$ as described by Noyce and Weingarten[19] to yield the methyl ester IXb, bp 105–106° (18 mm) (lit.[19] bp 117° (22 mm)), in addition to several other products. Hydrolysis yielded the acid IXa, mp 52–53° (lit.[19] mp 49.5–51.5°).

***cis*-4-Chlorocyclohexanecarboxylic Acid (Xa).** A mixture of 12.6 g (0.1 mole) of 3-cyclohexene-1-carboxylic acid and 30 ml of concentrated HCl was refluxed for 4 hr while a stream of gaseous HCl was passed through it. The resulting reaction mixture was extracted with $CHCl_3$, the extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. Glpc analysis of the methyl ester of a small sample showed that the crude acids contained *ca.* 5% unreacted starting material, 7% VIIIa, 31% IXa, 38% Xa, and 19% XIa. Dilution of the crude product with hexane gave, after prolonged standing, 2 g of Xa, mp 109–110°. A purified sample had mp 111–112.5°.

Anal. Calcd for $C_7H_{11}ClO_2$: C, 51.70; H, 6.82; Cl, 21.80. Found: C, 52.01; H, 7.06; Cl, 21.7.

The acid Xa was also isolated from a distillation cut, bp 105.5–109.5° (0.5 mm), resulting from chlorination of IVa.

Methyl *cis*-4-Cyclohexanecarboxylate (Xb). This was prepared by esterification of the acid Xa with BF_3–methanol or diazomethane. No boiling point determination was made due to the small quantities available, but a fraction, bp 64–66° (1.0 mm), was found to be rich in Xb. Spectral data are given in the tables.

***trans*-4-Chlorocyclohexanecarboxylic Acid (XIa) and Methyl Ester (XIb).** Rearrangement of *cis*-4-methoxycyclohexanecarboxylic acid with $SOCl_2$[19] gave the ester XIb, bp 110–112° (17 mm) (lit.[19] bp 119° (20 mm)). Hydrolysis of XIb with dioxane–H_2SO_4 gave, after recrystallization from hexane, the acid XIa, mp 158.5–159° (lit.[19] mp 159.0–159.8°).

Acknowledgment. We would like to thank Professors J. C. Martin and Martin Stiles for numerous stimulating discussions, and also Professors E. L. Eliel and F. R. Jensen for their comments and suggestions. H. W. Moll carried out some of the early gas chromatographic collection of the methyl esters Vb–XIb, F. L. Beman contributed much useful advice in determining the A-60 nmr spectra, and K. C. Whitman and T. E. Zurawic rendered valuable experimental assistance.

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(51) E. Gryszkiewicz-Trochimowski, W. Schmidt, and O. Gryszkiewicz-Trochimowski, *Bull. Soc. Chim. France*, 593 (1948).

(52) L. D. Metcalfe and A. A. Schmitz, *Anal. Chem.*, **33**, 363 (1961).

(53) C. C. Price and M. Schwarcz, *J. Am. Chem. Soc.*, **62**, 2891 (1940).

(54) J. Tsuji, M. Morikawa, and J. Kiji, *J. Am. Chem. Soc.*, **86**, 4851 (1964).