

appropriate chloro isomers. In each case, peak areas were in fact directly proportional to the mole ratios within experimental error (1%). Peak areas were determined by use of a Burrell Corp. planimeter as an average of three traces. The areas were checked by the method of peak height and width at half-height where possible. Preparative glpc separations were conducted on an Aerograph A-700 gas chromatograph using a 15 ft \times 0.25 in. stainless steel column packed with 20% DEGS on 60-80 Chromosorb W. Decomposition of the chlorinated substances during glpc was a serious problem in early experiments. Careful control of the injection port temperature ($\leq 175^\circ$) and a Pyrex insert greatly reduced decomposition. Treatment of the column with repeated injections of Silyl 8 column conditioner (Pierce Chemical Co.) essentially eliminated all decomposition.

Chloromethyl Cyclohexanecarboxylate (XI). Following the general procedure of Ulich and Adams,¹³ 25 g (0.17 mol) of cyclohexanecarbonyl chloride was added dropwise to 5.13 g (0.17 mol) of paraformaldehyde with magnetic stirring over a period of 30 min. After addition of 30 mg of zinc chloride, the mixture was heated at 90° for 3 hr and then distilled directly through a small column giving 14.7 g (54%) of XI: bp $80-82^\circ$ (5 mm); ir (CCl₄) 1760 (C=O), 745 (CCl), and 714 cm^{-1} (CCl); nmr (CCl₄) δ 5.67 (s, 2 H), 1.0-2.0 ppm (broad, 11 H).

Methyl *trans*-4-Methylcyclohexanecarboxylate (XXI). The procedure of Kwart and Scalzi²⁴ was followed with modification. Methyl *p*-toluate (60 g) was exhaustively hydrogenated in two batches each using 200 ml of acetic acid solvent and 4 g of 5% rhodium on aluminum at an initial pressure of 50 psi. After filtration of the catalyst and the normal work-up, glpc showed the products to be a mixture of 82% *cis* and 18% *trans* isomers. The mixture was refluxed 12 hr with 10% sodium methoxide in methanol. After cooling, the mixture was poured into dilute hydrochloric acid solution and worked up as usual. The mixture was now 20% *cis* and 80% *trans*. Distillation on an annular Teflon spinning band column gave XXI in 56% yield ($>99\%$ purity), bp $55-56^\circ$ (2 mm). The remaining 44% could either be reprocessed or converted to the acid and purified by crystallization.²⁴ With patience very high yields of XXI could be obtained.

To verify that in fact the *trans* isomer was the one isolated by distillation, 2.0 g of the ester mixture (20% *cis*, 80% *trans*) was refluxed for 12 hr with aqueous 20% potassium hydroxide, followed by cooling and acidification. The solid *trans*-acid was collected and recrystallized from hexane, mp $112-113^\circ$ (lit.²⁴ mp $113-113.5^\circ$). Treatment of this acid with ethereal diazomethane gave a compound identical with XXI in all respects.

Methyl *cis*-4-*t*-Butylcyclohexanecarboxylate (XVIII). *cis*-4-*t*-Butylcyclohexanecarboxylic acid was isolated via the ammonium salt as described²⁸ and crystallized from hexane, mp $116-118^\circ$ (lit.^{29,30} mp $117.5-118^\circ$). XVIII was prepared from the acid with ethereal diazomethane, bp $54-56^\circ$ (0.5 mm) [lit.³¹ bp $57-58^\circ$ (0.7 mm)] and by glpc contained no trace of the *trans* isomer within the limits of the thermal conductivity detector.

Methyl *trans*-4-*t*-Butylcyclohexanecarboxylate (XII). *trans*-4-*t*-Butylcyclohexanecarboxylic acid was prepared by the method of Curtin, *et al.*,³² mp $173-175^\circ$ (lit.^{28,29} mp $174-175^\circ$). XII was prepared from the acid with ethereal diazomethane, bp $67-69^\circ$ (0.2 mm) [lit.³¹ bp $65-66^\circ$ (0.8 mm)] in 99% purity with 1% of XVIII as impurity.

Treatment of the Chlorination Products of XII with Methanolic Potassium Hydroxide. A typical reaction mixture of the monochloro isomers of XII (1.0 g) and 5 ml of 25% potassium hydroxide in methanol was refluxed for 10 hr. After removal of the precipitated potassium chloride, the solvent was removed *in vacuo*, and water was added to the residue. The alkaline layer was acidified with dilute sulfuric acid and then extracted with ether. The ether layer was dried over magnesium sulfate and then treated with ethereal diazomethane. The mixture was worked up as usual and the solvent evaporated prior to glpc analysis.

(28) H. H. Lau and H. Hart, *J. Amer. Chem. Soc.*, **81**, 4897 (1969).

(29) M. Tichy, J. Jowás, and J. Sicher, *Collect. Czech. Chem. Commun.*, **24** 3434 (1969).

(30) R. D. Stolow and C. B. Boyce, *J. Org. Chem.*, **26**, 4726 (1961).

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

(32) D. Y. Curtin, R. D. Stolow, and W. Maya, *ibid.*, **81**, 3330 (1959).

Free-Radical Chlorination of Methyl Cyclohexanecarboxylates. II. Stereochemistry of the Hydrogen-Abstraction Step

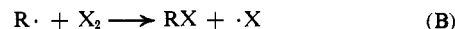
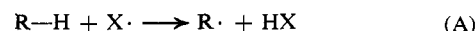
Charles C. Price and Charles D. Beard

Contribution from the Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104. Received January 16, 1970

Abstract: Catalytic hydrogenation of methyl perdeuteriobenzoate in acetic acid produced methyl cyclohexanecarboxylate with essentially all atoms *cis* to the ester deuterium. Similarly, catalytic addition of deuterium to methyl benzoate led to the analog with all atoms *trans* to the ester deuterium. Catalytic deuteration of methyl *p*-*t*-butylbenzoate also proceeded stereoselectively without significant exchange to give 78% methyl *cis*-4-*t*-butylcyclohexanecarboxylate-*d*₆. This product was epimerized by base, with exchange of the α -deuterium. Free-radical chlorination of these esters by sulfuryl chloride, followed by glpc separation of the monochloro isomers and determination of the H/D fraction on the chlorine-containing carbon, leads to the conclusion that the abstraction of hydrogen is governed by a normal H/D ratio of *ca.* 1.7 for free-radical chlorination but is unaffected by whether the hydrogen atom is *cis* or *trans* to the ester group or in an axial or equatorial position, *i.e.*, there is no significant stereoselectivity in the hydrogen-abstraction step.

Recently an explanation for the preferential formation of *trans* products (hereafter denoted "*trans* effect") in the free-radical chlorination of methyl cyclohexanecarboxylate and derivatives was proposed.¹ Electrostatic repulsions between the electronegative substituent and the chlorinating agent in the transition state for propagation step B were postulated as pri-

marily responsible for the stereoselectivity. Steric repulsions were apparently small compared with polar interactions.¹

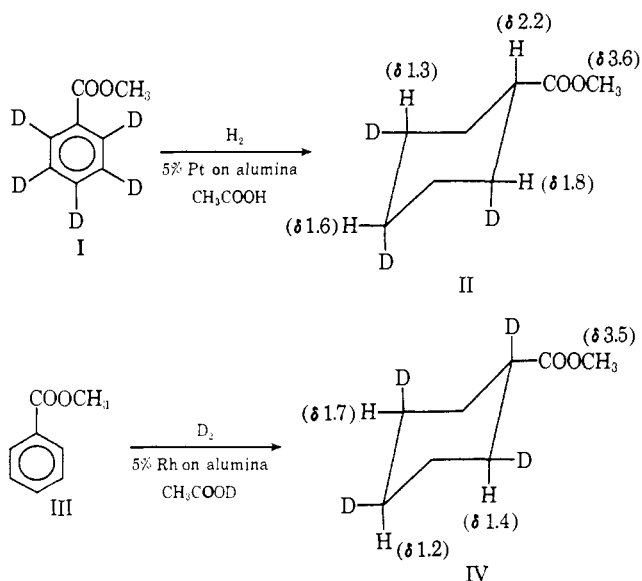


The "*trans* effect" is readily detected experimentally since it leads to a greater proportion of *trans* than of *cis* isomers. On the other hand, because of the

(1) C. C. Price, C. D. Beard, and K. Akune, *J. Amer. Chem. Soc.*, **92**, 5916 (1970).

configurational instability of a free radical, a system suitable for study of a steric preference in propagation step A, the abstraction of hydrogen, is more difficult to devise. The purpose of this paper is to report the development of such a system and the steric consequences of the abstraction of hydrogen during free-radical chlorination.

Experience indicated that stereospecifically deuterated methyl cyclohexanecarboxylate would perhaps be suitable. The most promising deuterium incorporation method appeared to be catalytic deuteration of methyl benzoate (III) leading to methyl cyclohexanecarboxylate- d_6 (IV) with all deuteriums *trans* to the ester group, or by hydrogenation of methyl benzoate- d_5 (I) to give methyl cyclohexanecarboxylate- d_5 (II) with all deuteriums *cis* to the ester group. In principle, if the attacking chlorine atom approached opposite to carbomethoxyl as does the chlorine molecule in step B, deuterium would be preferentially abstracted from IV and hydrogen from II. It would also be possible to determine whether axial or equatorial hydrogens were attacked preferentially. For example, in II, the 3-hydrogen is axial while in IV it is equatorial. The percentage hydrogen or deuterium actually abstracted would then be readily determined by integration of the downfield hydrogen α to chlorine in the nmr spectrum of each monochloro isomer.

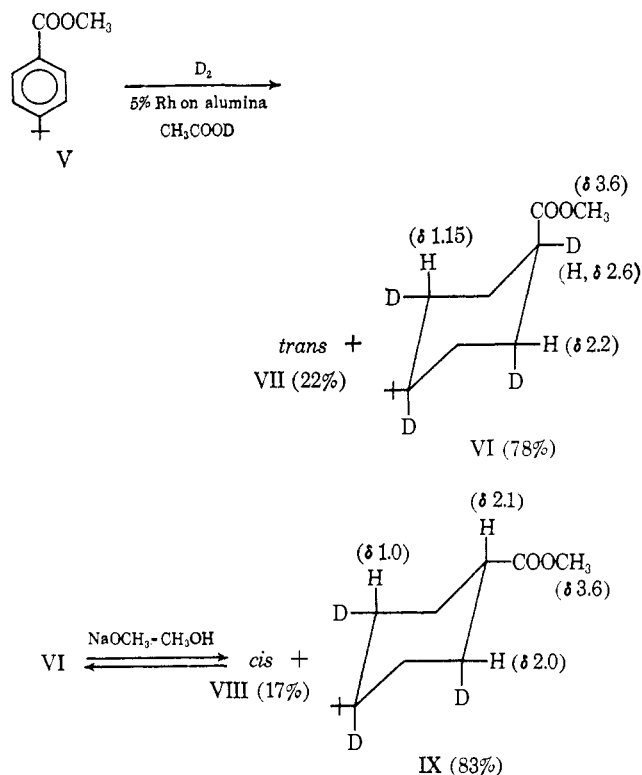


In order to provide an essentially "frozen" cyclohexyl system and thus minimize the variables associated with ring mobility and variable axial-equatorial environment,² methyl *trans*-4-*t*-butylcyclohexanecarboxylate- d_5 (IX) was prepared and chlorinated.

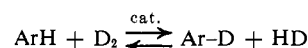
Proof of Structure. Catalytic hydrogenation and hence deuteration is an extremely complex reaction, but generally polysubstituted aromatic rings give a large predominance of *cis* isomer under mild conditions.³

(2) (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965, Chapter 2; (b) M. Hanack, "Conformation Theory," Academic Press, New York, N. Y., 1965, p 87.

(3) (a) R. L. Burwell, Jr., *Chem. Rev.*, **57**, 895 (1957); (b) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine, and R. B. Whetstone, *J. Amer. Chem. Soc.*, **64**, 1985 (1942); (c) M. Freifelder, D. A. Dunningan, and E. T. Baker, *J. Org. Chem.*, **31**, 3438 (1966); (d) P. N. Rylander, "Catalytic Hydrogenation over Platinum Metals," Academic Press, New York, N. Y., 1967, p 324; (e) R. L. Burwell, Jr., *Accounts Chem. Res.*, **2**, 289 (1969).



Catalytic deuteration presents two major problems: H-D exchange of the aromatic ring on the catalyst leading to products containing excess deuterium,⁴ and nonstereospecific or net "*trans*" addition of deuterium to the aromatic nucleus which may occur *via* discrete cyclohexene intermediates.⁵



The literature is of little aid in helping to define reaction conditions. The hydrogenation of many unsaturated systems using deuterium as a tracer has been studied, but usually the reactions were not allowed to proceed to completion and thin metal films rather than the normal supported catalysts were employed.⁴ There have been few attempts to use catalytic deuteration of aromatic rings for preparative purposes with two notable exceptions. Smith, Line, and Wyatt⁶ deuterated aniline using platinum oxide and Bissell and Finger⁷ deuterated furan using rhodium on alumina, but neither was able to determine accurately the amount of exchange or stereochemistry.

By consideration of the available literature and with the advice of Dr. R. L. Burwell, Jr.,⁸ the hydrogenation of methyl benzoate- d_5 and deuteration of methyl benzoate and methyl 4-*t*-butylbenzoate were completed using experimental conditions designed to minimize exchange and maximize *cis* addition.

To prepare methyl cyclohexanecarboxylate- d_5 (II), I was exhaustively hydrogenated at room temperature with an initial pressure of 50 psi using a 5% platinum-

(4) F. Hartog, J. H. Tebben, and C. A. M. Weterings in *Proc. Int. Congr. Catal.*, **3rd**, 1964, **2**, 1210 (1965).

(5) S. Siegel, G. V. Smith, B. Dmuchousky, P. Dubbell, and W. Halpern, *J. Amer. Chem. Soc.*, **84**, 3106 (1962).

(6) L. E. Line, Jr., B. Wyatt, and H. A. Smith, *ibid.*, **74**, 1808 (1952).

(7) E. R. Bissell and M. Finger, *J. Org. Chem.*, **24**, 1259 (1959).

(8) R. L. Burwell, Jr., Northwestern University, private communication, 1966.

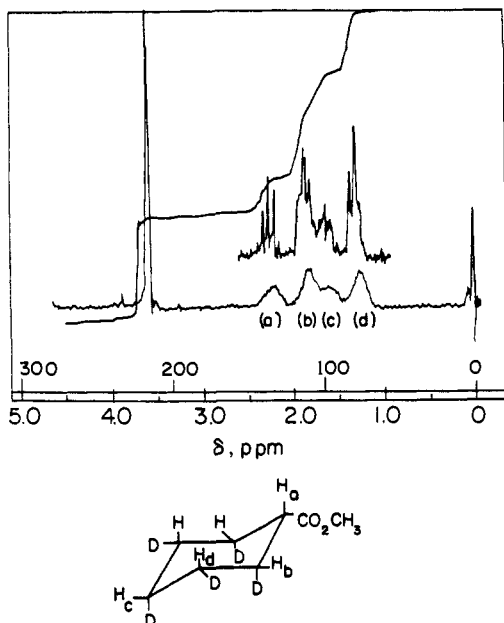


Figure 1. Nuclear magnetic resonance spectrum of methyl cyclohexanecarboxylate- d_5 (in carbon tetrachloride) with deuteriums decoupled.

on-aluminum catalyst and acetic acid as solvent. Analysis of the low-voltage mass spectrum by the method of Biemann⁹ indicated the empirical formula to be $C_8H_3D_5O_2$ with only *ca.* 3% D-H exchange. Deuterium analysis by the combustion and falling drop method confirmed this conclusion. The nmr spectrum of II (Figure 1) allows assignment of predominant stereochemistry. Assuming ΔG_{25}° ($COOCH_3$) = -1.27 kcal/mol,¹⁰ and that the conformational requirements of deuterium are similar to protium, then the equilibrium mixture would consist of 89% of the conformer with carbomethoxyl in an equatorial position and 11% of the axially oriented conformer. The spectrum can best be interpreted by considering it arises primarily from the equatorial arrangement, as little change was noted down to -80° .

The peaks (Figure 1) lettered (a)-(d) have integral ratios of 1:2:1:2. Carbomethoxyl substantially deshields hydrogens at positions 1 and 2 and has a negligible effect at 3 and 4. Positions 3 and 4 are then primarily governed by axial-equatorial chemical shift differences with the equatorial hydrogen at position 4 deshielded relative to the two axial hydrogens at 3. The decoupled spectrum, although not first order, allows assignment of an upper limit for the H_c-H_d coupling constant of $J \approx 3-4$ cps, consistent with a dihedral angle between hydrogens approximating 60° as required by *cis* hydrogenation.

In support of the assignments, the α -hydrogen of methyl cyclohexanecarboxylate is observed at essentially the same position as (a), and the axial and equatorial hydrogens of cyclohexane at low temperature have chemical shifts approximating (d) and (c), respectively.¹¹ The assignment seems fully justified but

(9) K. Biemann, "Mass Spectrometry Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 223.

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

(11) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Amer. Chem. Soc.*, **84**, 386 (1962).

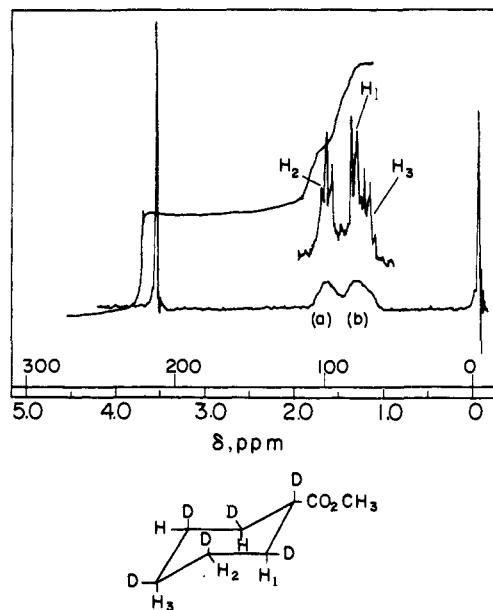


Figure 2. Nuclear magnetic resonance spectrum of methyl cyclohexanecarboxylate- d_6 (in carbon tetrachloride) with deuteriums decoupled.

it must be emphasized that a small amount of *trans* stereochemistry would be extremely difficult to detect. We are, however, confident in suggesting a predominantly *cis* hydrogenation ($\geq 90\%$) with negligible exchange.

Methyl Cyclohexanecarboxylate- d_6 (IV). III was exhaustively deuterated at 50 psi using a 5% rhodium-on-alumina catalyst.¹² Acetic acid- d_1 was required as solvent because gaseous deuterium rapidly exchanges with protic solvents on the catalyst.⁶ IV was obtained in quantitative yield containing a slight (2%) excess of deuterium.

The nmr peaks were assigned in analogy to II. Notable features were the absence of an α -hydrogen (at δ 2.28, compare Figure 1) and the relatively weak coupling ($J \approx 3-4$ cps) again consistent with *cis* deuteration and dihedral angles between hydrogens of 60° . Comparison of Figures 1 and 2 yields the data tabulated in Table I. The axial - equatorial chemical shift

Table I. Proton Magnetic Resonances in II and IV^a Relative to TMS

| Ring position | Axial | Equatorial | (A - E) |
|---------------|-------|------------|---------------|
| 2 | 83 | 110 | 27 (0.45 ppm) |
| 3 | 76 | 102 | 26 (0.43 ppm) |
| 4 | 73 | 96 | 23 (0.38 ppm) |

^a In cycles per second.

differences are in excellent agreement with published values for similar compounds, and strongly support the assignments.²

Methyl *cis*-4-*t*-Butylcyclohexanecarboxylate- d_6 (VI) and *trans*-4-*t*-Butylcyclohexanecarboxylate- d_6 (IX). V was deuterated as for III and the *cis* isomer VI isolated

(12) 5% platinum on alumina gave a product having low deuterium values perhaps because of hydrogen adsorbed on the catalyst during preparation.

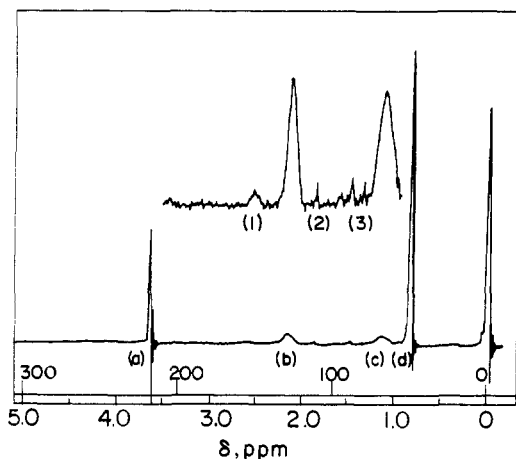


Figure 3. Nuclear magnetic resonance spectrum of methyl *cis*-4-*t*-butylcyclohexanecarboxylate-*trans*- d_6 (in carbon tetrachloride).

in 99.5% purity by fractional distillation on a spinning band column. Combustion analysis showed only 5.5 deuterium atoms, rather than six. Inspection of the nmr spectrum (Figure 3) provides an explanation for the discrepancy. Peaks (a)–(d) were assigned to methyl ester, equatorial hydrogens at position 2, axial hydrogens at 3, and *t*-butyl hydrogens, respectively, and are in the correct ratio of 3:1.9:2:9. Closer scrutiny (Figure 3) reveals several small peaks. Peak (1) (0.20 hydrogen) corresponds to an equatorial α -hydrogen suggesting that some exchange took place at the labile α position either during work-up or upon distillation. Peak (2) was a ^{13}C satellite from *t*-butyl. Peak (3) (0.25 hydrogen) could perhaps be a consequence of “*trans*” deuteration. For example, a 2-axial hydrogen in IX would appear as a triplet at about δ 1.4; the observed triplet in Figures 3 and 4 appears at δ 1.47 ppm, $J = 8$ cps. This 2-axial hydrogen cannot produce a triplet in VI; however, the peak at δ 1.3 in Figure 3 may be a spinning side band reducing the apparent triplet to the predicted doublet. The hydrogen in the 1 and 2 positions in VI could be explained by having 25% *cis* addition of H_2 to a Δ^1 -unsaturated intermediate and IX does indeed contain an excess of hydrogen consistent with 0.25 H extra, as would be expected for 0.25 H in the 2-axial position of IX.

VI was then equilibrated and epimerized three times with excess 5% sodium methoxide in methanol and the resulting *trans* isomer IX isolated in 99% purity by spinning hand distillation. The deuterium analysis now indicated 4.8 deuteriums confirming that much of the excess hydrogen in VI had been in the α position. The nmr spectrum of IX (Figure 4) shows the new axially oriented hydrogen at the α position at δ 2.1 ppm as expected. The major hydrogen ratios are 3:2.8:2:9. The hydrogens at carbon 3 are shielded by *ca.* 0.15 ppm relative to the *cis* isomer. Eliel¹³ has noted a similar perturbation of chemical shift positions for hydrogens close to a *t*-butyl holding group in *cis*-*trans* isomers. Thus it would appear that deuteration has been largely *cis* with little exchange, and indeed this may prove to be a valuable labeling technique.

(13) E. L. Eliel and J. L. Martin, *J. Amer. Chem. Soc.*, **90**, 682 (1968).

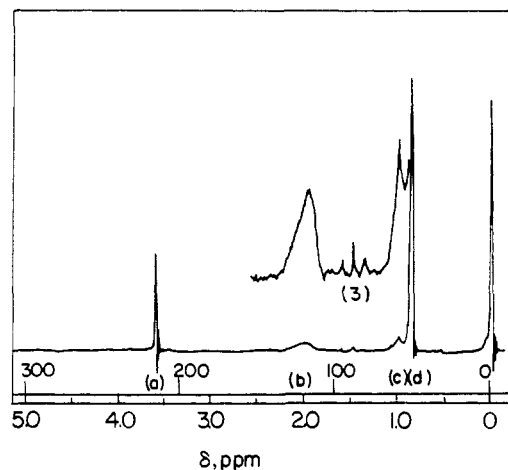


Figure 4. Nuclear magnetic resonance spectrum of methyl *trans*-4-*t*-butylcyclohexanecarboxylate-*cis*- d_3 (in carbon tetrachloride).

Discussion

II, IV, and IX were chlorinated with sulfur chloride and the monochloro isomers isolated by preparative gas chromatography as described.¹ The distribution of isomers and per cent chlorination at each position were identical with that obtained for the undeuterated analogs.¹ This is expected assuming that all carbons are substituted with one hydrogen and one deuterium and that the *trans*-*cis* ratios are determined by propagation step B. Presumably this is independent of H or D substitution provided that the steric requirements for H and D are comparable.

Analysis of the downfield hydrogen $>\text{CHCl}$ by nmr spectroscopy allows computation of the per cent hydrogen abstracted and thus also the amount of deuterium removed (Table II). The attacking radical may

Table II. Fraction of Hydrogen α to Chlorine, by Nmr^{a,b}

| Starting material | Monochloro product | | | | |
|-------------------|--------------------|---------------|-----------------|---------------|---------------|
| | <i>trans</i> -2 | <i>cis</i> -2 | <i>trans</i> -3 | <i>cis</i> -3 | <i>cis</i> -4 |
| II | 0.40 | 0.32 | 0.38 | 0.40 | 0.39 |
| IV | 0.36 | 0.35 | 0.41 | 0.37 | 0.38 |
| IX | 0.43 | 0.49 | 0.42 | 0.43 | |

^a Obtained by electronic integration of the nmr spectra with the methyl ester singlet taken as internal standard of three hydrogens.

^b For compounds II and IV the *trans*-4 and *cis*-2 isomers were not separable by glpc and were collected together. Overlap of peaks obscured data for the *trans*-4 and this experimental uncertainty is undoubtedly responsible for the low values for *cis*-2.

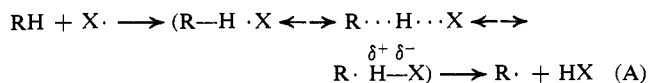
abstract either a hydrogen or a deuterium depending on the direction of approach. This direction could depend on the *cis* or *trans* orientation of the substituent groups (COOCH_3 or *t*-butyl) or the direction of attack might be influenced by the axial or equatorial character of the hydrogen (deuterium) being attacked. A primary kinetic isotope effect is expected and, in the absence of data for sulfur chloride, values obtained for chlorine of between 1.4 and 2.2 are a useful guide.¹⁴

The data in Table II may best be interpreted in terms of essentially random hydrogen abstraction, *i.e.*,

(14) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

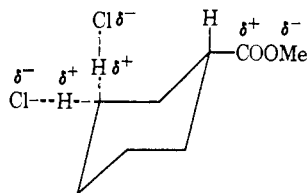
the values are essentially independent of the *cis-trans* orientation of the hydrogen abstracted to the substituent groups and of the axial-equatorial environment of the hydrogen (deuterium) involved. The values for IX appear to be slightly higher than the rest and if this trend is significant could be explained by steric interactions favoring attack by the chlorosulfonyl radical opposite to the bulky *t*-butyl group. The average deuterium isotope effect of *ca.* 1.67 is as expected. The fact that the same ratio of isomers is obtained from the deuterated as the undeuterated analogs and that there seems to be no steric factor favoring chlorine attack on either axial or equatorial hydrogen (other than the normal isotope effect) indicates (a) that chlorine can attack and remove axial hydrogen just as easily as equatorial and (b) that the resulting radical undergoes configurational equilibration more rapidly than it reacts with sulfonyl chloride.

An explanation of these phenomena may be found by consideration of polar contributions to the transition state.



The transition state for hydrogen abstraction can reasonably be depicted as having characteristics of both products and reactants. When the intermediate radical is very reactive, the Hammond¹⁵ postulate predicts a transition state resembling reactants, and only small contributions from ionic structures would be expected. On the other hand, Hodnett and Juneja^{16a} have presented experimental evidence in the form of β -secondary isotope effects in the photochlorination of 2-methylpropane-2-*t* which supports the concept of a small ionic contribution to the transition state. The preference for attack remote from the ester group is also readily explained by some developing ionic character in the new H-X bond.^{16b}

If attack on hydrogen remote from the ester group is indeed favored by a diminished unfavorable interaction of the dipoles in the ester group (or of the electric field generated by these dipoles) with the developing H-X dipole, one must explain why, for the same reason, the *cis*-hydrogen at carbon 3 is not favored over the *trans* or the *trans*-hydrogen at carbon 4 over the *cis*. This may be rationalized by more careful inspection of the geometry involved, as is illustrated below for the case of carbon 3.



While the *cis*-H is further from the ester group, the orientation between the dipoles is more favorable for greater interaction. The *trans*-H₃, while closer to the ester group, is oriented with respect to the ester

- (15) G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955).
 (16) (a) E. M. Hodnett and P. S. Juneja, *J. Org. Chem.*, **33**, 1233 (1968); (b) C. C. Price and H. Morita, *J. Amer. Chem. Soc.*, **75**, 3686 (1953).

dipole so as to decrease its interaction. These two factors, distance and dipole-dipole orientation, can thus counteract each other and offer a rational explanation of the absence of any significant *cis-trans* preference in hydrogen abstraction. A similar factor would be possible for the 4 position while the hydrogens in the 2 position are the same distance from the ester and would have the same dipole-dipole angles.¹⁷

Experimental Section

General. All temperature readings are uncorrected. Mass spectra were obtained on a Consolidated Electronics Model 21-130 cycloidal mass spectrograph. Infrared spectra were recorded on a Perkin-Elmer 521 spectrometer using the extended range interchange. Deuterium analyses were determined using the combustion and falling drop method by Josef Nemeth, Urbana, Ill. Deuterium decoupling experiments were performed by T. P. Churay of Nmr Specialties, Inc., New Kensington, Pa. Catalysts were purchased from Englehard Industries, Newark N. J., and used directly. Acetic acid was purified by distillation through a spinning band column. The chlorination procedure and separation of the isomeric chloroesters by preparative gas chromatography has been described.¹

Methyl Benzoate-*d*₅ (I). Benzene-*d*₆ (99.5%) was used directly as received from Volk Radiochemical Co. Following the general procedure of Best and Wilson,¹⁸ 30 g of bromine was added dropwise with stirring over a period of 45 min to 20 g of benzene-*d*₆ and 0.8 g of iron wire, and then warmed (50–60°) until the vapors of deuterium bromide were no longer visible. After cooling, the contents of the flask were extracted with ether, washed with saturated sodium carbonate solution, dried over magnesium sulfate, and distilled through a small column. Fractions of ether and benzene-*d*₆ were collected followed by a higher boiling fraction of bromobenzene-*d*₅ in 70% yield, bp 154–155° (755 mm) (lit.¹⁸ bp 154–155° (760 mm)).

The Grignard reagent was prepared from bromobenzene-*d*₅ and magnesium as described¹⁸ and transferred under nitrogen to a dropping funnel. The mixture was added dropwise to a well-stirred ethereal solution of powdered carbon dioxide.¹⁹ After evaporation of excess carbon dioxide, the mixture was acidified with congo red with 6 *N* hydrochloric acid and the organic layer washed with water. Extraction with 7.5 *N* ammonium hydroxide followed by acidification gave a 40% yield of benzoic acid-*d*₅ based on benzene-*d*₆, mp 121.5–122.5° (lit.²⁰ mp 121.7°). The benzoic acid-*d*₅ was treated with excess ethereal diazomethane giving an 89% yield of I after work-up: ir (CCl₄) 2297, 2275 (CD), 1720 (C=O), 1242 (OCH₃) and 1080 cm⁻¹ (OCH₃); nmr (CCl₄) δ 3.85 ppm (s); mass spectrum (76 eV) *m/e* (rel intensity) 142 (8), 141 (83), 111 (9), 110 (100), 82 (5).

Methyl Cyclohexanecarboxylate-*d*₅ (II). I (10 g), 3.0 g of 5% platinum on alumina,²¹ and 100 ml of acetic acid were placed in a hydrogenation bottle and charged with hydrogen to 50 psi on a Parr apparatus. Quantitative uptake of hydrogen was complete in 1 hr. After filtration of the catalyst, most of the solvent was removed at 10 mm with heating to 45°. The product was isolated either by direct distillation at 1–3 mm or by taking the material up in ether, washing twice with dilute sodium bicarbonate, drying over magnesium sulfate, concentrating on a rotary evaporator, and distilling. Both of these procedures gave products with identical spectral properties in 99.5% purity by glpc: ir (CCl₄) 2183 (CD), 1733 (C=O), 1189 (OCH₃) and 1167 cm⁻¹ (OCH₃); nmr (see Figure 1); mass spectrum (10 eV) *m/e* (rel intensity) 148 (2), 147

(17) By assuming the type of geometry above, with a $\pm 1.93 \times 10^{-10}$ esu dipole charge in the ester group (coaxial with the carbon-carbon bond to the ring) and with a $\pm 0.81 \times 10^{-10}$ esu dipole charge on the developing HCl bond, linear with the breaking C-H bond, we estimate the following electrostatic increments to the activation energy: H_{2-*cis*} = H_{2-*trans*} = 570 cal/mol; H_{3-*cis*} = 210; H_{3-*trans*} = 230; H_{4-*cis*} = 160; H_{4-*trans*} = 150.

(18) A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 239 (1946).

(19) A. S. Hussey, *J. Amer. Chem. Soc.*, **73**, 1364 (1957).

(20) H. Erlenmeyer, H. Lobeck, and A. Epprecht, *Helv. Chim. Acta*, **19**, 793 (1936).

(21) Preliminary experiments showed about 10–15% exchange with platinum oxide and *ca.* 5% exchange with rhodium on alumina.

(21), 146 (2), 116 (16), 115 (15), 89 (54), 88 (100), 87 (19), 86 (11), 76 (22), 75 (29), 74 (21), 73 (18), 72 (18).

Anal. Calcd for $C_8H_9D_6O_2$: D, 35.71. Found: D, 34.65.

Methyl Cyclohexanecarboxylate- d_6 (IV). Deuterium (99.97%) was used as received from Baker Chemical Co., Phillipsburg, N. J. Acetic acid- d_1 was prepared as described²² and used directly for the deuterations. A Parr apparatus was prepared for deuterium by alternately purging with nitrogen and evacuation. After a final evacuation at 0.1 mm the tank was charged with deuterium to 50 psi.

Methyl benzoate (5 g), 1.0 g of 5% rhodium on alumina catalyst, and 50 ml of acetic acid- d_1 were placed in a bottle under nitrogen. The bottle was then attached to the apparatus and evacuated. Nitrogen was admitted through a three-way stopcock and evacuated three times to purge the system. The theoretical volume of deuterium was consumed within 2 hr and the product was isolated as described for II in quantitative yield by distillation: ir (CCl_4), 2164 (CD), 1735 (C=O), 1251 (OCH₃) and 1072 cm^{-1} (OCH₃);

(22) G. Binsch and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 5158 (1965).

nmr (see Figure 2); mass spectrum (10 eV) *m/e* (rel intensity) 149 (5), 148 (12.4), 147 (6), 118 (6.0), 117 (14.9), 116 (16.2), 115 (11.0), 91 (16.2), 90 (61.5), 89 (100), 88 (24.4), 87 (16.2), 77 (17.6), 76 (38.4), 75 (32.5).

Anal. Calcd for $C_8H_9D_6O_2$: D, 42.86. Found: D, 43.70.

Methyl *cis*-4-*t*-Butylcyclohexanecarboxylate- d_6 (VI). Methyl 4-*t*-butylbenzoate (V) was exhaustively deuterated similarly to IV to give a quantitative yield of products; 78% *cis* (VI) and 22% *trans* (VII). The *cis* isomer (VI) was isolated in 99% purity by careful fractionation on a Nester-Faust Annular Teflon spinning band column in 50% yield based on V, bp 62–63° (0.1 mm).

Anal. Calcd for $C_{12}H_{16}D_8O_2$: D, 27.27. Found: D, 24.80.

Methyl *trans*-4-*t*-Butylcyclohexanecarboxylate- d_6 (IX). VI (40 g) was refluxed for 15 hr with 250 ml of 5% sodium methoxide in methanol under nitrogen. The methanol was then removed *in vacuo* and the same procedure was repeated twice more with fresh methanol. After work-up the mixture consisted of 17% *cis* (VIII) and 83% *trans* (IX) isomers. IX (18 g) was isolated in 99% purity by distillation on a spinning band column. A forerun of 20.5 g of a mixture of isomers could be treated with base and reprocessed ultimately leading to high yields (>90%) of IX.

Anal. Calcd for $C_{12}H_{17}D_8O_2$: D, 22.73. Found: D, 21.60.

Equilibrium and Kinetic Acidities of Nitroalkanes and Their Relationship to Transition State Structures¹

F. G. Bordwell, William J. Boyle, Jr.,² and K. C. Yee

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201. Received October 17, 1969

Abstract: The rates of deprotonation by base in 50% (v/v) H_2O -MeOH and the pK_a 's in this solvent have been determined for $ArCH_2CHMeNO_2$ (13 substituents) and for $ArCHMeNO_2$ (12 substituents). Log-log plots for one series against the other gave excellent lines showing that the relative influence of the substituents is the same in each series, despite the possibility of direct conjugative effects operating in one series but not the other. Although direct resonance effects for *p*-NO₂, *p*-CF₃, *p*-Cl, *p*-F, *p*-Me, and *p*-MeO groups are absent, indirect resonance effects, relayed by induction, are shown to be operative in each series. Substituents affect the rates of the forward (deprotonation) and reverse (protonation) reactions in the *same* manner. As a consequence the ρ 's are smaller for the equilibria (0.395 and 1.07) than for the forward rates (0.665 and 1.44). This leads to the unprecedented observation of Brønsted coefficients larger than one (1.61 and 1.37). The Brønsted coefficients for the reverse (protonation) reactions are negative (−0.61 and −0.37) because here the substituent effects are opposite in direction to those prevailing in the equilibria. Evidence concerning the structure of the transition state in the deprotonation of nitroalkanes by hydroxide ion is reviewed and the conclusion is drawn that the transition state is *not* product-like. The evidence points to a transition state in which there is about equal O–H bond making and H–C bond breaking, but with very little delocalization of the developing negative charge to the oxygen atoms of the nitro group.

In order to elucidate the effect of substituents on the rates of proton abstraction by bases from nitroalkanes and on the stereochemistry of the protonation of the corresponding nitronate ions with acids³ it became necessary to learn more about the nature of the transition state for these reactions. Considerable attention has been given to this question, but various approaches have led to quite different conclusions. Hammond pointed out that the rough parallelism between acidity and the rates of proton removal by bases from weak pseudoacids (nitroalkanes and ketones are implied by the referencing) to form carbanions is explicable on the basis of a carbanion-like transition

state "since these reactions are rather highly endothermic."⁴ Similarly, for the reverse reaction, protonation of the nitronate ion, the transition state has been assumed to resemble the nitronate ion (carbanion) in structure.⁵ It was also concluded that the transition state must be product-like for the reaction of hydroxide ion with nitroethane on the basis of a large negative entropy of activation (−15.5 eu) which corresponded closely to the equilibrium entropy (−18.3 eu) for this reaction.⁶ On the other hand, consideration of solvent deuterium isotope effects (k_{H_2O}/k_{D_2O}) on the rate of proton abstraction by hydroxide ion from nitromethane led Swain and Rosenberg to conclude that the transition state is

(1) For a preliminary account of this work see F. G. Bordwell, W. J. Boyle, Jr., J. A. Hautala, and K. C. Yee, *J. Amer. Chem. Soc.*, **91**, 4002 (1969).

(2) National Institutes of Health Predoctoral Fellow, 1967–1970.

(3) F. G. Bordwell and M. M. Vestling, *J. Amer. Chem. Soc.*, **89**, 3906 (1967).

(4) G. S. Hammond, *ibid.*, **77**, 334 (1955).

(5) H. E. Zimmerman, "Molecular Rearrangements," Vol. I., P. de Mayo, Ed., Interscience, New York, N. Y., 1963, p 346.

(6) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 16 (1963).