207. *Conformation and Reactivity. Part IV.*[1] *Preparation of the* trans-*Decalincarboxylic Acids: Kinetics of the Esterification with Diazodiphenylmethane in Ethanol of these Acids, and of the 4-t-Butylcyclohexanecarboxylic Acids and Cyclohexanecarboxylic Acid.*

By N. B. Chapman, J. Shorter, and K. J. Toyne.

The four *trans*-decalincarboxylic acids have been prepared; the compound with a 2-axial carboxyl group was previously unknown. The rates of esterification with diazodiphenylmethane in ethanol of these acids, of *cis*- and *trans*-4-t-butylcyclohexanecarboxylic acid, and of cyclohexanecarboxylic acid have been measured at several temperatures and the Arrhenius parameters have been determined. The results indicate that there is no polar effect of the 4-t-butyl group in this reaction, and that in ethanol, 77% of cyclohexanecarboxylic acid has the carboxyl group in the equatorial conformation. The rate coefficients for the reactions of the *trans*-decalin-2-carboxylic acids have nearly the same values as those for the reactions of their *cis*- and *trans*-4-t-butylcyclohexanecarboxylic acid counterparts at a given temperature. The rate coefficient for the reaction of the 1-axial acid is low because of three " 1,3-axial hydrogen atom " interactions, but the rate coefficient for the reaction of the 1-equatorial acid is ~20% higher than that of the 2-equatorial acid.

Previous papers in this series have dealt with the alkaline[2] and the acid-catalysed[1] hydrolysis of dimethyl cyclohexanedicarboxylates, and of methyl *cis*- and *trans*-4-t-butylcyclohexanecarboxylate. The intention was to correlate the reactivity and conformation

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[1] Part III, Chapman, Shorter, and Toyne, *J.*, **1961**, **2543**.

[2] Cavell, Chapman, and Johnson, *J.*, **1960**, **1413**.

of the several esters; in this paper we report the results of an extension of our studies as indicated in the title.

Since monosubstituted cyclohexane compounds do not have the substituent exclusively in one conformation, the conformation of the whole molecule must be locked if it is desired to study the properties of a particular substituent in the axial or the equatorial conformation. This may be done by appropriate further substitution. Winstein and Holness [3] suggested that the bulky t-butyl group would be so compressed in the axial conformation because of the 1,3-interactions, that it would be unlikely to take up this position. Therefore, a compound *cis*-4-t-butylcyclohexane-1-X will have the 1-substituent in the axial conformation, and the *trans*-isomer will have the 1-substituent in the equatorial conformation, provided that the substituent, X, is small compared with the t-butyl group. Increasing the size of X will gradually make the *cis*-isomer conformationally inhomogeneous.

This method of studying axial and equatorial groups has been widely used in kinetic work, but three assumptions involved in obtaining k_e and k_a (the rate coefficients for equatorial and axial groups, respectively) must be borne in mind. Eliel [4] has stated the assumptions thus: (*a*) the t-butyl group must not exert a polar effect at the reaction site; (*b*) the t-butyl group must not exert a direct steric effect on the reaction site; (*c*) the t-butyl group must not give rise to distortion of the ring, for, if it does, the geometry, and therefore the specific reaction rates of the 4-t-butyl compounds, might be different from those of the conformationally pure, unsubstituted cyclohexane compounds. Cavell, Chapman, and Johnson [2] studied the alkaline hydrolysis of the methyl 4-t-butylcyclohexanecarboxylates and methyl cyclohexanecarboxylate in 1 : 1 dioxan–water and their results suggest that the 4-t-butyl group does in fact exert a polar effect on the 1-ester group in this reaction. The second and the third assumption above appear reasonable in this case from a study of molecular models.

Because the first assumption above has been shown to be doubtful, and because the validity of the other assumptions is not easily proved, a further method of investigating the characteristics of axial and equatorial groups is desirable. This is provided by a study of *trans*-decalin derivatives, particularly the 2-derivatives.

In *trans*-decalin, cyclohexane rings are fused by two equatorial bonds. Consequently, any ring conversion would cause these bonds to become axial–axial: this is geometrically impossible, and therefore *trans*-decalin derivatives are conformationally rigid. Substituents at the 2-position are situated similarly to axial and equatorial groups in cyclohexane. The substituents at the 1-position, however, are situated rather differently from cyclohexane substituents [see p. 1085 and (I) and (II)].

We have therefore studied the alkaline and the acid-catalysed hydrolysis of the methyl *trans*-decalincarboxylates and related the results to those previously obtained; this work will be reported later. The present paper, however, extends the types of reaction studied to esterification with diazodiphenylmethane, a reaction which Smith and Hunt [5] have used in investigating the conformations of the cyclohexanedicarboxylic acids.

The mechanism of esterification of carboxylic acids with diazodiphenylmethane in ethanol involves the oxygen and hydrogen atoms of the carboxyl group,[6] *i.e.*, a site at least two bond-lengths removed from the ring in cyclohexanecarboxylic acids. (It is not established whether the carbonyl–oxygen or the hydroxyl–oxygen atom is involved.) This contrasts with the mechanisms for alkaline and acid-catalysed hydrolysis which involve attack at the carbonyl–carbon atom of the ester group. The esterification of cyclohexanecarboxylic acids with diazodiphenylmethane should, therefore, show the difference in environment at a distance of two bond-lengths from the ring of the axial and equatorial conformations of the carboxyl group.

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[3] Winstein and Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.
[4] Eliel, *J. Chem. Educ.*, 1960, **37**, 126.
[5] Smith and Hunt, *J. Amer. Chem. Soc.*, 1959, **81**, 590.
[6] Roberts, Watanabe, and McMahon, *J. Amer. Chem. Soc.*, 1951, **73**, 760.

The preparation of the *trans*-decalin-1- and -2-equatorial-carboxylic acids is well established [7,8] but not that of the axial acids. Nazarov, Kucherov, and Segal [9,10] have recently obtained the 1-axial acid, but the 2-axial acid has not been prepared previously. As all attempts to isolate the *trans*-decalin-1- and -2-axial acid from mixtures of isomers had failed, it was necessary to devise a series of stereospecific reactions which would give a single product at every stage. The four *trans*-1- and *trans*-2-decalyl toluene-*p*-sulphonates had been prepared [11] and we therefore investigated displacing the equatorial toluene-*p*-sulphonate group in a S_N2 reaction with a reagent containing a nucleophilic carbon atom, thus forming an axial group. We first studied the reaction of the equational *trans*-1- and *trans*-2-decalyl toluene-*p*-sulphonate with cyanide ion. However, interaction of sodium cyanide and the toluene-*p*-sulphonate in acetone, ethanol, or dimethyl sulphoxide at temperatures from room temperature to reflux temperature failed to give any of the nitrile. Shoppee and Stephenson,[12] however, showed that steroidal toluene-*p*-sulphonates reacted with diethyl sodiomalonate in toluene to give products with inverted configurations, and that the configurations of the side-chains were retained in subsequent reactions whereby the side-chain was converted into a carboxyl group. This reaction was carried out with the equatorial *trans*-1- and *trans*-2-decalyl toluene-*p*-sulphonate in toluene, and the products were hydrolysed and decarboxylated to give pure acids. These acids were then degraded by a modification of the Barbier–Wieland method [13] to give acids of m. p. different from those of the equatorial *trans*-decalin acids. The m. p. of the presumed 1-axial acid (127·5—129°) agreed with that recorded (127°) by the Russian authors.[10] Both the pure acids gave correct analyses and correct equivalent weights for *trans*-decalin acids and must therefore be the axial acids. The presumed 2-axial acid was converted by the Schmidt reaction into the amine, which was characterised as the axial amine by formation of the benzoyl derivative.

EXPERIMENTAL

Cyclohexanecarboxylic Acid.—The commercial acid (from British Drug Houses Ltd.) was distilled before use and had b. p. 116—118°/13 mm. (lit.,[14] 110°/8 mm.).

cis-4-t-*Butylcyclohexanecarboxylic Acid.*—This was prepared as described by Cavell, Chapman, and Johnson.[2] A 5% rhodium–alumina catalyst (Baker Platinum Co. Ltd.) in ethanol was less easily poisoned than Adams platinum catalyst and gave similar yields. The pure acid had m. p. 117·5—118·5° (lit.,[2] 118°).

trans-4-t-*Butylcyclohexanecarboxylic Acid.*—*p*-t-Butylbenzoic acid was hydrogenated in alkaline solution with a Raney nickel catalyst.[15] The mixed acids produced were separated by Stolow's method,[16] or by van Bekkum, Verkade, and Wepster's method,[17] the latter being more successful. The pure acid had m. p. 175—176° (lit.,[2] 174·5—175·5°).

trans-*Decalin*-1α-*carboxylic Acid.**—*trans*-1α-Decalol was prepared by Moritani,

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* We number *trans* decalin according to the Ring Index system; and we use the convention that the 4a-hydrogen atom is above the plane of the rings (β) when the molecule is oriented as in the figures below. Substituents lying above the plane and those lying below are denoted by β and α, respectively. The 1-equatorial acid is thus (±)-*trans*-decalin-1α-carboxylic acid. It would be possible to denote this acid as (±)-*trans*-4aβ-decalin-1α-carboxylic acid, thus defining the convention in the name, but we omit that refinement in the text of this paper. This convention is in effect the same as that used by Moritani *et al.*[11] and by Henbest *et al.* (*J.*, 1961, 4478) for similar compounds.

[7] Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420.
[8] Dauben and Tweit, *J. Amer. Chem. Soc.*, 1954, **76**, 3197.
[9] Nazarov, Kucherov, and Segal, *Izvest. Akad. Nauk S.S.S.R.*, *Otdel. khim. Nauk*, 1956, 1215.
[10] Kucherov, Segal, and Nazarov, *Izvest. Akad. Nauk S.S.S.R.*, *Otdel. khim. Nauk*, 1958, 367.
[11] Moritani, Nishida, and Murakami, *J. Amer. Chem. Soc.*, 1959, **81**, 3420.
[12] Shoppee and Stephenson, *J.*, 1954, 2230.
[13] Barbier and Locquin, *Compt. rend.*, 1913, **156**, 1443; Wieland, Schlichting, and Jacobi, *Z. physiol. Chem.*, 1926, **161**, 80.
[14] Roberts and Chambers, *J. Amer. Chem. Soc.*, 1951, **73**, 5030.
[15] Cooke and MacBeth, *J.*, 1939, 1245.
[16] Stolow, *J. Amer. Chem. Soc.*, 1959, **81**, 5806.
[17] van Bekkum, Verkade, and Wepster, *Koninkl. Ned. Akad. Wetenschapp.*, *Proc. Series* B**62**, 1959, No. **3**, 147.

Nishida, and Murakami's method,[11] and was converted (four stages), by a method similar to that of Dauben, Tweit, and Mannerskantz,[7] into pure *trans*-decalin-1α-carboxylic acid.

The Grignard reagent from *trans*-1-chlorodecalin was prepared by reaction with magnesium turnings (Eastman Kodak Co.) in dry tetrahydrofuran and carbonated (yield of crude acid 34%). Magnesium turnings from U.K. sources failed to work successfully and yields of only 3—4% were obtained.[18] The pure *trans*-decalin-1α-carboxylic acid had m. p. 103—104° (lit.,[7] 99·5—100·4°) (Found: C, 72·6; H, 9·7. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·95%). From 1800 g. of 1-naphthol 26·5 g. of pure acid was obtained, an overall yield of 1·16%.

trans-*Decalin*-1β-*carboxylic Acid.*—*trans*-1α-Decalol was prepared as described above and converted by Tipson's method [19] into the toluene-*p*-sulphonate, m. p. 97—99° (lit.,[11] 97—98°). The remaining stages were similar to a procedure used by Shoppee and Stephenson [12] with steroidal toluene-*p*-sulphonates.

trans-1β-*Decalylmalonic acid. trans*-1α-Decalyl toluene-*p*-sulphonate (73·4 g.) in dry toluene (900 ml.) was added to a solution of diethyl sodiomalonate, prepared by heating sodium (15·9 g.) and diethyl malonate (127 ml.) in dry toluene (900 ml.) under reflux until all the sodium had reacted; heating at the b. p. and stirring were continued for 20 hr. Sodium toluene-*p*-sulphonate was filtered off and washed with toluene; the toluene filtrates were evaporated under reduced pressure and the residue was dissolved in ether, washed with water, and dried ($MgSO_4$). After removal of the ether, the residue was hydrolysed by 24 hours' boiling with potassium hydroxide (120 g.) in methanol (300 ml.) and water (400 ml.). The mixture was poured into water and shaken with ether to remove neutral material. The alkaline solution was acidified to Congo Red with 36% hydrochloric acid and shaken with ether, and the ethereal extracts were dried ($MgSO_4$). After removal of the ether, the residue of *trans*-1β-decalylmalonic acid (36 g., 63%) had m. p. 143° (decomp.).

trans-1β-*Decalylacetic acid. trans*-1β-Decalylmalonic acid (36 g.) was heated at 180° until evolution of gas had ceased (20 min.). The resultant solid was dissolved in 2N-sodium hydroxide and the solution was washed with ether. The alkaline solution was filtered and the filtrate was acidified to Congo Red with 36% hydrochloric acid. The acidic solution was shaken with ether and the ethereal extracts were dried ($MgSO_4$). On removal of ether, slightly impure trans-1β-*decalylacetic acid* (25 g., 85%) was obtained and had m. p. 92—94° when recrystallised from light petroleum (b. p. 60—80°) (Found: C, 73·4; H, 10·3. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%).

Methyl trans-1β-*decalyl acetate.* Ethereal diazomethane, prepared by de Boer and Backer's method,[20] was added to an ethereal solution of *trans*-1β-decalylacetic acid (10 g.). The resulting *methyl* trans-1β-*decalylacetate* (10·5 g., 98%) was distilled and had b. p. 96—98°/0·1 mm. (Found: C, 74·0; H, 10·3. $C_{13}H_{22}O_2$ requires C, 74·2; H, 10·5%).

2-(trans-1β-*Decalyl*)-1,1-*diphenylethanol.* To phenylmagnesium bromide in dry ether (300 ml.) [from magnesium turnings (13·25 g.) and bromobenzene (87·7 g.)] methyl *trans*-1β-decalylacetate (39·1 g.) in dry ether (200 ml.) was added slowly and the mixture was heated under reflux for 2 hr. It was then poured on ice (500 g.) and 2N-sulphuric acid (300 ml.). The product was subjected to steam-distillation to remove biphenyl, and the residue was shaken with ether. The ethereal extracts were washed with brine and dried ($MgSO_4$). On removal of the ether, 2-(trans-1β-*decalyl*)-1,1-*diphenylethanol* (53 g., 85%) was obtained; recrystallised from methanol, it had m. p. 114—115° (Found: C, 86·0; H, 9·1. $C_{24}H_{30}O$ requires C, 86·2; H, 9·0%).

2-(trans-1β-*Decalyl*)-1,1-*diphenylethylene.* 2-(*trans*-1β-Decalyl)-1,1-diphenylethanol (12·5 g.) in pyridine (90 ml.) was cooled in ice–salt, and redistilled thionyl chloride (20 ml.) was added. The mixture was kept at 0° for 5 min. and then at room temperature for 50 min. Water (10 ml.) was added dropwise, the mixture being cooled in ice–salt and then poured into water (300 ml.) and shaken with ether. The ethereal extracts were washed with cold 2N-hydrochloric acid, then with water, and dried ($MgSO_4$), and the ether was removed to give a light brown oil. The oil was dissolved in light petroleum (b. p. 40—60°) and filtered through alumina. The solvent was removed to give a colourless oil (10 g.). The infrared spectrum

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[18] Kharasch and Reinmuth, " Grignard Reactions of Non-metallic Substances," Prentice-Hall, New York, 1954, p. 6.

[19] Tipson, *J. Org. Chem.*, 1944, **9**, 235.

[20] de Boer and Backer, *Rec. Trav. chim.*, 1954, **73**, 229.

showed that no alcohol or ether was present, but no conclusive evidence for an ethylenic linkage could be obtained.

trans-*Decalin-*1β*-carboxylic acid.* The above oily product (12·5 g.) was oxidised in chloroform (100 ml.) and glacial acetic acid (500 ml.) at room temperature with a saturated aqueous solution of chromium trioxide (33 g.). The mixture was kept overnight at room temperature, and then methanol was added to destroy the excess of chromium trioxide. The solvents were removed under reduced pressure; 2N-sulphuric acid (20 ml.) and water (300 ml.) were added, and the solution was shaken with ether. The ethereal layer was washed with brine and shaken with 2N-aqueous potassium hydroxide. The alkaline solution was filtered, acidified to Congo Red with 36% hydrochloric acid, and kept at 0° overnight. The crude acid (4·1 g.) was filtered off; after recrystallisation thrice from light petroleum (b. p. 60—80°), the pure *trans*-decalin-1β-carboxylic acid (3·9 g., 54%) had m. p. 127·5—129° (lit.,[10] 127°) (Found: C, 72·3; H, 9·75. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·95%). From 450 g. of 1-naphthol 22·3 g. of pure acid was obtained; an overall yield of 3·92%.

trans-*Decalin-*2α*-carboxylic Acid.*—*trans*-2β-Decalyl toluene-*p*-sulphonate was prepared as described by Moritani, Nishida, and Murakami,[11] except that 2-oxo-$\Delta^{1,9}$-octalin was reduced with sodium in liquid ammonia. The *trans*-2β-decalyl toluene-*p*-sulphonate had m. p. 61—63·5° (lit.,[11] 62·5—63°).

The remaining stages were essentially those described above for the preparation of *trans*-decalin-1β-carboxylic acid. *trans*-2α-Decalylmalonic acid (73% yield from the toluene-*p*-sulphonate) had m. p. 90° (decomp.); trans-2α*-decalylacetic acid* (89%) was recrystallised from light petroleum (b. p. 60—80°) and had m. p. 77—78·5° (Found: C, 73·7; H, 10·2. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%). Methyl *trans*-2α-decalyl acetate (97%) had b. p. 142—144°/15 mm. 2-(*trans*-2α-Decalyl)-1,1-diphenylethanol (90%) did not crystallise and was obtained as a pale yellow glass, but 2-(trans-2α*-decalyl*)-1,1*-diphenylethylene* (89%) was recrystallised from glacial acetic acid and had m. p. 80·5—82° (Found: C, 90·8; H, 8·8. $C_{24}H_{28}$ requires C, 91·1; H, 8·9%). Crude trans-*decalin-*2α*-carboxylic acid* (82%) was decolourised with charcoal in methanol and recrystallised from aqueous acetic acid, then having m. p. 80—81° (yield 36%) (Found: C, 72·6; H, 10·2. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·95%).

From cyclohexanone (1500 g.) 29·5 g. of pure *trans*-decalin-2α-carboxylic acid was obtained; an overall yield of 1·06%. The *trans*-decalin-2α-carboxylic acid was converted into the amine by a Schmidt reaction,[7] and the crude amine was converted into the benzoyl derivative which was recrystallised from ethanol. The benzoyl derivative of the axial amine had m. p. 177—178° (lit.,[7] 177°) (Found: C, 79·0; H, 8·9; N, 5·7. Calc. for $C_{17}H_{23}NO$: C, 79·3; H, 9·0; N, 5·4%).

trans-*Decalin-*2β*-carboxylic Acid.*—This was prepared by Dauben and Tweit's method.[8] Magnesium turnings from U.K. sources failed completely to give the Grignard reagent from mixed *trans*-chlorodecalins, so magnesium turnings from Eastman Kodak Ltd., U.S.A., were again used. The crude acid was recrystallised five times from light petroleum (b. p. 60—80°), to give pure *trans*-decalin-2β-carboxylic acid, m. p. 105—106° (lit.,[8] 105—106°) (Found: C, 72·3; H, 9·8. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·95%). From 1334 g. of decalin, 13·5 g. of pure *trans*-decalin-2β-carboxylic acid was obtained; an overall yield of 0·77%.

Purity.—The purity of each carboxylic acid was checked by three methods. (*a*) The neutralisation equivalents were determined, and indicated purities of 100 ± 0·2%. (*b*) Carbon and hydrogen analyses were satisfactory. (*c*) Small amounts of the acids were esterified with ethereal diazomethane and, after evaporation of the ether, the residues were analysed by vapour-phase chromatography, with an alkali-washed Celite column and 12% of Apiezon L as stationary phase. All the acids gave single peaks.

Solvent.—Pure ethanol was prepared by Lund and Bjerrum's method,[21] and had b. p. 78·5°/760 mm., n_D^{20} 1·3606 (lit.,[22] b. p. 78·33°/760 mm., n_D^{20} 1·3614).

Reagent.—Diazodiphenylmethane was prepared by oxidation of benzophenone hydrazone as described by Smith and Howard.[23] This crude product (m. p. 27—29°) was pure enough for the kinetic measurements and was immediately dissolved in dry ethanol to give an ~0·008M-solution.

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[21] Lund and Bjerrum, *Ber.*, 1931, **64**, 210.

[22] Weissberger, Proskauer, Riddick, and Toops, " Organic Solvents," Interscience Publ., Inc., New York, 1955, p. 91.

[23] Smith and Howard, *Org. Synth.*, 1944, **24**, 53.

Diazodiphenylmethane reacts with ethanol in the presence of acid, as well as with the acid itself.[6] The ratio (R) of the amount of diazodiphenylmethane consumed in the reaction with each acid to the total amount consumed was determined as described previously.[24] For this purpose diazodiphenylmethane was recrystallised from methanol, and its purity checked by treating it with AnalaR benzoic acid in AnalaR ether. The average value of R for allthe acids was 60·5% at 25°, with a maximum deviation of 1·5%.

Kinetic Procedure.—This has been described by Smith and Hunt,[5] and by Chapman, Shorter, and Utley.[24] The concentration of the acid was 0·0300M, and the concentration of the diazodiphenylmethane was 0·00400M. The optical density of the solution was determined throughout the reaction at 525 mμ, with pure ethanol in the standard cell, by using a Unicam S.P. 500 spectrophotometer. In most experiments 10—15 samples were taken and the results gave an excellent linear plot of log (optical density) against time. The first-order rate coefficient thus obtained was divided by the acid concentration to give a second-order coefficient.

DISCUSSION

Conformational Equilibrium Constant for Cyclohexanecarboxylic Acid in Ethanol.—The rate coefficients for the esterification of the monocarboxylic acids in pure ethanol are given in Table 1. At 30° the ratio of rate coefficients for equatorial and axial carboxyl groups, as given by the results for *trans*- and *cis*-4-t-butylcyclohexanecarboxylic acid is 1·49; and as given by the results for *trans*-decalin-2β- and -2α-carboxylic acid is 1·56; these ratios are considerably less than the value obtained from the kinetics of acid-catalysed hydrolysis[1] of the methoxycarbonyl group (4·8) in 1 : 1 dioxan–water at 90°, and still less than that obtained for the corresponding alkaline hydrolysis[2] (17·1) at 29·4°. The value of the ratio is reduced, at least in part, because the environment of an axial carboxyl group, which is more congested than that of an equatorial carboxyl group, is not so congested when a position two bond-lengths removed from the ring is considered as when carbonyl-carbon (one bond-length from the ring) is considered. However, the different susceptibilities of the two reactions to steric effects are probably superimposed upon this.

TABLE 1.

Rate coefficients (l. mole^{-1} sec.$^{-1}$) for esterification with diazodiphenylmethane in dry ethanol [water content (Karl Fischer titration), 0·05%].

	10^3k						
Acid	15·0°	25·0°	35·0°	45·0°	30·0° *	E (kcal./mole)	log A
Cyclohexanecarboxylic acids							
Parent	1·49	3·76	9·02	19·7	5·86	15·75	9·12
cis-4-t-Butyl	1·05	2·72	6·52	14·9	4·26	16·1	9·24
trans-4-t-Butyl	1·61	4·20	9·69	21·5	6·34	15·7	9·14
trans-*Decalincarboxylic acids*							
-1α-	2·01	5·06	12·0	26·4	7·83	15·7	9·21
-1β-	0·697	1·75	4·36	9·48	2·77	15·95	8·94
-2α-	1·00	2·53	6·44	14·3	4·09	16·3	9·35
-2β-	1·61	4·13	9·96	21·4	6·38	15·7	9·11

The rate coefficients are uncorrected for the reaction of diazodiphenylmethane with the solvent Such a correction is not necessary since R (see above) is the same for all the acids at 25° and Smith and Hunt[5] showed that R does not vary with temperature for the cyclohexanedicarboxylic acids.

* Calculated from Arrhenius parameters.

The rate coefficients were usually determined in duplicate and were reproducible within about 2%. Values of E are accurate to ±300 cal./mole, and those of log A to ±0·2 unit.

The conformational equilibrium constant for cyclohexanecarboxylic acid at 30°, as calculated from these results by Eliel's method,[4] is $K = 3{\cdot}33$, corresponding to 77% of equatorial carboxyl group. This value for the proportion of equatorial carboxyl group in

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[24] Chapman, Shorter, and Utley, *J.*, 1962, 1824.

cyclohexanecarboxylic acid is rather lower than that (100%) for the equatorial methoxycarbonyl group of methyl cyclohexanecarboxylate, as measured in acid-catalysed hydrolysis in 1 : 1 dioxan–water.[1] Any polar effect of the t-butyl group would retard the reaction and if allowance were made for this effect, the values of the conformational equilibrium constant and of the percentage of equatorial group would be even less. Smith and Hunt's work,[5] in conjunction with the present work, shows that the 4-methoxycarbonyl or 4-carboxyl group exerts a polar effect, relative to the 4-t-butyl group, on the 1-carboxyl group in this reaction; *e.g.*, the rate coefficients at 25° for the reactions of *trans*-4-t-butylcyclohexanecarboxylic acid and *trans*-cyclohexane-1,4-dicarboxylic acid (two equatorial carboxyl groups) are $4{\cdot}20 \times 10^{-3}$ and $11{\cdot}3 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$, respectively. (All rate coefficients mentioned henceforth are in l. mole^{-1} sec.$^{-1}$.) Siegel and Komarmy[25] also showed that a polar effect is observed in the reactions of *trans*-4-X-cyclohexanecarboxylic acids with diazodiphenylmethane in ethanol; *e.g.*, the rate coefficients at 24·9° for *trans*-4-hydroxy- and *trans*-4-cyanocyclohexanecarboxylic acid are $4{\cdot}84 \times 10^{-3}$ and $6{\cdot}22 \times 10^{-3}$, respectively.

In spite of these cases showing polar effects of substituents, it appears that the 4-t-butyl group exerts no noticeable polar effect on the 1-carboxyl group in this reaction. There are two lines of evidence in favour of this.

(*a*) The rate coefficients for the reactions of *cis*- and *trans*-4-t-butylcyclohexanecarboxylic acid are extremely close to the values obtained for the reactions of *trans*-decalin-2α- and -2β-carboxylic acid, respectively. This may mean either that the polar effects in the t-butyl and the decalin compounds are extremely small, or that they are appreciable but very similar; the latter possibility is rather unlikely.

(*b*) Although a considerable proportion of cyclohexanecarboxylic acid in ethanol has axial carboxyl groups, it seems likely that the proportion of diaxial conformation in *trans*-4-X-cyclohexanecarboxylic acid will be very small. If it is assumed that the acids studied by Siegel and Komarmy exist essentially in the diequatorial conformation, it should then be possible to correlate the rate coefficients they obtained with the polar constants, σ', of the substituents in the 4-position of a saturated cyclic system as calculated by Roberts and Moreland[26] from the reactions of the 4-X-bicyclo[2,2,2]octane-1-carboxylic acids and their esters. Extrapolating to $\sigma' = 0$ should then give the rate coefficient for an equatorial acid group subject to no polar effects. The substituents that are common to Roberts and Moreland's and to Siegel and Komarmy's studies are given in Table 2. Roberts and Moreland give the σ'-values for the ethoxycarbonyl and bromo-substituents whereas the methoxycarbonyl and chloro-substituents were investigated by Siegel and Komarmy, but the differences in σ' between ethoxycarbonyl and methoxycarbonyl, and between bromo- and chloro-substituents, should be very small. (The electron-attracting powers of chlorine and bromine as indicated by the strengths of monochloroacetic and monobromoacetic acid differ but slightly.[27])

TABLE 2.

Rate coefficients (l. mole^{-1} sec.$^{-1}$) for the esterification of certain *trans*-4-X-cyclohexanecarboxylic acids with diazodiphenylmethane in ethanol at 24·9°, and the substituent constants for the group (X) in the 4-bicyclo[2,2,2]octyl-1 system.

X	H	OH	CO_2Me	Cl	CN
10^3k_2 (from ref. 25)	3·57	4·84	4·95	5·64	6·22
σ' (from ref. 20)	0·000	0·283	0·297 *	0·454 †	0·579

* Et instead of Me. † Br instead of Cl.

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[25] Siegel and Komarmy, *J. Amer. Chem. Soc.*, 1960, **82**, 2547.

[26] Roberts and Moreland, *J. Amer. Chem. Soc.*, 1953, **75**, 2167.

[27] Kortüm, Vogel, and Andrussow (I.U.P.A.C.), "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworths, London, 1961.

A graph of log 10^3k_2 (24·9°) against σ' was plotted and the straight line obtained was extrapolated to $\sigma' = 0$ (see Figure). This gave log $10^3k_2 = 0{\cdot}587$, and therefore the rate coefficient for an equatorial acid group, subject to no polar effect, is $k_2 = 3{\cdot}86 \times 10^{-3}$. The observed value (Siegel and Komarmy [25]) for cyclohexanecarboxylic acid is $3{\cdot}57 \times 10^{-3}$, lower than the calculated value, and this suggests that, in ethanol, there is an appreciable proportion of the acid with an axial carboxyl group.

The rate coefficient for *trans*-4-t-butylcyclohexanecarboxylic acid at 24·9° obtained in the present work is $4{\cdot}00 \times 10^{-3}$, which is about 3% greater than the value calculated above (from Siegel and Komarmy's results) for an equatorial carboxyl group. This difference is not significant, since the rate coefficients are rather sensitive to traces of moisture in the ethanol,[6] and our value for cyclohexanecarboxylic acid at 24·9° is $3{\cdot}68 \times 10^{-3}$, which is also about 3% greater than Siegel and Komarmy's value, $3{\cdot}57 \times 10^{-3}$.

The polar effect of the 4-t-butyl group in the esterification with diazodiphenylmethane thus appears negligible, and therefore Eliel's simple equation can be used, as above, to calculate the conformational equilibrium constant, K (3·33), and the proportion (77%) of equatorial acid group for cyclohexanecarboxylic acid in ethanol at 30°. This suggests, by comparison with the values from acid-catalysed hydrolysis, that the carboxyl group in ethanol is effectively smaller than the methoxycarbonyl group in 1 : 1 dioxan–water,[1] and this may be due to the methoxycarbonyl group's being more strongly solvated in the aqueous solvent than the carboxyl group in the non-aqueous solvent.

The dissociation constants of certain cyclohexanecarboxylic acids in various solvents have been measured recently, and some of the values reported are shown in Table 3. In each solvent the *cis*-acid is much weaker than the *trans*-acid and this is due to steric inhibition of solvation in the *cis*-anion. If we assume that there is no polar effect of the t-butyl group influencing the dissociation constants, it appears that cyclohexanecarboxylic acid has almost 100% of its carboxyl groups equatorial; possibly solvation of the carboxyl group in aqueous solvents makes it larger than in non-aqueous solvents such as ethanol (see above). However, the values of the dissociation constants of *trans*-4-alkylcyclohexanecarboxylic acids in 50% v/v ethanol–water at 25° reported by van Bekkum, Verkade, and Wepster [28] indicate that there may be a balance between the 4-alkyl group increasing the proportion of equatorial 1-carboxyl group (lowering pK_a by a steric effect) and the 4-alkyl group influencing the acidity by a polar effect (raising pK_a); the pK_a values for the unsubstituted, *trans*-4-methyl, *trans*-4-ethyl, *trans*-4-isopropyl, and *trans*-4-t-butyl acids are 6·30, 6·26, 6·28, 6·26, and 6·28, respectively. The possibility of polar effects of these alkyl groups in acid dissociation is not incompatible with the absence of a polar effect of the 4-t-butyl group in the esterification with diazodiphenylmethane in ethanol (see above) as the latter reaction appears to be less sensitive to polar effects than the ionisation of acids. Siegel and Komarmy [25] give a value of 1·490 for ρ'' (polar susceptibility constant) for the ionisation of acids in 50% v/v aqueous ethanol, and a ρ'' value of 0·540 for the esterification of acids with diazodiphenylmethane in ethanol. This suggests that the ionisation of acids in solvents containing comparable amounts of organic component and

TABLE 3.

Dissociation constants (pK_a) of cyclohexanecarboxylic acids.

	A	B	C
Cyclohexanecarboxylic acid	7·43	7·82	6·30
trans-4-t-Butylcyclohexanecarboxylic acid	7·43	7·79	6·28
cis-4-t-Butylcyclohexanecarboxylic acid	7·91	8·23	6·78

(A) In 80% methyl cellosolve–20% water at 20° (Tichý, Jonáš, and Sicher, *Coll. Czech. Chem. Comm.*, 1959, **24**, 3434). (B) In 66% dimethylformamide–34% water at 25°.[16] (C) In 50% v/v ethanol–water at 25°.[28]

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[28] van Bekkum, Verkade, and Wepster, *Proc., k. ned. Akad. Wetenschap.*, 1961, B**64**, No. 1, 161.

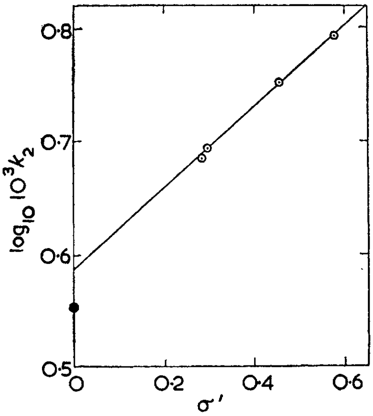
water is about three times more sensitive to polar effects than the esterification of acids with diazodiphenylmethane in ethanol. If a polar effect of the 4-alkyl group does influence the dissociation of the 1-carboxyl group in aqueous solvents, the percentage of equatorial carboxyl group in cyclohexanecarboxylic acid in these solvents is probably not so high as appears at first sight.

Activation Energies and log *A Values.*—For all the acids studied, the activation energies and log *A* values do not vary very greatly (see Table 1), ranging only from 15·7 to 16·3 kcal.

Relationship between the rate of reaction of *trans*-4-X-cyclohexanecarboxylic acids with diazodiphenylmethane and the polar effect of X.

○ Experimental points for *trans*-4-X-cyclohexanecarboxylic acids.

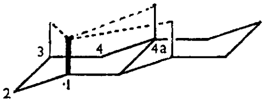
● Experimental point for cyclohexanecarboxylic acid.



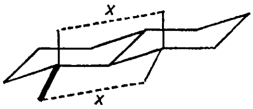
mole^{-1}, and from 8·94 to 9·35 units, respectively. The values for *cis*-4-t-butylcyclohexanecarboxylic acid and *trans*-decalin-2α-carboxylic acid, and for *trans*-4-t-butylcyclohexanecarboxylic acid and *trans*-decalin-2β-carboxylic acid are very similar, with the cyclohexanecarboxylic acid values lying very close to those of the compounds with equatorial acid groups. The compound with an equatorial acid group usually has the lower activation energy and lower log *A* value.

trans-*Decalin-carboxylic Acids.*—The *trans*-decalin-2-carboxylic acids give rate coefficients, activation energies, and log *A* values which agree very closely with their 4-t-butylcyclohexanecarboxylic acid counterparts.

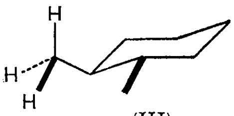
trans-Decalin-1β-carboxylic acid has an axial acid group subject to three " 1,3-axial hydrogen atom " interactions [see (I)], compared with two interactions for an axial group in the cyclohexane ring. It is thus not surprising that the rate coefficient for the 1-axial compound at 30° (2·77 × 10^{-3}) is lower than that for the 2-axial compound (4·09 × 10^{-3}).



(I) 1-Axial; 1β



(II) 1-Equatorial; 1α



(III)

trans-Decalin-1α-carboxylic acid has an equatorial acid group which is influenced by an interaction with the equatorial hydrogen atom at the 8-position [see (II)]; this equatorial–equatorial interaction is not present in cyclohexane compounds. The distance (*x*) between the 1-equatorial carboxyl group and the 8-equatorial hydrogen atom is the same as the distance between the 1-axial carboxyl group and the 8-axial hydrogen atom, *i.e.*, the distance of a normal axial–axial interaction.

For this reason the *trans*-decalin-1α-carboxylic acid might have been expected to show a reactivity intermediate between that of equatorial and axial carboxyl groups in the 2-position, *i.e.*, a rate coefficient at 30° between 6·38 and 4·09 × 10^{-3}. The observed rate coefficient is $7{\cdot}83 \times 10^{-3}$ which is about 20% higher than that of the 2-equatorial carboxyl group. Wepster and his co-workers have shown that *trans*-2-methylcyclohexanecarboxylic acid has a pK_a of 6·24 (in 50% (v/v) ethanol–water at 25°), which is lower than the pK_a of *trans*-4-methylcyclohexanecarboxylic acid (6·26) and the unsubstituted acid (6·30), and is in fact lower than that of any alkyl-substituted acid they studied.[28] The high rate coefficient of the *trans*-decalin-1α-carboxylic acid in esterification with diazodiphenylmethane, may be related to the enhanced acid strength of the *trans*-2-methylcyclohexanecarboxylic acid, as the carboxyl group of the *trans*-2-methylcyclohexanecarboxylic acid is in the same position relative to the hydrogen atom of the methyl group [see (III)] as the carboxyl group of *trans*-decalin-1α-carboxylic acid is to the 8-equatorial hydrogen atom [see (II)]. Further discussion of this point must await the results of measurements of pK_a for the *trans*-decalincarboxylic acids at present being undertaken by Ir. van Bekkum and Professor Wepster in Delft.

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