The above mixture of ester, acid, and lactide was esterified with methanol containing 1% of sulfuric acid and the crude esterification product was worked up as above. Vacuum distillation gave 23.3 g (83%) of methyl 2-hydroxyundecanoate, bp 80–82° (0.3 mm).

Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.6; H, 11.2; O, 22.2. Found: C, 66.9; H, 11.4; O, 22.3.

The nmr spectrum ($CDCl_3$) is characterized by a hydroxyl doublet at τ 7.32 (1 H), a methoxyl singlet at τ 6.27 (3 H), and a methinyl multiplet at τ 5.9 (1 H). Upon deuterium exchange, the doublet disappeared and the multiplet collapsed to a triplet. The spectrum of the product obtained from this reaction was essentially identical with the spectrum of an authentic sample of methyl 2-hydroxypalmitate.

The nmr spectrum of the product obtained from the reaction in which deuterium oxide was used instead of water was unchanged from the spectrum of the normal product. The area of the multiplet at τ 5.9 remained equivalent to one proton showing that no deuterium had been incorporated at the methinyl carbon.

ω,ω-Dideuterio-ω-(methylsulfinyl)acetophenone.—A mixture of 6.0 g (0.033 mole) of ω-methylsulfinylacetophenone, 2 drops of a 25% solution of sodium deuteroxide in deuterium oxide, and 20 ml of deuterium oxide was stirred overnight at room temperature. The mixture was then extracted with chloroform and the combined extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by recrystallization from 50 ml of a 1:1 mixture of benzene–hexane gave 5.3 g of the dideuterated sulfoxide.

The nmr spectrum of the starting material (CCl_4 solution) showed resonance at τ 1.9–2.7 (aromatic), 5.78 (methylene), and 7.32 (methyl). The spectrum of the product was free of the τ 5.78 resonance.

ω-Deuterio-ω,ω-(dimethoxy)acetophenone (4).—The Pummerer rearrangement of 3.7 g (0.020 mole) of ω,ω-dideuterio-ω-(methylsulfinyl)acetophenone was carried out as described previously[3] with 2.7 g (0.011 mole) of iodine in 30 ml of methanol-d_1. Part of the product was distilled, bp 79° (1.5 mm), and another part was purified by gas chromatography. The chromatographed material was analyzed by mass spectroscopy and was found to consist of 97% of the monodeuterated and 3% of the undeuterated α-keto acetal.

Reaction of Stannic Chloride with a Mixture of ω-Deuterio-ω,ω-(dimethoxy)acetophenone and 1,1-Dimethoxyundecan-2-one.—This reaction was performed as described above using 0.45 g (0.0025 mole) of ω-deuterio-ω,ω-(dimethoxy)acetophenone, 0.58 g (0.0025 mole) of 1,1-dimethoxyundecan-2-one, 1.3 g (0.59 ml, 0.005 mole) of anhydrous stannic chloride, and 0.63 g (0.035 mole) of water in 20 ml of dry dioxane. After esterification, the aliphatic and aromatic hydroxy esters were separated by gas chromatography and each was analyzed by nmr.

The nmr spectrum of the aliphatic hydroxy ester showed a multiplet at τ 5.9 (HCO), the area of which was equivalent to one (full) proton. The level of methinyl proton in the aromatic hydroxy ester was determined by comparing the area of the HCO peak in the nmr spectrum with the area of the C^{13} satellite of the CH_3O peak. This analysis was made with the aid of a Varian C-1024 time-averaging computer and showed that less than 2% of undeuterated aromatic hydroxy ester was present.[12]

Rearrangement of Benzil Dimethyl Ketal.—Benzil dimethyl ketal[13] (2.0 g, 0.0078 mole), 6.0 g (2.6 ml, 0.023 mole) of stannic chloride, and 0.99 g (0.055 mole) of water reacted in 20 ml of dry dioxane according to the general procedure described for the rearrangement of α-keto acetals. The esterification product (1.7 g) was found by infrared spectroscopy and gas and thin layer chromatography to consist of both benzil and methyl benzilate. Quantitative thin layer chromatography, using appropriate standard mixtures, indicated that the sample contained 20–25% of methyl benzilate. This represents an 18–22% yield of the ester.

Registry No.—2, 14919-24-5; 5, 14919-25-6; 1,1-dimethoxyundecan-2-one, 13133-49-8; ω,ω-dideuterio-ω-(methylsulfinyl)acetophenone, 7714-34-3.

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(12) The author wishes to thank Dr. J. J. McLeskey, III, for this analysis.
(13) R. Kuhn and H. Trischmann, *Chem. Ber.*, **94**, 2258 (1961).

Conformational Studies in the Ethyl 3-*t*-Butylcyclobutanecarboxylate System[1]

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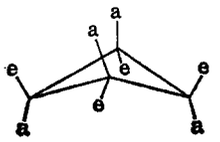
The syntheses of ethyl *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylates and the corresponding carboxylic acids are reported. The conformational studies made on these compounds are basic equilibration and rates of saponification of the esters and ionization constants of the acids. The results are explained on the basis of both planar and nonplanar conformers.

The cyclobutane ring has been shown to be nonplanar in a large number of cases such as cyclobutane,[2–5] octafluorocyclobutane,[6] octachlorocyclobutane,[7] *gem*-difluorocyclobutanes,[8] bromocyclobutane,[9] chlorocyclobutane,[10] methyl 3-methylcyclobutanecarboxylate,[11] 3-isopropylcyclobutyl alcohols and amines,[12] methyl 3-isopropylcyclobutanecarboxylate,[13] 2,2,4,4-tetramethylcyclobutane-1,3-dinitrile,[14] 1,3-dibromocyclobutane,[15] and *cis*-1,3-cyclobutanedicarboxylic acid.[16b] The nonplanar conformations lead to axial and equatorial positions similar to those of cyclohexane as indicated in Chart I.[17] However, whereas the

(1) Presented in part at the 20th Northwest Regional Meeting of the American Chemical Society, Corvallis, Ore., June 1965.
(2) J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952).
(3) G. W. Rathjens, Jr., N. K. Freeman, W. D. Gwinn, and K. S. Pitzer, *J. Am. Chem. Soc.*, **75**, 5634 (1953).
(4) R. C. Lord and I. Nakagawa, *J. Chem. Phys.*, **39**, 2951 (1963).
(5) S. Meiboom and L. C. Snyder, *J. Am. Chem. Soc.*, **89**, 1038 (1967).
(6) H. P. Lemaire and R. L. Livingston, *ibid.*, **74**, 5732 (1952).
(7) T. B. Owen and J. L. Hoard, *Acta Cryst.*, **4**, 172 (1951).
(8) J. B. Lambert and J. D. Roberts, *J. Am. Chem. Soc.*, **87**, 3884, 3891 (1965).
(9) (a) W. G. Rothschild and B. P. Dailey, *J. Chem. Phys.*, **36**, 2931 (1962); (b) W. G. Rothschild, *ibid.*, **45**, 1214 (1966).
(10) H. Kim and W. D. Gwinn, *ibid.*, **44**, 865 (1966).
(11) N. L. Allinger and L. A. Tushaus, *J. Org. Chem.*, **30**, 1945 (1965).
(12) I. Lillien and R. A. Doughty, *J. Am. Chem. Soc.*, **89**, 155 (1967).
(13) I. Lillien and R. A. Doughty, *Tetrahedron*, **23**, 3321 (1967).
(14) F. Lautenschlaeger and G. F. Wright, *Can. J. Chem.*, **41**, 863 (1963).
(15) K. B. Wiberg and G. M. Lampman, *J. Am. Chem. Soc.*, **88**, 4429 (1966).
(16) (a) T. N. Margulis and M. S. Fischer, *J. Am. Chem. Soc.*, **89**, 223 (1967); (b) E. Adman and T. N. Margulis, *Chem. Commun.*, 641 (1967).
(17) The Dreiding model of cyclobutane has been used. The bond angles are as follows: C–C–C, 88°; H–C–H, 113°; dihedral angle, 26°; bond lengths for C–C bonds in ring, 1.54 A. These values closely approximate the values obtained for bromocyclobutane, ref 9a.

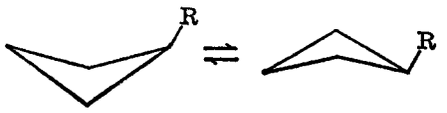
CHART I
AXIAL AND EQUATORIAL POSITIONS IN CYCLOBUTANE



conformational problems associated with the cyclohexane ring have been explored in detail,[18,19] relatively little is known about the cyclobutane derivatives.[8-15]

Certain problems arise in studying conformational effects in cyclobutanes that are not present or are reduced in cyclohexane. While the cyclohexane ring appears to maintain similar dihedral angles for axial and equatorial groups in substituted cyclohexanes, the dihedral angle in cyclobutane appears to be quite sensitive to the position of substitution on the ring. Thus, the axial conformer shown in Chart II has been shown

CHART II
CONFORMATIONAL EQUILIBRIUM IN SUBSTITUTED NONPLANAR CYCLOBUTANE



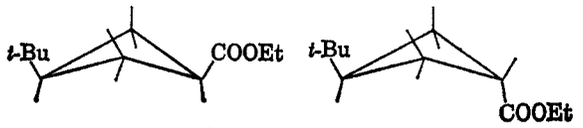
axial equatorial

to be nearly planar or planar for bromocyclobutane,[9b] *gem*-difluorocyclobutanes,[8] methyl *trans*-3-isopropylcyclobutanecarboxylate,[13] and *trans*-1,3-cyclobutanedicarboxylic acid.[16a] A planar axial conformer reduces the 1,3 interaction and angle strain[15] at the expense of increased torsional strain[15] and 1,2 interactions. However, significantly nonplanar axial conformers have been observed for *trans*-2,2,4,4-tetramethylcyclobutane-1,3-dinitrile[14] and *trans*-1,3-dibromocyclobutane.[15,20] Thus, it appears that an axial conformer may vary anywhere from a planar structure[16a] to a nonplanar one with a dihedral angle of about 34°.[15,20]

On the other hand, an equatorial conformer appears to be nonplanar as shown in Chart II at least at room temperature. Dihedral angles have been reported which vary from about 20[10] to 34°.[15,20] A nonplanar conformation may result from more satisfactory torsional angles[15] and 1,2 interactions than those for a planar conformation. Thus, it is possible that the equatorial and axial conformers may differ greatly in the degree of ring puckering.

In this paper, the syntheses of ethyl *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylates and the corresponding carboxylic acids are described. It is of interest to carry out conformational studies on these compounds such as basic equilibration and rates of saponification of the esters and ionization constants of the acids. The conformations shown in Chart III result if the *t*-butyl group is used as a holding group to fix the con-

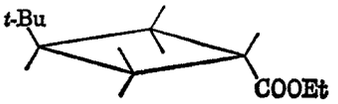
CHART III
NONPLANAR CONFORMATIONS OF ETHYL *cis*- AND *trans*-3-*t*-BUTYLCYCLOBUTANECARBOXYLATES



cis-equatorial *trans*-axial

formation at one carbon analogous to work done in cyclohexane.[21-23] However, the *trans* isomer is probably not puckered to the extent shown in Chart III, where serious 1,3 interactions occur but is probably intermediate between this structure and a planar one as shown in Chart IV.

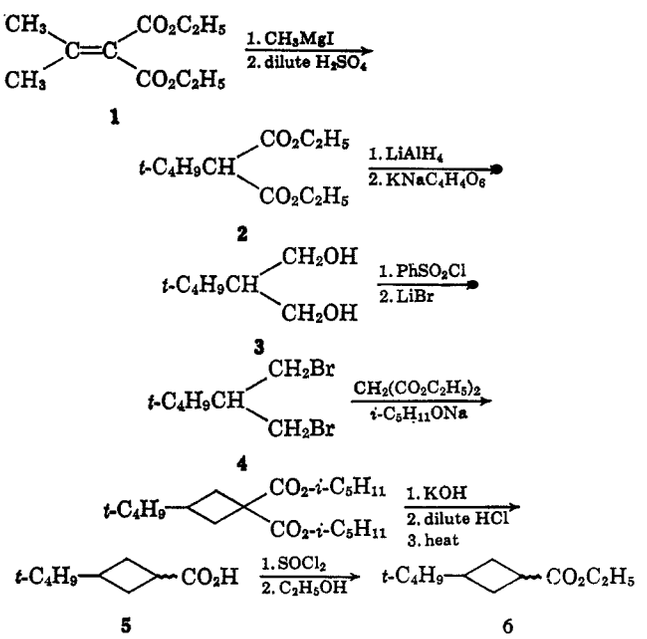
CHART IV
PLANAR CONFORMATION OF ETHYL *trans*-3-*t*-BUTYLCYCLOBUTANECARBOXYLATES



Synthetic Work

The synthesis of a mixture of the *cis* and *trans* esters is indicated in Scheme I. Methylmagnesium iodide

SCHEME I



was added 1,4 to diethyl isopropylidenemalonate (1) to give a *t*-butyl-substituted malonic ester **2**.[24] The diester was reduced with lithium aluminum hydride[25] to give the diol **3**. The dibromide **4** was prepared from the diol by means of lithium bromide on the di-

(18) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 204.

(19) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, p 36.

(20) L. Walløe and O. Bastiansen, private communication. An electron diffraction study indicated that the *cis*- and *trans*-1,3-dibromocyclobutanes were each puckered by about 33°.

(21) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(22) E. L. Eliel, H. Haubenstock, and R. V. Acharya, *ibid.*, **83**, 2351 (1961).

(23) The use of the *t*-butyl group as a holding group in kinetic and equilibrium studies has been recently criticized: J. L. Mateos, C. Perez, and H. Kwart, *Chem. Commun.*, 125 (1967); F. Shah-Malak and J. H. P. Utley, *ibid.*, 69 (1967).

(24) (a) S. Wideqvist, *Arkiv Kemi Mineral. Geol.*, **B23**, No. 4, 1 (1946); *Chem. Abstr.*, **41**, 1615*d* (1947); (b) M. T. Bush and W. D. Beauchamp, *J. Am. Chem. Soc.*, **75**, 2949 (1953).

(25) H. F. vanWoerden, *Rec. Trav. Chim.*, **82**, 920 (1963).

benzenesulfonate. Treatment of this dibromide with the anion of malonic ester, followed by saponification of the condensation product and decarboxylation give a mixture of the *cis* and *trans* acids **5**. The mixture of the acids were converted to the acid chlorides and then to a mixture of ethyl *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylates (**6**) which were separated by gas chromatography. Saponification of each of the isomers gave the separated *cis* and *trans* acids which could not be obtained directly from the mixture of acids **5**.

Peak one of a chromatograph of the esters corresponds to the *cis* isomer. This has been established in several ways. Methyl 3-methylenecyclobutanecarboxylate[26] was hydrogenated to methyl 3-methylcyclobutanecarboxylate which was in turn equilibrated with sodium methoxide. It was found that peak one was the larger as was also true with an equilibrated mixture of the 3-*t*-butyl esters. Since the *cis*-3-methyl ester is known to predominate at equilibrium,[11] the *cis*-3-*t*-butyl ester will most likely also. In addition, the equilibration of methyl 3-isopropylcyclobutanecarboxylate and analysis on the same column used in the present work (SE-30) gave a mixture where the larger peak one was again shown to be the *cis* isomer.[13]

The nuclear magnetic resonance (nmr) spectra of the esters provide some information on their stereochemistry. It has been found in many cases in cyclohexane that an equatorial proton is less shielded than the corresponding axial one.[27,28] It is convenient to observe the chemical shift for the proton on the carbon carrying the substituent since it is deshielded relative to the other ring protons and is found at low field. The same has been found true in cyclobutane in the present work. The *trans* ester (Chart III) has an equatorial proton at τ 7.20 and the *cis* ester has an axial proton at τ 7.26 consistent with the generalization. While the *trans* ester is not as puckered as shown in Chart III, the qualitative argument would probably still hold.[29]

Results and Discussion

Pure ethyl *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylates were each epimerized by means of sodium ethoxide in absolute alcohol at 80° to an equilibrium mixture of the two esters. Gas chromatographic analysis indicated that mixtures of the same composition were obtained from both esters, containing 71.1 ± 0.4% *cis* and 28.9 ± 0.4% *trans* isomers. Thus, the *cis* isomer is favored by an equilibrium constant of 71.1/28.9 or 2.46 ± 0.04. The free energy difference is −0.63 ± 0.02 kcal/mole at 80°. The greater thermodynamic stability of the *cis* isomer is readily accommodated by the structures shown in Chart III since the *trans* isomer would be destabilized by the 1,3 interaction. However, the results are also consistent with a planar *trans* isomer as shown in Chart IV where the structure is destabilized by torsional strain and 1,2 interactions. What may actually result is an axial conformation which is intermediate between a highly puckered one (Chart III) and a planar one (Chart IV). Such a structure would minimize the interactions and strain present in each of the extreme structures but would still be destabilized relative to the *cis* isomer.

Lillien and Doughty[13] have suggested that the results of the equilibration of methyl *cis*- and *trans*-3-isopropylcyclobutanecarboxylates may best be accommodated by a more nearly planar *trans* isomer and perhaps even a more nearly planar *cis* isomer. The latter suggestion could be substantiated by the observation that it requires only 1 kcal/mole to flex from the equatorial to the planar conformation in bromocyclobutane.[9b] This energy and more would be readily available in their chemical equilibration carried out at 65°. Thus, it may be possible that the *cis*-3-*t*-butyl ester may be less puckered than shown in Chart III considering the 80° equilibration temperature. In view of the apparent structural similarities between the 3-*t*-butyl esters and the 3-isopropyl esters, it is not surprising to find that the latter gave a free energy difference of −0.53 as compared to −0.63 obtained for the former.

The rates of saponification of the esters were measured. Data taken from a typical run are given in Table I.

TABLE I
SAPONIFICATION RATE OF ETHYL *cis*-3-*t*-BUTYLCYCLOBUTANECARBOXYLATE IN 70% ETHANOL AT 25.2°[a]

Time, sec	Corr titer, ml of 0.05066 *N* NaOH	*x*, mole/l.	*a* − *x*, mole/l.	Reaction, %	$k \times 10^4$, l. mole^{-1} sec^{-1}
0	6.216	0	0.02090	0	...
1545	6.750	0.00270	0.01819	13	4.61
4008	7.361	0.00580	0.01510	28	4.59
5916	7.722	0.00763	0.01327	37	4.65
7653	7.952	0.00880	0.01210	42	4.54
10035	8.248	0.01029	0.01061	49	4.63
11523	8.382	0.01097	0.00993	53	4.59
13059	8.516	0.01165	0.00925	56	4.62
14952	8.666	0.01241	0.00849	59	4.68
				Mean k =	4.61

[a] Base, 10 ml of 0.2097 *N* NaOH; ester equivalent, 0.3865 g; quench acid, 10 ml of 0.05239 *N* HCl; indicator, phenolphthalein; back titration base, 0.05066 *N* NaOH; blank, 0.094 ml; a = 0.02090 mole/l.

Table II gives a summary of the alkaline saponification rates of the *cis* and *trans* esters and ethyl cyclobutanecarboxylate in 70% aqueous ethanol at 25.2°.[22] The products of the saponification runs were shown to be the corresponding acids and therefore epimerization did not precede saponification. The *cis* isomer reacts at a faster rate than the *trans* isomer, although the difference is small. The *trans* conformations shown in Charts III and IV or an intermediate structure can accommodate such a finding. The nonplanar structure has a serious 1,3 interaction while the planar one would have repulsive 1,2 interactions. The *cis* isomer reacts more slowly than the unsubstituted ester. Since both may have equatorial carbethoxyl groups, the rate depression could be due to a steric effect of the

(26) H. N. Cripps, J. K. Williams, and W. H. Sharkey, *J. Am. Chem. Soc.*, **81**, 2723 (1959).

(27) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *ibid.*, **80**, 6098 (1958).

(28) E. L. Eliel and M. H. Gianni, *Tetrahedron Letters*, 97 (1962).

(29) The *cis*- and *trans*-3-*t*-butylcyclobutanols show a similar relationship to the 3-isopropyl alcohols,[12] again providing evidence of properly assigned stereochemistry. The preparation and equilibration of these compounds will be reported later.

TABLE II
SUMMARY OF SAPONIFICATION RUNS

Ethyl ester of acid	*a*, mole/l.	$k \times 10^3$, l. mole^{-1} sec^{-1}	Reaction, %
Cyclohexanecarboxylic	0.03122[a]	0.719 ± 0.009[a,b]	67[a]
Cyclobutanecarboxylic	0.03064[a]	7.70 ± 0.11[a]	78[a]
	0.02046	7.68 ± 0.06	69
	0.02090	7.53 ± 0.08	69
cis-3-*t*-Butylcyclobutanecarboxylic	0.02090	4.61 ± 0.03	59
	0.02043	4.67 ± 0.08	63
trans-3-*t*-Butylcyclobutanecarboxylic	0.02074	4.24 ± 0.04	58
	0.02043	4.25 ± 0.05	62

[a] These runs were carried out using 15 ml of 0.2 *N* NaOH and an equivalent amount of ester, each diluted to 50 ml of 70% ethanolic solution. Ethyl cyclobutanecarboxylate was found to saponify at too great a velocity under these conditions so that a lower initial concentration was used for most cyclobutane compounds. [b] This agreed well with previous work, 0.729×10^{-3}, ref 22.

t-butyl group interfering with the developing tetrahedral activated complex, but a more planar ring for the *cis* ester than present in the unsubstituted ester would cause a rate depression. In addition, an inductive effect of the *t*-butyl group may also account for the decreased reactivity of the *cis* and *trans* esters relative to the unsubstituted ester. Thus, a steric and/or inductive effect may be used to explain these results.

Table III gives a summary of the ionization constants of the *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylic acids and cyclobutanecarboxylic acid measured in 80% aqueous methyl cellosolve at 25.0°.[30] The *cis* isomer is more acidic than the *trans* isomer, although the difference is again small as found for the saponification of the esters. Likewise, the unsubstituted acid is more acidic than the *cis* acid. Both of these results may be explained in the same way as the ester saponification, except that a solvated anion would be substituted for a tetrahedral activated complex.

TABLE III
SUMMARY OF IONIZATION CONSTANTS IN 80% METHYL CELLOSOLVE AT 25.0°

Acid	pK_a	$K_a \times 10^5$
Cyclohexanecarboxylic	7.48 ± 0.01[a,b]	3.3 ± 0.1[a]
Cyclobutanecarboxylic	7.23 ± 0.01	5.9 ± 0.1
cis-3-*t*-Butylcyclobutanecarboxylic	7.34 ± 0.01	4.6 ± 0.1
trans-3-*t*-Butylcyclobutanecarboxylic	7.38 ± 0.01	4.2 ± 0.1

[a] Four 50-ml aliquots were titrated. [b] This value agreed well with previous work, 7.43, ref 30.

Although the exact degree of puckering is unknown for the isomeric esters and acids,[31] it may reasonably be assumed that the *trans* isomers are less puckered than the *cis* isomers. In addition, it seems reasonable that the *cis* isomers themselves will tend to be less puckered at a higher temperature than a lower one. In dealing with conformational effects in the cyclobutane ring, one must consider the possibility of conformations of varying dihedral angles since the system is highly flexible. The comparisons one makes with the more rigid cyclohexane ring may thus be limited.

(30) M. Tichý, J. Jonáš, and J. Sicher, *Collection Czech. Chem. Commun.*, **24**, 3434 (1959).

(31) It would be of considerable interest to investigate the solid *trans* acid by X-ray analysis. This is currently being tried.

Experimental Section

Diethyl *t*-Butylmalonate (2).—In a 3-l. three-necked flask, fitted with a stirrer, reflux condenser, and an addition funnel were placed 40.2 g (1.68 g-atoms) of magnesium turnings and 300 ml of dry ether. A solution of 240 g (1.69 moles) of methyl iodide dissolved in 240 ml of dry ether was added slowly to the flask with cooling and stirring. The ice bath was removed after the addition and the flask was heated under reflux for 15 min to give methylmagnesium iodide. To the cooled solution was added slowly with stirring 300 g (1.50 moles) of diethyl isopropylidenemalonate[32] (1) in 300 ml of dry ether. After the addition was complete, the ice bath was removed and the flask was heated under reflux for 20 min. The flask was cooled in an ice bath while 450 ml of an ice–water mixture was added to decompose the mixture in the flask. Dilute sulfuric acid was added until the contents were acidic to litmus. The two layers were separated and the water layer was extracted three times with 100-ml portions of ether. The organic layers were combined and washed with five 75-ml portions of a saturated aqueous solution of sodium bisulfite to reduce the free iodine. After drying over anhydrous magnesium sulfate, the ether was removed under vacuum and the residue was distilled to give 206 g (64%) of diethyl *t*-butylmalonate, bp 90–105° (9 mm), lit.[24] bp 98–101° (10 mm). During some of the distillations of this product, iodine was formed. This could be removed by repeating the washing procedure above and then redistilling the product.

2-*t*-Butyl-1,3-propanediol (3).—In a 1-l. three-necked flask, fitted with a stirrer, reflux condenser, and an addition funnel were placed 55.5 g (1.46 moles) of lithium aluminum hydride and 300 ml of dry ether. The flask was cooled in an ice bath as a solution of 200 g (0.93 mole) of **2** in 300 ml of dry ether was added slowly with stirring. The ice bath was removed and the flask was heated under reflux for 30 min. To the mixture was added slowly with cooling and stirring 30 wt % aqueous potassium sodium tartrate until the gray solid was replaced by a white solid (tartrate complex) and no aqueous layer was formed. The resulting tartrate complex was filtered from the ether solution of **3**. The complex was found to contain a considerable amount of **3** but this was removed by extraction with ether in a Soxhlet extractor for 36 hr. The extracts were combined with the ether solution and dried over magnesium sulfate. Following removal of the ether under vacuum, the residual semisolid was distilled through an air-cooled condenser to give 82.2 g (67.2%) of 2-*t*-butyl-1,3-propanediol, bp 117–127° (9–10 mm), a liquid that readily solidified. Recrystalization of a sample of this from benzene gave white crystals, mp 56.5–56.8°, lit.[25] mp 58–59°. *Anal.* Calcd for $C_7H_{16}O_2$: C, 63.6; H, 12.2. Found: C, 63.6; H, 12.2. Nmr (CCl_4)[33] gave τ 9.08, 8.52, 6.24, and 5.75, with ratio 9:1:4:2.

2-*t*-Butyl-1,3-dibromopropane (4).—The dibenzenesulfonate of 2-*t*-butyl-1,3-propanediol was first made by the following procedure. In a 2-l. flask were placed 90.0 g (0.72 mole) of **3** and 251 g (1.43 moles) of benzenesulfonyl chloride. The flask was cooled in an ice bath and 115 ml of pyridine (dried over sodium hydroxide) was added slowly with constant swirling. The reaction was very exothermic and must be kept cold for 30 min. After this time the mixture had completely solidified and was placed in a refrigerator for 24 hr. After warming to room temperature, 200 ml of water and 700 ml of ether were added to dissolve the solids. The layers were separated and the aqueous layer was extracted with two 150-ml portions of ether. The organic layers were combined and washed successively with 150 ml of water, 150 ml of 10% hydrochloric acid, 150 ml of 10% sodium carbonate, and 150 ml of water. The ether solution was dried over magnesium sulfate; the ether was removed under vacuum to give 281 g (94%) of solid dibenzenesulfonate used directly without further purification. Recrystalization of a sample of this from cyclohexane gave white crystals, mp 75.1–75.4°. *Anal.* Calcd for $C_{19}H_{24}O_6S_2$: C, 55.3; H, 5.9. Found: C, 55.5; H, 5.9. Nmr (CCl_4) gave τ 9.11, 8.58, 5.92, and 2.3, with ratio 9:1:4:10.

In a 3-l. three-necked flask, fitted with a stirrer and a reflux

(32) A. C. Cope and E. M. Hancock, *J. Am. Chem. Soc.*, **60**, 2644 (1938).

(33) The nmr spectra were obtained with a Varian A-60 spectrometer.

condenser, were placed 278 g (0.68 mole) of the above dibenzenesulfonate of **3**, 168 g (1.94 moles) of lithium bromide, and 800 ml of dry acetone. The contents were heated under reflux for 72 hr with stirring. After 20 min the lithium bromide had gone into solution and lithium benzenesulfonate had started to precipitate. After the acetone was distilled, the black residue was dissolved in 450 ml of water and 675 ml of ether. The layers were separated and the aqueous layer was extracted twice with 300-ml portions of ether. The combined organic layers were dried over magnesium sulfate. The ether was removed under vacuum and the residue was distilled through a 50-cm column packed with glass helices to give 144 g (78% from 3) of 2-*t*-butyl-1,3-dibromopropane, bp 76–96° (10 mm), but most boiled at 94° (10 mm). The nmr spectrum was consistent with the structure because of its similarity to both **3** and the dibenzenesulfonate of **3**; nmr (CCl_4) gave τ 8.97, 8.15, and 6.32, with ratio 9:1:4.

3-*t*-Butylcyclobutanecarboxylic Acid (5).—Diisoamyl 3-*t*-butylcyclobutane-1,1-dicarboxylate was first prepared by the following procedure. In a 3-l. three-necked flask, fitted with a stirrer, a reflux condenser, and an addition funnel was placed 500 ml of isoamyl alcohol. To this was added with stirring 9.8 g (0.43 g-atom) of sodium metal in portions and the temperature was maintained above the melting point of sodium. After the sodium had dissolved, 93.1 g (0.58 mole) of diethyl malonate was added slowly to the hot solution. The reflux condenser was replaced by a variable reflux distilling head and the mixture was heated under reflux as 50.0 g (0.194 mole) of **4** was added over a period of 2 hr. During this addition, 100 ml of a mixture of ethyl and isoamyl alcohol was distilled from the reaction flask. The mixture was heated under reflux with stirring for a total of 24 hr. Isoamyl alcohol (280 ml) was removed by distillation, the residue was cooled, and 10% hydrochloric acid (17 ml) was added until the contents were acidic to litmus. Water (100 ml) was added to dissolve the solids, the two layers were separated, and the water layer was extracted twice with 100-ml portions of ether. The combined organic layers were dried over magnesium sulfate and the ether and remaining isoamyl alcohol were removed under vacuum. The residue was distilled to give 89.5 g, bp 110–130° (1 mm), of mainly diisoamyl malonate and 40.7 g (63.2%), bp 130–152° (1 mm), of mainly diisoamyl 3-*t*-butylcyclobutane-1,1-dicarboxylate. This product was not further purified and was used directly for the preparation of **5**.

To 41 g of potassium hydroxide dissolved in 96 ml of 95% ethyl alcohol and 14 ml of water was added slowly with cooling and swirling, 20.3 g (0.06 mole) of diisoamyl 3-*t*-butylcyclobutane-1,1-dicarboxylate. The contents were heated under reflux for 1.5 hr. The solvent was removed under vacuum, the resulting solid was dissolved in a minimum amount of water while being cooled, and the alkaline solution was extracted twice with 100-ml portions of ether (discarded). The aqueous layer was acidified to pH 4 with concentrated hydrochloric acid (45 ml) with cooling. The precipitate which formed was dissolved in ether and the aqueous layer was extracted nine times more with 50-ml portions of ether. The ether solution was dried over magnesium sulfate, the ether was removed under vacuum, and the resulting solid diacid was heated at 220° until no more bubbles were observed (15 min). The residue was distilled to give 7.3 g (79%) of 3-*t*-butylcyclobutanecarboxylic acid, bp 89–96° (1 mm). A 20-ft 30% SE-30 on 45/60 Chromosorb W column at 200° at 200 ml/min indicated that about 80% of the distillate was **5** and was a mixture of the *cis* and *trans* acids with retention times of 12.5 and 13.0 min, respectively. A substantial amount of the impurity (10%) had a retention time of 14 min. Careful redistillation of the above mixture could not adequately remove this impurity. An attempt was also made to collect the *cis* and *trans* isomers together by gas chromatography and thus remove it from this impurity, but extremely poor recovery was made since they easily formed aerosols. Unsuccessful attempts were made to improve the resolution of the *cis* and *trans* isomers by changing the column conditions and also by use of a 12-ft 35% diethylene glycol succinate on 45/60 Chromosorb W column at 160° at 30 psi, which gave retention times of 2.40 and 2.50 hr, respectively.

Each of the *cis* and *trans* isomers of **5** were prepared pure by the saponification of their respective pure ethyl esters (**6**) obtained below. The procedure was as follows. *cis* **6** (0.69 g, 3.75 mmoles) was stirred with 20 ml of 0.2 *N* sodium hydroxide at 25° until a homogeneous solution was obtained (15 hr). The solution was acidified, extracted three times with 25-ml portions of ether, dried over magnesium sulfate, and the ether was removed under vacuum. The residue was distilled to give 0.44 g (75%) of *cis*-3-*t*-butylcyclobutanecarboxylic acid, bp 90–92° (1 mm). The retention time of this acid corresponded to the first peak in the mixture and the nmr spectrum was nearly identical with that of the *cis* ester precursor except for the ethyl group; nmr (CCl_4) gave τ 9.19, 7.91, 7.16, and −1.6, with ratio 9:5:1:1. *Anal.* Calcd for $C_9H_{16}O_2$: C, 69.2; H, 10.3. Found: C, 68.9; H, 10.1. The identical procedure was used to convert the *trans* ester to the *trans* acid except that a solid was obtained upon acidification, mp 47.5–48.0, in 77% yield. The retention time of this acid corresponded to the second peak in the mixture and the nmr spectrum was nearly identical with that of the *trans* ester precursor; nmr (CCl_4) gave τ 9.16, 7.75, 7.08, and −1.8, with ratio 9:5:1:1. *Anal.* Calcd for $C_9H_{16}O_2$: C, 69.2; H, 10.3. Found: C, 69.5; H, 10.4.

Ethyl 3-*t*-Butylcyclobutanecarboxylate (6).—To 9.7 g (0.062 mole) of impure **5** was added 8.3 ml (13.5 g, 0.113 mole) of thionyl chloride and the reaction mixture was allowed to react at room temperature for 22 hr. The reaction mixture was warmed on a steam bath for 30 min and the excess thionyl chloride was removed under vacuum. To this was added 36 ml of pyridine followed by 36 ml of ethyl alcohol dissolved in 20 ml of pyridine. The reaction mixture was allowed to stand at room temperature for 24 hr, poured into 72 ml of 10% hydrochloric acid, and extracted twice with 100-ml portions of ether. The combined ether layers were washed four times with 70-ml portions of 10% hydrochloric acid, followed by 70 ml of 10% sodium carbonate and 70 ml of water. The ether solution was dried over magnesium sulfate, the ether was removed under vacuum, and the residue was distilled to give 5.3 g (47%) of ethyl 3-*t*-butylcyclobutanecarboxylate, bp 85–86° (8 mm). The mixture foamed badly while being distilled.

The product was analyzed by gas chromatography and was shown to be a completely resolved 50:50 mixture of the *cis* and *trans* esters. The retention times on a 20-ft 30% SE-30 on 45/60 Chromosorb W column at 148° at 120 ml/min were 42 and 45 min and on a 12-ft 35% diethylene glycol succinate on 45/60 Chromosorb W column at 100° at 30 psi were 49 and 55 min. The isomers were separated on the 20-ft SE-30 column and collected. Each separated isomer was shown to be free of the other isomer by gas chromatography. The first peak was assigned the *cis* configuration principally because of the equilibration. *Anal.* Calcd for $C_{11}H_{20}O_2$: C, 71.7; H, 10.9. Found: C, 71.6; H, 10.8. Nmr (CCl_4) gave τ 9.17, 8.77, 7.97, 7.26, and 5.95, with ratio 9:3:5:1:2. The second peak was assigned the *trans* configuration as a result of the above-mentioned experiment. *Anal.* Calcd for $C_{11}H_{20}O_2$: C, 71.7; H, 10.9. Found: C, 71.4, H, 10.7. Nmr (CCl_4) gave τ 9.17, 8.75, 7.82, 7.20, and 5.91 with ratio 9:3:5:1:2.

Equilibration of Ethyl 3-*t*-Butylcyclobutanecarboxylate.—Ethyl *cis*-3-*t*-butylcyclobutanecarboxylate (0.100 g, 0.544 mmole) was mixed with 1.32 ml of a solution of sodium ethoxide made by dissolving 0.950 g (0.0413 g-atom) of sodium metal in 200 ml of dry ethanol.[34] The solution was distributed into four test tubes, flushed with dry nitrogen, sealed, and placed in a bath at 80.0 ± 0.1°. A tube was removed after 454 hr, opened, diluted with water, and extracted with ether. The extract was dried over magnesium sulfate, the ether was distilled, and the residue was analyzed directly by gas chromatography on the 12-ft 35% diethylene glycol succinate column. The same procedure was used with ethyl *trans*-3-*t*-butylcyclobutanecarboxylate with tubes removed at 449 and 1002 hr. The first peak was the larger one and was assumed to be the *cis* isomer. Calculations based on height times half-band-width measurements and weighing cutout models of the peaks showed the equilibration concentration to be 71.1 ± 0.4% *cis* and 28.9 ± 0.4% *trans* based on five chromatograms, corresponding to an equilibrium constant of 2.46 ± 0.04. A synthetic mixture consisting of 71.3% *cis* and 28.7% *trans* gave an analysis of 71.4% *cis* and 28.6% *trans*.

Rates of Saponification.—Ethyl cyclohexanecarboxylate was obtained from the acid by esterification in the usual way with ethanol and a catalytic amount of sulfuric acid, bp 78–80° (12 mm), $n^{20}D$ 1.4410, lit.[22] bp 82–83° (16 mm), $n^{20}D$ 1.4421. Ethyl cyclobutanecarboxylate was obtained from the acid in the same manner, bp 50–51° (17 mm). Both esters were shown to

(34) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 286.

be pure by gas chromatography. The ethyl *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylates were each shown to be pure as discussed previously.

The method and conditions used were essentially the same as used previously by Eliel and co-workers.[22] The alkali solution was prepared by diluting exactly 10 ml of standardized 0.2097 *N* carbonate-free aqueous sodium hydroxide with exactly 5 ml of carbon dioxide free water in a 50-ml volumetric flask and filled up to the mark with absolute ethanol. An amount of ester exactly equivalent to 10 ml of the 0.2097 *N* base was transferred to a 50-ml volumetric flask, exactly 15 ml of carbon dioxide free water was added, and filled up to the mark with absolute ethanol. Both solutions were placed in a constant-temperature bath at 25.2° for about 60 min and then mixed by pouring them through a wide-necked funnel into a 200-ml, glass-stoppered round-bottom flask in the bath. A 10-ml aliquot was withdrawn immediately and the clock was started. This sample and all other aliquots were quenched in a mixture of 10 ml of standardized 0.05 *N* hydrochloric acid and 15 ml of absolute ethanol, and back-titrated with standardized 0.05 *N* sodium hydroxide using phenolphthalein as the indicator. A blank was run at the start of each saponification run and was subtracted from the observed sodium hydroxide titers.

The specific rates were calculated from the equation $k = x/at(a - x)$, where t is the time in seconds, a is the initial concentration of ester or base in moles per liter, and x is the amount of ester or base, expressed in moles per liter, consumed in time t.

The data taken from a typical saponification run are shown in Table I. Table II summarizes the specific rates determined in this investigation.

The solutions from the *cis* saponification runs were combined, sodium hydroxide was added and the solutions were allowed to stand until approximately 100% completion. After acidification with 10% hydrochloric acid and the addition of water, the solution was extracted six times with 200-ml portions of ether. The ether extracts were dried over magnesium sulfate, the ether was distilled, and the residue was distilled to give 0.15 g of *cis*-3-*t*-butylcyclobutanecarboxylic acid as shown by gas chromatography and the infrared spectrum. No detectable amount of the *trans* acid was present. Similarily, the solutions from the *trans* saponification runs were combined and worked up in the same way. The solid obtained did not contain a detectable amount of the *cis* impurity as shown by gas chromatography and the infrared spectrum. Thus, very little or no equilibration occurred during the saponification runs.

Ionization Constants.—Cyclohexanecarboxylic acid and cyclobutanecarboxylic acid were redistilled before use and shown to be pure by gas chromatography. The *cis*- and *trans*-3-*t*-butylcyclobutanecarboxylic acids were each shown to be pure by gas chromatography. The solvent was prepared by mixing 2.0 l. of Methyl Cellosolve (Fisher Certified reagent ethylene glycol monomethyl ether redistilled, bp 124–125°) with 500.0 ml of carbon dioxide free water, both at 25.0° to give 80% Methyl Cellosolve–20% water.

Samples of each of the acids were dissolved in 80% Methyl Cellosolve to make approximately 0.01 *N* solutions. Four 25-ml aliquots of each solution were titrated with 0.1539 *N* carbonate-free sodium hydroxide at 25.0 ± 0.1°. Nitrogen, dried by passage through Drierite and potassium hydroxide pellets, was passed through a capillary into the solution to stir the solution and to provide a nitrogen atmosphere over the solution. The change in acidity of the solutions during the titrations was followed using an external glass electrode (Beckmen No. 40495) and a saturated potassium chloride calomel electrode with a Beckman Model G pH meter. The meter was standardized with a pH 4.01 buffer[35] and a pH 7.00 buffer (Beckman No. 3501) before and after the series of measurements for each solution. The change in water content of the solutions resulting from the addition of the sodium hydroxide solution was compensated by the addition of Methyl Cellosolve. Measurements made before and after solvent additions indicated an increase in pH of about 0.15 unit throughout the titration. Particular care was taken around the half-neutralization point and the equivalence point to correct for the change in solvent conditions.

The equivalence points in all cases were determined graphically and were sharp. From this, the pH and the volume of base at the approximate half-neutralization point, the pK was determined by the equation: $pK_a = pH - \log [A^-/HA]$. Four determinations were made on each acid, and the pK values are averaged. The results are summarized in Table III with the corresponding apparent ionization constants, K_a.

Methyl 3-Methylcyclobutanecarboxylate.—A solution of 5.0 g (0.04 mole) of methyl 3-methylenecyclobutanecarboxylate[26] in 15 ml of methanol containing 0.05 g of platinum oxide catalyst was reduced at 1 atm until hydrogen uptake ceased. The reaction mixture was filtered and the methanol was removed by distillation. The residue was distilled to give 3.0 g (59%) of methyl 3-methylcyclobutanecarboxylate, bp 145–146 and 58–60° (28 mm), $n^{25}D$ 1.4192, lit.[11] bp 146–147°, $n^{25}D$ 1.4213. Gas chromatography indicated a poorly resolved mixture of the *cis* and *trans* isomers with a 20-ft 30% SE-30 on 45/60 Chromosorb W column, at 78° at 300 ml/min. The peak with the shorter retention time was larger. When this mixture was equilibrated in the manner described[11] with sodium methoxide in methanol at 65° for 116 hr, the first peak still predominated. Allinger and Tushaus[11] have synthesized the *cis* isomer and have shown that it predominates at equilibrium. Therefore, as in their work the first and larger peak was due to the *cis* isomer.

Registry No.—**2**, 759-24-0; **3**, 2819-05-8; **4**, 14294-49-3; **5** (*cis*), 15043-69-3; **5** (*trans*), 14294-50-6; **6** (*cis*), 14294-51-7; **6** (*trans*), 14924-52-8; cyclobutanecarboxylic acid ethyl ester, 14924-53-9; cyclobutanecarboxylic acid, 3721-95-7; methyl 3-methylcyclobutanecarboxylate, 14924-54-0; dibenzenesulfonate of 2-*t*-butyl-1,3-propanediol, 14897-49-5.

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(35) R. G. Bates, "Electrometric pH Determination," John Wiley and Sons, Inc., New York, N. Y., 1954, p 74.