Synthesis and Ionization Constants of *meta*- and *para*-Substituted *cis*-3-Phenylcyclobutanecarboxylic Acids

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cis-3-Phenylcyclobutanecarboxylic acid and the *p*-OCH_3, *m*-CH_3, *p*-F, *m*-F, and *m*-CF_3 derivatives have been prepared from the appropriate arylmagnesium bromide and ethyl 3-ketocyclobutanecarboxylate, followed by palladium-catalyzed hydrogenolysis, and saponification. The *cis* configuration of each acid was established by the ruthenium tetroxide oxidation to *cis*-1,3-cyclobutanedicarboxylic acid. The ionization constants in 50% ethanol at 25° give $\rho = 0.256$ ($-\log K_0 = 5.985$) using σ^0 values.

Much work has been directed in recent years toward the evaluation of the ability of atoms and groups in various hybridizations and stereochemical configurations to transmit electronic effects.[2-7]

Attempts have been made to rationalize the decrease in the (Hammett equation) ρ value as transmitting groups, X, are inserted between the aromatic ring and the functional group. One might expect that each X group (-CH_2-, -CH=CH-, etc.) would have a characteristic and constant transmission factor,[2,7] and knowing this value and the ρ value for the ionization of benzoic acids, the ρ value for the phenylacetic acid series, for example, might be calculated. This approach does not give consistently satisfactory results,[4,5] and a range of transmission factors from 0.1 to 0.6 have been suggested at one time or another for the same transmitting group. Variations in the degree of direct resonance interaction between *para* substituents and the functional group *via* X may, in certain cases, account for variations in the apparent transmission coefficient of X. But in general the real variable involved may be the distance and orientation of the substituent dipole with respect to the reaction center, and not the number of atoms between them.[4,5]

The present study of the *meta*- and *para*-substituted *cis*-3-phenylcyclobutanecarboxylic acids begins an examination of those systems with three-carbon-atom transmitting groups. The use of cyclic transmitting units helps to avoid the ambiguity of chain conformation, which is a severe problem in studies of ω-arylalkanoic acid derivatives. Work in this area should provide some additional cases for comparison of the transmission coefficient concept[2,7] *vs.* the electrostatic transmission viewpoint.[4,5]

Results

The least-squares treatment of the ionization constants of *cis*-3-phenylcyclobutanecarboxylic acid and its *p*-OCH_3, *m*-CH_3, *p*-F, *m*-F, and *m*-CF_3 derivatives in 50% aqueous ethanol (by volume) at 25° (Table I) *vs.* σ^0 values[3] gives $\rho = +0.256$, with an average deviation of ± 0.013 pK_a, and $-\log K_0 = 5.985$.

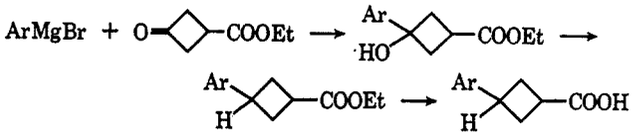
TABLE I

APPARENT DISSOCIATION CONSTANTS OF *meta*- AND *para*-SUBSTITUTED *cis*-3-PHENYLCYCLOBUTANECARBOXYLIC ACIDS IN 50% ETHANOL AT 25°

Substituent	σ^0	$-\log K$
H	0	5.98, 5.98
p-OCH_3	−0.16	6.02, 6.04
m-CH_3	−0.07	6.02, 6.00
p-F	0.17	5.92, 5.92
m-F	0.35	5.92, 5.93
m-CF_3	0.42	5.85, 5.88

Discussion

The acids were prepared by the addition of the arylmagnesium bromides to ethyl 3-ketocyclobutanecarboxylate at −80°. The resulting ethyl 3-aryl-3-hydroxycyclobutanecarboxylates underwent hydrogenolysis in the presence of palladium on charcoal to yield the ethyl 3-arylcyclobutanecarboxylates, which were converted by base-catalyzed hydrolysis into the 3-arylcyclobutanecarboxylic acids.



The determination of the stereochemistry of each of the 3-phenylcyclobutanecarboxylic acids was required before a meaningful comparison of ionization constants could be made. In the first step it seems likely that attack by the Grignard reagent on the ketone function will come from the side of the cyclobutane ring opposite the carbethoxyl group. The expected product, after hydrolysis of the magnesium salt, is the hydroxylated product with the carbethoxyl and aryl groups *trans* to one another, and the hydroxyl and carbethoxyl groups *cis*. Hydrogenolysis of this product over palladium on charcoal catalyst proceeds with inversion of configuration[8] yielding the ethyl *cis*-3-arylcyclobutanecarboxylate. Saponification of this product would not be expected to affect the stereochemistry of the resultant acid (provided that base-catalyzed epimerization does not occur) since the reaction site is the carbonyl carbon atom and not a ring carbon atom. On this basis the final products expected are the *cis*-3-arylcyclobutanecarboxylic acids and not the *trans* isomers.

The first member of the series prepared in this manner was the unsubstituted compound. Both *cis* and *trans* isomers of this compound are known,[9] and the product

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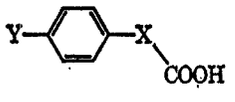
obtained proved to be the *cis* isomer. This result confirms the foregoing stereochemical predictions. Rigorously establishing the stereochemistry of the other acids of the series at first appeared to be difficult, since Beard and Burger[9] had previously treated the parent compound with ozone in a fruitless attempt to oxidize the aromatic ring. The oxidation of aromatic rings with ruthenium tetroxide had previously been reported,[10] but the products had not been isolated or identified. We have recently oxidized *cis*-2-phenylcyclobutanecarboxylic acid to *cis*-1,2-cyclobutanedicarboxylic acid, and *cis*-3-phenylcyclobutanecarboxylic acid to *cis*-1,3-cyclobutanedicarboxylic acid, both stereospecifically, with RuO_4.[11] These products were not isolated, but were directly converted into the dimethyl esters, which were found to have the same gas chromatographic retention times as authentic samples of the *cis*-esters,[12] but different from those of the *trans*-esters,[12] using two dissimilar capillary columns. Dimethyl 1,3-cyclobutanedicarboxylate from the RuO_4 oxidation was also subjected to mass spectral analysis and its spectrum was found to be identical with that of an authentic sample of the *cis* isomer, but different from that of the *trans* isomer.

All five *meta*- and *para*-substituted *cis*-3-phenylcyclobutanecarboxylic acids were oxidized with RuO_4, and converted into dimethyl 1,3-cyclobutanedicarboxylate by esterification with methanol. In every case the product was the *cis* isomer, with no detectable amounts of the *trans* isomer present.

Kirkwood and Westheimer[13] have attempted to calculate the transmission of polar effects by considering the direct electrostatic effect of a substituent group on ionization constants and on the relative rates of alkaline hydrolysis

$$\log k/k_0 = \frac{e\mu \cos\theta}{2.303kTD'r^2}$$

where μ is the dipole moment, e the electronic charge, k the Boltzmann constant, T the absolute temperature, D' the effective dielectric constant, r the distance between the midpoint of the dipole and the reaction center, and θ the angle between the line joining the reaction center and the center of the dipole, and the axis of the dipole. A number of studies, particularly with 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids, have demonstrated a dependence of the electrostatic effect on the model chosen for the calculation,[14] and a dependence of substituent effects on the solvent (particularly for charged substituents).[15] In various series of phenyl-substituted acids



for which pK_a values are determined in the same solvent, a number of simplifications can be made. The shape of the substituent end of the cavity model, the location of the substituent dipole in that cavity, and the apparent σ constant in that solvent need not be known precisely, since all of these factors will be identical for each series. In the comparison of two identically substituted members of different series, e, μ, and D' are also assumed to be constant, and the relative transmission of the substituent effect is determined by the factor $(\cos\theta)/r^2$ for each series.[4] Dividing ρ by $[10^2 (\cos\theta)]/r^2$ for related acid series (β-phenylpropionic, *trans*-2-phenylcyclopropanecarboxylic) lacking direct resonance interactions between aryl and carboxyl groups gives values of about 0.24. For *trans*-cinnamic, -benzoic, and -phenylpropiolic acids, values of 0.38 are obtained, indicating that substituent effects are transmitted to a larger extent than is predicted on a purely electrostatic basis. These are the very series in which direct resonance effects are possible. However, $\rho/[10^2 (\cos\theta)/r^2]$ for the *cis*-2-phenylcyclopropanecarboxylic acid series is 0.18; that is, ρ is smaller than would be predicted on this simplified electrostatic basis.

The ρ value for the *meta*- and *para*-substituted 3-phenylcyclobutanecarboxylic acids is +0.256. Skeletal measurements were taken directly from a Framework Molecular Model with a puckered cyclobutane ring, and the aryl and carboxyl groups in a pseudo-equatorial conformation. The distance r, measured from the p-carbon atom (the assumed center of the dipole) to a point 0.89 Å beyond the carbonyl atom,[4] is 7.9 Å. Cos θ is 0.885, and $[\rho/(\cos\theta)/r^2] \times 100 = 0.18$. Changes in the assumed conformation would alter the latter value slightly, so we attribute no particular significance to the observation that this value is identical with that for the *cis*-2-phenylcyclopropanecarboxylic acids. Molecules are considered in the Kirkwood–Westheimer treatment to be ellipsoid cavities of low dielectric constant (*ca.* 2.0) embedded in the solvent, which in this study has a high dielectric constant. If, for some compounds, the straight-line pathway over which the electrostatic interaction is transmitted passes through a volume of space, filled not by the molecule itself, but rather by solvent molecules, then the effective dielectric constant D' is not constant between series. This explanation seems particularly applicable to the *cis* series mentioned and suggests that the electrostatic theory will be least precise when the actual molecule deviates most from the ellipsoidal model.

From the transmission coefficient viewpoint the value of $\rho = +0.256$ is about that expected from the value of $\rho = +0.517$ for the *cis*-2-arylcyclopropanecarboxylic acids, and an apparent coefficient, ϵ, for sp^3 carbon of 0.48.[4] Unless modifications in ϵ are made, this treatment would predict identical values of ρ for the *trans*-2-arylcyclopropanecarboxylic acids ($\rho = +0.542$[4]), the *cis* isomers, and the β-arylpropionic acids ($\rho = +0.417$[4]). Neither this nor the electrostatic viewpoint can be applied at present with complete confidence to substantially nonellipsoidal molecules.

Experimental Section

Ethyl 3-Ketocyclobutanecarboxylate.—Benzyl bromide and epibromohydrin react in the presence of mercuric chloride to give 2-benzyloxy-1,3-dibromopropane[16] (77%), bp 109–112°

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(0.1 mm). The latter added to a solution of sodium in isoamyl alcohol and diethyl malonate gives diisoamyl 3-benzyloxycyclobutane-1,1-dicarboxylate[17] (64%), bp 180–185° (0.14 mm), which by saponification and monodecarboxylation afforded a 70% yield of 3-benzyloxycyclobutanecarboxylic acid,[16,17] bp 145–152° (0.3 mm).

Esterification of 3-benzyloxycyclobutanecarboxylic acid with ethanol gave a product which upon hydrogenolysis with 10% palladium on charcoal catalyst at a hydrogen pressure of 25 psi yielded ethyl 3-hydroxycyclobutane-1-carboxylate,[16,17] bp 97–115° (4 mm) (75%).

Ethyl 3-hydroxycyclobutanecarboxylate was oxidized[11] with RuO_4 to ethyl 3-ketocyclobutanecarboxylate,[16] bp 86–90° (0.55 mm) (78%). The proton magnetic resonance (pmr) spectrum of the product is as follows: a triplet at δ 1.27 (3 H, CH_3), multiplet centered at 3.25 (5 H), and a quartet at 4.15 (2 H, CH_2). The same product was obtained in 38% yield using CrO_3 as the oxidant.[16]

Ethyl 3-Phenyl-3-hydroxycyclobutane-1-carboxylate. Procedure A.—To a stirred solution of 3.1 g (0.022 mol) of ethyl 3-ketocyclobutane-1-carboxylate in 200 ml of ether at −80° under a nitrogen atmosphere was added dropwise over 1 hr a solution of 0.022 mol of phenylmagnesium bromide prepared from 4.60 g (0.029 mol) of bromobenzene in ether and 0.78 g (0.032 g-atom) of magnesium metal. The reaction mixture was allowed to warm to room temperature with stirring, and a saturated sodium sulfate solution was then added dropwise until a clear solution resulted. The ether phase was decanted, dried over magnesium sulfate, and the product isolated by removal of the solvent. The infrared spectrum of the neat oil is as follows: ν_{max} 3450 strong and broad (OH), 2980 medium (CH), 1730 very strong (C=O), 1443, 1370, 1345, 1240 strong, 1180 strong, (CO_2Et), 1090, 1025, 750, and 695 cm^{-1} strong. The pmr spectrum showed a triplet at δ 1.2 (3 H, CH_3), multiplet centered at 2.6 (5 H), quartet at 4.0 (2 H, CH_2), broad singlet at 4.5 (1 H, OH), and another multiplet centered at 7.3 (5 H, aromatic).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 71.34; H, 7.33.

Ethyl 3-Phenylcyclobutanecarboxylate. Procedure B.—Ethyl 3-hydroxy-3-phenylcyclobutanecarboxylate was hydrogenolyzed in 100 ml of 95% ethanol at a hydrogen pressure of 20 psi with 1 g of 10% palladium on charcoal catalyst. When the theoretical amount of hydrogen was taken up the solution was filtered and the solvent removed under vacuum. Distillation yielded a product of bp 76–85° (0.2 mm).

3-Phenylcyclobutanecarboxylic Acid. Procedure C.—Ethyl 3-phenylcyclobutane-1-carboxylate was dissolved in 70% ethanol and refluxed for 4 hr with an excess of KOH. The ethanol was removed by reduced-pressure evaporation and the residue was extracted with ether to remove nonacidic impurities, and then acidified with HCl and extracted with chloroform. After removal of the solvent, distillation yielded the product: bp 110–111° (0.15 mm); *p*-toluidine, mp 136–137° (lit.[9] mp 137–138.5°). The infrared spectrum of the neat oil is as follows: ν_{max} 2940, 2980, 3020 strong (COH), 1710 very strong (C=O), 1600, 1490, 1430, 1250, 930, 740 strong, and 690 cm^{-1} strong. The pmr spectrum in CCl_4 is as follows: a singlet at δ 11.9 (1 H, $-CO_2H$), multiplet at 7.12 (5 H, aromatic), quartetlike multiplet centered at 3.26 (1 H), another quartetlike multiplet centered at 2.98 (1 H), another multiplet centered at 2.48 (4 H).

Anal. Calcd for $C_{11}H_{12}O_2$: neut equiv, 176.2. Found: neut equiv, 176.8, 175.3.

3-(*p*-Fluorophenyl)cyclobutanecarboxylic Acid.—This synthesis was accomplished as outlined earlier by procedure A. *p*-Fluorophenylmagnesium bromide (0.022 mol) was added to ethyl 3-ketocyclobutane-1-carboxylate (3.1 g, 0.022 mol) to yield 3-(*p*-fluorophenyl)-3-hydroxycyclobutane-1-carboxylate with the following infrared spectrum: ν_{max} 3450 strong (OH), 2980 medium (CH), 1710 strong (C=O), 1600, 1510, 1370, 1350, 1250, 1190, 1160, 1090, and 830 cm^{-1}.

Hydrogenolysis, with 1 drop of $HClO_4$ catalyst (by procedure B) followed by saponification (by procedure C) yielded a solid: mp 81.5–83.6°; yield 0.75 g (18% over-all). The infrared spectrum of 3-(*p*-fluorophenyl)-cyclobutanecarboxylic acid is as follows: ν_{max}^{mull} 1700 strong (C=O), 1600, 1510, 1300, 1280, 1250, 1210, 1170, 1160, 1070, 1060, 820, 810, and 750 cm^{-1}. The pmr spectrum is as follows: a singlet at δ 11.7 (1 H, CO_2H), multiplet at 6.86 (4 H, aromatic), two adjacent multiplets (eight lines total) centered at 3.23 (1 H) and 2.88 (1 H), multiplet centered at 2.43 (4 H).

Anal. Calcd for $C_{11}H_{11}O_2F$: C, 68.03; H, 5171; neut equiv, 194.2. Found: C, 68.28; H, 5.87; neut equiv, 194.8, 193.7.

3-[*m*-(Trifluoromethyl)phenyl]cyclobutanecarboxylic Acid.—By procedure A *m*-(trifluoromethyl)phenylmagnesium bromide (0.050 mol), prepared from 15.0 g (0.067 mol) of *m*-bromo-α,α,α-trifluorotoluene and 1.62 g (0.067 g-atom) of magnesium, was added to ethyl 3-ketocyclobutanecarboxylate (7.11 g, 0.050 mol) to give 3-[*m*-(trifluoromethyl)phenyl]-3-hydroxycyclobutanecarboxylic acid whose infrared spectrum is as follows: ν_{max} 3450 strong and broad (OH), 2980 and 2940 (CH), 1720 very strong (C=O), 1610, 1600, strong, 1480, 1440, 1370, 1340, 1240, 1190, 1100, 1030, 920, 890, 870, 825, 780 strong, 690, and 660 cm^{-1}.

Hydrogenolysis, with 1 drop of $HClO_4$ catalyst, followed by saponification (procedures B and C, respectively) gave the title product: yield 3.0 g (25% over-all); bp 110–112° (0.2 mm); $n^{23.5}D$ 1.4842. The infrared spectrum of the product is as follows: ν_{max} 3000 very strong and very broad, 1710 very strong (C=O), 1490, 1425 strong, 1325 strong, 1230, 1215, 1200, 1158, 1115, 1065, 920 very broad, 790, 742, 692, and 647 cm^{-1}. The pmr spectrum is as follows: a broad singlet at δ 11.5 (1 H, CO_2H), multiplet centered at 7.34 (4 H, aromatic), two quartetlike multiplets centered at 3.40 (1 H) and 3.06 (1 H), and another multiplet centered at 2.52 (4 H).

Anal. Calcd for $C_{12}H_{11}O_2F_3$: C, 59.01; H, 4.54; F, 23.34; neut equiv, 244.2. Found: C, 58.69; H, 4.70; F, 23.03; neut equiv, 246.4, 247.0.

3-(*m*-Fluorophenyl)cyclobutanecarboxylic Acid.—By procedure A *m*-fluorophenylmagnesium bromide (0.050 mol) and ethyl 3-ketocyclobutane-1-carboxylate (7.11 g, 0.050 mol) yielded ethyl 3-(*m*-fluorophenyl)-3-hydroxycyclobutanecarboxylate whose infrared spectrum is as follows: ν_{max} 3440 strong and broad (OH), 2980 and 2940 (CH), 1720 very strong (C=O), 1610, 1590, 1480, 1440, 1370, 1340, 1270, 1240, 1190, 1100 broad, 1030, 915, 890, 775, 685, and 660 cm^{-1}.

Hydrogenolysis, with 1 drop of $HClO_4$ added (procedure B), yielded ethyl 3-(*m*-fluorophenyl)cyclobutanecarboxylate, bp 80–117° (0.1–0.2 mm).

Saponification (procedure C) yielded the title product, bp 102–107° (0.12 mm), 0.8 g (87%), whose infrared spectrum is as follows: ν_{max} 3000 strong and broad, 1710 strong (C=O), 1610, 1600, 1490, 1435 broad, 1250 broad, 1140, 960, 860, 825, 775, 740, and 680 cm^{-1}. The pmr spectrum of the product is as follows: a singlet at δ 10.1 (1 H, CO_2H), multiplet centered at 6.85 (4 H, aromatic), two adjacent multiplets at 3.20 (1 H), and 2.90 (1 H), and another multiplet centered at 2.40 (4 H).

Anal. Calcd for $C_{11}H_{11}O_2F$: C, 68.03; H, 5.71; neut equiv, 194.2. Found: C, 68.11; H, 5.93; neut equiv, 194.4, 193.3.

3-(*m*-Tolyl)cyclobutanecarboxylic Acid.—By procedure A *m*-tolylmagnesium bromide (0.050 mol) was added to ethyl 3-ketocyclobutanecarboxylate (7.11 g, 0.050 mol) to give ethyl 3-(*m*-tolyl)-3-hydroxycyclobutanecarboxylate whose infrared spectrum is as follows: ν_{max} 3450 strong and broad (OH), 2980 and 2930 (CH), 1720 strong (C=O), 1600, 1450 broad, 1370, 1340, 1240, 1180 broad, 1090, 1030, 775, 725, and 695 cm^{-1}.

Hydrogenolysis, with 1 drop of $HClO_4$ added (procedure B), gave ethyl 3-(*m*-tolyl)cyclobutanecarboxylate, bp 95–103° (0.4 mm), yield 5.4 g (50% over-all), whose pmr spectrum is as follows: a multiplet centered at δ 7.58 (4 H, aromatic), quartet at 4.68 (2 H, CH_2), two adjacent quartetlike multiplets centered at 3.88 (1 H) and 3.58 (1 H), another multiplet centered at 3.06 (4 H), a singlet at 2.92 (3 H, CH_3), and a triplet at 1.87 (3 H, CH_3).

Saponification (by procedure C) yielded 1.3 g (60%) of the title compound, bp 129–131° (0.4 mm), whose infrared spectrum is as follows: ν_{max} 2950 very strong and very broad, 1705 very strong (C=O), 1610, 1590, 1490, 1425 strong, 1330 broad, 1250 strong, 1220, 1090 broad, 1035, 930 broad, 820, 780, 740, 690, and 670 cm^{-1}. The pmr spectrum of the product is as follows: a singlet at δ 11.7 (1 H, CO_2H), multiplet at 6.86 (4 H, aromatic), two adjacent quartetlike multiplets centered at 3.16 (1 H) and 2.90 (1 H), another multiplet centered at 2.40 (4 H), and a singlet at 2.19 (3 H, CH_3).

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42; neut equiv, 190.2. Found: C, 75.72; H, 7.25; neut equiv, 191.0, 190.6.

3-(*p*-Methoxyphenyl)cyclobutanecarboxylic Acid.—By procedure A *p*-methoxyphenylmagnesium bromide (0.050 mol) was

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added to ethyl 3-ketocyclobutane-1-carboxylate yielding a product whose infrared spectrum is as follows: ν_{max} 3460 strong and broad (OH), 2980, 2950 and 2840 (CH), 1725 strong (C=O), 1600 strong doublet, 1590, 1510, 1500, 1450 broad, 1375, 1345, 1295, 1240 broad, 1175 broad, 1095, 1030 strong, 830 strong, 780, 750, and 690 cm^{-1}.

Hydrogenolysis, with 1 drop of $HClO_4$ added (by procedure B), yielded ethyl 3-(*p*-methoxyphenyl)cyclobutanecarboxylate, bp 114–115° (0.15 mm), 3.0 g (25% over-all).

Saponification (by procedure C) yielded the title compound, bp 129–150° (0.3–0.4 mm), which upon crystallization followed by two recrystallizations from ether at −80° gave the product, mp 70.5–72.0°, with the following infrared spectrum: ν_{max}^{mull} 1700 strong (C=O), 1610, 1580, 1515, 1460 strong, 1430, 1380, 1355, 1295, 1260, 1230, 1205, 1175, 1030, 930 broad, 805, and 750 cm^{-1}. The pmr spectrum of the product is as follows: a singlet at δ 12.0 (1 H, CO_2H), simplified AA'BB' four-line multiplet with halves centered at 6.96 and 6.60 (4 H, aromatic), singlet at 3.59 (3 H, OCH_3), two adjacent quartetlike multiplets centered at 3.17 (1 H) and 2.88 (1 H), another multiplet centered at 2.34 (4 H).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; neut equiv, 206.2. Found: C, 69.45; H, 6.80; neut equiv, 205.1, 207.3.

Instrumentation.—pK_a determinations in 50.0% (v/v) aqueous ethanol were carried out as previously reported.[6] Pmr spectra (100 mc) were run in CCl_4 solution containing 6% tetramethylsilane.

Registry No.—Ethyl 3-phenyl-3-hydroxycyclobutane-1-carboxylate, 16204-46-9; ethyl 3-phenylcyclobutanecarboxylate, 16204-47-0; 3-phenylcyclobutanecarboxylic acid, 16204-48-1; 3-(*p*-fluorophenyl)cyclobutanecarboxylic acid, 16204-49-2; 3-[*m*-(trifluoromethyl)phenyl]cyclobutanecarboxylic acid, 16204-50-5; 3-(*m*-fluorophenyl)cyclobutanecarboxylic acid, 16204-51-6; 3-(*m*-tolyl)cyclobutanecarboxylic acid, 16204-52-7; 3-(*p*-methoxyphenyl)cyclobutanecarboxylic acid, 16204-53-8.

Cyclopropanes. XXIII. An Optically Active Cyclopropylsodium[1]

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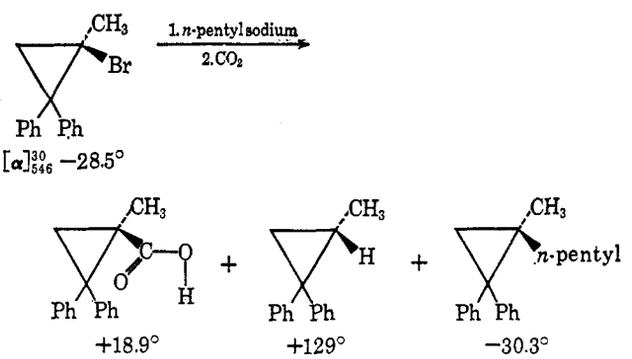
Halogen–metal exchange between (−)-(*R*)-1-bromo-1-methyl-2,2-diphenylcyclopropane and *n*-amylsodium yielded upon carbonation (+)-(*R*)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid (optical purity, 46%), (+)-(*S*)-1-methyl-2,2-diphenylcyclopropane (optical purity, 83%), and (−)-(*R*)-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane (optical purity, 66%) with over-all retention of configuration. In an ancillary study to the determination of the absolute configuration of (−)-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane it was found that the most effective method for the reduction of a vinylcyclopropane intermediate was by the use of diimide.

It has recently been established that organolithium[2] and magnesium[3] reagents derived from 1-bromo-1-methyl-2,2-diphenylcyclopropane are capable of maintaining their optical activity and configuration. In connection with our current studies on the reduction of this compound with sodium in liquid ammonia, we were interested in determining the effect on the optical stability of replacing lithium or magnesium by the less covalently bonded sodium. There was some evidence that 1-methyl-2,2-diphenylcyclopropylsodium would have at least some degree of optical stability since previous studies had shown that the reaction of the corresponding bromide with metallic sodium in benzene or toluene yielded 1-methyl-2,2-diphenylcyclopropane (optical purity 60–70%) with net retention of configuration.[2] Since carbonation, under these conditions, did not yield the corresponding acid and since the mechanism of direct metallation is still under investigation,[4] it was thought desirable to produce the intermediate organosodium derivative by halogen–metal exchange reaction.

Optically active 1-methyl-2,2-diphenylcyclopropylsodium has now been prepared by the reaction of *n*-pentylsodium with (−)-(R) - 1 - bromo - 1 - methyl - 2,2-diphenylcyclopropane in pentane solution. Carbonation followed by hydrolysis of the reaction mixture gave three main products, (+)-(R)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid in 10% yield (optical purity, 46%), (+)-(*S*)-1-methyl-2,2-diphenylcyclopropane, 45% yield (optical purity, 83%), and (−)-(*R*)-1-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane in 25% yield (optical purity, 66%).



All products were produced with over-all retention of configuration. The relative[2,5] and absolute configurations[6] of the cyclopropyl bromide, carboxylic acid and hydrocarbon have previously been established and the configuration of 1-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane was established by an independent synthesis starting from an alcohol of known absolute configuration.[6] Since none of the above reactions affect the optically active center in the starting carbinol, the configuration of the resulting (−)-1-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane must be identical with that of the starting material. Furthermore, in that the (−)-carbinol has been shown to have the same configuration

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(6) H. M. Walborsky and C. G. Pitt, *ibid.*, **84**, 4831 (1962).