Substituent Effect in the Ionization of *cis*-2-Substituted 1-Cyclopropanecarboxylic Acids

Yoshiaki KUSUYAMA

Department of Chemistry, Faculty of Education, Wakayama University, Masagocho 1-1, Wakayama 640

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Ten *cis*-2-substituted 1-cyclopropanecarboxylic acids (substituents: H, CH_3, C_6H_5, CH_3O, C_2H_5O, Cl, Br, CH_3CO, CH_3OCO, and C_2H_5OCO) were prepared, and their pK_a values were determined in water at 25 °C, along with those of the *trans*-2-chloro and 2-methoxy derivatives. The pK_a values for cis isomers are somewhat larger than those for the corresponding trans isomers, except for the chloro and bromo derivatives. The substituent effects obtained were in the usual order in the sense of the electronic effects, except for the phenyl group, which produced a decrease in acidity relative to the unsubstituted acid. It was shown that the carbon-13 chemical shifts for the methylene carbon of the ethyl group in the ethyl *cis*-2-substituted 1-cyclopropanecarboxylate obtained in deuteriochloroform gave a reasonable linear relation with the pK_a(*cis*) values.

It is well established that the C–C bonds of cyclopropane ring have π double-bond character[1] and can extend the chain of conjugation when a cyclopropane ring is directly attached to a π system of bonds.[2] The degree of the contributions of the conjugative effect of the cyclopropane ring has been estimated by several workers.[3–6] The degree of the transmission of the electronic effects through the cyclopropane ring, however, is still uncertain, since conflicting results have been reported. For example, the effective transmission or a greater polarizability of the trans system was indicated by spectroscopic measurements[6,7] and by the chemical reactivities,[8] including the ionization of 2-phenyl-cyclopropanecarboxylic acids.[9] On the other hand, the alkaline hydrolysis of ethyl 2-phenyl-1-cyclopropanecarboxylates afforded larger Hammett's ρ values for cis isomers than for trans isomers.[10] Thus, the abilities of the cis isomer relative to the trans isomer in 1,2-disubstituted cyclopropane in transmitting electronic effects have been a continued subject of controversy.[8,11]

In attempt to resolve the contradiction in the reported results on transmitting polar effects through cyclopropylene, it appeared to be of interest to examine the effects of substituents in the ionization of 2-substituted 1-cyclopropanecarboxylic acids. In a previous paper,[12] the pK_a values of *trans*-2-substituted 1-cyclopropanecarboxylic acids and their linear relation with σ_m were reported. A study of the substituent effect in the pK_a values of *cis*-2-substituted 1-cyclopropanecarboxylic acids and in the carbon-13 chemical shifts of the methylene carbon of the ethyl group in ethyl *cis*-2-substituted 1-cyclopropanecarboxylates has been undertaken in the present study.

The system is a very interesting one from another point of view. The rigidity of the cyclopropane ring offers an interesting tool for elucidating the mechanistic problems in the acidity-structure relationship where substituents are in a close proximity to the carboxyl group. In this field of chemistry[13,14] less progress has been reported than in those concerning the effects of remote substituent groups, which have been well explained by both inductive (including the effects through both the field and bonds) and resonance effects. It appears that the data reported herein will provide useful information in order to elucidate interaction mechanisms between the proximate substituent and the carboxyl group.

Results and Discussion

Unsubstituted,[15] *cis*-2-methyl-,[13a] and *cis*-2-phenyl-1-cyclopropanecarboxylic acids[16] were synthesized by the methods described in the literature. Other substituted cyclopropanecarboxylic acids were obtained by the hydrolysis of the respective ethyl esters prepared by the appropriate methods. The cis isomers of ethyl esters were separated conveniently by a combination of fractional distillation and preparative GPLC. Cis and trans mixtures of ethyl 2-methoxy- and 2-ethoxy-1-cyclopropanecarboxylate were synthesized by the copper(I)-catalyzed decomposition of ethyl diazoacetate in methyl vinyl ether and ethyl vinyl ether respectively.[12] By using the method of McCoy,[17] diethyl and dimethyl 1,2-cyclopropanedicarboxylates were obtained. The remaining derivatives were prepared by the routes shown in the following scheme:

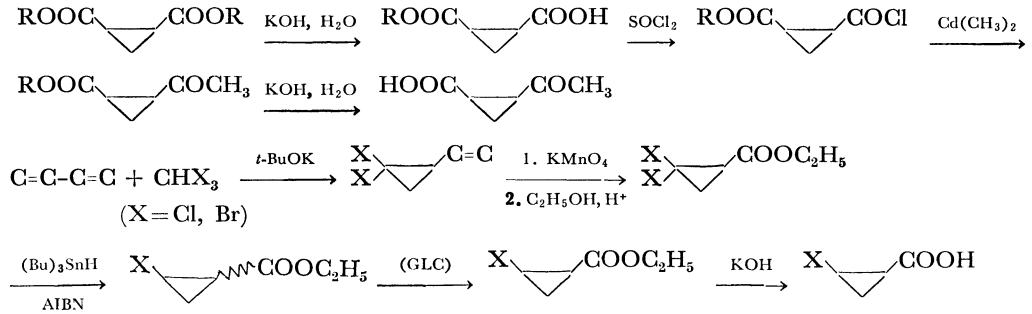


Table 1. pK_a values of 2-substituted cyclopropanecarboxylic acids in water at 25 °C

Substituent	*cis*	*trans*
H	4.83±0.01	4.84±0.01[c]
	4.83[a]	
CH_3	5.03±0.01	4.98±0.01[c]
	5.02[b]	5.00[b]
CH_3O	4.76±0.01	4.47±0.01
C_2H_5O	4.83±0.01	4.46±0.01
CH_3OCO	4.22±0.02	4.09±0.02[c]
C_2H_5OCO	4.26±0.02	4.10±0.02[c]
CH_3CO	4.19±0.01	4.08±0.01[c]
Cl	4.12±0.01	4.12±0.01
Br	4.09±0.01	4.09±0.01[c]
C_6H_5	4.95±0.02	4.57±0.02[c,d]

a) M. Kilpatric and J. O. Morse, *J. Am. Chem. Soc.*, **75**, 1854 (1953). b) Ref. 13(a). c) Ref. 12. d) Ref. 11.

Table 2. $\Delta pK_a(pK_a^X - pK_a^H)$ and $\Delta pK_a^{ct}(pK_{a_{cis}} - pK_{a_{trans}})$ values for 2-substituted cyclopropanecarboxylic acids in water at 25 °C

Substituent	$\Delta pK_a(cis)$	$\Delta pK_a(trans)$	ΔpK_a^{ct}
H	0.00	0.00	0.00
CH_3	0.20	0.14	0.05
CH_3O	−0.07	−0.37	0.29
C_2H_5O	0.00	−0.38	0.37
CH_3OCO	−0.61	−0.75	0.13
C_2H_5OCO	−0.57	−0.74	0.16
CH_3CO	−0.64	−0.76	0.11
Cl	−0.71	−0.72	0.00
Br	−0.74	−0.75	0.00
C_6H_5	0.12	−0.27	0.38

The pK_a values measured in water at 25 °C are listed in Table 1. The reproducibilities of the repeated runs are less than 0.01 pK_a unit except for the alkoxycarbonyls and the phenyl group (0.2 pK_a unit). This accuracy is considered to be sufficient for us to discuss the substituent effects. The values determined here for unsubstituted and *cis*-2-methyl derivatives showed a good agreement with those published by McCoy, within the limits of experimental error.[13a]

It is convenient to use the $\Delta pK_a^H(pK_a^X - pK_a^H)$ and $\Delta pK_a^{ct}(pK_{a_{cis}} - pK_{a_{trans}})$ values in discussing the substituent effects in comparison with various systems. These values are summarized in Table 2.

Since carbon-13 NMR chemical shifts are sensitive to changes in the electron density[18] and the stereochemical relationship of atoms in a molecule,[18,19] the application of this spectroscopic method to the methylene carbon of the ethyl group in ethyl 2-substituted 1-cyclopropanecarboxylates would provide additional insight into the substituent effect on pK_a values(*cis*) obtained here. Therefore, the substituent-induced chemical shifts(SCS)[20] for this carbon were determined under conditions essentially corresponding to an infinitive dilution in deuteriochloroform; the results are listed in Table 3, along with those of trans derivatives.[12] Both the cis and trans carbons showed "normal" substituent effects.

Table 3. ^{13}C Chemical shifts[a] for the methylene carbons of the ethyl group in ethyl 2-substituted cyclopropanecarboxylates in deuteriochloroform

Substituent	$\delta(cis)$[b,c]	$\delta(trans)$[d]	$\delta_{(cis)} - \delta_{(trans)}$
H	60.46	60.37	0.09
CH_3	60.15	60.19	−0.04
CH_3O	60.58	60.49	0.09
C_2H_5O	60.50	60.49	0.01
C_2H_5OCO	60.96	60.97	−0.01
CH_3CO	60.94	61.04	−0.10
Cl	61.04	61.04	0.00
Br	61.23	61.11	0.12
C_6H_5	60.14	60.61	−0.47
CN	61.70	61.73	−0.03

a) ppm from TMS as the internal standard. The errors are at least ±0.1 ppm. b) To be published in detail, along with the chemical shifts of cyclopropane-ring carbons. c) Measured on a Hitachi Perkin-Elmer R-22 spectrometer, with 22.6 MHz in the FT mode. d) Y. Kusuyama, *Bull. Chem. Soc. Jpn.*, **50**, 1784 (1977).

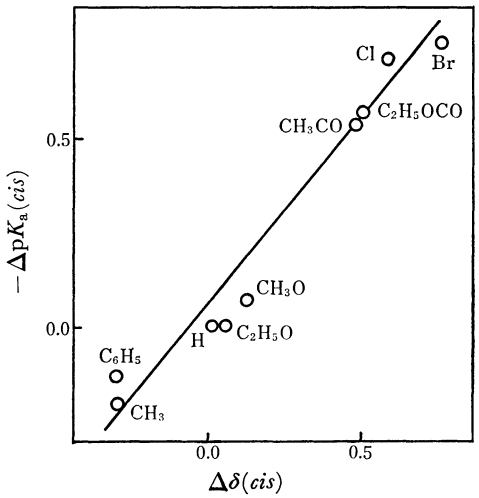


Fig. 1. Plots of ΔpK_a values for *cis*-2-substituted 1-cyclopropanecarboxylic acids at 25 °C in water *vs.* substituent induced ^{13}C chemical shifts of the methylene carbons of ethyl group in ethyl 2-substituted 1-cyclopropanecarboxylates.

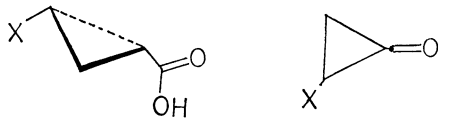
The general trend of the substituent effects obtained for $pK_a(cis)$ is similar to those in such 2-substituted cyclopropane systems[6,12,13a,21] as 2-substituted 1,2-dimethyl-1-cyclopropanecarboxylic acids; they may be explained by substituent electronic effects except for the case of the phenyl group.

The $\Delta pK_a(cis)$ values showed a good linear relation with the $\Delta\delta(cis)$ values (Fig. 1). Therefore, it is reasonable to consider that the special desolvation effect by the proximate *cis*-2-substituents does not contribute to the pK_a values. In the case of 2-substituted acrylic acids, appreciable contributions of the desolvation effect to the dissociation of cis isomers have been reported.[13d]

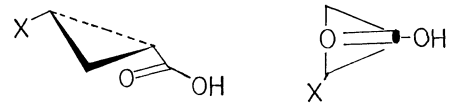
$\Delta pK_a(cis)$ values do not afford a linear relation with those of *o*-substituted benzoic acid, where the steric

inhibition of resonance between the benzene ring and the carboxyl group by the *o*-substituents causes a acid-strengthening effect relative to *p*-substituted benzoic acids.

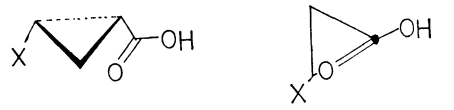
The cyclopropane ring is capable of overlaping with an adjacent p orbital of the substituents at the maximum in the *s-trans* or *s-cis* conformation.[6] In cyclopropanecarboxylic acid, the preferred conformation might be the *s-cis* conformer,[6] where the steric repulsion between the spherical *cis*-2-substituent and the carboxyl group is minor compared to those in ortho-substituted benzoic acids.[13c,22] Thus, spherical substituents would not prevent the resonance interaction between the cyclopropane ring and the carboxyl group. The acid-weakening effect of the *cis*-2-methyl group clearly



s-trans



s-cis



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showed the same direction as that observed in the trans isomer. Moreover, it may be thought that the steric inhibition of resonance is not of major importance for chloro and bromo derivatives, although for these substituents the same acidity as in the cis and trans series respectively resulted from the compensation of contributing factors. Substituents with p-orbitals tend to have the maximum overlap with the cyclopropane ring in the bisected conformation. In *cis*-2-acetyl, methoxycarbonyl- and ethoxycarbonyl-1-cyclopropanecarboxylic acids, the steric repulsion between the substituent and the carbonyl group of the carboxyl group increases and prevents cis substituents from having the maximum overlap with the cyclopropane ring relative to the corresponding trans isomer. Such substituents could lead in the direction of acid weakening relative to the trans isomer (Table 2).

The pK_a values for alkoxy groups and phenyl group are quite high relative to that of the parent compound and the corresponding trans derivatives, if they are considered only in terms of normal electronic substituent effects. The origin for this phenomenon can not be explained clearly at the present time. Only the phenyl group deviated appreciably in the $\Delta\delta(trans)$-$\Delta\delta(cis)$ plots to the high field from the regression line (Fig. 2), while no significant difference in the plots was detected for alkoxy groups. It is considered that the methylene carbon of the ethyl group is more deshielded by the proximate phenyl group in the cis isomer.

The substituent effects can generally be analysed

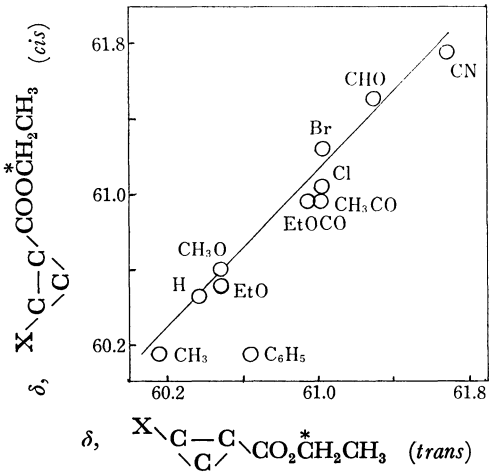
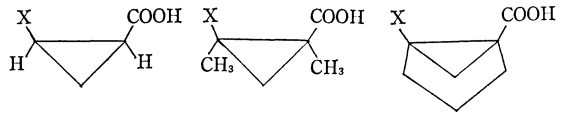


Fig. 2. Comparison of substituent-induced ^{13}C chemical shifts of the methylene carbons of ethyl group in ethyl 2-substituted 1-cyclopropanecarboxylates.

TABLE 4. THE SUBSTITUENT EFFECTS (ΔpK_a VALUES) OF METHOXYCARBONYL AND BROMINE IN THE *cis*-2-SUBSTITUTED CYCLOPROPYL FRAMEWORK



	(I)	(II)	(III)
H	0.00	0.00	0.00
CH_3OCO	−0.61	−1.019	−0.912
Br	−0.74	−1.276	−0.851

by the use of the linear free-energy relationship if only the electronic effect operates. The pK_a values for the trans series were excellently correlated by σ_m (correlation coefficient: 0.998; ρ: 1.99), indicating an appreciable contribution of the resonance effect.[12] The plots of the $\Delta pK_a(cis)$ against the substituent constants, σ^0, σ_p, and σ_I, failed to give a good linear relationship. The correlation coefficients proved to be from 0.83 to 0.89. A rather good correlation with the ρ value of 2.09 was obtained by means of σ_m with the correlation coefficient of 0.981. Although this correlation is not an excellent one, it appears that the special proximity effect is not of major importance in the dissociation of *cis*-2-substituted 1-cyclopropanecarboxylic acid.

In the series of *cis*-2-substituted 1-cyclopropanecarboxylic acids (I), the 2-substituted 1,2-dimethyl-1-cyclopropanecarboxylic acids (II), and 5-substituted bicyclo-[3.1.0]hexane-1-carboxylic acids (III)[14] effects of substituents (the values for methoxycarbonyl and bromo were available for comparison) increase in the order of I<III<II (Table 4), the same as the increasing order of the steric bulk of alkyl groups located behind the carboxyl group (hydrogen < trimethylene < two methyl groups). This order is also the same as that for the pK_a values for the parent acid of each series. Two explanations are possible for the phenomenon: (1) Bulky alkyl groups effectively desolvate the carb-

oxylate anion. The negative charge on the carboxylate does not disperse, though; accordingly, the electron density increases. (2) Alkyl groups shorten the distance between the substituent and the carboxyl group and increase the contribution of the field effect.

Experimental

The boiling points and melting points are uncorrected. The melting points were determined on a Yanaco Mp hot-stage melting-point apparatus. The ^{1}H NMR spectra were obtained on a JEOL JNM-C-60 HL spectrometer (60 MHz) and were reported in δ values relative to the internal TMS. The GLC analyses were carried out on a Yanaco GCG 550T, using a 1-m column of Silicone DC 550 or Silicone XF 1150. Preparative scale GLC separations were performed on a Yanaco G 80 aparatus equipped with an AP 11 collector.

The structure assignments for the geometrical isomers of alkyl 2-substituted 1-cyclopropanecarboxylates were made on the basis of the ^{1}H NMR spectra of ring protons by means of shift reagents, based on the generalization that the tendency of the shift of the signals of cis protons to carbonyl is larger than that of the shift of the trans protons.[23] The cis and trans isomers of alkyl 2-substituted 1-cyclopropanecarboxylates were well separated by GLC, and the cis isomer always showed a longer retention time than that of the corresponding trans isomer.

Ethyl cis-*2-Methoxy-1-cyclopropanecarboxylate.* The title compound was isolated by fractional distillation and by making two passes on the column (silicone DC 550 and silicone XF 1150) from a mixture of cis and trans isomers obtained by the reaction of ethyl diazoacetate with methyl vinyl ether.[12] Bp 81 °C/30 Torr, NMR (CCl_4) δ 0.75—1.75 (3H, m, ring), 1.24 (3H, t, J=8 Hz, CCH_3), 3.22 (3H, s, CH_3O), 3.23—3.65 (1H, m, ring), 4.05 (2H, q, J=8 Hz, CO_2CH_2C). Found: C, 58.72; H, 8.07%. Calcd: C, 58.31; H, 8.39%.

cis-*2-Methoxy-1-cyclopropanecarboxylic Acid.* Ethyl *cis*-2-methoxy-1-cyclopropanecarboxylate (1.3 g) was hydrolyzed by heating (40 °C) with sodium hydroxide (0.4 g) in 5 ml of water. After acidification to pH 3, extraction with ether, and the evaporation of the ether, *cis*-2-methoxy-1-cyclopropanecarboxylic acid was purified by short-column distillation; 0.3 g; bp 105 °C/10 Torr. NMR ($CDCl_3$) δ 0.90—2.70 (3H, m, ring), 3.34 (3H, t, J=7 Hz, CH_3), 3.30—3.7 (1H, m, ring, OCH), 7.75 (1H, s, OH). Found: C, 50.45; H, 7.55%. Calcd: C, 51.70; H, 6.94%.

Ethyl cis-*2-Ethoxy-1-cyclopropanecarboxylate.* The procedure used was the same as that employed above for the methoxy derivative; bp 103 °C/33 Torr. NMR (CCl_4) δ 0.7—1.75 (3H, m, ring), 1.10 (3H, t, J=8 Hz, $COCH_3$), 1.25 (3H, t, J=7 Hz, $COOCH_3$), 3.10—3.70 (3H, m, two methylene protons of the ethoxy group and one ring proton). Found: C, 60.76; H, 9.42%. Calcd: C, 60.74; H, 8.92%.

cis-*2-Ethoxy-1-cyclopropanecarboxylic Acid.* This compound was obtained by the alkaline hydrolysis of the corresponding ethyl ester; bp 135 °C/17 Torr. NMR ($CDCl_3$) δ 0.95—2.70 (3H, m, ring), 1.15 (3H, t, J=7 Hz, CH_3), 3.20—3.80 (3H, m, ring OCH and CH_2 of ethyl group) Found: C, 54.30; H, 7.86%. Calcd: C, 55.37; H, 7.74%.

Dimethyl and Diethyl cis-*1,2-Cyclopropanedicarboxylates.* These two esters were separated from mixtures[17] of the corresponding geometrical isomers. Dimethyl *cis*-1,2-cyclopropanedicarboxylate: bp 84 °C/4 Torr, 146—148 °C/45 Torr, lit, 110 °C/3 Torr.[24] Diethyl *cis*-1,2-cyclopropanedicarboxylate. Bp 138 °C/27 Torr, lit, bp 83—84 °C/1 Torr,[25] 124 °C/14 Torr.[24]

cis-*2-Methoxycarbonyl-1-cyclopropanecarboxylic Acid.* The alkaline hydrolysis[26] of dimethyl 1,2-cyclopropanedicarboxylate afforded *cis*-2-methoxycarbonyl-1-cyclopropanecarboxylic acid in a 30% yield; bp 147—148 °C/4.5 Torr, lit, 160 °C/3 Torr.[24]

cis-*2-Ethoxycarbonyl-1-cyclopropanecarboxylic Acid.* This compound was obtained by the alkaline hydrolysis of diethyl *cis*-1,2-cyclopropanedicarboxylate; bp 130—131 °C/3.5 Torr.

cis-*2-Ethoxycarbonyl-1-cyclopropanecarbonyl Chloride.* The treatment of *cis*-2-methoxycarbonyl-1-cyclopropanecarboxylic acid (9 g) with thionyl chloride (12 g) and subsequent distillation afforded the title compound (9 g); bp 84 °C/4 Torr. NMR (CCl_4) δ 1.00—2.00 (2H, m, ring CH_2), 1.25 (3H, t, J=7 Hz, CH_2 of the ethyl group).

Ethyl cis-*2-Acetyl-1-cyclopropanecarboxylate. A.* To dimethyl cadmium (*ca.* 0.05 mol) in benzene we added, drop by drop, 9 g (0.05 mol) of *cis*-2-ethoxycarbonyl-1-cyclopropanecarbonyl chloride in 10 ml of benzene. After a routine treatment, 3 g of crude ethyl *cis*-2-acetyl-1-cyclopropanecarboxylate were obtained. To this we then added 3 ml of water and stirred the mixture vigorously for 10 min. The organic layer was then separated and purified by distillation; 2 g; bp 95 °C/7 Torr.

Ethyl cis-*2-Acetyl-1-cyclopropanecarboxylate. B.* To a stirred mixture of 100 g of methyl vinyl ketone and 1 g of anhydrous copper(I) sulfate in 50 ml of hexane at 40 °C, 100 g of ethyl diazoacetate were added. After several minutes, the reaction took place suddenly. After the reaction was complete, the mixture was filtered and carefully distilled at atmospheric pressure in order to remove the excess methyl vinyl ketone and hexane. The residue was distilled *in vacuo* to yield 10 g of crude products; bp 70—88 °C/5.5 Torr. The fractional distillation afforded 3 g of the title compound, including 20% of impurities. Treatment with 2 ml of 0.5 M NaOH and subsequent GLC operation gave a pure material which showed essentially the same retention time in GLC and the same NMR spectrum as has been obtained by Method A.

cis-*2-Acetyl-1-cyclopropanecarboxylic Acid.* Ethyl *cis*-2-acetyl-1-cyclopropanecarboxylate (1 g) was hydrolyzed by heating (40 °C) with sodium hydroxide (0.24 g) in 6 ml of 50% ethanol to yield, after a routine treatment, *cis*-2-acetyl-1-cyclopropanecarboxylic acid (0.4 g); bp 143 °C/4 Torr. NMR ($CDCl_3$) δ 1.10—2.62 (m, 4H, ring), 2.24 (1H, s, CH_3), 8.30 (1H, s, OH). Found: C, 54.86; H, 6.62%. Calcd: C, 56.24; H, 6.30%.

1,1-Dichloro-2-vinylcyclopropane. This compound was prepared by adding potassium *t*-butoxide to a solution of 1,3-butadiene and chloroform and by a subsequent routine treatment,[27] bp 123—125 °C, lit, 122.5 °C/730 Torr.[28]

2,2-Dichloro-1-cyclopropanecarboxylic Acid. The oxidation of 1,1-dichloro-2-vinylcyclopropane with potassium permanganate in acetone gave a 2,2-dichloro-1-cyclopropanecarboxylic acid,[29] bp 92 °C/6 Torr, mp 74—75 °C, lit, mp 75—76 °C.[28]

Methyl 2,2-Dichloro-1-cyclopropanecarboxylate. This compound was obtained by the esterification of 2,2-dichloro-1-cyclopropanecarboxylic acid with methanol and sulfuric acid; bp 79 °C/23 Torr. NMR (CCl_4) δ 1.70—2.21 (2H, m, CH_2), 2.4—2.75 (1H, m), 3.76 (3H, s, CH_3).

Methyl cis-*2-Chloro-1-cyclopropanecarboxylate.* A mixture of 22 g (0.1 mol) of methyl 2,2-dichlorocyclopropane-carboxylate, 37 g (0.13 mol) of tributyltin hydride, and 1 g of AIBN was heated to about 90 °C. A vigorous reaction took place. After the mixture has then cooled to room temperature, cis and trans methyl 2-chloro-1-cyclopropane-carboxylate were obtained by fractional distillation through a small Widmer column; 8 g; bp 65—80 °C/33 Torr. A pure cis

isomer was obtained by a semi-preparative GLC operation; bp 100 °C/38 Torr. NMR (CCl_4) δ 1.10—1.68 (2H, m, CH_2), 1.73—2.15 (1H, m, CHCO), 3.00—3.45 (1H, m, CHCl), 3.70 (3H, s, CH_3). Ethyl *cis*-2-chloro-1-cyclopropanecarboxylate was prepared by the procedure described above for the methyl ester. NMR (CCl_4) δ 1.10—1.65 (2H, m, CH_2 of ring), 1.31 (3H, t, J=7 Hz, CH_3), 1.73—2.08 (1H, m, CHCO), 3.11—3.42 (1H, m, CHCl), 4.06 (2H, q, J=7 Hz, CH_2 of the ethyl group). Found: C, 48.75; H, 5.78%. Calcd: C, 48.52; H, 6.06%.

cis-*2-Chloro-1-cyclopropanecarboxylic Acid.* Ethyl *cis*-2-chloro-1-cyclopropanecarboxylate (1.1 g) was saponified by stirring with 0.4 g of sodium hydroxide in 6 ml of 30% ethanol to yield, after acidification, 0.7 g of *cis*-2-chloro-1-cyclopropanecarboxylic acid; bp 108—110 °C/5 Torr, mp 88—88.5 °C. NMR ($CDCl_3$) δ 1.2—1.6 (2H, m, CH_2), 1.6—2.27 (1H, q, J=7 Hz, CHCO), 3.13—3.57 (1H, q, J=7 Hz, CHCl), 5.5 (1H, s, OH). Found: C, 39.89; H, 3.97%. Calcd: C, 39.84; H, 4.17%.

Ethyl trans-*2-Chloro-1-cyclopropanecarboxylate.* This compound was obtained by GLC separation from a cis and trans mixture; bp 76—78 °C/36 Torr. NMR (CCl_4) δ 1.25 (3H, t, J=7 Hz, CH_3), 1.10—1.65 (2H, m, ring CH_2), 1.75—2.07 (1H, m, CHCO), 3.10—3.40 (1H, m, CHCl), 4.05 (2H, q, J=7 Hz, CH_2).

trans-*2-Chloro-1-cyclopropanecarboxylic Acid.* Ethyl *trans*-2-chloro-1-cyclopropanecarboxylate (1 g) was hydrolyzed with sodium hydroxide (0.4 g) in 40% ethanol (5 ml) to yield *trans*-2-chloro-1-cyclopropanecarboxylic acid; 0.5 g; bp 86 °C/4 Torr. Mp 59 °C. NMR ($CDCl_3$) δ 1.20—1.75 (2H, m, CH_2), 1.80—2.15 (1H, m, CHCO), 3.24—3.55 (1H, m, CHCl), 11.60 (1H, s, OH). Found: C, 40.05; H, 4.24%. Calcd: C, 39.85; H, 4.18%.

1,1-Dibromo-2-vinylcyclopropane. This compound was synthesized by the method described above for the chloro derivative; bp[30] 60 °C/22 Torr. lit, 69.5—70 °C/26 Torr[28] 53—56 °C/10 Torr.[31]

Methyl 2,2-Dibromo-1-cyclopropanecarboxylate. The oxidation of 1,1-dibromo-2-vinylcyclopropane (115 g), the same treatment as has been described for the preparation of 2,2-dichloro-1-cyclopropanecarboxylic acid, gave crude 2,2-dibromo-1-cyclopropanecarboxylic acid, which was then converted to the corresponding methyl ester by adding 200 ml of methanol and 5 ml of concentrated sulfuric acid and by refluxing the subsequent mixture for 10 h. After a routine work-up, methyl 2,2-dibromo-1-cyclopropanecarboxylate (40 g) was obtained; bp 90 °C/9 Torr. NMR (CCl_4) δ 1.76—2.70 (3H, m, ring), 3.73 (3H, s, CH_3). Found: C, 23.08; H, 2.25%. Calcd: C, 23.28; H, 2.35%.

Methyl cis-*2-Bromo-1-cyclopropanecarboxylate.* 34 g (0.13 mol) of methyl 2,2-dibromo-1-cyclopropanecarboxylate were added to 34 g (0.13 mol) of tributyltin hydride. The reaction took place immediately. After cooling to room temperature, methyl *cis*- and *trans*-2-bromo-1-cyclopropanecarboxylate were obtained by distillation; bp 65—95 °C/20 Torr. Subsequent distillation and GLC operation afforded pure methyl *cis*-2-bromo-1-cyclopropanecarboxylate; bp 108 °C/25 Torr. NMR (CCl_4) δ 1.25—1.58 (2H, m, CH_2), 1.75—2.15 (1H, q, J=8 Hz with a small splitting, CHCO), 2.95—3.33 (1H, q, J=8 Hz with a small splitting), 3.70 (3H, s, CH_3). Found: C, 33.80; H, 4.20%. Calcd: C, 33.52; H, 3.91%.

cis-*2-Bromo-1-cyclopropanecarboxylic Acid.* The alkaline hydrolysis of methyl *cis*-2-bromo-1-cyclopropanecarboxylate gave *cis*-2-bromo-1-cyclopropanecarboxylic acid; bp 120 °C/2 Torr; mp 68.5—70.5 °C. NMR ($CDCl_3$) δ 1.3—1.7 (2H, m, CH_2), 1.85—2.23 (1H, m, CHCO), 2.0—2.40 (1H, q, J=8 Hz with small spritting, CHBr), Found: C, 29.11; H, 2.82%. Calcd: C, 29.08; H, 3.05%.

The ionization constants were determined by the potentiometric titration of substituted cyclopropanecarboxylic acids (0.005 M) with sodium hydroxide (0.02 M) according to the previously outlined procedure.[3,12]

The ^{13}C NMR spectra were measured on a Hitachi Perkin-Elmer R-22 spectrometer, with 22.6 MHz in the FT mode. The measurement conditions will be described in detail elsewhere, along with the chemical shifts of the cyclopropane ring carbons.

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