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^{13}C NMR Spectroscopy. Substituent Effects in the Ethyl *trans*-2-Substituted Cyclopropanecarboxylates

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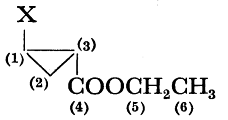
^{13}CFT NMR spectra have been obtained for ethyl *trans*-2-substituted cyclopropanecarboxylates. The chemical shifts have been compared with those of saturated and unsaturated compounds and with substituent constants. The chemical shifts of the methylene carbon of the ethyl group have been correlated linearly with σ_m.

A substantial body of evidence supporting resonance interactions between the cyclopropane ring and the p-orbital of substituents has been obtained from spectroscopic measurements and chemical reactions.[1] However, there has been little work suggesting such interactions based on ^{13}C NMR spectroscopy, which is a useful source of information on the nature of chemical bonds.[2] This paper will describe some characteristic results for the ^{13}C chemical shifts of ethyl *trans*-2-substituted cyclopropanecarboxylates. It is hoped that the effects of the substituents at the 2-position of the ring on the chemical shifts of ^{13}C of the ethyl group will provide a convenient tool for estimating the transmitting ability of the polar effect through a cyclopropane ring.

Results and Discussion

Proton-decoupled natural-abundance ^{13}CFT NMR spectra were obtained at 25.15 MHz at 30 °C. The samples were run as a 1.5±0.1 M solution in CDCl$_3$ containing tetramethylsilane as an internal reference. The signals have been assigned on the basis of the peak intensities and the chemical shifts reported in the literature.[3–5] The assignments of the ^{13}C resonances of the ethyl cyclopropanecarboxylates investigated in this work are shown in Table 1.



Ring carbons are strongly affected by the substituents. The screening at the carbons of the α and β positions relative to the substituents is influenced by several factors (inductive, steric, magnetic anisotropy, *etc.*) contributed by the substituents. One of the most common methods to interpret the substituent effects is a comparison with other similarly substituted compounds.

The best agreement of the cyclopropyl α-carbon shieldings of the monosubstituted cyclopropanes *vs.* the shieldings of substituted methanes was found by Weiner and Malinowski.[3] In addition to their results, a very high correlation of $C_{(1)}$ chemical shifts with the chemical shifts of substituted methanes[2a,3,6] or those of the α-position of 1-substituted pentanes[2a,2b] was obtained by others (slope, 0.80; Fig. 1.). Spiesecke and Schneider[6,7] reported that the chemical shifts of ^{13}C, to which substituents were attached, were correlated by the electronegativity (Ex) of the substituents. In Table 2, the relations of the relative substituent-induced chemical shifts of α-carbons to substituents(C_α-scs) and Ex[8] are summarized. The electronegativity of the group substituents, OCH$_3$, NH$_2$, and CH$_3$, was assumed to be that of the first atom in the group. Good correlations of C_α-scs with Ex were obtained except for the X-vinyl derivative. In the case of the X-vinyl derivative, neighbor-anisotropy may contribute considerably.[2,7] In all five series, bromine deviated from the correlation line because of the contribution of the heavy-atom effect.[2b,9,10] The ($C_{(\alpha)}$-scs *vs.* C_{X-Me}-scs) slopes were parallel to the ($C_{(\alpha)}$-scs *vs.* Ex) slopes. Thus, the electronegativity of the substituents is the most important factor in the ^{13}C chemical shifts of α-carbons.[6] It may be though that the hydridization of α-carbons is a result of the susceptibility of the electronegativity.

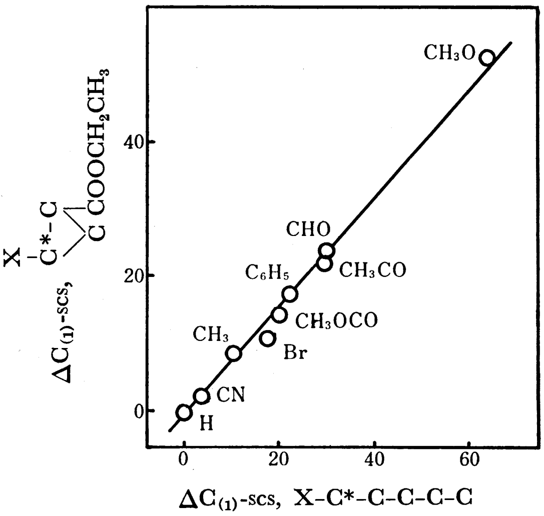
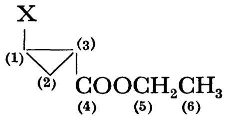


Fig. 1. Comparison of relative substituent-induced ^{13}C chemical shifts of the substituted carbons ($\Delta C_{(1)}$-scs) in 1-substituted pentanes and ethyl *trans*-2-substituted cyclopropanecarboxylates.

The chemical shifts of $C_{(3)}$ were slightly larger than those of $C_{(2)}$. There is a good linear relation between the shifts of $C_{(3)}$ and those of the β-carbons of 1-substituted pentanes for the methyl, bromo, and methoxyl groups,[11] while the cyano, formyl, methylcarbonyl, and acetyl groups are scattered (Fig. 2). Also the chemical shifts of $C_{(3)}$ can not be correlated by those of the β-carbons of substituted ethylenes.[2,12]

For the β-carbons to the substituents in the unsaturated frameworks, the substituent effects exhibit a much wider range of shifts than those observed in saturated frameworks.[2] The chemical shitfs may be indicated by the kinds of canonical resonance structures:

Table 1. ^{13}C Chemical shifts for ethyl *trans*-2-substituted cyclopropanecarboxylates
(The shifts are in PPM downfield from TMS)



X	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$
H	8.25(8.4)[a]	8.25(8.4)[a]	12.92(13.2)[a]	174.86(174.1)[a]	60.37(60.8)[a]	14.26(14.7)[a]
CH_3	17.87	17.05	21.30	174.32	60.19	14.26
C_6H_5	26.15(26.4)[a]	17.05(16.9)[a]	24.15(24.3)[a]	173.22(172.1)[a]	60.61(60.6)[a]	14.32(14.5)[a]
CH_3O	62.13	15.72	20.87	172.49	60.49	14.26
C_2H_5O	66.62	15.05	21.17	172.62	60.49	14.32
C_6H_5O	57.15	15.59	21.66	172.06	60.85	14.26
Br	15.17	18.87	23.78	171.46	61.10	14.20
CH_3OCO	22.45	15.35	22.15	171.65	61.10	14.20
C_2H_5OCO	22.33	15.23	22.33	171.65	60.97	14.20
CHO	30.70	14.80	22.15	171.09	61.28	14.14
CH_3CO	30.70	17.05	24.15	171.89	61.04	14.20
COCl	31.73	17.96	25.24	170.01	61.64	14.14
CN	5.64	14.50	21.05	170.06	61.70	14.08

a) O. A. Subbotin, A. S. Kozmin, Yu. K. Grishin, N. M. Sergeyev, and I. G. Bolesov, *Org. Magn. Reson.*, **4**, 53 (1972).

Table 2. Comparison of the substituent-induced chemical shifts of α-carbon ($C_{(\alpha)}$-scs) and the relation of $C_{(\alpha)}$-scs to the electronegativity (Ex)[a]

α-Carbon	($C_{(\alpha)}$-scs *vs.* C_{X-Me}-scs)Slope	($C_{(\alpha)}$-scs *vs.* Ex)Slope	f[b]
(1) X-Me	1.00	43.4(0.940, H, Me, Cl, Br, NH_2, MeO)[c]	1.00
(2) X-*c*-Pr	0.82[d]	31.1(0.983, H, Cl, Br, NH_2)	0.72
(3) X-vinyl	0.88[d]	15.7(0.738, H, Me, Cl, Br, F, MeO)	
		21.3(0.998, H, Me, MeO)	0.49
(4) X-Ph	0.54[d]	20.45(0.846, H, Me, Cl, Br, F, NH_2, MeO)	
		18.9(0.994, H, Me, F, NH_2, MeO)	0.44
(5) *trans*-2-X-*c*-Pr-CO_2Et	0.80	37.7(0.923, H, Me, Cl, Br, MeO)[e]	
		38.0(0.979, H, Me, Cl, MeO)	0.82

a) Ref. 8. b) Relative value of the ($C_{(\alpha)}$-scs *vs.* Ex)Slope. c) Correlation coefficient and the substituents included for the calculation. d) Ref. 3. e) The value of the methyl ester (δ 33.25) was used for chlorine.

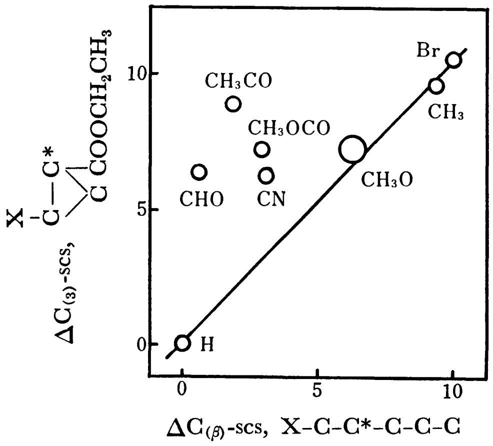
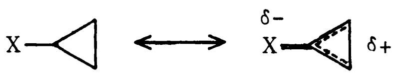


Fig. 2. Plots of the relative substituent-induced ^{13}C chmical shifts of $C_{(3)}$($\Delta C_{(3)}$-scs) in ethyl *trans*-2-substituted cyclopropanecarboxylates *vs.* the relative substituent-induced ^{13}C chemical shifts of β-carbons ($\Delta C_{(\beta)}$-scs) in 1-substituted pentanes.

$$X\text{-}C\text{=}C \leftrightarrow \overset{\delta-}{X}\text{=}C\text{-}\overset{\delta+}{C} \leftrightarrow \overset{\delta+}{X}\text{=}C\text{-}\overset{\delta-}{C}. \qquad (1)$$

The cyclopropane ring exhibits a considerable degree of π-bond character and interacts with the p-orbitals of the substituents, especially releasing electrons to substituents:[1,2]



(2)

The cyano, formyl, methoxycarbonyl, and acetyl groups are electron-attracting groups by means of their resonance and decrease the electron densities of $C_{(2)}$ and $C_{(3)}$, as is shown in (2). Accordingly, $C_{(2)}$ and $C_{(3)}$ shift downfield from those expected from the shift of the saturated frameworks. It may be thought that the interaction is responsible for the appreciable differences between the observed values and the predicted values (Table 3.) which were calculated by the simple additive rule.[5] The shift differences in $C_{(2)}$ is largest in the three ring carbons except for the $C_{(1)}$ of the bromo derivative, to which the heavy halogen atom effect may contribute,[2] In order to estimate semiquantitatively

TABLE 3. SHIFT DIFFERENCES BETWEEN THE OBSERVED VALUES AND THE PREDICTED ONE

	$\delta_{pred} - \delta_{obsd}$ (in ppm)		
	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$
C_6H_5	0.75	3.55	1.25
Br	6.13	5.03	1.22
$COCH_3$	2.20	4.35	2.05
COCl	3.77	5.64	3.16
CN	2.41	4.32	2.15

TABLE 4. Δ_R VALUES FOR THE $C_{(3)}$ OF ETHYL *trans*-2-SUBSTITUTED CYCLOPROPANECARBOXYLATES

Substituent	Δ_R
H	0.0
CH_3	−1.0
CH_3O	1.9
Cl	0.7
Br	0.9
CH_3OCO	6.3
CH_3CO	9.1
CHO	8.5
CN	4.9

the contribution of the ionic canonical form in (2), the differences (Δ_R) in the chemical shifts between $C_{(3)}$ (ethyl *trans*-2-substituted cyclopropanecarboxylate) and $C_{(\beta)}$(1-substituted pentane) were calculated (Table 4). For unsaturated frameworks, the substituent effects may be designated as follows:

$$\Delta\delta = \Delta\delta_{saturated} + \Delta_R. \qquad (3)$$

A linear correlation was obtained between Δ_R and σ_R^- for the electron-attracting groups by means of the resonance (slope, 15.97; r: correlation coefficient, 0.980). On the basis of these results, it seemed reasonable to assume that the resonance interaction of a cyclopropane with electron-attracting substituents plays an important role in the chemical shifts of $C_{(2)}$ and $C_{(3)}$.

The most striking result in the present investigation is a measurable chemical shift of $C_{(5)}$. In general, chemical shifts of the carbon of the δ position to substituents are correlated by a Hammett-type equation because of the absence of steric interaction between the substituents and δ-carbon. The present chemical shifts of $C_{(5)}$ are correlated with σ_m (slope, 2.07; r=0.985), and a more excellent correlation was obtained with σ_m° (slope, 2.17; r=0.994)[13] although σ_m and σ_m° were obtained from the reaction in hydroxylic solvents, and solvent-variable substituent constants are included in the calculations.

$$\Delta\delta_{(C5)} = 2.07\sigma_m,$$

$$\Delta\delta_{(C5)} = 2.17\sigma_m^\circ.$$

It is noteworthy that σ_m and σ_m° include considerable contributions of the resonance effects.[1,14]

$$\sigma_m = \sigma_I + 0.33\sigma_R,$$

$$\Delta\delta_{(C5)} = 2.1\sigma_I + 0.72\sigma_R.$$

On the basis of this correlation of $^{13}C_{(5)}$ chemical shifts, it seemed reasonable to assume that the cyclopropane ring can transmit the resonance effect, although its influence is rather small. The pK_a values of *trans*-2-substituted cyclopropanecarboxylic acids in water or in 50% aqueous alcohol were correlated by σ_m:[15]

$$\Delta pK_a = 1.99\sigma_m = 0.96\Delta\delta(C_{(5)}) \text{ (in water)}$$

$$\Delta pK_a = 2.92\sigma_m = 1.41\Delta\delta(C_{(5)}) \text{ (in 50\% alcohol)}$$

Thus, the relative acidities of carboxylic acids may be estimated by means of the ^{13}C chemical shifts of alkoxyl carbons of appropriate esters, in which substituents are sufficiently remote from the carboxyl group.

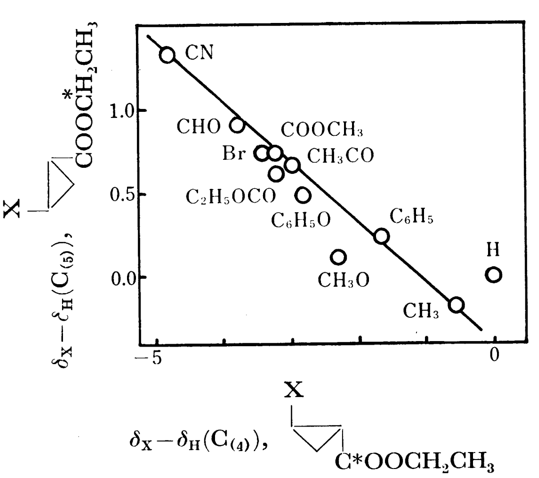


Fig. 3. Correlation between the ^{13}C chemical shifts of carbonyl carbons and those of alkoxy carbons in ethyl *trans*-2-substituted cyclopropanecarboxylates.

A linear correlation was observed between the ^{13}C chemical shifts of $C_{(4)}$ and those of $C_{(5)}$ (Fig. 3). The unsaturated compound, however, deviated from the correlation line. The direction of the chemical shifts of $C_{(4)}$ is reversed in terms of the substituent electronic properties. A "reverse" correlation has previously been reported for the chemical shifts of carboxyl carbons in the substituted benzoic acids[16] and benzocaine hydrochlorides[17] and of cyanide carbons in the substituted benzonitriles.[18] It appears that the large charge separation in the carboxyl group is responsible for the reversal in this direction of the substituent effects.

The $C_{(6)}$, which is most remote from the site of substitution, is practically not influenced at all by the substituent and has a chemical shift equal to 14.2±0.1 ppm from tetramethylsilane. This carbon seems too distant from the substituent for any substituent effect to be detected.

Experimental

^{13}C NMR Spectra. The ^{13}CFT NMR spectra were obtained at 25.15 MHz on a JEOL-JNM-PFT-100 apparatus at 30 °C. Samples were dissolved in $CDCl_3$ containing tetramethylsilane as the internal reference. The concentrations were 1.5±0.1 M. The measurement conditions were as follows: puls width, 15 μs(90°); repetition time, 2.5 s; frequency range, 6.25 KHz; data points, 8192. The accuracy is at least ±0.06 ppm.

Materials. The materials were identified on the basis of spectroscopic and gas-chromatographic measurement and elemental analysis. The NMR spectra were measured on a JEOL-JNM-C-60HL(60 MHz) spectrometer, with tetrameth-

TABLE 5. BOILING POINTS OF ETHYL *trans*-2-SUBSTITUTED CYCLOPROPANECARBOXYLATE (°C/Torr)

Substituent	Observed[a]	Lit, value
H	127	134—135[b], 50—51/4[c]
CH_3	144	76/70
C_6H_5	132—135/7	94—95.5/0.65[d] 105—106/0.2[e]
CH_3O	76—77/30	61—63/15[f]
C_2H_5O	95/32	66/9[f]
C_6H_5O[g]	87—90/1.5	
Br[h]	98/40	
CH_3OCO[i]	109/28	101—114/15[j]
C_2H_5OCO	101—103/5	117/17
CHO	97/20	45/<1[k]
CH_3CO	83/6	105/19[f]
COCl[l]	110/22	
CN	82/5	80—82/3

a) Uncorrected. b) S. R. Landor and N. Punja, *J. Chem. Soc.*, *C*, **1967**, 2495. c) A. F. Ferris, *J. Org. Chem.*, **20**, 780 (1955). d) C. H. Depuy, G. M. Duppen, K. L. Eilers, and R. A. Klein, *J. Org. Chem.*, **29**, 2813 (1964). e) M. Julia, S. Julia, and B. Bemont, *C. R. Acad. Sci.*, **245**, 2304 (1957). f) Ref. 15. g) Found: C, 69.28; H, 6.88%. Calcd for: C, 69.89; H, 6.84%, NMR (CCl_4) δ 0.75—1.58 (2H, m, CH_2, ring), 1,26(3H, t, J=7 Hz, CH_3), 1.68—2.02(1H, m, CHCO), 3.75—4.10(1H, m, OCH), 4.09(2H, q, J=7 Hz, OCH_2), 6.6—7.3(5H, m, C_6H_5). h) NMR(CCl_4) δ 1.27(3H, t, J=7Hz, CH_3), 1.2—1.7(2H, m, CH_2, ring), 1.80—2.20(1H, m, CHCO), 2.95—3.35(1H, m, CHBr), 4.16(2H, q, J=7 Hz, OCH_2). i) NMR(CCl_4) δ 2.25(3H, t, J=7 Hz, CCH_3), 1.30—1.50(2H, m, CH_2, ring), 1.86—2.20(2H, m, CH, ring), 3.61(3H, s, OCH_3), 4.06(2H, q, J=7 Hz. OCH_2C). j)Mixture of *cis-trans* isomers, L. L. McCoy, *J. Am. Chem. Soc.*, **80**, 6568(1958). k) Ref. 25. l) NMR(CCl_4) δ 1.27(3H, t, J=7 Hz, CH_3), 1.4—1.8(2H, m, CH_2, ring), 2.16—2.75(2H, m, CH), 4.11(2H, q, J=7 Hz, OCH_2).

ylsilane employed as the internal standard. Two geometrical isomers of ethyl 2-substituted cyclopropanecarboxylates were isolated by fractional distillation and/or by GLC. For the 2-phenyl derivative, the *trans*-isomer in a mixture of the two isomers was hydrolyzed to *trans*-2-phenylcyclopropanecarboxylic acid, which was then converted to the appropriate ethyl ester by the usual method.[19] The GLC analyses were carried out on a Yanaco GCG-550T, using a 1-m column of Silicone DC 550 or Silicone XF 1150. The *trans*-isomer always showed the shorter retention time. The separation of the two isomers were carried out on a Yanaco G80 apparatus equipped with AP11. The structure assignments for the geometrical isomers were made by means of the ^1H NMR spectra using shift reagents based on a generalization[20] that the tendency of the shift of the signal of the *cis* proton to ethoxycarbonyl is larger than that of the shift of the *trans* protons.

The ethyl 2-phenyl-, methoxy-, ethoxy-, phenoxy-, cyano-, and ethoxycarbonyl-cyclopropanecarboxylates were prepared by the reaction of ethyl diazoacetate with the appropriate alkene.[15] Ethyl *trans*-2-methylcyclopropanecarboxylate was obtained by the ethanolysis of the appropriate acid chloride,[21] itself prepared by the chlorination of *trans*-2-methylcyclopropanecarboxylic acid[21,22] with thionyl chloride. The ethyl 2-bromocyclopropanecarboxylate was synthesized by a Hunsdicker reaction[23,24] of silver *trans*-2-ethoxycarbonylcyclopropanecarboxylate using bromine. The *trans*-2-ethoxycarbonylcyclopropanecarboxylic acid[24] was chlorinated by thionyl chloride to *trans*-2-ethoxycarbonylcyclopropanecarbonyl chloride. The methanolysis of *trans*-2-ethoxycarbonylcyclopropanecarbonyl chloride afforded methyl ethyl cyclopropane-1,2-dicarboxylate. Ethyl 2-formyl- and 2-cyanocyclopropanecarboxylates were obtained by the reaction of ethyl (dimethylsulfuranylidene) acetate with acrolein and acrylonitrile respectively.[25] The boiling points of the ethyl *trans*-2-substituted cyclopropanecarboxylates are summarized in Table 5.

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