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Carbon 13 NMR Spectra of Dimethyl Fumarate and its Thioderivatives: Empirical Shielding Constants for the Methyl Ester and Thioester Substituents†

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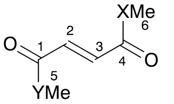
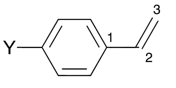
The assigned ^{13}C NMR spectroscopic data from *O,S*-dimethyl thiofumarate, *S,S*-dimethyl bis(thio)fumarate and the novel *S*-methyl *p*-methoxythiocinnamate are presented and the empirical shielding constants for the methoxycarbonyl and methylsulfanylcarbonyl groups determined for the first time.

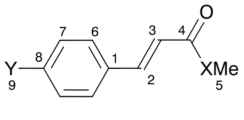
Our continued interest in the chemistry of organic sulfur compounds led us to prepare some thioderivatives (**1a**, **b**) of dimethyl fumarate (**1c**). When their ^{13}C NMR spectra were acquired (Table 1), as part of the characterization process, we were struck by the amazing similarity between the olefinic carbon's (C-2 and C-3) chemical shifts of compounds **1a** and **1c**, which hinders the assignment of the signals arising from C-2 and C-3 in compound **1b**.



1a X = Y = S
b X = O; Y = S
c X = Y = O



2a Y = H
b Y = Me
c Y = OMe
d Y = Cl
e Y = NO_2



3a X = S; Y = H
b X = S; Y = Me
c X = S; Y = OMe
d X = S; Y = Cl
e X = S; Y = NO_2

4a X = O; Y = H
b X = O; Y = Me
c X = O; Y = OMe
d X = O; Y = Cl
e X = O; Y = NO_2

To assign $\delta_{C\text{-}2}$ and $\delta_{C\text{-}3}$ in the spectrum of **1b** and in the hope of better understanding the results already obtained, we decided to calculate the expected chemical shifts of those signals, by using empirical shielding constants (Z_i). To our surprise, however, we have been unable to find the Z_i values for either the methylsulfanylcarbonyl or methoxycarbonyl substituent groups in the literature. Thus, we decided to determine these values by comparing the ^{13}C NMR data (Table 2) from a series of *p*-substituted styrenes (**2**) with the data from the corresponding series of *p*-substituted thiocinnamates (**3**) and cinnamates (**4**).

The results (Table 3) for –C(=O)OMe are consistent with the reported[2] empirical shielding constants for the carboxyl group ($Z_1 = 4.2$; $Z_2 = 8.9$), albeit less so with those for the ethoxycarbonyl substituent ($Z_1 = 6.3$; $Z_2 = 7.0$). No such comparisons are possible for –C(=O)SMe owing to the lack of previously published data. Hence, to test the accuracy of the newly determined Z_i values, we calculated the ^{13}C NMR chemical shifts for the olefinic carbons in *p*-nitrostyrene, using data both from the corresponding cinnamate and thiocinnamate and found the calculated values to be in good agreement with the experimental[3] values (Table 4).

We then calculated $\delta_{C\text{-}2}$ and $\delta_{C\text{-}3}$ for **1b**, using the experimental values of the chemical shifts owing to the olefinic carbons of **1a** (Table 1), by adding the Z_i values for –C(=O)OMe (Table 3) and subtracting those for –C(=O)SMe. Similarly, we obtained another pair of $\delta_{C\text{-}2/3}$ estimates from **1c**. Furthermore, as the above estimates are mutually independent, we assumed that their average should be the best estimated values available for $\delta_{C\text{-}2/3}$. These results (Table 5) led us to the assignments of $\delta_{C\text{-}2/3}$ for **1b** shown in both Tables 1 and 5. Moreover, from a comparison of the best calculated estimates of $\delta_{C\text{-}2/3}$ with the measured values of the same chemical shifts, we were able to determine the corresponding non-additivity corrections ($\tilde{N}_i$) for $\delta_{C\text{-}2/3}$ of **1b**. The non-zero value of these corrections suggests that there are subtle differences in the rotameric preferences of the –C(=O)OMe and –C(=O)SMe substituents, not taken into account by the model underlying the idea of empirical shielding constants. The fact that these $\tilde{N}_i$ are small enough to permit the application of Z_i to the assignment of ^{13}C NMR data is a triumph of this elegantly straightforward model.

In conclusion, it should be pointed out that the similarity of $\delta_{C\text{-}2/3}$ in compounds **1a** and **1c** is not accidental, but traceable, as we have shown, to a capricious combination of the effects governing the chemical shifts, the very same effects that lead to the different values of $\delta_{C\text{-}2}$ and $\delta_{C\text{-}3}$ observed for compound **1b**.

Table 1 $\delta_{^{13}C}$ of dimethyl fumarate and its thioderivatives[a]

Compound	X	Y	C-1	C-2	C-3	C-4	C-5	C-6
1a	S	S	189.2	133.4	133.4	189.2	12.0	12.0
1b	O	S	189.2	138.7	128.3	165.5	11.9	52.4
1c[b]	O	O	165.3	133.5	133.5	165.3	52.2	52.2

[a]5% v/v $CDCl_3$ solutions (TMS = 0 ppm), observed at 50 MHz. [b]Although the ^{13}C NMR spectrum of **1c** (in CCl_4) is published in ref. 1, we acquired it in $CDCl_3$, to ascertain that the observed similarity of $\delta_{C\text{-}2/3}$ in **1a** and **1c** was not owing to any spurious solvent effect. We found that both solvents led to identical spectra.

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 2 $\delta_{^{13}C}$ for signals of olefinic carbons[a] of substituted styrenes[b] (**2**), methyl thiocinnamates (**3**) and methyl cinnamates (**4**)

		$\delta_{^{13}C}$			$\delta_{^{13}C}$			$\delta_{^{13}C}$	
Y	Comp.	C-2	C-3	Comp.	C-2	C-3	Comp.	C-2	C-3
H	**2a**	137.0	113.5	**3a**	140.1	124.7	**4a**	144.7	118.1
Me	**2b**	136.9	112.5	**3b**	140.3	123.8	**4b**	144.8	116.6
MeO	**2c**	136.5	111.3	**3c**	140.0	122.5	**4c**	144.5	115.2
Cl	**2d**	135.7	114.2	**3d**	138.7	125.2	**4d**	143.4	119.4

[a] 5% (v/v) $CDCl_3$ solutions (TMS = 0 ppm), observed at 150 MHz. [b] Ref. 1.

Table 3 Calculated values of $\Delta\delta_{^{13}C}$[a] (ppm) and the Z_i[b,c] of esters and thioesters

	$\Delta\delta_{^{13}C}$			
	–C(=O)OMe		–C(=O)SMe	
Y	C-2	C-3	C-2	C-3
H	+7.7	+4.6	+3.1	+11.2
Me	+7.9	+4.1	+3.4	+11.3
MeO	+8.0	+3.9	+3.5	+11.3
Cl	+7.7	+5.2	+3.0	+11.0
Z_i[b,c]	+7.8	+4.5	+3.3	+11.2

[a] $\Delta\delta_{^{13}C} = \delta_{^{13}C}$ (**4** or **3**) $- \delta_{^{13}C}$ (**2**). [b] Z_i = avg. ($\Delta\delta_{^{13}C}$). [c] As in ref. 2, thus: $i = 2$ for C-2 and $i = 1$ for C-3.

Table 4 Calculated and experimental $\delta_{^{13}C}$ for the olefinic carbons in *p*-nitrostyrene (**2e**)

Compound		$\delta_{^{13}C}$[a]		$\delta_{^{13}C}$(**2e**)	
No	Z	C-2	C-3	C-2	C-3
3e	NO_2	137.0	128.4	133.7[b]	117.2[b]
4e	NO_2	141.8	122.0	134.0[c]	117.5[c]
2e	NO_2	Exptl.[d] values		134.8	117.9

[a] At 50 MHz, 5% (v/v) $CDCl_3$ solutions (TMS = 0 ppm). [b] $\delta_{^{13}C}$(**3e**) $- Z_i$[–C(O)SMe]. [c] $\delta_{^{13}C}$(**4e**) $-Z_i$[–C(O)OMe]. [d] At 15 MHz, in 1,4-dioxane (CS_2 = 192.6 ppm), *cf.* ref. 3.

Table 5 Calculated and experimental $\delta_{^{13}C}$ for the olefinic carbons in compound **1b** and the values for the corresponding non-additivity correction ($\tilde{N}_i$)

$\delta_{^{13}C}$(**1b**)		$\tilde{N}_i$[a]	
C-2	C-3	C-2	C-3
137.9[b]	126.7[b]	+0.8	+1.6
140.2[c]	129.0[c]	–1.5	–0.7
139.1[d]	127.9[d]	–0.4	+0.4
138.7[e]	128.3[e]	–	–

[a] $\tilde{N}_i = \delta_{^{13}C}$(exptl.) $- \delta_{^{13}C}$(calcd.). [b] $\delta_{^{13}C}$(**1a**) $- Z_i$[–C(O)SMe] $+ Z_i$[–C(O)OMe]. [c] $\delta_{^{13}C}$(**1c**) $- Z_i$[–C(O)OMe] $+ Z_i$[–C(O)SMe]. [d] Average estimates. [e] Experimental values, see Table 1.

Experimental

Materials.—Deuterochloroform and compounds **1c** and **4a** were used as-received from Aldrich, after being checked for purity. Compounds **1a**, **1b**, **3a**, **3b**, **3d**, **3e** and **4b–e** were prepared by literature[4–8] procedures; all liquid compounds were distilled under reduced pressure, while the solids were recrystallized, until the final purity attained for each of these compounds was at least 98% (both by GLC and ^1H NMR). The complete assigned ^{13}C NMR dataset for compounds **3a–e** is presented in Table 6.

Methyl p-*methoxythiocinnamate* **3c**.—Thionyl chloride (6.5 cm^3, 91 mmol) was added dropwise to a stirred solution of *p*-methoxythiocinnamic acid (8.0 g; 45 mmol) in 50 cm^3 of anhydrous diethyl ether, the resulting mixture being held under reflux during 5 h. The solvent and excess thionyl chloride were removed by evaporation under reduced pressure and the greyish solid obtained was redissolved in a further 50 cm^3 of anhydrous diethyl ether. This solution was cooled in a dry-ice/acetone bath, 5.5 cm^3 (10 mmol) of liquefied methanethiol was added to it, in a single portion, followed by 4.0 cm^3 (50 mmol) of pyridine, added dropwise. After removing the cooling bath, the reaction mixture was boiled under reflux for 5 h (NB. all preceding operations were performed under a moisture-free atmosphere) and then quenched with water and extracted with dichloromethane. The combined extracts were dried over anhydrous magnesium sulfate, the solvent removed and the crude product recrystallized from ethanol. Compound **3c** (3.93 g, 18.9 mmol) was obtained as a colourless microcystalline solid of mp = 82–85 °C (Found: C, 63.0; H, 5.7. $C_{11}H_{12}O_2S$ requires C, 63.44; H, 5.81%). Yield: 42%, purity: 99% (both by GLC and ^1H NMR). δ_H ($CDCl_3$) 2.42 (s, 3 H, H-5), 3.84 (s, 3 H, H-9), 6.63 (d, 1 H, J_{23} 16 Hz, H-2), 6.91 (d, 2 H, J_{76} 8 Hz, H-7, H-6), 7.50 (d, 2 H, J_{67} 8 Hz), 7.58 (d, 1 H, J_{32} 16 Hz, H-3).

Instruments and Methods.—See ref. 9.

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References

1 *Sadtler Standard Carbon-13 NMR Spectra*, Sadtler Research Laboratories, Inc: Philadelphia 1976, S229C [**1c**]; S4006C [**2a**]; S12461C [**2b**]; S1965C [**2c**]; S12345C [**2d**].

2 E. Pretsch, T. Clerc, J. Seibl and W. Simon, in *Tablas para la Elucidación Estructural de Compuestos Orgánicos por Métodos Espectroscópicos*, Alhambra Longman, Madrid, 1996, p. C90.

3 K. S. Dhami and J. B. Stothers, *Can. J. Chem.*, 1965, **43**, 510.

4 P. G. Campbell, G. Sumrell and C. H. Schramm, *J. Org. Chem.*, 1961, **26**, 697.

5 G. Sumrell, M. Zief, E. J. Huber, G. E. Ham and C. H. Schramm, *J. Am. Chem. Soc.*, 1959, **81**, 4313.

6 S. Rondestvedt, Jr and C. D. Ver Nooy, *J. Am. Chem. Soc.*, 1955, **77**, 4878.

7 B. Myrboh, H. Ila and H. Junjappa, *J. Org. Chem.*, 1983, **48**, 5327.

8 J. Bestmann, G. Schmid and D. Sandmeier, *Chem. Ber.*, 1980, **113**, 912.

9 A. de B. Rezende, M. R. Alcantara, I. P. de Arruda Campos, V. G. Toscano, G. Ebeling and J. C. D. Lopes, *Tetrahedron*, 1997, **53**, 10113.

Table 6 $\delta_{^{13}C}$ of methyl thiocinnamates[a]

Compound	Y	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
3a	H	133.9	140.1	124.7	190.0	11.5	–[b]	–[b]	–[b]	–
3b	Me	131.3	140.3	123.8	190.3	11.6	128.4	129.7	141.0	21.5
3c	OMe	126.9	140.0	122.7	190.2	11.6	129.0	114.3	161.6	55.4
3d	Cl	132.6	138.7	125.2	190.0	11.7	129.2	129.5	138.4	–
3e	NO_2	140.3	137.0	128.5	189.6	11.9	129.0	124.2	148.6	–

[a] 5% (v/v) $CDCl_3$ solutions (TMS = 0 ppm), observed at 50 MHz. [b] 127.7 or 130.8.