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Carbon-13 NMR Spectra of 1,3-Dioxolanes

I—New Parameters for *cis*- and *trans*-4-Methyl Groups in 2,4-Disubstituted Derivatives

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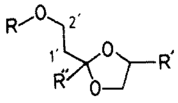
The ^{13}C NMR spectra of 24 1,3-dioxolane derivatives are reported in an attempt to propose parameters for the C-2, C-4 and C-5 shifts from the 2-Me and 4-Me substituents, based on the ring stereochemistry. These parameters are obtained from simultaneous equations, and clearly agree with those calculated by the use of pattern molecules. The calculated parameter for the C-4 shift due to a 2-Me group differs notably from that proposed by other workers.

KEY WORDS 1,3-dioxolane derivatives ^{13}C NMR Shift parameters

INTRODUCTION

Despite the conformational flexibility of five-membered rings, it has been possible to establish some rules related to the additivity of shift effects that substituents exert on the ^{13}C NMR chemical shifts of ring carbon atoms. Thus, Pihlaja and Nurmi,[1] Anteunis and Daneels[2] and Eliel *et al.*[3] have described cases of the additivity of such shift effects in 1,3-dioxolane derivatives. Eliel *et al.*[3] proposed values for the shift effects of substituents such as 2-Me, 4-Me and 2-Et on the 1,3-dioxolane C-2, C-4 and C-5 carbon atoms. However, parameters based on the ring stereochemistry have never been proposed.

In this work we studied the ^{13}C chemical shifts of 24 1,3-dioxolane derivatives, corresponding to general formula I, in order to try to propose parameters for



the C-2, C-4 and C-5 shifts due to 2-Me and 4-Me substituents, based on the ring stereochemistry.

RESULTS AND DISCUSSION

The ^{13}C chemical shifts of 24 1,3-dioxolane derivatives are summarized in Table 1; the reference compounds 1,3-dioxolane and 2-methyl-1,3-dioxolane[3] have also been included.

The compounds fall into four categories: (a) 2-alkoxyethyl-1,3-dioxolanes (seven cases), (b) 2-alkoxyethyl-2-methyl-1,3-dioxolanes (five cases), (c) *cis*-2-alkoxyethyl-4-methyl-1,3-dioxolanes (six cases) and (d) *trans*-2-alkoxyethyl-4-methyl-1,3-dioxolanes (six cases).

The parameters for the calculated shifts for C-2, C-4 and C-5 are shown for the above-mentioned substituent groups in Tables 2 and 3.

Two different methods for calculating the parameters and their standard errors were used: (1) the use of pattern molecules and (2) resolution of the simultaneous equations which result from the consideration of the chemical shift for a carbon atom C_i as the sum of a set of additive values, as follows:

$$\delta_{C_i} = \delta_0 + \sum \Delta_i$$

The use of pattern molecules implies that, if molecular conformation is independent of the composition and/or configuration, the differences observed in the experimental values for the C-2, C-4 and C-5 chemical shifts between any compound which belongs to the (b), (c) or (d) series and the analogous compound of the (a) series can be interpreted as shift effects due to the different substituent groups.

On the other hand, provided that in each class of compounds the various members differ only in the nature of the R group, it is possible to obtain a set of several values for each shift parameter. Starting from these data, the average value and its standard error expressed as σ_{n-1} can be obtained. Thus, the 6.20 ± 0.32 parameter, calculated for the shift on C-2 of a 2-Me group, obtained from the C-2 chemical shifts in **14**, **15**, **16**, **17** and **18**, substituted with a 2-Me group, and those of the **3**, **5**, **7**, **9** and **13** pattern compounds, respectively, which lack this group. The value calculated by other workers by means of linear regression analysis from 58 1,3-dioxolane derivatives[3] is 6.20 ± 0.16.

Similarly, the parameters for the C-2 shifts of 4-Me-*cis*(0.13 ± 0.14) and 4-Me-*trans* (−0.83 ± 0.17) were obtained from the set of calculated values, using

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Table 1. Experimental ^{13}C shifts for 1,3-dioxolanes[a]

Entry No.	R	R′	R″	C-2	C-4	C-5	C-1′	C-2′	Other carbons
1	H	H	H	103.50	64.86	64.86	35.84	53.81	
2*c*[b]	H	Me	H	103.55	72.89	70.89	36.34	58.21	18.65
2*t*[b]	H	Me	H	102.59	72.00	71.72	36.24	58.21	18.38
3	Me	H	H	102.16	64.47	64.47	33.94	58.16	68.04
4*c*[b]	Me	Me	H	102.05	72.28	70.42	34.24	58.00	67.86; 18.17
4*t*[b]	Me	Me	H	101.15	71.25	71.25	34.24	58.00	67.86; 17.86
5	Et	H	H	102.56	64.85	64.85	34.55	66.24	15.20; 66.24
6*c*[c]	Et	Me	H	102.79	72.70	70.90	34.94	66.01	18.83; 14.91 65.96
6*t*[c]	Et	Me	H	101.83	71.67	71.67	34.89	66.00	18.16; 14.88 66.00
7	*n*-Pr	H	H	102.52	64.81	64.81	34.42	66.33	10.53; 22.88 72.74
8*c*[c]	*n*-Pr	Me	H	102.67	72.58	70.84	34.88	66.17	18.46; 10.23 72.58; 22.76
8*t*[c]	*n*-Pr	Me	H	101.92	71.75	71.75	35.01	66.32	18.04; 10.13 72.72; 22.90
9	*i*-Pr	H	H	102.51	64.79	64.79	34.79	63.66	22.07; 71.55
10*c*[c]	*i*-Pr	Me	H	102.79	72.70	70.90	35.33	63.53	18.55; 21.97 71.38
10*t*[c]	*i*-Pr	Me	H	101.50	71.66	71.66	34.93	63.16	17.81; 21.97 71.33
11	*t*-Bu	H	H	102.61	64.78	64.78	35.29	57.34	27.55; 72.77
12*c*[c]	*t*-Bu	Me	H	102.79	72.61	70.84	35.91	57.23	17.56; 27.43 72.61
12*t*[c]	*t*-Bu	Me	H	101.91	71.61	71.61	35.83	57.26	17.19; 27.45 72.56
13	CH_2-CH_2OH	H	H	102.64	64.83	64.83	34.11	66.75	61.54; 72.70
14	Me	H	Me	108.62	64.17	64.17	38.43	68.35	23.85; 58.11
15	Et	H	Me	108.21	63.82	63.82	38.37	65.83	23.57; 65.34 14.49
16	*n*-Pr	H	Me	108.75	64.24	64.24	38.68	66.45	24.04; 72.39 22.70; 10.35
17	*i*-Pr	H	Me	108.85	64.29	64.29	39.15	63.81	24.10; 71.22 21.90
18	CH_2-CH_2OH	H	Me	108.85	64.34	64.34	38.45	66.48	24.05; 71.92 61.37
19	1,3-Dioxolane			95.00	64.54	64.54			
20	2-Methyl-1,3-dioxolane			101.51	64.86	64.86			19.78

[a] Spectra run in $CDCl_3$–TMS at room temperature.

[b] Values obtained from a mixture of *cis–trans* stereoisomers.

[c] *c* (*cis*) and *t* (*trans*) stereoisomers were separated by GLC using Carbowax 20M as the stationary phase.

as patterns the compound pairs **1–2*c***, **3–4*c***, etc., or **1–2*t***, **3–4*t***, etc. The parameter for the C-2 shift of a 4-Me group (for molecules without *cis–trans* stereoisomerism) is -0.35 ± 0.17; this was obtained by averaging the calculated values for the parameters of the 4-Me-*cis* and 4-Me-*trans* groups, and it differs from the value proposed by other workers (0.08 ± 0.11).[3] Finally, the parameter of the C-2 shift due to the 2-alkoxyethyl group (7.56 ± 0.35) was obtained from **3**, **5**, **7**, **9** and **13**, which were related to 1,3-dioxolane, and **14**, **15**, **16**, **17** and **18**, which were related to 2-methyl-1,3-dioxolane. No additional effect due to the 2-*gem*-Me-alkoxyethyl group was observed, since the values for the parameters of each of the two series are analogous.

Table 2. Parameters for the C-2 chemical shifts in 1,3-dioxolanes

Group	Value and error		No. of occurrences
2-Me	6.20 ± 0.32[a]	6.01 ± 0.23[b]	5
2-$ROCH_2CH_2$	7.56 ± 0.35[a]	7.64 ± 0.37[b]	3
4-Me	-0.35 ± 0.17[a]	-0.35 ± 0.44[b]	12
4-Me-*cis*	0.13 ± 0.14[a]	0.13 ± 0.43[b]	6
4-Me-*trans*	-0.83 ± 0.17[a]	-0.83 ± 0.44[b]	6

[a] Values calculated by the pattern molecule method.

[b] Values calculated by the simultaneous equation method.

With regard to the parameters for the C-4 and C-5 shifts (Table 3), it should be noted that (a) the approaches used for the parameter calculations have already been described and (b) the calculated parameter for the C-4 shift due to the 2-Me group (-0.58 ± 0.27) differs notably from that proposed by other workers (0.51 ± 0.14).[3]

We accept Eliel's *et al.* value[3] for the parameter for

Table 3. Parameters for the C-4 and C-5 shifts in 1,3-dioxolanes

Group	Value and error C-4		C-5		No. of occurrences
2-Me	-0.58 ± 0.27^a	-0.59 ± 0.43^b			5
2-ROCH$_2$CH$_2$	0.27 ± 0.02^a	0.23 ± 0.40^b			12
4-Me	7.38 ± 0.13^a	7.34 ± 0.18^b	6.43 ± 0.17^a	6.45 ± 0.05^b	12
4-Me-*cis*	7.86 ± 0.09^a	7.85 ± 0.18^b	6.02 ± 0.17^a	6.04 ± 0.05^b	6
4-Me-*trans*	6.90 ± 0.13^a	6.84 ± 0.16^b	6.84 ± 0.16^a	6.85 ± 0.05^b	6

[a] Values calculated by the pattern molecule method.
[b] Values calculated by the simultaneous equation method.

the C-4 shift of a methyl group, and we extend our findings to the shift value of a second methyl group which forms part of a geminal group at C-2. Thus, a 2-*gem*-di-Me group will bring about a total substitution effect at C-4 of $0.51 + (-0.58) = -0.07$ (Eliel *et al.* assigned the value $0.51 + 0.51 + (-0.80) = 0.22$ to this parameter; in this calculation -0.80 represents an additional effect due to the 2-*gem*-di-Me group[3]).

The values of the C-2, C-4 and C-5 shift parameters due to the above-mentioned substituents, obtained from simultaneous equations, are also shown in Tables 2 and 3. These are in clear agreement with those calculated by the use of pattern molecules.

Table 4 summarizes the ^{13}C experimental and calculated C-2, C-4 and C-5 chemical shifts of several 2,4-disubstituted-1,3-dioxolane *cis–trans* stereoisomers. For the calculation of the theoretical values for the 2-Me, 2-Et, 2-*i*-Pr, 2-*t*-Bu and 2-Ph groups, both the shift parameters proposed by Eliel *et al.*[3] and those which we have proposed for the 2-*gem*-Me, 4-Me-*cis* and 4-Me-*trans* groups have been used.

The results obtained indicate that it is possible to propose the C-2, C-4 and C-5 shift parameters due to 4-Me-*cis* and 4-Me-*trans* groups in 4-methyl-2-substituted-1,3-dioxolanes.

EXPERIMENTAL

The ^{13}C NMR spectra were recorded on Varian CFT-20 (20 MHz) and on Bruker HX-90-E (25.2 MHz) spectrometers, for CDCl$_3$ solutions using TMS as internal standard. ^{1}H NMR spectra (60 MHz, internal TMS), were recorded on a Perkin–Elmer R-20B spectrometer, IR spectra with a Pye Unicam SP 1000 instrument and mass spectra with a Hewlett-Packard 5930 A mass spectrometer. GLC was performed at 100 °C on a Carlo-Erba Fractovap G gas chromatograph equipped with a flame-ionization detector and a glass column (2 m × 1.75 mm i.d.) packed with Carbowax 20M. The nitrogen flow-rate was 125 ml min^{-1}, the injection port temperature 130 °C, and the zone detector temperature 120 °C, TLC was performed on silica gel G (Merck), using iodine detection and diethyl ether–hexane as the developing solvent. Column chromatography was performed on silica gel (Merck 7734). Concentration of the solutions was carried out under reduced pressure at 40 °C using a rotatory evaporator.

Syntheses

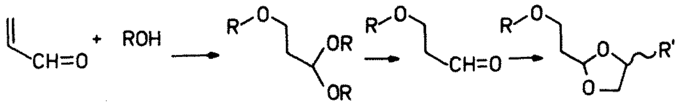
The syntheses of some products in Table 1 have been previously reported. Thus, **13** was obtained by acid-catalysed addition of ethylene glycol to acrolein.[4] Compounds **5**–**10*t*** were obtained by alcohol interchange reactions, under reflux, between **13** or the mixture of *cis–trans* stereoisomers of 2-[2-(2-hydroxypropoxy)ethyl]-4-methyl-1,3-dioxolane and EtOH, *n*-PrOH and *i*-PrOH.[5] Their configurational assignments were established on the basis of that described by Willy *et al.*[6] for 2,4-disubstituted-1,3-dioxolanes, taking account of the fact that the *cis* isomer shows an upfield shift for the acetal proton compared with the corresponding *trans* analogue. The **11**, **12*c*** and **12*t*** derivatives[7] were obtained in a similar way. Compound 18 was obtained by acid-catalysed addition of ethylene glycol to methyl vinyl ketone.[8] The alcohol interchange between **18** and MeOH,

Table 4. Experimental and calculated shift values in 2,4-disubstituted-1,3-dioxolanes

Compound	Substituent	C-2 Exptl.	C-2 Calc.	C-4 Exptl.	C-4 Calc.	C-5 Exptl.	C-5 Calc.
21	2,2-Di-Me	108.34	107.40	64.44	64.48	64.44	64.48
22	2-Me-2-*t*-Bu	113.79	114.19	65.03	64.41	65.03	64.41
23	*cis*-2,4-Di-Me	101.54	101.31	72.87	72.88	70.97	71.09
24	*trans*-2,4-Di-Me	100.56	100.35	71.88	71.90	71.73	71.90
25	*cis*-2-Et-4-Me	105.47	105.29	72.73	72.78	70.99	70.99
26	*trans*-2-Et-4-Me	104.62	104.33	71.80	71.80	71.80	71.80
27	*cis*-2-*i*-Pr-4-Me	108.34	108.40	72.63	72.62	71.04	70.83
28	*cis*-2-*t*-Bu-4-Me	110.38	110.24	72.63	72.81	71.23	71.02
29	*trans*-2-*t*-Bu-4-Me	109.62	109.28	72.38	71.83	72.08	71.83
30	*cis*-2-Ph-4-Me	103.91	103.85	73.32	73.36	72.18	72.38

EtOH, *n*-PrOH and *i*-PrOH leads to **14–17**,[8] respectively. 2-(2-Methoxyethyl)-2-methyl-1,3-dioxolane: ^{1}H NMR, δ 1.29 (s, 3H), 1.87 (t, 2H), 3.25 (s, 3H), 3.42 (t, 2H), 3.85 (s, 4H); MS (70 eV) *m/z* (rel. intensity), $(M-\text{Me})^{+\cdot}$ 131(8), 115(<1), 101(7), 87(100), 73(<1), 59(3) and 45(55). 2-(2-Ethoxyethyl)-2-methyl-1,3-dioxolane: ^{1}H NMR, δ 1.10 (t, 3H), 1.20 (s, 3H), 1.74 (t, 2H), 3.30 (q, 2H), 3.33 (t, 2H), 3.76 (s, 4H); MS (70 eV) *m/z* (rel. intensity), $(M-\text{Et})^{+\cdot}$ 131(10), 115(<1), 99(23), 87(100), 73(2), 59(3) and 45(49). 2-(2-*n*-Propoxyethyl)-2-methyl-1,3-dioxolane: ^{1}H NMR, δ 0.88 (t, 3H), 1.28 (s, 3H), 1.46 (m, 2H), 1.87 (t, 2H), 3.28 (t, 2H), 3.44 (t, 2H), 3.82 (s, 4H); MS (70 eV) *m/z* (rel. intensity), $(\text{M}-\text{Me})^{+\cdot}$ 159(5), 131(5), 115(2), 101(1), 87(100), 73(6) and 57(3). 2-(2-Isopropoxyethyl)-2-methyl-1,3-dioxolane: ^{1}H NMR, δ 1.12 (d, 6H), 1.30 (s, 3H), 1.85 (t, 2H), 3.42 (T, 2H), 3.45 (m, 1H), 3.85 (s, 4H); MS (70 eV) *m/z* (rel. intensity), $(M-\text{Et})^{+\cdot}$ 145(6), 115(3), 99(18), 87(100), 73(5), 57(3) and 43(98).

Compounds **1**, **2***c* and **2***t* were prepared from 2-(2-chloroethyl)-1,3-dioxolane and the 2-(2-chloroethyl)-4-methyl-1,3-dioxolane *cis–trans* mixture, respectively. Replacement of the chlorine atom was carried out by heating the chlorinated substrates with Na_2CO_3–NaOH in a sealed tube at 160 °C. Isomers **2***c* and **2***t* were separated by GLC. The chloroethyldioxolanes were prepared by reaction between acrolein and ethylene glycol or 1,2-propylene glycol in the presence of dry HCl.[9]



R' = H **3**
R' = Me **4**

Compounds **3**, **4***c* and **4***t* are new, and were obtained by acid-catalysed reactions between 3-methoxypropanal and ethylene glycol or 1,2-propylene glycol. The **4** *cis–trans* stereo-isomers were separated by GLC. 3-Methoxypropanal was prepared by hydrolysis from 1,1,3-trimethoxypropane, which was obtained by alcohol interchange between **13** and MeOH[5] or by addition of MeOH to acrolein.[10]

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