Long-range Coupling in the Nuclear Magnetic Resonance Spectra of Some 2,5-Disubstituted 1,3-Dioxolan-4-ones

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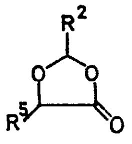
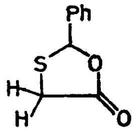
The n.m.r. spectra of both the *cis*- and *trans*-forms of five 2,5-disubstituted 1,3-dioxolan-4-ones show long-range coupling between 2-H and 5-H thus confirming that the mere presence of such coupling cannot be used to assign a *cis*-relationship to the substituents at C-2 and C-5.

LONG-RANGE coupling between protons at C-2 and C-5 in 2,5-disubstituted 1,3-dioxolan-4-ones was first reported[1] for the three compounds 'active lactic acid chloralide' (I; $R^2 = CCl_3$, $R^5 = Me$), 'malic acid chloralide' (I; $R^2 = CCl_3$, $R^5 = CH_2CO_2H$), and 'chloralide' (I; $R^2 = R^5 = CCl_3$). Subsequently several mixtures of the *cis*- and it was reported[2] that such long-range coupling is only present in one of the forms, which was always assigned a *cis*-geometry, on the basis of the deshielding effects of substituents at C-2 or C-5 on protons on the same side of the ring at C-5 or C-2. However, more recently it has been shown[3] that in one of these cases (I; $R^2 = CCl_3$, $R^5 = Ph$) long-range coupling is in fact present in both of the isomers. We have confirmed this correction and have now examined again the three other previously reported[2] cases, together with two other pairs of *cis*- and *trans*-forms [(I; $R^2 = CCl_3$, $R^5 = Me$) and (I; $R^2 = CBr_3$, $R^5 = Me$)] and can report that long-range coupling of *ca.* 1 Hz is observed with both the *cis*- and *trans*-forms of all these pairs of compounds. The results are set out in the Table. In those cases where the C-5 substituent was phenyl the signals due to 5-H were complicated by additional 'benzylic' coupling to the aromatic protons,[4] but the values of $J_{2,5}$ could


(I)


(II)

N.m.r. spectra in $CDCl_3$ at 100 MHz of 2,5-disubstituted 1,3-dioxolan-4-ones (chemical shifts in τ; J in Hz)

Substituent at C-2	C-5	Form	$J_{2,5}$	2-H	5-H	5-Me	$J_{H,5Me}$	2-Me	$J_{H,2Me}$	5-Ph
CCl_3	Me	(±), M.p. 55°	1·4	4·15(d)	5·17(dq)	8·46(d)				
CCl_3	Me	(±) Liquid	1·1	4·17(d)	5·30(dq)	8·40(d)	7·0			
CCl_3	Me	+, M.p. 88°	1·4	4·17(d)	5·17(dq)	8·45(d)	7·0			
CCl_3	Me	From *S*-lactic acid	0·9	4·19(d)	5·33(dq)	8·38(d)	7·0			
CBr_3	Me	M.p. 133°	1·4	4·25(d)	5·10(dq)	8·43(d)	6·8			
CBr_3	Me	Minor form	1·0	4·37(d)	5·33(dq)	8·34(d)	6·8			
Me	Ph	*ca.* 50 : 50 Mixture	0·8	4·19(dq)	4·75(c)			8·56(d)	5·0	2·79 (c)
Me	Ph		1·1	4·47(dq)	4·96(c)			8·62(d)	5·0	2·79
Me	Me	Major form	1·0	4·41(dq)	5·68(dq)	8·52(d)	7·0	8·46(d)	5·0	
Me	Me	Minor form	0·9	4·21(dq)	5·53(dq)	8·57(d)	7·0	8·49(d)	5·0	
CBr_3	Ph	Major form	1·5	4·07(d)	4·30(c)					2·67 (c)
CBr_3	Ph	Minor form	1·3	4·26(d)	4·54(c)					2·67

and *trans*-forms of compounds of this type [(I; $R^2 = CCl_3$, $R^5 = Ph$), (I; $R^2 = Me$, $R^5 = Ph$), (I; $R^2 = CBr_3$, $R^5 = Ph$), and (I; $R^2 = R^5 = Me$)] were examined,

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[1] M. P. Baron and D. P. Hollis, *Rec. Trav. chim.*, 1965, **84**, 1109.

[2] M. Forines and J. Soulier, *Bull. Soc. chim. France*, 1970, 332.

[3] L. A. Cort and R. A. Stewart, *J. Chem. Soc.* (*C*), 1971, 1386.

[4] S. Sternhell, *Quart. Rev.*, 1969, **23**, 236.

readily be obtained from the splitting of the signals due to 2-H. The signals for the methyl groups in each of the forms of 2,5-dimethyldioxolan-4-one (I; $R^2 = R^5 = Me$) occur at very similar chemical shifts, but it is possible to assign them to particular methyl groups on the basis of the coupling constants to the adjacent protons. One methyl group in each form has J 7 Hz, as observed for the other 1,3-dioxolan-4-ones with a single methyl group at C-5, but the other methyl group in each form has J 5 Hz, as observed for the compounds with a single methyl group at C-2. Our results reinforce the recent warning[3] that the mere presence or absence of long-range coupling in 2,5-disubstituted 1,3-dioxolan-4-ones (I) does not permit any conclusion to be drawn about the relative geometries of 2-H and 5-H. The values for the long range coupling constants in each pair of compounds which we have studied are not identical. Unfortunately the form having the greater value for $J_{2,5}$ does not always correspond to the form assigned a *trans*-arrangement of substituents at C-2 and C-5 on the basis of the criteria used earlier.[2] For example in the case of 5-methyl-2-trichloromethyl-1,3-dioxolan-4-one (I; $R^2 = CCl_3$, $R^5 = Me$) the previously investigated[1,3] *trans*-form shows the absorption for 5-H at lower field and this form has the higher value of $J_{2,5}$ but for 2-methyl-5-phenyl-1,3-dioxolan-4-one (I; $R^2 = Me$, $R^5 = Ph$) where the *trans*-form also shows the absorption for 5-H at lower field[2] this form has the lower value of $J_{2,5}$. It appears that the magnitude of $J_{2,5}$ in 2,5-disubstituted 1,3-dioxolan-4-ones (I), which may only differ by 0·1 Hz [*e.g.* for (I; $R^2 = R^5 = Me$)], cannot be used to draw conclusions about the relative geometries of 2-H and 5-H. However on the basis of the criteria used earlier[2,3] the major product from the preparation of 5-methyl-2-tribromomethyl-1,3-dioxolan-4-one (I; $R^2 = CBr_3$, $R^5 = Me$), having the absorption of 5-H at lower field, should be the *trans*-form.

In view of the above results it is perhaps surprising that only one of the two protons at C-5 in (I; $R^2 = CHPh_2$, $R^5 = H$)[5] and in (I; $R^2 = CCl_3$, $R^5 = H$)[3] couples with 2-H, but we have confirmed the latter result and have also observed that the same coupling behaviour is manifest in 2-tribromomethyl-1,3-dioxolan-4-one (I; $R^2 = CBr_3$, $R^5 = H$), where only one arm of the AB quartet due to the C-5 protons is split by coupling to 2-H. In contrast it has recently been shown[6] that both analogous protons at C-4 in 2-phenyl-1,3-oxathiolan-5-one (II) couple weakly with 2-H.

The preparations of several of the mixtures of *cis*- and *trans*-forms of 1,3-dioxolan-4-ones used in this work require brief comment. A mixture of the two 2,5-dimethyl-1,3-dioxolan-4-ones (I; $R^2 = R^5 = Me$)[2] could only be obtained by semi-preparative g.l.c., as the redistilled material was contaminated by 2,4,6-trimethyl-1,3,5-trioxan, identified by its n.m.r. spectrum. The product from the condensation of bromal with (±)-lactic acid[7] was clearly (n.m.r.) a mixture of both forms of (I; $R^2 = CBr_3$, $R^5 = Me$); we were able to isolate one of the components by fractional crystallisation. In agreement with Shah and Alimchandani[8] we find that chloral condenses with (±)-lactic acid in concentrated sulphuric acid to give a mixture of a solid and a liquid 'chloralide.' The two forms have been separated by preparative g.l.c. The solid form, m.p. 55° (lit.,[8] 56—57°), was also obtained by separating the solid portion of the semi-solid mixture and repeated crystallisation as described by Shah and Alimchandani. We have not encountered a form of (±)-'lactic acid chloralide' (I; $R^2 = CCl_3$, $R^5 = Me$), m.p. 82°, which has recently been reported.[3] We have also established that chloral condenses with *S*-lactic acid to give a mixture (g.l.c.; n.m.r.) of two forms of 'active lactic acid chloralide,' from which the 'active lactic acid chloralide,' m.p. 88°, first reported by Baron and Hollis[1] can be obtained by the procedure used to isolate the corresponding solid (±)-'lactic acid chloralide.'

EXPERIMENTAL

N.m.r. spectra were recorded on a Varian HA 100 spectrometer in $CDCl_3$ solution with tetramethylsilane as internal standard. The integrations were in every case in agreement with the proton assignments. Chemical shifts are recorded in τ units and multiplicities are recorded as d (doublet), q (quartet), and c (complex). Long-range coupling constants are based on the average of the appropriate peak separations measured from spectra run at 100 Hz sweep width. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. M.p.s were determined on a Kofler block. Light petroleum had b.p. 60—80°.

1,3-*Dioxolan*-4-*ones*.—Mixtures of the *cis*- and *trans*-forms of 2,5-dimethyl-, 2-methyl-5-phenyl-, and 5-phenyl-2-tribromomethyl-1,3-dioxolan-4-one were prepared as described previously.[2] The sample of the 2,5-dimethyl-1,3-dioxolan-4-ones, b.p. 60—62° at 22 mmHg (lit., 45° at 2 mmHg), showed absorption at *inter alia* τ 4·98 and 8·69 (J 5 Hz) (due to 2,4,6-trimethyl-1,3,5-trioxan). A pure (n.m.r.; g.l.c.) sample of *cis*- and *trans*-2,5-dimethyl-1,3-dioxolan-4-one was obtained by semipreparative g.l.c. (F and M 720; 6 ft; Apiezon L; 60°). The mixture was resolved into its components by analytical g.l.c. (F 11; 50 ft capillary; E 301 silicone rubber; 60°). 2-*Tribromomethyl*-1,3-*dioxolan*-4-*one* was prepared by the condensation of glycollic acid (3·8 g) and bromal (14·1 g) in 36N-sulphuric acid (20 ml) and had m.p. 74° (from light petroleum), τ 4·21 (d, J 1·4 Hz) and an AB system, τ_A 5·30, τ_B 5·50 ($J_{A.B}$ −15, J_A 1·4 Hz) (Found: C, 14·2; H, 1·2; Br, 70·8%. $C_4H_3Br_3O_3$ requires C, 14·2; H, 0·9; Br, 70·8%). A mixture of the *cis*- and *trans*-forms of 5-methyl-2-tribromomethyl-1,3-dioxolan-4-one, m.p. 100—125° (lit.,[7] 94—97°) was prepared similarly from (±)-lactic acid. Repeated crystallisation from ether–light petroleum gave one form of 5-*methyl*-2-*tribromomethyl*-1,3-*dioxolan*-4-*one*, m.p. 133° (Found: C, 17·2; H, 1·5; Br, 67·9. $C_5H_5Br_3O_3$ requires C, 17·1; H, 1·4; Br, 68·0%). (±)-5-Methyl-2-

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[5] R. Soulier and J. Soulier, *Bull. Soc. chim. France*, 1969, 2048.

[6] M. Brink, *Org. Mag. Res.*, 1972, **4**, 195.

[7] *Cf.* O. Wallach, *Annalen*, 1878, **193**, 1.

[8] N. M. Shah and R. L. Alimchandani, *J. Univ. Bombay*, 1936, **5**, 132 (*Chem. Abs.*, 1937, **31**, 3003).

trichloromethyl-1,3-dioxolan-4-one, b.p. 117° at 20 mmHg (lit.,[8] 110—112° at 15 mmHg) was prepared from technical (±)-lactic acid (Emanuel), α_D^{22} +0·002° (0·1 dm) by the method of Shah and Alimchandani [8] and was shown to be a mixture of the *cis*- and *trans*-forms by its n.m.r. spectrum. The liquid portion of the distillate was separated by filtration through a sintered glass disc and the resultant solid, after five crystallisations from light petroleum, had m.p. 54° (lit.,[8] 56—57°). A pure sample of this form, m.p. 55°, and a sample of the liquid form, were obtained by preparative g.l.c. (Pye 105; 15 ft; silicone rubber; 150°) on the distillate. Analytical g.l.c. (Pye 105; 6 ft; Carbowax 20M; 180°) showed that the ratio of the solid to the liquid isomer in the distillate was *ca.* 2 : 1. The sample of *S*-lactic acid (Fluka; *ca.* 90% Ph. Helv. V) which was condensed with chloral had a negative rotation α_D^{23} −1·33° (0·1 dm) due to the presence of laevorotatory cyclic derivatives of *S*-lactic acid.[9] The optical purity and configuration of the acid were checked by converting some of it into ethyl *S*-lactate, b.p. 61—63° at 18 mmHg, $\alpha_D^{26\cdot5}$ −1·037° (0·1 dm) [lit.,[10] 54—56° at 22 mmHg, α_D^{18} −11·15° (1·0 dm)]. The material, b.p. 120° at 25 mmHg, obtained by condensing *S*-lactic acid with chloral in the same way [8] as for the (±)-acid was shown by its n.m.r. spectrum and by g.l.c. (F.11; 6 ft; OV 17; 110°) to be a mixture of 2*S*,5*S*- and 2*R*,5*S*-5-methyl-2-trichloromethyl-1,3-dioxolan-4-ones. The solid isomer was separated as for the (±)-case and had m.p. 88° (lit.,[1] 88°), $[\alpha]_D^{23}$ +23·35° (*c* 0·9; $CHCl_3$).

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[9] Personal communication, through J. Davis, Fluka AG. *Cf.* L. N. Owen and M. B. Rahman, *J. Chem. Soc.* (*C*), 1971, 2432.

[10] W. Gerrard, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 1937, 153.