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Studies of Saturated Heterocyclic Compounds. Preparations and PMR Spectra of *cis* and *trans* 2,5-Disubstituted 1,3-Dioxolan-4-ones[1]

Yoshihiro ASABE, Shoji TAKITANI, and Yojiro TSUZUKI*

Faculty of Pharmaceutical Sciences, Science University of Tokyo, Ichigayafunagawara-machi, Shinjuku-ku, Tokyo

**Department of Chemistry, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo*

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Although a number of investigations have been made into the chemistry of 1,3-dioxolan-4-ones,[2-5] studies of their geometrical isomers have been left undeveloped, presumably because of the difficulty in the isolation and identification of each isomer. The present work aims at isolating the *cis* and *trans* isomers of some 2,5-disubstituted homologues by means of preparative thin-layer chromatography (tlc) and at assigning these isomers by means of PMR spectroscopy. The product of 2-trichloromethyl-5-phenyl-1,3-dioxolan-4-one(I) was found by PMR spectral studies to be a mixture of *cis* and *trans* isomers. The integrated signal intensities really showed the mixture to be in a ratio of about 1: 1.3(=b: a). Each isomer (a: mp 67—68°C, in the upper band; b: mp 88—89.5°C, in the lower band) was isolated from the mixture by means of tlc; the identification of the 1,3-dioxolan-4-one ring of each isomer was made by studying the stretching vibrations ($\nu_{C=O}$) in their IR spectra.[5,6] In Fig. 1, the PMR spectra of the a-isomer are shown; signals due to 5-H and 2-H appear at τ 4.43 and τ 4.03 respectively, and signals due to the phenyl-ring protons are observed as an almost single peak at τ *ca.* 2.63. On the other hand, as is shown in Fig. 2, the b-isomer gives signals arising from 5-H and 2-H at τ 4.56 and τ 4.13 respectively, and shows signals due to the phenyl-ring protons as complicated multiplets at τ *ca.* 2.56. No detectable change in the spectral pattern was observed at elevated temperatures (to *ca.* 100°C, in $CCl_2=CCl_2$). In the *trans* form, it is expected that the phenyl-ring protons give a spectral pattern similar to those of the 5- or 2-phenyl derivatives. On the other hand, it may be expected for the *cis* form that the phenyl-ring protons will give a complicated spectral pattern because of larger chemical-shift differences among the ring protons due to the predominant anisotropic effect of the Cl atoms in the trichloromethyl group,[5] which is located on the same side as the phenyl group in the five-membered ring. In this regard, the isomer in the lower band (b-isomer) on the tlc, which shows the phenyl-ring proton signals as a complicated spectrum, should be *cis*, and the isomer in the upper band (a-isomer) on the tlc, which gives the phenyl-ring proton signals as a simple pattern, much like those of the 5- and 2-phenyl-1,3-dioxolan-4-ones (III and IV respectively), should be assigned as the *trans* form. Although the spectra of the phenyl-ring protons in $CCl_2=CCl_2$ as well as in $(CD_3)_2CO$ and $CDCl_3$ differ from those in CCl_4 because of the solvent effect, the same conclusion was derived for the same reasons.[7] As is shown in Fig. 1,

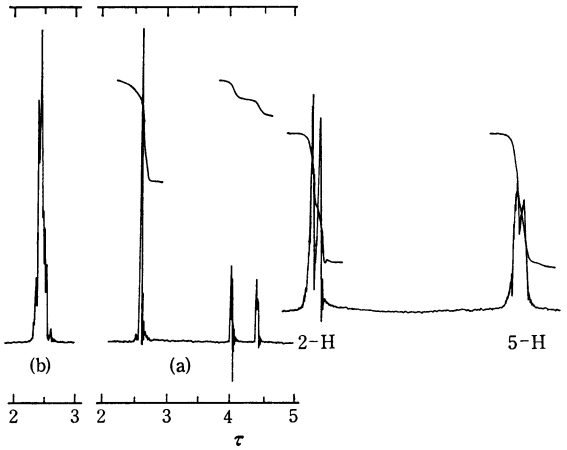

Fig. 1. 100 MHz PMR spectra of the isomer in the upper band (a-isomer, *trans*) (a): in CCl_4 (b): in $(CD_3)_2CO$.

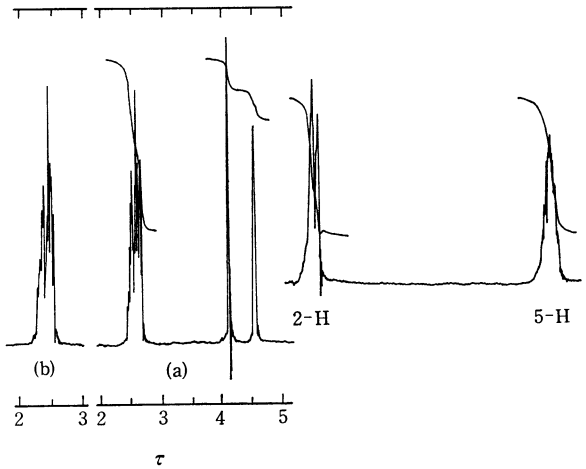

Fig. 2. 100 MHz PMR spectra of the isomer in the lower band (b-isomer, *cis*) (a): in CCl_4 (b): in $(CD_3)_2CO$.

1) Presented at the Annual Meeting of the Pharmaceutical Society of Japan, April, 9, 1971 (Fukuoka).

2) R. C. Elderfield and F. W. Short, "Heterocyclic Compounds," Vol. 5, ed. by R. C. Elderfield, John Wiley & Sons, New York (1957), Chap. 1.

3) E. L. Salmi and A. Pohjolaninen, *Ber.*, **72**, 798 (1939).

4) M. Baron and D. P. Hollis, *Rec. Trav. Chim. Pays-Bas*, **84**, 1109 (1965).

5) M. Farines and J. Soulier, *Bull. Soc. Chim. Fr.*, **1970**, 332.

6) N. J. Turro, S. S. Edelson, J. R. Williams, and T. R. Darling, *J. Amer. Chem. Soc.*, **90**, 1926 (1968).

7) In a paper recently published, Cort and Stewart gave the same assignment on the basis of the PMR spectra of the phenyl rings as well as on that of the dipole-moment measurements of Compound (I). Since they obtained an equal value for the *cis* and *trans* coupling of the long-range couplings between 2-H and 5-H, they claimed that the characteristic long-range couplings could not be used for assignment in the stereochemistry of these compounds. However, our results on the long-range couplings are different from theirs. See L. A. Cort and R. A. Stewart, *J. Chem. Soc. C*, **1971**, 1386.

Table 1. The PMR spectral data of the compounds

Compound		Chemical shift (τ)[a] 2-H *cis*[b]	2-H *trans*[c]	5-H *cis*[d]	5-H *trans*[e]	Phenyl protons	Coupling constant, J (Hz) $\lvert J_{2H-5H}\rvert$	$\lvert J_{gem}\rvert$
I	*trans*	4.03		4.43		*ca.* 2.63 s	1.4	
	cis		4.13		4.56	*ca.* 2.56 c	1.1	
II	*trans*	3.23		5.09		*ca.* 2.60 s	1.6	
	cis		3.58		5.11	*ca.* 2.55 c	1.1	
III		4.54	4.47	4.93		*ca.* 2.68 s	0.7	0.4
							0.4	
IV		3.55		5.80	5.47	*ca.* 2.55 s	1.0	15.0
							0.4	

a) in CCl_4. b) *cis* to the 5-substituent group. c) *trans* to the 5-substituent group. d) *cis* to the 2-substituent group. e) *trans* to the 2-substituent group. s: almost single peak. c: complicated multiplet.

two doublets are observed due to long-range couplings through the oxygen atoms ($|J|=1.4$ Hz) for expanded patterns of the 2-H and 5-H signals in the a-isomer; the 5-H doublet is further broadened because of the long-range couplings with the phenyl-ring protons. Similarly, the 2-H in the b-isomer gives a doublet ($|J|=1.1$ Hz), and the 5-H gives a more broadened signal than that shown in Fig. 1 for the same reason (see Fig. 2). Accordingly, the absolute magnitude of the long-range couplings between the 2-H and the 5-H *via trans*($|J|=1.4$ Hz) was found to be larger than that of the coupling *via cis*($|J|=1.1$ Hz). As is given in Table 1, the *trans* coupling ($|J|=1.6$ Hz) is, in a similar manner, larger than the *cis* coupling ($|J|=1.1$ Hz) in the 2-phenyl-5-trichloromethyl derivative (II), a structural isomer of Compound(I). As is given in Table 1, the 5-H and the 2-H signal in Compound(I) both appear at a slightly higher field in the *cis* than in the *trans* isomer, but the 5-H signals of both isomers of Compound(II) have equal chemical shifts. Therefore, the assignments of the isomers on the basis of the chemical shift seem very difficult. Although the magnitude of the long-range couplings between the 2-H and 5-H signals of these compounds and the differences between the two couplings, are very small, it is possible to distinguish between them, at least, by comparing them with each other in the samples containing both isomers.

This result is in accordance with one of the empirical generalizations for 2,5-dihydrofurans,[8,9] which may be considered to be isoelectronic with 1,3-dioxolan-4-ones. This coupling mechanism is regarded as the same as in 2,5-dihydrofurans in view of the contribution of the $C-\underset{\underset{O}{\|}}{C}-O-C \longleftrightarrow C-\overset{|}{\underset{O^-}{C}}=\overset{+}{O}-C$ of the planar lactone function[10,11] in the 1,3-dioxolan-4-one ring.[5] The assignment based on the long-range couplings on the methylene protons of the C-2 and C-5 signals of Compounds-(III) and (IV) was in accordance with that made on the basis of the deshielding effects of their phenyl group. Hardly no solvent effect was observed on the long-range couplings.

Experimental

Preparation of Materials. *2-Trichloromethyl-5-phenyl-1,3-dioxolan-4-one (I)*: This was prepared by the reaction of *dl*-mandelic acid, chloral, and phosphorus pentoxide in tetrachloroethane (at *ca.* 100°C); the *cis*, *trans* mixture was purified by recrystallization from CCl_4–ligroin. Mp 66—67°C. Yield, 51.3%. Each isomer was separated by preparative tlc[12] from the mixture, and was recrystallized from petroleum ether. The upper band (a-band, *trans* isomer) yielded colorless needles; mp 67—68°C. Found: C, 42.77; H, 2.73%. Calcd for $C_{10}H_7O_3Cl_3$: C, 42.67; H, 2.51%. The lower band (b-band, *cis* isomer) gave colorless plates; mp 88—89.5°C. Found: C, 42.16; H, 2.49%.

2-Phenyl-5-trichloromethyl-1,3-dioxolan-4-one (II): This was similarly prepared by the reaction of *dl*-β,β,β-trichlorolactic acid with benzaldehyde; then the excess benzaldehyde was removed by distillation under reduced pressure, and the residue was treated in the same manner as Compound (I). Mp 74—76°C. Yield, 52.8%. The upper band (*trans* isomer) on the tlc gave colorless needles; mp 86—87°C. Found: C, 42.50; H, 2.22%. The lower band (*cis* isomer) gave colorless plates; mp 88—89.5°C. Found: C, 42.75; H, 2.41%. 5-Phenyl-1,3-dioxolan-4-one (III, colorless liquid, bp 124—125 °C/5 mmHg) and 2-phenyl-1,3-dioxolan-4-one (IV, colorless liquid, bp 123—124°C/5 mmHg) were prepared from the corresponding α-hydroxycarboxylic acids and aldehydes by Gerhardt's method[2,3] with a slight modification; they were purified by repeated distillation before use.

Measurements. All the melting points and boiling points are uncorrected. The PMR spectra were measured with a Varian A-60 spectrometer and a JNM-4H-100 spectrometer at room temperature. Carbon tetrachloride, chloroform-*d*, acetone-d_6, and tetrachloroethylene were used as the solvents (the concentrations were about 60—70 mg/0.5 ml), and TMS was used as the internal reference; none of the samples were degassed.

8) C. Barbier, D. Gagnaire, and P. Vottero, *Bull. Soc. Chim. Fr.*, **1968**, 2330; D. Gagnaire and P. Vottero, *ibid.*, **1970**, 164.

9) M. Barfield, R. J. Spear, and S. Sternhell, *J. Amer. Chem. Soc.*, **93**, 5322 (1971).

10) G. A. Jeffrey and S. H. Kim, *Chem. Commun.*, **1966**, 211.

11) E. A. Noe and J. D. Roberts, *J. Amer. Chem. Soc.*, **93**, 7261 (1971), and the referencs cited therein.

12) Two-layer, one-dimensional tlc plates coated with Merck Silica gel HF_{254}-Kieselguhr G (the thickness was 0.5 mm) were used, and benzene or benzene–ligroin mixed solvents were used as the developers.