

¹³C NMR STUDIES ON LICODIONE AND RELATED COMPOUNDS
 IN EQUILIBRIUM MIXTURE OF KETO AND ENOL FORMS

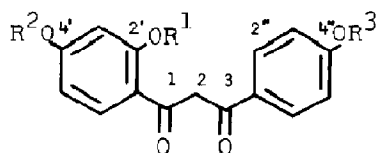
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Abstract: ¹³C NMR data of licodione and its methylated derivatives in keto-enol tautomeric mixture are given, and evidence for correct assignment of α-proton and methyl signals in ¹H NMR is presented.

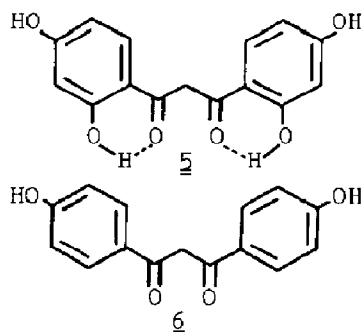
Proton magnetic resonance (¹H NMR) spectroscopy has been one of the most useful methods for elucidation of the ratio of keto, enol and hemiketal forms of substituted dibenzoylmethanes existing in tautomeric mixture in solution.¹⁾ Correct assignments of signals of α-protons are critical for this purpose, but reported assignments for naturally occurring dibenzoylmethanes seem to be ambiguous.²⁾ Now, ¹³C NMR studies on licodione(1), a component of *Glycyrrhiza* cell culture,^{3a)} and its methylated derivatives(2-4)^{3b)} have been carried out to confirm the assignments of ¹H NMR signals. In this paper, we will discuss mainly on the assignments of α-atom signals and demonstrate the utility of ¹³C NMR for elucidation of the existing forms of dibenzoylmethanes.

Spectra were recorded at 25.15MHz with JEOL PS-100 instrument with JEOL EC-100 computer at 22°(1-3, 5,6) and 30°(4). Samples were dissolved in acetone-d₆ at the concentration of 0.5-0.7 M with TMS as internal standard (δ0). Chemical shifts of observed signals are summarized in Table 1.

Observation of the spectra of symmetrical model compounds, 2'-hydroxy-(5) and 2'-deoxy-(6) licodiones,^{3c)} established that α-carbon of keto form gives a signal at δ49-55 and enol form δ 90-97. In the spectrum of 5, which exists exclusively in keto form because of two intra-molecular hydrogen bondings, only a signal at δ49.3 (triplet in off-resonance spectrum) is



- 1: R¹=R²=R³=H
2: R¹=CH₃, R²=R³=H
3: R¹=R²=H, R³=CH₃
4: R¹=H, R²=R³=CH₃



observed, while 6 gives a signal at δ 91.4 (doublet) and methylene carbon signal is hardly detectable, indicating predominant enol form. Proton selective decoupled spectra clarified that protons attaching to α -carbon give signals at δ 4.65 in 5 and δ 6.98 in 6. These findings were applied to the assignment of ^{13}C NMR spectrum of licodione(1), in which both olefinic(δ 90.5) and methylene(δ 49.0) carbon signals, although the latter is very weak, are detected. ^1H NMR spectrum of 1 shows olefinic(δ 6.97) and methylene(4.62) proton signals which integrate 0.7 and 0.6 protons respectively, indicating 1 exists in 70% enol and 30% keto forms.

Differences in chemical shifts of aromatic carbons between keto and enol forms were also observed (see Table 1).

4''-O-Methyl-(3) and 4',4''-di-O-methyl-(4) licodiones give the ^{13}C NMR spectra which are essentially the same as that of 1, except for appearance of one methyl signal in each.

In higher magnetic field of ^{13}C NMR spectrum of 2'-O-methyl-licodione(2), readily assignable methyl signal at δ 56.1 and two more minor peaks at δ 54.4 and 55.6 appear. The signal at δ 54.4 was assigned to methylene carbon referring the spectrum recorded after the addition of D_2O . As shown in Fig.1, intensity of signals of α -carbons, which bear labile protons in keto form, remarkably decreases by the addition of D_2O . The signal at δ 55.6, remaining unchanged by D_2O addition, would be then assigned to methyl carbon of the minor (keto) form.

These ^{13}C NMR assignments were successfully utilized to confirm the assignment of ^1H NMR signals. ^1H NMR of 2 reveals small peaks at δ 3.61(0.5H) and δ 4.45(0.3H) in addition to the signal of olefinic proton of enol form at δ 7.23(0.8H), while no signals at δ 3-4 appear in the spectra of 3, 4 and 4'-O-methyl-licodione. We tentatively assigned the signal at δ 3.61 to methyl proton of keto form regarding the unusual intensity of another methyl signal at δ 3.97(2.4H), in accordance with high field shift of *ortho*-methoxy signal in keto form of a synthetic dibenzoylmethane noted by Wagner et al.^{1a)} Reported ^1H NMR data of natural products, milletenone^{2a)} and ovalitenone^{2c)} (*glabra*-I),^{2d)} fit with the observed spectrum of 2, but in these reports signals at δ 3.6-4.0 have been assigned to methylene proton of keto form and δ 4.4-4.5 to olefinic proton of enol form assuming a particular conformation with a twisted benzene ring.

Unambiguous assignments of higher field signals in ^{13}C NMR of 2 were made by comparing ^1H noise decoupled, ^1H coupled and ^1H selective decoupled spectra recorded at 67.89 MHz with Bruker WH-270 instrument (Fig.2). A weak signal at δ 55.6, which splits to quartet in ^1H coupled spectrum, is now surely assigned to methyl carbon of keto form, and this carbon is shown to bear protons giving a peak at δ 3.61 in ^1H NMR spectrum. Thus the unusual features of ^1H NMR spectra of *ortho*-methoxy-dibenzoylmethanes should be attributed to the difference of chemical shifts of α -proton signals and also methoxy signals in keto and enol forms.

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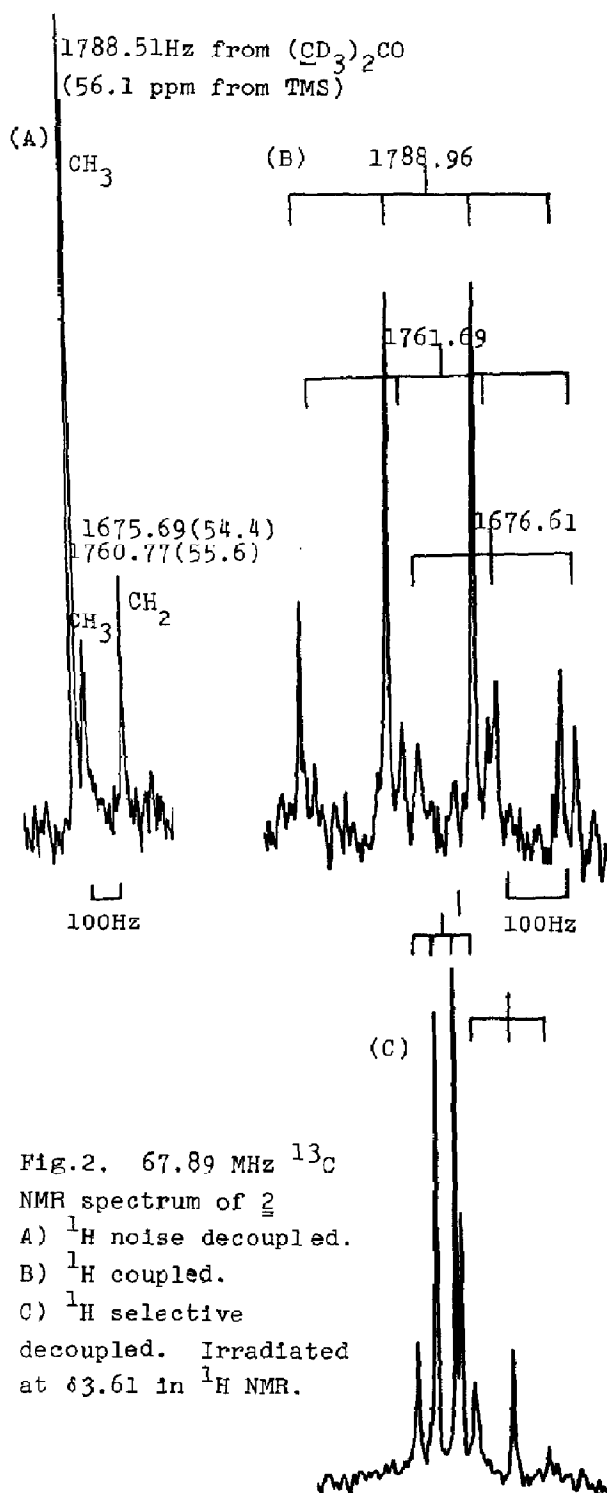
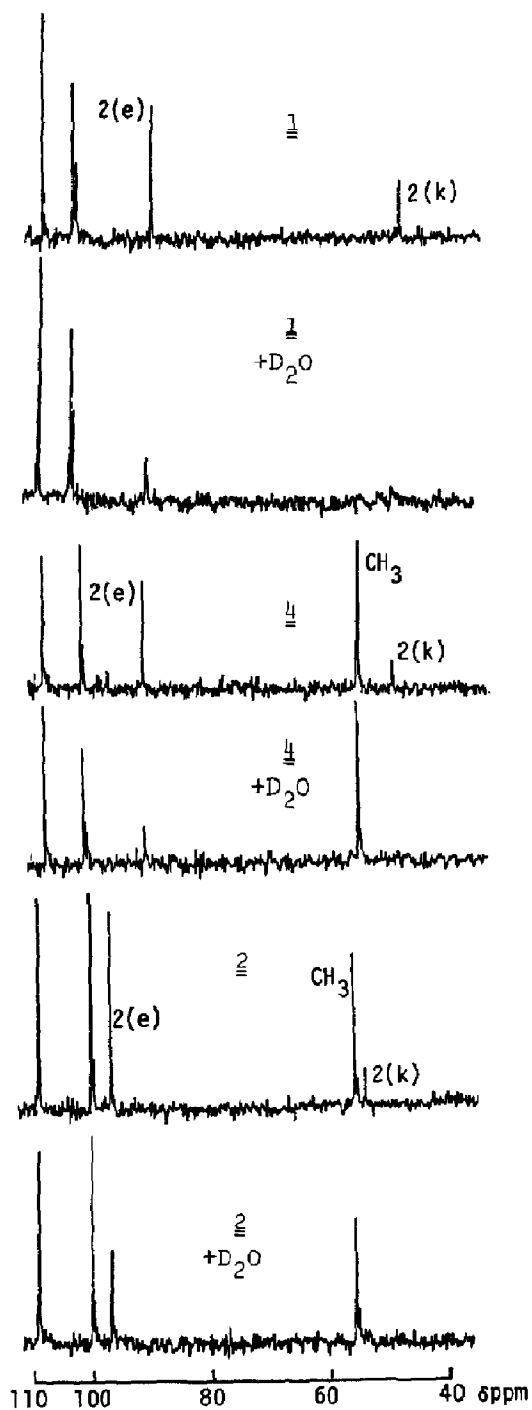


Table 1. ^{13}C NMR Chemical Shifts of Licodione and Related Compounds (25.15MHz, $(\text{CD}_3)_2\text{CO}$, TMS as internal standard)^{a)}

Carbon No.	Compounds									
	<u>5</u> keto	<u>6</u> ca.90% enol	enol	<u>1</u> keto	enol	<u>2</u> keto	enol	<u>3</u> keto	enol	<u>4</u> keto
1,3	199.5	185.4	200.3 194.9 ^{b)} 193.0 177.3		193.2 186.6 182.4		200.0 195.0 192.9 176.8		195.1 177.3	
2	49.3	91.4	91.1	49.7	96.8	54.4	91.4	49.7	91.6	49.9
1'	114.1	-	112.8	114.2	116.6		112.8	114.2 ^{f)}	113.3	
2'	166.4 ^{c)}	-	165.9 ^{d)}	166.4 ^{d)}	163.3 ^{e)}	164.3 ^{e)}	165.2 ^{g)}	165.8 ^{g)}	164.1 ^{h)}	164.9 ^{h)}
3'	103.6	-	104.1	103.5	100.1	99.7	104.0	103.5	102.0	101.6
4'	166.0 ^{c)}	-	165.1 ^{d)}		161.9 ^{e)}		163.9 ^{g)}	164.7 ^{g)}	166.8 ^{h)}	167.4 ^{h)}
5'	109.1	-	109.0		108.7	108.9	109.0		108.3	
6'	134.5	-	132.1	134.6	132.4	133.4	132.1	134.4	131.7	134.0
1''	-	127.8	125.6		128.5		126.6		126.6	
2'',6''	-	130.1 132.0 ⁱ⁾	129.8	129.6	130.1	131.4	129.4	131.7	129.6	130.4
3'',5''	-	116.2	116.3	116.1	116.2	116.0	114.8	114.5 ^{f)}	114.9	114.7
4''	-	162.2	162.2	163.2	162.1 ^{e)}	162.6 ^{e)}	165.9 ^{g)}	166.4 ^{g)}	166.0 ^{h)}	166.4 ^{h)}
CH ₃	-	-	-	-	56.1	55.6	55.8		55.9	

a) Recording conditions were as follows: pulse width, 20 μsec (45°); repetition time, 2.0 sec; frequency range, 6250 Hz; data points, 8191; number of scans, 1200-1800. Error of the shift value is about 0.1 ppm. b) Assignments of distinct signals have not been made. c-h) Assignments bearing the same superscript may be interchanged. i) Possibly the signal of the minor (keto) form is observed.

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