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Intramolecular Hydrogen Bonds. VII.[1] Methyl Mandelates and Related Compounds

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The infrared OH spectra of an $ArCH(OH)(CH_2)_nCOOMe$ series ($n=0$ and 1) in dilute carbon tetrachloride solutions have been measured at 25°C with a Perkin-Elmer 21 spectrometer. A comparison of the data with those of other related compounds shows that the OH group forms a hydrogen bond predominantly with the carbonyl-oxygen atom and also with the ether-oxygen atom and/or the π-electrons of the phenyl group, while, practically speaking, no free OH group is present. Further, the NMR chemical shifts of the methine- and the methyl-protons when $n=0$, as measured with a Varian A-60 spectrometer, have been correlated with the Hammett substituent constants; the shift of the methine-proton, when the ring-substituent is a halogen, does not fall on the correlation line, but falls on a separate line.

The infrared spectrum of ethyl mandelate in a dilute carbon tetrachloride solution exhibits, in the OH-stretching region, a very strong band at 3534 cm^{-1} and a weak shoulder at 3602 cm^{-1}.[2] Flett[2] assigned the former to the OH group bonded to the carbonyl-oxygen atom of the ester group and the latter to the free OH group, mainly on the basis of a comparison of the frequencies and the half-band widths; he also suggested that the lowering of the free OH frequency from that of ca. 3625 cm^{-1} characteristic of secondary alcohols is to be attributed to the electrostatic influence of the adjacent ester group. However, the assignment of the shoulder seems doubtful because the frequency is very close to that of the OH group internally bonded to the ether-oxygen atom of an alkoxycarbonyl group in aliphatic α-hydroxycarboxylates[3] and to that of the OH group bonded to the π-electrons of a phenyl group in α-phenylalkanols.[4]

This paper will report on an investigation which has solved this problem by measuring the infrared spectra of a variety of methyl mandelates in dilute carbon tetrachloride solutions. Further, this paper will deal with their characteristics in nuclear magnetic resonance, and also with the intramolecular hydrogen bonding in two methyl β-phenyl-β-hydroxypropionates.

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[1] Part VI: N. Mori, S. Ōmura and Y. Tsuzuki, This Bulletin, **38**, 2199 (1965).

[2] M. St. C. Flett, *Spectrochimica Acta*, **10**, 21 (1957).

[3] N. Mori, S. Ōmura, N. Kobayashi and Y. Tsuzuki, This Bulletin, **38**, 2149 (1965).

[4] M. Ōki and H. Iwamura, ibid., **32**, 950 (1959).

Experimental

Samples.—All the esters investigated, some of which have hitherto been unknown, are listed in Table I. The mandelates, except for Nos. 4 and 6, were prepared in the usual way[5-7] by the conversion of the corresponding benzaldehyde-cyanohydrins into the iminomethylether hydrochlorides, followed by hydrolysis. The cyanohydrins were synthesized by treating a suspension of the corresponding substituted benzaldehyde in glacial acetic acid with potassium cyanide[5,6] (in the case of Nos. 1 and 2) or by treating a mixture of the corresponding benzaldehyde and potassium cyanide with concentrated hydrochloric acid[7] (in the case of Nos. 3, 5, 7 and 8); they were used without further purification for the preparation of the esters. The ester of No. 4 was derived from *p*-bromoacetophenone by way of *p*-bromomandelic acid,[8] while the ester of No. 6 was prepared by the conversion of the benzaldehyde into mandelic acid,[9] followed by esterification. Methyl β-phenyl-β-hydroxypropionates 9 and 10 were prepared by the Reformatsky reaction[10] from benzaldehydes and methyl bromoacetate. All the esters were purified by recrystallization from a mixture of benzene and ligroin or by fractional distillation; their physical constants and the data of analysis are summarized in the table. The constants of the known esters agree closely with those reported in the literature.

Infrared and NMR Measurements.—The infrared measurements in the OH-stretching region were carried out, by the method previously described,[3] at 25°C with a Perkin-Elmer 21 spectrometer equipped with a lithium fluoride prism and a cell 3 cm. long. The concentrations were about 0.004 mol./l. in carbon tetrachloride, at which concentration no intermolecularly hydrogen-bonded OH band was observed; however, a very weak absorption, due to the overtone of a carbonyl-stretching vibration, appeared at ca. 3460 cm^{-1}.

The NMR spectra were measured at ca. 25°C using a Varian A-60 spectrometer on pre-calibrated chart paper, in which TMS was used as the internal standard. The concentration was 5 w./v. % in carbon tetrachloride and in chloroform. Preliminary measurements with solutions from 0.5 to 40% in both solvents showed that the resonance positions of the methine- and the methyl-protons were constant[*1] within the limits of experimental accuracy ($\pm$0.5 c. p. s.). The NMR data listed in Table III are the average of two measurements.

Results and Discussion

The infrared OH spectra of the mandelates apparently consist of two resolved bands, whose frequencies are in the range from 3601 to 3611 cm^{-1} and from 3526 to 3536 cm^{-1} respectively; the higher frequency band is much weaker than the lower frequency band, as Fig. 1 shows, and the separation between the two peaks is constant to 77 cm^{-1}. It should be noted that the stronger band is located at ca. 3526 cm^{-1} and that it is somewhat broadened

TABLE I. THE PHYSICAL CONSTANTS AND ANALYSIS OF METHYL MANDELATES (Nos. 1—8) AND METHYL β-PHENYL-β-HYDROXYPROPIONATES (Nos. 9 and 10)

No.	Substituent	M.p., °C (B.p., °C/mmHg)	Anal., %			
			Calcd.		Found	
			C	H	C	H
1	*p*-NO$_2$	86.5—87[6,11]				
2	*m*-NO$_2$	63[12]				
3	*m*-Cl	83—84[13]				
4	*p*-Br	61	For $C_9H_9O_3Br$ (245.09) 44.11	3.70	44.24	3.89
5	*p*-Cl	55[13] (131/5)				
6	H	57[14]				
7	*p*-Me	49 (130/6)	For $C_{10}H_{12}O_3$ (180.20) 66.65	6.71	66.60	6.57
8	*p*-MeO	36 (152/5.5)	For $C_{10}H_{12}O_4$ (196.20) 61.21	6.17	61.12	6.27
9	H	(150/10)[15]				
10	*p*-MeO	(159—162/3.5)	For $C_{11}H_{14}O_4$ (210.22) 62.84	6.71	62.91	6.45

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5) G. Heller, *Ber.*, **46**, 280 (1913).

6) L. S. Fosdick and G. D. Wessinger, *J. Am. Chem. Soc.*, **60**, 1465 (1938).

7) E. Knorr, *Ber.*, **37**, 3172 (1904).

8) T. L. Cairns, Editor-in-Chief, "Organic Syntheses," **35**, 11 (1955).

9) H. Gilman, Editor-in-Chief, ibid., Coll. Vol. I, 336 (1941).

10) E. C. Horning, Editor-in-Chief, ibid., Coll. Vol. III, 408 (1955).

11) C. Engler and O. Zielke, *Ber.*, **22**, 207 (1889).

12) L. S. Fosdick and J. C. Calandra, *J. Am. Chem. Soc.*, **63**, 1101 (1941).

13) S. S. Jenkins, ibid., **53**, 2341 (1931).

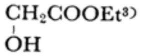
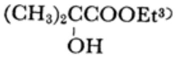
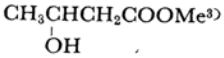
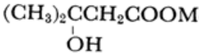
14) S. F. Acree, *Ber.*, **37**, 2767 (1904).

15) A. McKenzie and C. Martin, *J. Chem. Soc.*, **103**, 112 (1913).

[*1] It is noteworthy that the methine-proton resonance of aliphatic α- and β-hydroxycarboxylates depends on the concentration in carbon tetrachloride.[16]

16) N. Mori, S. Omura, O. Yamamoto, T. Suzuki and Y. Tsuzuki, This Bulletin, **36**, 1401 (1963).

TABLE II. THE INFRARED DATA OF METHYL SUBSTITUTED MANDELATES (Nos. 1—8) AND METHYL β-SUBSTITUTED PHENYL-β-HYDROXYPROPIONATES (Nos. 9 AND 10) AS WELL AS SOME RELATED COMPOUNDS (Nos. 11—16)

No.	Substituent	Band*	ν_{OH}, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	D**
1	p-NO_2	I	3526	37	0.58
		II, III	3602	ca. 18	0.10
2	m-NO_2	I	3525	40	1.03
		II, III	3601	ca. 18	0.13
3	m-Cl	I	3526	42	0.86
		II, III	3603	ca. 25	0.14
4	p-Br	I	3526	35	1.17
		II, III	3606	ca. 25	0.19
5	p-Cl	I	3532	41	0.92
		II, III	3611	ca. 22	0.16
6	H	I	3536	44	0.89
		II, III	3610	ca. 25	0.16
7	p-Me	I	3532	44	0.79
		II, III	3610	ca. 24	0.15
8	p-MeO	I	3536	40	0.61
		II, III	3611	ca. 26	0.09
9	H	I	3537	102	0.47
		II	3588	38	0.06
		III	3618	23	0.28
10	p-MeO	I	3545	100	0.37
		II	3587	31	0.04
		III	3618	22	0.23
11	 $\underset{OH}{\underset{\mid}{CH_2}}COOEt$[3]	I	3550	46	0.68
		II	3618	25	0.13
12	 $(CH_3)_2\underset{OH}{\underset{\mid}{C}}COOEt$[3]	I	3544	48	0.43
		II	3606	21	0.09
13	 $CH_3\underset{OH}{\underset{\mid}{C}}HCH_2COOMe$[3]	I	3559	82	0.49
		II	3592	32	0.08
		IV	3622	30	0.16
14	 $(CH_3)_2\underset{OH}{\underset{\mid}{C}}CH_2COOMe$[3]	I	3537	54	0.59
		II	3588	20	0.04
		IV	3613	22	0.06
15	$C_6H_5CH_2OH$[4]	III	3617		
		IV	3636		
16	$C_6H_5C(CH_3)_2OH$[4]	III	3607		
		IV	3620		

* Bands I, II and III denote those due to the OH groups bonded to the proton-acceptors, =O, -O- and π-electrons, respectively, and band IV means the free OH band.

** $D = \log I_0/I$, for the apparent OH band in the case of Nos. 1—8 and for the separated OH band-component in the case of Nos. 9—14.

on the higher frequency side (the most broadened position being at ca. 3535 cm^{-1}) when the ring-substituent is of an electron-attracting nature (Nos. 1—4), while it appears at ca. 3534 cm^{-1} and is substantially symmetric in respect to the ordinate at the maximum when the substituent is a p-chlorine or hydrogen atom or an electron-repelling group (Nos. 5—8). The reason for this is not clear at the present time. The β-hydroxy-esters 9 and 10 show a strong, broad band around 3540 cm^{-1} and a sharp band at 3618 cm^{-1}, the former being highly broadened on the higher frequency side; each of the observed spectra can be graphically separated into three symmetric components,*2 as is shown in Fig. 2.

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*2 Although it is not clear whether or not the individual band-components are intrinsically symmetric, their symmetry is, at any rate, assumed to simplify the graphical separation. This separation was thus made by reflecting the major component about the ordinate at the apparent maximum and by subtracting the mirror image from the observed spectrum. The residual minor part, which had a shoulder at ca. 3590 cm^{-1}, was then similarly separated into two. Alternatively, by reflecting the minor component and subtracting the mirror image, the major part remained; this was highly broadened around 3590 cm^{-1}. It is unlikely that either the major or the minor component is intrinsically unsymmetric with the broadening or the shoulder at 3590 cm^{-1}. Rather, the part at 3590 cm^{-1} may reasonably be attributed to an absorption of another bonded OH group, as will be discussed in detail later.

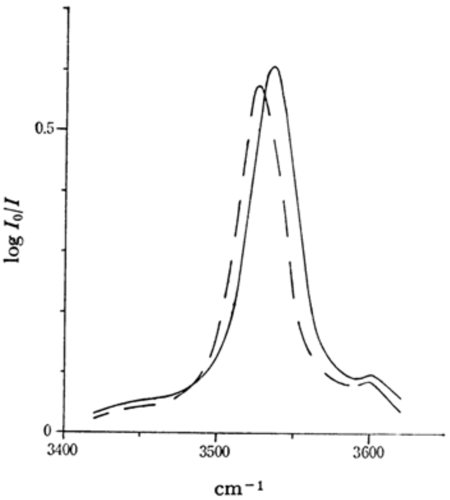

Fig. 1. IR spectra of methyl *p*-nitromandelate (– –) and *p*-methoxymandelate (——).

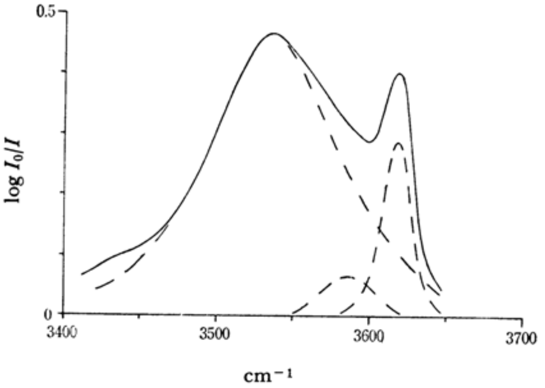

Fig. 2. IR spectrum of methyl β-phenyl-β-hydroxypropionate.

Table II includes the IR data of the apparent OH bands of the mandelates and the OH band-components separated from the observed spectra of the β-phenyl-β-hydroxypropionates, together with those of some related compounds for the purpose of comparison.

In order to assign the bands, it is convenient to take account of the six hydrogen-bonded conformations possible by rotation around the C–O axis; these conformations are shown in Fig. 3. Further, there must be considered the electrostatic and the steric influence on the OH frequency of the phenyl group and the methoxycarbonyl group, both skew

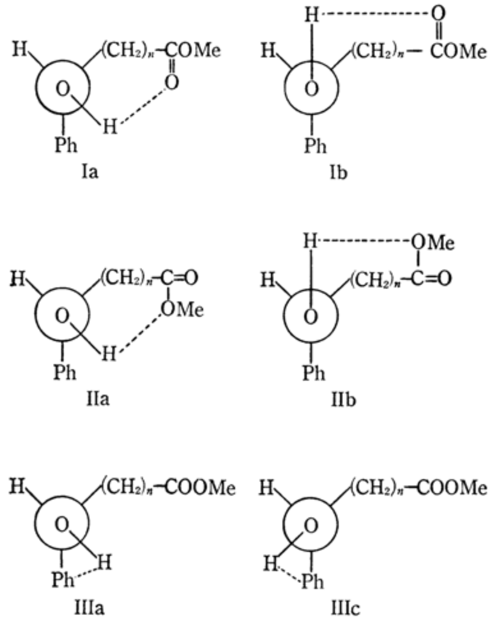

Fig. 3. Hydrogen-bonded conformations possible around the C–O axis.

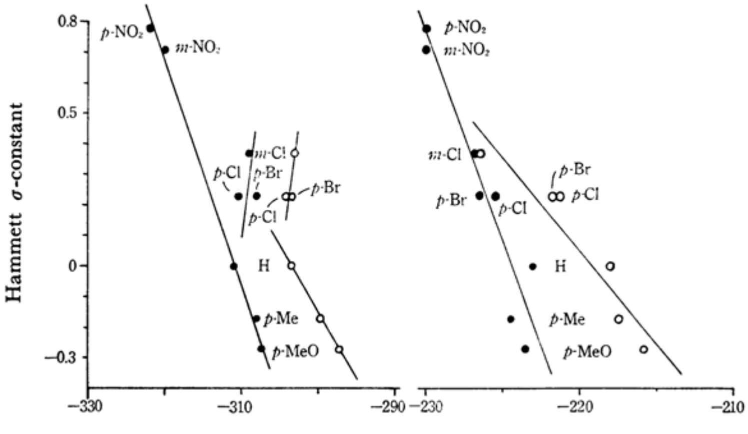

Fig. 4. Chemical shifts vs. Hammett σ-constants for: (left) the methine- and (right) the methyl-protons in chloroform (-●-) and carbon tetrachloride (-○-).

to the OH group. Fortunately, it is known that the influences both of an unsubstituted and a substituted phenyl group are substantially of the same degree as those of a methyl group,[4,17] while the electron-attracting nature of the methoxycarbonyl group lessens the OH frequency by 10 cm^{-1} at most.[3]

In the mandelates (n=0 in Fig. 3), the lower frequency band is undoubtedly due to the OH group bonded to the carbonyl-oxygen atom in form Ia and to the bonded OH group in form Ib, since its frequency agrees with that of band I of the comparative α-hydroxycarboxylates. The higher frequency band should not be attributed to a free OH group, since it is considerably lower than the frequency of 3620 cm^{-1} or more which is to be expected for the OH group in form Ib, IIb or IIIc, if it is not hydrogen-bonded. The frequency is also lower than the 3618 cm^{-1} of band II of ethyl glycolate 11 in a form corresponding to form IIb, but it is rather close to the 3606 cm^{-1} of band II of ethyl α-hydroxyisobutyrate 12 in a form corresponding to form IIa. On the other hand, the bonded OH frequencies of forms IIIa and IIIc may fall within the frequency range from 3601 to 3611 cm^{-1}, if the lowering of frequency due to the electron-attracting nature of the methoxycarbonyl group is 7 cm^{-1} and this is then subtracted from the bonded OH frequencies of 3607 and 3617 cm^{-1} of phenyldimethylcarbinol 16 and benzylalcohol 15. Consequently, the band is due to the bonded OH group in at least one of the forms, IIa, IIb, IIIa and IIIc. For a more detailed discussion, it is necessary to investigate the electronic effect of a ring-substituent influencing on the band-intensity. Unfortunately, however, the observed absorbance is too low and inexact to make such an investigation possible.

In the β-phenyl-β-hydroxypropionates (n=1 in Fig. 3), the three bands can easily be assigned by comparing their frequencies with those of aliphatic β-hydroxycarboxylates and α-phenylalkanols, as, practically speaking, it is not necessary to take account of the frequency-lowering effect of the methoxycarbonyl group.[3] The band at around 3540 cm^{-1} can undoubtedly be assigned to the OH group bonded to the carbonyl-oxygen atom in form Ia and the bonded OH group in form Ib, while the band at ca. 3590 cm^{-1} may be assigned to the OH group bonded to the ether-oxygen atom in forms IIa and IIb for two reasons: (1) such forms should be present to some extent, though less stable than forms Ia and Ib, and (2) the frequency closely agrees with the ν_{OH} of 3590—3600 cm^{-1} of some 1, 3-diol monoacetates[18] in a similar six-membered ring formed through the intramolecular hydrogen bonding. On the other hand, the highest frequency band may be due to the OH group bonded to the π-electrons of the phenyl group in forms IIIa and IIIc, rather than due to a free OH group. This assignment may be further supported by the fact that the relative intensity of band III to II is higher than those of the free OH band, IV, to band II in β-hydroxycarboxylates 13 and 14; this heightening may result from the hydrogen bonding of the OH group with the π-electrons. As can be seen from a comparison of the data of esters 9 and 10, the p-methoxy substituent appears to raise the relative intensity of band III to II; this is in agreement with the effect of an electron-repelling substituent in strengthening the bonded OH band in series of α- and β-phenylalkanols.[17,19] Thus, no free OH group is present in these esters, since there is no absorption in the frequency region around 3627 cm^{-1} characteristic of the free secondary OH group of α-phenylalkanols.[4]

The above assignments are reasonable also in view of the half-band widths. Thus, the $\Delta\nu_{1/2}$ values of bands I and II (or III) of the mandelates are essentially equal to those of the α-hydroxycarboxylates 11 and 12. The same relationship can be found between the two series of β-hydroxycarboxylates (9 and 10) and (13 and 14).

The Correlation of the Chemical Shift with the Hammett σ-Constant.—Table III includes the NMR data of the methine- and the methyl-protons of the mandelates.

The chemical shifts of protons not directly bonded to the aromatic ring in some aryl compounds have recently been correlated with the Hammett σ-constants.[20] In Fig. 4 the chemical shifts of the methine- and methyl-protons in the mandelates are plotted vs. the Hammett σ-constants.*3 When the substituent is a halogen, the methine-proton point in both solvents does not fall on the correlation line, but falls on a separate line. A similar deviation of the halogens from the correlation line has been obtained when they are plotted vs. the σ^0-values reported by Taft.[21] This at present admits of no explanation. However, it is noteworthy that the falling of the halogens on a separate line is

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[17] M. Ōki and H. Iwamura, This Bulletin, **35**, 1552 (1962).

[18] H. B. Henbest and B. J. Lovell, *J. Chem. Soc.*, **1957**, 1965; R. West, J. J. Korst and W. S. Johnson, *J. Org. Chem.*, **25**, 1976 (1960).

[19] M. Ōki and H. Iwamura, This Bulletin, **32**, 1135 (1959).

[20] Y. Yukawa, M. Sakai and K. Kabazawa, *Memoirs of Sci. & Ind. Research Osaka Univ.*, **17**, 185 (1960); Y. Yukawa and H. Yamada, *J. Chem. Soc. Japan, Pure Chem. Sect.* (*Nippon Kagaku Zasshi*), **85**, 501 (1964); R. E. Klinick and J. B. Stothers, *Can. J. Chem.*, **40**, 1071 (1962); W. G. Paterson and N. R. Tipman, ibid., **40**, 2122 (1962); C. Heathcock, ibid., **40**, 1865 (1962); C. D. Cook and S. S. Danyluk, *Tetrahedron*, **19**, 177 (1963).

*3 The constants are those based on the ionization of substituted benzoic acids, as reported by D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

[21] R. W. Taft, Jr., *J. Phys. Chem.*, **64**, 1805 (1960).

TABLE III. THE NMR DATA ($-\delta$, IN c.p.s. FROM TMS)

No.*	in $CHCl_3$		in CCl_4	
	-CH-	$-COOCH_3$	-CH-	$-COOCH_3$
1	322.0	229.8	Insoluble	
2	320.0	229.8	Insoluble	
3	309.0	226.8	303.1	226.6
4	307.9	226.5	303.5	221.8
5	310.5	225.5	304.1	221.3
6	311.0	223.0	303.5	218.0
7	308.0	224.5	299.5	217.5
8	307.5	223.5	297.0	215.8

* The number refers to that used for the ester described in Tables I and II.

found for the α-protons in *p*-substituted ethylbenzenes[22] and in the plotting of NMR substituent constants vs. Hammett σ_p-constants for a series of *p*-disubstituted benzenes.[23]

The authors wish to thank Mr. Teruo Kajiura and Mr. Tadao Tamura of the Government Chemical Industrial Research Institute, Tokyo, for their infrared measurements.

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[22] K. L. Williamson, N. C. Jacobus and K. T. Soucy, *J. Am. Chem. Soc.,* **86**, 4021 (1964).

[23] G. W. Smith, *J. Mol. Spectroscopy,* **12**, 146 (1964).