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NMR SPECTRA OF INTRAMOLECULARLY HYDROGEN-BONDED COMPOUNDS—I

β-DIKETONES, *o*-HYDROXYALDEHYDES, AND *o*-HYDROXYKETONES

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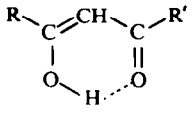
Abstract—The NMR spectra of a series of β-diketones, *o*-hydroxyaldehydes, and *o*-hydroxyketones have been measured. The influence of steric and electronic effects on the position of the enolic signal and hence on the strength of the intramolecular hydrogen bond is discussed.

THE enol forms of *o*-hydroxyaldehydes and ketones (I) and of β-ketoesters and β-diketones (II) form strong intramolecular hydrogen-bonded chelate rings. The strengths of the hydrogen bonds in these compounds have been studied using the



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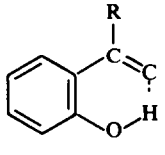

II

IR absorptions of the CO and OH groups, and the chemical shifts of the enolic proton in the NMR spectra; the significance of these values as a measure of the strength of the hydrogen bond having been clearly demonstrated in these investigations.[1]

The influence of steric and electronic effects on the strength of the hydrogen bond in these classes of compound has not been examined in detail though Fórsen and Akermark[2] considered steric effects to be unimportant in their examination of the NMR spectra of OMe derivatives of salicyldehyde and *o*-hydroxyacetophenone. The present work involves a more detailed study of these effects using NMR spectroscopy as a measure of the hydrogen bond strength.

Table 1 summarizes the important features of the NMR spectra of the enolic forms of a range of β-diketones. Assignment of the lines in Table 1 is unambiguous: it is based on chemical shifts, relative intensities, and rapid deuterium exchange of the enolic protons and slow exchange of the vinyl protons. The position of the enolic signal in the spectra of β-diketones containing terminal alkyl groups is strongly dependent on the size of the alkyl group. Bulky groups cause an appreciable downfield shift with consequent sharpening of the normally broad enolic signal. This effect is also apparent in benzoylacylmethanes. The downfield shift is of too great a magnitude to be explained only by electronic effects and must therefore have a steric origin. In β-diketones containing bulky alkyl groups, e.g. dipivaloylmethane

TABLE 1. NMR SPECTRA OF β-DIKETONES

	Solvent	Enolic (τ)	Vinylic proton (τ)	Methyl protons (τ)	$W^{1/2}$ (c/s)*
Acetylacetone	CCl_4	−5·0	4·6	8·0	18
Trifluoroacetylacetone	$CDCl_3$	−4·1	4·1	7·8	
Hexafluoroacetylacetone	$CDCl_3$	−2·4	3·63		
Acetylpivaloylmethane	CCl_4	−5·9	4·45	7·95	6
Di-n-butyrylmethane	CCl_4	−5·3	4·6		15
Di-isobutyrylmethane	CCl_4	−5·75	4·5		5
Dipivaloylmethane	CCl_4	−6·3	4·4		3
Di-t-butylacetylmethane	CCl_4	−5·9	4·65		8
Benzoylacetone	CCl_4	−6·1	3·9	7·85	12
p-Chlorobenzoylacetone	$CDCl_3$	−6·0	3·88	7·83	
p-Nitrobenzoylacetone	CCl_4	−5·8	3·7	7·75	
Mesitoylacetone	CCl_4	−5·4	4·56	7·96	
Benzoyltrifluoroacetylmethane	$CDCl_3$	−4·6	3·48		
Benzoyl-n-butyrylmethane	CCl_4	−6·1	3·9		18
Benzoylisobutyrylmethane	CCl_4	−6·2	3·9		15
Benzoylpivaloylmethane	CCl_4	−6·7	3·8		3
p-Nitrobenzoylpivaloylmethane	CCl_4	−6·4	3·65		3
Dibenzoylmethane	$CDCl_3$	−6·9	3·1		
p-Methoxydibenzoylmethane	$CDCl_3$	−7·0	3·22		
p-Methyldibenzoylmethane	$CDCl_3$	−7·05	3·25		
p-Chlorodibenzoylmethane	$CDCl_3$	−7·0	3·25		
Di-*p*-bromobenzoylmethane[8]	$CDCl_3$	−6·6	3·3		
Mesitoylbenzoylmethane	CCl_4	−6·3	3·82		
Picolinylbenzoylmethane	$CDCl_3$	−6·3			
2-Thenoylbenzoylmethane	$CDCl_3$	−6·28	3·38		
2-Furoylbenzoylmethane	CCl_4	−5·8	3·35		
α-Chloroacetylacetone	CCl_4	−5·4		7·8	2
α-Bromoacetylacetone	CCl_4	−5·8		7·6	2
α-Methylacetylacetone	CCl_4	−6·35		7·9	2
α-n-Propylacetylacetone	CCl_4	−6·55		7·9	2
α-Phenylacetylacetone	CCl_4	−6·6		8·2	2
α-Cyanoacetylacetone[9]	CCl_4	−6·8			
Triacetylmethane[7]	CCl_4	−7·41		7·89	

* This applies only to the enolic proton peak.
$W_{1/2}$ = Peak width at half height.

(I, R = R′ = Bu^t) the size of the alkyl groups forces the CO groups together.[3] The resultant electronic repulsion is released by the formation of a strong hydrogen bond with the interposition of the hydrogen between the two oxygen atoms. With smaller alkyl groups the oxygen atoms will be further apart and the resultant hydrogen bond weaker.

α-Substituted β-diketones all have the enolic signal displaced to lower field with respect to the parent diketone and also the signal is sharper. Again these substituents cause the CO groups in the enolic form to be forced closer together such that a strong hydrogen bond is formed. These results are consistent with those of Burdett and Rogers[4] for α-substituted β-ketoesters except that the magnitudes of the downfield shifts are greater for the diketones in which steric effects are more important.

The broadening of the enolic signal in the NMR spectra of β-diketones is probably due to exchange of the enolic protons on different β-diketone molecules. That it is not due to a rapidly equilibrating mixture of the keto and enol forms, is indicated by the rapid deuterium exchange of the enolic signal (virtually completely exchanged within 5 min) and the very slow exchange of the vinylic signal (only partially exchanged after 24 hr). A sharp enolic signal in the NMR spectrum thus indicates slow intermolecular exchange of the enolic protons. It is reasonable that this should be so in β-diketones containing a strong hydrogen bond.

Bulky alkyl groups also result in the deshielding of the vinyl protons (protons attached to the α-carbon in the enolic form). Inductive electron-donating effects which would be greater with a t-butyl than with a Me group would cause increased shielding of the vinyl protons. On the other hand ring-current effects[5] would enhance the shifts to low field and these may well be more important in diketones with bulky alkyl groups and consequently stronger hydrogen bonds.

Similar conclusions of the influence of steric effects on hydrogen bond strength can be drawn from a study of the NMR spectra of Me, OMe, and chloro derivatives of salicylaldehyde. Substituents *ortho* to the OH or formyl groups result in a strengthening of the hydrogen bond and an enhanced ring current as indicated by downfield shifts of the enolic and aldehydic protons (Table 2). In drawing these conclusions it is necessary to eliminate the influence of electronic effects by comparing the spectra of the 3- and 5-substituted salicylaldehydes, and of the 4- and

TABLE 2. NMR SPECTRA OF *o*-HYDROXYCARBONYL COMPOUNDS

Compound	Solvent	Enolic signal (τ)	Aldehydic signal (τ)	Methyl signal (τ)
Salicylaldehyde	CCl_4	−1·00	0·20	
3-Methylsalicylaldehyde	CCl_4	−1·25	0·15	7·70
4-Methylsalicylaldehyde	CCl_4	−0·92	0·25	7·65
5-Methylsalicylaldehyde	CCl_4	−0·70	0·20	7·70
6-Methylsalicylaldehyde	CCl_4	−1·80	−0·22	7·45
3-Methoxysalicylaldehyde	CCl_4	−0·83	0·09	6·15*
4-Methoxysalicylaldehyde[2]	CCl_4	−1·36	0·35	6·17*
5-Methoxysalicylaldehyde	CCl_4	−0·68	0·12	6·20*
6-Methoxysalicylaldehyde[2]	CCl_4	−1·84	−0·25	6·17*
3-Chlorosalicylaldehyde	CCl_4	−1·32	0·18	
4-Chlorosalicylaldehyde	CCl_4	−1·05	0·22	
5-Chlorosalicylaldehyde	CCl_4	−0·80	0·20	
6-Chlorosalicylaldehyde	CCl_4	−1·80	−0·35	
4-Isopropylsalicylaldehyde[10]	$CDCl_3$	−1·00	0·02	
5-Bromosalicylaldehyde	$CDCl_3$	−1·00	0·10	
5-Nitrosalicylaldehyde	$CDCl_3$	−1·60	0·02	
2-Hydroxyacetophenone	CCl_4	−2·18		
2-Hydroxybenzophenone	CCl_4	−1·83		
1-Hydroxy-2-naphthaldehyde	CCl_4	−2·60	0·15	
2-Hydroxy-1-naphthaldehyde	CCl_4	−3·10	−0·72	
1-Hydroxy-2-acetonaphthone[6]	CCl_4	−3·98		7·38
2-Hydroxy-1-acetonaphthone[6]	CCl_4	−3·40		7·18
2-Hydroxy-1-benzonaphthone	$CDCl_3$	−1·15		

* OMe signal.

6-substituted salicylaldehydes. When this is done it is seen that the downfield shift is greater with substituents in the 6-position than in the 3-position as a consequence of the greater steric interaction between the aldehydic proton and the substituent than between the OH group and the substituent. An examination of 'Dreiding' models revealed that the distance between the Me group and the aldehydic proton is 1·6Å whereas the distance between the Me group and the OH oxygen is 2·2Å. Secondly, effects are greater with Me than OMe substituents owing to the greater effective size of the Me group as the preferred orientation of the OMe will have the O—Me bond directed away from neighbouring substituents. The chloro and Me derivatives of salicylaldehyde have very similar spectra which is not unexpected from the similar sizes of a chlorine atom and a Me group.

The difference in the chemical shifts of the enolic signals for 1-hydroxy-2-naphthaldehyde and 2-hydroxy-1-naphthaldehyde can similarly be accounted for on steric grounds in that in the latter compound, there will be steric interaction between the peri hydrogen in the 8 position and the aldehydic hydrogen.

If, however, the steric interaction becomes too great such that the intramolecularly hydrogen-bonded chelate ring is forced out of planarity, the resultant hydrogen bond is weakened.[6] Thus the downfield shift between 2-hydroxy-1-acetonaphthone and 2-hydroxy-1-naphthaldehyde is less than one might have expected (0·3 τ). The corresponding shifts between 1-hydroxy-2-naphthaldehyde and 1-hydroxy-2-acetonaphthone, and between salicylaldehyde and *o*-hydroxyacetophenone are 1·4 and 1·2 τ respectively. The effect is much more pronounced in the case of 2-hydroxy-1-benzonaphthone where an upfield shift of 1·95 τ was observed. A downfield shift of about 0·8 τ would have been expected if steric effects had not intervened; this being the difference in chemical shifts for the enolic protons in salicylaldehyde and 2-hydroxybenzophenone. Models indicate that in these compounds the chelate ring cannot be planar.

Fórsen and Akermark[2] claimed in their study of the OMe derivatives of salicylaldehyde and *o*-hydroxyacetophenone that the downfield shift caused by the OMe group in the 3 and 6 positions was of electronic and not steric origin. They stated if it were of steric origin a greater displacement would be expected for 6-methoxy-2-hydroxyacetophenone than for 6-methoxysalicylaldehyde whereas the shifts were about the same. However for the 3-OMe compounds a significantly greater shift was observed with 3-methoxy-2-hydroxyacetophenone (0·63 τ) than for 3-methoxysalicylaldehyde (0·15 τ) when compared with the corresponding 5-OMe compounds. This is attributed to greater steric interaction in the 3-methoxy-2-hydroxyacetophenone than in 3-methoxysalicylaldehyde. In 6-methoxy-2-hydroxyacetophenone steric interaction becomes so severe that there is a distortion of the chelate ring accompanied by a slight relative weakening of the hydrogen bond.

Examination of the spectra also indicates that the aldehydic protons, in cases where there is appreciable steric interaction, are also at significantly lower field, thus a comparison of 6- and 4-methylsalicylaldehydes shows a shift of 0·47 τ. As indicated for the diketones this could signify a stronger ring current in the chelate ring.

A further steric effect is seen by comparison of the spectra of mesitoylacetone with dibenzoylmethane and benzoylacetone respectively. The enolic signals of the mesitoyl compounds are significantly less downfield than in the corresponding benzoyl

compounds. Electronic effects would cause the enolic signal to move downfield. The signals of the vinylic protons are similarly shifted upfield. The chemical shifts of the enolic and vinylic protons are much closer to those found in benzoylacetone and acetylacetone than in dibenzoylmethane and benzoylacetone suggesting that the mesityl group is forced out of coplanarity with the chelate ring. Models show that it would not be possible to achieve anything approaching coplanarity of the rings. This is further confirmed by comparing the chemical shifts of the acetyl protons in mesitoylacetone with those in benzoylacetone and acetylacetone. Again there is an upfield shift to a value similar to that of acetylacetone.

Burdett and Rogers have shown that electron-withdrawing α-substituents in β-diketones and β-ketoesters cause a deshielding of the enolic proton.[4] These results have been confirmed and extended. No explanation has, however, been advanced for the fact that introduction of an electron-withdrawing group at the terminal position of the β-dicarbonyl compound results in the enolic signal being displaced upfield though the degree of enolization is increased.[5] This is particularly well illustrated by the replacement of a Me by a trifluoromethyl group and to a lesser extent by replacement of a Ph by a *p*-nitrophenyl group. An electron-withdrawing group adjacent to a CO group causes the CO oxygen to be less electronegative with consequent strengthening of the bond between the other oxygen and the hydrogen-bonded hydrogen, i.e. in a loss of symmetry and a consequent weakening of the hydrogen bond. Consistent with this the enolic signal of 2-thenoylbenzoyl-methane is further downfield than that of 2-furoylbenzoylmethane and similarly that of dibenzoylmethane is further downfield than that of picolinylbenzoylmethane.

In salicylaldehyde derivatives, it is necessary to compare the influence of substituents in the 4 and 5 positions to examine electronic effects without the intervention of steric effects. The results show that the electron-withdrawing nitro group in the 5 position causes strengthening of the hydrogen bond by virtue of weakening the oxygen-hydrogen bond of the OH group *para* to the nitro group thereby strengthening the hydrogen bond. Conversely a similarly situated OMe group weakens the hydrogen bond whereas a 4-OMe group, which by mesomeric electron release increases the electronegativity of the CO oxygen, strengthens the hydrogen bond. From these studies it can be concluded that the hydrogen bond in an intramolecularly hydrogen-bonded chelate ring is strengthened by factors which increase its symmetry or shorten the O—H═O bond.

EXPERIMENTAL

Materials. The compounds were either commercial samples or were prepared by standard procedures. Purification was achieved by distillation or recrystallization until the correct m.p. or b.p. was obtained.

p-Nitrobenzoylpivaloylmethane. p-Nitrobenzoyldipivaloylmethane in 95% AcOH was refluxed for 12 hr. The soln was cooled, neutralized with dil NaOH aq, and extracted several times with ether. The ethereal extracts were washed, dried, and distilled. The oily residue, on treatment with aqueous alcoholic copper acetate, gave *copper p-nitrobenzoylpivaloylmethane*, m.p. 300–302° dec. (Found: C, 55·2; H, 4·7; N, 5·5. $C_{26}H_{28}CuN_2O_8$ requires: C, 55·7; H, 5·0; N, 5·0%). The chelate was dissolved in CH_2Cl_2 and shaken with dil HCl. The organic layer was washed with water, $NaHCO_3$ aq water, dried and evaporated to dryness, giving *p-nitrobenzoylpivaloylmethane* crystallizing from MeOH as colourless plates, m.p. 106–107°. (Found: C, 62·95; H, 6·2. $C_{13}H_{15}NO_4$ requires: C, 62·6; H, 6·1%).

The NMR spectra were recorded at 40 Mc on a Perkin Elmer R10 spectrometer. Chemical shifts were reported on the τ-scale using TMS as an internal reference.

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