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One-bond C–H Coupling Constants of Acetyl Groups as Possible Monitors of CH Hydrogen Bonds and Electric Field Effects*

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C–H coupling constants of acetyl groups of a series of substituted 2-hydroxyacetophenones have been measured. These ^{1}J(C,H) couplings are then intercompared and compared to acetophenone in order to elucidate the cause of the variation. Structures are calculated using *ab* initio DFT methods. A comparison of 2-hydroxyacetophenone and acetophenone shows an increase of ~0.5 Hz. An OR group in the 6-position of 2-hydroxyacetophenone leads to an increase of ^{1}J(C,H) of ~1 Hz and substitution of an acetyl group at 3- or 5-positons likewise leads to an increase, whereas OR groups in 3-, 4- or 5-positions lead to small negative changes compared to the corresponding 2-hydroxyacetophenones. The variations in the ^{1}J(C,H) coupling constants of 6-OR substituted 2-hydroxyacetophenones are discussed as a function of C–H hydrogen bonding and electric field effects. The former is shown not to be at play, whereas the latter is clearly active, but in some instances in an indirect fashion.

Key words: one-bond carbon-hydrogen coupling constants, electric field effects, CH hydrogen bonds, *ortho*-hydroxyacetophenones, DFT calculations

Recently, CH one-bond couplings have been used to discuss both electric field effects [1,2] and hydrogen bonds involving CH bonds [3,4,5,6]. The seminal work of Steiner [7,8] and Desiraju [9] has laid the ground for the CH…X type of interaction and shown how these interactions although weak may have an importance in crystals. The basis for a C–H bond taking part in hydrogen bonding is clearly that the C–H bond must be polarized. This can be caused by substituents such as the case for the CH_α bond of *e.g.* amino acids [10]. The theoretical work of Scheiner *et al.* [11,12,13] has pointed out some other very important conditions such as: i) the C–H bond should point in a directional way towards the lone pair of the acceptor; ii) electron withdrawing substituents must be present; iii) hybridization plays a role.

Some of the compounds investigated show rather strong hydrogen bonds, *e.g.* **11** and especially **13** and **14**. The strength of the hydrogen bonds is stemming not only from electronic effects, but also from steric compression involving the CH_3 group and the OR group at position 6 (relative to an acetyl group at position 1) [14,15,16].

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* Dedicated to Prof. M. Szafran on the occasion of his 70th birthday.

Compounds like *ortho*-hydroxyacetophenones with a hydroxy or a methoxy group in 6-position offer a test ground for some of the above mentioned ideas as they *via* the 2-hydroxy group confine the CH_3CO groups to the ring plane positioning this to be able to interact with the oxygen at position 6. Theoretical calculations of DFT type [17,18,19] may be very helpful in describing the geometries of these compounds.

RESULTS AND DISCUSSION

C–H coupling constants have been measured from reverse gated ^{13}C spectra (non-decoupled spectra with NOE effect). The results are shown in Table 1. The compounds cover a wide range in order to have good reference values. The variations are small, but it should be considered that three CH bonds are involved and they are not perturbed to the same extent all three (see later).

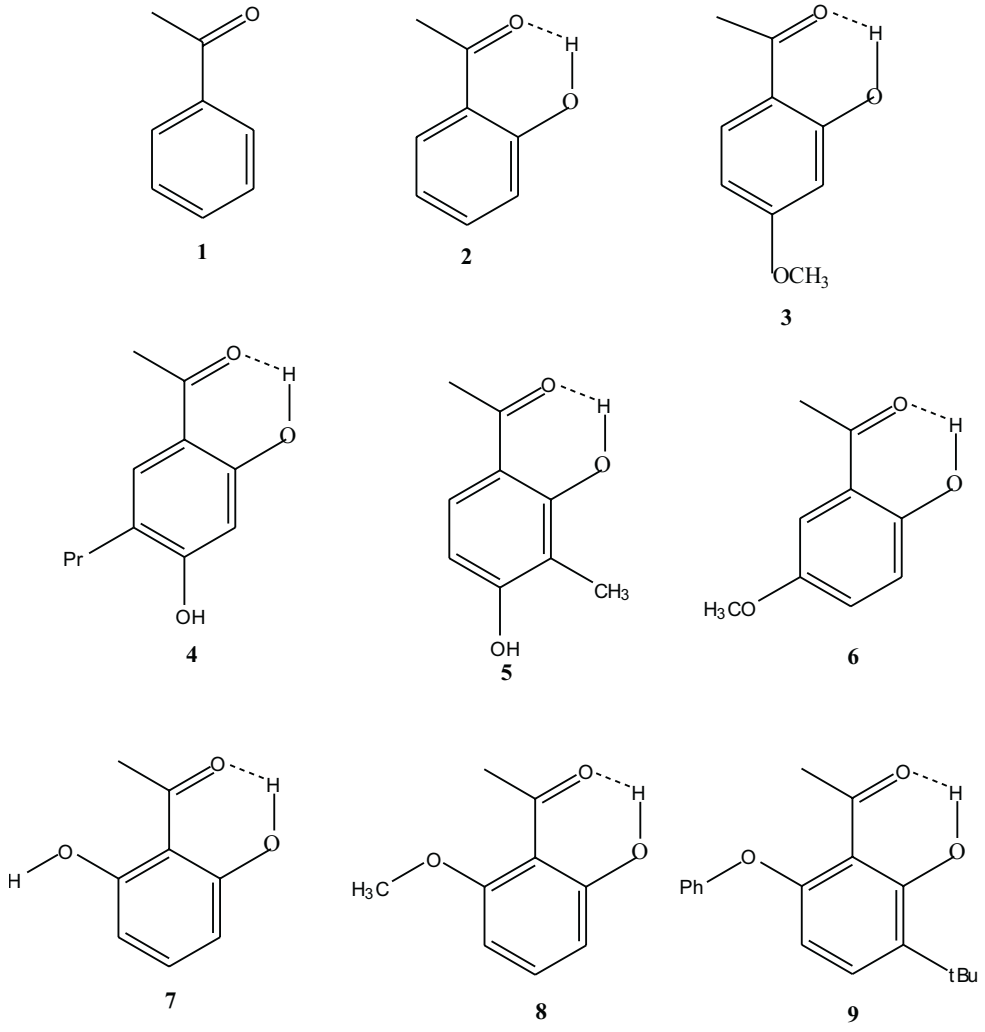
Table 1. C–H bond lengths of methyl groups.

Compound	R C–H (gauche)[1]	R C–H (periplanar)	R C–H (average)	$^1J(C,H)$[3]
1	1.10192	1.09640	1.10000	127.50
2[6]	1.0131	1.09644	1.09968	128.13
3	1.10135	1.09654	1.09974	127.95
4	1.10142	1.09659	1.09981	127.93
5	1.10134	1.09656	1.09975	127.97
6	1.10140	1.09647	1.09975	128.09
7	1.09070	1.09695	1.09878	129.25
8	1.09954	1.09713	1.09875	129.15
9	1.09925	1.09721	1.09855	129.28
10	1.09969	1.09696	1.09878	128.97
11	1.09955	1.09721	1.09877	128.99
12[6]	1.10129	1.9633	1.09964	128.26[5]
13[2,7]	1.09932	1.09712	1.09860	129.36
	1.09962	1.09716	1.09880	129.44
14	1.09945	1.09707	1.09866	129.84
15[2,6]	1.10132	1.10130	1.09969	[4]
	1.09977	1.09699	1.09884	
16	1.10009	1.0988	1.09955	[4]
17	1.09960	1.09687	1.09859	[4]

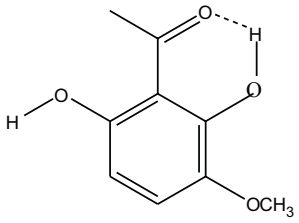
[1]Gauche in relation to carbonyl group. [2]Acetyl group at C-1. [3]All values are better than ±0.04 Hz. [4]Not recorded. [5]Only based on one measurement. [6]Distance data taken from [16]. [7]Distance data taken from [17].

It is obvious from Table 1, that the CH coupling constants of the CH_3CO groups vary. A comparison of the values for compounds **1** and **2** shows that the OH group in 2-position leads to a small increase ~0.5 Hz. It is also seen that that an OR group at the

6-position leads to an increase of approximately 1 Hz (compounds **7–9** *vs*. **2**). A comparison of compounds **7**, **8** and **9** reveals also that an OH group gives a slightly larger increase than an OCH_3 group. However, introduction of an OR group at position 4 leads to small negative change as seen comparing compounds **3**, **4** and **5** with **2**. This comparison also reveals that the effect of alkyl groups is non-significant and that the OH and OR groups in this context are similar. An OR group at position 5 has virtually no effect (compare compounds **6** and **2**). Substitution at position 3 can be judged by comparing compounds **10** and **7** (small negative effect). The introduction of extra acetyl groups can be judged by comparing compounds **12** and **4**. An increase of ~0.3 Hz is found. Finally, the rather large increase seen between compounds **13** and **14** relative to compound **11** can thus be ascribed to the two extra acetyl groups.



Scheme 1. Investigated compounds.



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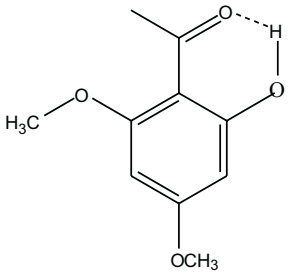

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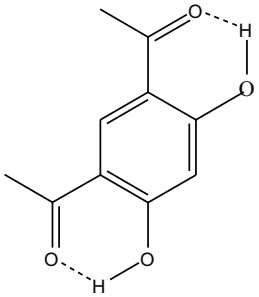

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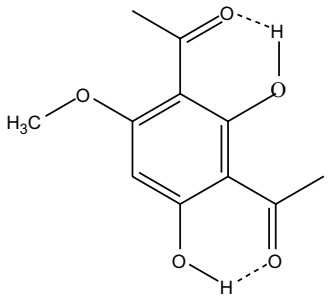

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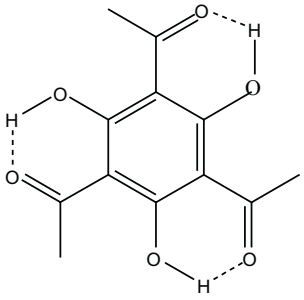

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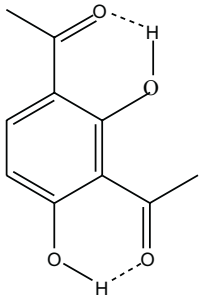

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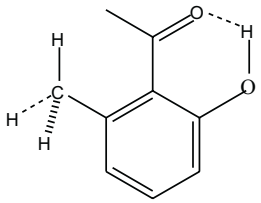

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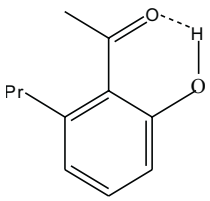

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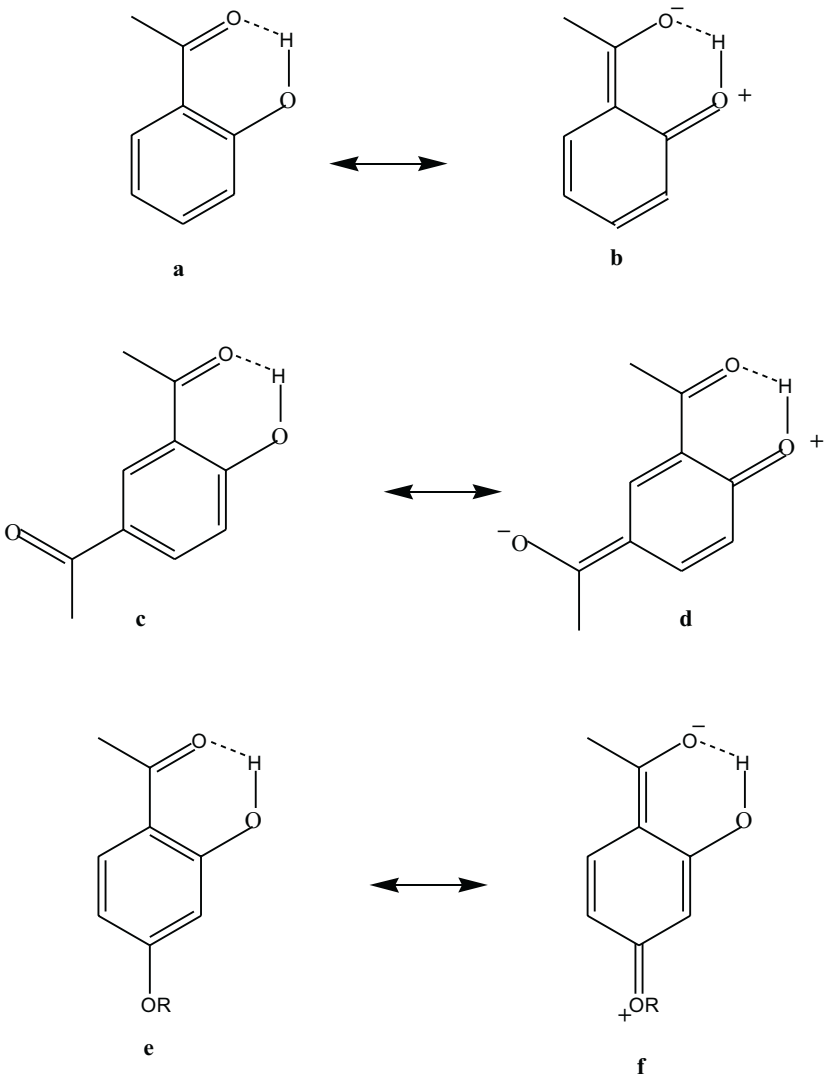
Scheme 1. (continuation).

The variation in $^1J(C,H)$ coupling constants can be ascribed to hybridization effects, electronic effects, electric field effects or to CH hydrogen bonding if a proper acceptor like an OR in 6-position is available in compound with an acetyl group at position 1 and an OH group at position 2 [1,2,3,20]. For acetophenone (**1**) the C–H bond periplanar with the C=O group is shorter than for the $C–H_{gauche}$. This can partly be ascribed a conjugation effect. The formation of a hydrogen bond as found in 2-hydroxyacetophenone (**2**) has very little effect at the C–H periplanar bond length, but decreases the length of the $C–H_{gauche}$ bond. From a resonance point of view (see Scheme 2a,b) the mixing of resonance form b would be expected to decrease the size of the periplanar bond as this is most strongly conjugated. This is not found.



Scheme 2. Resonance structures.

The finding that both OR (R = H or alkyl) at 6-position and OH groups at the 2-position lead to an increase in the one-bond C–H coupling, whereas OR substituents at 4-position lead a decrease eliminates simple electronic effects. The OH group in 2-position takes up a special function as discussed above as it takes part in Resonance assisted hydrogen bonding [21,22] leading to the resonance forms 2a and 2b of Scheme 2. The effects of an acetyl group in the 5-position leads also to a positive charge built up at O-2 (Scheme 2d). This provides a field effect leading to a net polarization of the C–H bonds and to a slight increase of the $^1J(C,H)$ coupling. For the oxygen at position 6, the opposite position and charge as substitution at position 2 leads to a similar polarization of the C–H bonds. The effect of an OR substituent at position 4 is not a direct electric field effect as the OR groups at position 5 shows no effect and the latter is much closer. This conclusion is contrary to that reached for 5-nitrosalicylaldehyde [1], in which it was assumed that the effect was caused by a direct electric field effect origination from the nitro group. For **3** – we find it much more likely that the effect is indirect and in our case mediated *via* the $C–O^-$ of the acetyl group (see Scheme 2f).

Could the effect caused by an OR group at position 6 be caused by a CH…..O hydrogen bond. Probably not, firstly because the criteria set up by Scheiner *et al.* [11,12,13] are not fulfilled (see previously) and secondly because an atom in molecules (AIM) [23,24] analysis showed [15] that no bond path exists between the C–H and the oxygen, but rather a C–H …O bond path for **14**. **14** is by far the most likely to show a C–H….O hydrogen bond as the steric strain ensures a close contact between the C–H and the oxygen so the conclusion is that no CH…O bond exists. This fact puts a question mark after recent work of (1-adamantyl) alkyl ketones [25], in which a CH…O hydrogen bond is suggested between the C=O oxygen and the CγH´s of adamantane. The same is true for intermolecular CH…O hydrogen bonds suggested in 4-ethoxybenzaldehyde [3]. This also calls for caution as the behaviour seen in this paper is very similar to those described in other papers, in which CH….X hydrogen bonds are suggested [4,5,26].

A plot of the average C–H bond length vs. the $^1J(C,H)$ coupling constant is seen to give a decent correlation (Fig. 2). If we look at the individual components (Table 1), the increase of the $CH_{periplanar}$ bond is more than outweighed by the decrease of the CH_{gauche} one. The finding that the CH periplanar and the gauche CH bonds change size in opposite directions is in good agreement with the change being caused by an electric field effect.

Including compounds **16** and **17** in which only steric effects are at play shows that for **16** virtually no effects is seen on the average C–H bond length, whereas this is the case for **17** in which a more direct interaction takes place between the C–H bonds. A plot of the O…O distance *vs*. the average C–H bond length shows some correlation, but also that **16** falls clearly outside again supporting that hydrogen bonding as such has only a small effect, but that steric perturbation, which in principle could also be found in the 6-OR derivatives, may lead to an effect.

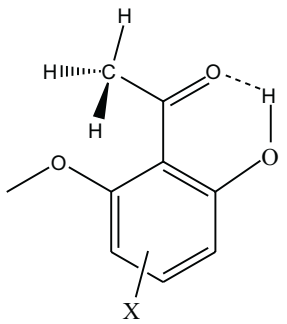


Figure 1. Conformations of methyl group.

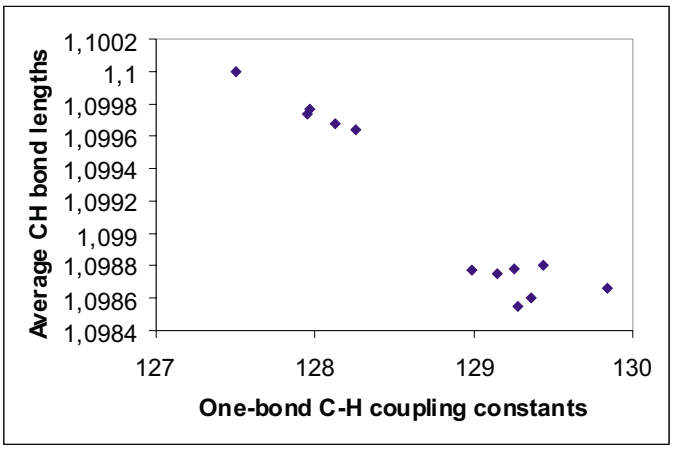


Figure 2. Correlation between the average calculated C–H bond length and the $^{1}J(C,H)$ coupling constants.

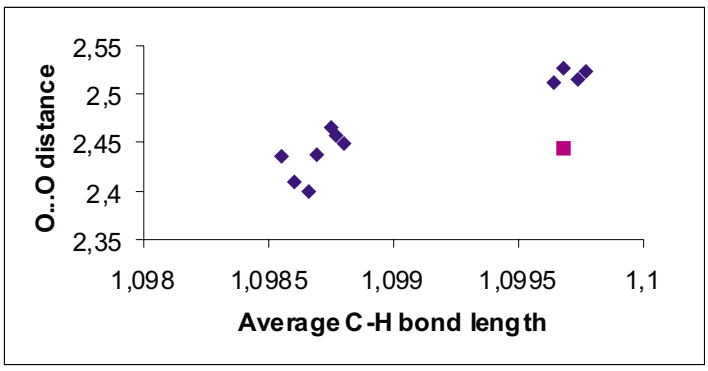


Figure 3. Correlation between the O…O distance and the average calculated C–H bond length. Data for compound **16** marked with square.

EXPERIMENTAL

Compounds: Compounds **1**–**3**, **6**, **7**, **11** and **12** were purchased from Sigma-Aldrich. Those of **4**, **5**, **9**, **10** and **14** from Maybridge Chemical Comp., Tintagel, UK and those of **8** [27]and **14** [14] are described previously.

NMR measurements: The NMR spectra have been recorded on a Varian Mercury 300 NMR spectrometer. The C–H coupling constants are measured using reverse gated decoupling. Spectral parameters: SW 8000 Hz, digital resolution 0.125 Hz, solvent $CDCl_3$, temperature 278 K. The data given are the average of two measurements.

Theoretical calculations: Geometries have been calculated using the Gaussian program [28] and the Density Functional Theory in the BPW 91 [17,18,19] using a mixed basis set 6-31G(d,p). Some of the data have been taken from [14,15]. All calculations show that the CH_3 group is having a non-directional approach *versus* the oxygen at position 6 (see Fig. 1).

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