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SPIN-SPIN COUPLING CONSTANTS FOR METHYLENE GROUPS ADJACENT TO CARBONYL GROUPS

Takeshi Takahashi
Research Laboratories, Takeda Chemical Industries, LTD.
Higashiyodogawa-ku, Osaka, Japan

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GUTOWSKY, Karplus and Grant[1] have found that the spin-spin coupling constant between methylene protons depended on the H-C-H bond angle of the methylene group and also suggested that some other factors might be responsible for the magnitude of the coupling constant. Thereafter, Bannwell, Sheppard and Turner[2] reported that the vicinal and geminal coupling constants in mono-substituted ethylenes decreased linearly with the increasing electronegativity of the substituent. We now wish to report the third factor which exerts a pronounced influence on the magnitudes of the coupling constants for the methylene protons adjacent to carbonyl groups.

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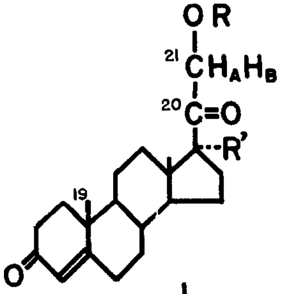
[1] H.S.Gutowsky, M.Karplus and D.M.Grant, J. Chem. Phys. **31**, 1278 (1959).

[2] C.N.Bannwell, N.Sheppard and J.J.Turner, Spectrochim. Acta **16**, 794 (1960).

The impetus to the present study arose from the finding,[3] in the NMR spectra of 19,21-dihydroxypregn-4-ene-3,20-dione and related compounds, that the coupling constants for the 21-methylene protons show



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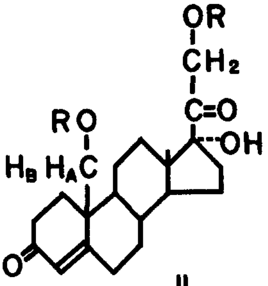

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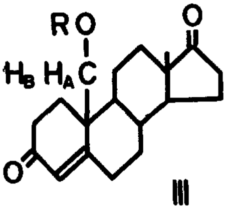

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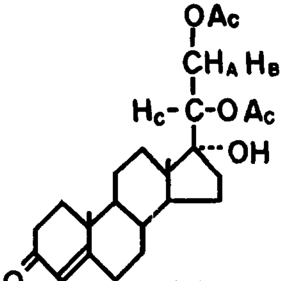

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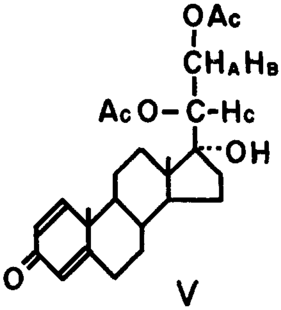

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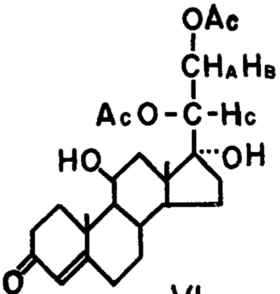

VI

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[3] T.Takahashi, Agr. Biol. Chem. 27, 633 (1963).

exceptionally large absolute values compared with those for the 19-

TABLE I

Spin-spin Coupling Constants (J_{AB}) for the Methylene Protons in 19,21-Dihydroxypregn-4-ene-3,20-dione and Related Compounds

Compound			Position of methylene group	J_{AB} (c.p.s.)[a,b]
	R	R'		
Ia	H	OH	21	-19.5
IIa	H		21	-19.7[c]
Ib	Ac	OH	21	-17.6
IIb	Ac		21	-17.5
Ic	Ac	H	21	-16.9
Id	Ac	OAc	21	-16.8
Ie	Cl	OH	21	-16.7
IIa	H		19	-11.4[c]
IIb	Ac		19	-11.4
IIIa	H		19	-11.0
IIIb	Ac		19	-11.2
IV			21	-12.0[d]
V			21	-12.0[d]
VI			21	-12.0[d]

a: All values were obtained in 10% solution in $CDCl_3$ on a Varian A-60 spectrometer, unless otherwise noticed and are believed to accurate to within 0.2 c.p.s.

b: Recently Buckingham and McLauchlan (Proc. Chem. Soc. 144 (1963) reported that the absolute sign of the ^{13}C-H coupling was positive. On the other hand Anet (J. Am. Chem. Soc. 84, 3767 (1962)) found that the geminal proton-proton coupling constant and $J_{C^{13}-H}$ were of opposite signs. Accordingly the geminal coupling constant (J_{AB}) should be negative, provided the carbon atom concerned is SP^3 hybridized.

c: This value was obtained in pyridine.

d: This value was obtained from analysis of a spectrum due to ABC spin system by the iterative method as outlined by Arata, Shimizu and Fujiwara (J. Chem. Phys. 36, 1951 (1962)) using an NEAC 2203 computer.

methylene protons as shown in Table I. This anomaly observed in the coupling constants for the 21-methylene protons seemed to be ascribable to the presence of the 20-carbonyl groups, and this assumption has received further support by the finding that the coupling constants for the 21-methylene protons in 20α,21-diacetoxypregn-4-en-17α-ol-3-one (IV) and other 20,21-diacetoxysteroids (V and VI) were all -12.0 c.p.s. (Table I).

The fact that the absolute values of the spin-spin coupling constants between methylene protons increase remarkably in the compounds which bear the methylene groups adjacent to the carbonyl groups will be in this communication referred to as 'carbonyl effect' on the coupling constants for the methylene groups. The validity of the carbonyl effect can also be confirmed by other examples including those compounds which are shown in Tables II and III.

It will be impertinent, however, to consider that there may be a relation between the carbonyl effect and the H-C-H bond angle dependence[1] of the coupling constants, because it was known[5] that the H-C-H bond angles in the methylene groups adjacent to carbonyl groups

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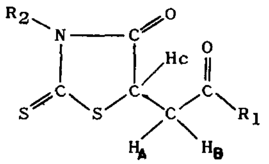
[5] N.Kwak, J.H.Goldstein and J.W.Simmons, J. Chem. Phys. 25, 1203 (1956)

TABLE II

J_{AB} Values for the Methylene Protons in 3-Substituted 5-Carboxymethyl-2-thiothiazolidine-2,4-dione and Related Compounds



VII -16.6 ∼ -18.8 c.p.s.

Compound			J_{AB} ^{a,b} (c.p.s.)
	R_2	R_1	
VIIa	C_2H_5	C_6H_5	-18.8
VIIb	$CH_2C_6H_5$	C_6H_5	-18.4
VIIc	n-C_6H_{13}	C_6H_5	-18.8
VIId	CH_3	OH	-17.6
VIIe	$CH_2C_6H_5$	OH	-17.5^c
VIIf	CH_3	OCH_3	-17.8
VIIg	C_2H_5	OCH_3	-17.4
VIIh	$CH_2C_6H_5$	OCH_3	-17.4
VIIi	$CH_2C_6H_5$	OC_2H_5	-17.6
VIIj	$CH_2C_6H_5$	$OCH_2C_6H_5$	-17.6
VIIk	CH_3	NHC_2H_5	-16.7
VIIl	C_2H_5	NHC_2H_5	-16.2

a: All values were obtained in $CDCl_3$, unless otherwise noticed.

b: See footnotes b and d in Table I.

c: Obtained in pyridine.

were not always smaller than the normal tetrahedral angle. No simple relationship of the carbonyl effect to the electronegativity[2] of the carbonyl group is also evident from the comparison of Ib with IV or V in Table I.

Careful inspection of Tables I and II, however, led us to two possible mechanisms through which some influences may be exerted on the carbonyl effect: the first is that the effect may be weakened by an electron donating group adjacent to the carbonyl group and the second is that the effect may be strengthened by a hydrogen-bond in which the carbonyl group takes part as a proton acceptor. The first mechanism can be seen from Table II. Thus the absolute value of the coupling constant decreases depending on the group adjacent to the carbonyl group in the following order:

$CO\text{-}C_6H_5$ (18.7 c.p.s.) CO-OR (17.6 c.p.s.) CO-NHR (16.5 c.p.s.)

Although this order accords with that of contributions of substituents (X) to the acidity of the pseudoacids, $CH_3COCH_2\text{-}X$[6], it is not reasonable to conclude that the carbonyl effect is due to the stabilization by the carbonyl group, of the ionic structures of the methylene group in the ground state, because[7] the absolute values of the coupling constant of 13.5 c.p.s. has been found for the methylene protons adjacent to

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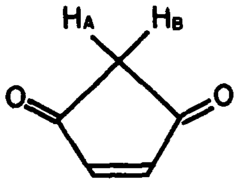
[6] R.G.Pearson and R.L.Dillon, J. Am. Chem. Soc. 75, 2439 (1953).

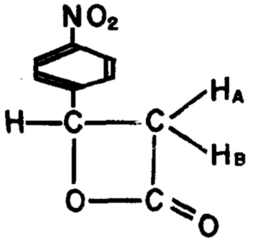
[7] C.C Price and S Oae, "Sulfur Bonding", The Ronald Press Comp., New York, 1962, Chapter 3.

TABLE III

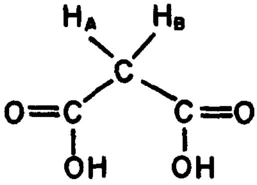
J_{AB} Values for Methylene Protons Adjacent to Carbonyl Groups



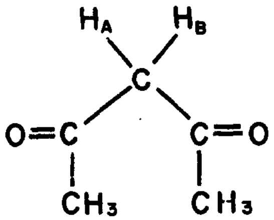
VIII^{a} -21.5 cps



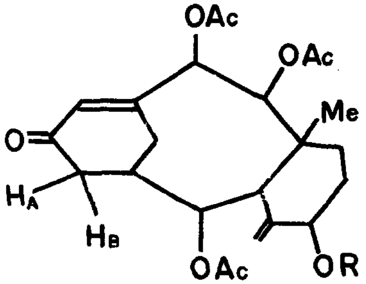
IX^{a}-16.6



X^{b}-15.9 ± 1.0



XI^{c}-17.5 ± 1.5



XII^{d} -20.5

a: Ref. (1). b: Obtained from J_{HD} – value measured in D_2O solution.

c: Obtained in D_2O-pyridine.

d: Reported by K. Nakanishi at the VIIth meeting for symposium on natural organic compounds at Fukuoka, Oct. 1963.

a sulfonyl group[8]. Another factor which has to be taken into account is an interaction of the π-electrons of the carbonyl group with the σ-electrons of the methylene group, thereby resulting in a significant increase of the deviation from perfect paring that occurs in the group. In this case, the interaction may be dependent on the angle formed by the π-electron orbitals of the carbonyl group and the σ-bonds of the methylene group.

The second mechanism can be suggested from the data on Ia, Ib, Ic and Id in Table I. Thus the absolute value of the coupling constant for Ia in which the 20-carbonyl group is known to form a strong hydrogen-bond with the 21-hydroxyl group[9] is 19.7 c.p.s., whereas that for Ib in which the 20-carbonyl group forms a weak hydrogen-bond with the 17α-hydroxyl group is 17.6 c.p.s. and those of Ic and Id where the 20-carbonyl groups can not form hydrogen-bonds are 16.9 c.p.s. and 16.8 c.p.s., respectively. The second mechanism is, however, open to doubt, because a preliminary experiment attempted to confirm the mechanism afforded a contradictory result.

Further aspects of 'carbonyl effect', including quantitative treatise and the influence of substituents are under investigation.

Acknowledgement The author wishes to thank Dr. S. Noguchi and Mr. K. Nagase of these Laboratories for many compounds studied in this work. He is also deeply indebted to the staff of the computer center of Takeda Chem. Ind. for their valuable cooperation.

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[8] Y.Asahi and M.Numata, private communication.

[9] T.Takahashi, to be published.