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CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY OF NATURALLY OCCURRING SUBSTANCES. PROSTAGLANDINS [1,2]

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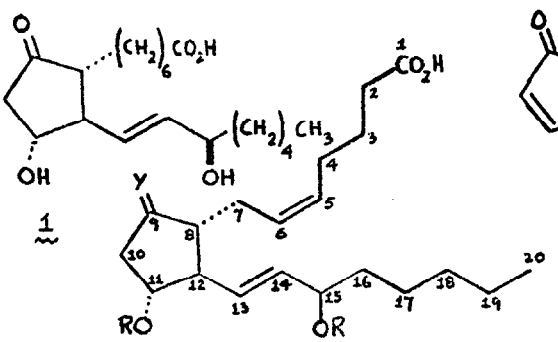
We wish to report the first natural abundance ^{13}C nmr study of the prostaglandins,[3] chemical shift analysis of members of the PGE (1, 2a), PGF (2b-d) and PGA (3) groups and interpretation of the data in terms of the solution behavior of these biologically important substances.

The shifts (Table 1) of carbons 1, 2, 3, 9, 18, 19 and 20 of PGE_1 (1) and PGE_2 (2a) and C(6) of the former are based on models.[4] Those of carbons 4, 5 and 7 of 1 and 4 and 7 of 2 are founded on the calculated effect of a double bond upon its neighbors.[5] Being a α-keto-α'-hydroxycarbinylmethylene, C(10) is the lowest-field methylene in the two substances. Its signal disappears in the spectrum of dienone 3. The C(16) and C(17) shifts are consistent



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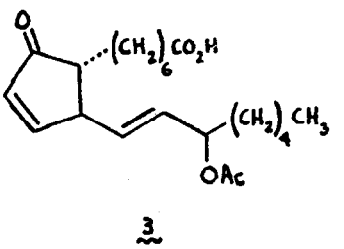

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2a, R = H, Y = O
b, R = H, Y = α-OH, β-H
c, R = H, Y = α-H, β-OH
d, R = Ac, Y = α-OAc, β-H

among all C(15) alcohols and change predictably in their acetates. The PGE methines C(8) and C(12) are undifferentiable, while C(11) and C(15) are distinguished by the shift constancy of the latter in all 15-ols. The structural difference of PGE_1 and PGE_2 identifies the olefinic carbon pairs. Calculation[5] distinguishes C(5) from C(6), whereas differentiation of C(13) from C(14) emanates from analysis of the PGF series (vide infra).

The shifts of the acid sidechain of PGA_1 acetate (3) are recognized from the spectrum of 1, those of the ester sidechain from that of 2d (vide infra) and those of C(9), C(10) and C(11) from that of cyclopentenone.[6] C(8) and C(12) are undifferentiable. Shift assignment of C(1), C(20) and the methylenes of PGF_2 alcohols 2b and 2c stems from spectral comparison with PGE_2 (2a) and expected shift changes at C(10), C(16) and C(17) in $PGF_{2\alpha}$ triacetate (2d).[7] C(8) and C(12) show a greater shift disparity in the PGF than PGE series, C(8) being predictably shielded in the 9-ols. The C(15) shift being established (vide supra), the remaining oxymethine signals of 2b and 2c are identified from spectra of 9-deuterio compounds (from borodeuteride reduction of PGE_2).

Comparison of the cmr data of PGE_1 (1) and PGA_1 acetate (3) in light of the magnitude and direction of the allyl acetate effect[6,8] differentiates C(13) from C(14) in the two compounds as well as in PGE_2 (2a) and $PGF_{2\alpha}$ acetate (2d). Similar comparison of $PGF_{2\alpha}$ (2b) and its triacetate (2d) leads to shift assignment of the olefinic carbon pair in 2b and 2c. The C(5) and C(6) shifts of 2d, as those of 2a (vide supra), are obtained by calculation.[5] While the C(5) and C(6) resonances of the PGF_2 alcohols are at lower field than those of 2a and 2d, they maintain their shift relationship to each other.

The anomalous shifts of the Δ^{13}-linkage in the 11α-alcohols, as calculated from the allyl acetate effect, and of the Δ^{5}-linkage in the 9-alcohols indicate hydrogen bonding between nuclear hydroxyl groups and their double bond neighbors in chloroform solution. The shift deviation is similar for the two Δ^{5}-carbons but dissimilar for the Δ^{13}-carbons, reflecting symmetrical hydrogen bonding in the former situation and unsymmetrical bonding favoring C(14) in the latter case. These interactions, difficulty assessable by physical means other than cmr spectroscopy, are illustrated in the $PGF_{2\beta}$ stereostructure (4).

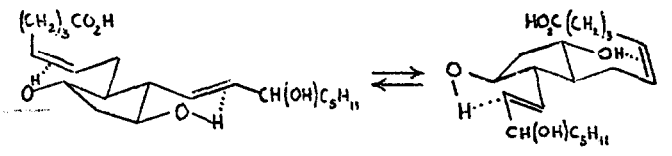

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Table 1. Cmr Chemical Shifts[a]

	1[b]	2a[b]	2b[b]	2c[b]	2d[c]	3c
C(1)	176.7	177.2	176.6	180.3	175.9	173.2
C(2)	33.8	33.4	33.2	33.1	32.9	34.0
C(3)	24.5	24.6	24.5	24.5	24.4	24.5
C(4)	29.0	26.5	26.3	26.3	26.1	28.9
C(5)	28.6	131.0	132.8	133.2	131.1	28.6
C(6)	26.3	126.7	128.9[d]	127.8	127.3	26.5
C(7)	27.4	25.2	25.1	25.1	24.4	28.2
C(8)	54.6[d]	54.6[d]	49.9	51.7	47.0	51.8[d]
C(9)	215.2	215.4	71.8	f	74.0	197.1
C(10)	45.9	46.2	42.6	41.9	38.4	132.9[e]
C(11)	71.6	72.0	77.2	73.7	77.6	164.7
C(12)	54.2[d]	53.6[d]	55.0	55.8	51.5	51.0[dg]
C(13)	131.9	131.7	129.1[d]	130.0	131.9	132.3[e]
C(14)	136.6	136.7	135.0	135.0	129.6	130.0
C(15)	72.9	73.2	72.9	72.9	74.0	74.1
C(16)	36.9	37.0	36.8	36.9	33.9	34.8
C(17)	25.0	25.2	25.1	25.1	24.4	23.8
C(18)	31.5	31.8	31.5	31.6	31.1	31.2
C(19)	22.5	22.7	22.4	22.4	22.1	22.2
C(20)	13.8	14.1	13.9	14.0	13.6	13.9

[a]Spectra taken at 15.08 MHz on a Fourier transform spectrometer ; chemical shifts in parts per million downfield from TMS.

[b]In ca. 10:1 v/v chloroform-methanol solution ; $\delta^{TMS} = \delta^{CHCl_3} + 77.2$ ppm.

[c]In ca. 10:1 v/v deuteriochloroform-methanol solution ; $\delta^{TMS} = \delta^{CDCl_3} + 76.9$ ppm.

[d, e]Values in any vertical column may be reversed. [f]Signal absent, C(9) deuterated.

[g]Center of broad signal in spectrum of highly dilute solution.

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