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CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY OF C/D-CIS POLYOXYPREGNANES. I

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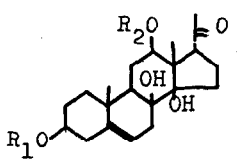
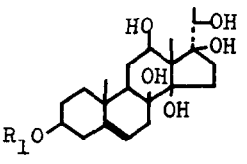
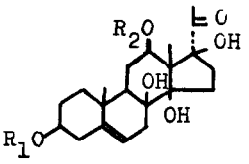
Carbon-13 NMR spectra of about 40 polyoxypregnanes were determined at 25.146 MHz on a Pulsed FT NMR spectrometer (1). C-13 NMR spectra have been far more informative than proton NMR spectra for structural analyses of the C/D-cis polyoxypregnanes,* both because of the enormous sensitivity of C-13 chemical shifts to structural changes and because of large differences in chemical shifts (the order of ca. 200 ppm). All of the skeletal atoms of the polyoxypregnanes were assigned by the techniques such as noise-modulated total proton decoupling (Fig. 1a), off-resonance proton decoupling (Fig. 1b), and substituent influences on chemical shifts in analogous compounds. Carbons in ring A and B are assignable by comparison with the spectra of cynanchogenin (Ib) and its acetate (Ic) with the spectra of cholesterol and cholesteryl acetate (2). Carbons C-1 to C-7 in these compounds have almost equal chemical shifts to their counterparts in the cholesterol series. In addition, C-1, C-2, C-4 and C-5 exhibit similar upfield shifts when the oxygen at C-3 is acetylated, while C-3 and C-5 shift downfield. Carbons C-3, C-5, C-6, C-17, C-20 and C-21 in lineolon (Ia) can be clearly assigned by comparison with the spectrum of pregnenolone (2). Three resonances of Ia (33.37, 20.81 and 60.00 ppm) (3) are significantly changed on introduction of a hydroxyl function at C-17 to form deacylmetaplexigenin (III), and these can be assigned to C-15, C-16 and C-17, respectively. Of the remaining unassigned atoms in ring C, C-11, C-12 and C-13 are assignable by comparison of spectra of Ia and Ib. Further predictable changes occur in C-11, C-12 and C-13 on benzoylation of the C-12 hydroxyl group in Ia. The highest-field methyl resonance (13.83 ppm) of Ia moves 2.5 ppm upfield in III, and this can be assigned to C-18. Four resonances of carbinyl carbons (C-3, C-8, C-12, and C-14) in Ia were classified as quarternary (C-8 and C-14)

and tertiary (C-3 and C-12) carbons by the off-resonance decoupling technique. The C-14 signal was assigned to the resonance shifted downfield by hydroxylation at C-17 (III). The resonances of C-3 and C-12 were also assigned by a downfield shift with acylation (eg. acetylation, benzoylation, etc.) of each carbinol. The assignments for these compounds are listed in the Table and correlated in Figs. 1~3.



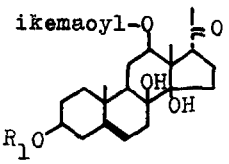




1a: $R_1=R_2=H$
1b: $R_1=H$, R_2=ikemaoyl
1c: R_1=Ac, R_2=ikemaoyl
1d: $R_1=R_2=Bz$

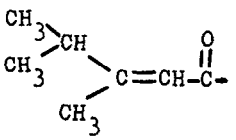
IIa: $R_1=H$
IIb: $R_1=Bz$

III



IV

ikemaoyl:



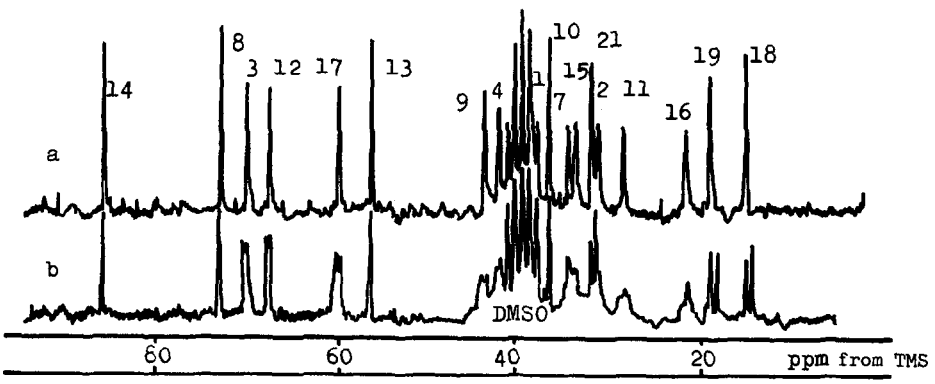


Fig. 1. Carbon-13 NMR spectra of lineolon (Ia) with off-resonance decoupling (b) and noise proton decoupling (a).

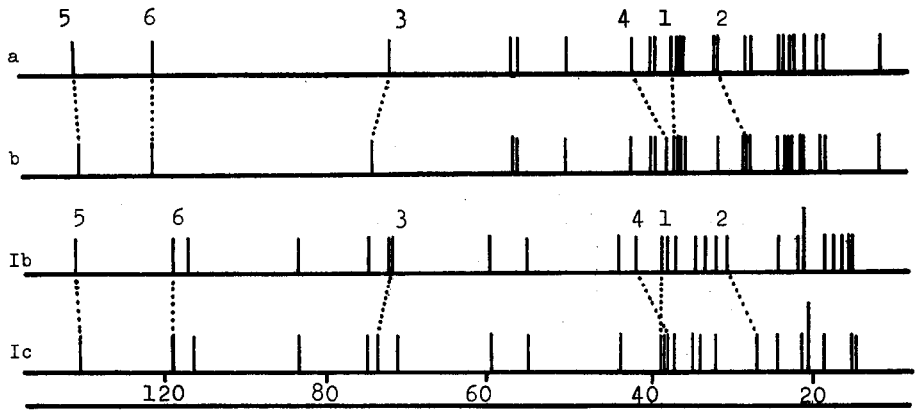


Fig. 2. Correlation of C-13 chemical shifts for (a) cholesterol, (b) cholesterol acetate, (Ib) cynanchogenin, and (Ic) 3-O-acetyl-cynanchogenin.

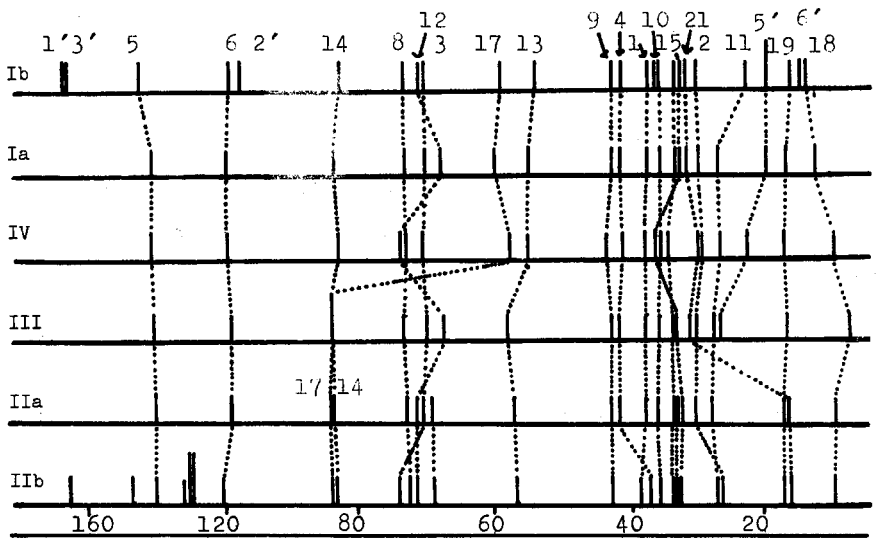


Fig. 3. Correlation of C-13 chemical shifts for Ia, Ib, IV, IIa, IIb, and III.

Table

Carbon-13 Chemical Shifts of Skeletal Atoms

	Ia	Ib	Ic	Id	IIa	IIb	III	IV
C-1	38.22	38.76	38.47	38.04	38.24	38.89	38.34	38.95
C-2	30.82	30.76	26.88	27.06	31.06	27.79	31.06	31.06
C-3	70.26	71.53	73.72	74.38	70.49	72.93	70.37	71.96
C-4	42.05	41.86	37.92	37.92	42.22	37.34	42.22	42.23
C-5	139.06	140.81	140.28	139.06	139.17	137.18	139.17	139.18
C-6	117.88	117.45	118.55	119.98	118.18	120.13	118.06	118.85
C-7	34.22	34.64	34.52	34.52	34.21	34.22	34.09	37.07
C-8	73.29	74.56	74.75	74.38	73.04	74.20	73.16	74.87
C-9	43.68	44.06	43.99	43.87	43.19	43.02	43.55	44.41
C-10	36.28	37.06	37.13	37.07	36.27	36.22	36.27	37.07
C-11	27.91	24.38	24.33	24.27	28.02	26.94	28.02	24.38
C-12	67.77	71.22	70.99	72.62	71.71	71.65	67.70	73.90
C-13	56.36	55.14	55.09	55.45	57.27	57.15	58.72	54.06
C-14	86.33	86.88	86.76	86.82	87.60	87.55	88.45	86.33
C-15	33.37	33.36	33.43	33.61	33.36	33.49	33.36	35.55
C-16	20.81	20.93	21.29	21.48	33.36	33.25	27.29	24.69
C-17	60.00	59.94	59.94	59.76	88.09	87.85	91.12	57.64
C-18	13.83	15.10	14.99	15.12	10.43	10.31	8.73	12.01
C-19	17.84	18.62	18.69	18.38	17.95	17.66	17.95	18.20
C-20	209.32	209.73	209.32	209.98	69.52	69.35	208.09	217.51
C-21	31.43	31.91	31.91	31.97	17.22	17.05	31.54	32.94

REFERENCES

1 All of the ^{13}C-FT-NMR spectra were obtained at 25.1 MHz using a JEOL PS-100/PFT-100 spectrometer system, and facilitated by the complete proton noise decoupling technique. The measurement conditions are as follows: rf pulse width, 10μsec ($\pi/4$ pulse); data points, time domain 8192 points, frequency domain 4096 points.

2 H.J. Reich, M. Jautelate, M.T. Messe, F.J. Weigert, and J.D. Roberts, J. Amer. Chem. Soc. 17, 7445 (1969).

3 The data recorded are in ppm downfield from the carbon resonance of internal tetramethylsilane and thought to be accurate to ± 0.05 ppm.

4 Ia, IIa, IIb, and IV were measured in Me_2SO-d_6. Ib, Ic, Id, and IV were measured in $CDCl_3$.

* C-13 NMR analyses for other steroids were refered to the following article: K. Tori, H. Ishii, Z.W. Wolkowski, C. Chachaty, M. Sangare, F. Piriou and G. Lukacs, Tetrahedron Letters, 1077 (1973).