

Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring
Substances ^{1,2} Lanosterol and Dihydrolanosterol.

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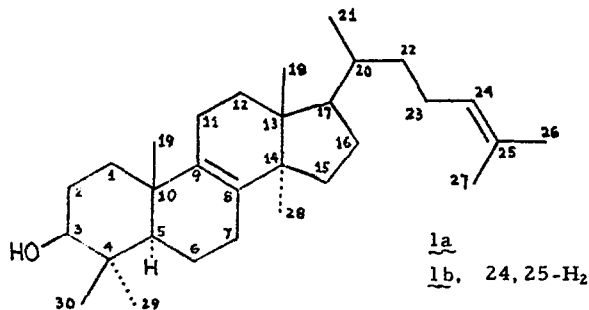
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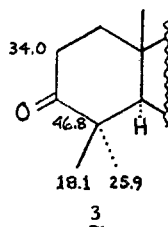
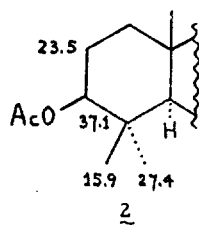
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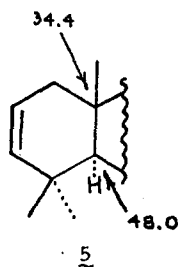
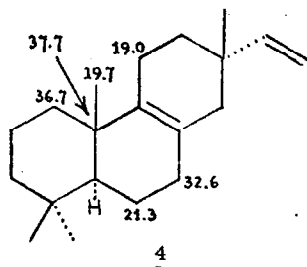
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In continuation of our ¹³C nmr study of terpenic natural products^{1,2} the natural abundance ¹³C nmr spectra of lanosterol (1a), dihydrolanosterol (1b) and related substances were recorded. Noise decoupled, single frequency off-resonance decoupled⁴ and, whenever needed, noise off-resonance decoupled spectra⁵ yielded chemical shift data, differentiated carbon types and in the end led to the assignments in the Table. This constitutes the first cmr analysis of triterpenes.



Comparison of the δ values of 1a and 1b with those of 2,6-dimethyloctane⁴ and 2-methyl-2-heptene⁶, respectively, permits assignment of the C-17 sidechain shifts. Chemical shift theory⁷ indicates the farthest downfield signals of non-protonated carbons to be olefinic C-8 and C-9 and the downfield methine to be C-3, thus leaving the remaining methine signals to C-5 and C-17. Conversion of dihydrolanosterol to its acetate (2) and ketone (3) and comparison of the ring A shifts of these derivatives with those of 1a and 1b yield the values of C-2, C-4 and the C-4 methyl groups.^{4,8,9} Finally, comparison of the spectra of 1a and 1b with the cmr spectrum of $\Delta^{8(9)}$ -sandaracopimaradiene (4)¹⁰ reveals the values of the C-10 angular methyl group, the C-10 quaternary carbon center and the C-1, C-6 and C-11 methylene functions. Since the C/D trans fusion in the triterpenes changes their ring C conformation from that of 4¹⁰ and imposes non-bonded interactions between the C-11 hydrogens and the α hydrogen and the C-10 and C-13 angular methyl groups, the shifts of all carbons affected by the interactions and their neighbors, i. e. C-9 and C-10, are upfield in 1a and 1b. Another striking conformational effect first noted among piperideines¹⁰ and in the diterpene field¹¹, —the upfield shift of homoallyl carbons within a six-membered ring into which a double bond has been introduced, —is apparent in the Δ^2 compound 5 from dihydrolanosterol (1b). The C-5 and C-10 shifts, of 5 are ca. 2 ppm upfield those of 1b.





Consideration of the cmr spectrum of cholestanol⁴ and the expected consequence of the introduction of a C-14 angular methyl group on the basis of chemical shift theory⁷ leads to the shift assignment of C-13 and C-14 and their methyl groups in 1a and 1b. The cmr data of 7-ketodihydrolanosteryl acetate are in consonance with this assignment. The 7-keto group leaves C-13 and its methyl group nearly **unchanged** (44.2 and 15.3 ppm, respectively), while modifying the δ values of C-14 (47.1 ppm) and its methyl group (24.3 ppm). An evaluation of the effect of the 14 α methyl function on C-12 and C-16, i. e. more shielding than in their cholestanic environment, yields the two carbon shifts. Finally, the C-14 methyl group is expected to shield C-7 in 1a and 1b (in contrast to C-7 in 4), thereby differentiating the remaining methylenes at C-7 and C-15.

Table. Cmr Chemical Shifts

C	<u>1a</u>	<u>1b</u>	C	<u>1a</u>	<u>1b</u>	C	<u>1a</u>	<u>1b</u>
1	35.0	35.1	11	17.6	17.6	21	18.4	18.5
2	27.4	27.4	12	25.8	25.8	22	35.1	35.8
3	78.3	78.3	13	43.7	43.8	23	24.2	23.6
4	38.1	38.2	14	49.1	49.1	24	124.7	38.9
5	49.8	49.8	15	30.2	30.3	25	130.2	27.4
6	20.3	20.5	16	30.2	30.3	26	24.9	22.3
7	27.4	27.4	17	49.8	49.8	27	16.9	22.0
8	133.9	133.9	18	15.3	15.2	28	23.5	23.6
9	133.9	133.9	19	18.0	18.1	29	27.4	27.4
10	36.3	36.5	20	35.1	35.8	30	14.8	15.0

References

1. V. For previous paper see G. Lukacs, X. Lusinchi, E. W. Hagaman, B. L. Buckwalter, F. M. Schell, and E. Wenkert, C. R. Acad. Sci., Paris, C, 274, 1458 (1972).
2. XII. For previous paper see J. Polonsky, Z. Baskevitch, N. Cagnoli-Bellavita, P. Ceccherelli, B. L. Buckwalter, and E. Wenkert, J. Amer. Chem. Soc., 94, 4369 (1972).
3. The spectra of deuteriochloroform solutions were taken on Fourier Transform spectrometers at 15.08, 22.63, and 25.15 MHz. TMS was used as internal reference for all spectra except the one of lanosterol and the signals recorded in ppm downfield of TMS. The δ values of lanosterol are relative to the solvent ($\delta_{\text{TMS}} = \delta_{\text{CDCl}_3} + 77.3$ ppm).
4. H. J. Reich, M. Jautelat, M. T. Messe, F. J. Weigert, and J. D. Roberts, J. Amer. Chem. Soc., 91, 7445 (1969).
5. E. Wenkert, A. O. Clouse, D. W. Cochran, and D. Doddrell, J. Amer. Chem. Soc., 91, 6879 (1969).
6. D. E. Dorman, M. Jautelat, and J. D. Roberts, J. Org. Chem., 36, 2757 (1971); E. Wenkert and E. W. Hagaman, unpublished observations.
7. J. B. Stothers, Quart. Rev., Chem. Soc., 19, 144 (1965); E. F. Mooney and P. H. Winson, Annu. Rev. Nucl. Resonance Spectrosc., 2, 153 (1969).
8. J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Reich, J. Amer. Chem. Soc., 92, 1338 (1970).
9. F. J. Weigert and J. D. Roberts, J. Amer. Chem. Soc., 92, 1347 (1970).
10. D. W. Cochran, Ph.D. dissertation, Indiana University, 1971.
11. E. Wenkert and B. L. Buckwalter, J. Amer. Chem. Soc., 94, 4367 (1972).