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# CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTRAL ANALYSIS OF CYCLOARTANOL AND RELATED COMPOUNDS [1]

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During the past two decades a vast amount of research has been directed toward the structure elucidation of triterpenic substances. A prerequisite for the use of $^{13}C$ nmr in this field is the unambiguous assignment of the carbon signals of the parent compounds. Upon completion of the $^{13}C$ nmr spectral analysis of lanosterol [2] a similar study on cycloartanol was undertaken. We report here the assignment of the carbon signals of cycloartanol 1, cycloeucalenol 4 and some of their derivatives, pollinastanol acetate 7 and cyclolaudanol 8. The basic differences in structure between the compounds studied and that of 5α-cholestane, whose $^{13}C$ nmr spectrum has already been interpreted [3] are the B/C-cis ring junction, the cyclopropane unit, the ring-C boat conformation [4] and the extra methyl groups.

The $^{13}C$ nmr spectra of cycloartanol 1 and its derivatives 2 and 3 as well as pollinastanol acetate 7 show eight carbons whose resonances are also present in the spectrum of 5α-cholestane [3] which has the same sidechain. Some of these signals are absent in the $^{13}C$ nmr spectra of cycloeucalenol 4 and cyclolaudanol 8 whose sidechain carbons are assigned by calculation in terms of the Grant rules [5] and these attributions are corroborated by SFORD experiments.

Consideration of chemical shift rules [6] and of the $^{13}C$ nmr spectrum of lanosterol [2] leads to the shift assignments of the quaternary carbons C-13 and C-14 while the location of the C-4 signals is based on acetylation [3] and methyl substitution effects [7]. The remaining two quaternary carbon signals at much higher field (26.0 and 20.0 ppm in the spectrum of 1 and 29.5 and 23.5 ppm in the spectrum of 4) represent the cyclopropane carbons C-10 and C-9 respectively. Their differentiation was acheived with the aid of chemical shift reagent studies on the spectrum of 8 [++].

Among the four methine resonances of the tetracyclic skeleton of 1 the lowest field one is assigned to the oxymethine carbon while the signal at 52.2 ppm is attributed to C-17 on comparison with the $^{13}C$ nmr spectrum of lanosterol [2]. The two other methine resonances due to C-5 and C-8 are differentiated by chemical shift reagent studies and methyl substitution effects [7].

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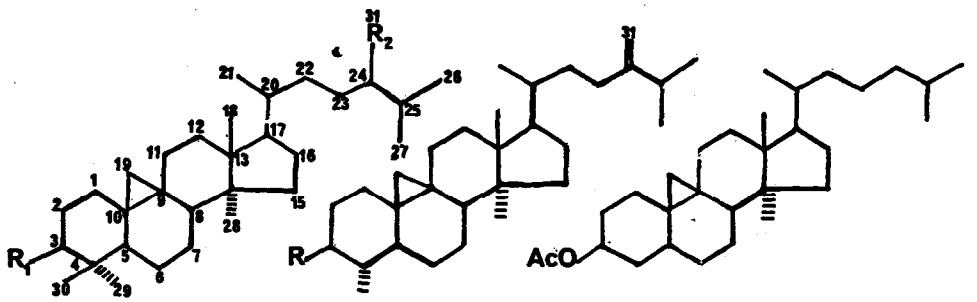
[++] In the $^{13}C$ nmr spectrum of cycloeucalenone-2,2,4-$d_3$ 6-$d_3$ neither high field quaternary carbon signal shows any significant line broadening. Such a phenomenon would be expected for C-10 as a result of $^3J$ type couplings with the three deuterium atoms.



1 $R_1$=OH ; $R_2$=H  4 R= H  7

2 $R_1$= OAc ; $R_2$=H  5 R=OAc

3 $R_1$= =O; $R_2$=H  6 R= =O

8 $R_1$=OH; $R_2$=$CH_3$

Among the methylene resonances of 1 representing the carbons of its skeleton, the two lowest field ones at 35.5 and 32.8 ppm are assigned to the neopentylic sites C-12 and C-15 respectively.Their differentiation is based on an investigation of the spectra of cycloartanol related 11-keto alkaloids [8].Two other methylene signals exhibit practically no shift variation.The lower field signal among them at 28.0 ppm in the spectrum of 1 is assigned to C-7 and the other at 26.5 ppm to C-16.These assignments are in good agreement with the $^{13}C$ nmr spectrum of lanosterol whose corrected C-16 shift is 25.8 ppm [2],[3].Based on the shift contrast of the various spectra studied, three further methylene resonances due to C-2, C-1 and C-6 can be easily assigned.The expected consequence of the replacement of C-30 by a hydrogen atom is to deshield the C-2 and C-6 signals by elimination of a steric $\gamma$-effect. In pollinastanol acetate 7 C-6 resonates further downfield as a result of the absence of any peri-interaction affecting the hydrogens attached to this site.The highest field methylene signal in the spectrum of 1 represents C-6.

Grover and Stothers have shown [9] that in direct contrast to the well established trends for $\gamma$-effects,steric crowding of $\delta$ nuclei causes marked downfield shifts.This deshielding $\delta$-effect (syn-axial interaction) ranging up to 3.4 ppm in several steroids [9] has been found to offer valuable help in stereochemical assignments.A recent study of the $^{13}C$ nmr spectra of steroidal epoxides [10] and episul-

TABLE 1.

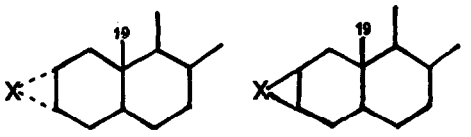
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| C-1 | 31.9 | 31.5 | 33.3 | 30.7 | 30.4[a] | 32.8 | 31.4[a] | 31.9 |
| C-2 | 30.3 | 26.7 | 37.2 | 34.8 | 30.9[a] | 40.8 | 30.4[a] | 30.3 |
| C-3 | 78.5 | 80.3 | 215.1 | 76.3 | 78.5 | 212.2 | 73.7 | 78.5 |
| C-4 | 40.3 | 39.4 | 50.0 | 44.5 | 41.4 | 49.8 | 38.5 | 40.4 |
| C-5 | 47.0 | 47.0 | 48.3 | 43.2 | 43.3 | 45.9 | 37.1[b] | 47.0 |
| C-6 | 21.0 | 20.8 | 21.5 | 24.6 | 24.6 | 25.1 | 28.1[b] | 21.1 |
| C-7 | 28.0 | 28.0 | 27.9 | 28.0 | 28.0 | 28.0 | 27.8[b] | 28.0 |
| C-8 | 47.8 | 47.6 | 47.7 | 46.7 | 46.7 | 46.9 | 46.1 | 47.8 |
| C-9 | 20.0 | 20.1 | 21.0 | 23.5 | 23.6 | 24.9 | 23.5 | 20.0 |
| C-10 | 26.0 | 26.0 | 26.0 | 29.5 | 29.3 | 29.3 | 29.8[c] | 26.0 |
| C-11 | 26.0 | 25.8 | 26.0 | 25.1 | 24.9 | 25.8 | 24.6 | 26.0 |
| C-12 | 35.5 | 35.4 | 35.5 | 35.2 | 35.3 | 35.3 | 35.2 | 35.5 |
| C-13 | 45.1 | 45.1 | 45.2 | 45.2 | 45.2 | 45.2 | 45.3 | 45.1 |
| C-14 | 48.7 | 48.6 | 48.5 | 48.7 | 48.7 | 48.7 | 49.0 | 48.7 |
| C-15 | 32.8 | 32.8 | 32.8 | 32.8 | 32.8 | 32.8 | 32.9 | 32.9 |
| C-16 | 26.5 | 26.5 | 26.7 | 26.9 | 26.9 | 26.9 | 27.1 | 26.5 |
| C-17 | 52.2[a] | 52.2[a] | 52.2[a] | 52.0[a] | 52.0[b] | 52.1[a] | 52.3[d] | 52.1[a] |
| C-18 | 17.9[a] | 17.9[a] | 18.1[a] | 17.7[a] | 17.7[b] | 17.9[a] | 17.5[c] | 17.9[a] |
| C-19 | 29.8 | 29.6 | 29.5 | 26.9 | 26.9 | 27.1 | 25.7 | 29.6 |
| C-20 | 36.0[a] | 36.0[a] | 36.0[a] | 36.0[a] | 36.0[b] | 36.0[a] | 36.2[b] | 36.5[a] |
| C-21 | 18.3[a] | 18.3[a] | 18.1[a] | 18.3[a] | 18.3[b] | 18.3[a] | 18.5[b] | 18.4[a] |
| C-22 | 36.4 | 36.4 | 36.4 | 35.0 | 35.0 | 35.0 | 36.5 | 33.9 |
| C-23 | 24.0 | 24.1 | 24.1 | 31.3 | 31.3 | 31.3 | 24.2 | 31.4 |
| C-24 | 39.4 | 39.4 | 39.4 | 156.2 | 156.1 | 156.1 | 39.6 | 39.0 |
| C-25 | 28.0 | 28.0 | 27.9 | 33.7 | 33.7 | 33.7 | 28.1 | 30.9 |
| C-26 | 22.5 | 22.5 | 22.5 | 21.8 | 21.9 | 21.8 | 22.9 | 20.5[b] |
| C-27 | 22.7[a] | 22.7[a] | 22.7[a] | 21.8[a] | 21.9[b] | 21.8[a] | 22.9[b] | 17.6[a] |
| C-28 | 19.3[a] | 19.2[a] | 19.3[a] | 19.1[a] | 19.1[b] | 19.1[a] | 19.0[b] | 19.3[a] |
| C-29 | 25.4 | 25.3 | 26.0 | 14.4 | 14.4 | 10.7 | - | 25.4 |
| C-30 | 14.0 | 15.1 | 20.6 | - | - | - | - | 14.0[b] |
| C-31 | - | - | - | 105.6 | 105.6 | 105.6 | - | 15.5 |
| OCOCH$_3$ | - | 170.0 | - | - | 170.1 | - | 170.0 | - |
| OCOCH$_3$ | - | 21.2 | - | - | 21.2 | - | 21.5 | - |

$^{13}$C nmr chemical shifts for cycloartanol 1 and related compounds. Spectra were recorded in $CDCl_3$ solution on a Bruker HX 90E F.T. spectrometer at 22.63 MHz. Chemical shifts are given in ppm with respect to TMS used as an internal standard. [a.b.c.d.] assignments may be reversed although those given here are preferred.

fides [1] illustrated this effect between an axial methyl group and a cis-oriented three membered ring. In 9a the oxirane ring has a trans- while in 10a a cis-configuration with respect to C-19 which resonates at 12.9 ppm in the former and at 14.0 ppm in the latter compound. The C-19 signal of the corresponding epimeric thiiranes 9b and 10b indicated a 2.3 ppm lower field shift for the cis- compared to the trans-compound.

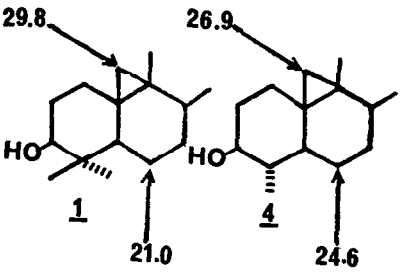
While on going from 1 to 4 , C-11 is not expected to undergo any significant change, the 2.9 ppm higher field shift of C-19 in 4 can be explained in view of the loss of the $\delta$ interaction between C-30 and C-19.Thus the remaining methylene resonances at 26.0 ppm and 29.8 ppm in 1 are assigned to C-11 and C-19 respectively.

The lowest and highest field methyl signals of 1 are assigned to the equatorial and axial methyls C-29 and C-30 respectively by comparison with the spectrum of lanosterol.The other methyl resonances due to C-18, C-21 and C-28 cannot be differentiated.




9a X=O; C-19 12.9ppm 10a X=O;C-19 14.0ppm

9b X=S; C-19 12.6ppm 10b X=S; C-19 14.9ppm

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