Tetrahedron Vol 33, pp 2997 to 2998 Pergamon Press 1977 Printed in Great Britain

THE ^{13}C-NMR SPECTRUM AND STEREOCHEMISTRY OF HETERONEMIN

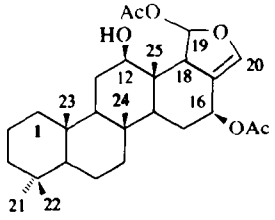
Y. KASHMAN* and A. RUDI
Department of Chemistry, Tel-Aviv University, Tel-Aviv, Israel

(*Received in UK 22 March 1977; Accepted for publication 14 June 1977*)

Abstract—The ^{13}C-NMR spectrum of heteronemin (**1**), a new sesterterpene from marine origin is reported. Assignment of most of the signals was accomplished by a combination of off-resonance decoupling, PRFT measurement, comparison with suitable known model compounds and LIS measurements. An all *trand*-anti-*trans* configuration is suggested from **1** according to the ^{13}C-NMR data.

Several tetracarbocyclic sesterterpenes have been found in sponges of the genus *Cacospongia* and in the taxonomically related *Spongia*.[1]

This report describes ^{13}C-NMR studies aimed at the elucidation of the stereochemistry of a new sesterterpene (**1**) from *Heteronema Erecta* a sponge collected at the Gulf of Eilat (the Red Sea). This new compound was assumed, on the basis of its spectral properties, to be identical to heteronemin,† a tetracarbocyclic sesterterpene of the scalarin type which has been recently reported.[2]



1

The ^{13}C-NMR spectrum, taken in $CDCl_3$ solution, exhibited 27 resonance lines from the 29 C-atoms (25 skeleton and 4 of the two acetate groups). The multiplicity of the different resonance lines (Table 1) was established by the PRFT technique (to determine quaternary C-atoms) and by several off-resonance decoupling experiments. The signals were assigned to the various C-atoms by comparison with model compounds, taking into consideration substituent effects, the known chemical shifts of the functional groups present, and by LIS measurements. The signals that were not shifted‡ upon addition of $Eu(fod)_3$ to a $CDCl_3$ solution of **1** could be related to C atoms C_1–C_7, C_{10} and to the three Me groups (C_{21}, C_{22} and C_{23}). These C atoms are relatively far away from the C_{12}-OH group, expected to be the main complexation site; the signals could hence be essentially uninfluenced by $Eu(fod)_3$ addition. The 11 unchanged resonance lines (asigned to C_1–C_7, C_{10} and C_{21}–C_{23}) were found to be in good agreement with the corresponding A/B ring C atom signals of α and β-amyrin,[3] labdane diterperoids,[4] and podocarpane derivatives[5] [after correction for the expected substituent effect of an additional C_8-Me group[6] (Table 1)]. Such agreement suggest a *trans* A/B ring junction in **1** since it is well known that the ^{13}C δ-values of the methyldecalin moiety are a good probe for the ring fusion mode.[7] The signals belonging to carbons C_{12}, C_{16}, C_{17}, C_{19} and C_{20} were determined according to known chemical shifts and substituent effects.[6a] The differentiation between the lines, with the same multiplicity (C_8 and C_{13}(s), C_9, C_{14} and C_{18}(d), C_{11} and C_{15}(t) and C_{24} and C_{25}(q)) was achieved by applying substituent effects and LIS measurements (Table 1).

The chemical shifts of C_8 and C_9 (39.9 and 58.6 ppm respectively) are very similar to those of C_{10}, C_5 (37.3 and 56.4 ppm) and C_{13}, C_{14} (38.0 and 54.6 ppm respectively) indicating a *trans*-anti-*trans* configuration, (see below). More specifically, the chemical shifts of C_8 and C_9, the B/C ring junction C atoms, agreee with the chemical shifts expected for the models described above as well as for those obtained from other steroid models—taking into consideration the additional influence of the 24-Me group (α-effect on C_8 and β-effect on C_9).[6] A B/C *cis* fusion could influence strongly the C_{24}-Me group which may cause an over 10 ppm down field shift in comparison with the B/C *trans* isomer. In a similar fashion carbons C_1, C_5, C_{12} and C_{14} could be strongly influenced by intramolecular γ-effects.§

Examinations of rings C and D C-atom signals, pointed also at *trans*-anti-*trans* fusion (*vide supra*). Each of the three alternative ring junctions is excluded by at least part of the signals; i.e. in the chair–chair A/B *trans*-anti-C/D-*cis* isomer the C_{24}-Me should be strongly influenced by two δ-effects[8] of C_{16} and C_{18} and could thus be 4-7 ppm paramagnetically shifted. (The second, less probable twisted boat–boat conformer of this *cis* isomer does not fit the δ-values nor the LIS values measured for C_{19}.) Similarly in a B/C *trans*-syn-C/D *cis* isomer it would be difficult to explain the high field resonance line of C_{25}, appearing at δ 8.8 ppm, as well as the chemical shifts of the C_7, C_9 and C_{24} atoms.

Accordingly the δ-values and LIS measurements suggest that an all *trans*-anti-*trans* configuration seems to be the most fitting stereochemistry for **1**.

The ^{1}H-NMR of **1**, recorded on a 270 MHz instrument, was taken in d_6-acetone which gave a better resolution than $CDCl_3$ (Experimental).

†Unfortunately we could not yet get a sample for unequivocal comparison.

‡Shifts of 0–0.4 ppm for $Eu(fod)_3$/substrate ratio of 0.25 equ. are in the same order of magnitude as the shift of $CDCl_3$, relative to internal TMS and are thus considered as uninfluenced by the shift reagent.

§A good example for the variation with *cis*/*trans* configuration is the spectral data of cholestane vs coprostane.[7b]

Table 1. ^{13}C-NMR spectrum of **1**

Carbon No.	Chemical shift* & multiplicity	Δδ**	Model compound*** δ-value
1	41.7 t	0.4[a]	39.2
2	18.2 t	0.3[b]	18.7
3	42.6 t	0.4[a]	42.2
4	33.1 s	0.2	33.3
5	56.4 d	0.2	56.5
6	18.6 t	0 [b]	19.9
7	41.9 t	0.2[a]	43.0
8	39.9 s	0 [e]	
9	58.6 d	0.7[f]	58.3
10	37.3 s	0.4[e]	36.8
11	27.9 t	1.8[g]	
12	80.3 d	4.3	
13	38.0 s	0.7[e]	
14	54.6 d	1.1[f]	
15	27.2 t	1.3[g]	
16	69.1 d	0.7	
17	113.9 s	1.4	
18	64.0 d	2.2	
19	101.2 d	3.3	
20	154.9 d	1.4	
21	21.2 q	0 [c]	21.5
22	33.1 q	0.2	33.4
23	26.3 q	0.2[d]	15.7
24	17.3 q	0.4[d]	
25	8.8 q	1.1	
OAc	21.2 q	1.1	
OAc	20.9 q	0.4[c]	

a,b,c,d - Assignments may be reversed. e,f,g - Assignments based on LIS-values.

*δ-values relative to TMS. **Δδ(ppm) for Eu(fod)$_3$/Substrate ratio of 0.25.

***According to α and β-amyrin, manoyl oxide, and cholestane taking into account substituent effects.

The H-12 dd (J = 10.5 and 4.3 Hz) and the H-16 ddt (J = 10.2, 6 and ~ 1.7 Hz) coupling constants agree with the suggested $C_{12}$and C_{16} equatorial hydroxy and acetoxy configurations, suggested by Wells according to $\Delta W_{1/2}$ values (100 MHz spectrum).[2]

The C_{19} stereochemistry seems to us ambiguous since a J_{18-19} larger than 2 Hz would be expected for both possible configurations.

EXPERIMENTAL

Instrumentation: IR: Perkin-Elmer 257. UV: Cary 14. ^{1}H-NMR: Varian 270 MHz. Mass spectrum: Varian MAT CH-7.

Isolation of heteronemin(**1**). Freeze-dried *Heteronema Erecta* collected at the Gulf of Eilat (100 g) was extracted during a period of 24 hr with light petroleum in a soxhlet. the concentrated extract gave after cooling a crystalline ppt of **1**. (*ca.* 1 g); m.p. 182° (uncorrected), ν_{max}^{KBr} 3500, 3180, 2930, 1735, 1385, 1365, 1240, 1100, 1085, 1060, 1025, 936 cm^{-1}, λ_{max} 210 nm (s, ε 17,000), mass spectrum: *m/e*: 428.291 ($C_{27}H_{40}O_4$, M-HOAc, 14.7%), 386.282 (M-HOAc-CH_2=C=O, 8.3%; m* (428→386) at 348), 368.273 (M-2HOAc, 17.0%; m*(428→368) at 317), 350.259 ($C_{25}H_{34}O$, M-2HOAc-H_2O, 3.6%; m* (368 → 350) at 333), 191.179 ($C_{14}H_{23}$, 7.5%). NMR (Varian 270 MHz, d_6-acetone): 6.9 d (H_{19}, J = 2 Hz), 6.16 brt (H_{20}, J ≈ 1.7 Hz), 5.34 ddt (H_{16}, J = 10.2, 6 and ~ 1.7 Hz), 3.45 dd (after addition of D_2O) (H_{12}, J = 10.5 and 4.3 Hz), 2.57 brs (H_{18}), 2.06 and 1.99 (two OAc groups), 0.893 s (2 Me groups), 0.871 s, 0.866 s and 0.833 s (3 Me groups).

Recording of ^{13}C-NMR *spectra.* ^{13}C-NMR chemical shifts were obtained at 22.62 MHz with a Brucker WH-90 spectrometer which incorporates the B-NC-12 data system with 12 K memory. The proton noise decoued FT technique was used. The r.f. pulse width was 5–13 μsec, corresponding to a pulse angle of 30–90°, and a pulse repetition rate was 0.6–10 sec. The chemical shifts were determined with an accuracy of ±0.1 ppm, at 27°, in a 10 mm diameter tube. Spectra were measured for $CDCl_3$ solutions at a concentration of 10% to enable use of the deuterium resonance as internal lock signal. TMS was used as an internal standard.

REFERENCES

[1] [a]E. Fattorusso, S. Magno, C. Santacroce and D. Sica, *Tetrahedron* **28**, 5993 (1972); [b]G. Cimino, S. De Stefano and L. Minale, *Experientia* **29**. 934 (1973); [c]G. Cimino, S. De Stefano and L. Minale, *Ibid.* **30**, 846 (1974).

[2] R. Kazlauskas, P. T. Murphy, R. J. Quinn and R. J. Wells, *Tetrahedron Letters* 2631 (1976).

[3] S. A. Knight, *Org. Mag. Res.* **6**, 603 (1974).

[4] S. O. Almqvist, C. R. Enzell and F. W. Wehrli, *Acta. Chem. Scan.* **B29**, 695 (1975); and refs therein.

[5] I. Wahlberg, S. O. Almqvist, T. Nishida and C. R. Enzell, *Ibid.* **B29**, 1047 (1975).

[6] [a]J. B. Stothers, *Carbon-13 NMR Spectroscopy*. Academic Press, New York (1972); [b]L. P. Lindeman and J. Q. Adams, *Analyt Chem.* **43**, 1245 (1971); [c]D. K. Dalling and D. M. Grant, *J. Am. Chem. Soc.* **89**, 6612 (1967); [d]J. D. Roberts, F. J. Weigert, J. I. Kroschwitz and H. J. Reich, *Ibid.* **92**, 1338 (1970).

[7] [a]D. K. Dalling, D. M. Grant and E. G. Paul, *Ibid.* **95**, 3718 (1973); [b]D. Leibfritz and J. D. Roberts, *Ibid.* **95**, 4996 (1973).

[8] S. H. Grover, J. P. Guthrie, J. B. Stothers and C. T. Tan, *J. Mag. Res.* **10**, 227 (1973)