MAGNETIC RESONANCE IN CHEMISTRY
Magn. Reson. Chem. **36**, 539–541 (1998)

Note

NMR Assignments and conformation of taraxerenes

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Received 19 December 1997; revised 10 February 1998; accepted 10 February 1998

ABSTRACT: Complete ^1H and ^{13}C NMR chemical shift assignments were made for taraxerene from HMQC and HMBC spectra. Methyl proton shifts were assigned for 11 other taraxerenes. Molecular mechanics calculations and NMR evidence supported the *p*-bromobenzyl acetylaleuritolate x-ray conformation for taraxerenes in solution. © 1998 John Wiley & Sons, Ltd.

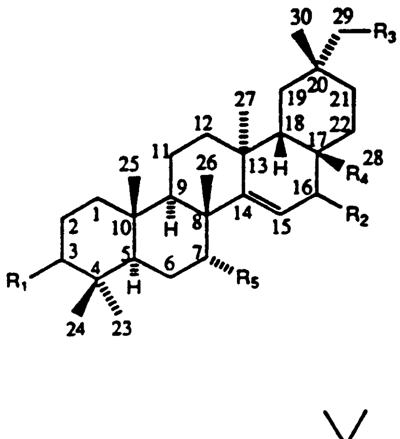
KEYWORDS: NMR; ^1H NMR; ^{13}C NMR, triterpenes; taraxerenes

INTRODUCTION

Our recent finding of taraxerene derivatives **1c**, **1f** and **2** in a Costa Rican plant[1] prompted us to carry out an HMQC/HMBC NMR study on taraxerene (**1a**) which permits assignments of all of its 50 protons and 30 carbons (Table 1) and provides a basis for assigning methyl shifts for taraxerene derivatives **1b**–**k** and **2** (Table 2). This work complements 2D NMR studies on 3-acetylaleuritolic acid (**1j**),[6] whose ^1H and ^{13}C NMR assignments serve as excellent models for those taraxerenes with 28-carboxyl groups such as **1k**,[7] and on a mixture of the *trans*- and *cis*-*p*-hydroxycinnamoyl esters of taraxerol (**1m** and **1n**).[8]

RESULTS AND DISCUSSION

An x-ray study on *p*-bromobenzyl acetylaleuritolate (**1l**) showed the A and B rings to be chairs and the C and E rings to be twist-boats.[9] The similarity of our ^1H and ^{13}C NMR shifts for **1a** to those found for **1j**,[6] molecular mechanics calculations we have carried out on tarax-



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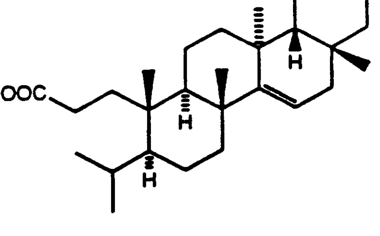
	R_1	R_2	R_3	R_4	R_5
a	H	H	H	CH_3	H
b	H	H	H	CH_3	OH
c	ß-OH	H	H	CH_3	H
d	α-OH	H	H	CH_3	H
e	ß-OH	α-OH	H	CH_3	H
f	=O	H	H	CH_3	H
g	=O	=O	H	CH_3	H
h	=O	H	OH	CH_3	H
i	ß-OAc	H	OAc	CH_3	H
j	ß-OAc	H	H	CO_2H	H
k	α-OAc	H	H	CO_2H	H
l	ß-OAc	H	H	[a]	H
m	[b]	H	H	CH_3	H
n	[c]	H	H	CH_3	H

[a] $CO_2CH_2C_6H_4Br$-*p*
[b] ß-O(CO)CH=CHC$_6$H$_4$OH-*p* (*trans*)
[c] ß-O(CO)CH=CHC$_6$H$_4$OH-*p* (*cis*)



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CCC 0749-1581/98/070539-03 $17.50

Table 1. NMR assignments for 1a

Atom	δ_c	δ_H (*J*, Hz)	Atom	δ_c	δ_H (*J*, Hz)
1	39.4	α 0.78 m, β 1.54 m	16	37.8	α 1.92 dd (14.7, 3.1) β 1.63 m
2	18.5	α 1.36 m, β 1.57 m	17	35.8	
3	42.1	α 1.11 m, β 1.34 m	18	48.8	0.95 m
4	33.1		19	36.7	α 1.30 m, β 0.96 m
5	56.6	0.81 m	20	28.8	
6	19.1	α 1.60 m, β 1.41 m	21	33.1	α 1.23 m, β 1.33 m
7	41.4	α 1.34 m, β 2.01 m	22	35.2	α 1.38 m, β 1.01 m
8	39.2		23	33.4	0.850 s
9	49.4	1.44 m	24	21.6	0.830 s
10	38.3		25	15.4	0.923 s
11	17.5	α 1.66 m, β 1.46 m	26	26.0	1.090 s
12	33.8	α 1.61 m, β 1.54 m	27	21.3	0.915 s
13	37.6		28	29.8	0.823 s
14	158.5		29	33.4	0.951 s
15	116.6	5.53 dd (8.2, 3.1)	30	29.9	0.911 s

erene (**1a**) and the appearances of various HMQC, HMBC and NOESY peaks strongly suggest that in solution **1a** has essentially the same minimum energy conformation as observed in the x-ray structure of **11**.[9]

The connectivity in **1a** was established with certainty from the one-, two- and three-bond CH couplings. Assignments within the two *gem*-dimethyl groups and 11 methylene groups were then made as follows.

The *gem*-dimethyls were assigned from γ-effects on the methyl carbon shifts. Equatorial methyl carbon C-23 on ring A absorbs 11.8 ppm further downfield than axial carbon C-24, since the former has two anti-γ interactions and the latter has none. For the ring E *gem*-dimethyls, since in the favored conformation C-29 has one near-anti-γ-interaction (C-29—C-20—C-19—C-18 = 159° in both the molecular mechanics minimum energy and x-ray structures) and C-30 has none, C-29 was assigned to the peak which is 3.5 ppm further downfield. This was supported by a large NOESY peak between the 19α and 29 protons.

The assignments of protons within each of the 11 methylene groups were made most easily from the HMQC spectrum, with support in every case from both the HMBC and NOESY spectra. From the HMQC peaks for each pair of methylene protons, it was clear how many large vicinal couplings were present in addition to the large geminal coupling. The five methylenes in the A and B rings were easily assigned in this way. Those in the C and E rings (twist-boat) and D ring (cyclohexene) were assigned with the aid of the calculated coupling constants from the molecular mechanics program: 16α, 19β, 21α and 22β have no large vicinal

Table 2. ^{1}H NMR chemical shifts (δ) for methyl groups in 1a–k, m and *n* and 2

		Atom							
Compound	Ref.	23	24	25	26	27	28	29	30
1a	this work	0.850	0.830	0.923	1.090	0.915	0.823	0.951	0.911
1b	2	0.879	0.823	0.921	1.156	0.904	0.823	0.951	0.904
1c	1	0.979	0.803	0.927	1.090	0.909	0.821	0.950	0.906
1d	3	1.10	0.85	0.95	1.10	0.92	0.82	0.95	0.92
1e	4	0.97	0.79	0.92	1.10	0.79	0.79	0.97	0.91
1f	1	1.082	1.068	1.140	1.089	0.916	0.831	0.955	0.909
1g	3	1.10	1.08	1.20	1.10	1.01[a]	0.98[a]	0.95	0.93
1h	5	1.07	1.07	1.13	1.07	0.93	0.85	—	0.93
1i	5	0.88	0.88	0.97	1.10	0.91	0.88	—	0.97
1j	6	0.85	0.89	0.955	0.955	0.92	—	0.94	0.91
1k	7	1.07[a]	1.03[a]	1.03[a]	0.92	0.88	—	0.90	0.88
1m	8	0.901	0.957	0.986	1.104	0.917	0.826	0.956	0.913
1n	8	0.864	0.833	0.966	1.090	0.908	0.824	0.956	0.913
2	1	0.832 d	0.912 d	0.891	1.098	0.919	0.824	0.955	0.912

[a] May be interchanged within row.

couplings, 12β has one, 11β and 12β have two and 11α has three. The HMBC verifications of these methylene assignments came from the very strong peaks observed for the many near-anti three-bond CH couplings which occur in this structure. For example, H-16β gives a far larger crosspeak with C-18 than does H-16α.

The methyl proton shifts in Table 2 for other natural taraxerenes **1b**–**k** and **2** were assigned from the shifts for **1a**, **1j**,[6] **1m** and **1n**.[8] H-29 and H-30 (not distinguished earlier) in **1i** and **1j** can be assigned by analogy with **1a**, **1m** and **1n**. For **1b**–**h** and **k**, the methyls were either unassigned or between two and seven of the eight methyls were misassigned. The ring A methyls in the 3β-ols were assigned by analogy with other triterpenes[10] and in the 3-ketones by analogy with moretenone.[6] That the methyl shifts of taraxerenes **1a**–**k**, **m** and **n** and **2** fit so well suggests that the x-ray/molecular mechanics conformation[9] predominates in solution for all of them.

EXPERIMENTAL

NMR spectra were measured in $CDCl_3$–TMS at 500 MHz (^1H) on a Bruker AM-500 spectrometer. The HMBC spectrum was optimized for 10 Hz CH couplings. Molecular mechanics calculations with MACROMODEL[11] showed the x-ray conformation to be the global minimum, with the only other minimum within 3·6 kcal mol^{-1} being one 1.7 kcal mol^{-1} higher with a ring E chair obtained by rotating 120° about the C-21—C-22 bond.

Acknowledgements

We thank Professor S. K. Paknikar for a gift of taraxerene (**1a**).

REFERENCES

1. W. N. Setzer, M. C. Setzer, A. L. Hopper, D. M. Moriarty, G. K. Lehrman, K. L. Niekamp, S. M. Morcomb, R. B. Bates, K. J. McClure, C. C. Stessman and W. A. Haber, *Planta Med.* submitted for publication.
2. H. Ageta and Y. Arai, *Phytochemistry* **22**, 1801 (1983).
3. R. E. Corbett, S. D. Cumming and E. V. Whitehead, *J. Chem. Soc., Perkin Trans. 1* 2827 (1972).
4. W.-H. Hui and M.-M. Li, *J. Chem. Soc., Perkin Trans. 1* 897 (1977).
5. W.-H. Hui and M.-M. Li, *J. Chem. Soc., Perkin Trans. 1* 23 (1976).
6. S. McLean, M. Perpick-Dumont, W. F. Reynolds, H. Jacobs and S. Lachmansing, *Can. J. Chem.* **65**, 2519 (1987).
7. T. K. Razdan, S. Harkar, V. Kachroo and G. L. Koul, *Phytochemistry* **21**, 2339 (1982).
8. S. McLean, W. F. Reynolds, J. P. Yang, H. Jacobs and L. L. Jean-Pierre, *Magn. Reson. Chem.* **32**, 422 (1994).
9. A. T. McPhail, D. R. MacPhail, M. C. Wani, M. E. Wall and A. W. Nicholas, *J. Nat. Prod.* **52**, 212 (1989).
10. W. F. Reynolds, S. McLean, J. Poplawski, R. G. Enriquez, L. I. Escobar and I. Leon, *Tetrahedron* **42**, 3419 (1986).
11. F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson and W. C. Still, *J. Comput. Chem.* **11**, 440 (1990).