Tetrahedron Letters,Vol.30,No.34,pp 4563-4564,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

STEREOSTRUCTURAL REVISION OF AURICULARIC ACID SYNTHESIS OF 4-EPI-AURICULARIC ACID

A. Abad*, C. Agulló, M. Arnó*, and R.J. Zaragozá

Departamento de Química Orgánica, Universidad de Valencia
Dr. Moliner 50, 46100 Burjasot, Valencia, Spain.

Summary: Cleistanth-13,15-dien-18-oic acid (1) has been synthesised from methyl 13-keto-podocarp-8(14)-en-18-oate (3). It is demonstrated that auricularic acid is an epimer at C-4 of 1, so it must be reformulated as cleistanth-13,15-dien-19-oic acid (2).

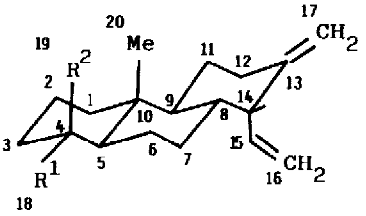
Auricularic acid is an spasmolytic cleistanthane type diterpenoid with a completely reduced C-ring. It and its 7-hydroxy derivative were isolated from *Pogostemon auricularis* Hassk by Prakash and coworkers[1a,b] in 1986.

The structure 1 for auricularic acid was proposed on the basis of degradative and spectroscopic studies. We have prepared this compound from enone 3[2] by a method that does not disturb the stereochemistry of ring A (see Scheme) but have found that its properties differ from those reported by Prakash for the natural product. The differences observed in the ^{13}C n.m.r. spectra of both compounds are specially significant (see Table).

Table. ^{13}C and ^{1}H Chemical Shifts of Auricularic Acid (AA) and 1.

Carbon	δc **AA**[a]	δc **1**[b]	Proton[c]	δH **AA**[a]	δH **1**[b]
1	38.0[d]	38.4	H-14	2.82(dd,9.2, 4.6)	2.77(dd,9.2, 4.3)
2	19.5	18.0			
3	39.7	36.9			
4	43.9	47.35	H-15	6.0(ddd,17.3, 10.3,9.2)	6.01(ddd,17.5, 9.4,9.2)
5	56.4	49.35			
6	23.2	24.2			
7	32.7	31.2	H-16	5.02(dd,10.3, 1.7)	5.01(dd,9.4, 1.8)
8	40.9	40.6			
9	48.9	49.1			
10	37.7	36.4	H-16'	5.04(dd,17.3, 1.7)	5.02(dd,17.5, 1.8)
11	27.4	26.7			
12	31.5[d]	31.6			
13	152.2	152.4	H-17	4.65	4.62(d,2.2)
14	54.7	54.7			
15	137.7	137.7	H-17'	4.57	4.52(m)
16	115.7	115.9			
17	106.5	106.4	Me-4	1.22(s)	1.15(s)
Me-4	29.0	16.6			
Me-10	12.8	14.15	Me-10	0.71(s)	0.82(s)
COOH	184.0	185.7			

[a] These data have been taken from reference 1. [b] In $CDCl_3$. [c] J-Values (Hz) are given in parentheses. [d] We have reversed the signals previously attributed to C-1 and C-12 since we believe the chemical shift assignments for these atoms were incorrect (see ref 5).

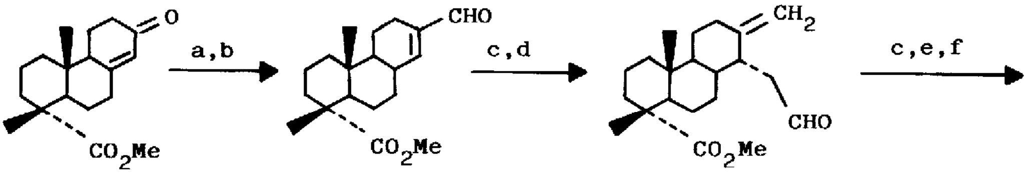


1 : R^1 = COOH, R^2 = Me

2 : R^1 = Me , R^2 = COOH

Thus, comparison of the ^{13}C chemical shifts reveals that the greatest difference observed for auricularic acid with respect to **1** lies in the values for C-5 and Me-4 which are shifted downfield by 7 and 12.4 ppm, respectively.[3] These differences are sufficiently characteristic to demonstrate that auricularic acid is an epimer at C-4 of structure 1, so it must be re-formulated as cleistanth-13,15-dien-19-oic acid and stereochemically represented as **2**.

Scheme[6]



3

1

a) $Ph_3P{=}CHOCH_3$, THF, then NaH, DMF. b) HCOOH, DMF. c) $NaBH_4$, CH_3OH. d) $Hg(OAc)_2$, $CH_3CH_2OCH{=}CH_2$, 195 °C. e) o-NO_2PhSeCN, Bu_3P, THF, then H_2O_2. f) NaSePh, THF, HMPT.

Acknowledgements: Finaltial support from CICYT (Grant N° PB86-0578) is gratefully acknowledged. We also thank Dr D. Craig for manuscript revision.

References and notes

1 (a) O. Prakash, R. Roy, S. Agarwal, F.A. Hussaini, and A. Shoeb, *Tetrahedron Lett.*, 1987, **28**, 685; (b) F.A. Hussaini, S. Agarwal, R. Roy, O. Prakash, and A. Shoeb, *J. Nat. Prod.*, 1988, **51**, 212.

2 Prepared from abietic acid as described in: A. Abad, M. Arnó, L.R. Domingo, and R.J. Zaragozá, *Tetrahedron*, 1985, **41**, 4937.

3 Previous studies on ^{13}C n.m.r. spectra of various abietane and podocarpane type diterpenoids[4] have demonstrated that the presence of an equatorial carboxyl group at C-4 results in shielding of the β-carbon atoms (specially C-5 and C-19) with respect to their axial counterpart. Thus, when the values for the compounds having an axial carboxyl group at C-4 are compared with that having the same group equatorial, the C-5 appears at 53-56 instead of 45-50 ppm and the methyls linked to C-4 at 28-29 instead of 16-18 ppm.

4 (a) T. Nishida, I. Wahlberg, and C.R. Enzell, *Org. Magn. Reson.*, 1977, **9**, 203; (b) B. Delmond, M. Taran, and J. Valade, *Org. Magn. Reson.*, 1981, **17**, 207; (c) S. Valverde, J.C. Lopez, R.M. Rabanal, and J. Escudero, *Tetrahedron*, 1986, **42**, 573; (d) A.C. Pinto, D.H.T. Zocher, P.P.S. Queiroz, and A. Kelecom, *Phytochemistry*, 1987, **26**, 2409.

5 (a) T.S. Kaufman, M.P. Mischne, M. Gonzalez-Sierra, and E.A. Ruveda, *Can. J. Chem.*, 1987, **65**, 2024; (b) R.W. Dunlop, *Phytochemistry*, 1985, **24**, 977.

6 The details of this transformation shall be published elsewhere.

(Received in UK 4 July 1989)