NOVEL TRITERPENES, HANCOLUPENONE AND HANCOLUPENOL, FROM *CYNANCHUM HANCOKIANUM*

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The absolute stereochemistry of hancolupenone and hankolupenol, novel triterpenes, isolated from *Cynanchum hancokianum*, has been determined by spectroscopy and X-ray analysis.

KEYWORDS *Cynanchum hancokianum*; pentacyclic triterpene; hancolupenone; hankolupenol; absolute stereochemistry; 2D NMR; X-ray; CD

Cynanchum hancokianum (Maxim.) Al. Ilujinski. (Asclepiadaceae), distributed in Inner Mongolia, is known as a chinese folk medicine with antitumor activity. We previously reported the isolation of a new pentacyclic triterpene, hancokinol, from the ethanol extract of this plant.[1)] Our further studies have led to the isolation of two new pentacyclic triterpenes, named hancolupenone and hancolupenol, from the same source. We now report the structure of these compounds as determined by spectroscopy and X-ray analysis.

Hancolupenone (1),[2)] $C_{30}H_{48}O$, colorless plates, mp 241-242℃ (MeOH), $[\alpha]_D^{29}$ +14.4° (c=0.2, $CHCl_3$), showed an IR carbonyl band at 1702 cm^{-1}. Its protons and carbons were assigned by 2D NMR spectroscopy[3)] (Table I).

DEPT experiments provided eight methyls, nine methylenes, six methines and seven quaternary carbons. The presence of an iso-propyl comprised of two *sec*-methyls (H_3-29, H_3-30) and a methine (H-20) was confirmed by ^1H-^1H COSY experiments. The ^1H-^1H and ^1H-^{13}C correlations of a methylene (C-22) to a methylene (C-21) and a methyl (C-28), which was correlated to a methine (C-18), suggested Pr^i-19. A one-proton signal at δ_H 5.31 was attributed by ^1H-^1H COSY experiments to a trisubstituted olefinic proton (H-11) containing a neighboring methylene (H_2-12). A carbonyl carbon (C-3) was deduced from its correlation to a methylene (Hα-2) in the ^1H-^{13}C (long-range) COSY spectrum. ^1H-^1H COSY experiments related a methine (H-8) to a neighboring methylene (Hβ-7).

The EIMS displayed a characteristic fragment at *m/z* 206 arising from a retro-Diels-Alder fission, suggesting a 13-methyl-26-norlup-9(11)-en-3-one for 1 by combining the NMR data.

Assuming a chair form for each ring-A, -B and -D and a half-chair form for ring-C, A/B *trans*, C/D *trans* and D/E *cis* were assigned on the basis of the orientations of each angular methyl and bridge head hydrogen deduced by NOE difference experiments (Chart 1). The enhancements linking to H_3-25 and H_3-27 suggested Hβ(ax)-8 with respect to ring-B and -C. An NOE observed between H-19 and H_3-27 led to $Pr^i\alpha$-19.

X-ray analysis proved the above-deduced stereochemistry to be correct (Fig. 1).[4)]

Aborinone (3) and lanost-9(11)-en-3-one (4) show a negative ORD Cotton effect in the carbonyl $n \rightarrow \pi^*$ region.[5)] Cylindrin (5), 4,4-dimethyl-5α,14β-cholest-9(11)-en-3 -ol acetate (6) and 4 exhibit a positive CD cotton effect in the olefinic $\pi \rightarrow \sigma^*$ region.[6)] A negative CD Cotton effect at 306 nm and a positive one at 201 nm observed for 1 assigned the 10*S*- and 8*S*,10*S*-configurations for 1, respectively, on the basis of the structural similarities of ring-A, -B, and -C. Thus, the absolute stereochemistry of 1 was determined to be the 5*R*, 8*S*, 10*S*, 13*R*, 14*S*, 17*S*, 18*S*, 19*S*-configuration (13β-methyl-26-nor-17α-lup-9(11)-en-3-one).

Hancolupenol (2),[7] $C_{30}H_{50}O$, colorless plates, mp 215-217℃ (MeOH), $[\alpha]_D^{29}$ +14.9° (c=0.4, $CHCl_3$), showed an IR hydroxyl band at 3602 cm^{-1}.

^{1}H-NMR spectroscopy revealed that 1 and 2 possess the same structure except the

Table I. NMR Data for 1[a]

Carbon No	δ_C		Correlated H[b] δ_H			H coupled with C[c]	H coupled with H[d]
1	36.50	t	Hα-1	1.80 (5.5, 13.5)	dt	H_3-25	Hβ-1, H_2-2
			Hβ-1	2.05 (13.5, 6.0, 3.0)	ddd		Hα-1, H_2-2
2	34.90	t	Hα-2	2.40 (15.5, 5.5, 3.0)	ddd		H_2-1, Hβ-2
			Hβ-2	2.72 (15.5, 13.5, 6.0)	ddd		H_2-1, Hα-2
3	217.34	s				Hα-2	
4	47.65	s				H-5, H_3-23, H_3-24	
5	53.39	d	H-5	1.36 (12.0, 3.0)	dd		H_2-6
6	22.82	t	Hα-6	1.70	m	Hα-7	H-5, Hβ-6, Hβ-7
			Hβ-6	1.55	m		H-5, Hα-6, Hα-7
7	26.72	t	Hα-7	1.14	m	H-5, H_2-6, H-8	Hβ-6, Hβ-7
			Hβ-7	1.88 (12.0, 4.0)	dq		Hα-6, Hα-7, H-8
8	42.25	d	H-8	2.00 (12.0)	brd	H_3-27	Hβ-7
9	146.78	s				H_3-25	
10	39.18	s				H_3-25	
11	115.04	d	H-11	5.31 (3.0)	t	H_2-12	H_2-12
12	36.95	t	H_2-12	1.71 (3.0)	d	H_3-27	H-11
13	36.99	s				H-8, H-18, H-19, H_3-26, H_3-27	
14	37.34	s				H_3-26, H_3-27	
15	27.91	t	Hα-15	1.31	m	H_2-16, H_3-26	Hβ-15, H_2-16
			Hβ-15	1.44	m		Hα-15
16	32.23	t	H_2-16	1.45	m	Hα-22, H_3-28	Hα-15
17	41.16	s				H_3-28	
18	54.17	d	H-18	1.55	m	H_3-28	
19	49.53	d	H-19	1.49	m		Hβ-21
20	35.94	d	H-20	1.53	m	H-19, Hα-21	H_3-29, H_3-30
21	28.90	t	Hα-21	1.51	m	H-19, Hβ-22	Hβ-21, H_2-22
			Hβ-21	1.76	m		H-19, Hα-21, Hα-22
22	38.46	t	Hα-22	1.12	m	H-19, Hα-21, H_3-28	H_2-21, Hβ-22
			Hβ-22	1.76	m		Hα-21, Hα-22
23	25.55	q	H_3-23	1.07	s	H_3-24	
24	22.00	q	H_3-24	1.06	s	H-5, H_3-23	
25	21.30	q	H_3-25	1.20	s	Hα-1, H-5	
26	15.95	q	H_3-26	0.75	s		
27	15.67	q	H_3-27	0.74	s	H-18	
28	32.60	q	H_3-28	0.92	s	H_2-16, H-18, H-19, Hα-21	
29[e]	22.32	q	H_3-29	0.88 (5.8)	d	H_3-30	H-20
30[e]	23.42	q	H_3-30	0.90 (5.8)	d	H_3-29	H-20

a) Spectra were taken on a Varian XL-400 (^{1}H, 400 MHz; ^{13}C, 100.6 MHz) in $CDCl_3$.
b) ^{1}H-^{13}C (one-bond) COSY. Figures in parentheses are coupling constants (Hz).
c) ^{1}H-^{13}C (long-range) COSY. d) ^{1}H-^{1}H COSY. e) These are exchangeable.

3-substituents. Sodium borohydride reduction of 1 afforded 2. Coupling (dd, J=11.5, 4.0 Hz) observed for H-3 indicated HOβ(eq)-3, *i.e.* the 3S-configuration.

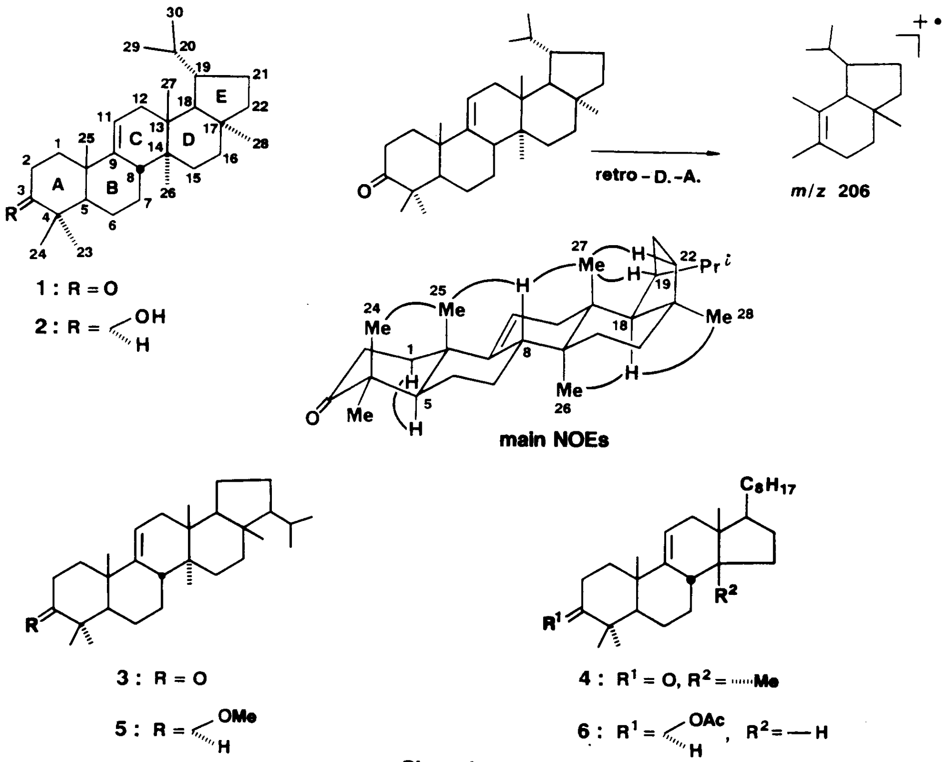

Chart 1

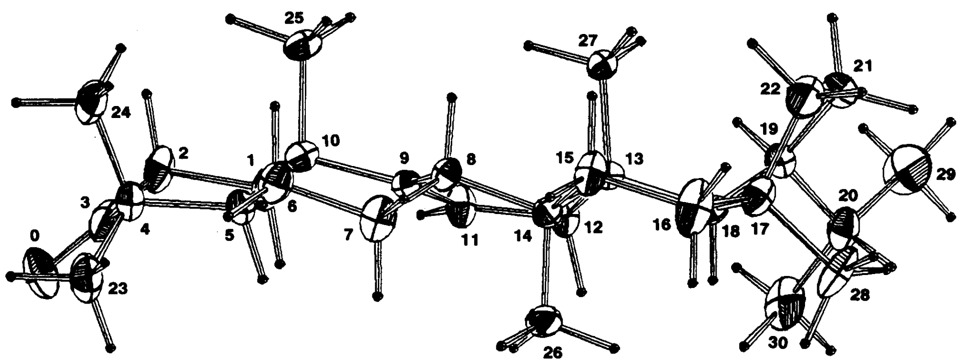

Fig. 1. ORTEP-View of X-Ray Structure of 1

REFERENCES AND NOTES

1) Y. Konda, M. Iguchi, Y. Harigaya, X. Li, H. Lou, and M. Onda, *Tetrahedron Lett.*, accepted for publication.
2) CD $[\theta]^{28}$ (nm): 0 (339), -328 (319)(sh), -480 (306)(negative maximum), -433 (296)(sh), 0 (263), +31000 (201)(positive maximum)(c=1.45$\times$ 10^{-3}, n-hexane). EIHRMS m/z: M^+, 424.3698 (424.3707 for $C_{30}H_{48}O$).
3) The experimental conditions for the ^1H-^1H and ^1H-^{13}C COSY spectra will be described in the full paper.
4) The crystal data were: 1, $C_{30}H_{48}O$, Mol. Wt.=424.68, Triclinic, space group P1, Z=2. Lattice constants, a=12.280 (2), b=14.296 (2), c=8.314 (2)Å, α=101.20 (1), β= 100.09 (2), γ=113.07 (1)°, V=1265.2Å^3, D_{calc}=1.115 g/cm^{-3}, μ for CuKα=0.602 cm^{-1}. A total of 3509 reflections were measured as being above the 3σ (I) level in the 2θ range of 0-150°. The crystal structure was elucidated by the direct method and atomic parameters were refined by block-diagonal least squares procedure. The final R value was 0.078 for 3509 reflections including 96 hydrogen atoms for which isotropic thermal parameters were applied. The details will be presented eleswhere.
5) H. Vorbrüggen, S. C. Pakrashi, and C. Djerassi, *Liebigs Ann. Chem.*, 668, 57 (1963).
6) J. Hudec and D. N. Kirk, *Tetrahedron*, 32, 2475 (1976); M. Legrand and R. Viennet, *Comp. Rend. C*, 262, 1290 (1966).
7) EIHRMS m/z: M^+, 426.3846 (426.3860 for $C_{30}H_{50}O$).

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