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Prelacinan-7-ol, a Novel Sesquiterpene from *Rudbeckia laciniata*

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Abstract : A new tricyclic sesquiterpene, prelacinan-7-ol (**1**) was isolated from the roots of *Rudbeckia laciniata*. The structure was determined on the base of the extensive 2D NMR analyses The absolute configuration was established by derivatizing to axially chiral 2-(2'-methoxy-1'-naphthyl)-3,5-dichlorobenzoic acid (MNCB, **3**) and 2'-methoxy-1,1'-binaphthyl-2-carboxylic acid (MBNC, **4**) esters. For the same purpose, "Modified Mosher's method" was inapplicable

The chemical constituents of *Rudbeckia laciniata* L. (Asteraceae) have previously been studied in some detail[1]. This weed was naturalized in Japan, and forms colonies along roadsides and field. Our reinvestigation with allelopathic interest gave a phytotoxic and unique sesquiterpene alcohol (**1**).

The ethyl acetate extracts (7g) from 2kg (fr. wt.) of *R. laciniata* roots were fractionated by silica-gel column chromatography (Hexanc:EtOAc=9:1) and preparative TLC on silica-gel (CH_2Cl_2) to afford prelacinan-7-ol (**1**)[2] 60mg as colourless prisms. The ^1H and ^{13}C NMR data[3] of 1 are summarized in Table 1.

Table 1 ^1H and ^{13}C NMR Data of Prelacinan-7-ol (**1**)

Position	δC[a]	DEPT	δH[b] (*J*=Hz)	^1H-^1H COSY	HMBC	NOESY	δC[c]	δH
1	53.48	C	-	-	2,3β,5,10αβ,11αβ,12	-	53.87	-
2	39.05	CH	1.72 ddq (9,10,7)	3β,12	3β,4β,5,10β,12	11β	39.52	1.77
3	30.55	CH_2	α 1.09 dddd (4.5,9,10,12)	3β,4αβ	2,4α,12	12	30.98	1.11
			β 1.81 dddd (7,8,9,12)	3α,4αβ		5		1.81
4	21.37	CH_2	α 1.47 m	3αβ,4β	3αβ,5	14	21.76	1.50
			β 1.54 m	3αβ,4α		13		1.55
5	54.11	CH	1.53 dd (5.5,9)	4α	3β,4α,7,10αβ,11αβ,13,14	3β,11β,13	54.59	1.78
6	37.48	C	-	-	4β,5,13,14	-	38.10	-
7	84.37	CH	3.10 bd (6)	-OH	9αβ,11α,13,14,15	13,14	83.52	3.26
8	46.29	C	-	-	9αβ,10β,11α,15	-	47.01	-
9	34.56	CH_2	α 1.65 ddd (2,10,11)	9β,10β	10β,11β,15	14	34.79	1.68
			β 1.34 m	9α,10α		10α		1.34
10	21.71	CH_2	α 1.22 ddd (2,10,11)	9β,10β	2,9β,11β	3α,9β,14	22.23	1.22
			β 1.37 m	9α,10α		11α		1.40
11	42.61	CH_2	α 1.18 dd (1.5,11)	11β	7,9α,10α,15	12	43.18	1.24
			β 1.28 ddd (2,2,11)	11α		2,5		1.75
12	14.27	CH_3	0.84 d (7)	2	2,3α	3α,11α	14.59	0.87
13	29.67	CH_3	0.98 s	-	5,14	5	30.71	1.22
14	24.58	CH_3	1.01 s	-	5,7,13	9α,10α	25.00	1.05
15	25.59	CH_3	1.13 s	-	9β,11α	9β	26.45	1.36
OH			1.50	7				5.71

[a] In $CDCl_3$. [b] From HMQC. [c] In C_5D_5N.

The molecular formula was determined to be $C_{15}H_{26}O$ by HRMS. The IR spectrum showed the absorption of a hydroxy group at 3350 cm^{-1}, and the presence of a hydroxymethine proton (δ 3.10) in ^1H NMR spectrum indicated it to be a secondary alcohol. The DEPT sequence showed the presence of four methyls, five methylenes, three methines and three quaternary carbons. The ^1H-^1H COSY spectrum showed the correlations between 1) H-12, H-2, H-3, H-4 and H-5, 2) H-9 and H-10 (dotted lines in Figure 1'). The HMBC spectrum showed the following correlations between 1) H-15 and C-7, 8, 9, 11, 2) H-14 and C-5, 6, 7, 13, 3) H-13 and C-5, 6, 7, 14, 4) H-12 and C-1, 2, 3 (bold-faced bonds in Figure 1'), and 5) H-10 and C-1, 2, 5, 8, 9, 11 (arrows in Figure 1'). Thus, the planar structure for prelacinan-7-ol should be expressed a tricyclo-[6,2,1,$0^{1,5}$]undecane skeleton as shown in Figure 1'. The other correlations of the ^1H-^1H COSY and HMBC spectra supported this structure.

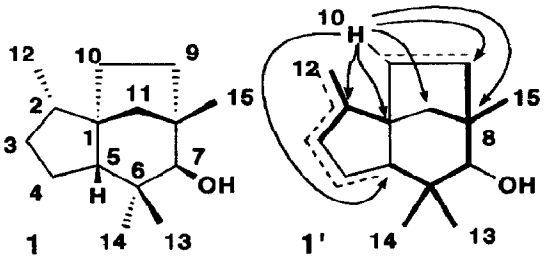


Figure 1 Structure of prelacinan-7-ol (1), with ^1H-^1H connectivities represented by dotted lines, the methyls' long-range ^1H-^{13}C HMBC correlations indicated by bold-faced bonds and those of H-10's indicated by arrows (1').

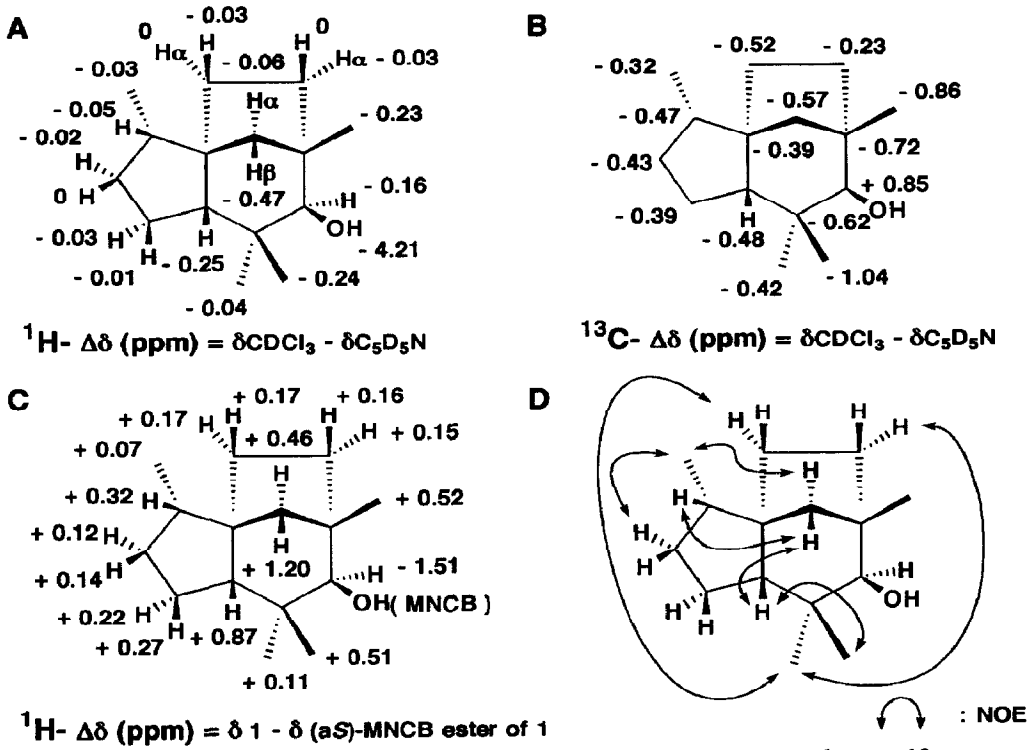


Figure 2 Pyridine-Induced Solvent Shifts: Δδ(=δCDCl3-δC5D5N) in ^1H and ^{13}C NMR obtained for **1** (**2A**, **B**), MNCB Shifts[5]: Δδ(=δ**1**-δ(a*S*)-MNCB ester of **1**) in ^1H NMR (CDCl3) (**2C**) and NOEs detected by NOESY spectrum for **1** (**2D**).

The relative stereochemistry of **1** was elucidated as shown in Figure 2 based on the following lines of evidence. **1)** W-type long-range couplings between Hβ-11 and Hα-10 (J=2Hz), Hβ-11 and Hα-9 (J=2Hz), and also Hα-11 and H-7 (J=1.5Hz). **2)** The arrangement of the large pyridine-induced solvent shifts[4] of signals near the hydroxyl group in the ^{1}H and ^{13}C NMR spectra (Figures **2A** and **2B**). **3)** The arrangement of the Δδ(=δalcohol-δMNCB ester)[5,9] values of signals near the hydroxyl group in the ^{1}H NMR spectrum (Figure **2C**). **4)** The observation of NOEs detected by NOESY spectrum in Figure **2D**.

To determine the absolute configuration of **1**, it was esterified with (*R*)- and (*S*)-α-methoxy-α-trifluoromethylphenylacetic acids (MTPA, **2**)[6], (a*R*)- and (a*S*)[7]-2-(2'-methoxy-1'-naphthyl)-3,5-dichlorobenzoic acids (MNCB, **3**), and also (a*R*)- and (a*S*)-2'-methoxy-1,1'-binaphthyl-2-carboxylic acids (MBNC, **4**)[8,9]. As pointed out by Ohtani *et al.*[6], since the hydroxy group of **1** is oriented in axial direction, "Modified Mosher's method" was inapplicable to **1** (Figure **3A**). On the other hand, MNCB and MBNC methods are applicable to sterically hindered alcohols[8]. So by these methods (Figure **3B**), the absolute configuration of **1** was established as depicted in formula **1**[10].

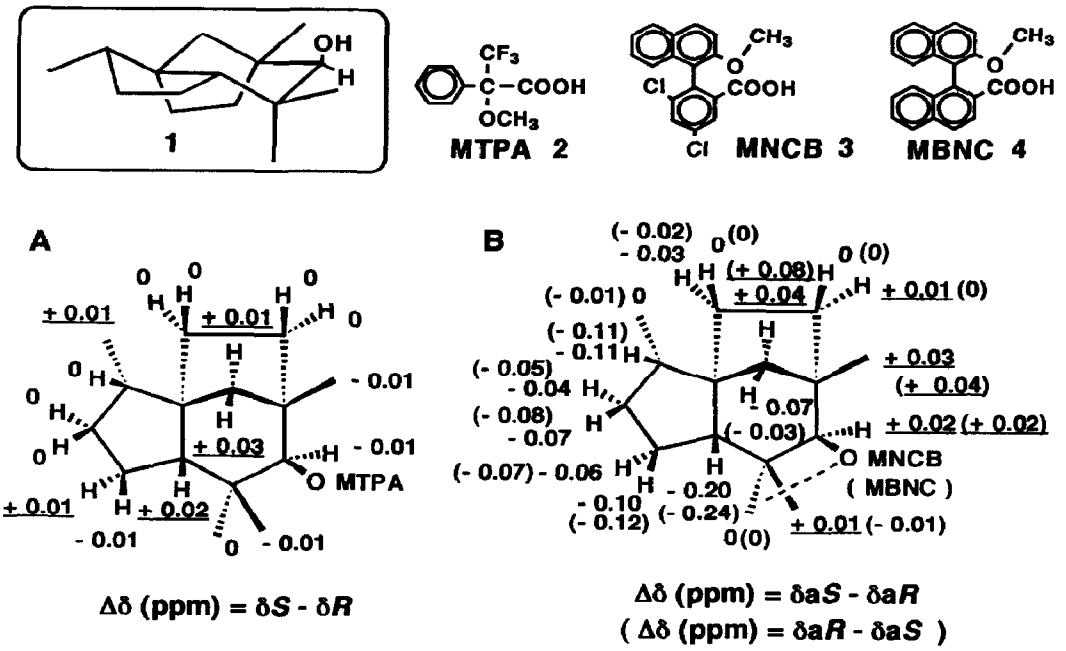
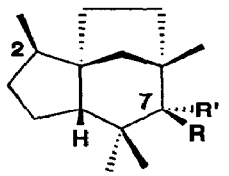


Figure 3 Δδ values in ^{1}H NMR obtained for the MTPA, MNCB and MBNC esters of **1**. Border plane is shown by a dotted line.



5 R=H, R'=OH
6 R, R'=O

Two sesquiterpenes (**5**, **6**) with the same skeleton of prelacinan-7-ol have been found in *Eremophila georgei* (Myoporaceae) and the abusolute cofiguration of **5** was determined by X ray analysis of *p*-bromobenzoate of **5**[11]. Prelacinan-7-ol, a 2,7-diepimer of **5**, is biogenetically interesting[11,12]. And it is phytotoxic to seedlings of *Nasturtium officinale* and *Phleum pratense* at 50 ppm.

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2. mp 32.5-34.5°C (hexane), $[\alpha]^{23}_{D}$ -13.8° (*c* 0.87, $CHCl_3$), HRMS: m/z 222.1987,$C_{15}H_{26}O$ requires 222.1985; MS (EI) m/z 222 (M^+, 32%), 207 (10), 204 (12), 191 (57), 161 (37), 135 (37), 134 (10), 121 (100). IR (KBr): 3350, 2950, 2870, 1445, 1040, 1020, 985 cm^{-1}.

3. A JEOL EX 270 and a Bruker AM 500 spectrometers were used to record ^1H and ^{13}C NMR spectra in $CDCl_3$ or C_5D_5N (ambient temperature). Proton and carbon chemical shifts were determined in δ units relative to TMS

4 Demarco P.V.;Farkas E.;Doddrell D.;Mylari B.L.;Wenkert E. *J.Am.Chem.Soc.* **1973**, *90*, 5480-5486. Pyridine-induced solvent shifts are observed in ^{13}C NMR as well as in ^1H NMR and useful for stereochemical investigation.

5. Fukushi Y.;Yazima C.;Endo K.;Mizutani J. The 38th Symposium on the Chemistry of Terpenes, Essential Oils, and Aromatics, Niigata, Japan, October 8-10, **1994**, 2-III-12 in press. Δδ defined as $\Delta\delta=\delta_{alcohol}-\delta_{MNCB\ ester}$ for each proton leads to the conformation and/or configuration of the compound in question. These shifts are named MNCB shifts, and MBNC shifts are used for MBNC derivatives.

6. Ohtani I.;Kusumi T.;Kashman Y.;Kakisawa H. *J.Am.Chem.Soc.* **1991**, *113*, 4092-4096.

7. The descriptors (a*R*) and (a*S*) refer to axial chirality.

8 Fukushi Y.;Yajima C.;Mizutani J. *Tetrahedron Lett.* **1994**, *35*, 599-602. In the present case, this rule was inapplicable in ^{13}C NMR.

9. The ^1H NMR data (in $CDCl_3$) for the alcohol moieties of the respective diastereomers are summarized as the following order :(2, 3α, 3β, 4α, 4β, 5, 7, 9α, 9β, 10α, 10β,11α, 11β, 12, 13, 14, 15). (*S*)-MTPA ester. (1.73, 1.10, 1.81, 1.46, 1.53, 1.49, 4.88, 1.74, 1 42, 1.25, 1.38, 1.24, 1.31, 0.85, 0.76, 1.11, 0.93), (*R*)-: (1.73, 1.10, 1.81, 1.45, 1.54, 1.47, 4.89, 1.74, 1.42, 1.25, 1.38, 1.23, 1.28, 0.84, 0.77, 1.11, 0.94), (a*S*)-MNCB ester: (1.40, 0.97, 1.67, 1.25, 1.27, 0.66, 4.61, 1.50, 1.18, 1.05, 1.20, 0.72, 0.08, 0.77, 0.47, 0.90, 0.61), (a*R*)-: (1.51, 1.01, 1.74, 1.31, 1.37, 0.86, 4.59, 1.49, 1.18, 1.08, 1.20, 0.68, 0.15, 0.77, 0.46, 0.90, 0.58), (a*R*)-MBNC ester: (1.45, 0.98, 1.68, 1.26, 1.27, 0.72, 4.70, 1.54, 1.20, 1.08, 1.22, 0.77, 0.22, 0.77, 0.54, 0.93, 0.69), (a*S*)-. (1.56, 1.03, 1 76, 1.33, 1.39, 0.96, 4.68, 1.54, 1.20, 1 10, 1.22, 0.69, 0.25, 0.78, 0.55, 0 93, 0.65)

10. The IUPAC name of **1** is (1*R*, 2*S*, 5*R*, 7*S*, 8*S*)-2, 6, 6, 8-tetramethyltricyclo[6, 2, 1, $0^{1,5}$]undecan-7-ol.

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