Pergamon

Tetrahedron Letters, Vol. 37, No. 21, pp. 3757-3760, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00640-5

Novel Tricyclic Sesquiterpenes from *Juniperus thurifera* L. Chemical Confirmation of the Duprezianane Skeleton

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Abstract: Three tricyclic sesquiterpenes, sesquithuriferol (**1**), α- (**3**) and β-duprezianene (**4**) were isolated from the essential oil of the wood of *Juniperus thurifera* L. The structure and absolute configuration of **1** was established on the basis of 2D INADEQUATE and other 2D NMR spectra, as well as by chemical correlations. The structure of **3** and **4** were elucidated by 2D NMR spectra and confirmed by their synthesis from tosyl-solvolysis rearrangement of **1**.

During the last few years the essential oils from wood of different species of the genus *Juniperus*[1,2] have been revealed as important sources of new sesquiterpenic compounds. Following the authors' research in this field, sesquithuriferol (**1**),[3] a new sesquiterpene alcohol $[\alpha]^{20}_{D}$=-58.8 (*c* 1.0, Cl_3CH), has been isolated as a colourless crystalline solid from *Juniperus thurifera* L. The structure of **1** and its O-acetyl derivative **2**[3] was established on the basis of the 2D INADEQUATE, DQF-COSY, HMQC and HMBC spectra (Table 1). The spectroscopic data of **1**[3] were not in accordance with those of the previously reported sesquiterpene alcohols **5**[4a,5] and **7**,[6] which have the same skeleton. For this reason **1** must be a stereoisomer. The relative stereochemistry of **1** was established on the basis of the following data: **A**) W-type long-range couplings between H-11β and H-10α (*J*=2.2Hz), H-11β and H-9α (*J*=2.2Hz), H-11α and H-7 (*J*=1Hz); **B**) the pyridine-induced solvent shifts[7] observed in the ^1H and ^{13}C NMR spectra (Figure 1); **C**) nOes shown by the NOESY spectrum (Table 1).

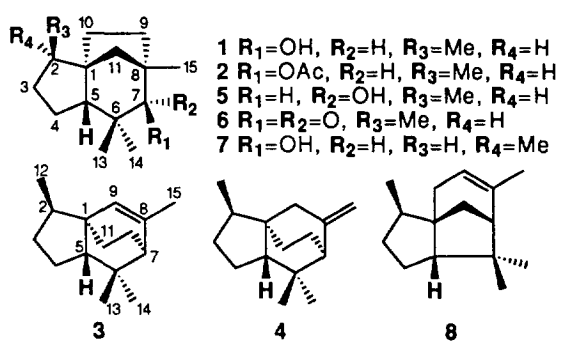


Figure 1. Compounds **1-8** and pyridine-induced solvent shifts in ^1H and ^{13}C NMR spectra for **1**.

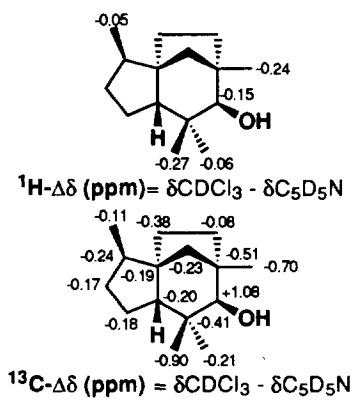


Table1. ^1H (400 MHz) and ^{13}C NMR (100 MHz) chemical shift data[8] ($CDCl_3$) of **1** and **2**

		Compound 1		Compound 2			Compounds 1 and 2		
n° C	DEPT	$\delta^{13}C$	$\delta^{1}H^{*}$ (*J*=Hz)	$\delta^{13}C$	2D INAD.	$\delta^{1}H^{*}$	COSY	HMBC	NOESY
1	C	54.11	–	53.97	2,5,10,11	–	–	2,3α,4α,5,10αβ 11αβ,12	–
2	CH	40.72	1.68, *dq* (11.1,7.2,3.8)	40.77	1,3,12	1.71	3β,12	3α,10β,12	3αβ,10β,12
3	CH_2	31.29	1.90, α, *dddd* (13,11.1,8.5,2.7)	31.27	2,4	1.91	3β,4αβ	4α,12	2,3β,4αβ,12
			1.08, β, *dddd* (13,12.4,8.5,3.8)			1.07	2,3α,4αβ		2,3α,4αβ,5,12
4	CH_2	22.98	1.42,α, *m*	22.98	3,5	1.42	3αβ,4β,5	3αβ,2,5	3αβ,4β,13
			1.56,β, *m*			1.56	3αβ,4α		3αβ,4α,12,13
5	CH	49.69	1.57, *m*	50.62	1,4,6	1.57	4α	2,3αβ,4αβ,7, 10αβ,11β,13,14	3β,12,13
6	C	37.39	–	36.89	5,7,13,14	–	–	4α,5,7,13,14	–
7	CH	84.22	3.05, *br s*	84.46	6,8	4.59	11α	9αβ,11αβ,13, 14,15	9α,13,14,15
8	C	47.03	–	46.23	7,9,11,15	–	–	7,9αβ,10α, 11αβ,15	–
9	CH_2	34.66	1.58, α, *dddd* (13.8,4.8,4.4,2.2)	34.21	8,10	1.63	9β,10αβ,11β	7,10αβ,11αβ,15	7,9β,10αβ,14,15
			1.38, β, *ddd* (13.8,12.8,4.6)			1.38	9α,10αβ		9α,10αβ,15
10	CH_2	33.51	1.74, α, *dddd* (13.4,4.6,4.4,2.2)	33.60	1,9	1.77	9αβ,10β,11β	2,9αβ,11β	9αβ,10β,14
			1.14,β, *ddd* (13.4,12.8,4.8)			1.17	9αβ,10α		2,9αβ,10α
11	CH_2	41.04	1.08, α, *dd* (11,1)	42.26	1,8	1.14	7,11β	7,9α,10α,15	11β,12,15
			1.50, β, *ddd* (11,2.2,2.2)			1.52	9α,10α,11α		11α,12,13,15
12	CH_3	19.95	0.85, *d* (7.2)	19.91	2	0.87	2	3αβ,2	2,3αβ,4β,5,11αβ
13	CH_3	30.03	0.98, *s*	29.40	6	0.84	14	5,14	4αβ,5,7,11β,14
14	CH_3	24.73	0.99, *s*	24.37	6	1.06	13	5,7,13	7,9α,10α,13
15	CH_3	25.79	1.12, *s*	25.07	8	0.94	–	7,9β,11α	7,9αβ,11αβ
MeCO	CH_3	–	–	21.03	–	2.06,*s*	–	–	–
MeCO	C	–	–	170.8	–	–	–	–	–

*From HMQC

The absolute configuration of **1** was determined by chemical correlation with **5**. The treatment of **1** with Jones reagent afforded the ketone **6**,[4a] which gave the alcohol **5**[4a] on stereoselective reduction with sodium borohydride. The absolute configuration of **5** had been previously determined by X ray analysis of its *p*-bromobenzoate derivative.[4b] **5** had $[\alpha]^{20}_D$=-34 (*c* 0.8, Cl_3CH) [lit. $[\alpha]^{20}_D$=-32 (*c* 1.1, Cl_3CH)] and its spectroscopic data were identical to those previously reported.[4a,5]

Two sesquiterpene hydrocarbons, α-duprezianene (**3**[9]) and **4**[9], a new natural product, were also isolated from the essential oil of *Juniperus thurifera* L.. **3** had been previously isolated from *C. dupreziana* by Piovetti *et al*[10a] as an unknown sesquiterpene and its tricyclo[5.2.2.$0^{1,5}$]undecane skeleton tentatively assigned by Kirtany *et al*[10b] on the basis of limited spectral data[10a], its co-occurrence with (+)-α-funebrene (**8**) and biogenetic considerations. The structures of **3** and **4** were elucidated through 2D NMR spectroscopy. The DQF-COSY spectrum of **4** (Table 2) established the presence of three molecular frameworks (Figure 2), whose connections were established by the analysis of the HMBC spectrum (Table 2 and Figure 2). The relative stereochemistry of **4** was established from the following data: W-type long range couplings between H-

5 and H-11β (J=1.7 Hz), H-9 and H-15 and between H-9 and H-11α (DQF-COSY, Table 2) together with nOes shown by the NOESY spectrum (Table 2, selected nOes are depicted in Figure 2).

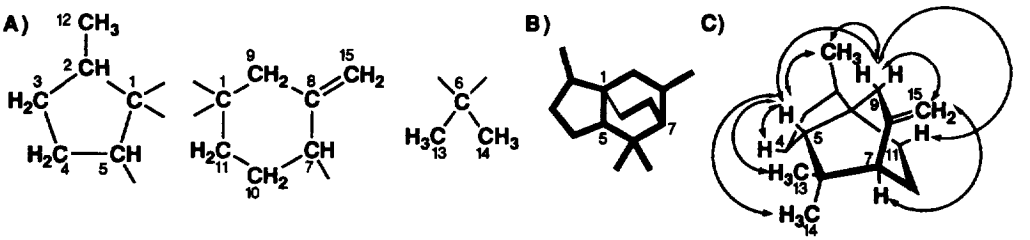


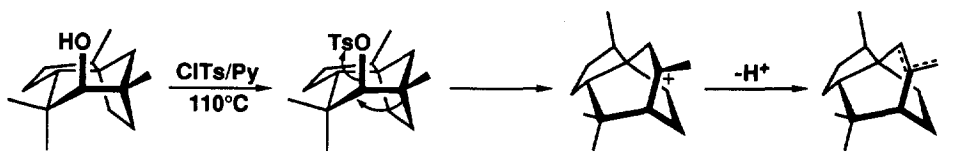
Figure 2. A)DQF-COSY proton-coupled systems. B)HMBC correlations are indicated by bold-faced bonds. C) nOes observed in the NOESY spectrum of **4**.

Table 2. ^{1}H (500 and 400 MHz) and ^{13}C NMR (100 MHz) chemical shift data[4] ($CDCl_3$ and C_6D_6*) of **4**

nºC	DEPT	δ^{13}C	δ^1H#(J=Hz)	COSY	HMBC	NOESY	δ^{13}C*	δ^1H*
1	C	43.56	–	–	2,3α,4α,5,9,12	–	43.64	–
2	CH	39.29	1.48, *m*	3β,12	3β,4α,12	3α,12	39.45	1.52
3	CH_2	34.43	1.98,α,*dddd*(12.9,8.3,8.3,2.2)	3β,4αβ	2,4β,12	2,3β	34.61	2.03
			1.01,β,*m*	2,3α,4β		3α,12		1.04
4	CH_2	23.84	1.50,α,*m*	3α,5	5	4β	23.99	1.57
			1.39,β,*m*	3αβ,5		4α,5		1.43
5	CH	52.80	1.21,*ddd*(12.3,6.9,1.7)	4αβ	3α,4β,7,9,13,14	4β,9,12,13,14	52.98	1.30
6	C	32.71	–	–	4β,5,13,14	–	33.07	–
7	CH	48.93	1.63,*dd*(3.4,2.2)	10αβ	10αβ,11α,13, 14,15	10α,13,14,15	49.07	1.72
8	C	152.00	–	–	7,9,10αβ,15	–	151.60	–
9	CH_2	37.66	2.07,*m*	11α,15	2,5,7,15	5,11β,12,15	37.76	2.18
10	CH_2	23.07	1.83,α,*dddd*(12.4,10.8,3.4,2)	7,10β,11αβ	5,11α	7,10β,11α,14	23.23	1.86
			1.40,β,*dddd* (12.4,10.5,2.2,2)	7,10α,11β		10α,11β		1.55
11	CH_2	28.64	1.44,α,*m*	9,10α	2,5,7,9,10β	10α,11β,14	28.80	1.45
			1.06,β,*dddd*(11.3,10.5,2,1.7)	10αβ		9,10β,11α		1.09
12	CH_3	18.23	0.79,*d*(7.2)	2	2,3αβ	2,3β,5,9	18.25	0.86
13	CH_3	31.82	0.90,*s*	–	5,14	5,7	31.90	1.14
14	CH_3	23.65	0.91,*s*	–	13	5,7,10α,11α	23.63	0.98
15	CH_2	107.35	4.71,*m*	9	7,8,9	7,9	107.94	5.02,*m* 4.99,*m*

#From HMQC

Furthermore, the structure and stereochemistry of the duprezianane skeleton of these compounds were unequivocally established by chemical correlation with **1**. Thus, as would be expected, the tosyl-solvolysis of **1** afforded a 1:1 mixture of **3** and **4** (Scheme 1).



1 **3** and **4** (1:1)

Scheme 1

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3. **Compound 1**: crystalline colourless solid, mp 44-5°C; $[\alpha]^{20}_D$=-58.8° (*c* 1.0, Cl_3CH); IR (neat): υ 3461, 2950, 2867, 1455, 1390, 1374, 1019; EIMS *m/z* (rel. int.): 222 (M^+, 32), 207 (M^+-CH_3, 37), 204 (M^+-H_2O, 2), 191 (M^+-CH_2OH, 100), 179 (31), 166 (18), 161(17), 149 (12), 135 (28), 121 (54), 108 (49), 95 (40), 81 (58), 69 (29), 55 (32), 41 (61). **Compound 2**: crystalline colourless solid, mp 63-4°C; $[\alpha]^{20}_D$=-42.6° (*c* 1.0, Cl_3CH); IR (neat): υ 2955, 2870, 1731, 1457, 1390, 1373, 1243, 1021; EIMS *m/z* (rel. int.): 264 (M^+,14), 249 (M^+-CH_3,4), 222 (M^+-CH_2CO, 6), 204 (M^+-CH_3COOH, 37), 191 (34), 189 (M^+-CH_3COOH-CH_3,30), 176 (13), 175 (13), 161 (31), 148 (26), 135 (23), 121 (36), 119 (34), 108 (20), 107 (30), 93 (30), 81 (31), 69 (30), 55 (24), 43 (CH_3CO^+,100), 41 (39).
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8. Bruker AMX 300, ARX 400 and AMX 500 spectrometers were used to record ^1H and ^{13}C NMR spectra (room temperature). Proton and carbon chemical shifts are given in δ units relative to TMS.
9. **Compound 3**. Colourless oil; $[\alpha]^{20}_D$=+17.6° (*c* 1.0, Cl_3CH); IR (neat): υ 3071, 2925, 2857, 1646, 1460, 1382, 1375; EIMS *m/z* (rel. int.): 204 (M^+,55), 189 (M^+-CH_3,42), 161 (M^+-CH_3-C_2H_4, 100), 148 (34), 137 (21), 133 (24),119 (M^+-CH_3-C_2H_4-C_3H_6, 91), 105 (61), 93 (74), 79 (47), 69 (55), 55 (37), 41 (73). **Compound 4**. Colourless oil; $[\alpha]^{20}_D$=+28.2° (*c* 1.0, Cl_3CH); IR (neat): υ 3029, 2952, 2869, 1460, 1373, 1360; EIMS *m/z* (rel. int.): 204 (M^+, 28), 189 (M^+-CH_3, 5), 176 (M^+-C_2H_4, 5) 161 (M^+-CH_3-C_2H_4, 25), 147 (4), 133 (M^+-CH_3-C_2H_4-C_2H_4, 15), 119 (M^+-CH_3-C_2H_4-C_3H_6, 100), 105 (24), 93 (19), 91 (19), 77 (11), 69 (7), 55 (10), 41 (21). ^1H NMR (500 MHz, $CDCl_3$): δ 5.88 (*br s*, H-9), 2.06 (*dddd*, *J*=13.2, 9,8,2.1, H-3α), 1.81 (*d*, *J*=1.7, H-15), 1.78 (*m*, H-7), 1.74 (*dddd*, *J*=12.2, 9.3, 2.5, 2.5, H-10α), 1.70 (*ddq*, *J*=8, 7.2, 4.4, H-2), 1.49 (*dddd*, *J*=12.5, 9, 8, 2.2, H-4α), 1.38 (*m*, H-4β), 1.38 (*m*, H-11α), 1.19 (*ddd*, *J*=12.5, 7.3, 2.2, H-5), 1.14 (*dddd*, *J*=13.2, 8.8, 8.8, 4.4, H-3β), 1.00 (*dddd*, *J*=12.2, 12.2, 5.8, 2.5, H-10β), 0.93 (*d*, *J*=7.2, H-12), 0.89 (*s*, H-14), 0.80 (*s*, H-13), 0.70 (*dddd*, *J*=12.2, 12.2, 2.5, 2.2, H-11β). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.40 (C, C-1), 36.97 (CH, C-2), 33.80 (CH_2, C-3), 22.93 (CH_2, C-4), 52.66 (CH, C-5), 31.91 (C, C-6), 49.59 (CH, C-7), 142.86 (C, C-8), 127.03 (CH, C-9), 23.23 (CH_2, C-10), 25.90 (CH_2, C-11), 20.05 (CH_3, C-12), 33.24 (CH_3, C-13), 24.67 (CH_3, C-14), 22.23 (CH_3, C-15).
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(*Received in UK* 25 *March* 1996; *accepted* 3 *April* 1996)