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Sesquiterpenes from *Juniperus thurifera* L. Stereochemistry in Unusual Cedrane and Duprezianane Series

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Abstract—The analysis of the essential oil from the wood of *Juniperus thurifera* has provided the isolation of seven new natural products, including the first described examples of 2-*epi*-cedranes and 2-*epi*-duprezianane. The co-occurrence in the oil of the three cedrane-type arrangements (cedrane, 1,7-*diepi*-cedrane and 2-*epi*-cedrane) has permitted, after a thorough 2D NMR analysis the unequivocal spectroscopical assignment of each of the three cedrane skeletons, and subsequently the development of an unambiguous method for establishing their stereochemistries. A useful pattern for distinguishing between the two duprezianane stereochemistries is also given.

Introduction

As a result of the previous studies by the authors,[1–3] the essential oils from the wood of different species of *Juniperus* have been revealed as sources of new sesquiterpene compounds, including junicedranol,[2] a sesquiterpene with a novel carbon skeleton, as well as the rare α and β-duprezianene (**11** and **12**). This finding provided the first complete NMR analysis of the duprezianane skeleton.[3] Continuing our research on the genus *Juniperus*, we report in this paper the results obtained from the study of the essential oil from the wood of *Juniperus thurifera*. The occurrence in this oil of unusual tricyclic sesquiterpenes, some of them presenting some ambiguities in their structural assignment, justifies the herein described approach to overcome the controversy in the elucidation of this kind of compounds.

Results and Discussion

Seven new tricyclic sesquiterpenes have been isolated from the wood of *J. thurifera*: 2-*epi*-α-cedren-3-one (**1**), 2-*epi*-β-cedren-3-one (**2**), 1,7-*diepi*-α-cedrenal (**3**), α-cedren-4-one (**5**), 2-*epi*-β-duprezianen-3-one (**6**), β-duprezianene (**12**) and sesquithuriferol (**14**); together with known 1,7-*diepi*-α-cedrenol (**4**), α-cedrene (**7**), β-cedrene (**8**), α-cedrenal (**9**), α-cedrenol (**13**), 1,7-*diepi*-β-cedrene (**10**), α-duprezianene (**11**) and sesquithuriferone (**15**) (Fig. 1).

Compound **1** presented in its IR spectrum absorptions due to a trisubstituted double bond (ν 3020 and 805) and a carbonyl group (ν 1737). Its molecular formula $C_{15}H_{22}O$ was deduced from its HR-EI-MS. The ^{1}H NMR spectrum showed signals due to an olefinic proton (δ 5.28), and to three methyls, two of them appear as a singlet (δ 1.11 and 0.90) and the third as a doublet (δ 0.96, J=7 Hz). The multiplicities in the ^{13}C NMR spectrum indicate the presence of three rings in the structure. Combined analysis of the HETCOR, COSY-DQF and HMBC experiences allow the assignment for this compound of an α-cedrene skeleton, possessing a carbonyl at C3. Comparison of the ^{13}C NMR data of **1** with those of α-cedrene (**7**) confirms the location of the keto group. In order to establish the relative configuration, the NOESY spectrum of **1** was performed. So, the NOE correlations of H5 with H13, H10β and H4β, and the ones of H14 with H11α and H4α indicate that the configuration at C1, C5 and C7 coincide with those of the normal series. Nevertheless, the existence of NOE between H12 and H11α, and between H2 and H4β, H10, reveals a change in the configuration at C2 (Fig. 2). This is the first described example of a cedrane skeleton showing at C2 the opposite configuration to that presented by the normal series.

Compound **2** has the molecular formula $C_{15}H_{22}O$, as can be deduced from its HR-EI-MS. The IR spectrum showed bands corresponding to an exocyclic double bond and a carbonyl group (ν 1640, 890 and ν 1737). The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of β-cedrene (**8**).[4] The 2D NMR (HETCOR on reverse phase, COSY and HMBC) experiences confirm the structure of **2** to be cedren-3-one, having the double bond located at $\Delta^{8(15)}$. The assignment of the stereochemistry was achieved, as in the previous case, on the basis of the NOESY experience.

Keywords: natural products; terpenoids; stereochemistry.

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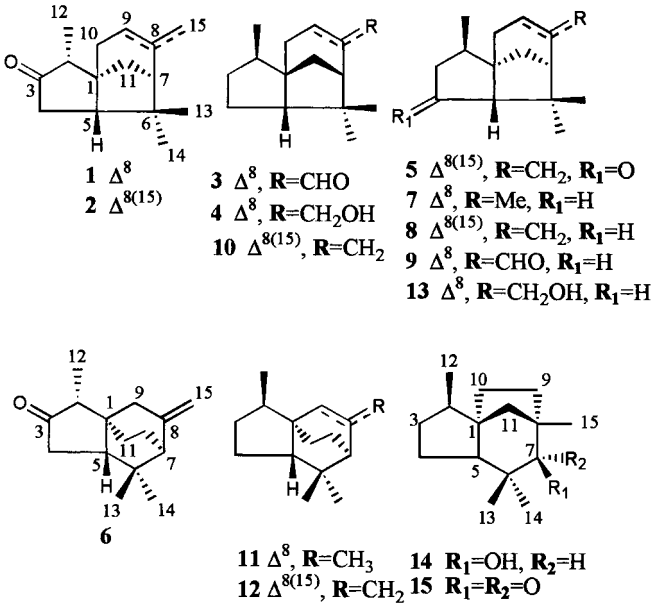


Figure 1.

And again, the correlations observed showed that Me-12 is located in the α face of the molecule (Fig. 2). Then, the structure of 2-*epi*-β-cedren-3-one is assigned to **2**.

Besides the NOE correlations, the ^{13}C NMR data of both **1** and **2** also show evidence of the stereochemistry change, these NMR data change are in according to γ-gauche effects observed after inspecting the models,[5] so looking through the C1–C2 bond, an eclipsed disposition of Me-12 with C11 in the 2-*epi* series, and with C10 in the normal series, is observed (Fig. 3).

These different dispositions justify the variations on the chemical shifts of C10 and C11 for both stereochemistries.

Compound **3** presents in its IR spectrum absorptions characteristic of α,β-unsaturated aldehyde (ν 2710 and 1683). Its molecular formula, $C_{15}H_{24}O$, was determined via HR-EI-MS. The combined spectroscopical analyses of **3** showed the presence of similar features of those of α-cedrenal (**9**),[6] but at the same time clearly demonstrated its non-identity with **9**. The cedrane skeleton was confirmed after 2D NMR analysis, including COSY-DQF, HETCOR, and HMBC experiences. The correlations displayed in the NOESY experiment led to assign to **3** the structure of 1,7-*diepi*-α-cedrenal. The observed NOE correlations of H5 with H12, H13 and H11β, and the one of H2 with H10β were conclusive to determine the relative stereochemistries of 1,7-*diepi*-cedranes (Fig. 2). This study represents the first complete NMR analysis of 1,7-*diepi*-cedranes (Table 1).

An enantiomer of **3** was tentatively assigned on the basis of uncompleted spectroscopic data (no α_D value is given) and biogenetic reasons.[7]

1,7-*diepi*-α-cedren-15-ol (**4**) was prepared from **3** by reduction with $NaBH_4$, and identified in the oil. Since the spectroscopical data of **4** were reported only partially,[8] the complete assignation of this compound has been realized after 2D NMR analyses (DQF-COSY, HMQC and NOESY).

The spectroscopic data of 1,7-*diepi*-β-cedrene (**10**), also present in the oil, was extensively studied using 2D NMR spectroscopy (^{13}C NMR of this compound has not previously reported in literature). As in the case of **3** and **4**, the assignment of the 1,7-*diepi*-cedrane stereochemistry was confirmed after noticing the existence of NOE in H12,

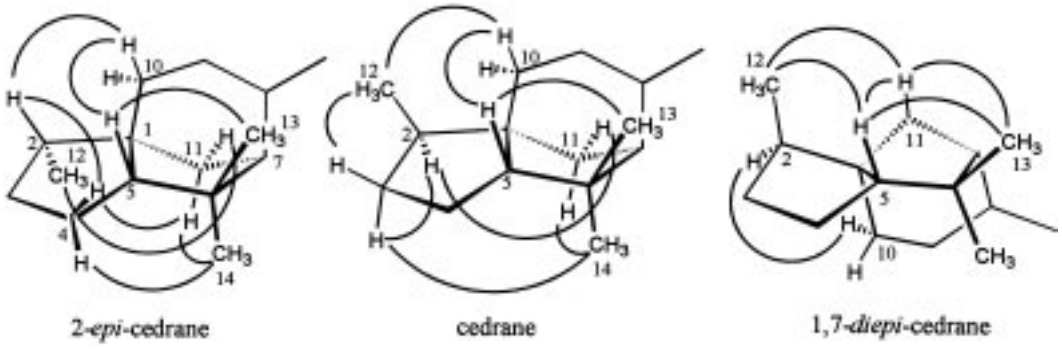


Figure 2. Characteristic NOEs for the cedrane, 2-*epi*-cedrane and 1,2-*diepi*-cedrane series.

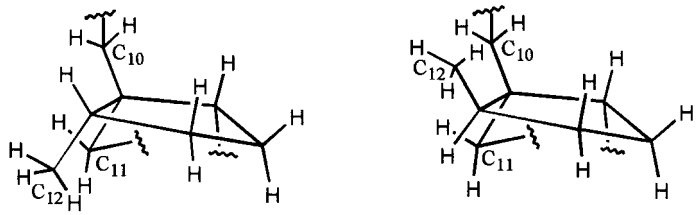


Figure 3. γ-Gauche effects observed when comparing ^{13}C NMR data of 2-*epi*-cedranes with those of normal series.

H13 and H11β after irradiating H5; and of H10β after irradiating H2 (Fig. 2). Furthermore, the obtention of **10** from 1,7-*diepi*-α-cedrenal (**3**), by treating **3** with *p*-toluenesulfonylhydrazine dissolved in DMF/sulfolane containing TsOH, and then heating the crude with $NaBH_3CN$, confirmed the structural relationship between these two compounds.

Compound **5** possesses a molecular formula of $C_{15}H_{22}O$, as deduced from its HR-EI-MS. The IR spectrum shows absorptions due to a double bond and ketone carbonyl (ν 1639 and 1730). The combined analysis of the ^1H NMR, ^{13}C NMR, HETCOR and COSY-DQF spectra indicated an α-cedrene skeleton containing a carbonyl group. The correlations of the carbonyl carbon with H2, H3 and H5 permitted its location at C4. The resonances of H5 (singlet) and H3 (both double doublet) in the ^1H NMR spectrum confirm this assignment.

As it happens in **1** and **2**, the enhancements observed in H13 and H10β after irradiating H5, and in H11α and H3α after irradiating H14, discarded the 1,7-*diepi*-cedrane stereochemistry for this compound. Considering the relative configuration at C2, the enhancements produced in H3α and H11β after irradiation at H2, and in H3β and H10β when H12 is irradiated, confirm unambiguously the β orientation of Me-12; and then, the assignment of the normal cedrane series stereochemistry for **5**.

The NOEs characteristic for each of the three cedrane arrangements depicted in Fig. 2, together with the compared ^{13}C NMR data shown in Table 2 and Fig. 3, afford an empirical method for distinguishing among the three different stereochemistry series.

In addition to the NOEs analysis, comparison of the ^{13}C NMR data of **3**, **4** and **10** and their corresponding isomers of the normal series (α-cedrenal and α-cedrenol, both present in the oil as traces, were prepared from α-cedrene via allylic oxidation with selenium dioxide) provided a second procedure to distinguish between both stereochemistries (Table 2).

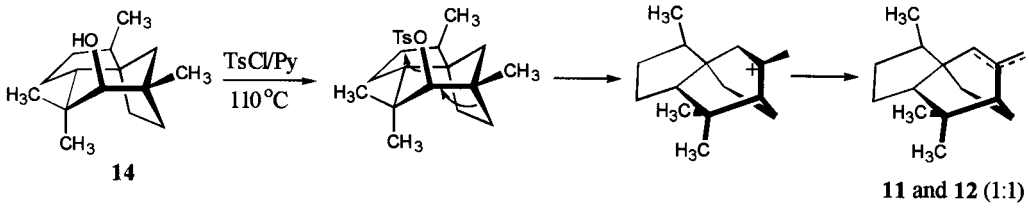
The essential oil of *J. thurifera* has also afforded three tricyclic sesquiterpenes presenting the unusual duprezianene skeleton (**6**, **11** and **12**). This finding led to the first complete structural study of this tricyclic structure via 2D NMR. The new natural product sesquithuriferol (**14**)[3] was also obtained from this plant. The NOEs observed between H7 and H9α and also between H12 and H15 permitted us to

Table 1. ^1H and ^{13}C NMR, DQF-COSY, HMBC and NOEDIFF data for Compound **3**

C	$\delta^{13}C$	DEPT	δ^1H (*J*=Hz)	COSY	HMBC	NOES
1	56.33	C	–	–	2,7,9,10αβ,11β,12	–
2	37.15	CH	1.50 (8.7, 1.2), *dq*	3αβ,12	3αβ,10α,11β,12	3α,10β,12
3	36.63	CH_2	α, 2.34, *m*	2,3β,4	–	2,4,10α
			β, 1.45, *m*	2,3α,4	4,5,12	3α
4	17.94	CH_2	α+β, 1.35, *m*	3αβ,5	2,3αβ,5	2,3α,10α,14
5	61.34	CH	2.06 (12.1, 1.8), *dd*	4αβ	2,3β,4αβ,7,9,10αβ 13,14	4,11β,12,13
6	36.43	C	–	–	7,11α,13,14	–
7	48.77	CH	3.01 (5.0), *d*	11β	9,11β,13,14,15	11β,13 14
8	149.44	C	–	–	7,10αβ	–
9	149.39	CH	α, 6.56 (3.6, 3.6, 1.1), *ddd*	10αβ	7,9,10αβ,11α,13 15	10αβ,15
10	38.53	CH_2	α, 2.54 (21.4, 3.6), *dd*	9,10α	–	3α,4,10β
			β, 2.14 (21.4, 3.6), *dd*	9,10β	2,5,9, 11β	2,9,10α
11	32.92	CH_2	α, 1.13 (10.8), *d*	11β	–	11β
			β, 1.73 (10.8, 5.0), *dd*	7, 11α	5,7,10β	9,5,7,11α 12
12	18.42	CH_3	0.91 (7.1), *d*	2	2, 3αβ,	2,11β,5
13	33.33	CH_3	1.11, *s*	14	5,7,14	5,7, 11β
14	22.55	CH_3	0.63, *s*	13	5,13	4,7,10α
15	191.82	CH	9.37, *s*	–	7,9	9

Table 2.

C	β-Cedrene	1,7-Di*epi*-β-cedrene	Δδ	α-Cedrenal	1,7-Di*epi*-α-cedrenal	Δδ	α-Cedrenol	1,7-Di*epi*-α-cedrenol	Δδ
4	25.7	19.5	−6.2	24.9	17.9	−7.0	24.9	18.1	−6.8
6	42.3	34.1	−8.2	48.0	36.4	−11.6	48.4	36.8	−11.6
11	45.1	34.3	−10.8	39.7	32.2	−7.5	40.7	33.9	−6.8
12	15.4	18.4	+3.0	15.6	18.4	+2.8	15.5	18.5	+3.0
13	25.9	35.3	+9.4	24.9	33.3	+8.4	25.6	33.9	+8.3
14	26.6	21.7	−4.9	27.4	22.6	−4.8	27.8	22.5	−5.3



Scheme 1.

distinguish between **14** and their epimers at C2 (isolated from *Rudbeckia laciniata*[9]) and C7 (isolated from *Eremofila georgei*[10]). Previously, only **11** had been tentatively reported to possess the duprezianane skeleton on the basis of partial spectral data and biogenetic considerations.[11] The structural and stereochemical assignation of α and β-duprezianene (**11** and **12**) was further confirmed by chemical correlation with sesquithuriferol. Thus, the treatment of **14** with tosyl chloride in pyridine produced, as was anticipated, a mixture of **11** and **12** (Scheme 1).

Compound **6** presents in its IR spectrum signals due to a carbonyl group and a double bond (ν 1741 and 1645). The HR-EI-MS is concordant with the molecular formula $C_{15}H_{22}O$. The ^1H and ^{13}C NMR spectra show a great resemblance with those of β-duprezianene, differing only in the additional presence of a carbonyl group.

Since the duprezianene skeleton has been spectroscopically fully characterized only in two previous occasions,[3,12] the detailed analysis of 2D NMR experiences (HETCOR, COSY-DQF and HMBC) has been included in Table 3.

The location of the ketone at C3 was confirmed after noticing the α-effect of the carbonyl group at C2 and C4 in the ^{13}C NMR spectrum, so the chemical shifts of these two carbons appear highly shielded with respect to the values found in **9** ($\Delta\delta_{C2}$ approx. 15 ppm, $\Delta\delta_{C4}$ approx. 13 ppm).

NOEDIFF experiences were performed in order to confirm the relative stereochemistry. Most of the enhancements observed were comparable to those observed in **12**. However, the NOEs observed for H2 and H12 indicate a change in the configuration at C2 with respect to α and β-duprezianene (Fig. 4).

Finally, the oxidation of sesquithuriferol (**14**) with Jones reagent gave the corresponding ketone **15**, also identified in the oil. This ketone had been previously isolated from *Eremophilia georgei* Diels and its synthesis acomplished,[13]

Table 3. ^1H and ^{13}C NMR, DQF-COSY, HMBC and NOEDIFF data for Compound **6**

C	$\delta^{13}C$	DEPT	δ^1H (*J*=Hz)	DQF-COSY	HMBC	NOES
1	42.9	C	–	–	2,4β,5,9α,11αβ	–
2	54.5	CH	1.89 (7.1, 1.1), *dq*	4β,12	12,9α	–
3	220.1	C	–	–	–	–
4	36.4	CH_2	α, 2.12 (19.1, 12.1), *dd*	4β,5	5	11α,14,5
			β, 2.28 (19.1, 9, 1.1), *ddd*	2,4α,5		–
5	48.5	CH	1.63 (12.1, 9, 1.9), *ddd*	4αβ,11β	4αβ,7,9α,11β,1314	2,9β,4β,13
6	32.6	C	–	–	4α,5,7,10β,13,14	–
7	48.2	CH	1.80 (3.6, 2), *dd*	10αβ	10β,15[a]b	–
8	149.3	C	–	–	9αβ,10αβ	–
9	40.8	CH_2	α, 2.01 (16.3), *br d*	9β,11α,15ab	2,5,7,11α,15ab	9β,11β,12
			β, 2.53 (16.3, 2.6, 2.6), *ddd*	9α,15ab	–	5,9α,15b
10	21.9	CH_2	α, 1.92, *m*	7,10β,11αβ	–	–
			β, 1.49 (13.5, 11.5, 9.3, 2), *dddd*	7,10α,11αβ	–	–
11	19.2	CH_2	α, 1.10, *m*	9α,10αβ,11β	2,5,7,9αβ,10αβ	–
			β, 1.28 (13.5, 9.3, 2, 1.9), *dddd*	5,10αβ,11α	–	9α,11α,12
12	7.9	CH_3	0.91 (7.1), *d*	2	2	4α,9α,11β
13	31.8	CH_3	1.02, *s*	14	5,7,14	5,4β,9β,7,15a
14	24.0	CH_3	0.94, *s*	13	5,13	4α,7,10α,11α
15	108.4	CH_2	a, 4.80, *m*	9αβ	7,9β	7,13
			b, 4.79, *m*	9αβ	–	9αβ,7

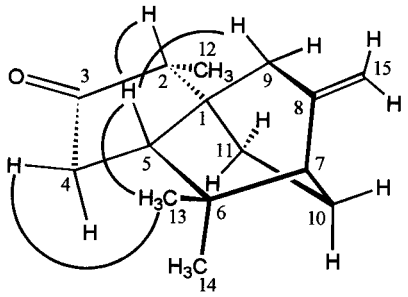


Figure 4. NOEs observed for **6**.

however the ^{13}C NMR data of this compound remained undescribed (Table 5).

Experimental

Optical rotations were determined on a Perkin–Elmer Model 141 polarimeter, using $CHCl_3$ as solvent. ^1H NMR, ^{13}C NMR and 2D NMR spectra were performed on a Bruker AMX 300 (^1H 300 MHz/^{13}C 75 MHz), Bruker ARX 400 (^1H 400 MHz/^{13}C 100 MHz) and Bruker AMX 500 (^1H 500 MHz/^{13}C 125 MHz) spectrometers using TMS as internal standard and $CDCl_3$ or C_6D_6 as solvents. Chemical shifts (δ) are expressed in parts per million (ppm) and coupling constants (J) in hertz. IR spectra were recorded on a Perkin–Elmer Model 983 G spectrometer with samples between sodium chloride plates (film). All mass spectra were registered on a Hewlett–Packard 5972A mass spectrometer using an ionizing voltage of 70 eV (EIMS) coupled to Gas Chromatograph Hewlett–Packard 5890A. HR-EIMS were registered on an Autospec-Q VG-Analytical (FISONS) mass spectrometer. Chromatographic separations were carried out by conventional column (or impregnated on 20% $AgNO_3$) on Merck silica gel 60 (70–230 mesh) using hexane/*t*-butylmethyl ether mixtures of increasing polarity or by flash chromatography on Merck silica gel 60 (230–400 mesh).

Isolation. The oil was obtained by steam distillation (1.8 kg of wood) using a circulatory Clevenger-type apparatus. 47.5 g (2.7%) of essential oil was obtained. Successive chromatographies on silica gel, silica gel impregnated on 20% silver nitrate and crystallizations led to the isolation of 40 mg of **1**, 51 mg of **2**, 53 mg of **3**, 6 mg of **5**, 5 mg of **6**,

Table 4. ^1H NMR data for compounds **1**, **2**, **4** and **5**

H	1	2	4	5
2	2.08 (7, 1.7), *dq*	2.08 (7, 1.9), *dq*	1.45, *m*	2.09 (8.0, 7.3, 2.2), *ddq*
3	–	–	α, 2.32, *m*	α, 2.78 (17.2, 8), *dd*
	–	–	β, 1.37, *m*	β, 1.96 (17.2, 2.2), *dd*
4	α, 2.17 (19.3, 5.5), *dd*	α, 2.23 (19.3, 5.2), *dd*	α, 1.37, *m*	–
	β, 2.45 (19.3, 12.3, 1.7), *ddd*	β, 2.44 (19.3, 12.4, 1.9), *ddd*	β, 1.31, *m*	–
5	1.98 (12.3, 5.5), *dd*	2.15 (12.4, 5.2, 1.3), *ddd*	1.99 (12.5, 6.8), *br dd*	1.94, *s*
7	1.76 (4.0), *d*	2.16 (4.7), *br d*	2.27 (5), *br d*	2.25 (4.6), *br d*
9	5.28, *br s*	α, 2.50, *m*	5.38, *m*	6.56 (3.6, 3.6, 1.1), *ddd*
	–	β, 2.38 (15.9, 7), *br dd*		
10	α, 1.86 (17), *br d*	α, 1.50 (7.9, 7, 2.9), *ddd*	α, 2.32, *m*	α, 1.78 (12.2, 8.1, 3.0), *ddd*
	β, 2.48 (17), *br d*	β, 1.85 (7,7), *dd*	β, 1.85, *m*	β, 1.49 (12.2, 6.7), *ddd*
11	α, 1.46 (12.2, 4.0), *dd*	α, 1.56 (11.7, 4.7, 2.9), *ddd*	α, 1.38 (10.2), *d*	α, 2.18 (11.9, 4.6, 3), *ddd*
	β, 1.32 (12.2), *d*	β, 1.13 (11.7), *br d*	β, 1.67 (10.2, 5), *dd*	β,1.36 (11.9), *br d*
12	0.96 (7.0), *d*	0.93 (7.0), *d*	0.88 (7.2), *d*	0.88 (7.3), *d*
13	1.11, *s*	1.02, *s*	1.07, *s*	1.08, *s*
14	0.90, *s*	0.90, *s*	0.82, *s*	0.99, *s*
15	1.70 (1.7), *bd*	a, 4.64 (2.4, 2.4), *dd*	a, 3.97 (14, 1.9), *dd*	a, 4.66 (2.5, 2.5), *dd*
	–	b, 4.58 (2.4, 2.4), *dd*	b, 3.92 (14, 1.9), *dd*	b, 4.60 (2.5, 2.5), *dd*

Table 5. ^{13}C NMR data for compounds **1**, **2**, **4**, **5**, **10** and **15**

C	1	2	4	5	10	15
1	51.73 (C)	52.76 (C)	56.02 (C)	53.76 (C)	55.73 (C)	54.01 (C)
2	51.82 (CH)	52.53 (CH)	37.45 (CH)	33.70 (CH)	37.47 (CH)	40.37 (CH)
3	219.88 (C)	219.81(C)	36.68 (CH_2)	47.83 (CH_2)	36.69 (CH_2)	31.70 (CH_2)
4	38.08 (CH_2)	38.04 (CH_2)	18.11 (CH_2)	220.19 (C)	19.50 (CH_2)	22.96 (CH_2)
5	52.46 (CH)	48.35 (CH)	61.30 (CH)	61.16 (CH)	59.89 (CH)	54.32 (CH)
6	48.79 (C)	43.16 (C)	36.83 (C)	45.28 (C)	34.11 (C)	45.72 (C)
7	52.55 (CH)	57.63 (CH)	53.84 (CH)	59.02 (CH)	63.08 (CH)	220.00 (C)
8	140.51 (C)	149.51 (C)	145.40 (C)	149.67 (C)	152.60 (C)	53.51 (C)
9	118.86 (CH)	29.23 (CH_2)	120.03 (CH)	29.90 (CH_2)	27.61 (CH_2)	35.31 (CH_2)
10	41.73 (CH_2)	37.79 (CH_2)	36.97 (CH_2)	33.27 (CH_2)	29.79 (CH_2)	33.52 (CH_2)
11	34.48 (CH_2)	38.24 (CH_2)	33.91 (CH_2)	44.47 (CH_2)	34.28 (CH_2)	45.35 (CH_2)
12	8.42 (CH_3)	8.85 (CH_3)	18.53 (CH_3)	18.26 (CH_3)	18.39 (CH_3)	19.94 (CH_3)
13	27.87 (CH_3)	25.99 (CH_3)	33.91 (CH_3)	26.25 (CH_3)	35.16 (CH_3)	29.48 (CH_3)
14	27.21 (CH_3)	27.90 (CH_3)	22.49 (CH_3)	26.30 (CH_3)	21.70 (CH_3)	24.79 (CH_3)
15	24.80 (CH_3)	109.17 (CH_2)	66.85 (CH_2)	109.07 (CH_2)	106.75 (CH_2)	21.81 (CH_3)

740 mg of **7**, 90 mg of **8**, 32 mg of **10**, 23 mg of **11**, 52 mg of **12**, and 46 mg of **14**.

2-*epi*-α-Cedren-3-one (1). Colourless oil. $[\alpha]_D=-71.9°$ (*c* 1.0, $CHCl_3$). IR (neat): ν 3020, 2961, 2870, 2826, 1737, 1451, 1371, 1373, 805. EIMS *m/z* (rel. int.): 218 (M^+, 75), 203 (M^+-CH_3, 3), 190 (6), 175 (13), 161 (13), 147 (28), 133 (9), 121 (100), 111 (17), 105 (44), 93 (62), 91 (38), 77 (27), 69 (33), 57 (35), 41 (34). HR-EIMS observed *m/z* 218.1675, required 218.1671. ^{1}H NMR ($CDCl_3$, 400 MHz, Table 4). ^{13}C NMR ($CDCl_3$, 100 MHz, Table 5).

2-*epi*-β-Cedren-3-one (2). Colourless oil. $[\alpha]_D=-13.4°$ (*c* 1.0, $CHCl_3$). IR (neat): ν 3069, 2965, 2931, 2870, 1737, 1640, 1367, 888. EIMS *m/z* (rel. int.): 218 (M^+, 64), 203 (M^+-CH_3, 52), 190 (3), 175 (13), 162 (14), 149 (24), 146 (16), 133 (5), 121 (74), 105 (22), 93 (100), 91 (38), 79 (40), 69 (48), 53 (15), 41 (38). HR-EIMS observed *m/z* 218.1672, required 218.1671. ^{1}H NMR ($CDCl_3$, 400 MHz, Table 4). ^{13}C NMR ($CDCl_3$, 100 MHz, Table 5).

1,7-*diepi*-α-Cedrenal (3). Colourless oil. $[\alpha]_D=+25°$ (*c* 1.1, $CHCl_3$). IR (neat): ν 2954, 2873, 2806, 2710, 1683, 1645, 1378, 1365, 815. EIMS *m/z* (rel. int.): 218 (M^+, 24), 203 (M^+-CH_3, 13), 200 (M^+-H_2O, 6), 189 (14), 175 ($M^+-C_3H_7$, 34), 162 (18), 147 (25), 133 ($M^+-C_3H_7-C_3H_6$, 100), 123 (20), 105 (58), 91 (56), 79 (40), 69 (54), 55 (29), 41 (61). HR-EIMS observed *m/z* 218.1675, required 218.1670. ^{1}H NMR ($CDCl_3$, 400 MHz, Table 1), ^{13}C NMR ($CDCl_3$, 75 MHz, Table 1).

Synthesis of 1,7-*diepi*-α-cedrenol (4) from 3. To a solution of 23 mg of **3** (0.11 mmol) in absolute ethanol, 10 mg (0.15 mmol) of $NaBH_4$ were added. After stirring for 1 h, 10 ml of brine were added and the mixture extracted with ether. Usual work-up gave a crude which was concentrated to obtained 2 mg of **4** (H:E 9:1, 0.009 mmol, 8%). Colourless oil. $[\alpha]_D=+36.8°$ (*c* 0.2, $CHCl_3$). IR (neat): ν 3366, 2925, 2857, 1645, 1375, 1363, 1041, 804. EIMS *m/z* (rel. int.): 220 (M^+, 10), 202 (M^+-H_2O, 3), 189 (M^+-CH_2-OH, 7), 177 ($M^+-C_3H_7$,13), 159 (6), 147 (14), 135 ($M^+-C_3H_7-C_3H_6$, 100), 121 (15), 105 (29), 91 (34), 79 (43), 69 (24), 55 (17), 41 (26). ^{1}H NMR ($CDCl_3$, 400 MHz, Table 4). ^{13}C NMR ($CDCl_3$, 100 MHz, Table 5).

α-Cedren-4-one (5). Colourless oil. $[\alpha]_D=+97.6°$ (*c* 0.5, $CHCl_3$). IR (neat): ν 3071, 2934, 1730, 1639, 886. EIMS *m/z* (rel. int.): 218 (M^+, 55), 203 (M^+-CH_3, 5), 200 (M^+-H_2O, 1), 176 (24), 161 (5), 148 (66), 133 (21), 120 (100), 105 (28), 91 (29), 83 (36), 67 (7), 55 (15), 41 (20). HR-EIMS observed *m/z* 218.1672, required 218.1671. ^{1}H NMR ($CDCl_3$, 400 MHz, Table 4). ^{13}C NMR ($CDCl_3$, 100 MHz, Table 5).

2-*epi*-β-Duprezianen-3-one (6). Colourless oil. $[\alpha]_D=-36.0°$ (*c* 0.43, $CHCl_3$). IR (neat): ν 3066, 2957, 2870, 1741, 1645, 1375, 1364, 875. EIMS *m/z* (rel. int.): 218 (M^+, 53), 203 (M^+-CH_3, 3), 200 (M^+-H_2O, 0.3), 190 ($M^+-C_2H_4$, 2), 162 (6), 147 (8), 133 (5), 121 (100), 105 (25), 91 (37), 79 (24), 69 (93), 53 (14), 41 (44). HR-EIMS observed *m/z* 218.1672, required 218.1671. ^{1}H NMR ($CDCl_3$, 400 MHz, Table 3). ^{13}C NMR ($CDCl_3$, 100 MHz, Table 3). COSY-DQF ($CDCl_3$, 400 MHz, Table 3). HETCOR ($CDCl_3$, ^{1}H 400 MHz/^{13}C 100 MHz). HMBC ($CDCl_3$, ^{1}H 400 MHz/^{13}C 100 MHz, Table 3). NOEDIFF ($CDCl_3$, 500 MHz, Table 3).

1,7-*diepi*-β-Cedrene (10). Colourless oil. IR (neat): ν 3067, 2951, 2870, 1640, 1374, 1363, 880. EIMS *m/z* (rel. int.): 204 (M^+, 17), 189 (M^+-CH_3), 147 (9), 133 (40), 120 (39), 109 (22), 105 (33), 93 (59), 91 (56), 79 (34), 69 (84), 55 (36), 41 (65). HR-EIMS observed *m/z* 204.1889, required 204.1878. ^{13}C NMR ($CDCl_3$, 100 MHz, Table 5).

Synthesis of 1,7-*diepi*-β-cedrene (10) from 1,7-*diepi*-cedrenal (3). To a solution of 55 mg (0.25 mmol) of **3** and 63 mg (0.32 mmol) of tosylhidrazine in 1.6 ml of DMF/Sulfolane (1:1) 6.0 mg of anhydrous TsOH were added under inert atmosphere. The mixture was heated to 100°C and after 10 min 63 mg of $NaBH_3CN$ (1 mmol) were added. After stirring for 10 min, 1.6 ml of anhydrous cyclohexane were then added. After 6 h, the usual work-up[14] yielded 45 mg of reaction mixture, which was cc to give 1,7-*diepi*-β-cedrene (**10**, 15 mg, 0.07 mmol, *R*=28%) and 57 mg of the corresponding tosylhydrazone (0.16 mmol, *R*=64%).

Oxidation of α-cedrene with SeO_2. To 220 mg α-cedrene (1.1 mmol) in 1.5 ml of ethanol, a solution of 480 mg (4.32 mmol) of SeO_2 was added dropwise. After refluxing for 17 h, 10 ml of water were added, and then the mixture was worked-up as usual. The reaction mixture was chromatographed to yield 175 mg of cedrenal (**9**, 73%) and cedrenol (**13**, 10 mg, 5%).

Obtention of sesquithuriferona (15) from sesquithuriferol (14). Jones reagent was added dropwise to a solution of 22 mg (0.1 mmol) of **14** in acetone (5 ml) at 0°C. After TLC control, usual work-up gave 20 mg of **15** (0.09 mmol, *R*=90%). Colourless oil, $[\alpha]_D=+5.7°$ (*c* 1.0) IR (neat): ν 2956, 2870, 1699, 1375,1358, 1040 and 1021. EIMS *m/z* (rel. int.): 220 (M^+, 42), 205 (M^+-CH_3, 8), 202 (M^+-H_2O, 5), 192 ($M^+-C_2H_4$, 32), 177 (13), 149 (23), 147 (27), 136 (16), 121 (100), 108 (45), 93 (28), 81 (70), 67 (18), 55 (23), 41 (47). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.13 (3H, *s*, H-15), 1.10 (3H, *s*, H-13), 1.10 (3H, *s*, H-14), 0.90 (3H, *d* (*J*=7.1 Hz), H-12). ^{13}C NMR ($CDCl_3$, 75 MHz, Table 5).

Solvolysis of the tosylate derivative of sesquithuriferol (14) to give α and β-duprezianene (11 and 12). To 27 mg of **14** (0.12 mmol) in 4 ml of pyridine, 116 mg (0.6 mmol) of TsCl were added under inert atmosphere. The resulting solution was refluxed for 6 h. Addition of water, extraction with ether and washing of the organic extracts with $KHSO_4$ led to obtain 40 mg of reaction crude, which was chromatographed with silica gel impregnated on 20% $AgNO_3$ to give 17 mg of **11** (0.05 mmol, 34%) and 17 mg of **12** (0.05 mmol, 34%).

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