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TETRAHEDRON

Allohimachalane, *seco*-allohimachalane and himachalane sesquiterpenes from *Illicium tsangii*.

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Abstract: The dichloromethane extract of *I. tsangii* has yielded ten novel sesquiterpenes (**1-4**, **6-11**) possessing or derived from the very rare allohimachalane skeleton, in addition to one new himachalane (**12**) and a new megastigmane (**14**). It is suggested that the novel skeletons possesed by *seco*-allohimachalanes **8-11** are the result of carbon-carbon bond cleavage reactions associated with hydroperoxide autoxidation products (e.g. **6**, **7**) of the tri-substituted double bond.

INTRODUCTION

Illicium tsangii A.C. Sm. (Illiciaceae) is a poisonous shrub from southern China which is used in traditional medicine for treating pain.[1] No previous phytochemical investigations of *I. tsangii* have been reported, although the Illicium family is known to be characterized by oligomeric neolignans,[2-6] prezizaane sesquiterpenes [8-21] and cycloartane triterpenes.[3]

RESULTS AND DISCUSSION

Extraction of the aerial parts of *I. tsangii* with CH_2Cl_2 followed by separation by CC and HPLC has yielded thirteen sesquiterpenoids **1-13**, of which eleven are novel. The molecular formula of compound **1** was established as $C_{15}H_{26}O_2$ by HREIMS. Analysis of 1D-NMR and IR spectra revealed the presence of one endocyclic double bond (δ_C 138.6 C; 130.1 CH; δ_H 5.41, d, J = 5.6 Hz) and two secondary hydroxyl groups (δ_C 78.4 CH, 71.2 CH; δ_H 3.83, d, J = 10.7 Hz, 4.13 br d; IR ν_{max} 3435 (br)). In consequence, compound **1** must be a bicyclic sesquiterpene. The allohimachalane skeleton of **1** was established by means of HSQC (Tables 1 and 2), HMBC (Figure 1) and ^{1}H-^{1}H COSY (Figure 1) 2D-NMR experiments. Analysis of coupling constants and NOESY correlations (Figure 2) established the relative configuration of **1** to be as shown.

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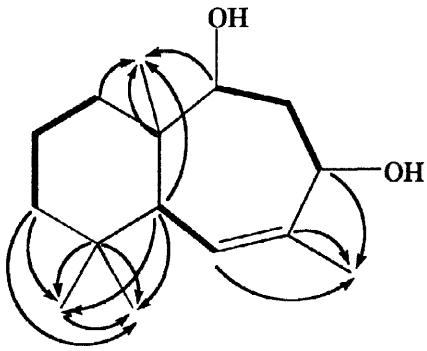


Figure 1. HMBC correlations (indicated by arrows from ^{13}C to ^{1}H) and ^{1}H-^{1}H COSY correlations (indicated by heavy lines) used in assigning the structure of **1**

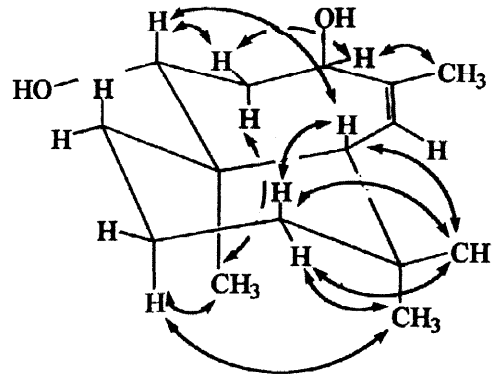
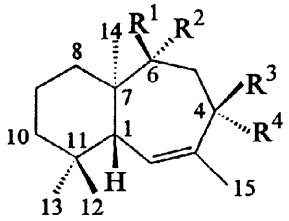
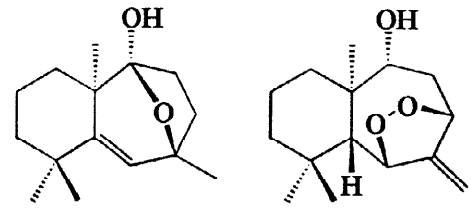


Figure 2. Critical NOESY correlations used in establishing the relative configuration of **1** (indicated by double-headed arrows from ^{1}H to ^{1}H)



1 $R^1 = R^4 = H$, $R^2 = R^3 = OH$
2 $R^1 = H$, $R^2 = OH$, R^3, $R^4 = O$
3 R^1, $R^2 = O$, $R^3 = OH$, $R^4 = H$
4 R^1, $R^2 = O$, $R^3 = R^4 = H$
5 $R^1 = R^3 = R^4 = H$, $R^2 = OH$



6 **7**

Compound **2** was shown to be the 4-keto derivative of **1** and compound **3** was assigned as the isomeric 6-keto analogue from results of rigorous 2D-NMR analysis. Similarly, compound **4** is the 4-deoxy analogue of **3**, whilst compound **5** is the known natural product allohimachalol which has been reported previously as a constituent of *Cedrus deodara*,[22] *Schistostephium crataegifolium*[23] and *Artemisia vestita*.[24] To the best of our knowledge, only one other representative of the allohimachalane class of sesquiterpenes is known as a natural product: dipterolone[25] from *Dipterocarpus macrocarpus*, which was isolated in 1974 and assigned a *cis* ring junction, by analogy with allohimachalol, as formulated at that time.[26,27] Allohimachalol is now thought to be *trans*-ring fused and more recent reports of the ^{13}C NMR spectrum[28] and partial ^{1}H NMR data[23] for allohimachalol gave excellent agreement with our NMR data for **5** (Tables 1 and 2). NOESY correlations for **5** were similar to those observed for **1** which confirmed the expected relative stereochemistry at the 1, 6 and 7-positions (including the *trans*-ring fusion). The absolute stereochemistry of the secondary alcohol was established by derivitization with the (*S*)-(+)- and (*R*)-(-)- forms of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPCl) to form Mosher esters[29] **5a** and **5b**, respectively (Figure 3). Calculation of differences for all ^{1}H chemical shifts of the two esters (Δ $\delta^{1}H$ NMR values for the (*S*)-OMTP ester minus the (*R*)-OMTP ester)[29] indicated the absolute stereochemistry at C-6 to be *R*. Compound **5** is therefore 1*R*, 6*R*, 7*R* and all other allohimachalanes reported herein are assumed to share the same stereochemistry.

Table 1 ^{13}C NMR assignments for compounds **1-13**

Atom	1	2	3	4	5	6	7	8	9	10	11	12	13
1	48.0	51.4	47.5	47.7	49.2	149.2	58.5	82.3	218.0	214.5	48.9	38.7	45.3
2	130.1	140.8	129.7	126.1	126.5	126.1	89.8	97.4	161.0	-	50.8	64.5	72.1
3	138.6	139.6	136.1	134.5	138.1	79.7	149.1	209.3	207.8	206.9	217.3	57.5	135.2
4	71.2	202.8	71.3	32.0	29.8	37.7	85.3	41.4	40.0	37.0	66.5	27.9	127.3
5	37.1	47.9	46.9	37.1	31.1	34.2	38.9	21.8	22.7	32.0	35.5	19.6	26.5
6	78.4	77.5	218.0	218.3	86.3	107.5	77.5	85.1	77.1	206.9	74.1	43.6	45.8
7	41.2	42.4	52.5	54.9	39.2	45.9	42.5	47.2	51.5	62.4	40.4	74.5	74.2
8	38.3	38.6	35.0	35.2	38.8	32.9	38.9	30.5	32.0	35.2	37.3	40.5	41.5
9	18.3	18.8	18.4	18.4	18.3	19.2	18.8	17.7	17.2	18.3	18.2	18.6	18.3
10	42.2	41.3	41.3	41.5	42.4	43.2	42.3	38.2	38.6	39.9	43.4	44.2	44.8
11	35.5	33.5	32.5	32.8	33.3	37.2	33.5	36.1	44.6	46.2	34.1	36.5	35.8
12	33.2	33.5	33.4	33.4	33.3	32.2	33.8	27.1	27.1	26.0	36.5	32.2	32.2
13	22.0	21.4	20.8	21.2	22.6	26.4	23.8	22.8	28.1	26.8	22.7	28.4	28.7
14	12.6	16.3	17.1	16.9	13.7	20.3	13.7	16.2	22.3	24.0	12.1	32.3	31.9
15	25.3	19.1	23.0	25.5	25.8	24.4	102.5	29.9	30.0	30.0	33.9	24.3	21.1

Table 2 ^{1}H NMR assignments for compounds **1-13**

Atom	1	2	3	4	5	6	7	8	9	10	11	12	13
1	2.12	2.16	2.96	2.78	1.66	-	1.49	-	-	-	1.94	2.46	2.13
2	5.41	6.32	5.53	5.36	5.26	5.40	5.34	5.38	8.02	-	2.90	3.09	3.88
4α	4.13	-	4.16	2.44	1.83	1.77	5.00	2.49	2.48	2.60	3.94	2.00	5.61
4β	-	-	-	2.15	2.17	1.77	-	2.71	2.45	2.69	-	1.78	
5α	1.70	2.93	3.65	3.46	1.37	2.50	1.83	1.49	1.63	2.49	1.55	1.34	2.00
5β	2.00	2.86	2.72	2.23	1.64	1.69	2.55	1.62	1.88	2.88	1.94	1.50	2.00
6	3.83	3.61	-	-	3.18	-	4.00	3.94	5.35	-	3.75	1.97	1.99
8α	1.90	1.52	1.40	1.46	1.93	1.69	1.75	1.36	1.97	2.53	1.84	1.39	1.47
8β	1.14	1.18	1.32	1.38	1.09	1.55	1.09	1.36	1.69	1.42	1.06	1.68	1.75
9α	1.53	1.73	1.67	1.63	1.54	1.83	1.69	1.59	0.79	1.62	1.60	1.43	1.40
9β	1.44	1.54	1.55	1.51	1.44	1.59	1.55	1.47	1.77	1.86	1.47	1.70	1.67
10α	1.45	1.52	1.51	1.48	1.44	1.54	1.43	1.41	1.68	1.69	1.35	1.47	1.38
10β	1.15	1.12	1.15	1.16	1.11	1.21	1.28	1.37	1.62	1.63	1.28	1.65	1.56
12	0.86	0.86	0.95	0.92	0.83	1.02	1.04	0.87	1.05	1.04	0.71	1.10	1.01
13	0.98	1.06	0.99	0.97	1.01	1.15	0.96	1.04	1.14	1.11	1.03	1.00	0.71
14	0.81	1.05,	1.10	1.12	0.79	1.27	1.23	1.02	1.15	1.31	0.96	1.21	1.26
15	1.82	1.86	1.82	1.68	1.77	1.37	4.89 4.88	2.14	2.13	2.19	2.44	1.32	1.81

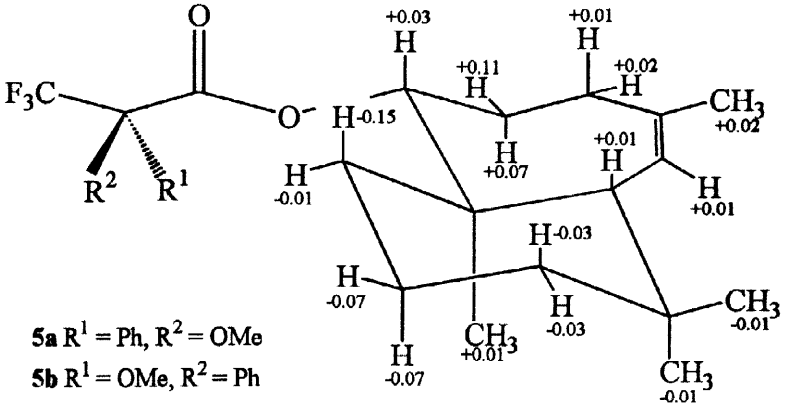
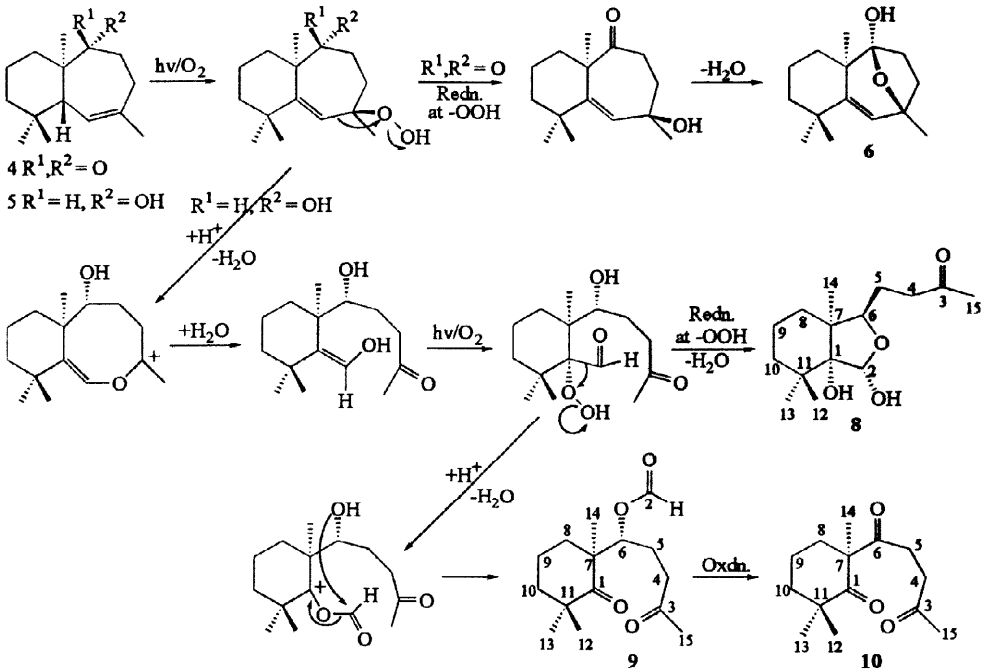


Figure 3. Δ δ^1H NMR values for **5b** - **5a** used in determining the absolute stereochemistry of **5**.

The results of 2D-NMR spectroscopy established that the double bond in compound **6** had shifted to the 1-position and that an oxygen substituent had been introduced at the 3-position. The structure of **6** is suggestive of autoxidation at the tri-substituted Δ^2-double bond of **4**, occurring by addition of singlet molecular oxygen *via* an "ene-type" mechanism,[30] followed by reduction of the resulting tertiary hydroperoxide group and ensuing intramolecular cyclization of the 3-hydroxyl group with the 6-ketone group to form a hemi-ketal as shown in Scheme 1. ^{13}C/DEPT NMR spectra of **7** showed the presence of three oxygenated carbons (δ_C 89.8 CH, 85.3 CH, 77.5 CH) one of which was substituted by a hydroxyl group, as demonstrated by an upfield shift in resonance following exchange with D_2O (δ_C 77.5 Δ δ^{13}C +0.13 ppm; other resonances showed no significant change).[31] The endoperoxide group in compound **7** might also be rationalized as the product of autoxidation proceeding *via* an alternative "ene-type" reaction at the Δ^2-double bond of compound **1** which forms a secondary allylic hydroperoxide as the initial product (rather than a tertiary hydroperoxide as for **6**). NOESY experiments confirmed that the oxidation products **6** and **7** shared the same relative stereochemistry as the allohimachalanes **1-5** and indicated that the oxygen of the new heterocyclic ring was β-oriented in both cases. Hashidoko *et al.*[32-34] have obtained similar oxygenated cyclic intermediates which are proposed to arise during the autoxidation of carotane sesquiterpenes.

The allohimachalane skeleton can be seen to have undergone carbon-carbon bond cleavage in compounds **8-11**. ^{13}C/DEPT NMR spectra of **8** revealed three oxygenated carbons (δ_C 97.4 CH, 85.1 CH, 82.3 C), two of which underwent significant upfield shifts as a result of secondary isotope effects associated with the conversion of an -OH group to an -OD group (δ_C 97.4 Δ δ^{13}C +0.14 ppm; δ_C 82.3 Δ δ^{13}C +0.12 ppm) and therefore bear hydroxyl groups.[31] The structure of **8** was established as a 2,3-*seco*-allohimachalane incorporating a tetrahydrofuran ring vicinally substituted by these two hydroxyl groups by 2D-NMR (Tables 1 and 2; Figure 4). Compounds **9** and **10** were shown to be *bis*-1,2-2,3-*seco*-allohimachalanes in the same manner. The relative stereochemistry of *seco*-sesquiterpenes **8, 9** and **10** as established by NOESY was consistent with their formation from allohimachalanes such as **1-5** by oxidative cleavage of the 2,3-double bond.



Scheme 1. Possible biogenesis of **6**, **8**, **9** and **10** from **4** and **5** by autoxidation reactions.

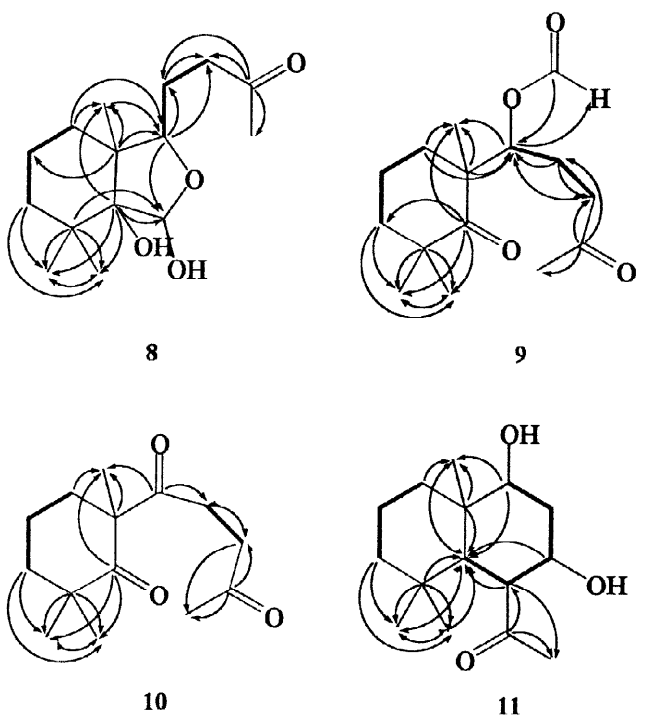
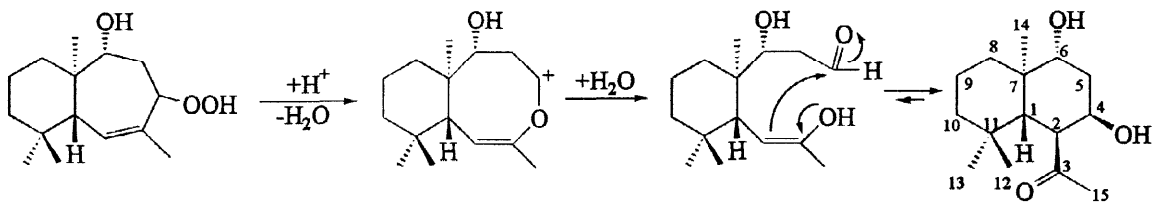


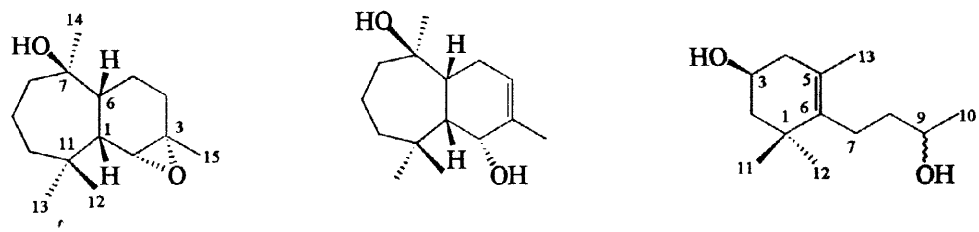
Figure 4. 2,3-*seco*-Allohimachalane skeleton of **8**; *bis*-1,2-2,3-*seco*-allohimachalane skeleton of **9** and **10**; and 3,4-*seco*-allohimachalane skeleton of **11** as established by HMBC (arrows from ^{13}C to ^{1}H) and ^{1}H-^{1}H COSY (heavy lines).

We propose that autoxidation of allohimacholol **5** initially produces a tertiary hydroperoxide analogous to that postulated in the biogenesis of **6** from **4**. This hydroperoxide is unable to undergo hemiketal formation; instead, protonation of the terminal oxygen atom and ensuing loss of water accompanied by a 1,2-shift of the alkene group to the developing carbocation on the internal oxygen atom leads to 2,3-bond cleavage and ultimately to production of a 2-enol 3-ketone intermediate. Haynes and Vonwiller[35] have provided evidence for just such a 1,2-shift in the rearrangement of a tertiary allylic hydroperoxide[30] derived from artemisinic acid which was proposed to account for carbon-carbon bond cleavage in the biogenesis of the important anti-malarial compound, qinghaosu (artemisinin). Following a second autoxidation reaction of the more nucleophilic enolic double bond, reduction of the new tertiary hydroperoxide group and intramolecular ketalization, compound **8** is obtained. Alternatively, elimination of water from this new hydroperoxide accompanied by rearrangement (as before) may lead to a second cleavage, this time at the 1,2-bond, resulting in product **9**. Further oxidation of the formyl ester group in **9** yields the triketone **10**. The structure of compound **11** can be rationalized as that of a 3,4-*seco*-allohimachalane, perhaps produced by intramolecular aldol condensation of the enol and aldehyde groups generated during an analogous 3,4-bond scission process associated with the transposed secondary allylic hydroperoxide autoxidation product shown in Scheme 2. The 2-acetyl and 4-hydroxyl substituents on the new cyclohexane ring in **11** generated by this proposed aldol reaction were both shown to be on the β-face of the molecule by NOESY. This configuration allows formation of an intramolecular hydrogen bond between these two functional groups, which is consistent with new 2,4-carbon-carbon bond formation of the more thermodynamically favoured diastereoiosmer occurring by a reversible aldol reaction.



11

Scheme 2. Possible formation of **11** by aldol reaction of a 3,4-*seco*-allohimachalane



12 **13** **14**

Compounds **12** and **13** were shown to belong to the himachalane series of sesquiterpenes by 2D-NMR in the same manner as for compounds **1-11**. Although far from common, the himachalane skeleton is

much more frequently reported[36-43] in the literature than the allohimachalane skeleton. The novel himachalane **12** is formally the epoxide of the known compound himachalol for which a *cis* ring-fusion has been proposed.[44] Compound **13** is the known compound centdarol[45,46] which can be formally derived from **12** by epoxide ring opening. The ^{1}H NMR (as reported by Kulshreshtha and Rastogi[45]) and ^{13}C NMR data (as reported by Prakash *et al.*[47]) of centdarol agreed well with that for compound **13** (reversed assignments for C-2/7 C-5/10 are corrected in Table 1), even though the stereochemistry at the 7-position of centdarol was differently assigned in the two reports. Our own independent analysis by NOESY confirmed that the 14-methyl group for both **12** and **13** is correctly assigned to the α-configuration (as reported for centdarol by Prakash *et al.*[47]) and also confirmed the *cis*-ring junction.

Compound **14** (relative stereochemistry only indicated) was shown to be a novel megastigmane by 2D-NMR. Megastigmanes are believed to be produced by photo-oxygenation reactions of tetraterpenes such as β-carotene, yielding degraded C_{11} and C_{13} products.[48,49] It is interesting to note that the mechanism for oxidative cleavage of the unsaturated β-carotene chain has been postulated to involve initial reaction of singlet molecular oxygen with double bonds, producing allylic hydroperoxides, which then become involved in promoting carbon-carbon bond cleavage reactions in a manner reminiscent of that postulated for the the *seco*-allohimachalanes in this study.

EXPERIMENTAL

Chemical shifts are expressed in ppm (δ) relative to TMS as internal standard. All NMR experiments were run on a Bruker DRX 500 instrument with $CDCl_3$ as solvent. HSQC and HMBC experiments were recorded with 2048 data points in F_2 and 128 data points in F_1. HREIMS were recorded at 70 eV on a Finnigan-MAT 95 MS spectrometer. FTIR spectra were recorded in $CHCl_3$ on a Shimadzu FTIR-8201 PC instrument. TLC plates were developed using *p*-anisaldehyde. Column chromatography was performed using silica gel 60-200 μm (Merck). HPLC separations were performed using a PREP-SIL 20 mm x 25 cm column, flow rate 8 ml/min.

Extraction and Separation Leaf tissue of *I. tsangii* (750 g) was obtained from Conghua county, Guangdong province, China; a voucher specimen (Q. Lin and G. Hao 939) has been deposited in the herbarium of the University of Hong Kong (HKU) and the IBSC herbarium. The sample was ground to a fine powder under liq. N_2 and immediately extracted with CH_2Cl_2. The organic extract was then dried and solvent removed under red. pres. to yield a dark green oil (16.6 g; 2.2 % w/w) which was separated chromatographically: **1** (28 mg, R_f 30.3 min, 50% EtOAc/hexane/1% AcOH), **2** (21 mg, R_f 47.6 min, 18% EtOAc/hexane); **3** (25 mg, R_f 34.3 min, 23% EtOAc/hexane), **4** (8 mg, R_f 24.6 min, 2% EtOAc/hexane); **5** (232 mg, R_f 18.4 min, 15% EtOAc/hexane); **6** (35 mg, R_f 20.5 min, 16% EtOAc/hexane); **7** (9 mg, R_f 41.6 min, 35% EtOAc/hexane), **8** (162 mg, R_f 22.8 min, 45% EtOAc/hexane); **9** (110 mg, R_f 33.9 min, 18% EtOAc/hexane), **10** (3.7 mg, R_f 20.7 min, 20% EtOAc/hexane), **11** (9 mg, R_f 38.7 min, 50% EtOAc/hexane/1% AcOH); **12** (2 mg, R_f 24.0 min, 23% EtOAc/hexane), **13** (4 mg, R_f 28.2 min, 50% EtOAc/hexane/1% AcOH); **14** (11 mg, R_f 19.7 min, 50% EtOAc/hexane/1% AcOH).

Tsangane A (4β,6α-dihydroxyallohimachal-2-ene) (1): Crystal. mp 212-213°C; $[\alpha]_D$ +59.4° (*c* 0.1, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3435 (br), 2928, 2851, 1437, 1373 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.41 (1H, d, *J* = 5.6 Hz), 4.13 (1H, br d), 3.83 (1H, d, *J* = 10.7 Hz), 2.12 (1H, d, *J* = 5.6 Hz), 1.82 (3H, s), 0.98 (3H, s), 0.86 (3H, s), 0.81 (3H, s). HREIMS *m/z* (rel. int.) 238.1928 [M^+, $C_{15}H_{26}O_2$ requires 238.1932] (8), 220 (8), 205 (25), 202 (2), 177 (13), 155 (25), 135 (29), 123 (49), 109 (60), 99 (100).

Tsangane B (6α-hydroxyallohimachal-2-en-4-one) (2): Oil. $[\alpha]_D$ +73.4° (*c* 0.11, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3422 (br), 3015, 2957, 2930, 2874, 1717, 1661, 1458, 1375 cm^{-1}. ^1H NMR δ ($CDCl_3$): 6.32 (1H, dd, *J* = 6.6, 1.4 Hz), 3.61 (1H, br m), 2.93 (1H, dd, *J* = 16.4, 6.7 Hz), 2.86 (1H, dd, *J* = 16.4, 2.3 Hz), 2.16 (1H, d, *J* = 6.6 Hz), 1.86 (3H, s), 1.06 (3H, s), 1.05 (3H, s), 0.86 (3H, s) HREIMS *m/z* (rel. int.) 236.1769 [$M^{+\cdot}$ $C_{15}H_{24}O_2$ requires 236.1776] (60), 221 (14), 192 (100), 177 (74), 149 (35), 135 (40), 123 (70), 122 (70), 109 (65), 95 (49).

Tsangane C (4β-hydroxyallohimachal-2-en-6-one) (3): Oil. ^1H NMR δ ($CDCl_3$): 5.53 (1H, dd, *J* = 6.4, 1.4 Hz), 4.16 (1H, dd, *J* = 10.1, 7.2 Hz) 3.65 (1H, dd, *J* = 10.9, 10.1 Hz), 2.96 (1H, d, *J* = 6.4 Hz), 2.72 (1H, dd, *J* = 10.9, 7.2 Hz), 1.82 (3H, s), 1.10 (3H, s), 0.99 (3H, s), 0.95 (3H, s). HREIMS *m/z* (rel. int.) 236.1775 [M^+, $C_{15}H_{24}O_2$ requires 236.1776] (12), 218 (13), 179 (16), 173 (27), 149 (84), 121 (86), 109 (100), 93 (64).

Tsangane D (Allohimachal-2-en-6-one) (4): Oil. $[\alpha]_D$ -61.1° (*c* 0.27, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3020, 2930, 2855, 1686, 1541, 1458, 1375 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.36 (1H, d, *J* = 5.2 Hz), 3.46 (1H, td, *J* = 11.4, 6.5 Hz), 2.78 (1H, d, *J* = 5.2 Hz), 2.44 (1H, m), 2.23 (1H, ddd, *J* = 11.4, 6.1, 3.7 Hz), 2.15 (1H, m), 1.68 (3H, s), 1.12 (3H, s), 0.97 (3H, s), 0.92 (3H, s). HREIMS *m/z* (rel. int.) 220.1823 [M^+, $C_{15}H_{24}O$ requires 220.1827] (100), 205 (44), 177 (43), 163 (54), 138 (76), 121 (66), 107 (68).

Allohimachalol (6α-Hydroxyallohimachal-2-ene) (5): Oil. $[\alpha]_D$ +27.8° (*c* 3.1, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3342 (br), 2930, 2870, 2855, 1458, 1369 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.26 (1H, d, *J* = 4.9 Hz), 3.18 (1H, dd, *J* = 11.3, 3.4 Hz), 2.17 (1H, t, *J* = 13.5 Hz), 1.77 (3H, s), 1.01 (3H, s), 0.83 (3H, s), 0.79 (3H, s). HREIMS *m/z* (rel. int.) 222.1976 [M^+, $C_{15}H_{26}O$ requires 222.1984] (33), 204 (51), 189 (33), 163 (64), 123 (52), 119 (66), 107 (100), 93 (77).

Tsangane E (3β,6β-epoxy-allohimachal-1-en-6α-ol) (6): Oil. $[\alpha]_D$ -12.6° (*c* 0.78, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3300 (br), 2934, 2870, 1460, 1377 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.40 (1H, s), 2.69 (1H, br s, -OH), 2.50 (1H, m), 1.37 (3H, s), 1.27 (3H, s), 1.15 (3H, s), 1.02 (3H, s). HREIMS *m/z* (rel. int.) 236.1782 [M^+, $C_{15}H_{24}O_2$ requires 236.1776] (41), 221 (100), 203 (18), 193 (19), 180 (49), 161 (68), 133 (22), 121 (45), 107 (73), 93 (39).

Tsangane F (2β,4β-Epidioxy-allohimachal-3(15)-en-6α-ol) (7): Oil $[\alpha]_D$ +14.4° (*c* 0.1, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3400 (br), 2932, 2872, 2854, 1458, 1373, 1016 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.34 (1H, s), 5.00

(1H, dd, J = 4.6, 1.1 Hz), 4.89 (1H, d, J = 1.0 Hz), 4.88 (1H, s), 4.00 (1H, dd, J = 10.1, 5.5 Hz), 2.55 (1H, m), 1.23 (3H, s), 1.04 (3H, s), 0.96 (3H, s). CIMS *m/z* (rel. int.) 253 [M+1] (3), 251 (7), 237 (10), 235 (19), 219 (57), 217 (100), 201 (46). HREIMS *m/z* (rel. int.) 236.1763 [M^+-O, $C_{15}H_{24}O_2$ requires 236.1776] (2), 234 (M^+-H_2O) (5), 203 (13), 175 (17), 149 (60), 121 (41), 109 (59), 95 (59).

Tsangane G (**8**): Oil. $[\alpha]_D$ +30.5° (*c* 2.15, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3485 (br), 2939, 2872, 1713, 1514, 1464, 1367 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.38 (1H, s), 4.49 (1H, br s, exch. D_2O), 3.94 (1H, dd, J = 10.8, 1.7 Hz), 3.00 (1H, br s, exch. D_2O), 2.71 (1H, ddd, J = 17.8, 9.5, 5.4), 2.49 (1H, ddd, J = 17.8, 9.2, 6.1), 2.14 (3H, s), 1.04 (3H, s), 1.02 (3H, s), 0.87 (3H, s). CIMS *m/z* (rel. int.) 271 [M+1] (5), 253 (M^+-H_2O) (30), 235 (100), 207 (77), 189 (19).

Tsangane H (**9**): Oil. $[\alpha]_D$ +3.2° (*c* 2.3, $CHCl_3$). IR υ_{max} ($CHCl_3$) 2941, 1720, 1697, 1464, 1379, 1362 cm^{-1}. ^1H NMR δ ($CDCl_3$): 8.02 (1H, s), 5.35 (1H, d, J = 10.8 Hz), 2.50-2.43 (2H, m), 2.13 (3H, s), 1.15 (3H, s), 1.14 (3H, s), 1.05 (3H, s). HREIMS *m/z* (rel. int.) 268.1688 [M^+, $C_{15}H_{24}O_4$ requires 268.1675] (2), 236 (16), 222 (88), 164 (25), 151 (69), 140 (67), 109 (63), 95 (72), 82 (100).

Tsangane I (**10**): Oil. $[\alpha]_D$ -64.8° (*c* 0.19, $CHCl_3$). IR υ_{max} ($CHCl_3$) 2934, 1717, 1688, 1456 cm^{-1}. ^1H NMR δ ($CDCl_3$): 2.88 (1H, ddd, J = 18.3, 7.2, 5.3 Hz), 2.69 (1H, ddd, J = 18.1, 7.2, 5.4 Hz), 2.60 (1H, ddd, J = 18.1, 6.7, 5.3 Hz), 2.53 (1H, m), 2.49 (1H, ddd, J = 18.3, 6.7, 5.4 Hz), 2.19 (3H, s), 1.31 (3H, s), 1.11 (3H, s), 1.04 (3H, s). HREIMS *m/z* (rel. int.) 238.1631 [M^+, $C_{14}H_{22}O_3$ requires 238.1569] (4), 195 (2), 141 (67), 140 (61), 125 (28), 99 (100).

Tsangane J (**11**): Oil. $[\alpha]_D$ -4.3° (*c* 0.2, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3422 (br), 2932, 2874, 1688, 1360 cm^{-1}. ^1H NMR δ ($CDCl_3$): 4.11 (1H, br s, -OH), 3.94 (1H, br), 3.75 (1H, dd, J = 11.9, 4.1 Hz), 2.90 (1H, dd, J = 11.8, 1.8 Hz), 2.44 (3H, s), 1.03 (3H, s), 0.96 (3H, s), 0.71 (3H, s). HREIMS *m/z* (rel. int.) 254.1887 [M^+, $C_{15}H_{26}O_3$ requires 254.1882] (3), 236 (47), 208 (19), 193 (29), 178 (43), 149 (31), 135 (44), 123 (40), 109 (100), 95 (54).

Tsangane K (2α,3α-epoxy-himachal-7β-ol) (**12**): Oil. $[\alpha]_D$ +2.8° (*c* 0.31, $CHCl_3$). IR υ_{max} ($CHCl_3$) 2930, 2856, 1474, 1458 cm^{-1}. ^1H NMR δ ($CDCl_3$): 3.09 (1H, d, J = 2.9 Hz), 2.46 (1H, br), 1.32 (3H, s), 1.21 (3H, s), 1.10 (3H, s), 1.00 (3H, s).

Centdarol (2α,7β-Dihydroxyhimachal-3-ene) (**13**): Oil. $[\alpha]_D$ -60.8° (*c* 0.18, $CHCl_3$). IR υ_{max} ($CHCl_3$) 3393 (br), 2961, 2932, 1468, 1456 cm^{-1}. ^1H NMR δ ($CDCl_3$): 5.61 (1H, d, J = 3.3 Hz), 3.88 (1H, s), 1.81 (3H, s), 1.26 (3H, s), 1.01 (3H, s), 0.71 (3H, s). HREIMS *m/z* (rel. int.) 238.1913 [M^+, $C_{15}H_{26}O_2$ requires 238.1932] (10), 220 (38), 205 (18), 177 (41), 150 (27), 137 (55), 135 (84), 121 (44), 109 (100).

Tsangane L (3,9-Dihydroxy-megastigma-5-ene) (**14**): Oil. IR υ_{max} ($CHCl_3$) 3368 (br), 3011, 2930, 2965 cm^{-1}. ^1H NMR δ ($CDCl_3$): 3.93 (1H, m, H-3), 3.79 (1H, m, H-9), 2.22 (1H, m, H-4), 2.06 (1H, m, H-

7), 1.98 (1H, m, H-7), 1.96 (1H, m, H-4), 1.72 (1H, m, H-2), 1.60 (3H, s, H-13), 1.51-1.48 (2H, m, H-8), 1.42 (1H, m, H-2), 1.21 (3H, d, J = 6.6 Hz, H-10), 1.04 (3H, s, H-12), 1.01 (3H, s, H-11). ^{13}C NMR 136.8 C (C-6), 124.1 C (C-5), 68.8 CH (C-9), 65.4 CH (C-3), 48.4 CH_2 (C-2), 42.1 CH_2 (C-4), 39.6 CH_2 (C-8), 37.9 C (C-1), 29.7 CH_3 (C-12), 28.5 CH_3 (C-11), 24.4 CH_2 (C-7), 23.2 CH_3 (C-10), 19.7 CH_3 (C-13). HREIMS *m/z* (rel. int.): 212.1769 [M^+, $C_{13}H_{24}O_2$ requires 212.1776] (2), 179 (3), 161 (11), 138 (28), 121 (33), 107 (100).

Preparation of Mosher esters 5a and 5b from 5. (*S*)-(+)-MTPCl (0.03 ml) was added to allohimachalol (**5**) (10 mg) in pyridine (0.3 ml) and the solution stirred overnight at room temperature. *N,N*-Diisopropylethylamine (0.021 ml) was added to the solution and stirring continued for a further 10 min. Following removal of solvent the (*R*)-OMTP ester **5a** (11 mg; 53 %) was isolated directly from the reaction mixture by column chromatography. ^{13}C NMR δ ($CDCl_3$): 165.8 (C-1'), 138.5 (C-3), 132.5 (C-3'), 129.3 (C-6'), 128.3 (C-5'/7'), 127.8 (C-4'/8'), 126.3 (C-2), 123.2 (q, J = 285 Hz, CF_3), 90.7 (C-6), 84.5 (q, J = 28 Hz, C-2'), 55.4 (2'-OMe), 48.8 (C-1), 42.0 (C-10), 39.1 (C-7), 38.3 (C-8), 33.3 (C-12), 32.1 (C-11), 29.0 (C-4), 28.0 (C-5), 25.7 (C-15), 22.5 (C-13), 18.1 (C-9), 14.9 (C-14). ^{1}H NMR δ ($CDCl_3$): 7.51 (2H, m, H-4'/H-8'), 7.39 (3H, m, H-5'-7'), 5.27 (1H, d, J = 4.4 Hz, H-2), 4.73 (1H, dd, J = 11.5, 3.5 Hz, H-6), 3.49 (3H, s, 2'-OMe), 2.25 (1H, t, J = 13.7 Hz, H-4), 1.77 (3H, s, H-15), 0.99 (3H, s, H-13), 0.84 (6H, s, H-12/14). Treatment of **5** with (*R*)-(-)-MTPCl, under the same conditions, resulted in the (*S*)-OMTP ester **5b** (10 mg; 50%).^{13}C NMR δ ($CDCl_3$): 165.5 (C-1'), 138.2 (C-3), 132.3 (C-3'), 129.5 (C-6'), 128.2 (C-5'/7'), 127.3 (C-4'/8'), 126.3 (C-2), 123.2 (q, J = 285 Hz, CF_3), 90.5 (C-6), 84.5 (q, J = 28 Hz, C-2'), 55.4 (2'-OMe), 48.8 (C-1), 42.0 (C-10), 39.2 (C-7), 37.8 (C-8), 33.3 (C-12), 32.1 (C-11), 29.0 (C-4), 28.2 (C-5), 25.6 (C-15), 22.5 (C-13), 18.0 (C-9), 14.8 (C-14). ^{1}H NMR δ ($CDCl_3$): 7.54 (2H, m, H-4'/H-8'), 7.39 (3H, m, H-5'-7'), 5.28 (1H, d, J = 4.6 Hz, H-2), 4.76 (1H, dd, J = 11.5, 3.5 Hz, H-6), 3.56 (3H, s, -OMe), 2.27 (1H, t, J = 13.8 Hz, H-4), 1.79 (3H, s, H-15), 0.98 (3H, s, H-13), 0.85 (3H, s, H-14), 0.83 (3H, s, H-12).

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REFERENCES

1. Lin, Q. "Systematics and Evolution of the family Illiciaceae" Ph.D thesis, Forestry College, South China Agricultural University, Guangzhou (1997).
2. Sy, L.-K; Brown, G. D. *Phytochemistry* **1996**, *43*, 1417 (see also *erratum* in *Phytochemistry* **1997**, *45*, 211).

3. Sy, L.-K.; Saunders, R. M. K.; Brown G. D. *Phytochemistry* **1997**, *44*, 1099.
4. Kouno, I.; Morisaki, T.; Hara, Y.; Yang, C.-S. *Chem. Pharm. Bull.* **1991**, *39*, 2606.
5. Kouno, I.; Hashimoto, A.; Kawano, N.; Yang, C.-S. *Chem. Pharm. Bull.* **1989**, *37*, 1291.
6. Kouno, I.; Iwamoto, C.; Kameda, Y.; Tanaka, T.; Yang, C.-S. *Chem. Pharm. Bull.* **1994**, *42*, 112.
7. Sy, L.-K.; Brown, G. D. *Phytochemistry* (in press).
8. Yang, C.-S.; Kouno, I.; Kawano, N.; Sato, S. *Tetrahedron Lett.* **1988**, *29*, 1165.
9. Kouno, I.; Baba, N.; Hashimoto, M.; Kawano, N.; Takahashi, M.; Kaneto, H.; Yang, C.-S. *Chem. Pharm. Bull.* **1990**, *38*, 422.
10. Kouno, I.; Baba, N.; Hashimoto, M.; Kawano, N.; Yang, C.-S.; Sato, S. *Chem. Pharm. Bull.* **1989**, *37*, 2427.
11. Kouno, I.; Baba, N.; Hashimoto, M.; Kawano, N.; Takahashi, M.; Kaneto, H.; Yang, C.-S.; Sato, S. *Chem. Pharm. Bull.* **1989**, *37*, 2448.
12. Wong, M.-G.; Gulbis, J. M.; Mackay, M. F.; Craik, D. J.; Andrews, P. R. *Aust. J. Chem.* **1988**, *41*, 1071.
13. Kouno, I.; Irie, H.; Kawano, N.; Katsube, Y., *Tetrahedron Lett.* **1983**, *24*, 771.
14. Manabe, S.; Wakamatsu, K.; Hirata, Y.; Yamada, K. *Tetrahedron* **1979**, *35*, 1925.
15. Fukuyama, Y.; Shida, N.; Kodama, M. *Planta Med.* **1993**, *59*, 181.
16. Kouno, I.; Mori, K.; Akiyama, T.; Hashimoto, M. *Phytochemistry* **1991**, *30*, 351.
17. Yamada, K.; Takada, S.; Nakamura, S.; Hirata, Y. *Tetrahedron* **1968**, *24*, 199.
18. Yamada, K.; Takada, S.; Nakamura, S.; Hirata, Y. *Tetrahedron Lett.* **1965**, 4797.
19. Kouno, I.; Irie, H.; Kawano, N. *J. Chem. Soc. Perkin Trans. I* **1984**, 2511.
20. Kouno, I.; Kawano, N.; Yang C.-S. *J. Chem. Soc. Perkin Trans. I*, **1988**, 1537.
21. Okuyama, E.; Nakamura, T.; Yamazaki, M. *Chem. Pharm. Bull.* **1993**, *41*, 1677.
22. Agrawal, P. K.; Rastogi, R. P. *Biochem. Syst. Ecol.* **1984**, *12*, 133.
23. Bohlmann, F.; Jakupovic, J.; Ahmad, M.; Schuster, A. *Phytochemistry* **1983**, *22*, 1623.
24. Weyerstahl, P.; Kaul, V. K.; Weirauch, M.; Marschall-Weyerstahl, H. *Planta Med.* **1987**, *53*, 66.
25. Krishnamurty, H. G.; Parkash, B.; Parthasarathy, M. R.; Seshadri, T. R. *Ind. J. Chem.* **1974**, *12*, 520.
26. Bisarya, S. C.; Dev, S. *Tetrahedron* 1968, *24*, 3869.
27. Bisaraya, S. C.; Dev, S. *Tetrahedron Lett.*, 1964, *49*, 3761.
28. Agrawal, P.K. *Fitoterapia* 1990, *LXI*, 466.
29. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.
30. Sy, L.-K.; Brown, G. D.; Haynes, R. *Tetrahedron* 1998, *54*, 4345.
31. Christofides, J. C.; Davies, D. B. *J. Am. Chem. Soc.* 1983, *105*, 5099.
32. Hashidoko, Y.; Tahara, S.; Mizutani, J. *J. Chem. Soc. Chem. Commun.* **1991**, 1185.
33. Hashidoko, Y.; Tahara, S., Mizutani, J. *Phytochemistry* **1989**, *28*, 425.
34. Hashidoko, Y.; Tahara, S.; Mizutani, J. *J. Chem. Soc. Perkin Trans. I* **1991**, 211.
35. Haynes, R. K.; Vonwiller, S. C. *Acc. Chem. Res.* **1997**, *30*, 73.
36. Bernharref, A.; El-Jamili, H.; Lassaba, E. *Acta Cryst.* **1995**, *C51*, 2658.
37. Joseph, T. C.; Dev, S. *Tetrahedron* 1968, *24*, 3809.

38 Joseph, T. C.; Dev, S. *Tetrahedron* **1968**, *24*, 3841.
39. Challand, B. D.; Hikino, H.; Kornis, G.; Lange, G.; de Mayo, P. *J. Org. Chem.* **1969**, *34*, 794.
40. Chiaroni, A.; Pais, M.; Riche, C.; Bernharref, A.; Chekaroun, A.; Lavergne, J.-P. *Acta Cryst.* **1991**, *C47*, 1945.
41. Chiaroni, A.; Riche, C.; Bernharref, A.; Chekroun, A.; Lavergne, J.-P. *Acta Cryst.* **1992**, *C48*, 1720.
42. Narula, A. P. S.; Dev, S. *Tetrahedron* **1977**, *33*, 813.
43. Suginome, H.; Nakayama, Y. *Tetrahedron* **1994**, 7771.
44. Bisarya, S. C.; Dev, S. *Tetrahedron* **1968**, *24*, 3861.
45. Kulshreshtha, D. K.; Rastogi, R. P. *Phytochemistry* **1975**, *14*, 2237.
46 . Kulshreshtha, D. K.; Rastogi, R. P. *Phytochemistry* **1976**, *15*, 557.
47. Prakash, O. M.; Roy, R.; Kulshreshtha, D. K. *Mag. Res. Chem.* **1988**, *26*, 47.
48. Izoe, S.; Hyeon, S. B.; Sakan, T. *Tetrahedron Lett.* **1969**, 279.
49. Powell, R. G.; Weisleder, D.; Smith, C. R.; Boettner, F. E. *J. Org. Chem.* **1986**, *51*, 1074.