Constituents of *Sindora sumatrana* MIQ. II.[1] Five New Sesquiterpenoids from the Dried Pods

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Further investigation of the neutral fraction of the methanolic extract of *Sindora sumatrana* MIQ. (Leguminosae) has yielded five new sesquiterpenoids: a new *trans*-isodaucane diol (1), two caryophyllane-type epoxydiols (2, 3), the diacetate of a caryophyllane-type trialcohol (4) and a caryolane-type hydroxy-ketone (5) which possesses an α-C-12 methano bridge. The structure elucidation of the compounds was based mainly on two-dimensional NMR techniques. The biosynthetic significance of the acid-catalyzed rearrangement of 5 to give a clovane-type hydroxyketone (10) is also discussed.

Keywords *Sindora sumatrana*; Leguminosae; sesquiterpenoid; *trans*-isodaucane; isocaryolane; caryophyllane

In a previous paper,[1] we reported the isolation and structure elucidation of three new sesquiterpenoids and nine known ones from the neutral fraction of the dried pods of *Sindora sumatrana* MIQ. (Leguminosae). Among the nine known sesquiterpenoids, three were new natural products. In the present paper, we report the isolation and identification from the neutral fraction of a new *trans*-isodaucane sesquiterpene diol (**1**) and four other new sesquiterpenoids (**2**, **3**, **4**, **5**) along with the diacetate (**6**) of caryolane-1,9β(*S*)-diol.[1]

Compound **1** was obtained as a pale yellowish amorphous solid, $[\alpha]_D$ +1.8° ($CHCl_3$). It showed a molecular ion peak at *m/z* 236 in the MS and its molecular formula was determined by high-resolution MS (HR-MS) to be $C_{15}H_{24}O_2$. The MS also showed fragment peaks at *m/z* 221 ($M^+ - 15$) and 218 ($M^+ - 18$) and the IR spectrum showed a broad absorption around 3400 cm^{-1} (OH). The ^1H- and ^{13}C-NMR spectra showed signals due to two oxygenated methine groups (δ_H 4.48, dd, J=6.0, 1.5 Hz, δ_C 77.8, d, C-8; δ_H 3.63, t, J=9.0 Hz, δ_C 83.0, d, C-2) together with a tertiary methyl (δ_H 0.79, 15-H_3) and a vinyl methyl (δ_H 1.70, 13-H_3). Distortionless enhancement by polarization transfer (DEPT) NMR analysis showed the presence of two sp^2 methylene (δ_C 111.7, C-12; δ_C 112.5, C-14) and two sp^2 quaternary carbons (δ_C 149.2, C-11; δ_C 154.2, C-7).

From the analysis of the ^1H–^1H and ^1H–^{13}C shift correlation spectroscopy (COSY) spectra of **1**, partial structures A, B and C were obtained (Fig. 1). In addition, the ^1H–^{13}C long-range COSY revealed long-range correlations which led to the planar structure (D) of **1**.

Next, a series of difference nuclear Overhauser effect (NOE) experiments were carried out on **1** in order to determine the relative stereochemistry of the molecule. As shown in Fig. 2, irradiation of the methyl protons at δ_H 0.79 (15-H_3) caused an enhancement of the intensity of both 6-H (δ_H 2.00) and 4-H (δ_H 2.29), but did not cause any enhancement of the 5-H signal (δ_H 2.11). It was thus concluded that the isopropenyl substituent at position 4 is in the α configuration and that the two rings of the molecule are condensed in the *trans* mode. NOE was also observed between 5-H and the methine proton attached to the hydroxyl-bearing carbon (δ_H 3.63, 2-H). This result clearly showed that the 2-hydroxyl substituent is in the β-configuration. The configuration at the remaining C-8 chiral center was determined from the analysis of the vicinal coupling constants of the 10-, 9- and 8-protons. The ^1H–^1H COSY revealed a long-range coupling between the 15-methyl protons and 10-H at δ_H 1.54, which indicated that this 10-H is in a pseudo-axial orientation with the α configuration. Thus, from the vicinal coupling constants with 10-H_2, 9-H at δ_H 1.69 (tdd, J=14, 4,

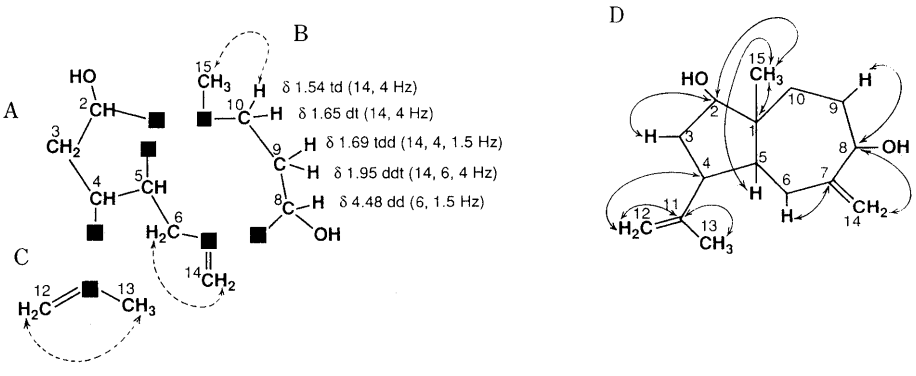

Fig. 1. Partial Structures (A, B, C) Deduced by ^1H–^1H and ^1H–^{13}C COSY and Long-Range Connectivities (D) Observed in the ^1H–^{13}C Long-Range COSY of **1** (in Methanol-d_4)

Long-range correlations observed in ^1H–^1H COSY.

1.5 Hz) was determined to be in a pseudo-axial orientation with the β configuration and 9-H at δ_H 1.95 (ddt, $J=14$, 6, 4 Hz) to be in the α-pseudo-equatorial orientation. In turn, from the inspection of Dreiding models and from its vicinal coupling constants ($J=6$, 1.5 Hz), 8-H was considered to be pseudo-equatorial in character and in the α-configuration. These deductions and the observation of NOE between the 14-olefinic proton (δ_H 4.87) and 8-H in the difference NOE spectrum established the relative stereochemistry of the molecule to be as shown in Fig. 2.

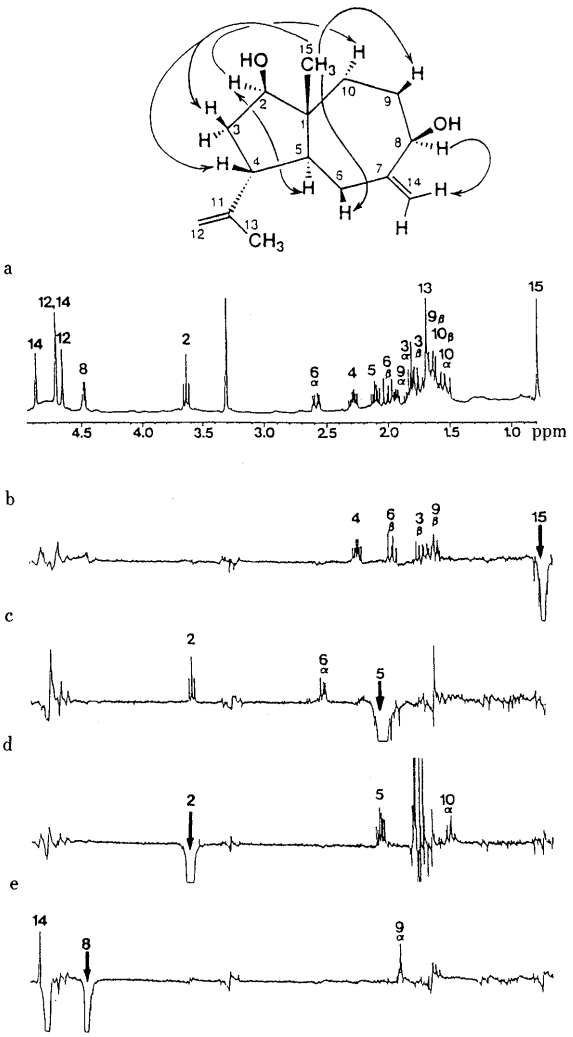

Fig. 2. Normal ^{1}H-NMR and NOE Difference Spectra of **1** (in Methanol-d_4)

a) Normal spectrum. b—e) NOE difference spectra on irradiation at δ 0.80, 2.11, 3.63 and 4.48, respectively.

Compound **1** is a new compound belonging to the rare group of sesquiterpenoids having the isodaucane skeleton and it appears to be the first report of a *trans*-isodaucane sesquiterpenoid.[2)]

Compound **2**, colorless amorphous solid, $[\alpha]_D$ $-22°$ ($CHCl_3$), and compound **3**, colorless needles, mp 118—119 °C, $[\alpha]_D$ $-5.0°$ ($CHCl_3$), had the same molecular formula of $C_{15}H_{26}O_3$ (*m/z* 254). The IR spectra of the two compounds showed broad hydroxyl absorption bands near 3450 cm^{-1}. The two compounds also showed similar ^{1}H- and ^{13}C-NMR spectra (Tables I and II) to each other. The doublet signals at δ_H 3.09 and 3.62 (both $J=10.5$ Hz) and the AB quartet (δ_H 3.16, 3.26, $J_{AB}=11$ Hz) observed in the ^{1}H-NMR spectra of **2** and **3**, respectively, were indicative of a disubstituted epoxide in both compounds. In addition, the ^{13}C-NMR signals at δ_C 75.2 (d) and 77.5 (s) in **2** and at δ_C 70.3 (d) and 78.1 (s) in **3** suggested the presence of both secondary and tertiary alcohol groups in the two compounds. Detailed analysis of their ^{1}H- and ^{13}C-NMR data with the aid of ^{1}H–^{1}H, ^{1}H–^{13}C and long-range ^{1}H–^{13}C COSY established the planar structures of both **2** and **3** to be 1(12)-epoxycaryophyllane-8,9-diol.

A series of difference NOE experiments of **2** and **3** established their respective ring A/B junctions to be *trans*, *viz.*; NOE's were observed between the 14-methyl protons and the 5-protons and between the 13-methyl protons and the 2-protons. The results of difference NOE experiments, together with the vicinal coupling constants of 9-H and the 10-methylene protons and the inspection of Dreiding models of the molecules, also confirmed their relative stereochemistry at the C-8 and C-9 chiral centers to be identical (Fig. 3).

With regard to the stereochemistry of the exocyclic epoxide rings in **2** and **3**, difference NOE experiments revealed a clear NOE between the 12-methylene proton at δ_H 3.62 and 5-H (δ_H 2.14) in **2**, while a clear NOE was observed between the 12-methylene proton at δ_H 3.26 and 2-H (δ_H 2.02) in **3**. Thus it was clear that **2** is the α-epoxide, and **3** is the β-isomer.

Biosynthetically, it appears the two compounds originated from the epoxide ring opening of β-caryophyllene 8*R*,9*R*-oxide (**7**) with the epoxidation of the 1(12)-olefinic group.

Compound **4** was isolated as a diacetate, colorless

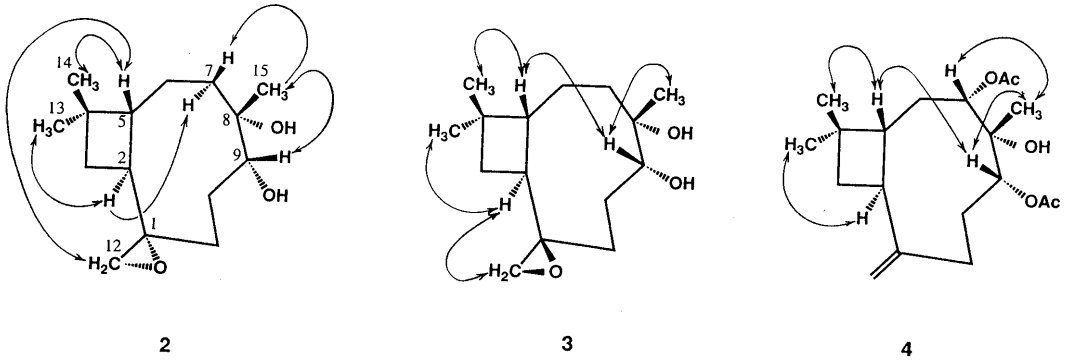

Fig. 3. NOE Correlations Observed in **2**, **3** and **4**

TABLE I. 400 MHz ^{1}H-NMR Data for **1**, **2**, **3**, **4**, **5**, **8**, **6** and **10**

	1[a]	**2**[b]	**3**[b]	**4**[b]	**5**[a]	**5**[b]	**8**[b,c]	**6**[b]	**10**[b]
2	3.63 t (9)	2.53 ddd (12, 10, 8)	2.02 ddd (11.5, 10.5, 7.5)	2.49 ddd (10.5, 7.5, 4.5)	2.08 ddd (11, 10, 8.5)	2.05 td (10.5, 8)	1.74 q-like	2.35 ddd (12, 10.5, 8)	3.87 dd (7, 5.5)
3	1.77 ddd (13.5, 10.5, 9)	1.34 t (10)	1.18 t (10.5)	1.65 dd (10.5, 7.5)	1.50 t (10)	1.48 t (10.5)	1.61 dd (9.5, 8)	1.27 t (10.5)	1.60 dd (13, 7)
	1.84 ddd (13.5, 9, 5.5)	1.41 dd (10, 8)	1.47 dd (10.5, 7.5)	1.82 t (10.5)	1.53 dd (10, 8.5)	1.54 dd (10.5, 8)	1.66 t (9.5)	1.74 dd (10, 8)	1.90 dd (13, 5.5)
4	2.29 td (11, 5.5)	—	—	—	—	—	—	—	—
5	2.11 td (11, 5.5)	2.14 ddd (12, 10, 6)	1.92 ddd (11.5, 10, 5.5)	1.83 ddd (12, 10, 4.5)	1.24 td (11, 6.5)	1.29 m	1.76 m	1.93 ddd (12, 8, 7)	1.78 t (7)
6	2.00 dd (15, 11)	1.45 dddd (13.5, 6, 4.5, 3.5)	1.45 dddd (14.5, 10, 7.5, 6.5)	1.66 ddd (14, 10, 3.5)	1.41 m	1.36 m	1.27 tdd (13, 12, 5)	1.38 dddd (13, 9, 8, 3.5)	1.61 dt (10, 7) (2H)
	2.58 ddt (15, 5.5, 2)	1.66 tdd (13.5, 10, 3.5)	1.55 ddt (14.5, 6.5, 5.5)	1.78 ddd (14, 12, 10.5)	1.47 m	1.51 m	1.46 ddt (13, 5.5, 2)	1.55 dddd (13, 9, 7, 3.5)	
7	—	1.35 dt (13.5, 3.5)	1.69 ddd (14.5, 7.5, 5.5)	5.18 dd (10.5, 3.5)	1.45 m	1.42 dd (14, 8)	1.06 td (13, 5.5)	1.23 ddd (12.5, 9, 3.5)	1.51 m (2H)
		1.92 td (13.5, 4.5)	1.82 dt (14.5, 6.5)		2.09 td (15, 6)	2.16 ddt (12, 8, 2)	2.10 ddd (13, 5, 1.5)	1.48 ddd (12.5, 9, 3.5)	
8	4.48 dd (6, 1.5)	—	—	—	—	—	—	—	—
9	1.69 tdd (14, 4, 1.5) 1.95 ddt (14, 6, 4)	3.42 dd (11, 5)	3.55 dd (6.5, 3)	5.05 dd (8.5, 3.5)	—	—	—	4.73 dd (4.5, 3.5)	—
10	1.54 td (14, 4)	1.82 dtd (13, 5, 2.5)	1.71 dtd (13, 6.5, 5.5)	1.60 tdd (14, 7, 3.5)	2.23 ddd (15, 8, 1.5)	2.30 m	2.37 ddd (16.5, 10, 4)	1.82 ddt (15, 6, 4)	2.40 ddd (16.5, 6.5, 2.5)
	1.65 dt (14, 4)	1.95 tdd (13, 11, 4)	2.09 dddd (13, 9.5, 6.5, 3)	2.29 dddd (14, 8.5, 6, 5)	2.91 ddd (15, 11.5, 10)	2.83 m	2.79 ddd (16.5, 12, 4.5)	1.95 dddd (15, 12, 6, 3.5)	2.64 ddd (16.5, 12, 8)
11	—	1.39 ddd (13, 4, 2.5)	1.54 dt (13.5, 6)	2.10 td (14, 5)	1.91 ddt (14, 11.5, 10)	1.95 br t (12.5)	1.86 dddt (12, 10, 4.5, 1.5)	1.73 td (12, 6)	1.75 ddt (13, 8, 2.5)
		2.04 td (13, 5)	1.84 ddd (13.5, 9.5, 6.5)	2.48 ddd (14, 7, 6)	2.37 dddd (14, 10, 8, 1)	2.38 m	2.00 td (12, 4)	2.47 dddd (12.5, 6, 4, 2.5)	1.89 ddd (13, 12, 6.5)
12	4.65 q (1)	3.09 d (10.5)	3.16 d (11)	4.92 s	1.67 dd (13, 1)	1.69 dd (13, 1)	2.03 br s (2H)	1.69 d (13)	1.49 dd (13.5, 2.5)
	4.71 br s	3.62 d (10.5)	3.26 d (11)	4.98 s	2.36 dd (13, 1.5)	2.38 dd (13, 1.5)		1.80 dd (13, 2.5)	1.54 d (13.5)
13	1.70 s	1.00 s	1.018 s	1.00 s	1.00 s	0.99 s	0.96 s	0.99 s	1.00 s
14	4.71 br s 4.87 br s	1.01 s	1.023 s	1.02 s	0.98 s	0.98 s	1.01 s	0.99 s	1.12 s
15	0.79 s	1.20 s	1.21 s	1.16 s	1.06 s	1.09 s	1.12 s	0.87 s	1.03 s
$OCOCH_3$	—	—	—	2.09 s, 2.11 s	—	—	—	2.00 s, 2.06 s	—

Coupling constants in parenthesis. *a*) Values obtained in methanol-d_4. *b*) Values obtained in chloroform-*d*. *c*) Reference 1.

TABLE II. 100 MHz ^{13}C-NMR Data for **1**, **2**, **3**, **4**, **5**, **8**, **6** and **10**

	1[a]	**2**[b]	**3**[b]	**4**[b]	**5**[a]	**5**[b]	**8**[b,c]	**6**[b]	**10**[b]
1	49.1 s	73.6 s	75.8 s	149.9 s	71.8 s	70.6 s	69.4 s	82.5 s	44.5[d] s
2	83.0 d	35.6 d	44.5 d	42.7 d	48.0 d	46.6 d	43.0 d	40.8 d	80.2 d
3	37.8 t	33.1 t	34.9 t	36.2 t	35.2 t	33.0 t	34.4 t	38.7 t	48.5 t
4	51.9 t	35.1 s	36.8 s	33.7 s	37.1 s	35.6 s	33.6 s	34.5 s	38.7 s
5	47.0 t	43.2 d	47.2 d	48.6 d	46.4 d	44.4 d	45.0 d	45.6 d	50.6 d
6	36.9 t	18.7 t	23.5 t	29.8 t	23.4 t	21.6 t	25.6 t	21.8 t	20.7 t
7	154.2 s	29.1 t	38.8 t	74.9 d	38.1 t	36.3 t	38.6 t	36.5 t	34.2 t
8	77.8 d	77.5 s	78.1 s	76.2 s	47.2 s	45.3 s	46.8 s	38.2 s	45.1[d] s
9	34.6 t	75.2 d	70.3 d	75.2 d	222.1 s	218.1 s	216.8 s	73.9 d	216.1 s
10	36.4 t	24.8 t	25.4 t	30.7 t	37.8 t	36.0 t	34.5 t	25.6 t	35.9 t
11	149.2 s	29.6 t	19.2 t	33.4 t	31.8 t	30.3 t	36.9 t	31.4 t	32.3 t
12	111.7 t	66.6 t	69.3 t	111.5 t	54.4 t	53.0 t	49.2 t	41.6 t	42.0 t
13	19.9 q	20.9 q	20.7 q	22.2 q	23.5 q	22.3 q	21.8 q	20.5 q	26.5 q
14	112.5 t	30.5 q	30.4 q	30.0 q	31.2 q	30.1 q	30.8 q	30.4 q	32.5 q
15	11.7 q	26.7 q	28.0 q	20.6 q	31.8 q	30.6 q	31.2 q	27.0 q	25.1 q
$OCOCH_3$	—	—	—	21.1 q, 21.2 q	—	—	—	21.2 q, 22.1 q	—
$OCOCH_3$	—	—	—	170.2 s, 170.5 s	—	—	—	169.8 s, 170.5 s	—

a) Values obtained in methanol-d_4. *b*) Values obtained in chloroform-*d*. *c*) Reference 1. *d*) Assignments may be interchanged.

amorphous substance, $[\alpha]_D$ −22° ($CHCl_3$), and its MS showed the molecular ion peak at *m/z* 338 ($C_{19}H_{30}O_5$). The IR spectrum showed a broad absorption centered around 3450 cm^{-1} and an intense peak at 1730 cm^{-1} indicative of a hydroxy and an ester function, respectively. The ^{1}H-NMR spectrum showed signals due to two acetoxy methyl groups at δ_H 2.09 and 2.11 and also signals due to three methyl groups at δ_H 1.00 (13-H_3), 1.02 (14-H_3) and 1.16 (15-H_3). The broad singlets observed at δ_H 4.92 and 4.98 (12-H_2) in the ^{1}H-NMR spectrum and the signals at δ_C 111.5 (t, C-12) and 149.9 (s, C-1) in the ^{13}C-NMR spectrum indicated the presence of an exocyclic double

bond in the molecule. These data and the ^{1}H- and ^{13}C-NMR patterns of the compound led us to assume that **4** probably has the caryophyllane skeleton. The ^{13}C-NMR signal at δ_C 76.2 (s) also suggested the presence of a tertiary alcohol group in the molecule, in addition to the two acetoxy substituents.

Further analysis of the ^{1}H- and ^{13}C-NMR spectra of **4** with the aid of ^{1}H–^{1}H and ^{1}H–^{13}C COSY clearly established that **4** is the diacetate derivative of a trihydroxy caryophyllane-type sesquiterpenoid.

Next, the results of a series of difference NOE experiments on the molecule confirmed the junction of rings A and B to be *trans* as shown in Fig. 3. NOE's were also observed between 5β-H (δ_H 1.83) and 9-H (δ_H 5.05) and between 15-H$_3$ (δ_H 1.16) and 9-H. These observations suggested that both the 9-acetoxy and the 8-hydroxy substituents are in the α configuration. NOE was also observed between 7-H (δ_H 5.18) and 15-H$_3$. From the inspection of Dreiding models and from the vicinal coupling constants of 7-H (dd, J=10.5, 3.5 Hz) it was concluded that 7-H is pseudo-axial and β. The 7-acetoxy substituent is therefore in the α configuration.

With regard to the biosynthesis, as in the case of both **2** and **3**, **4** is probably also formed *via* epoxide ring opening of **7** followed by enzymatic hydroxylation of an intermediate.

Compound **5** was isolated as a colorless amorphous solid, $[\alpha]_D$ +94° ($CHCl_3$), and the molecular formula was determined by HR-MS as $C_{15}H_{24}O_2$ (*m/z* 236). The IR spectrum showed a broad absorption at 3400 cm^{-1} due to a hydroxy group and an intense absorption at 1690 cm^{-1} due to a ketone group.

The ^{1}H-NMR spectrum of the compound (in methanol-d_4) showed signals due to an isolated methylene group at δ_H 1.67 (dd, J=13, 1 Hz) and 2.36 (dd, J=13, 1.5 Hz) in addition to three methyl singlets at δ_H 1.00 (13-H$_3$), 0.98 (14-H$_3$) and 1.06 (15-H$_3$), whilst the DEPT NMR spectral analysis indicated the presence of both a tertiary alcohol (δ_C 71.8, C-1) and a ketone group (δ_C 222.1, C-9). These

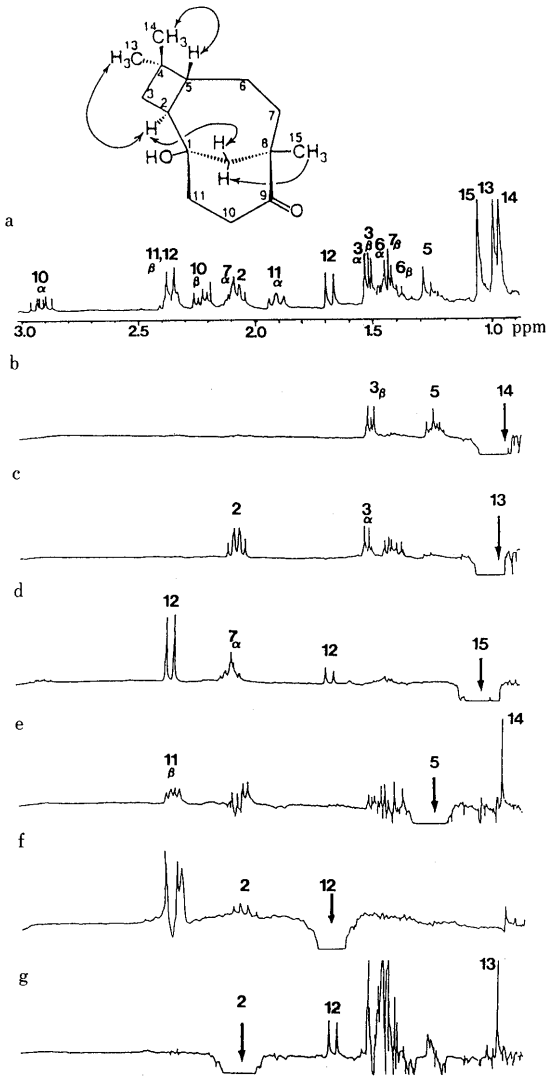

Fig. 4. Normal ^{1}H-NMR and NOE Difference Spectra of **5** (in Methanol-d_4)

a) Normal spectrum. b—g) NOE difference spectra on irradiation at δ 0.98, 1.00, 1.06, 1.24, 1.67, and 2.08, respectively.

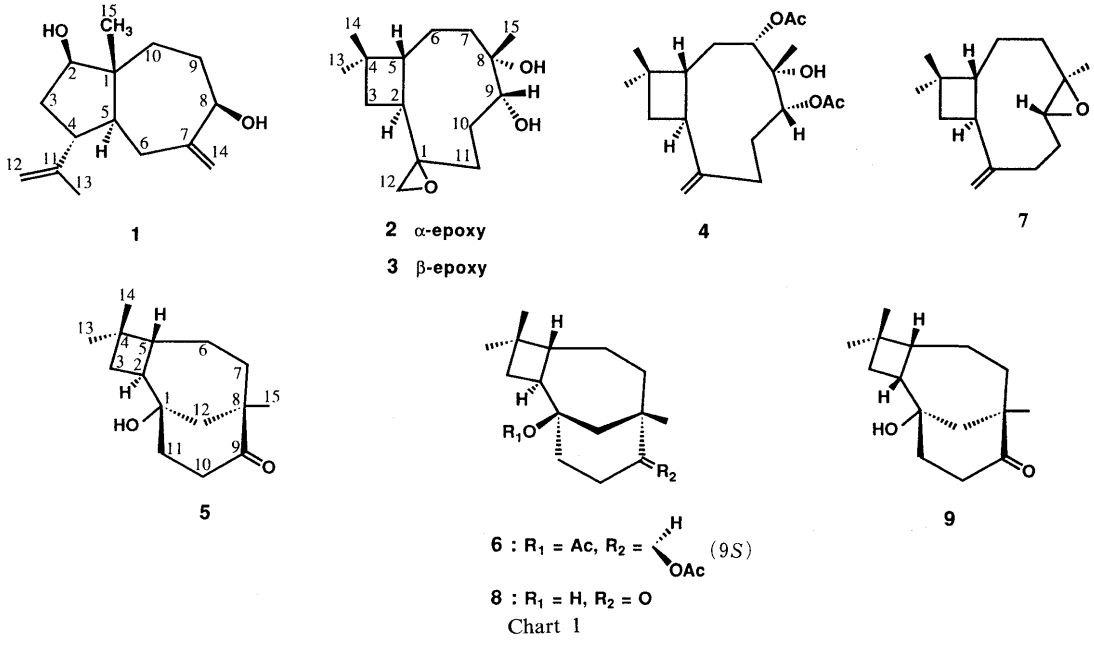

Chart 1

spectral data suggested that **5** is probably of the same skeletal type as 1-hydroxy-9-oxocaryolane (**8**), which had been isolated earlier from *S. sumatrana*.[1] Further analysis of the ^{1}H- and ^{13}C-NMR spectra of **5** with the aid of ^{1}H–^{1}H, ^{1}H–^{13}C and long-range ^{1}H–^{13}C COSY established its planar structure to be the same as that of **8**, thus indicating a probable stereoisomeric relationship between the two compounds.

The relative stereochemistry of **5** was next investigated by means of a series of difference NOE experiments (Fig. 4), in which NOE's were observed between the 14-methyl protons (δ_H 0.98) and 5-H (δ_H 1.24) and between the 13-methyl protons (δ_H 1.00) and 2-H (δ_H 2.08), indicating that the cyclobutane ring of the molecule is condensed in the *trans* mode. On the other hand, irradiation of 2-H caused an enhancement of the signal of a methano bridge proton at δ_H 1.67 (12-H) and *vice versa*. Irradiation at the frequency of the 15-methyl protons (δ_H 1.06) also caused a sharp enhancement in the intensity of the other 12-H signal at δ_H 2.36. From these results and from the inspection of Dreiding models it was concluded that the methano bridge in **5** is in the α-disposition, as opposed to the β-orientation in **8**.

A similar hydroxyketone **9**, possessing an α-methano bridge but having a *cis* stereochemistry at the junction of rings A and B, has been obtained by the Collins oxidation of senecrassidiol.[3] Compound **5** thus appears to be a new compound with a novel stereochemical structure for which we propose the name "isocaryolane".

The acid-catalyzed cyclization of caryophyllene to give a variety of rearranged skeletal types is well described in the literature.[4,5] As previously discussed,[1] the epoxidation reaction of β-caryophyllene could lead to the formation of both the 8*R*,9*R*- and the 8*S*,9*S*-epoxides. Whilst transformations of the latter could lead to the caryolane-type compounds (**6**, **8**), those of the former could lead to the clovane-type compounds (for example: **11a**) *via* a tricyclic intermediate, 1,9α(*R*)-dihydroxyisocaryolane, of the type envisaged by Aebi *et al.*[4] and having the same stereochemical structure as that of **5**.[6]

On treatment with concentrated sulfuric acid in anhydrous ether, compound **5** gave the product **10**, $C_{15}H_{24}O_2$, $[\alpha]_D$ −74° ($CHCl_3$). Analysis of the ^{1}H- and ^{13}C-NMR spectra of **10** with the aid of ^{1}H–^{1}H and ^{1}H–^{13}C COSY, together with a series of difference NOE experiments, established its structure as that of 2β-hydroxyclovan-9-one. Furthermore, compound **10** was found to be identical to a synthetic sample prepared from 2β-acetoxyclovan-9α(*R*)-ol (**11c**) (Chart 2).

It is thus clear that 1,9α(*R*)-dihydroxyisocaryolane is an intermediate in the biosynthetic pathway from caryophyllene to the clovane-type compounds. The co-occurrence of **5** and **8** in *S. sumatrana* is of particular interest with regard to the reversal in stereochemistry which occurs in the course of the biosynthesis of the caryolane- and clovane-type sesquiterpenoids.

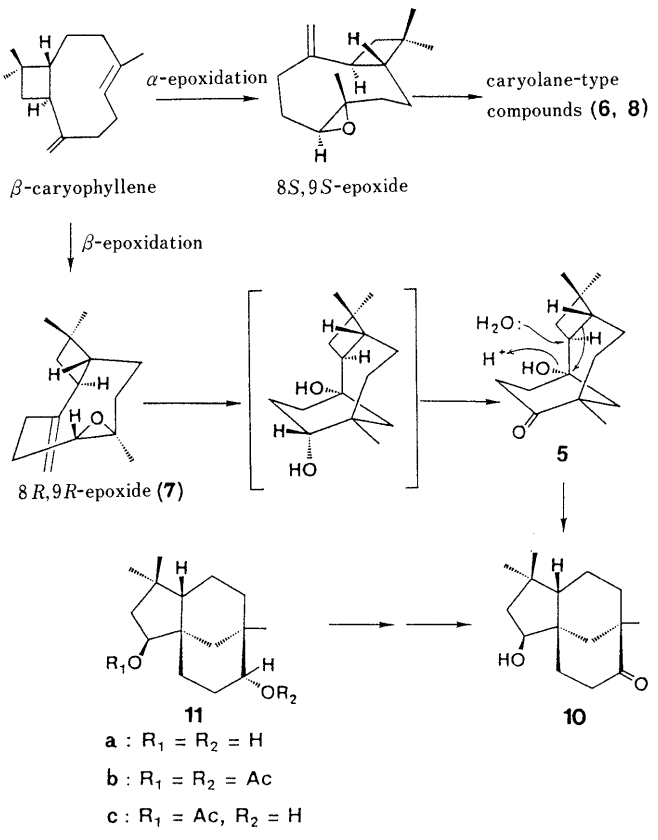

Chart 2

Experimental

Melting point was determined on a Yanagimoto micro-melting point apparatus and is uncorrected. Optical rotations were measured on a JASCO DIP-140 digital polarimeter at 26 °C. IR spectra were taken in $CHCl_3$ solutions on a JASCO IR-2 or a Hitachi 260-10 IR spectrophotometer. MS and HR-MS measurements were obtained on a JEOL D-300 spectrometer using a direct inlet system at the ionization voltage of 70 eV. ^{1}H-, ^{13}C- and two dimensional (2D) NMR and difference NOE spectra were taken with a JEOL JNM-GX400 spectrometer in $CDCl_3$ solutions (unless otherwise stated) and with tetramethylsilane as an internal standard. Chemical shifts are recorded in δ values and coupling constants in hertz (Hz). Multiplicities of ^{13}C-NMR signals were determined by means of the DEPT method and are indicated as s (singlet), d (doublet), t (triplet) and q (quartet).

Analytical TLC and preparative TLC were carried out on precoated Merck Kieselgel 60 F_{254} plates (0.25, 0.5, 1.0, 2.0 mm). Detection was done with $Ce(SO_4)_2$–10%H_2SO_4 (1:99) spray reagent. Elution of separated bands was done with MeOH–CH_2Cl_2 (15:85) and the eluates were concentrated *in vacuo*.

Isolation of Compounds The extraction and isolation of the sesquiterpenoids from the dried pods of *Sindora sumatrana* MIQ. (4 kg) were described in a previous paper.[1] The unidentified compounds, tentatively named SS1 and SS2 which were obtained from fractions 8 and 10—11, respectively, were further purified by preparative TLC using Et_2O–hexane (80:20). Compound **5** (25 mg) was obtained from SS1, whilst compound **1** (24 mg) and a minor compound **2** (5 mg) were obtained from SS2.

Fractions D-15 to D-25, reported in a previous paper,[1] were combined and separated by preparative TLC using Et_2O–hexane (80:20) to give compound **3** (92 mg).

Separation of the acetylated product of fr. 13—15 by preparative TLC gave the unidentified compound tentatively named SS3[1] and the polar fraction. These were further subjected to preparative TLC using acetone–benzene (10:90). SS3 gave 1,9β(*S*)-diacetoxycaryolane (**6**, 30 mg), whilst the polar fraction gave 1-hydroxy-9β(*S*)-acetoxycaryolane (50 mg) and compound **4** (6 mg).

Compound 1 (2β,8β-Dihydroxy-7(14),11-isodaucadiene) Pale yellowish amorphous solid, $[\alpha]_D$ +1.8° (*c*=1.6, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1440, 1220, 1020. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 236 (M^+, 13), 221 (10), 218 (100), 203 (40), 200 (24), 175 (96), 150 (38), 148 (41), 135 (41), 121 (63), 120 (56), 109 (53), 93 (51). HR-MS: Found 236.1786, Calcd for $C_{15}H_{24}O_2$ (M^+) 236.1776; Found 218.1673,

Calcd for $C_{15}H_{22}O$ ($M^+ - H_2O$) 218.1671.

Compound 2 (1α,12-Epoxy-8α(*S*),9α(*R*)-dihydroxycaryophyllene) Colorless amorphous solid, $[\alpha]_D$ −22° (c=0.38, $CHCl_3$). IR ν_{max} cm^{-1}: 3500 (br), 1190, 1050. ^1H- and ^{13}C-NMR: Tables I and II. MS m/z (%): 254 (M^+, 10), 236 (18), 218 (9), 202 (22), 180 (21), 175 (21), 162 (27), 151 (36), 135 (38), 126 (52), 123 (71), 111 (53), 109 (58), 108 (100), 95 (63), 93 (69). HR-MS: Found 254.1888, Calcd for $C_{15}H_{26}O_3$ (M^+) 254.1882; Found 236.1777, Calcd for $C_{15}H_{24}O_2$ ($M^+ - H_2O$) 236.1776.

Compound 3 (1β,12-Epoxy-8α(*S*),9α(*R*)-dihydroxycaryophyllene) Colorless needles ($CHCl_3$–hexane), mp 118—119 °C. $[\alpha]_D$ −5.0° (c=2.1, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1450, 1200, 1030. ^1H- and ^{13}C-NMR: Tables I and II. MS m/z (%): 254 (M^+, 6), 236 (8), 223 (38), 218 (10), 205 (36), 193 (22), 175 (39), 135 (61), 126 (100), 123 (60), 108 (90), 93 (46). HR-MS: Found 254.1885, Calcd for $C_{15}H_{26}O_3$ (M^+) 254.1882; Found 236.1802, Calcd for $C_{15}H_{24}O_2$ ($M^+ - H_2O$) 236.1776.

Compound 4 (7α(*S*),9α(*R*)-Diacetoxy-8α(*R*)-hydroxy-1(12)-caryophyllene) Colorless amorphous solid, $[\alpha]_D$ −22° (c=0.36, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1730, 1460, 1370, 1250, 1210, 1020. ^1H- and ^{13}C-NMR: Tables I and II. MS m/z (%): 338 (M^+, 16), 278 (9), 262 (12), 220 (58), 218 (58), 202 (95), 187 (28), 164 (38), 162 (41), 125 (100). HR-MS: Found 338.2093, Calcd for $C_{19}H_{30}O_5$ (M^+) 338.2093; Found 278.1882, Calcd for $C_{17}H_{26}O_3$ (M^+ − AcOH) 278.1882; Found 218.1683, Calcd for $C_{15}H_{22}O$ (M^+ − 2AcOH) 218.1671.

Compound 5 (9-Oxoisocaryolane-1-ol) Colorless amorphous solid, $[\alpha]_D$ +94° (c=1.05, $CHCl_3$). IR ν_{max} cm^{-1}: 3400 (br), 1690, 1450, 1200. ^1H- and ^{13}C-NMR: Tables I and II. MS m/z (%): 236 (M^+, 13), 218 (100), 178 (62), 163 (60), 161 (97), 153 (40), 144 (60), 135 (28), 125 (27), 123 (71), 121 (43). HR-MS: Found 236.1776, Calcd for $C_{15}H_{24}O_2$ (M^+) 236.1776; Found 218.1686, Calcd for $C_{15}H_{22}O$ ($M^+ - H_2O$) 218.1670.

Compound 6 (1,9β(*S*)-Diacetoxycaryolane) Colorless amorphous solid, $[\alpha]_D$ +42° (c=0.69, $CHCl_3$). IR ν_{max} cm^{-1}: 1720, 1460, 1370, 1250, 1210, 1030. ^1H- and ^{13}C-NMR: Tables I and II. MS m/z (%): 322 (M^+, 2), 262 (27), 220 (21), 202 (19), 187 (38), 161 (22), 159 (23). HR-MS: Found 262.1913, Calcd for $C_{17}H_{26}O_2$ (M^+ − AcOH) 262.1932; Found 202.1723, Calcd for $C_{15}H_{22}$ (M^+ − 2AcOH) 202.1722. This compound was identified as 1,9β(*S*)-diacetoxycaryolane by comparison ($[\alpha]_D$, IR, ^1H- and ^{13}C-NMR) with the diacetate obtained by the pyridine–acetic anhydride acetylation of 1-hydroxy-9β(*S*)-acetoxycaryolane.

Acid-Catalyzed Rearrangement of 5 A solution of **5** (3 mg) in anhydrous ether (1 ml) was added dropwise, with stirring, to a mixture (1 ml) of concentrated H_2SO_4 (1 ml) and anhydrous ether (7 ml) at 0°C. The mixture was stirred for 20 min at 0 °C and then for 30 min at room temperature. The reaction mixture was diluted with ice water, neutralized with 2 N NaOH solution and extracted with ether. The ether solution was washed with brine, dried over anhydrous $MgSO_4$ and evaporated to yield compound **10** (2.5 mg), colorless oil, $[\alpha]_D$ −74° (c=0.25, $CHCl_3$). IR ν_{max} cm^{-1}: 3500 (br), 1700. ^1H- and ^{13}C-NMR: Tables I and II. MS m/z (%): 236 (M^+, 20), 221 (18), 203 (24), 180 (100), 161 (46), 149 (45), 121 (56), 107 (46), 85 (29), 55 (35). HR-MS: Found 236.1767, Calcd for $C_{15}H_{24}O_2$ (M^+) 236.1776.

Partial Acetylation of Clovane-2β,9α(*R*)-diol (11a) Partial acetylation of **11a** (30 mg) was carried out with Ac_2O (0.8 ml) in pyridine (0.8 ml) at room temperature for 1.5 h. After the usual work-up, the product was separated by preparative TLC using acetone–benzene (10 : 90) to yield 2β,9α(*R*)-diacetoxy-clovane (**11b**, 12 mg) and 2β-acetoxyclovan-9α(*R*)-ol (**11c**, 18 mg). The spectral data (^1H- and ^{13}C-NMR) for **11b** and **11c** were identical with those of authentic samples.[1)]

Jones Oxidation and Subsequent Hydrolysis of 11c A solution of **11c** (18 mg) in acetone (2 ml) was treated with Jones reagent (4 drops) at 0 °C for 30 min. Usual work-up of the reaction mixture gave an oxidation product (16 mg), MS m/z 278 (M^+). This was dissolved in methanol (0.5 ml) and treated with 5% methanolic K_2CO_3 (0.6 ml) overnight at room temperature. The reaction mixture was treated in the usual manner to give **10** (10 mg), colorless oil, $[\alpha]_D$ −92° (c=0.60, $CHCl_3$).

References and Notes

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2) J. D. Connolly, R. A. Hill, "Dictionary of Terpenoids," Vol. 1, Chapman and Hall, London, 1991, p. 575. Only *cis*-isodaucanes are reported in this reference.
3) H. Iwabuchi, N. Kato, M. Yoshikura, *Chem. Pharm. Bull.*, **38**, 1405 (1990).
4) A. Aebi, D. H. R. Barton, A. W. Burgstahler, A. S. Lindsey, *J. Chem. Soc.*, **1954**, 4659.
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6) Even though Aebi *et al.* (reference 4) did not isolate any compound having the stereochemistry of the intermediate that they envisaged, they attempted a rearrangement of caryolane-1,9β(*S*)-diol in acetone using aqueous sulfuric acid. Initially this led to recovery of the starting material. Further addition of sulfuric acid resulted in an intractable gummy material from which they could not isolate clovanediol.