Constituents of *Sindora sumatrana* MIQ. I. Isolation and NMR Spectral Analysis of Sesquiterpenes from the Dried Pods

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Investigation of the neutral fraction of the dried pods of *Sindora sumatrana* MIQ. has resulted in the isolation of three new sesquiterpenoids (2, 6 and 8) together with nine known ones (1, 3, 4, 5, 7, 9, 10, 11a and 12a), of which three (7, 10 and 12a) are reported for the first time from a natural source. One other compound, 4-stigmasten-3-one (13) (together with a sterol mixture; β-sitosterol, stigmasterol and campesterol) was also obtained. The structures of all the isolated sesquiterpenes were determined by means of spectroscopic methods, mainly two-dimensional NMR techniques, and the compounds were found to have the caryophyllane, humulane, clovane and caryolane skeletons. The NMR data of the isolated sesquiterpenes are also discussed.

Keywords *Sindora sumatrana*; sesquiterpenoid; NMR spectrum; clovane; caryolane; caryophyllane

Sindora sumatrana MIQ. (Leguminosae) is an Indonesian medicinal plant known traditionally as "Seperantu." The pods are used for the treatment of fever, syphyllis and gonorrhoea.[1] The plant does not appear to have been the subject of any previous chemical study, and in this and subsequent communications, we wish to report on the analysis of the chloroform-soluble fraction of the methanolic extract of the powdered dried pods. This fraction has been found to contain a complex mixture of several sesquiterpenoids bearing the clovane, caryophyllane,[2] humulane,[2] and caryolane skeletons together with both neutral and acidic clerodane-type diterpenoids. In this paper, we describe the isolation and structure elucidation of the sesquiterpenoids from the neutral fraction.

The methanolic extract of the powdered dried pods of *Sindora sumatrana* was fractionated into chloroform-soluble (*ca.* 90%), and ethyl acetate-soluble (*ca.* 1%) fractions in addition to a methanol-soluble residue (*ca.* 9%) in that order. The chloroform-soluble fraction was

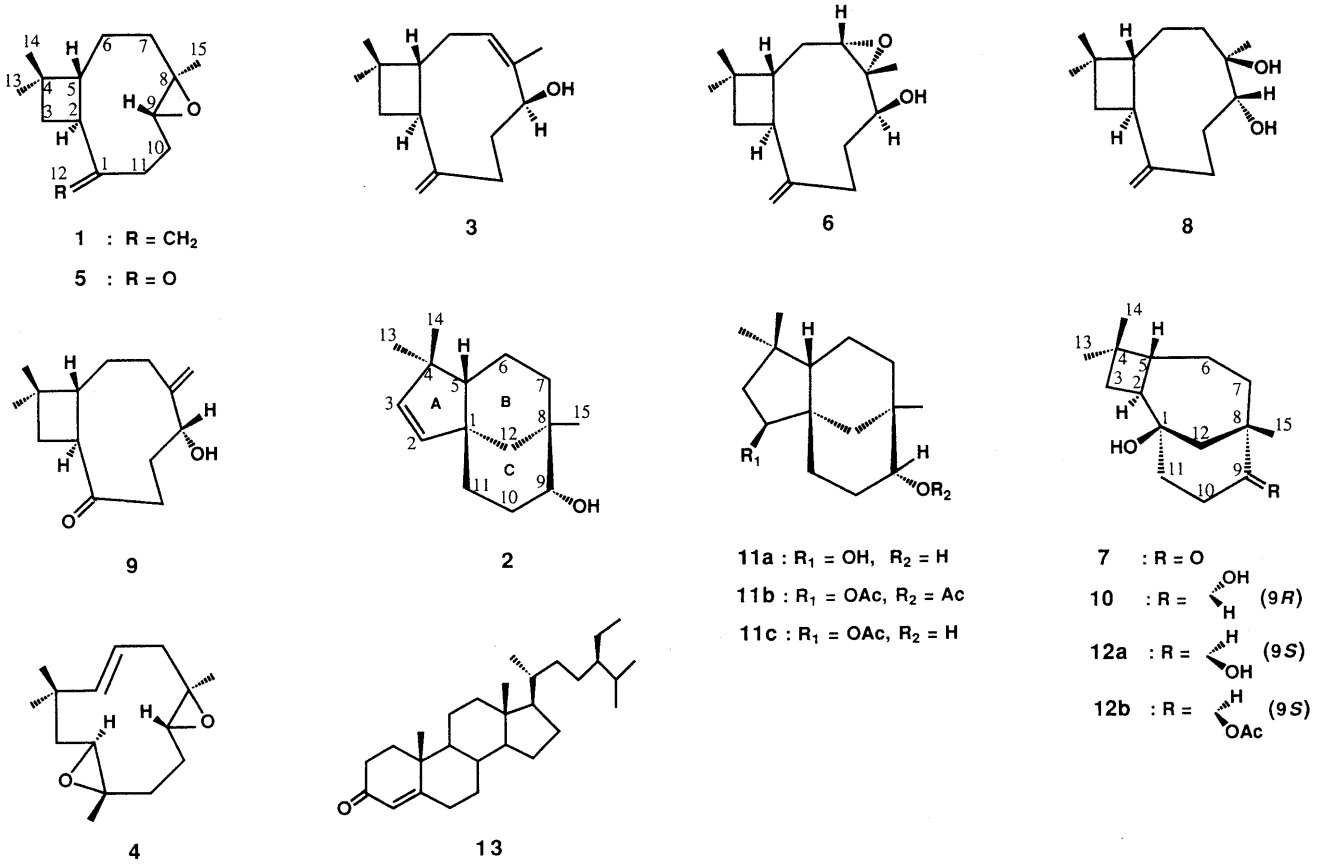

Chart 1

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TABLE I. 400 MHz ^{1}H-NMR Data for **1**, **3**, **6**, **8**, **5**, **9**, and **4** in $CDCl_3$ (Coupling Constants in Parenthesis)

	1	**3**	**6**	**8**	**5**	**9**	**4**
2	2.62 dt (10, 9.5)	2.68 qt (9.5, 2)	2.58 qt (9, 2)	2.37 td (10, 8)	3.06 td (9, 8)	3.07 td (10, 7.5)	2.48 d (9.5)
3	1.62 t (10)	1.57 t (9.5)	1.68 dd (10, 9)	1.59 dd (10.5, 8)	1.65 dd (10.5, 8)	1.42 dd (10, 7.5)	1.38 dd (14, 9.5)
	1.69 dd (10, 8)	1.97 dd (10, 8.5)	2.01 dd (10.5, 8.5)	1.75 t (10.5)	2.07 t (10)	2.06 t (10)	1.61 d (14)
5	1.76 t (10)	1.55 ddd	1.77 ddd	1.63 m	1.94 ddd	1.86 m	5.31 d (16)
		(11.5, 9.5, 1.5)	(12, 8.5, 1)		(10.5, 9, 1.5)		
6	1.43 tdd	1.92 ddd	1.35 ddd	1.32 dddd	1.53 dddd	1.73 m (2H)	5.49 ddd
	(13.5, 10.5, 4)	(13.5, 9, 1.5)	(14.5, 12, 9.5)	(15, 10, 8, 1.5)	(14.5, 13.5, 10.5, 3.5)		(16, 10.5, 5)
	1.65 dddd	2.09 ddd	2.20 ddd	1.65 m	1.66 dtd		
	(13.5, 5, 3.5, 1)	(13.5, 11.5, 8)	(14.5, 6, 1)		(14.5, 4, 1.5)		
7	0.97 td (13, 5)	5.55 tq (9, 1)	2.93 dd (9.5, 6)	1.54 ddd	0.95 td (13, 4)	1.86 m	1.65 t (10.5)
				(14.5, 8.5, 2)			
	2.09 dt (13, 3.5)			1.92 ddd	2.15 dt (13, 3.5)	2.60 dt (14, 4.5)	2.64 dd (10.5, 5)
				(14.5, 11, 1.5)			
9	2.87 dd (11, 4)	4.78 dd (11.5, 5.5)	3.74 dd (11, 6)	3.57 t (5.5)	2.69 dd (10, 5)	4.14 dd (10, 4.5)	2.73 dd (10,5)
10	1.32 dddd	1.62 td (13, 6)	1.72 dddd	1.58 m	1.44 dddd	2.02 m	1.38 dddd
	(12.5, 11, 8, 4.5)		(13.5, 12, 6, 1.5)		(13, 10.5, 6, 5)		(13.5, 10, 4, 2.5)
	2.25 ddt (12, 8, 4)	1.70 dddd	1.80 dddd	1.74 dddd	2.40 dddd	2.22 tdd	2.21 tt (13.5, 5)
		(13, 11.5, 6.5, 2)	(13.5, 11, 7.5, 1.5)	(14, 9.5, 5.5, 4)	(13, 10, 6.5, 5)	(11.5, 9, 1.5)	
11	2.11 ddd	1.84 br t (14)	2.09 br dd	2.07 dddd	2.53 m	2.29 td (11.5, 2)	1.08 td (13, 5)
	(12.5, 8, 4.5)		(13.5, 12)	(13.5, 9, 4, 1)			
	2.34 ddd	2.17 ddd	2.32 ddd	2.42 ddd	2.57 m	2.43 m	2.13 ddd
	(12.5, 8, 4.5)	(14, 7, 1.5)	(13.5, 7.5, 1.5)	(13.5, 9.5, 4.5)			(13, 6, 2.5)
12	4.86 d (1)	4.49 t (2)	4.55 t (2)	4.92 br s	—	—	1.31 s
	4.97 d (1)	4.73 q (1.5)	4.80 q (1.5)	4.94 br s			
13	1.01 s	1.01 s	0.98[a] s	0.98 s	1.040[b] s	1.03[b] s	1.20[c] s
14	0.98 s	0.97 s	0.98[a] s	1.00 s	1.035[b] s	1.02[b] s	1.08[c] s
15	1.20 s	1.64 br s	1.28 s	1.13 s	1.32 s	4.93 br s	1.31 s
						5.01 br s	

a) In benzene-d_6, 13-H_3 and 14-H_3 resonate at δ 0.80 and 0.85, respectively (difference NOE experiments). *b*) Assignments are based on correlation with the respective ^{13}C-signals in the ^{1}H–^{13}C COSY. *c*) Assignments may be interchanged.

TABLE II. 100 MHz ^{13}C-NMR Data for **1**, **3**, **6**, **8**, **5**, **9**, and **4** in $CDCl_3$

	1	**3**	**6**	**8**	**5**	**9**	**4**
1	151.8 s	154.6 s	153.8 s	151.8 s	214.0 s	213.3 s	60.1 s
2	48.7 d	42.5 d	42.8 d	42.3 d	52.6 d	46.6 d	64.7 d
3	39.8 t	39.7 t	40.2 t	36.0 t	35.3 t	33.0 t	38.4 t
4	34.1 s	33.2 s	32.8 s	34.1 s	34.5 s	34.2 s	35.7 s
5	50.8 d	50.3 d	44.2 d	57.1 d	51.4 d	51.3 d	142.9 d
6	27.2 t	28.6 t	32.1 t	23.2 t	26.5 t	27.1 t	122.6 d
7	39.2 t	125.9 d	63.7 d	40.8 t	39.0 t	29.8 t	43.4 t
8	59.8 s	138.0 s	63.6 s	75.0 s	58.9 s	147.4 s	60.1 s
9	63.7 d	69.7 d	71.2 d	73.3 d	61.6 d	76.3 d	60.4 d
10	30.3 t	34.3 t	34.0 t	32.5 t	24.8 t	29.6 t	25.2 t
11	29.8 t	32.5 t	30.9 t	34.7 t	37.7 t	40.5 t	34.9 t
12	112.8 t	109.7 t	110.5 t	110.4 t	—	—	16.6 q
13	21.7 q	22.8 q	22.8 q	22.1 q	22.3 q	22.3 q	23.4[a] q
14	29.9 q	30.0 q	30.1 q	30.0 q	29.4 q	29.3 q	30.8[a] q
15	17.0 q	15.6 q	15.9 q	21.4 q	16.2 q	116.9 t	16.6 q

a) Assignments may be interchanged.

separated into neutral and acidic fractions. The neutral fraction was then separated by a series of column chromatography and preparative TLC procedures to give twelve sesquiterpenes along with 4-stigmasten-3-one (**13**) and a sterol mixture comprising β-sitosterol, stigmasterol and campesterol.

Compounds **1**, colorless oil, $[\alpha]_D$ −54.7° (chloroform), and **3**, colorless oil, $[\alpha]_D$ +119.6° (chloroform), had the same molecular formula of $C_{15}H_{24}O$ and showed closely related NMR spectra (Tables I and II).

Detailed analysis of the respective ^{1}H–^{1}H and ^{1}H–^{13}C shift correlation spectroscopy (COSY) coupled with the respective ^{1}H–^{13}C long-range COSY spectra of **1** and **3** established their planar structures as those of caryophyllene oxide and caryophyllenol, respectively. The results of a series of difference nuclear Overhauser effect (NOE) experiments on **1** clearly showed that the cyclobutane ring is condensed in the *trans* mode and that 9-H is situated in close proximity to 5-H. These findings confirmed the structure of **1** to be that of β-caryophyllene 8*R*,9*R*-oxide[3] which has been found in the essential oils of various plants belonging to the families Myrtaceae,[4] Dipterocarpaceae,[5] Zingiberaceae,[6] Labiatae,[7] *etc.* It has also been obtained as the major product of the epoxidation reaction of β-caryophyllene.[8,9]

The ^{1}H- and ^{13}C-NMR data of **3** were identical to those reported for caryophyllenol-II,[9,10] thus establishing the identity of **3** as caryophyllenol-II. However, there appears to be some confusion in the literature regarding the stereochemistry of the 7,8-endocyclic double bond. This has been reported as *Z* by Gupta *et al.*,[5] whilst Groweiss *et al.*[9] and Connolly *et al.*[11] have reported it as *E*. We therefore proceeded to reexamine the relative stereochemistry of the compound. The results of a series of difference NOE experiments on **3**, obtained in this study, showed clear NOE between the 15-methyl protons (δ_H 1.64) and the 7-olefinic proton (δ_H 5.55) as shown in Fig. 1, thus confirming the *Z* configuration of the 7,8-endocyclic double bond. As in the case of **1**, the cyclobutane ring in **3** was also found to be condensed in the *trans* mode. Furthermore, NOE was also observed

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between the proton attached to the hydroxyl-bearing carbon (δ_H 4.78, 9-H) and 2-H (δ_H 2.68), indicating the spatial proximity of the two protons.

Both caryophyllenol-II (**3**) and its 9-OH epimer, caryophyllenol-I, have been isolated from *Dipterocarpus pilosus* (Dipterocarpaceae).[5] Monache *et al.*[12] have also reported the isolation of α-multijugenol, a compound similar to caryophyllenol-II, from *Copaifera multijuga*, belonging to the Leguminosae family. Caryophyllenol-II has also been obtained as one of the minor products of the oxidation of β-caryophyllene.[9,10] With regard to its biosynthesis, **3** is thought to be derived from the epoxide ring opening of β-caryophyllene 8*S*,9*S*-oxide.[9]

Compounds **5**, colorless oil, $[\alpha]_D$ −106.3° (chloroform), and **9**, colorless needles, mp 108—109 °C, $[\alpha]_D$ −29.4° (chloroform), were also shown to be isomeric compounds having the same molecular formula of $C_{14}H_{22}O_2$. Analysis of their ^1H–^1H and ^1H–^{13}C COSY spectra established their structures as the nor-sesquiterpene ketone kobusone[13] and its isomer isokobusone,[13] respectively. These compounds have been reported from species belonging to the Cyperaceae and Labiatae families.[13,14]

Compounds **6**, $[\alpha]_D$ +74.8° (chloroform), and **8**, $[\alpha]_D$ −26.0° (chloroform), were both obtained as amorphous solids and their molecular formulas were determined as $C_{15}H_{24}O_2$ and $C_{15}H_{26}O_2$, respectively, by high-resolution MS (HR-MS). Both compounds contained a hydroxy function(s) as indicated by broad absorptions near 3400 cm^{-1} in their IR spectra. They also showed NMR spectra similar to those of caryophyllenol-II (**3**) and β-caryophyllene 8*R*,9*R*-oxide (**1**) (Tables I and II) although a few signals showed significant differences.

A comparison of the ^{13}C-NMR spectrum of **6** with that of **3** clearly showed the loss of two sp^2 carbon signals (δ_C 125.9 and 138.0 in **3**) in the spectrum of **6**. The appearance, however, of carbon signals at δ_C 63.7 (d, C-7) and 63.6 (s, C-8) in the ^{13}C-NMR spectrum of **6** suggested that the unsaturation at these positions in **3** has been replaced by C–O bonds in an epoxide ring. On the other hand a comparison of the ^{13}C-NMR spectra of **8** and **1** clearly showed that the carbon signals at δ_C 59.8 (s, C-8) and 63.7 (d, C-9) in **1** have shifted downfield to δ_C 75.0 (s) and 73.3 (d), respectively, in the case of **8**. From the presence of a proton signal at δ_H 3.57 (t, J=5.5 Hz) in the ^1H-NMR spectrum of **8**, coupled with the broad absorption at 3500 cm^{-1} in the IR spectrum, it was concluded that the epoxide ring in **1** had been opened to give the 8- and 9-hydroxyl substituents in **8**. Further analysis of the ^1H- and ^{13}C-NMR data with the aid of ^1H–^1H and ^1H–^{13}C COSY spectra established the planar structures of both **6** and **8**.

A series of difference NOE experiments on both **6** (in C_6D_6) and **8** established their respective ring A/B junctions to be *trans*; *viz.* NOE's were observed between the 14-methyl protons and the 5-H signals and between the 13-methyl protons and the 2-H signals, respectively, in the two compounds. In the case of **6**, NOE's were also observed between 2α-H and 9-H, and between 7-H and the 15-methyl protons. These results, coupled with the vicinal coupling constants of 7-H and of 9-H, confirmed the relative stereochemistry of **6** (Fig. 1). In **8**, NOE was observed between 5β-H and 9-H although irradiation at the frequency of 15-H_3 did not cause an enhancement of the intensity of 9-H. From these results, the relative stereochemistry of **8** was deduced to be as shown in Fig. 1.

Compound **8** appears to be a new oxygenated caryophyllane-type sesquiterpene, reported here for the first time. With regard to its biosynthesis, the compound appears to arise from the epoxide ring opening of β-caryophyllene 8*R*,9*R*-oxide (**1**) in a stepwise fashion, in which an allylic 9*R*-alcohol intermediate such as 2*S*,5*R*,9*R*-caryophylla-1(12),8(15)-dien-9-ol or 2*S*,5*R*,9*R*-caryophylla-1(12),7-dien-9-ol (caryophyllenol-I) could be involved. Experimental results have shown that the exocyclic olefin compound, 2*S*,5*R*,9*R*-caryophylla-1(12),8(15)-dien-9-ol, is the major product obtained in the epoxide ring opening of **1**.[10] It is thus possible that this 8(15)-ene form may be the preferred intermediate in the formation of **8**.

On the other hand, **6** appears to be identical to an epoxyalcohol obtained by Groweiss *et al.*[9] as a minor product of the *m*-chloroperbenzoic acid epoxidation of β-caryophyllene. Although the stereochemistry of the epoxide ring was not indicated, the significant ^1H- and ^{13}C-NMR data reported for this compound show close similarities to those of **6**. Groweiss and Kashman[9] suggested that this epoxyalcohol probably arose from the epoxidation of the allyl alcohol, caryophyllenol-II (**3**), which was formed from the epoxide ring opening of the unstable intermediate, β-caryophyllene 8*S*,9*S*-oxide.

Compound **4** was obtained as colorless needles, mp 106—107°C, $[\alpha]_D$ −5.6° (chloroform), and the molecular

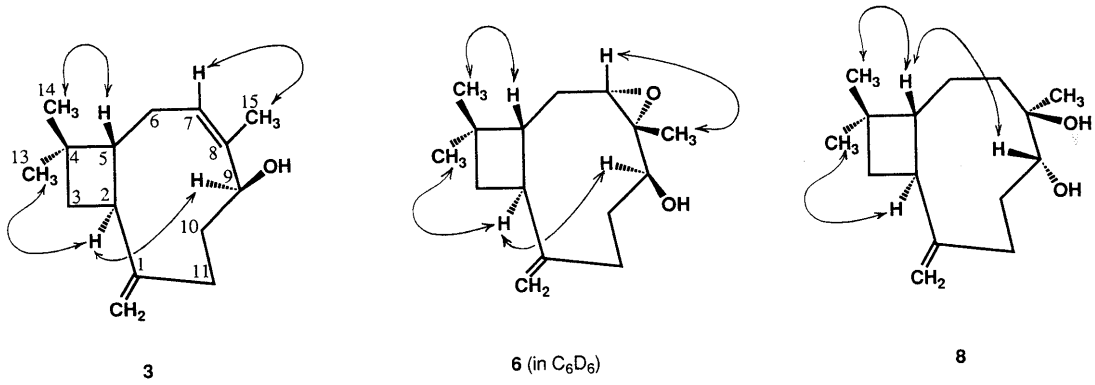

Fig. 1. NOE Correlations Observed in **3**, **6** and **8**

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formula was determined by HR-MS as $C_{15}H_{24}O_2$. Detailed analysis of the ^1H–^1H and ^1H–^{13}C COSY spectra confirmed compound **4** to be humulene diepoxide A, previously isolated from hops.[15] This compound has also been obtained from the essential oil of wild ginger (*Zingiber zerumbet*, FAM. Zingiberaceae).[6] The absolute configuration of the optically resolved (−)-humulene-1,12:8,9-diepoxide, $[\alpha]_D$ −83.5° (chloroform), has been determined by X-ray crystallographic studies.[16] However the $[\alpha]_D$ value of **4**, obtained in this study, is extremely small compared to that of the optically resolved humulene diepoxide, thus suggesting that **4** is probably a racemate.

Compound **11a**, one of the major components of the neutral fraction, was obtained as colorless needles, mp 152—153 °C, $[\alpha]_D$ +3.2° (chloroform), and the molecular formula was determined by HR-MS as $C_{15}H_{26}O_2$. Acetylation of **11a** with excess acetic anhydride–pyridine at room temperature afforded a diacetate **11b**, colorless needles, mp 96—97 °C, $C_{19}H_{30}O_4$ and a monoacetate **11c**, amorphous solid, $C_{17}H_{28}O_3$.

Detailed analysis of the ^1H–^1H, ^1H–^{13}C and ^1H–^{13}C long-range COSY spectra of both **11a** and **11b** confirmed the planar structure of **11a** to be that of clovanediol.[5,17–21]

The stereochemistry of clovanediol had been proposed by Aebi *et al.*[21] based on chemical and IR spectroscopic evidence. We now report a reinvestigation of this stereochemistry based on ^1H-NMR coupling constants and the results of a series of difference NOE experiments on both **11a** and its diacetate derivative **11b**.

Irradiation of the 14-methyl protons (**11a**: δ_H 1.04; **11b**: δ_H 1.06) caused an enhancement of the intensity of the 5-H signal (**11a**: δ_H 1.42; **11b**: δ_H 1.53). NOE was also observed between 2-H (δ_H 3.79) and both the signals at δ_H 0.86 (13-H_3) and 0.91 (12-H), respectively, in **11a**. Based on these observations the stereochemistry of the C-12 methano bridge was elucidated to be α and that of the 2-OH substituent to be β.

With regard to the conformation of ring C of **11a**, NOE was observed between the 10-methylene proton at δ_H 1.99 and the 5-H signal at δ_H 1.42 and between the 12-methylene proton at δ_H 1.56 and the 11-H signal (δ_H 1.66, m). In the chair conformation both 12-H (δ_H 1.56) and 11-H (δ_H 1.66) would be in a 1,3-diaxial relationship and therefore in spatial proximity. Similarly, 10-H (δ_H 1.99) would be axial and hence spatially close to the 5-methine proton. Furthermore, the ^1H–^1H COSY revealed long-range couplings between the proton signal at δ_H 0.91 (12β-H) and the proton signals at δ_H 1.07 (11β-H) and 3.32 (9-H), respectively, which could be explained in terms of long-range coupling *via* W-interaction. Based on these results and also the broad singlet nature of 9-H, the stereochemistry of the 9-hydroxysubstituent was defined as α(9*R*). In ring B of the molecule, the boat conformation may be preferred to the chair form in terms of stability. In the chair conformation, the 6- and 10-protons may be forced near each other, thus leading to instability due to steric factors as rationalized by Aebi *et al.*[21]

TABLE III. 400 MHz ^1H-NMR Data for **2**, **11a**, **11b**, **7**, **12a**, **12b** and **10** in $CDCl_3$ (Coupling Constants in Parenthesis)

	2	**11a**	**11b**	**7**	**12a**	**12b**	**10**
2	5.27 d (5.5)	3.79 dd (10.5, 5.5)	4.86 dd (8, 6)	1.74 q-like	2.22 ddd (12, 10, 8.5)	2.23 ddd (12.5, 10.5, 8)	2.30 ddd (12.5, 10.5, 8)
3	5.35 d (5.5)	1.51 dd (11.5, 10)	1.57 dd (13, 8)	1.61 dd (9.5, 8)	1.49 dd (10, 9)	1.48 t (10.5)	1.44 t (10)
		1.71 dd (11.5, 5.5)	1.82 dd (13, 6)	1.66 t (9.5)	1.54 t (10)	1.54 dd (10.5, 8)	1.53 dd (10, 8)
5	1.52 m	1.42 m	1.53 m	1.76 m	1.89 ddd (12, 9, 6)	1.89 ddd (12.5, 9, 6)	1.88 ddd (12.5, 9, 6)
6	1.46 m	*ca.* 1.32 m	1.38 dddd (16, 14, 12, 5.5)	1.27 tdd (13, 12, 5)	1.39 m	1.40 ddt (13, 6, 4)	1.43 ddt (14, 6, 4.5)
	1.50 m	*ca.* 1.35 m	1.49 m	1.46 ddt (13, 5.5, 2)	1.53 m	1.54 m	1.51 tdd (14, 10, 3)
7	1.18 ddd (14, 11, 5.5)	*ca.* 1.11 m	1.22 ddd (13.5, 10, 5.5)	1.06 td (13, 5.5)	1.15 m	1.21 ddd (13.5, 8, 4.5)	1.11 dt (13.5, 4)
	1.38 ddd (14, 5.5, 4)	*ca.* 1.50 m	1.42 ddd (13.5, 6, 2)	2.10 ddd (13, 5, 1.5)	1.42 m	1.44 br t (14)	1.64 td (13.5, 4.5)
9	3.35 br s	3.32 br s	4.55 br s	—	3.44 t (3)	4.66 t (3)	3.37 dd (11, 5.5)
10	1.62 ddt (14.5, 5, 2)	1.64 m	1.68 ddt (15.5, 5, 2.5)	2.37 ddd (16.5, 10, 4)	1.77 ddt (15, 5, 3)	1.81 ddt (15, 5, 3)	1.76 dddd (14, 13, 11, 4.5)
	2.05 dddd (14.5, 13, 5.5, 3.5)	1.99 m	1.95 dddd (15.5, 13.5, 5, 3.5)	2.79 ddd (16.5, 12, 4.5)	2.04 dddd (15, 12.5, 5.5, 3)	2.03 dddd (15, 12, 6, 3)	1.85 dtd (14, 5.5, 2.5)
11	1.11 ddt (13, 5.5, 2)	1.07 m	1.26 ddt (13.5, 5, 2.5)	1.86 dddt (12, 10, 4.5, 1.5)	1.51 m	1.53 m	1.50 td (13, 2.5)
	1.70 td (13, 5)	1.66 m	1.47 td (13.5, 5)	2.00 td (12, 4)	1.64 td (12.5, 5)	1.58 td (12.5, 5.5)	1.65 m
12	0.99 ddd (13, 2, 1)	0.91 br d (12.5)	1.10 dt (13, 2)	2.03 br s (2H)	1.42 d	1.49 br s (2H)	1.08 d (13)
	1.44 d (13)	1.56 d (12.5)	1.54 d (13)		1.47 d		1.67 d (13)
13	0.96 s	0.86 s	0.93 s	0.96 s	1.00[a] s	1.01 s	1.015[a] s
14	1.07 s	1.04 s	1.06 s	1.01 s	1.02[a] s	1.03 s	1.020[a] s
15	0.94 s	0.96 s	0.85 s	1.12 s	0.93 s	0.85 s	0.97 s
$OCOCH_3$			2.05 s 2.06 s			2.05 s	

a) Assignments are based on correlation with the respective ^{13}C-signals in the ^1H–^{13}C COSY.

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TABLE IV. 100 MHz ^{13}C-NMR Data for **2**, **11a**, **11b**, **11c**, **7**, **12a**, **12b** and **10** in $CDCl_3$

	2	**11a**	**11b**	**11c**[a)]	**7**	**12a**	**12b**	**10**
1	50.0 s	44.6 s	44.6 s	44.5 s	69.4 s	70.7 s	70.5 s	70.4 s
2	136.4 d	80.8 d	82.2 d	82.1 d	43.0 d	38.0 d	38.1 d	37.4 d
3	138.9 d	47.5 t	44.5 t	44.4 t	34.4 t	34.0 t	34.0 t	34.0 t
4	47.9 s	37.1 s	38.4 s	38.1 s	33.6 s	35.0 s	35.2 s	35.3 s
5	49.7 d	50.6 d	50.2 d	50.3 d	45.0 d	43.8 d	43.9 d	43.8 d
6	21.2 t	20.7 t	20.7 t	20.8 t	25.6 t	20.3 t	20.4 t	20.0 t
7	33.7 t	33.2 t	32.9 t	31.4 t	38.6 t	35.3 t	35.1 t	29.45 t
8	34.3 s	34.7 s	33.6 s	33.1 s	46.8 s	39.3 s	38.4 s	38.8 s
9	74.4 d	75.1 d	76.7 d	74.9 d	216.8 s	72.1 d	74.2 d	78.2 d
10	27.3 t	26.0 t	24.1 t	25.4 t	34.5 t	28.1 t	25.7 t	29.52 t
11	33.5 t	26.4 t	27.99 t	27.4 t	36.9 t	33.3 t	33.8 t	38.0 t
12	35.5 t	35.6 t	36.4 t	35.5 t	49.2 t	42.4 t	43.2 t	47.5 t
13	24.9 q	25.4 q	25.5 q	26.4 q	21.8 q	20.8 q	20.8 q	20.7 q
14	32.8 q	31.4 q	31.5 q	29.7 q	30.3 q	30.5 q	30.6 q	30.6 q
15	28.4 q	28.4 q	28.02 q	28.3 q	31.2 q	26.7 q	26.8 q	28.7 q
$OCO\underline{C}H_3$	—	—	21.3 q (2C)	21.3 q	—	—	21.2 q	—
$O\underline{C}OCH_3$	—	—	170.8 s (2C)	171.0 s	—	—	170.6 s	—

a) Assignments are based on comparison with ^{13}C-NMR data for **11b**.

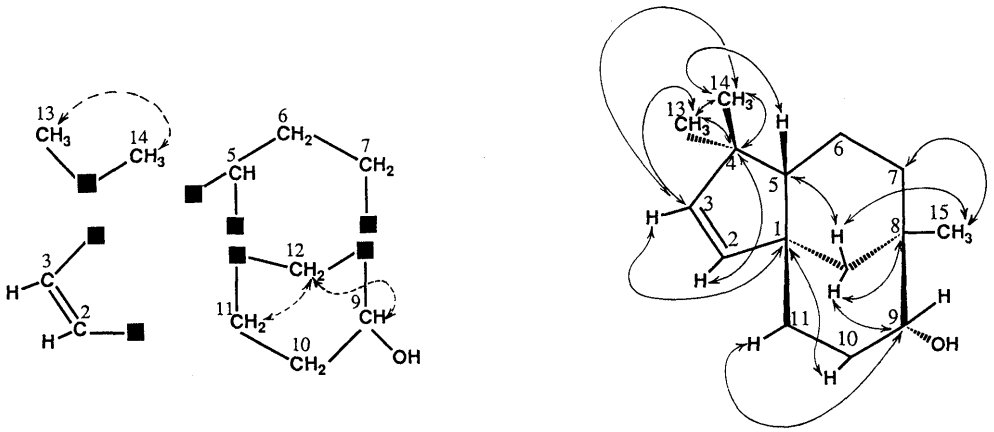

Fig. 2. Partial Structures Deduced by ^{1}H–^{1}H and ^{1}H–^{13}C COSY (Left) and Long-Range Connectivities Observed in ^{1}H–^{13}C Long-Range COSY (Right) of **2**

, long-range correlations observed in ^{1}H–^{1}H COSY.

Our results, based on NMR experimental evidence, thus confirm the stereochemistry proposed for clovane-diol.

Compound **2** was obtained as colorless needles, mp 79—80°C, $[\alpha]_D$ −39.3° (chloroform). The MS of **2** showed the molecular ion peak at *m/z* 220 and the molecular formula was determined by HR-MS to be $C_{15}H_{24}O$. The IR spectrum showed a broad hydroxy absorption at 3470 cm^{-1}. The ^{1}H- and ^{13}C-NMR spectra indicated the presence of a secondary alcohol group (δ_H 3.35, br s; δ_C 74.4) and olefinic signals (δ_H 5.27, 5.35, each d, J=5.5 Hz; δ_C 136.4, 138.9) along with three tertiary methyl, five methylene, four methine and three quaternary carbons (Tables III and IV). These ^{1}H- and ^{13}C-NMR data were found to be very similar to those obtained for clovane-2β,9α-diol (**11a**) except for the appearance of two new signals due to an olefinic group (C-2 and C-3) in **2** instead of the signals due to a secondary hydroxyl (δ_H 3.79; δ_C 80.8, C-2) and a methylene group (δ_C 47.5, C-3) in **11a**. These data suggested that **2** could be a dehydrated derivative of **11a**. This was supported by two-dimensional (2D) NMR analysis, in which partial structures from ^{1}H–^{1}H and ^{1}H–^{13}C COSY and connectivities found in ^{1}H–^{13}C long-range COSY were obtained as shown in Fig. 2.

The stereochemistry at the C-5 and C-9 chiral centers and also for the C-12 methano bridge in **2** were also confirmed by evidence obtained from NMR data as in the case of **11a**. The broad singlet exhibited by the methine proton attached to the hydroxyl-bearing carbon (9-H) and the coupling constants of 10-H_2 (δ_H 1.62, ddt, J= 14.5, 5, 2 Hz; δ_H 2.05, dddd, J=14.5, 13, 5.5, 3.5 Hz) and 11-H_2 (δ_H, 1.11, ddt, J=13, 5.5, 2 Hz; δ_H 1.70, td, J=13, 5 Hz) confirmed that ring C of **2** also exists in the preferred chair coformation with the 9-OH substituent in an axial disposition. This was further supported by the observation of NOE's between the methine proton at δ_H 1.52 (5-H) and the axial 10-H signal (δ_H 2.05) and between the 12-methylene proton at δ_H 1.44 and the axial 11-H signal (δ_H 1.70).

Clovane-2β,9α-diol has been isolated from a number of species belonging to the Dipterocarpaceae,[5)] Labiatae,[19)]

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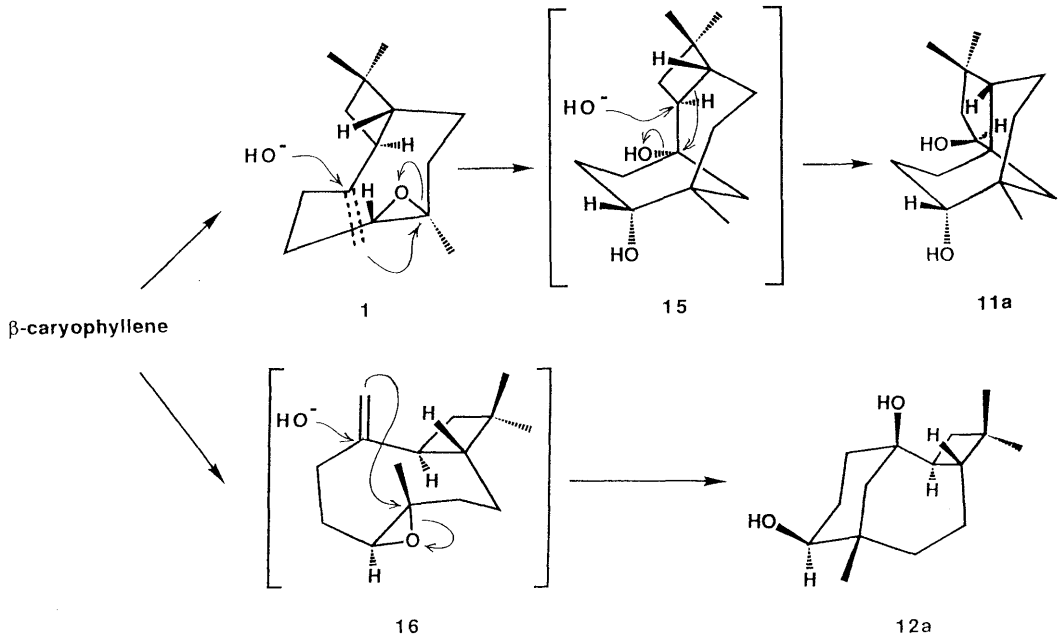

Chart 2

and Compositae families.[20] This compound has also been obtained as a product from the acid-catalyzed cyclization of β-caryophyllene 8*R*,9*R*-oxide (**1**).[17,18] However, **2** appears to be a new clovane-type sesquiterpene, reported here for the first time.

Compound **7**, colorless prisms, mp 100—101 °C, $[\alpha]_D$ −62.0° (chloroform), and compound **12a**, a pale yellowish oil, $[\alpha]_D$ +2.1° (chloroform), had the molecular formulas $C_{15}H_{22}O_2$ and $C_{15}H_{24}O_2$, respectively. Their IR spectra showed broad hydroxyl absorptions at 3450 cm^{-1} and 3400 cm^{-1}, respectively. In addition, that of **7** showed an intense carbonyl absorption at 1690 cm^{-1}. The two compounds also showed closely related NMR spectra (Tables III and IV) except for a few significant differences which suggested that the secondary hydroxyl group in **12a** was probably replaced by a ketone group in **7**.

Jones oxidation of **12a** gave **7**, thus confirming that **7** was the hydroxyketone derivative of **12a**. On acetylation with acetic anhydride–pyridine at room temperature, **12a** afforded an acetate **12b**, as colorless prisms, mp 103—104 °C. Detailed analysis of the ^1H–^1H, ^1H–^{13}C and long-range ^1H–^{13}C COSY spectra of both **12a** and the acetate **12b** established the planar structure of **12a**, which was found to be identical to that of both caryolane-1,9-diol[7,13] and senecrassidiol,[22] respectively.

Thus, in order to establish the identity of **12a**, its relative stereochemistry was investigated based on its ^1H-NMR coupling constants and on a series of difference NOE experimental results obtained for the acetate **12b**. Irradiation of the 14-methyl protons (δ_H 1.03) caused an enhancement of the intensity of 5-H (δ_H 1.89), whilst irradiation of the 13-methyl protons (δ_H 1.01) caused an enhancement of 2-H (δ_H 2.23). It was therefore concluded that the cyclobutane ring of the molecule is condensed in the *trans* mode. NOE correlation was also observed between 5-H (δ_H 1.89) and 12-H_2 (δ_H 1.49), suggesting that the stereochemistry of the 12-methano bridge is β.

With regard to the confomation of the six-membered ring of the molecule, inspection of Dreiding models coupled with the ^1H-NMR coupling constants of the 9- and 10-protons suggested that it probably exists in the chair conformation. This was confirmed by the observation of clear NOE between the 2α-methine proton and the axial 10-proton (δ_H 2.03, dddd, J=15, 12, 6, 3 Hz). From the inspection of Dreiding models these observations could be explained in terms of a chair conformation of the six-membered ring in which the axial 10-H is in an α configuration and therefore in spatial proximity to 2α-H. The triplet signal due to the methine proton on the hydroxyl-bearing carbon (δ_H 4.66, J= 3.0 Hz, 9-H) would then suggest an equatorial disposition of the 9-proton. Hence the 9-hydroxyl substituent would be axial and its stereochemistry defined as β(9*S*). These results thus confirmed the structure of **12a** as caryolane-1,9β-diol.[7,13]

Compound **10** was obtained as colorless needles, mp 136.5—137.5 °C, $[\alpha]_D$ −5.60° (chloroform), and the molecular formula was determined by HR-MS as $C_{15}H_{26}O_2$. The ^1H- and ^{13}C-NMR spectra of **10** were similar to those of **12a** (Tables III and IV). Detailed analysis of the ^1H–^1H, ^1H–^{13}C and long-range ^1H–^{13}C COSY of **10** and the ^1H-NMR double doublet splitting pattern of the methine proton attached to the hydroxyl-bearing carbon (δ_H 3.37, J=11, 5.5 Hz, 9-H) showed that the two compounds were epimeric at the C-9 position. This epimeric relationship of the two compounds was confirmed by the Jones oxidation of **10** to give the hydroxyketone **7**.

From these data and from comparisons with the literature data, **7**, **12a** and **10** were identified as 9-oxocaryolane-1-ol, caryolane-1,9β-diol and caryolane-1,9α-diol, respectively.[18,21]

Caryolane-1,9β-diol has been reported as a by-product of the epoxidation of β-caryophyllene.[8,21] Oxidation of

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this compound yielded the hydroxyketone **7**, which, on subsequent reduction with sodium and propanol afforded the 9-OH epimer **10**.[21] However, this is the first time any of these compounds has been isolated from a natural source.

The co-occurrence of clovane-type (**2**, **11a**) and caryolane-type (**7**, **10**, **12a**) sesquiterpenoids in the same mixture is of great interest. The presence of β-caryophyllene 8*R*,9*R*-oxide (**1**) itself in this mixture is also very significant.

With regard to the probable biosynthesis of these sesquiterpenoids, it would thus appear that epoxidation of β-caryophyllene could lead to the formation of both the 8*R*,9*R*- and 8*S*,9*S*-epoxides (Chart 2). Subsequent transformations of the 8*R*,9*R*-epoxide, involving a transannular cyclization could lead to an intermediate tricyclic compound **15** of the type envisaged by Aebi *et al.*[21] Subsequent bond migration could then lead to the formation of the clovane-type compounds **2** and **11a**. On the other hand, the 8*S*,9*S*-epoxide could also undergo transformation through a transannular cyclization of the 9-membered ring to form tricyclic compounds of the caryolane-type in which bond migration is unfavourable in steric terms, unlike in the case of its 8*R*,9*R*-epimer.

In addition, the presence of caryophyllane-, humulane-, clovane- and caryolane-type sesquiterpenoids in *S. sumatrana* is of chemotaxonomic interest as it offers further evidence of the co-occurrence of these structural types within the Leguminosae.[23]

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are 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 IR 260-10 spectrophotometer. MS and HR-MS measurements were done on a JEOL D-300 spectrometer using a direct inlet system at the ionization voltage of 70 eV. ^1H-, ^{13}C- and 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 distortionless enhancement by polarization transfer (DEPT) method and are indicated as s (singlet), d (doublet), t (triplet) and q (quartet).

Column chromatography was carried out over silica gel (Mallinkrodt, 100 mesh) and the eluates were monitored by TLC. Analytical TLC and preparative TLC were carried out on precoated Merck Kieselgel 60 F_{254} plates (0.25, 0.5, 1.0 and 2.0 mm). Detection of separated spots was done by spraying with $Ce(SO_4)_2$–10% H_2SO_4 (1:99) reagent. Elution of separated bands was done with MeOH–CH_2Cl_2 (15:85) and the eluates were concentrated *in vacuo*.

Gas chromatography (GC) analyses were done on a Shimadzu GC-6A gas chromatograph, using a flame ionization detector and a 2% OV-17 column (on Gas Chrom. Q, 2 m × 3 mm i.d. glass tube) at an injection temperature of 290 °C and a column temperature of 280 °C. Nitrogen was used as the carrier gas.

Extraction and Fractionation The powdered dried pods of *Sindora sumatrana* MIQ. (4 kg) was extracted by refluxing with MeOH (7 l, 4 h, × 3) and the combined extracts were concentrated *in vacuo* at 40 °C to give a syrupy residue. This residue was next separated into $CHCl_3$- and AcOEt-soluble fractions by successively shaking with $CHCl_3$ (1.6 l × 3) and AcOEt (1 l × 3) in that order, leaving a syrupy residue (71 g) which was soluble in MeOH. The bulked $CHCl_3$ and AcOEt-soluble fractions were respectively concentrated *in vacuo* to give a syrupy $CHCl_3$-soluble fraction (900 g) and an AcOEt-soluble fracion (8.6 g).

A portion of the $CHCl_3$-soluble fraction (260 g) was dissolved in Et_2O and extracted with 5%Na_2CO_3. The Et_2O layers were washed with water, dried and concentrated to give the neutral fraction (80 g). The aqueous layer was acidified with 5% HCl and extracted with Et_2O. The Et_2O extract was washed with water, dried and concentrated to give the acidic fraction (160 g).

Separation of Neutral Fraction The neutral fraction (80 g) was chromatographed on a silica gel (1 kg) column with hexane–$CHCl_3$ (50:50, 3 l), $CHCl_3$ (3 l) and MeOH–$CHCl_3$ (5:95, 3 l; 10:90, 3 l; 20:80, 3 l; 30:70, 1 l) gradient mixtures. Eluates were collected in 250 ml portions, monitored by TLC and subsequently combined into a total of seventeen fractions [fr. 1, hexane–$CHCl_3$ (50:50) eluate; frs. 2—5, $CHCl_3$ eluate; frs. 6—10, MeOH–$CHCl_3$ (5:95) eluate; frs. 11—13, MeOH–$CHCl_3$ (10:90) eluate; fr. 14, MeOH–$CHCl_3$ (10:90, 20:80) eluates; fr. 15, MeOH–$CHCl_3$ (20:80) eluate; fr. 16, MeOH–$CHCl_3$ (20:80, 30:70) eluates; fr. 17, MeOH–$CHCl_3$ (50:50) eluate].

Treatment of Fractions 2, 3 and 4 Fractions 2, 3 and 4 were combined (9.4 g) and rechromatographed on a silica gel (200 g) column with hexane, $CHCl_3$–hexane (25:75, 50:50, 75:25) gradient mixtues and $CHCl_3$. The eluates were combined into a total of nineteen fractions (frs. A-1 to A-19).

Fractions A-2 (1.5 g) and A-3 (1.1 g) [$CHCl_3$–hexane (50:50) eluates] were respectively rechromatographed on silica gel (50 g) columns with benzene. The less polar fractions were combined and again chromatographed on a silica gel (80 g) column with benzene–hexane gradient mixtures to afford compound **1** (β-caryophyllene 8*R*,9*R*-oxide, 498 mg). Also the more polar fractions were combined and purified by silica gel column chromatography to give 4-stigmasten-3-one (**13**, 38 mg) which was identified by GC comparison with an authentic sample.

Fraction A-8 [$CHCl_3$–hexane (50:50) eluate] yielded a crystalline mass which was recrystallized from MeOH to afford colorless plates (94 mg). GC analysis of this substance, using authentic samples, revealed the presence of β-sitosterol, campesterol and stigmasterol (intensity ratio 76:12.5:11.5). The mother liquor from fr. A-8 was combined with frs. A-4 to A-7 (2.0 g) and rechromatographed over silica gel (120 g) with benzene–hexane (20:80, 30:70, 50:50, 70:30) gradient mixtures, benzene and AcOEt–benzene (10:90, 50:50) gradient mixtures. An eluate with benzene–hexane (70:30) was further purified by repeated preparative TLC using AcOEt–hexane (10:90) to afford compound **2** (25 mg), while a benzene–hexane (50:50, 70:30) eluate was also purified by preparative TLC to give compound **3** (caryophyllenol-II, 19 mg).

Fractions A-12 to A-14 [$CHCl_3$–hexane (50:50, 75:25) eluates] were subjected to preparative TLC using AcOEt–hexane (10:90) and the fractions obtained were further purified by preparative TLC using acetone–hexane (10:90) to yield compound **4** (humulene diepoxide A, 10 mg) and compound **5** (kobusone, 100 mg).

Treatment of Fractions 5, 6 and 7 Fractions 5, 6 and 7 were combined (17.8 g) and rechromatographed over silica gel (500 g) with $CHCl_3$–hexane (20:80, 30:70) gradient mixtures, $CHCl_3$ and MeOH–$CHCl_3$ (5:95, 15:85) gradient mixtures. The eluates obtained were monitored by TLC and combined into twenty-four fractions (frs. B-1 to B-24).

Fractions B-4 to B-7 [$CHCl_3$–hexane (20:80) eluates] were respectively subjected to preparative TLC with AcOEt–hexane (10:90) and benzene–CH_2Cl_2–Et_2O (45:45:10) to give additional crops of **1** (146 mg) and **2** (160 mg).

Fractions B-10 and B-11 [$CHCl_3$–hexane (20:80) eluate] were combined and subjected to preparative TLC using acetone–benzene (5:95) to afford **3** (19 mg). Fraction B-13 [$CHCl_3$–hexane (20:80) eluate] was separated by preparative TLC using benzene–CH_2Cl_2–E_2O (45:45:10) to yield compound **6** (8 mg).

Frations B-14 to B-21 [$CHCl_3$–hexane (20:80, 30:70) eluates] afforded an additional crop of steroidal mixture (298 mg).

Treatment of Fraction 8 Fraction 8 (15.6 g) was rechromatographed on a silica gel (700 g) column with $CHCl_3$–hexane (30:70, 40:60, 50:50, 70:30, 90:10) gradient mixtures, $CHCl_3$ and MeOH–$CHCl_3$ (5:95). The eluates obtained were combined into fifty-five fractions (frs. C-1 to C-55). These fractions were further separated by preparative TLC using Et_2O–hexane (80:20). Fractions C-3 to C-5 [$CHCl_3$–hexane (40:60) eluates] gave compound **7** (24 mg). Fractions C-10 to C-12 [$CHCl_3$–hexane (40:60, 50:50) eluates] gave an unidentified compound (tentatively named SS1, 26 mg). Fractions C-20 and C-21 [$CHCl_3$–hexane (50:50) eluates] gave compound **8** (38 mg) and frs. C-34 to C-37 [$CHCl_3$–hexane (50:50) eluate] gave compound **9** (isokobusone, 41 mg).

Treatment of Fractions 10 and 11 Fractions 10 and 11 were combined (5.25 g) and rechromatographed on a silica gel (230 g) column with $CHCl_3$–hexane (30:70, 50:50, 70:30, 90:10) gradient mixtures, $CHCl_3$ and MeOH–$CHCl_3$ (5:95). The eluates obtained were combined into

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thirty-two fractions (frs. D-1 to D-32) and further separated by preparative TLC using Et_2O–hexane (80:20). Fractions D-9 to D-14 [$CHCl_3$ eluates] gave an impure compound (tentatively named SS2) from the less polar fraction and a crystalline mass from the more polar fraction. The latter was recrystallized from $CHCl_3$ to yield **10** (68 mg). Fractions D-15 to D-25 [$CHCl_3$ and MeOH–$CHCl_3$ (5:95) eluates] contained complex mixtures of sesquiterpenoids whose separation is still in progress, whilst frs. D-27 and D-28 [MeOH–$CHCl_3$ (5:95) eluates] gave compound **11a** (clovane-2β,9α-diol, 63 mg).

Treatment of Fraction 13 Fraction 13 (5.9 g), on dissolution in $CHCl_3$–hexane (30:70) mixture, afforded a crystalline mass, which was recrystallized from $CHCl_3$–hexane to give **11a** (clovanediol, 296 mg). The mother liquor was concentrated and chromatographed on a silica gel (200 g) column with $CHCl_3$–hexane (50:50, 80:20) gradient mixtures, $CHCl_3$ and MeOH–$CHCl_3$ (5:95) mixture. The eluates obtained were combined into a total of twenty-four fractions (frs. 13-1 to 13-24).

Fraction 13-15 [MeOH–$CHCl_3$ (5:95) eluate, 430 mg] was found to be a complex mixture and this was acetylated with Ac_2O in pyridine at room temperature over a period of 10 d and the reaction mixture was worked up in the usual manner to afford the acetylated product. Separation of this substance by preparative TLC using acetone–benzene (10:90), gave a small amount of an unidentified compound tentatively named SS3.

Fractions 13-16 and 13-17 [MeOH–$CHCl_3$ (5:95) eluates] yielded **12a** (296 mg) as an oily substance, whilst fr. 13-19 [MeOH–$CHCl_3$ (5:95) eluate] gave an additional crop of **11a** (342 mg). The mother liquor from fr. 13-19 was treated overnight with Ac_2O in pyridine at room temperature and the reaction mixture was worked up in the usual manner to give the actylated product. This was then separated by preparative TLC using acetone–benzene (10:90) to give **11b** (2β,9α-diacetoxyclovane, 140 mg).

Fraction 13-20 [MeOH–$CHCl_3$ (5:95) eluate] was acetylated with Ac_2O and pyridine to give **11b** (2β,9α-diacetoxyclovane, 180 mg).

Compound 1 (β-Caryophyllene 8*R*,9*R*-Oxide) Colorless oil, $[\alpha]_D$ $-57.7°$ ($c=0.6$, $CHCl_3$). IR ν_{max} cm^{-1}: 1450, 1380, 1210. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 220 (M^+, 37), 205 (18), 204 (30), 192 (33), 176 (29), 166 (31), 151 (44), 148 (79), 147 (60), 137 (59), 106 (82), 93 (100). HR-MS: Found 220.1831, Calcd for $C_{15}H_{24}O$ (M^+) 220.1828.

Compound 2 (Clov-2-ene-9α-ol) Colorless needles (acetone), mp 79—80 °C. $[\alpha]_D$ $-39.3°$ ($c=1.6$, $CHCl_3$). IR ν_{max} cm^{-1}: 3400 (br), 1466, 1452, 981, 964. ^{1}H- and ^{13}C-NNR: Tables III and IV. MS *m/z* (%): 220 (M^+, 3), 205 (42), 202 (15), 187 (54), 174 (14), 161 (100), 159 (14), 145 (14), 131 (16). HR-MS: Found 220.1830, Calcd for $C_{15}H_{24}O$ (M^+) 220.1828.

Compound 3 (Caryophyllenol-II) Colorless oil, $[\alpha]_D$ $+119.6°$ ($c=1.27$, $CHCl_3$). IR ν_{max} cm^{-1}: 3400 (br), 1700, 1440, 1200, 1040. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 220 (M^+, 53), 205 (54), 202 (69), 187 (84), 164 (71), 161 (100), 159 (75), 149 (91), 135 (92), 123 (77), 121 (80), 109 (91), 107 (75), 93 (73).

Compound 4 (Humulene Diepoxide A) Colorless needles ($CHCl_3$), mp 106—107 °C. $[\alpha]_D$ $-5.6°$ ($c=0.80$, $CHCl_3$). IR ν_{max} cm^{-1}: 1440, 1380, 1210, 970. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 236 (M^+, 37), 218 (49), 203 (19), 200 (15), 185 (21), 175 (20), 157 (22), 145 (37), 144 (29), 119 (23), 111 (100), 109 (43), 107 (29), 93 (41). HR-MS: Found 236.1774, Calcd for $C_{15}H_{24}O_2$ (M^+) 236.1775.

Compound 5 (Kobusone) Colorless oil, $[\alpha]_D$ $-106.3°$ ($c=2.53$, $CHCl_3$). IR ν_{max} cm^{-1}: 1685, 1450, 1220, 1200. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 222 (M^+, 13), 207 (10), 194 (27), 193 (18), 165 (65), 149 (24), 137 (36), 114 (27), 112 (33), 96 (100), 95 (37).

Compound 6 (7,8-Epoxy-1(12)-caryophyllene-9β-ol) Amorphous solid, $[\alpha]_D$ $+74.8°$ ($c=0.53$, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1200. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 236 (M^+, 23), 221 (40), 218 (33), 206 (19), 173 (33), 161 (68), 151 (80), 137 (68), 111 (89), 107 (78). HR-MS: Found 236.1751, Calcd for $C_{15}H_{24}O_2$ (M^+) 236.1775.

Compound 7 (9-Oxocaryolane-1-ol) Colorless prisms ($CHCl_3$–hexane), mp 100—101 °C. $[\alpha]_D$ $-62.0°$ ($c=1.6$, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1690, 1420, 1210. ^{1}H- and ^{13}C-NMR: Tables III and IV. MS *m/z* (%): 236 (M^+, 20), 219 (7), 218 (100), 203 (16), 179 (38), 164 (52), 161 (41), 154 (22), 126 (29), 125 (27), 123 (38). HR-MS: Found 236.1769, Calcd for $C_{15}H_{26}O_2$ (M^+) 236.1763; Found 218.1670, Calcd for $C_{15}H_{22}O$ (M^+-H_2O) 218.1670.

Compound 8 (8,9-Dihydroxy-1(12)-caryophyllene) Amorphous solid, $[\alpha]_D$ $-26.0°$ ($c=2.5$, $CHCl_3$). IR ν_{max} cm^{-1}: 3500 (br), 1450, 1375, 1210. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 238 (M^+, 7), 237 (38), 223 (24), 203 (47), 177 (36), 163 (33), 149 (87), 135 (56), 123 (53), 109 (100), 91 (72). HR-MS: Found 238.1941, Calcd for $C_{15}H_{26}O_2$ (M^+) 238.1933.

Compound 9 (Isokobusone) Colorless needles ($CHCl_3$–hexane), mp 108—109 °C. $[\alpha]_D$ $-29.4°$ ($c=2.73$, $CHCl_3$). IR ν_{max} cm^{-1}: 3485 (br), 1680, 1450, 1370, 1210, 1035, 1010. ^{1}H- and ^{13}C-NMR: Tables I and II. MS *m/z* (%): 222 (M^+, 72), 212 (31), 204 (100), 189 (48), 175 (42), 166 (50), 151 (52), 119 (51), 109 (52), 107 (61), 95 (68), 81 (44).

Compound 10 (Caryolane-1,9α-diol) Colorless needles ($CHCl_3$), mp 136.5—137.5 °C. $[\alpha]_D$ $-5.6°$ ($c=2.05$, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1450, 1200, 1050. ^{1}H- and ^{13}C-NMR: Tables III and IV. MS *m/z* (%): 238 (M^+, 1), 223 (2), 220 (76), 202 (100), 187 (53), 179 (40), 166 (44), 161 (60), 159 (38), 127 (73), 123 (58), 109 (49). HR-MS: Found 238.1948, Calcd for $C_{15}H_{26}O_2$ (M^+) 238.1933; Found 220.1827, Calcd for $C_{15}H_{24}O$ (M^+-H_2O) 220.1827; Found 202.1723, Calcd for $C_{15}H_{22}$ (M^+-2H_2O) 202.1721.

Compound 11a (Clovane-2β,9α-diol) Colorless needles ($CHCl_3$–hexane), mp 152—153 °C. $[\alpha]_D$ $+3.19°$ ($c=2.27$, $CHCl_3$). IR ν_{max} cm^{-1}: 3450 (br), 1460, 1200, 1065. ^{1}H- and ^{13}C-NMR: Tables III and IV. MS *m/z* (%): 238 (M^+, 27), 220 (54), 205 (24), 202 (100), 187 (59), 174 (44), 164 (34), 161 (51), 159 (46), 146 (54), 135 (21), 133 (21), 130 (20), 121 (18), 107 (16), 105 (17), 94 (17). HR-MS: Found 238.1925, Calcd for $C_{15}H_{26}O_2$ (M^+) 238.1935; Found 202.1745, Calcd for $C_{15}H_{22}$ (M^+-2H_2O) 202.1722.

Compound 12a (Caryolane-1,9β-diol) Yellow oil. $[\alpha]_D$ $+2.1°$ ($c=3.08$, $CHCl_3$). IR ν_{max} cm^{-1}: 3400 (br), 1450, 1200, 1050, 1015. ^{1}H- and ^{13}C-NMR: Tables III and IV. MS *m/z* (%): 238 (M^+, 1), 223 (2), 220 (83), 202 (100), 187 (67), 179 (54), 161 (63), 159 (37), 127 (54), 123 (46), 109 (44). HR-MS: Found 238.1933, Calcd for $C_{15}H_{26}O_2$ (M^+) 238.1933; Found 220.1825, Calcd for $C_{15}H_{24}O$ (M^+-H_2O) 220.1827.

Jones Oxidation of 10 Oxidation of **10** (20 mg) in acetone (2 ml) was done with Jones reagent (4 drops) at 0 °C for 1 h. After the usual work-up, the oily substance obtained was subjected to preparative TLC using Et_2O–hexane (80:20). The crystalline substance obtained was recrystallized from $CHCl_3$-hexane to give 9-oxocaryolane-1-ol (**7**, 12 mg), colorless prisms, mp 100—101 °C. $[\alpha]_D$ $-60°$ ($c=0.80$, $CHCl_3$).

Jones Oxidation of 12a Oxidation of **12a** (20 mg) was conducted according to the method described above to yield 9-oxocaryolane-1-ol (**7**, 10 mg). $[\alpha]_D$ $-54.4°$ ($c=0.67$, $CHCl_3$).

Acetylation of 12a Acetylation of **12a** (50 mg) was carried out overnight with excess Ac_2O in pyridine at room temperature. The reaction mixture was worked up in the usual manner to give a gummy product, which was subjected to preparative TLC using acetone–benzene (10:90). The crystalline mass obtained was recrystallized from Et_2O to give the acetate **12b** (70 mg): Colorless prisms (Et_2O), mp 103–104 °C, $[\alpha]_D$ $+16.7°$ ($c=0.77$, $CHCl_3$). IR ν_{max} cm^{-1}: 3400 (br), 1740, 1450, 1370, 1250, 1210, 1020. ^{1}H- and ^{13}C-NMR: Tables III and IV. MS *m/z* (%): 280 (M^+, 6), 262 (38), 220 (51), 202 (100), 187 (27), 179 (29), 162 (41), 161 (66), 159 (26), 149 (24), 123 (61), 109 (87), 95 (20). HR-MS: Found 262.1948, Calcd for $C_{17}H_{26}O_2$ (M^+-H_2O) 262.1933; Found 220.1797, Calcd for $C_{15}H_{24}O$ (M^+-AcOH) 220.1827.

Acetylation of 11a Acetylation of **11a** (50 mg) was conducted in the same manner as described for **12a** to yield both the diacetate **11b** (72 mg) and the monoacetate **11c** (6 mg). **11b**: Colorless needles (Et_2O), mp 96—97 °C. $[\alpha]_D$ $-45.7°$ ($c=0.73$, $CHCl_3$). IR ν_{max} cm^{-1}: 1720, 1375, 1260, 1100, 1040. ^{1}H- and ^{13}C-NMR: Tables III and IV. MS *m/z* (%): 262 (M^+-AcOH, 45), 220 (10), 202 (100), 187 (22), 174 (10). HR-MS: Found 262.1935, Calcd for $C_{17}H_{26}O_2$ (M^+-AcOH) 262.1933; Found 202.1728, Calcd for $C_{15}H_{22}$ (M^+-2AcOH) 202.1722.

11c: Colorless amorphous solid. IR ν_{max} cm^{-1}: 3400 (br), 1720, 1250, 1035. ^{1}H-NMR δ: 0.92, 0.95, 1.05 (each 3H, s, 15-H_3, 13-H_3 and 14-H_3 respectively), 2.04 (3H, s, $OCOCH_3$), 3.31 (1H, br s, 9-H), 4.84 (1H, dd, $J=9$, 6 Hz, 2-H). ^{13}C-NMR: Table IV. These NMR data were obtained by comparison with the ^{1}H- and ^{13}C-NMR data of **11b**. MS *m/z* (%): 280 (M^+, 0.5), 262 (13), 247 (4), 220 (7), 202 (100), 187 (46), 174 (27), 159 (40). HR-MS: Found 280.2011, Calcd for $C_{17}H_{28}O_3$ (M^+) 280.2037; Found 220.1821, Calcd for $C_{15}H_{24}O$ (M^+-AcOH) 220.1826; Found 202.1728, Calcd for $C_{15}H_{22}$ (M^+-AcOH$-H_2O$) 202.1821.

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