Pergamon

Tetrahedron, Vol. 52, No. 23, pp. 7961-7972, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00367-5

The Cleavage of Caryophyllene Oxide Catalysed by Tetracyanoethylene

Isidro G. Collado[†], James R. Hanson[†*] and Antonio J. Macías-Sánchez[*]

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz, Apartado 40, 11510 Puerto Real, Cádiz, Spain.

[*]The School of Chemistry and Molecular Sciences, University of Sussex, Brighton, Sussex, BN1 9QJ Great Britain

Abstract: The cleavage of caryophyllene oxide under novel, mild and clean conditions, using tetracyanoethylene as a catalyst, is described. Alcoholysis leads to clovenol-2-ether derivatives as major products. When dipolar aprotic solvents were used, rearrangement products were not formed and compounds from elimination reaction were obtained. The ratio of cyclization to elimination products reflects the extent to which the partially delocalized carbocation may be stabilized by the nucleophilic solvent. Copyright © 1996 Elsevier Science Ltd

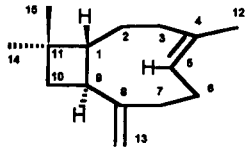
INTRODUCTION

The acid-catalysed cyclization of caryophyllene (**1**) leads to a complex mixture of products the detailed composition of which depends upon the reaction conditions[1]. In the first instance two groups of compounds with skeleta related to caryolan-1-ol (**2**) and clovene (**3**) are formed[1] which then undergo further rearrangement[2]. A more complex pattern has emerged from the rearrangement of caryophyllene oxide (**4**)[1]. A significant inhibition of the growth of *Botrytis cinerea* has been observed when it is incubated with compounds obtained from the rearrangement of isocaryophyllene (**5**)[3,4]. In order to obtain further compounds for study we have examined the alcoholysis of caryophyllene oxide under novel mild, clean conditions using tetracyanoethylene (TCNE) as a catalyst[5a,b]. Tetracyanoethylene behaves as a mild π-acid catalyst and in the steroid series, it affords the products of trans-diaxial opening of epoxides[6].

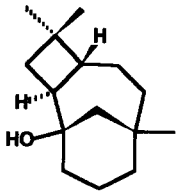
RESULTS AND DISCUSSION

Caryophyllene-4β,5α-oxide (**4**), free from isomeric epoxides[7], was stirred in methanol with tetracyanoethylene (0.1 mol equiv.) for 12 hr. at room temperature. The readily separable products were the 2β-monomethyl ether (**7**) of clovan-2β,9α-diol (**6**), the simple alcoholysis product (**14**) and the elimination product (**13**). The major product (**7**) (40% yield) was characterized by its NMR spectra (for ^{13}C NMR spectra see table 1). The ^{1}H-NMR spectrum showed signals at δ 3.36 ppm (s,OMe), 3.32 ppm (dd, 1H, J=5.5,10.3 Hz, C<u>H</u>(OMe)) and 3.30 ppm (s br, C<u>H</u>(OH)), assigned to -OMe(β), H-2α and H-9β, respectively. Nuclear Overhauser enhancement and 2D COSY studies led to a full assignment of the ^{1}H-NMR

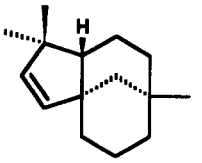
† Authors to whom correspondence should be addressed.



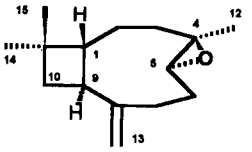
1



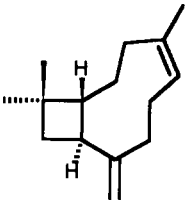
2



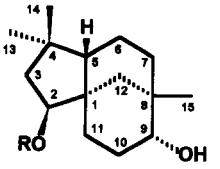
3



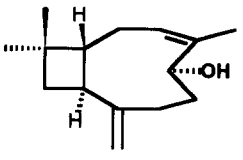
4



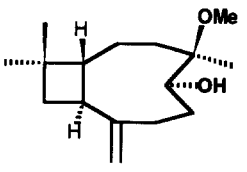
5



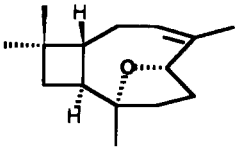
6 R = H
7 R = CH_3
8 R = $C(CH_3)_3$
9 R = CH_2CH_2Cl
10 R = CH_2CH_2OH
11 R = $CH_2CH_2NO_2$
12 R = $CH_2CH{=}CH_2$



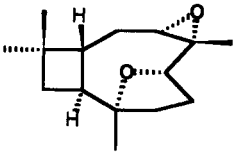
13



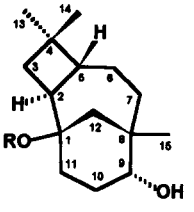
14



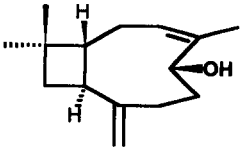
15



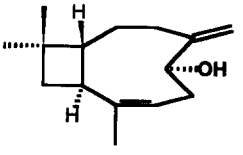
16



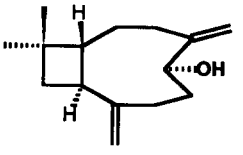
17 R = H
18 R = CH_2CH_2OH
19 R = $CH_2CH{=}CH_2$



20



21



22

spectrum and are fully consistent with the stereochemistry. This data was very similar to that of the known clovan-2β,9α-diol (**6**)[8]. The elimination product (**13**) possessed both the exocyclic alkene resonance of caryophyllene (δ 4.86 , 4.83 (2s, 2H)), a trisubstituted double-bond (δ 5.42 (t br, 1H, J=7.7Hz)) and a methine hydrogen, α to an hydroxy group (δ 4.60 (dd, 1H, J=5.3,9.6Hz)). The Z geometry of the double bond and the α stereochemistry for the hydroxy group were established by n.O.e. effects between H-3 and the vinylic methyl and between H-5β and H-1β, respectively. The simple alcoholysis product (**14**) possessed the signals characteristic of a methoxyl group (δ 3.19 (3H, s)) and a secondary alcohol (δ 3.70 (dd, 1H, J=4.5,7.1Hz)). It was assigned the stereochemistry β-OMe, H-5β on the basis of n.O.e. effects between the methoxy group and H-5 and between H-5 and H-1β (see figure 1).

The reaction was then repeated with a number of alcohols (see table 2). The clovandiol-2-ethers derivatives (**8-12**) were obtained as the major products. The structures were elucidated by extensive NMR investigation (see experimental for ^{1}H NMR and table 1 for ^{13}C NMR data). In two cases, caryolane-1-ethers (**18,19**) were also isolated. Their structures were established by comparision of their ^{1}H and ^{13}C NMR data with that of caryolan-1,9α-diol (**17**).

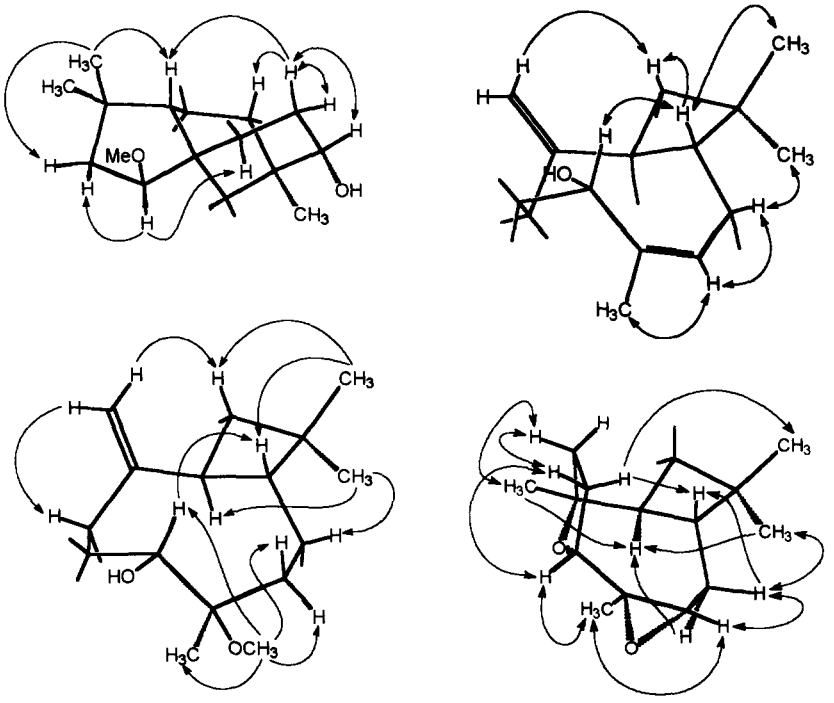


Figure 1. Selected n.O.e. correlations observed in **7**, **13**, **14**, and **16**

When 2-chloroethanol was used as a solvent, a cyclic ether (**15**) was obtained as the minor product and no compound **13** was detected. Compound **15** showed ^{1}H-NMR signals at δ 5.35 (qd, 1H, J=1.5,8.5Hz, H-3) and 4.48 (dd, 1H, J=9.4,5.5 Hz, H-5β), which correspond to an olefinic proton on a trisubstituted double

Table 1. 50 MHz and 100 MHz ^{13}C NMR data for **6**, **7** ,**8** , **9**, **10**, **11**, **12** **17**, **18**, **19** in $CDCl_3$.

	6	**7**	**8**	**9**	**10**	**11**	**12**	**17**	**18**	**19**
1	44.6 s	*44.15 s	• 43.81 s	*44.43 s	†44.33 s	*44.63 s	*44.38 s	70.4 s	75.30 s	75.78 s
2	80.8 d	90.08 d	79.51 d	89.11 d	88.70 d	89.36 d	87.78 d	37.4 d	38.53 d	38.80 d
3	47.5 t	44.04 t	47.87 t	44.49 t	44.46 t	43.96 t	44.60 t	34.0 t	35.86 t	29.05 t
4	37.1 s	*36.96 s	• 36.67 s	*37.14 s	†37.09 s	*37.42 s	*37.10 s	35.3 s	35.29 s	*35.24 s
5	50.6 d	50.57 d	49.69 d	50.42 d	50.55 d	50.32 d	50.55 d	43.8 d	44.80 d	44.81 d
6	20.7 t	20.53 t	*20.68 s	•20.56 t	*20.53 t	•20.60 t	20.61 t	20.0 t	20.72 t	20.88 t
7	33.2 t	33.09 t	*33.31 s	•33.05 t	*33.02 t	•33.02 t	33.19 t	29.45 t	35.76 t	35.89 t
8	34.7 s	*34.69 s	• 34.75 s	*34.68 s	†34.86 s	*34.62 s	*34.72 s	38.8 s	39.06 s	*38.99 s
9	75.1 d	75.16 d	75.25 d	75.11 d	75.12 d	75.03 d	75.20 d	78.2 d	72.39 d	72.39 d
10	26.0 t	25.97 t	25.97 t	26.03 t	25.92 t	26.08 t	26.10 t	29.52 t	28.04 t	28.05 t
11	26.4 t	26.52 t	27.05 t	26.69 t	26.71 t	26.55 t	26.83 t	38.0 t	28.80 t	36.13 t
12	35.6 t	36.49 t	35.73 t	36.33 t	36.36 t	36.20 t	36.46 t	47.5 t	40.23 t	40.84 t
13	25.4 q	25.35 q	†25.25 q	25.39 q	25.34 q	25.43 q	25.37 q	20.7 q	20.55 q	20.61 q
14	31.4 q	31.25 q	31.23 q	31.27 q	31.26 q	31.29 q	31.31 q	30.6 q	30.53 q	30.40 q
15	28.4 q	28.36 q	†28.43 q	28.34 q	28.32 q	28.31 q	28.36 q	28.7 q	26.85 q	26.70 q
1'	-	58.22 q	28.76 3q	70.51 t	71.29 t	65.68 t	71.17 t	-	*62.45 t	63.37 t
2'	-	-	72.39 s	43.11 t	62.06 t	75.51 t	135.68 d	-	*62.57 t	136.12 d
3'	-	-	-	-	-	-	115.89 t	-	-	115.51 t

Data for **6** and **17** taken from ref. 8; *,†,• interchageable signals

bond and to a hydrogen atom in an α position to the oxygen atom of a cyclic ether. The stereochemistry of the compound was carefully established through a full set of n.O.e. experiments (see figure 1) with the epoxide (**16**), obtained from peracid epoxidation of **15**.

Attempts to introduce nitrogen nucleophiles by carrying out the reaction in the presence of diethylamine, ethanolamine or sodium azide were unsuccessful. However when the reaction was carried out in a dipolar aprotic solvent, in the presence of lithium bromide, cyclization products were on the whole not formed and the products were those of elimination (see table 3) comprising different proportions of the exo- (**22**) and endo- (**13**) alkenes. They were distinguished by their ^{1}H-NMR spectra (**22** δ 4.95, 5.04 (2H, 2s, C=CH_2, H-12,12'), **13** δ 5.42 (br dd, 1H, J=7.7,7.7Hz, H-3 (C=CH))). When one equivalent of hydroxylamine hydrochloride in acetone was used (an effective way of releasing an accurate amount of HCl) the minor products included caryophyllenol-II[9] (**20**), the double bond isomer (**21**) and the cyclic ether (**15**). Compound **15** was the only reaction product when compound **13** was dissolved in acetone and treated with TCNE and hydroxylamine hydrochloride. This is in accordance with the stereochemistry of **15** that we assigned through n.O.e. experiments of the epoxide (**16**).

The formation of these cyclization products under mild conditions can be rationalized in terms of the possible conformations of caryophyllene oxide in which the exocyclic alkene may act as an internal nucleophile. The ratio of cyclization to elimination products reflects the extent to which the partially delocalized carbocation may be stabilized by the nucleophilic solvent.

A different situation can be depicted for compounds **15** and **21**. Once caryophyllene oxide is isomerized to **13** and **22**, a protonation of the exocyclic double bond[10] takes place and elimination (to give **21**) or etherification (to give **15**) then occurs.

Table 2

4 (mg)	Alcohol	TCNE (mol eq)	Temp. (°C)	Time(hr	Product (yield)
510	CH_3OH	0.1	25	12	**7** (40%), **13** (22%), **14** (8%)
250	t-BuOH	0.1	80	12	**8** (32%), **13** (15%)
500	$HOCH_2CH_2Cl$	0.1	25	12	**9** (34%) , **15** (8%)
1000	$HOCH_2CH_2OH$	0.1	25	48	**10**(32%), **18**(12%), **13**(5%), **22** (5%)
1250	$HOCH_2CH_2NO_2$	0.1	25	48	**11** (30%), **13** (8%), **22** (7%)
1100	$HOCH_2CH=CH_2$	0.1	25	12	**19** (4%),**12** (30%), **13** (5%), **22** (5%)

Table 3.

4 (mg)	Alcohol	Reagent (mol eq.)	Temp. (°C)	Time (hr.)	Product (yield)
420	acetone	TCNE (0.2) + LiBr (5)	25	1	**13** (22%), **22** (71%)
250	acetone	TCNE (0.2) + NH_2OHHCl (1)	25	3	**13** (34%), **15** (6%), **20** (5%), **21** (8%), **22** (5%)
500	DMSO	TCNE (0.1)	25	12	**13** (46%) , **22** (18%)

Table 4. 50 MHz and 100 MHz ^{13}C NMR data for **13**, **14**, **15**, **16**, **20**, **21**, **22** in $CDCl_3$.

	13	**14**	**15**	**16**	**20**	**21**	**22**
1	52.82 d	55.13 d	45.72 d	44.12 d	50.3 d	48.73 d	54.23 d
2	26.92 t	*22.39 t	26.61 t	29.56 t	28.6 t	29.42 t	*37.06 t
3	125.62 d	*32.38 t	140.03 s	62.68 d	125.9 d	30.30 t	*32.58 t
4	*136.92 s	79.93 s	122.66 d	*64.59 s	138.0 s	*150.23 s	+151.34 s
5	69.65 d	72.87 d	80.48 d	77.62 d	69.5 d	76.29 d	75.22 d
6	36.66 t	*34.27 t	34.56 t	32.13 t	34.3 t	34.11 t	*32.51 t
7	32.33 t	36.29 t	31.23 t	31.71 t	32.5 t	118.43 d	*32.83 t
8	*153.26 s	153.06 s	85.13 s	*86.66 s	154.6 s	*141.82 s	+152.46 s
9	42.88 d	41.99 d	49.30 d	48.90 d	42.5 d	40.76 d	43.83 d
10	37.17 t	*33.02 t	36.18 t	36.09 t	39.7 t	37.56 t	*30.67 t
11	33.78 s	33.94 s	34.16 s	34.11 s	33.2 s	33.70 s	33.83 s
12	16.82 q	15.55 q	26.07 q	22.70 q	15.6 q	112.70 t	113.39 t
13	109.88 t	110.48 t	26.47 q	26.74 q	109.7 t	22.18 q	109.14 t
14	22.17 q	22.19 q	*29.83 q	29.76 q	22.8 q	*21.97 q	†30.00 q
15	30.18 q	30.18 q	*21.04 q	21.08 q	30.0 q	*30.06 q	†21.97 q
1'	-	48.50 q	-	-	-	-	-
2'	-	-	-	-	-	-	-

Data for **20** taken from ref. 8; *,†,•,+ interchageable signals

EXPERIMENTAL

Melting points were measured with a Kofler block Reichert-Jung apparatus and are uncorrected. Optical rotations were determined with a Perkin -Elmer 241 polarimeter. IR spectra were recorded on a Perkin-Elmer 881 spectrophotometer or on a Bio-Rad FTS-7 Fourier-Transfom spectrophotometer. ^1H and ^{13}C NMR measurements were obtained on Varian Gemini 200 and Varian Unity 400 NMR spectrometers with $SiMe_4$ as internal reference. Mass spectra were recorded on VG 12-250 spectrometer at 70 eV. HPLC was performed with a Hitachi/Merck L-6270 apparatus equiped with a UV-VIS detector (L 4250) and a differential refractometer detector (RI-71). TLC was performed on Merck Kieselgel 60 F_{254}, 0.2 mm thick. Silica gel (Merck) was used for column chromatography. Purification by HPLC was accomplished using a Si gel column (Hibar 60, 7 μm, 1 cm wide, 25 cm long).

General procedure for the alcoholysis of 4 with TCNE. Caryophyllene oxide (**4**) dissolved in the alcohol (10 cm^3) was treated with TCNE. The progress of the reaction was monitored by TLC. When the epoxide was consumed (see table 2) the solvent was either evaporated under vacuum or washed with brine. The resulting gum was redissolved in a more volatile solvent (AcOEt) and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether (reaction conditions, products and

yields in table 2), giving **7**, **8**, **9**, **10**, **11**, **12**, **13**, **14**, **15**, **18**, **19**, **21**, **22**

General procedure for the reaction of 4 with TCNE in dipolar aprotic solvents. Caryophyllene oxide (**4**) was dissolved in 10 ml of solvent and LiBr, NH_2OH•HCl or neither of these were added (see reaction conditions in table 3). Then a catalytic amount of TCNE was added and reaction mixture was stirred for different times. Once the reaction was complete (TLC control), it was worked-up in the same way as described in the general procedure for alcoholysis, to yield **13**, **15**, **20**, **21**, **22**.

Treatment of 13 with hydroxylamine hydrochloride and TCNE in acetone. Compound **13** (176 mg) was dissolved in acetone (10 ml). To this mixture, NH_2OH•HCl (70 mg) and TCNE (25 mg) were added and reaction was stirred overnight. The reaction was worked up following the procedure described previously to yield **15** (96 mg, 54%).

2β-Methoxyclovan-9α-ol (**7**). White crystals, mp 51-52 °C. $[\alpha]_D^{25}$ + 6 (c = 0.005, $CHCl_3$). Anal. Found: C,76.1;H,11.3. $C_{16}H_{28}O_2$ requires C,76.1;H,11.2%. **IR**(film) 3454, 2937, 2865, 1462, 1385, 1279, 1194, 1108, 1053, 991, 946, 915, 843 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.86 (s, 3H, H-13α), 0.97 (s, 3H, H-15), 0.99 (m, 1H, H-12), 1.03 (brs, 3H, H-14β), 1.05-1.15 (2H, H-11α,H-7β), 1.30-1.44 (2H, H-6,H-6') 1.40 (m, 1H, H-7α), 1.42 (m, 1H, H-5β), 1.47 (dd, 1H, $J_{3\beta\text{-}2\alpha}$= 10.3Hz, $J_{3\beta\text{-}3\alpha}$= 11.8 Hz, H-3β), 1.56-1.66 (2H, H-10α,H-12'), 1.69 (brdd, 1H, $J_{11\beta\text{-}10\beta}$= 5.0 Hz, $J_{11\beta\text{-}11\alpha}$= 13.6Hz, H-11β), 1.72 (dd, 1H, $J_{3\alpha\text{-}2\alpha}$= 5.5 Hz, $J_{3\alpha\text{-}3\beta}$= 11.8 Hz, H-3α), 1.98 (dddd, 1H, $J_{10\beta\text{-}11\alpha}$= 14.2 Hz, $J_{10\beta\text{-}10\alpha}$= 14.2 Hz, $J_{10\beta\text{-}11\beta}$= 5.0 Hz, $J_{10\beta\text{-}9\beta}$= 3.1 Hz, H-10β), 3.32 (dd, 1H, $J_{2\alpha\text{-}3\alpha}$= 5.5 Hz, $J_{2\alpha\text{-}3\beta}$= 10.3 Hz, H-2α), 3.30 (m, 1H, H-9β), 3.36 (s, 3H, -OMe(H-1')). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 1). **EIMS** *m/z* (70 eV) 252 (15.3)[M^+], 237(19)[M^+-15], 220(10)[M^+-15-17], 205(17), 196(16), 193(32), 178(45), 163(26), 161(25), 150(27), 137(40), 135(40), 133(20), 121(15), 105(25), 99(100), 91(30), 85(34), 79(30), 77(26), 69(27), 67(24), 55(40), 41(50). **HREIMS** 252.2082 ($C_{16}H_{28}O_2$ requires 252.2082).

2β-t-Butoxyclovan-9α-ol (**8**). White crystals, mp 81-83 °C. $[\alpha]_D^{25}$ + 16 (c = 0.021 ,$CHCl_3$). Anal. Found: C,77.4;H,12.0. $C_{19}H_{34}O_2$ requires C,77.5;H,11.6%. **IR**(film) 3420, 2949, 2865, 1464, 1388, 1362, 1197, 1167, 1128, 1087, 1044, 992, 970, 944, 888 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H, H-13α), 0.88 (m, 1H, H-12), 0.93 (s, 3H, H-15), 0.98 (brs, 3H, H-14β), 1.04 (ddd, 1H, $J_{11\text{-}11'}$= 13.8 Hz, $J_{11\text{-}10'}$= 4.6 Hz, $J_{11\text{-}10}$= 2.2 Hz, H-11), 1.10 (m, 1H, H-7), 1.14 (brs, 9H, -C(CH_3)$_3$), 1.35-1.40 (4H, H-5β,H-6,H-6',H7'), 1.46-1.50 (3H, H-3,H-3',H-12'), 1.55 (dddd, 1H, $J_{10\text{-}10'}$= 14.2 Hz, $J_{10\text{-}9\beta}$= 2.3 Hz, $J_{10\text{-}11}$= 2.2 Hz, $J_{10\text{-}11'}$= 4.6 Hz, H-10), 1.66 (ddd, 1H, $J_{11'\text{-}10'}$= 14.1 Hz, $J_{11\text{-}11'}$= 13.8 Hz, $J_{11'\text{-}10}$= 4.6 Hz,H-11'), 1.95 (dddd, 1H, $J_{10\text{-}10'}$= 14.2 Hz, $J_{10'\text{-}11'}$= 4.6 Hz, $J_{10'\text{-}9\beta}$= 3.2 Hz, $J_{10'\text{-}11'}$= 14.1 Hz, H-10'), 3.27 (m, 1H, H-9β), 3.50 (dd, 1H, $J_{2\alpha\text{-}3'}$= 6.4 Hz, $J_{2\alpha\text{-}3}$= 10.0 Hz, H-2α). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 1). **EIMS** *m/z* (70 eV) 294 (2.8)[M^+], 279(2)[M^+-15], 262(0.1)[M^+-15-17], 237(2.5)[M^+- C(CH_3)$_3$)], 221(8)[M^+- OC(CH_3)$_3$)], 203(29)[M^+- OC(CH_3)$_3$)], 177(4), 163(8), 142(13), 141(100), 139(20), 121(10), 85(39), 69(8), 57(18). **HREIMS** 294.2557 ($C_{19}H_{34}O_2$ requires 294.2550).

2β-(2-Chloroethoxy)-clovan-9α-ol (**9**). White crystals, mp 81.5-83.5 °C. $[\alpha]_D^{25}$ + 12 (c = 0.011, $CHCl_3$). Anal. Found: C,67.8;H,10.3. $C_{17}H_{29}ClO_2$ requires C,67.9;H,9.7%. **IR**(film) 3429, 2949, 2866, 1464, 1362, 1196, 1131, 1108, 1052, 991, 944, 752, 673 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H, H-13α),

0.94 (s, 3H, H-15), 0.99 (d, 1H, $J_{12\text{-}12'}$=12.6 Hz, H-12), 1.01 (s, 3H, H-14β), 1.05-1.14 (2H, H-11,H-6), 1.27 (m, 1H, H-7), 1.34-1.43 (3H, H-5β,H-7',H-6'), 1.50 (dd, 1H, $J_{3\text{-}3'}$= 11.8 Hz, $J_{3\text{-}2\alpha}$= 10.1 Hz, H-3), 1.57 (d, 1H, $J_{12\text{-}12'}$= 12.6 Hz, H-12'), 1.59 (dddd, 1H, $J_{10\alpha\text{-}9\beta}$=$J_{10\alpha\text{-}11}$=$J_{10\alpha\text{-}11'}$= 3.6 Hz, $J_{10\alpha\text{-}10\beta}$= 14.2 Hz, H-10α), 1.67 (dd, 1H, $J_{3'\text{-}3}$= 11.8 Hz, $J_{3'\text{-}2\alpha}$= 5.5 Hz, H-3'), 1.68 (m, 1H, H-11'), 1.95 (dddd, 1H, $J_{10\beta\text{-}11'}$= 3.2 Hz, $J_{10\beta\text{-}10\alpha}$= 14.2 Hz, $J_{10\beta\text{-}11}$= 4.7 Hz, $J_{10\beta\text{-}9\beta}$= 3.1 Hz, H-10β), 3.30 (brs, 1H, H-9β), 3.42 (dd, 1H, $J_{2\alpha\text{-}3'}$= 5.5 Hz, $J_{2\alpha\text{-}3}$= 10.0 Hz, H-2α), 3.57 (m, 2H, H-2'), 3.69 (m, 2H, H-1'). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 1). **EIMS** *m/z* (70 eV) 302 (2.8)[M^++2], 300 (8.4)[M^+], 287 (5.7)[M^++2-15], 285 (19.7)[M^+-15], 243(8), 241(12), 226(26), 220(10)[M^+-$HOCH_2CH_2Cl$], 205(24), 187(17), 176(11), 164(31), 163(43), 161(29), 150(44), 149(49), 147(100), 137(27), 135(41), 133(37), 121(18), 107(20), 105(28), 93(17), 91(15), 79(30), 77(14), 69(24), 62(27), 55(18), 43(18), 41(30). **HREIMS** 300.1850 ($C_{17}H_{29}O_2Cl$ requires 300.1848).

2β-(2-Hydroxyethoxy)-clovan-9α-ol (10). White crystals, mp 81.5-83 °C. $[\alpha]_D^{25}$ + 6 (c = 0.02, $CHCl_3$). Anal. Found: C,70.3;H,10.4. $C_{17}H_{30}O_3 \cdot 0.5H_2O$ requires C,70.0;H,10.7%. **IR**(film) 3399, 2948, 2866, 1463, 1384, 1365, 1111, 1053, 944, 755 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H, H-13α), 0.93 (s, 3H, H-15), 0.96 (d, 1H, $J_{12\text{-}12'}$= 12.2 Hz, H-12), 1.01 (s, 3H, H-14β), 1.05-1.13 (2H, H-11,H-7), 1.28 (m, 1H, H-6), 1.34-1.42 (3H, H-5β,H-7',H-6'), 1.48 (dd, 1H, $J_{3\text{-}3'}$= 11.9 Hz, $J_{3\text{-}2\alpha}$= 10.2 Hz, H-3), 1.58 (d, 1H, $J_{12\text{-}12'}$= 12.2 Hz, H-12'), 1.59 (m, 1H, H-10), 1.64-1.74 (2H, H-11',H-3'), 1.95 (dddd, 1H, J= 3.2,14.1,14.1,5.0, H-10'), 3.30 (brs, 1H, H-9β), 3.44 (dd, 1H, $J_{2\alpha\text{-}3'}$= 5.5 Hz, $J_{2\alpha\text{-}3}$= 10.2 Hz, H-2α), 3.54 (m, 2H, H-2'), 3.67 (m, 2H, H-1'). **^{13}C NMR** ($CDCl_3$, 100 MHz) (see table 1). **EIMS** *m/z* (70 eV) 282 (23)[M^+], 267 (18)[M^+-15], 265 (14)[M^+-17], 264 (10)[M^+-H_2O], 234(9), 220(32)[M^+-$HOCH_2CH_2OH$], 203(86), 202(26), 164(40), 163(33), 161(32), 150(44), 129(100), 121(13), 105(12), 93(11), 85(11), 69(11), 45(11), 41(13). **HREIMS** 282.2194 ($C_{17}H_{30}O_3$ requires 282.2187).

2β-(2-Nitroethoxy)-clovan-9α-ol (11). White crystals, mp 61-62 °C. $[\alpha]_D^{25}$ + 14 (c = 0.004, $CHCl_3$). Anal. Found: C,65.6;H,9.5;N,4.3. $C_{17}H_{29}NO_4$ requires C,65.6;H,9.4;N,4.5%. **IR**(film) 3433, 2944, 2866, 1720, 1646, 1562, 1463, 1424, 1372, 1291, 1221, 1118, 1050, 993, 946, 879 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H, H-13α), 0.93 (s, 3H, H-15), 0.98 (d, 1H, $J_{12\text{-}12'}$= 12.6 Hz, H-12), 0.99 (s, 3H, H-14β), 1.06-1.13 (2H, H-11,H-7), 1.24-1.42 (4H, H-5β,H-7',H-6,H-6'), 1.50 (dd,1H,$J_{3\text{-}3'}$= 12.1 Hz, $J_{3\text{-}2\alpha}$= 9.5 Hz, H-3), 1.52 (d, 1H, $J_{12\text{-}12'}$= 12.6 Hz, H-12'), 1.52-1.62 (2H, H-10,H-11'), 1.66 (dd, 1H, $J_{3\text{-}3'}$= 12.1 Hz, $J_{2\alpha\text{-}3'}$= 5.5 Hz, H-3'), 1.93 (dddd, 1H, J= 3.2,4.9,13.4,13.4 H-10'), 3.29 (brs, 1H, H-9β), 3.41 (dd, 1H, $J_{2\alpha\text{-}3}$= 9.5 Hz, $J_{2\alpha\text{-}3'}$= 5.5 Hz, H-2α), 3.96 (m, 2H, H-1'), 4.48 (m, 2H, H-2'). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 1). **EIMS** *m/z* (70 eV) 311 (5.7)[M^+], 295(23)[M^+-16], 294(100)[M^+-17], 278(3.8), 254 (11), 252(23), 237(16), 220(46), 203(89), 164(27), 163(47), 161(25), 158(27), 137(33), 135(36), 133(24), 121(20), 107(27), 105(18), 95(13), 91(6). **HREIMS** 311.2100 ($C_{17}H_{29}NO_4$ requires 311.2088).

2β-(2-Propenyloxy)-clovan-9α-ol (12). White crystals, mp 56.5-58.5 °C. $[\alpha]_D^{25}$ + 7 (c = 0.018, $CHCl_3$). Anal. Found: C,77.5;H,11.2. $C_{18}H_{34}O_2$ requires C,77.6;H,10.9%. **IR**(film) 3440, 3088, 2950, 2865, 1647, 1467, 1344, 1283, 1217, 1138, 1089, 1053, 994, 945, 923, 773 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H, H-13α), 0.94 (s, 3H, H-15), 0.96 (m, 1H, H-12), 1.01 (s, 3H, H-14β), 1.02-1.16 (2H, H-11α,H-7β), 1.20-1.44 (4H, H-6,H-6,H-7',H-5β), 1.49 (dd, 1H, $J_{3\beta\text{-}2\alpha}$= 10.2 Hz, $J_{3\beta\text{-}3\alpha}$= 11.8 Hz, H-3β), 1.57 (m, 1H, H-10), 1.58 (d, 1H, $J_{12\text{-}12'}$= 12.8 Hz) 1.67 (dd, 1H, $J_{3\alpha\text{-}2\alpha}$= 5.7 Hz, $J_{3\alpha\text{-}3\beta}$= 11.8 Hz, H-3α), 1.70 (m, 1H, H-11'), 1.96 (dddd, 1H, J=14.2,14.2,5.0,3.2 Hz, H-10'), 3.29 (m, 1H, H-9β), 2.44 (ddd, 1H, $J_{3\beta\text{-}2\alpha}$= 10.2 Hz, $J_{2\alpha\text{-}3\alpha}$= 5.7

Hz, H-2α), 3.98 (ddd, 1H, $J_{1'-3'a}$=$J_{1'-3'b}$= 1.5 Hz, $J_{1'-2'}$= 5.3 Hz, H-1'), 5.11 (ddd, 1H, $J_{3'b-1'}$= 1.5 Hz, $J_{3'b-3'b}$= 3.1 Hz, $J_{3'b-2'}$= 10.2 Hz, H-3'b), 5.24 (ddd, 1H, $J_{3'a-1'}$= 1.5 Hz, $J_{3'a-3'b}$= 3.1 Hz, $J_{3'a-2'}$= 17.3 Hz, H-3'a), 5.88 (ddd, 1H, $J_{1'-2'}$= 5.3 Hz, $J_{3'a-2'}$= 17.3 Hz, $J_{2'-3'b}$= 10.2 Hz, H-2'). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 1). **EIMS** *m/z* (70 eV) 278 (2.7) [M^+], 263 (4) [M^+-15], 236 (4) [M^+-$HOCH_2CH{=}CH_2$], 236 (5), 220 [M^++1-H_2O], 205 (5), 203 (23), 180 (3), 163 (12), 137 (8), 135 (22), 125 (100), 105 (17), 93 (21), 83 (25), 69 (17), 55 (21), 41 (41)

5α-Hydroxycaryophylla-3,8(13)-diene (13). White crystals, mp 66-68 °C. $[\alpha]_D^{25}$ - 70 (c = 0.007, $CHCl_3$). Anal. Found: C,77.9;H,10.7. $C_{15}H_{24}O{\cdot}0.5H_2O$ requires C,78.5;H,11.0%. **IR**(film) 3327, 2950, 2929, 2860, 1636, 1450, 1368, 1044, 1017, 996, 886, 564 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.97 (s, 3H, H-14α), 0.99 (s, 3H, H-15β), 1.56-1.62 (2H, H-10,H-10'), 1.66 (brs, 3H, H-12), 1.70-1.80 (3H, H-6, H-6', H-7'), 1.97 (ddd, 1H, $J_{2\beta-2\alpha}$= 16.2 Hz, $J_{2\beta-3}$= 7.7 Hz, $J_{2\beta-1\beta}$= 7.7 Hz, H-2β), 2.07 (ddd, 1H, $J_{1\beta-9\alpha}$= 9.5 Hz, $J_{1\beta-2\alpha}$= 7.7 Hz, $J_{1\beta-2\beta}$= 7.7 Hz, H-1β), 2.20-2.40 (2H, H-2α,H-7), 2.34 (brddd, 1H, $J_{9\alpha-1\beta}$= 9.5 Hz, $J_{9\alpha-10}$= 9.5 Hz, $J_{9\alpha-10'}$= 9.5 Hz, H-9α), 4.83 (brs, 1H, H-13), 4.86 (brs, 1H, 0H-13'), 4.60 (dd, 1H, $J_{5\beta-6}$= 5.3 Hz, $J_{5\beta-6'}$= 9.6 Hz, H-5β), 5.42 (brt, 1H, J_{3-2}= $J_{3-2'}$= 7.7 Hz, H-3). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 4). **EIMS** *m/z* (70 eV) 220 (0.5)[M^+], 205(3)[M^+-15], 202(2.3)[M^+-H_2O], 187(13)[M^+-15-H_2O], 161(12), 149(14), 131(20), 123(23), 121(23), 109(37), 107(37), 93(42), 91(44), 79(46), 55(43), 43(62), 41(100). **HREIMS** 220.1828 ($C_{15}H_{24}O$ requires 220.1821).

4β-Methoxycaryophyllene-5α-ol (14). Oil, $[\alpha]_D^{25}$ -36 (c = 0.004, $CHCl_3$). **IR** (film) 3450, 3078, 2949, 2933, 2863, 2829, 1636, 1460, 1379, 1279, 1085, 1049, 888 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 500 MHz) δ 0.97 (s, 3H, H-14α), 1.01 (s, 3H, H-15β), 1.07 (s, 3H, H-12α), 1,29 (dddd, 1H, $J_{1\beta-2\beta}$= 4.0 Hz,$J_{2\beta-3\alpha}$= 7.3 Hz,$J_{2\beta-3\beta}$= 10.4 Hz, $J_{2\beta-2\alpha}$= 14.9 Hz, H-2β), 1.50-1.80 (5H, H-6,H-6',H-2α,H-3,H-3'), 1.60 (dd, 1H, $J_{10\alpha-10\beta}$= 10.0 Hz, $J_{10\alpha-9\alpha}$= 10.0 Hz, H-10α), 1.72 (dd, 1H, $J_{10\beta-10\alpha}$= 10.0 Hz, $J_{10\beta-9\alpha}$= 10.0 Hz, H-10β), 1.79 (ddd, 1H, $J_{1\beta-9\alpha}$= 10.0 Hz, $J_{1\beta-2\alpha}$= 10.0 Hz, $J_{1\beta-2\beta}$= 4.0 Hz, H-1β), 2.05 (ddd, 1H, $J_{7\alpha-6'}$= 4.1 Hz, $J_{7\alpha-6}$= 9.8 Hz, $J_{7\alpha-7\beta}$= 13.7 Hz, H-7α), 2.37 (ddd, 1H, $J_{9\alpha-1\beta}$= 10.0 Hz, $J_{9\alpha-10\alpha}$= 10.0 Hz, $J_{9\alpha-10\beta}$= 10.0 Hz, H-9α), 2.46 (ddd, 1H, $J_{7\beta-6}$= 4.8 Hz, $J_{7\beta-6'}$= 8.1 Hz, $J_{7\alpha-7\beta}$= 13.7 Hz, H-7β), 2.85 (s, 1H, -OH), 3.20 (s, 3H, H-16β), 3.70 (dd, 1H, $J_{5\beta-6}$= 4.5 Hz, $J_{5\beta-6'}$= 7.1 Hz, H-5β), 4.91 (s, 2H, H13, H-13'). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 4). **EIMS** *m/z* (70 eV) 252 (0.7)[M^+], 237 (1.6)[M^+-15], 220 (4.5)[M^+-15-17], 195(6), 176(16), 163(12), 164(11), 140(27), 139 (27), 125(53), 105(28), 93(38), 90(39), 84(49), 68(50), 54(41), 42(43), 41(100). **HREIMS** 252.2072 ($C_{16}H_{28}O_2$ requires 252.2059).

Caryophyll-13-ene-5,8-epoxide (15). Oil. $[\alpha]_D^{25}$ - 35 (c = 0.019, $CHCl_3$). **IR**(film) 2952, 2885, 2726, 1458, 1372, 1291, 1258, 1218, 1165, 1115, 1093, 1061, 902, 806 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.97 (s, 3H, *H-15β), 0.98 (s, 3H, *H-14α), 1.17 (s, 3H, H-13), 1.20 (m, 1H, H-10), 1.50-1.60 (3H, H-10',H-7α, H-1β), 1.64 (s, 3H, H-12), 1.90-2.05 (3H, H-2,H-2',H-6β), 2.09 (ddd, 1H, J=10.8,10.8,7.9 Hz, H-9α), 2.17 (ddd, 1H, $J_{7\beta-7\alpha}$= 13.1 Hz, $J_{7\beta-6\alpha}$= 4.0 Hz, $J_{7\beta-6\beta}$= 9.5 Hz, H-7β), 2.44 (dddd, 1H, $J_{6\alpha-6\beta}$= 12.8 Hz, $J_{6\alpha-7\beta}$= 4.0 Hz, $J_{6\alpha-5\beta}$= 9.3 Hz, $J_{6\alpha-7\beta}$= 11.1 Hz, H-6α), 4.48 (dd, 1H, $J_{5\beta-6\alpha}$= 9.4 Hz, $J_{5\beta-6\beta}$= 5.5 Hz, H-5β), 5.35 (qd, 1H, J= 1.5,8.5 Hz, H-3), (* interchangeable signals). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 4). **EIMS** *m/z* (70 eV) 220 (0.1)[M^+], 202(2)[M^+-H_2O], 187(1.0)[M^+-15-H_2O], 164(2), 162(3), 147(5), 121(6), 119(11), 107(14), 106(22), 95(38), 93(41), 81(37), 79(39), 69(32), 67(33), 55(50), 43(100). **HREIMS** 220.1830 ($C_{15}H_{24}O$ requires 220.1821).

1-(2-Hydroxyethoxy)-caryolan-9α-ol (18). White crystals, mp 61-62 °C. $[\alpha]_D^{25}$ + 14 (c = 0.008, $CHCl_3$). Anal. Found: C,69.3;H,10.8. $C_{17}H_{30}O_3 \cdot 0.5H_2O$ requires C,70.0;H,10.7%. **IR**(film) 3397, 2949, 2869, 1463, 1382, 1288, 1255, 1217, 1051, 969, 950, 894, 757, 668 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.90 (s, 3H, H-15), 0.95 (s, 3H, H-13α), 0.98 (brs, 3H, H-14β), 1.10-1.16 (2H, H-7,H-7'), 1.29-1.42 (2H, H-6,H,H-6'), 1.45-1.54 (3H, H-11,H-12,H,H-12'), 1.59 (dd, 1H, $J_{3\text{-}2\alpha}$= 8.3 Hz, $J_{3\text{-}3\alpha}$= 8.3 Hz, H-3), 1.61 (dd, 1H, $J_{3'\text{-}2\alpha}$= 8.3 Hz, $J_{3'\text{-}3}$= 8.3 Hz, H-3'), 1.68-1.81 (2H, H-10,H-11'), 1.88 (ddd, 1H, $J_{5\beta\text{-}6}$= 7.5 Hz, $J_{5\beta\text{-}6'}$= 7.5 Hz, $J_{5\beta\text{-}2\alpha}$= 12.3 Hz, H-5β), 2.00 (m, 1H, H-10'), 2.13 (ddd, 1H, $J_{3\text{-}2\alpha}$= 8.3 Hz, $J_{2\alpha\text{-}3'}$= 8.3 Hz, $J_{2\alpha\text{-}5\beta}$= 12.0 Hz, H-2α), 3.36 (ddd, 1H, $J_{1'a\text{-}1'b}$= 9.5 Hz, $J_{1'a\text{-}2'a}$= 4.3 Hz, $J_{1'a\text{-}2'b}$= 5.2 Hz, H-1'a), 3.42 (m, 1H, H-9β), 3.50 (ddd, 1H, $J_{1'a\text{-}1'b}$= 9.5 Hz, $J_{1'b\text{-}2'a}$= 3.6 Hz, $J_{1'b\text{-}2'b}$= 6.5 Hz, H-1'b), 3.66 (2H, H-2'a,H-2'b). **^{13}C NMR** ($CDCl_3$, 50 MHz)(see table 1). **EIMS** *m/z* (70 eV) 278 (2.7)[M^+], 277 (1.8)[M^+-1], 261(14)[M^++1-H_2O], 237(6), 221(14), 220(14), 219(62), 203(41), 168(16), 167(100), 163(17), 161(15), 149(12), 135(7), 121(15), 109(12), 107(12), 95(10), 91(4), 69(10), 67(10), 55(14), 41(33). **HREIMS** 282.2194 ($C_{17}H_{30}O_3$ requires 282.2187).

1-(2-Propenyloxy)-caryolan-9α-ol (19). White crystals, mp 87-89 °C. $[\alpha]_D^{25}$ + 19 (c = 0.012, $CHCl_3$). Anal. Found: C,74.8;H,10.7. $C_{18}H_{30}O_2 \cdot 0.5H_2O$ requires C,75.0;H,10.9%. **IR**(film) 3362, 3096, 2949, 2865, 1645, 1463, 1407, 1380, 1317, 1285, 1215, 1131, 1095, 1049, 964, 917, 784 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.89 (s, 3H, H-15), 0.96 (s, 3H, H-13α), 0.98 (brs, 3H, H-14β), 1.09-1.15 (2H, H-7,H-7'), 1.34-1.54 (4H, H-12,H-12',H-6,H-6'), 1.52 (dd, 1H, $J_{3\beta\text{-}2\alpha}$= 9.6 Hz, $J_{3\beta\text{-}3\alpha}$= 9.6 Hz, H-3β), 1.59 (m, 1H, H-11), 1.65 (dd, 1H, $J_{3\alpha\text{-}2\alpha}$= 7.7 Hz, $J_{3\alpha\text{-}3\beta}$= 9.6 Hz, H-3α), 1.68-1.82 (2H, H-10,H-11'), 1.91 (ddd, 1H, $J_{5\beta\text{-}6\alpha}$= 7.4 Hz, $J_{5\beta\text{-}6\beta}$= 7.4 Hz, $J_{5\beta\text{-}2\alpha}$= 12.0 Hz, H-5β), 1.98 (m, 1H, H-10'), 2.12 (ddd, 1H, $J_{3\beta\text{-}2\alpha}$= 9.6 Hz, $J_{2\alpha\text{-}3\alpha}$= 7.7 Hz, $J_{2\alpha\text{-}5\beta}$= 12.0 Hz, H-2α), 3.43 (m, 1H, H-9β), 3.75 (dddd, 1H, $J_{1'a\text{-}3'a}$=$J_{1'a\text{-}3'b}$= 1.4 Hz, $J_{1'a\text{-}2'}$= 5.4 Hz, $J_{1'a\text{-}1'b}$=12.6Hz, H-1'a), 3.91 (dddd, 1H, $J_{1'b\text{-}3'a}$=$J_{1'b\text{-}3'b}$= 1.4 Hz, $J_{1'b\text{-}2'}$= 5.4 Hz, $J_{1'a\text{-}1'b}$= 12.6 Hz, H-1'b), 5.09 (ddd, 1H, $J_{3'a\text{-}1'a}$=$J_{3'a\text{-}1'a}$= 1.4 Hz, $J_{3'a\text{-}2'}$= 10.3 Hz, H-3'a), 5.25 (ddd, 1H, $J_{3'b\text{-}1'a}$=$J_{3'b\text{-}1'b}$= 1.4 Hz, $J_{3'b\text{-}2'}$= 17.1 Hz, H-3'b), 5.89 (dddd, 1H, $J_{1'a\text{-}2'}$=$J_{1'b\text{-}2'}$= 5.4 Hz, $J_{3'a\text{-}2'}$= 10.3 Hz, $J_{2'\text{-}3'b}$= 17.2 Hz, H-2'). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 1). **EIMS** *m/z* (70 eV) 278 (2.7)[M^+], 277 (1.8)[M^+-1], 261(14)[M^++1-H_2O], 237(6), 221(14), 220(14), 219(62), 203(41), 168(16), 167(100), 163(17), 161(15), 149(12), 135(7), 121(15), 109(12), 107(12), 95(10), 91(4), 69(10), 67(10), 55(14), 41(33)

5α-Hydroxycaryophylla-4(12),7-diene (21). Oil. $[\alpha]_D^{25}$ - 82 (c = 0.027, $CHCl_3$). **IR** (film) 3338, 3069, 2953, 2929, 2860, 1638, 1456, 1375, 1029, 895, 832, 799 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.96 (s, 3H, *H-15β), 0.98 (s, 3H, *H-14α), 1.56-1.70 (2H, H-10,H-10'), 1.63 (s, 3H, H-13), 1.71-1.79 (3H, H-2',H-2,H-3), 1.81 (m, 1H, H-1β), 2.35-2.52 (3H, H-3',H-6,H-6'), 2.76 (brdd, 1H, J= 9.2,9.2 Hz, H-9α), 4.13 (dd, 1H, J= 9.2,4.2 Hz, H-5β), 4.79 (s, 1H, H-12), 4.86 (s, 1H, H-12'), 5.09 (brdd, 1H, J= 7.2,7.2 Hz, H-7), (* interchangeable signals). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 4). **EIMS** *m/z* (70 eV) 220(1.4)[M^+], 205(3)[M^+-15], 202(11)[M^+-H_2O], 187(5)[M^+-15-H_2O], 177(5), 164(6), 159(11), 146(10), 137(18), 120(14), 109(16), 107(24), 95(52), 81(55), 79(57), 69(54), 67(48), 55(54), 53(42) 41(100). **HREIMS** 220.1819 ($C_{15}H_{24}O$ requires 220.1827).

5α-Hydroxycaryophylla-4(12),8(13)-diene (22). Oil. $[\alpha]_D^{25}$ + 25 (c = 0.011, $CHCl_3$. **IR**(film) 3360, 3074, 2953, 2928, 2861, 1639, 1450, 1456, 1365, 1282, 1022, 901, 868 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.97 (s, 6H, H-14α,H-15β), 1.50-2.10 (9H, H-3,H-2,H-2',H-1β,H-10,H-10',H-7,H-6,H-6'), 2.28 (m, 1H, H-7'), 2.32 (ddd, 1H, $J_{9\alpha\text{-}10\alpha}$= 8.5 Hz, $J_{9\alpha\text{-}10\beta}$= 8.5 Hz, $J_{9\alpha\text{-}1\beta}$= 8.5 Hz, H-9α), 2.51 (brddd, 1H, J= 3.9,3.8,13.5

Hz, H-3'), 4.08 (dd, 1H, J= 3.6,8.9 Hz, H-5), 4.77 (s, 1H, H-13), 4.78 (s, 1H, H-13') 4.95 (s, 1H, H-12), 5.04 (s, 1H, H-12'). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 4). **EIMS** *m/z* (70 eV) 220(0.6)[M^+], 205(3)[M^+-15], 202(1.7)[M^+_2O], 187(8)[M^+-15-H_2O], 177(7), 159(14), 149(11), 137(16), 136(100), 135(25), 121(20), 119(21), 117(25), 109(35), 107(33), 105(33), 95(32), 93(34), 91(53), 79(39), 69(32), 55(23), 53(16) 41(38). **HREIMS** 220.1517 ($C_{15}H_{24}O$ requires 220.1827).

Epoxidation of 15 with m-chloroperbenzoic acid (MCPBA). Compound **15** (80 mg) was dissolved in chloroform (5 ml). To this mixture, MCPBA (65 mg) was added and the reaction mixture was stirred for 5 hours. Then the solvent was evaporated under low pressure to yield an amorphous solid that was purified by column chromatography on silica gel, with an increasing gradient of ethyl acetate in petroleum ether to afford **caryophyllen-3,4;5,8-diepoxide (16)** (62 mg, 77%) as an oil. $[\alpha]_D^{25}$ - 5 (c = 0.005, $CHCl_3$. **IR**(film) 2954, 2929, 2868, 1458, 1373, 1116, 1061, 876, 759 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 0.95 (s,3H, H-15β), 0.98 (s, 3H, H-14α), 1.13 (s, 3H, H-13), 1.15 (s, 3H, H-12), 1.14 (m, 1H, H-10α), 1.49-1.55 (2H, H-10β, H-1β), 1.63 (ddd, 1H, $J_{7\alpha\text{-}6\beta}$= 10.1 Hz, $J_{7\alpha\text{-}6\alpha}$= 11.5 Hz, $J_{7\alpha\text{-}7\beta}$= 11.5 Hz, H-7α), 1.76 (ddd, 1H, $J_{2\alpha\text{-}3\beta}$= 2.3 Hz, $J_{1\beta\text{-}2\alpha}$= 11.0 Hz, $J_{2\beta\text{-}2\alpha}$= 15.0 Hz, H-2α), 1.98 (dddd, 1H, $J_{6\alpha\text{-}5\beta}$= 6.8 Hz, $J_{6\beta\text{-}6\alpha}$= 12.4 Hz, $J_{6\beta\text{-}7\alpha}$= 10.1 Hz, $J_{7\beta\text{-}6\beta}$= 10.1 Hz, H-6β), 2.00 (ddd, 1H, $J_{9\alpha\text{-}10\alpha}$= 10.4 Hz, $J_{9\alpha\text{-}10\beta}$= 10.4 Hz, $J_{9\alpha\text{-}1\beta}$= 10.4 Hz, H-9α), 2.07 (ddd, 1H, $J_{1\beta\text{-}2\beta}$= 2.0 Hz, $J_{2\beta\text{-}3\beta}$= 8.8 Hz, $J_{2\beta\text{-}2\alpha}$= 15.0 Hz, H-2β), 2.15 (ddd, 1H, $J_{7\beta\text{-}6\alpha}$= 2.3 Hz, $J_{7\beta\text{-}6\beta}$= 10.1 Hz, $J_{7\beta\text{-}7\alpha}$= 11.5 Hz, H-7β), 2.39 (dddd, 1H, $J_{7\beta\text{-}6\alpha}$= 2.3 Hz, $J_{6\alpha\text{-}5\beta}$= 8.8 Hz, $J_{6\alpha\text{-}6\beta}$= 12.4 Hz, $J_{6\alpha\text{-}7\alpha}$= 11.5 Hz, H-6α), 2.96 (dd, 1H, $J_{2\alpha\text{-}3\beta}$= 2.3 Hz, $J_{2\beta\text{-}3\beta}$= 8.8 Hz, H-3β), 4.43 (dd, 1H, $J_{6\beta\text{-}5\beta}$= 6.8 Hz, $J_{5\beta\text{-}6\alpha}$= 8.8 Hz, H-5β). **^{13}C NMR** ($CDCl_3$, 50 MHz) (see table 4). **EIMS** *m/z* (70 e/v) 236 (14) [M^+], 221 (1) [M^+-17], 220 (1) [M^+-H_2O], 205 (4), 180 (5), 175 (5), 167 (5), 163 (5), 149 (17), 147 (6), 139 (10), 137 (13), 134 (8), 125 (17), 123 (16), 121 (22), 119 (19), 111 (13), 109 (40), 107 (46), 96 (23), 97 (100), 81 (41), 69 (29), 55 (23), 43 (63). **HREIMS** 236.1760 ($C_{15}H_{24}O_2$ requires 236.1776).

ACKNOWLEDGEMENTS

This research was supported by grants from C.I.C.Y.T. PB92-1101 and AGF95-0779 and by fellowship (to AJMS) from Ministerio de Educacion y Ciencia (M.E.C.). AJMS acknowledges the facilities provided by The School of Chemistry and Molecular Sciences, University of Sussex (UK) and by Departamento de Química Orgánica, Universidad de Cádiz (Spain).

REFERENCES

1. Tkachev, A.V. *Chemistry of Natural Compounds* **1987**, 393 (translation of Tkachev, A.V *Khim. Prir. Soedin* **1987**, 475)

2. Gatilova, V.P.; Korchagina, D.V.; Bagryanskaya, I.Yu.; Gatilov, Yu. V; Dubovenko,. Zh. V.; Barkhash, V.A.; Koptyug, V.A. *Zh. Org. Khim.* **1985**, *21*, 7

3. Collado, I.G.; Aleu, J.; Macias-Sanchez, A.J.; Hernandez-Galan, R. *J. Nat. Products* **1994**, *57*, 738

4. Collado, I.G.; Aleu, J.; Macias-Sanchez, A.J.; Hernandez-Galan, R. *J. Chem. Ecol.* **1994**, *20*, 2631

5. a) Masaki, Y.; Miura, T.; Ochiai, M. *Synlett* **1993**, 847; b) Masaki, Y.; Miura, T.; Ochiai, M. *Chemistry Letters* **1993**, 17

6. Boynton, J.A.; Hanson, J.R.; Uyanik, C. *J. Chem. Research (S)* **1995**, 334

7. a) Gatilov, Yu. V.; Tkachev, A.V.; Dubovenko, Z.V. *Chemistry of Natural Products* **1983**, 677 (translation of Gatilov, Yu. V.; Tkachev, A.V.; Dubovenko, Z.V. *Khim. Prir. Soedin.* **1982**, 715). b) Krebs, H. C.; Rakotoarimanga, J. V.; Habermehl, G. G. *Magnetic Resonance in Chemistry* **1990**, *28*, 124

8. Hermann, H.; Tezuka, Y.; Kikuchi, T.; Supriyatna, S.; *Chem. Pharm. Bull.* **1994**, 42, 138

9. Gupta, A.S.; Dev, S. *Tetrahedron* **1971**, 27, 635

10. Fitjer, L.; Malich, A.; Paschke, C.; Kluge, S.; Gerke, R.; Rissom, B.; Weiser, J.; Noltemeyer, M.; *J. Am. Chem. Soc.* **1995**, 117, 9180

(*Received in UK* 13 *March* 1996; *accepted* 12 *April* 1996)