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EIGHT NEW XENIA DITERPENOIDS FROM THREE SOFT CORALS OF THE RED SEA

AMIRAM GROWEISS and YOEL KASHMAN*
Department of Chemistry, Tel-Aviv University, Tel Aviv 69978, Israel

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Abstract—Investigation of the terpenoid content of three soft corals from the Gulf of Eilat (The Red Sea), *Xenia macrospiculata*, *X. obscuronata* and *X. lilielae* resulted in the isolation of 8 new diterpenes. Two of the new compounds belong to the xeniolides (xenialactol-D (**10a**) and xeniolide-E (**1**)) and the other six (4,14-di-epoxyxeniaphyllene (**15**), 4,5 - epoxyxeniaphyllan - 14,15 - diol (**17**), 4,14 - diepoxy - xeniaphyllenol - A (**21a**), xeniaphyllenol-B (**23a**), xeniaphyllenol-C (**24a**) and xeniaphyllantriol (**25**)) are new xeniaphyllanes (prenylated caryophyllanes). The structure determination of the various compounds is based on chemical transformations as well as on the ^1H and ^{13}C NMR spectra. Several known caryophyllene derivatives have been synthesised for ^{13}C NMR spectra and chemical comparisons. The ^{13}C NMR has proven to be an excellent probe for structural and stereochemical determinations.

Xenicin (**1**), isolated in 1977 from the soft coral *Xenia elongata*,[1] was the first reported diterpene with a fused dihydropyrane-cyclononane skeleton. From that time, many other xenicins (varying in their functional groups), xeniolides (the corresponding lactones) as well as the closely related xeniaphyllanes have been isolated from different *Xenia* species (*X. macrospiculata*, *X. obscuronata*[2] and *X. novae-britanniae*[3]). Diterpenes from this group were also isolated from other soft corals (*Nephthea* and *Alcyonium* spp.),[4,5] as well as from gorgonians.[6]

Representatives of these diterpenes, which we isolated from *X. macrospiculata*,[2] xeniculin (**2**), xeniolide-A (**3**) and xeniaphyllenol-A (**4**) are given in Chart 1.† In a recent paper,[7] Coll *et al.* have reported the isolation of xenicins from *X. crassa* including the isolation of a modified tricyclic xenicin from *X. viridis* for which structure **5** was determined. Another closely related compound, alcyonolide (**6**), was isolated from the Okinawan soft coral of the genus *Alcyonium*.[5]‡

The carbon framework of this δ-lactone, (**6**), corresponds to a seco-type variety of xenicin. The changes in the latter two compounds, **5** and **6**, indicate the type of variations which might be expected to be found in the future for this class of compounds.

The isolation by Scheuer of the coraxeniolides (e.g. **7**) from the Hawaiian pink coral, *Corallium* sp.,[6] demonstrated that the xenicin diterpenes are not exclusive to soft corals. Of special interest, from the biogenetic point of view, is corabohcin (**8**).[6] This compound, possessing a functionalized 18-Me (as a terminal methylene), may represent a possible intermediate in the biogenesis of the xenicins starting from xeniaphyllanes. Cyclononane diterpenoids (e.g. **9**) has been described also by Finer *et al.* from the brown algae *Dictyota crenulata*,[9] and *D. flabellata*, by Wells *et al.* from *D. profilicans*[10] and from the sea hare, *Aplysia depilans*.[9]

In a previous report, we have published the results of the investigation of one collection of *X. obscuronata* and two of *X. macrospiculata*.[2] Herein we report the isolation of eight new compounds from collections of the above two soft corals and from the hitherto uninvestigated species *X. lilielae*. As was reported in the past for other soft corals, we have also found remarkable variations in the secondary metabolite contents of the herewith explored 3 *xenia* species (Table 1).

From various collections of all three *xenia* spp. we have isolated in small amounts a new compound designated *xenialactol*-D (**10a**). Another xeniolide which was purified in minute amounts only, from *X. obscuronata*, is compound **13**. In addition to these two, the structure of six new xeniaphyllanes (**15**, **17**, **21**, **23–25**) isolated from one or more of the above *Xenia* spp (Table 1) will be discussed.

Compound **10a**, $C_{20}H_{30}O_4$ *m/e* 334 (6 unsaturations) is an oil. Its NMR spectra indicates clearly the existence of three double bonds ( , -CH=C(Me)- and ) an epoxide (), a secondary allyl alcohol and a lactol (Tables 2 and 3). The latter two moieties were confirmed by acetylation, which afforded the expected 1,9-diacetate. Comparisons of the ^1H and ^{13}C-NMR spectra of **10a** with the data of the previously isolated *xenia* diterpenes revealed, the bicyclic skeleton of **10a** to be identical with that of xenialactol-C (**11a**) (Tables 2 and 3). The NMR data of the ring system of the corresponding diacetates **10b** and **11b** was also in excellent agreement. From the UV, IR and NMR data it was obvious that xenialactols C and D differ only in the structure of the side chain. The almost identical chemical shifts of H-3, 3′ in **10a** and **11a** (both in the allylic position, Table 3) suggested that the third double bond of

†The absolute configuration of the xenicins and xeniaphyllanes is as yet unknown. In order to avoid confusion, we have written the formula of the xenicins and xeniaphyllanes in the same manner as has already been published, i.e. with the 4a-α, 11a-β and 1β, 9α proton orientations respectively. As we believe the two groups to be biogenetically related, one of the systems has to be enantiomeric with the present representation and will have to be changed in the future.

‡The only diterpenoids that could have been revealed by us in two other soft corals of this genus, *A. flaccidum* and *A. utinomii*, were cembranoids.[8]

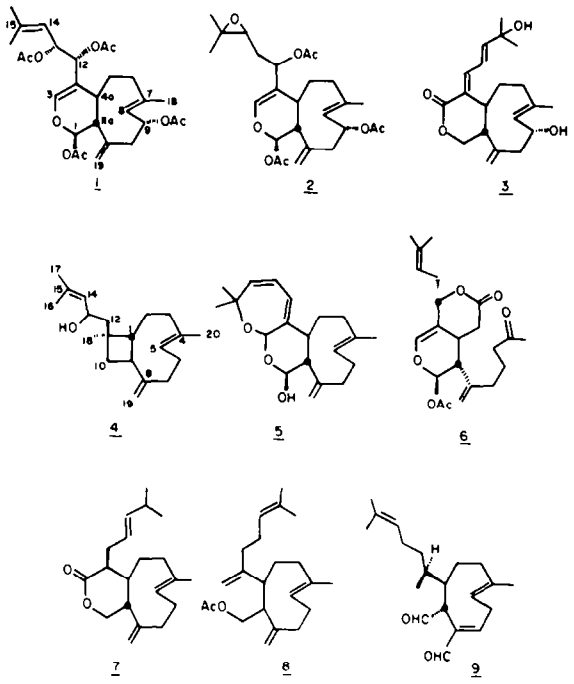


Chart 1.

Table 1. Percentage natural abundance of the xenia diterpenoids

	X. macrospiculata		X. obscuronata	X. lilielae
	Dec. 1978	Feb. 1979	April 1979	Nov. 1980
Dry weight	ca. 250 gm	293 gm	620 gm	710 gm
Petroleum ether extract	8.0 gm	9.5 gm	21.6 gm	23 gm
Ethyl acetate extract	9.2 gm*	4.0 gm*	13.4 gm	17 gm
Compound no.				
2	0.19	0.07		
3			0.02	0.11
10a	*	*	0.05	0.08
11a	*	*	0.06	0.07
12a	*	*	0.13	0.18
12b	*	*	0.06	0.06
13	*	*	< 0.01	
14				0.04
15				0.33
4	0.10	0.14	0.10	0.09
20	0.22	0.05	0.09	0.38
21				0.09
38**		0.02		
16	0.01	< 0.01	0.06	
17		0.04	0.03	0.04
18	0.06	0.02		
19	0.04	0.03		
23a	0.02			
24a		< 0.01		
25			< 0.01	
37			0.02	

*The composition of the 1977 EtOAc extracts have already been reported.[2]

**38 = 4,5-epoxyisoxeniaphyllenol.

Table 2. ^{13}C NMR data of several xenicins xeniolides and xenialactols

C	m	10a	10b	11a	11b	2	12b	12b-OAc
1	d	99.8	97.2	99.9	97.4	91.9	172.7s	172.4s
3	t	69.5	69.4	69.8	69.8		71.4	71.4
4	s	140.2	139.2	139.5	138.2		139.1[a]	138.2
4a	d	43.7	43.4	44.1	43.5	37.2	35.9	36.3
5	t	35.7	35.5	35.5	35.5	30.5	36.1[b]	35.9
6	t	40.1	40.2	40.2	40.4	40.0	38.7[b]	38.8
7	s	133.2	134.3	132.9	134.1	134.4	60.2	59.5
8	d	130.4	126.0	130.5	126.1	126.3	67.3	64.0
9	d	67.6	70.6	67.6	70.7	70.6	70.4	72.6
10	t	47.0	43.4	46.9	43.9	43.0	37.9	35.0
11	s	151.6	149.4	151.2	149.1	146.9	137.0[a]	136.9
11a	d	57.3	53.5	57.5	53.9	49.8	57.4	57.2
18	q	17.7	17.7	17.7	17.7	17.7	19.7	19.6
19	t	111.9	114.2	112.4	114.6	116.1	121.8	122.6
12	d	117.4	118.9	122.2	123.6		128.5	128.6
13		27.2t	27.4t	120.9d	120.6d		121.0d	120.9d
14	d	63.6	63.4	142.5	143.1		145.8	145.9
15	s	58.8	58.6	71.0	70.7		70.8	70.8
16	q	18.8	18.9	29.9	30.1		30.0	29.9
17	q	24.8	24.8	30.1	30.1		30.0	29.9
$CH_3\underline{C}O_2$	s		170.7		170.			
	s		169.6		169.			170.3
$\underline{C}H_3CO$	q		21.4		21.4			21.2
	q		21.0		21.2			

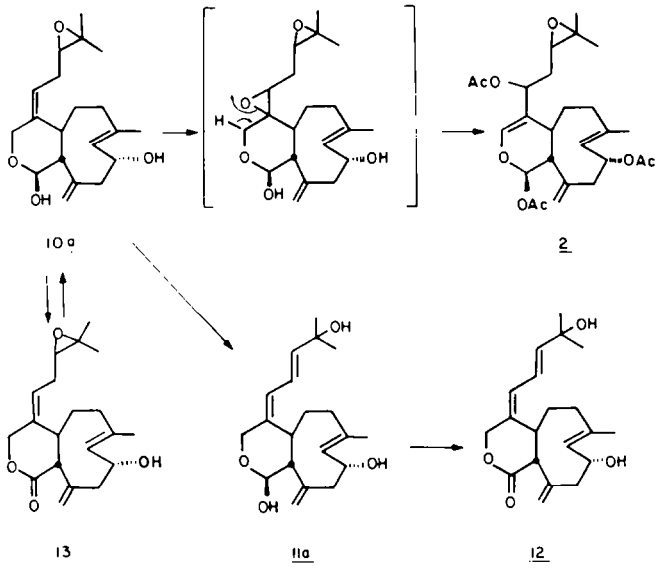
a,b - These signals may be interchanged.

Table 3. ^{1}H NMR of several xeniolides and xenialactols

H	10a	11a	10b	11b	12a	13
1	4.65*	4.60 d	5.53 d	5.49 d		
3	4.65 d	4.66 d	4.63 d	4.66 d	4.88 d	4.83 d
3'	4.32 d	4.29 d	4.37 d	4.37 d	4.43 d	4.45 d
8	5.23 bd	5.28 bd	5.28 bd	5.35 bd	5.40 bd	5.31 bd
9	4.78 m	4.85 m	5.68 bt	5.68 bt	4.69 dt	4.71 ddd
12**	5.33 bt	5.84 d	5.39 bt	5.89 d	6.06 d	5.63 bt
13	2.32 m	6.43 dd		6.44 dd	6.40 dd	2.78 ddd
13'	2.32 m					2.70 dt
14	2.71 t	5.82 d	2.73 t	5.88 d	5.97 d	2.81 dd
Me-16	1.32 s	1.34 s	1.33 s	1.36 s	1.38 s	1.35 s
Me-17	1.32 s	1.34 s	1.33 s	1.25 s	1.37 s	1.34 s
Me-18	1.75 bs	1.74 bs	1.80 bs	1.81 bs	1.67 bs	1.67 bs
19	4.95 bs	4.93 bs	4.91 bs	4.92 bs	5.07 bs	5.06 bs
19'	4.78 bs	4.75 bs	4.86 bs	4.86 bs	5.00 bs	4.98 bs
O						
CCH_3			2.09 s	2.10 s		
			2.04 s	2.03 s		

* partially obscured signal.

** The mutual relationship between H-12 - H-14 in compounds 10a & 13 was established by a double irradiation experiment.



Scheme 1.

10a was at the 4 (12) position. A 14,15-epoxy terminus, suggested on the basis of the NMR spectrum (δ_H 2.71(1H) and 1.32(6H) and δ_c 63.6 and 58.8) completed the structure of the side chain. The relationship of the proposed two functionalities of the side chain was confirmed by a double irradiation experiment (linking the vinyl H-12 to the 14-epoxide proton). A 12% enhancement of H-3 (δ 4.32) caused by irradiation of H-12 (NOE) determined a 4(12)Z-configuration, thus completing the structure of the molecule.

Compound **10a** is of special interest from the biogenetic point of view as it might be an intermediate in the biosynthesis of xenicins on one hand and of xeniolides like xeniolide-B (**12a**) on the other hand (Scheme 1).†

Compound **13**, designated xeniolide-E, was derived from *Xenia obscuronata* in only very small amounts. The compound $C_{20}H_{28}O_4$, ν_{max} 1740 cm^{-1} (7 unsaturations; 3 double bonds, an epoxide, a lactonic CO and the bicyclic framework) is somewhat less polar than **10a**. Comparison of the ^{1}H-NMR spectrum with that of the previously isolated compounds suggested that **13** has the same skeleton as xeniolide-B (**12a**) and the side chain of **10a**. Thus, compound **13** is the lactone counterpart of **10a** (a relationship which is similar to the one between xenialactol-C (**11a**) and xeniolide-B (**12a**), Chart 2).

The almost identical δ-values of molecules which possess the same functionalities on the bicyclic skeleton (e.g. **10a** and **11a** or **12a** and **13**, Tables 2 and 3), and the differences on the other hand, observed with slight changes in the functional groups (e.g. replacement of a lactol by a lactone) exhibit clearly the sensitivity of the

†Noteworthy, in this context, is a possible biogenetic route from compounds like **8** to xenialactol-D (**10a**).

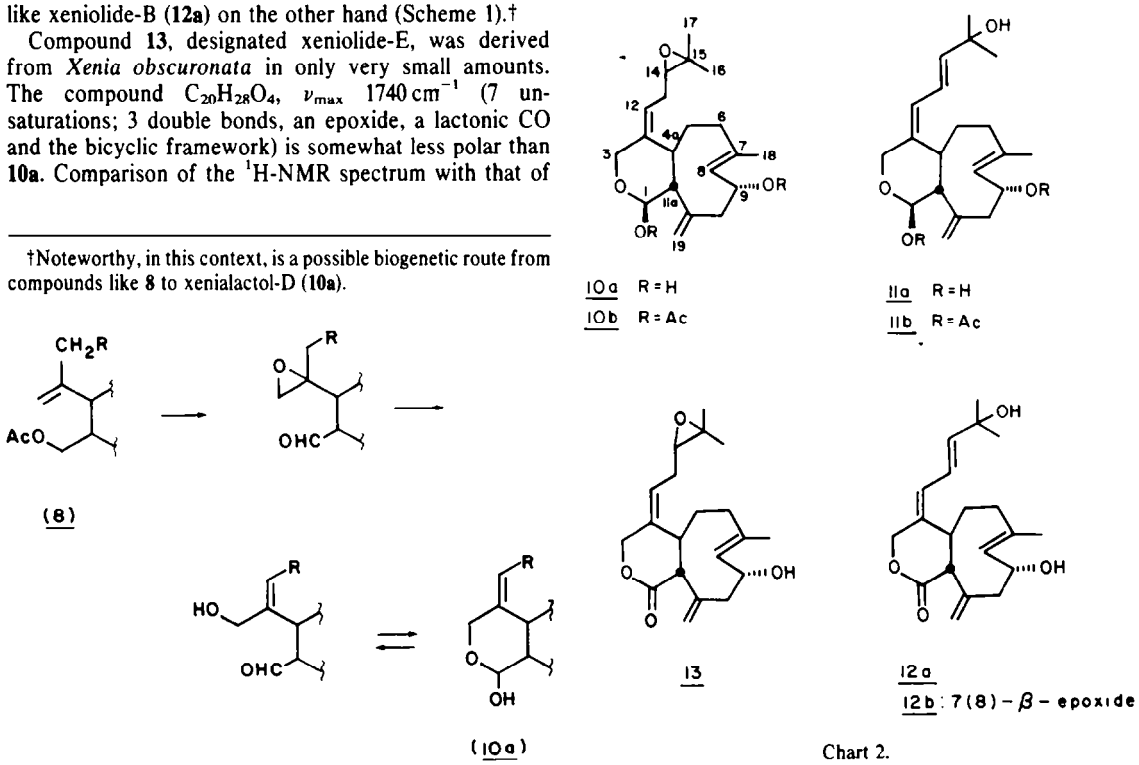


Chart 2.

Table 4. Some torsion angles of crystalline derivatives

Angle[b]	1	a	5	7
11-11a-4a-5*	-134	-132	-123	-121
11a-4a-5-6	83	85	81	85
4a-5-6-7	- 50	- 52	- 56	- 57
5-6-7-8	89	88	92	89
6-7-8-9	-158	-161	-159	-159
7-8-9-10	69	76	75	74
Me(18)7-8-9	14	7	13	12
8-9-10-11	35	35	31	37
9-10-11-11a	-83	-87	-90	-92
9-10-11-19	97	93	88	89
10-11-11a-4a	117	117	124	118
4-4a-5-6	-149	-146	-153	-152
4-4a-11a-11*	97	98	114	115
1-11a-11-10	-114	-113	-111	-118
1-11a-4a-5*	99	99	112	116

a. 13-Epi-9-desacetoxyxenicin, see ref. 3

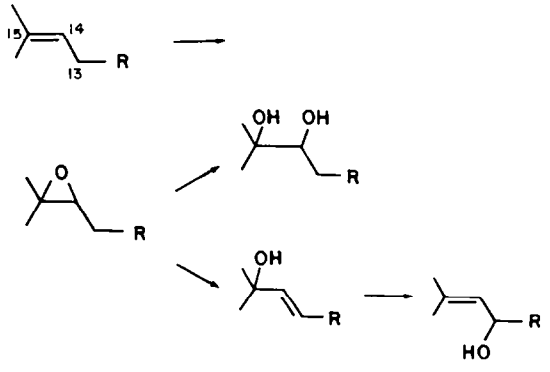
b. The dihedral angles were calculated from the published positional coordinates.

* The most affected angles, around the 4a-11a bond.

NMR and its usefulness as a structural probe in this series. The small changes in the chemical shift might well originate from variations in the conformation of the cyclononane ring due to small alterations in the 4-4a-11a-11 dihedral angle caused by fusion to different ring systems. Comparing the X-ray data of four reported xenia-diterpenoids (two pairs) (Table 4) show clearly the changes in the above angle. The latter comparison demonstrates a very similar conformation of the cyclononane ring in all four compounds. (A conformation in which the 11(19) methylene points in the same direction as H-4a and the 18-Me group is in the opposite direction (the same as the H-11a atom)). From a Dreiding model of these compounds it can be seen that the cyclononane ring is quite rigid due to the ring fusion as well as the two double bonds. This is similar to the situation in caryophyllene for which two conformers of the cyclononene ring in a ratio of 76 : 24, based on the ^{13}C NMR spectrum, have been proposed.[11] At this stage it is difficult because of minor accompanying impurities, to determine unequivocally whether such conformers also exist here, however, if such is the case, the ratio must be much higher.

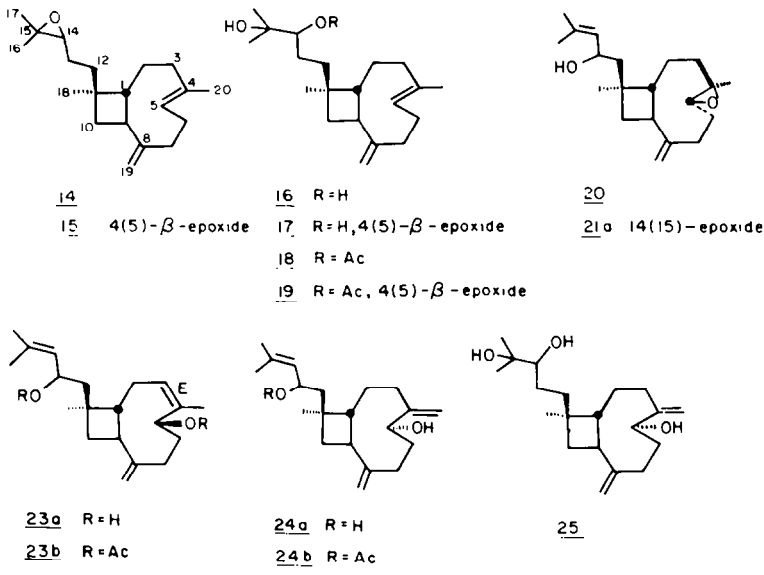
As discussed in his work on xenicin (1), Schmitz proposed a possible biosynthesis of **1**, suggesting a prenylated caryophyllene as one of two possible precursors.[1] Interesting in this context was the isolation from *X. macrospiculata* and *X. obscuronata* of the xeniaphyllanes–prenylated caryophyllenes†. Whether these compounds are, indeed, intermediates in the biosynthesis of the xenicins remains an open question.

We report the isolation of seven xeniaphyllanes, from the three investigated *Xenia species* in addition to the seven previously reported (Table 1).[2] Biosynthetically, the structure of all the former as well as novel xeniaphyllanes can readily be explained as being derived from the 4 (5) and/or 14 (15) epoxides. The new compounds can be divided into two groups; compounds **14**, **15**, **17** and **21** all possess the 4(5) double bond or epoxide, with different substituted side chains, and compounds **23–25** which differ in the cyclononane substitution pattern. The biosynthesis of the various side chains can readily be explained in the following sequence:



It was interesting in this context to isolate from *X. lilielae*, in small amounts 14(15)-epoxyxeniaphyllene (**14**).[12] This compound was found to be identical in all respects with the material isolated by Coll *et al.* from *Nephthea chabrolii*.[4] As mentioned earlier, the ^{13}C NMR spectra of these compounds which can be compared with caryophyllene and its derivatives, is an excellent probe

†As mentioned above, compounds like **8** might be the first oxidatively cleaved products obtained from the xeniaphyllanes.



14

15 4(5)-β-epoxide

16 R=H

17 R=H, 4(5)-β-epoxide

18 R=Ac

19 R=Ac, 4(5)-β-epoxide

20

21a 14(15)-epoxide

23a R=H

23b R=Ac

24a R=H

24b R=Ac

25

Chart 3.

for the structure determination including the stereochemistry. This made possible the assignment of the relative configuration of C-1, C-9 and the E configuration of the 4(5) double bond—all being the same as in caryophyllene.

Together with **14**, we have isolated from the same soft coral the 4,14-diepoxide **15**, $C_{20}H_{32}O_2$ *m/e* 304. In the light of the previous isolation of three pairs of 4(5) olefin/epoxides from *X. macrospiculata* the isolation of **15** was expected. Although the ease by which the Δ^4-undergoes epoxidation, even by air, **15** does not seem to us to be an artifact as the ratio between **14** and **15** (and other pairs) on storage remains stable. As mentioned in the past, the crude extract of many soft corals seem to contain natural antioxidants that protect the compounds from oxidations.

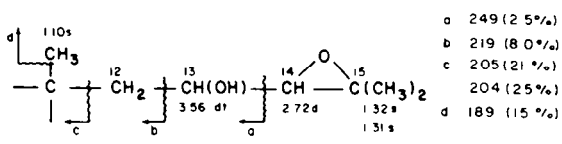
The structure of **15** (5 unsaturations: -CH(O)CMe$_2$, -CH(O)C(Me)-, >C=CH$_2$ and two rings, see Tables 5 and 6) was readily determined by comparison of the ^{13}C NMR lines of the skeleton with the resonances of caryophyllene oxide, and the lines of the side chain with those of compound **14**. The comparison of the ^{13}C NMR lines of the skeleton established also the stereochemistry at C-1,4,5 and 9. We also propose for **15** the stereochemistry at C-11—the atom bearing the gem-dimethyl in caryophyllene. These two Me groups in caryophyllene and caryophyllene oxide resonate at 22 and 30 ppm.

According to the X-ray diffraction analysis of two caryophyllene derivatives[13,14] and observations of Dreiding models within the series, the **11α** Me is pseudo axial and closer to C-2 than the **11β** Me† (resulting in a γ-effect), therefore, the 22 ppm signal was assigned to the **10α** Me. Hence, the 18.9 ppm‡ signal of the 18-Me of **15**, suggests it is in the α-orientation and the side chain in the β-position.

The structure of the two other new compounds of this group, **17** and **21a**, was determined by the ^{1}H NMR spectra, and especially, as before, on the basis of ^{13}C NMR data.

Compound **17** isolated from *X. macrospiculata*, was assigned the 14,15-xeniaphyllandiol - 4,5 - epoxide structure—the epoxy counterpart of the previously isolated xeniaphyllandiol (**16**). Compounds **16** and **17** isolated also from *X. obscuronata* are the parent alcohols of **18** and **19**.

Compound **21a**, derived from *X. lilielae*, was shown, on the basis of the ^{13}C NMR spectrum, to possess the following functionalities; a secondary alcohol (IR, ν_{max} 3640 cm^{-1}), affording a monoacetate by treatment with Ac$_2$O/Pyr, at r.t.), two epoxides (-HC(O)CMe$_2$ and -(CH$_3$)C(O)CH-) and a terminal methylene (>C=CH$_2$). Although the molecular ion was absent in the mass spectrum (the highest peak was observed at the odd *m/e* 249), the $C_{20}H_{32}O_3$ formula was clear from the ^{13}C NMR. Comparison of the NMR data of **21a** with the spectra of previously isolated xeniaphyllanes determined unequivocally the skeleton of **21a** as the 4(5) β-epoxide (Tables 5 and 6). The side chain was determined from the ^{1}H NMR data (including a double irradiation experiment of H-12, 13 and 14), and the mass spectrum:



The structure of **21** is closely related to the structure of the pair **4** and **20**, which we isolated previously from *X. macrospiculata* and *X. obscuronata* and also found in the extract of *X. lilielae*.

Epoxidation of **20** with *m*-chloroperbenzoic acid gave as the major epoxide **21** accompanied by small amounts of the

†Values of $d_{C_2\text{-}11\beta Me} = 3.57$ Å and $d_{C_2\text{-}11\alpha Me} = 3.07$ Å have been measured for buddledin-A bromohydrine and values of $d_{C_2\text{-}11\beta Me} = 3.77$ Å and $d_{C_2\text{-}11\alpha Me} = 3.21$ Å for β-caryophyllene chloride.[14]

‡A value of *ca* 19 ppm is characteristic for the whole series of the xeniaphyllanes.

Table 5. ^{13}C NMR chemical shifts (ppm) of the new 4(5)-epoxyxeniaphyllanes

C	m	Caryophyllene-Oxide	15	17	21
1	d	50.8	49.7	50.0	49.4
2	t	27.2[b]	27.8[b]	27.9[b]	27.8[b]
3	t	39.1	39.0	39.1	39.1
4	s	59.8	59.7	59.9	59.9
5	d	63.7	63.8	63.9	63.9
6	t	30.2	30.2	30.2	30.3
7	t	29.9[b]	29.7[b]	29.8[b]	29.4[b]
8	s	151.8	151.7	151.8	151.7
9	d	48.7	48.6	48.7	49.1
10	t	39.8	38.5	38.4	38.9
11	s	34.1	36.8	37.0	35.9
18	q	21.7	18.9[c]	19.0	19.5[a]
19	t	112.8	113.1	113.1	113.1
20	q	17.0	17.0	17.1	17.1
	q	29.9			
12	t		40.3	41.2	47.4
13	t		23.7	25.9	68.3[c]d
14	d		64.6	79.2	68.0[c]
15	s		58.4	73.2	59.9
16	q		18.6[c]	23.3	19.2[a]
17	q		24.9	26.7	24.9

a, b, c - These signals may be interchanged.

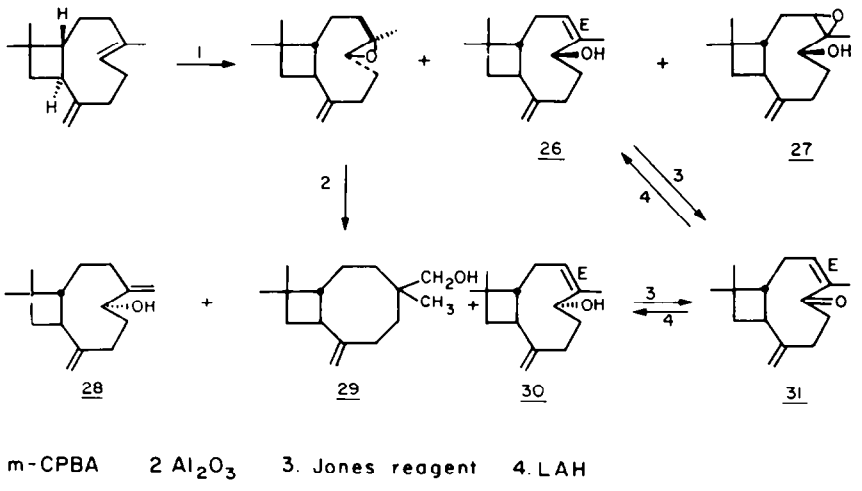
triepoxide **22** (the epoxidation of **4** to **20** was accomplished earlier).[2]

The first of the second subclass of the xeniaphyllanes (**23–25**) (*vide supra*) was designated xeniaphyllenol-B (**23a**), $C_{20}H_{32}O_2$, ν_{max} 3350 cm^{-1}. Compound **23a**, obtained from one collection of *X. macrospiculata*, is a diallyl alcohol. NMR comparisons of the side chain of **23a** (Tables 7 and 8) proved its structure to be identical with that of **4**. This is also in full agreement with the results of a double irradiation experiment (H-12 to H-15) as well as the *m/e* 85 fragment ($(CH_3)_2$ C=CHCH=$\overset{+}{O}$H) in the mass spectrum. Of the two remaining double bonds in the molecule, one was assigned the 8(19) position while the location of the other (the -CH=C(CH_3)- was not self evident.

In the course of the synthesis of caryophylene derivatives for NMR comparison purposes (Scheme 2), we

Table 6. ^1H NMR chemical shifts of the new 4(5)-epoxyxeniaphyllanes

H	Caryophyllene Oxide	15	17	21
H-5	2.88 dd	2.89 dd(J=11,4)	2.88 dd(11,4)	2.91 dd(10,4)
H-19	4.97 bs	4.98 bs	4.97 bs	4.97 bs
H-19'	4.85 bs	4.87 bs	4.85 bs	4.86 bs
CH_3-20	1.20 s	1.20 s	1.20 s	1.19 s
CH_3-18	1.01 s	1.03 s	1.02 s	1.10 s
H-13				3.56 dt(8,8,3)
H-14		2.68 t(J=6.2)	3.28 dd(10,2)	2.72 d (8)
CH_3-16		1.31 s	1.19 s	1.32 s
CH_3-17		1.27 s	1.15 s	1.31 s



Scheme 2.

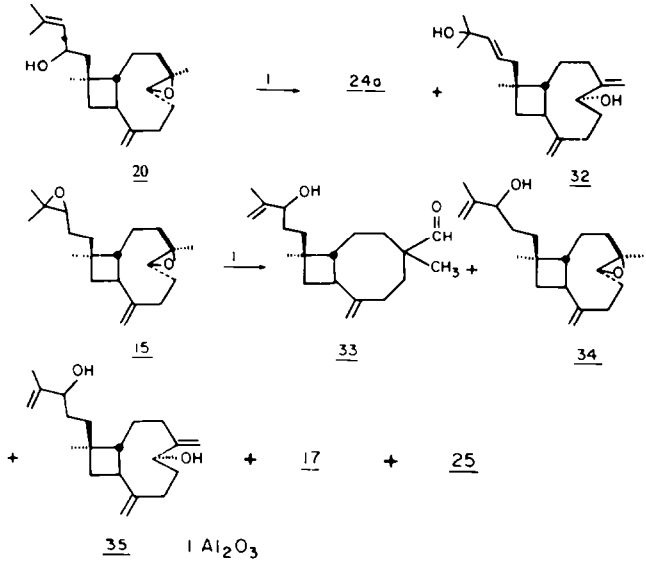
have treated caryophyllene with 1 equiv of *m*-chloroperbenzoic acid. In addition to the expected caryophyllene oxide (79%), we have also isolated two other compounds; an allyl alcohol **26** (8%) and a hydroxy epoxide **27** (9%).

The skeleton of **26** is identical to that of **23a**.

In contrast to the single epoxide obtained by the epoxidation of caryophyllene, xeniaphyllenol-A (**4**) afforded on epoxidation under similar conditions a 1 : 5 mixture of two epoxides—the 4(5) α and 4(5) β epoxides respectively. The stereochemistry of the major β-isomer was determined by comparison of its NMR spectrum with that of caryophyllene oxide whose β configuration was determined by Barton.[15]

We assume that caryophyllene also affords two epoxides with *m*-chloroperbenzoic acid. However, the α-epoxide being unstable under the acidic conditions of the reagent undergoes ring opening to give the Δ^3-5β-ol (**26**) which in part undergoes further epoxidation to furnish the 3,4 - epoxy - 5β - ol (**27**). Compound **26** is a natural compound, caryophyllenol-II, isolated by Dev from the oleoresin of *Dipterocarpus pilosus*.[16] Comparison of the NMR data of xeniaphyllenol-B (**23a**), its acetate (**23b**), caryophyllenol-II (**26**) and its acetate (Tables 7 and 8) showed very good agreement. The stereochemistry of C-5 in the natural **26**, was determined by Dev to be epimeric with that of a Δ^3-5-ol (**30**) obtained synthetically from caryophyllene oxide. The β-epoxide ring of the latter opens on contact with active Al_2O_3 to give the $\Delta^{4(20)}$-5α-ol (**28**),† the Δ^3-5α-ol (caryophyllenol-I, **30**) and a bicyclo [6.2.0]decan-11-ol (**29**) (Scheme 2). As the 5α stereochemistry of the OH group in **30** is determined by the parent epoxide, the C-5 configuration in **26**, and hence also in xeniaphyllenol-B (**23a**), is the 5β one. The epimeric relationship of **26** and **30** was confirmed by their Jones oxidation to the unsaturated Δ^3-5-one (**31**) and back reduction of the latter with LAH to the two epimeric 5-ols (**26** and **30**).

†Numbers according to the diterpene.



Scheme 3.

Table 7. ^{13}C NMR chemical shifts of several caryophyllene and xeniaphyllane derivatives

C	m	26	23a	28	24a	4	25
1	d	50.2	49.8	54.3	53.7		53.4
2	t	28.5[a]	28.8[a]	30.6[a]	30.8[a]		31.1[a]
3	d	125.6	126.1	32.7[a]t	32.9[a]t		32.6[a]t
4	s	138.0	137.6	151.2[b]	151.4[b]		151.2[b]
5	d	69.3	69.7	75.2	75.5		75.4
6	t	32.5[b]	32.5[b]	32.4[b]	32.6[b]		32.5[b]
7	t	34.1[a]	34.3[a]	32.7[a]	32.8[a]		32.6[a]
8	s	154.7	154.7	152.4[b]	152.5[b]		152.3[b]
9	d	42.5	43.0	43.7	44.2		43.5
10	t	39.6	39.3	37.0	36.7		35.7
11	s	33.1	35.1	33.4	35.5		36.3
18	q	22.7	20.4	22.0	19.9		19.4
19	t	109.6	109.8	109.1[b]	109.3[b]		109.4[b]
20	q	15.7	15.6	113.6[b]t	113.9[b]t		113.9[b]t
	q	30.0		30.1			
12	t		51.1		51.3	51.2	41.3
13	d		66.1		66.1	66.0	26.0 t
14	d		129.1		129.3	129.5	79.3
15	s		134.1		134.3	133.7	73.3
16	q		18.1		18.1	18.1	23.3
17	q		25.8		25.8	25.7	26.6

a Tentative assignment

b Assignment based on LIS experiments.

Table 8. ^{1}H NMR chemical shift of several caryophyllene and xeniaphyllane derivatives

H	26	23a	28	24a	4	25
H-3	5.56 bt	5.55 bt				
H-5	4.78 dd	4.78 dd	4.07 dd	4.10 dd		4.11 dd
H-19	4.74 bs	4.75 bs	4.94 bs	4.94 bs		4.96 bs
H-19'	4.49 bs	4.49 bs	4.78 bs	4.80 bs		4.80 bs
Me-20	1.64 bs	1.63 bs				
H-20			5.04 bs	5.04 bs		5.06 bs
H-20'			4.76 bs	4.77 bs		4.78 bs
Me-18	1.01 s	1.08 s	0.98 s	1.05 s	1.04 s	1.01 s
*	0.96 s		0.98 s			
H-13		4.43 dt		4.44 dt	4.46 dt	
H-14		5.17 bd		5.19 bd	5.20 bd	3.29 dd
Me-16		1.70 bs		1.71 bs	1.70 bs	1.22 s
Me-17		1.69 bs		1.70 bs	1.70 bs	1.17 s

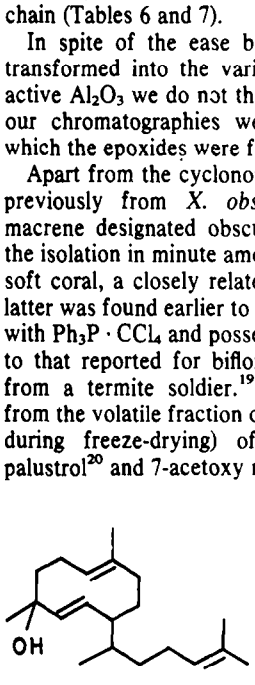
* The second (β)methyl at C-11.

Xeniaphyllenol-C (**24a**), $C_{20}H_{32}O_2$ was isolated from *X. macrospiculata*. As before, the structure of **24a** was determined by comparison of its NMR spectra and especially the ^{13}C-NMR with that of the already established structures. Thus, it could be suggested that the side chain of **24a** is identical with that of xeniaphyllenols-A and B (compounds **4** and **23a**, respectively) and that the skeleton of xeniaphyllenol-C is the same as the major Al_2O_3 ring opened product of caryophyllene oxide (**28**, Scheme 2). The proximity of the 5α-ol to H-20 suggested by the relative large Δδ value of H-20 and H-20' was also supported by a 6% NOE between H-5α and H-20. Unequivocal proof of the structure of **24a**, was obtained by treating **20** with neutral active Al_2O_3,[17] a reaction which afforded two $\Delta^{4(20)}5\alpha$ alcohols (Scheme 3). One of the isomers was identical in all respects with **24a** while the other (**32**) possessed the same skeleton but a Δ^{13}-15-ol side chain (the allylic rearranged alcohol, Scheme 3).

Diepoxide **15** on contact with active Al_2O_3 is transformed into 5 compounds. Among the five was a polar triol identical in all respects with a natural triol **25** isolated from *X. obscuronata*. The structure of **25** was established by comparison with **24a** and **28** (the same skeleton) as well as **16** and **17**—the same 14,15-diol side chain (Tables 6 and 7).

In spite of the ease by which the 4,5-epoxides are transformed into the various alcohols on contact with active Al_2O_3 we do not think that **23–25** are artifacts; all our chromatographies were carried out on Si_2O_3 on which the epoxides were found to be stable for 4 days.[18]

Apart from the cyclononane diterpenoids we obtained previously from *X. obscuronata* a prenylated germacrene designated obscuronatin (**36**). We now report the isolation in minute amounts (< 10 mg) from the same soft coral, a closely related bicyclic compound **37**. The latter was found earlier to result from the treatment of **36** with $Ph_3P \cdot CCl_4$ and possesses very similar spectral data to that reported for biflora-4, 10(19), 15-triene isolated from a termite soldier.[19] Noteworthy is the isolation from the volatile fraction of *X. macrospiculata* (obtained during freeze-drying) of the marine sesquiterpenes palustrol[20] and 7-acetoxy muurolene.[21]



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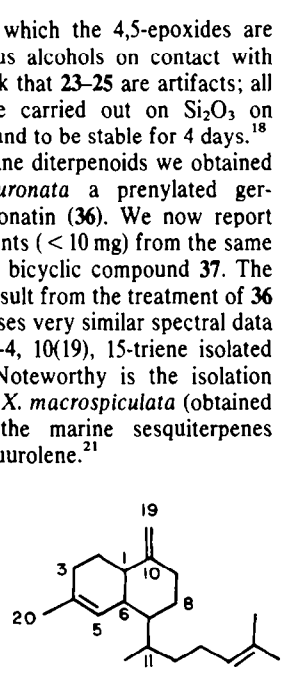

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EXPERIMENTAL

IR spectra were recorded on a Perkin–Elmer model 177 spectrophotometer. UV spectra were recorded on a Varian Cary 219 spectrophotometer in MeOH solns. Optical rotations were measured with a Bellingham and Stanley or Perkin–Elmer model 141 polarimeters in $CHCl_3$ solns. M.ps were determined on a Thomas–Hoover capillary m.p. apparatus and are uncorrected. Mass spectra were taken with a Du Pont 21-491B instrument. Parent peaks of the compounds were analyzed on a HRMS Varian Mat 731 instrument. ^{13}C NMR were measured with a Bruker WH-300 (75.46 MHz) and a Bruker WH-90 (22.63 MHz) in $CDCl_3$ or C_6D_6 solutions. ^1H NMR spectra were recorded, unless stated otherwise, on a Bruker WH-270 spectrometer. Chemical shifts are reported in δ-values downfield from internal TMS and the coupling constants are quoted in Hz. All solvents used were either spectral grade or freshly distilled ones.

Collection and extraction of soft corals and isolation of diterpenoids—a general procedure

The natural products were obtained from four collections of *Xenia* soft corals from the Red Sea. Two samples of *Xenia macrospiculata* were collected at a depth of 3–5 m in Marsa-el-Muqubila (the Gulf of Eilat) in December 1978 and February 1979, another sample of *X. obscuronata* was obtained in April 1979 from Ras Garah (the Gulf of Suez) and a specimen of *Xenia lilielae* was collected near Dahab (the Gulf of Eilat) in November 1980. In all cases freeze dried material was ground and extracted in ambient petroleum ether, then in hot petroleum ether in a Soxhlet (24 hr) and finally extracted with EtOAc (or occasionally CH_2Cl_2). Both petroleum ether extracts were combined as no differences between them could be revealed.

In all cases petroleum ether and EtOAc extracts were treated separately as they were found to give different compounds.

The crude extracts were separated in combinations of silica gel and Sephadex LH-20 column chromatographies. Each petroleum ether extract was separated on a silica gel H column under suction, individual fractions were combined and then separated from accompanying glycerides and sterols on a Sephadex LH-20 column (prepared and eluted with 7 : 3 $CHCl_3$-hexane). Final purifications were achieved following a second silica gel (extra pure) chromatography.

The EtOAc extracts were separated on a Sephadex LH-20 column, prepared and eluted with a solvent mixture of 2 : 1 : 1 hexane-$CHCl_3$-MeOH to give the main xeniolides fraction. This fraction was further separated with the aid of several silica gel H columns, using in all cases solvent mixtures of petroleum ether–EtOAc with increasing polarity.

The materials obtained from each specimen and their relative abundance are summarized in Table 1.

Xenialactol-D (**10a**) This compound was obtained as a viscous oil; IR($CHCl_3$) 3560, 3410, 3050, 2910, 2840, 1665, 1630, 1445, 1375, 1115, 1070, 1020, 1000, 955, 900 and 860 cm^{-1}; mass spectrum (10 eV), *m/e* (relative intensity) 316 (M^+–H_2O, $C_{20}H_{28}O_3$, 0.5), 300(0.6), 273(0.9), 243(1), 215(2), 187(3), 159(3), 145(3), 105(4), 97(6), 87(12), 85(80) and 83(100%); ^1H NMR 5.33 bt (J = 7.5), 5.23 bd (J = 7.3), 4.95 bs, 4.78 m (2H), 4.65 (2H, m + d (J = 14)), 4.32 d (J = 14), 2.71 (2H, m + t (J = 6)), 2.59 dd (J = 13.8, 6.6), 2.41 d(J = 13.8), 2.32 m (2H), 2.20 m (2H), 2.00 m, 1.75 bs (3H), 1.54 m, 1.32 s (6H); for ^{13}C NMR, Table 2.

Acetylation of xenialactol-D (**10a**) *to* **10b**. Ac_2O (1 ml) was added to a soln of **10a** (150 mg) in pyridine (1 ml), and the mixture was stirred at room temp over night. The excess reagents were then removed *in vacuo*, and the oily residue chromatographed on a short silica gel-H column. Elution with 1 : 4 EtOAc—petroleum ether afforded **10b** (120 mg) as an oily material; IR (neat) 3055, 2950, 2920, 2840, 1715 (strong) 1630, 1440, 1370, 1315, 1245, 1025, 980 and 905 cm^{-1}; mass apectrum (12 eV), *m/e* (relative intensity) 359 (M^+OA_c, $C_{22}H_{31}O_4$, 4) 358(8), 328(4), 298(12), 285(16), 269(13), 268(61), 227(28), 211(24), 199(44), 197(100%), 183(68), 71(57) and 43(46); ^1H NMR 5.68 bt (J = 7.3), 5.53 bd (J = 8.2), 5.39 bt (J = 7) 5.28 bd (J = 7–8), 4.91 bs, 4.86 bs 4.63 d(J = 13), 4.37d (J = 13), 2.73 t (J = 6), 2.09 s (3H), 2.04 s (3H), 1.80 bs (3H), 1.33 s (6H); for ^{13}C NMR see Table 2.

Xeniolide-E (**13**). This compound was obtained in minute quantities (ca. 18 mg) and was found to be very sensitive to air oxidation; ^1H NMR 5.63 bt (J = 7), 5.31 bd (J = 8.5), 5.06 bs, 4.98 bs, 4.83 bd (J = 12), 4.71 ddd (J = 8.5, 7.6, 5.6), 4.45 bd (J = 12), 2.81 dd (J = 7, 5), 2.78 ddd (J = 14, 7, 5), 2.70 dt (J = 14, 7), 1.67 bs (3H), 1.35 s (3H) and 1.34 s (3H).

14,15-*Epoxyxeniaphylla*-4,8(19)-*diene* ("*Xeniaphyllene*-14, 15-*oxide*", **14**). This oily compound was obtained in only small amounts (30 mg, unseparable from accompanying glycerides); ^1H NMR 5.29 m, 4.93 bs, 4.83 bs, 2.69 t (J = 6), 1.61 bs (3H) 1.31 s (3H), 1.27 s (3H) and 0.99 s (3H).

4,5 14,15-*Diepoxyxeniaphyll*-8(19)-*ene* ("*Xeniaphyllene-dioxide*", **15**). An oil, $[\alpha]_D^{25}$ + 21° (c, 3.4, $CHCl_3$); IR (neat 3060,

2930, 2910, 2840, 1620, 1450, 1445, 1370, 1250, 1115, 960, 905, 890 and 860 cm^{-1}; mass spectrum (10 eV), *m/e* (relative intensity) 304(M^+, $C_{20}H_{32}O_2$, 0.3) 289(1), 271(2), 253(1), 215(4), 205(10), 187(13), 161(17), 159(18), 149(25), 135(28), 121(43), 108(55), and 71(100%); for ^1H NMR see Table 6 and for ^{13}C NMR Table 5.)

4,5-*Epoxyxeniaphyll-8(19)-en*-14, 15-*diol* ("*Epoxyxeniaphyllandiol*", **17**). An oil, $[\alpha]_D^{25}$ + 31° (c, 0.9, $CHCl_3$); IR (neat) 3430, 3050, 2920, 2860, 1620, 1450, 1445, 1372, 1250, 1160, 1067, 885 and 860 cm^{-1}; mass spectrum (10 eV), *m/e* (relative intensity) 304 ($C_{20}H_{32}O_2$, M^+-H_2O, 3), 289(3), 286(2), 271(4), 245(11), 205(25), 189(21), 187(43), 149(52), 147(51), 143(79), 133(60), 121(69), 109(69), 107(73), 95(63) and 71(100%); ^1H NMR see Table 6 and for ^{13}C NMR Table 5.

4,5, 14,15-Diepoxyxeniaphyll-8(19)-en-13-ol ("Diepoxy-xeniaphyllenol-A", **21a**). An oil, $[\alpha]_D^{25}$ + 23° (c, 1.1, $CHCl_3$); IR($CHCl_3$) 3640, 3400, 3060, 2920, 1622, 1455, 1445, 1376, 1245, 895 and 865 cm^{-1}; mass spectrum (12 eV), *m/e* (relative intensity) 249(2.5), 248(2), 232(4), 230(7), 219(8), 205(21), 204(24), 187(40), 155(52), 138(47), 123(48), 120(68), 109(78), 107(64), 95(79) and 72(100%); for ^1H NMR see Table 6 and for ^{13}C NMR Table 5.

Xeniaphylla-3,8(19), 14-*trien*-5β, 13-*diol* ("*Xeniaphyllenol-B*", **23a**). An oil, $[\alpha]_D^{25}$ −47° (c, 1.1, $CHCl_3$); IR (neat) 3350, 3080, 2930, 2850, 1625, 1440, 1377, 1255, 1145, 1050, 1020, 885 and 785 cm^{-1}; mass-spectrum (14 eV), *m/e* (relative intensity) 304 (M^+, $C_{20}H_{32}O_2$, 0.3), 289(0.6), 286(1.3), 271(2), 257(2), 205(5), 204(5), 189(6), 187(12), 159(12), 147(23), 133(22), 121(29), 109(37), 107(54) and 85(100%); ^1H NMR 5.55 bt (J = 7.8), 5.17 bd (J = 8.7), 4.78 dd (J = 6.1, partially obscured), 4.75 bs, 4.49 bs, 4.43 dt (J = 8.7, 7.2), 1.70 bs (3H), 1.69 bs (3H), 1.63 bs (3H) and 1.08 s (3H); for ^{13}C NMR see Table 7.

Xeniaphylla-4(20), 8(19), 14-*trien*-5α, 13-*diol* ("*Xeniaphyllenol-C*, **24a**). Only 14 mg of this compound were obtained in pure form; IR($CHCl_3$) 3640, 3570, 3400 br, 3060, 2920, 2850, 1632, 1440, 1375 and 1005 cm^{-1}; mass spectrum (10 eV), *m/e* (relative intensity) 286 (M^+-H_2O, $C_{20}H_{30}O$, 2), 271(2), 268(1.5), 253(2.5), 222(4), 205(5), 187(15), 147(18), 136(64), 122(39), 107(37), 85(65) and 83(100%); ^1H NMR 5.19 bd (J = 9), 5.04 bs, 4.94 bs, 4.80, 4.77 bs, 4.44 dt (J = 9, 6.4), 4.10 dd (J = 8.1, 4.1), 1.71 bs (3H), 1.70 bs (3H) and 1.05 s (3H); for ^{13}C NMR (75.46 MHz) see Table 7.

Xeniaphylla-4(20), 8(19)-*dien*-5α, 14,15-*triol* ("*Xeniaphyllantriol*", **25**). This compound was obtained as an oil with *ca* 90% purity, $[\alpha]_D^{25}$ + 17°(c, 0.85, $CHCl_3$); IR ($CHCl_3$) 3640, 3570, 3380 br, 2910, 2850, 1620, 1442, 1372, 1070 and 910 cm^{-1}; mass spectrum (10 eV), *m/e* (relative intensity) 304(1.3) 290(1), 287(1), 245(4), 207(5), 205(22), 189(9), 187(34), 164(10), 159(17), 147(22), 143(40) and 136(100); ^1H NMR 5.06 bs, 4.96 bs, 4.80 bs, 4.78 bs, 4.11 dd (J = 9, 4), 3.29 dd (J = 10, 1.8), 1.22 s (3H), 1.17 s (3H) and 1.01 s; for ^{13}C NMR see Table 7.

Epoxidation of epoxyxeniaphyllenol-A (**20**) *to give diepoxide* **21a**. To a soln of **20** (60 mg) in $CHCl_3$ (15 ml) at 2° was added dropwise with stirring a soln of *m*-chloroperbenzoic acid (56 mg, 1.4 equiv) in $CHCl_3$ (7 ml) during a period of 1.5 hr. After 1 hr the excess of the peracid was removed with 15% Na_2CO_3 aq and water (5 ml) was added. The organic phase was separated and the aqueous residue reextracted with $CHCl_3$. The combined $CHCl_3$ soln was dried over $MgSO_4$ and evaporated to yield 50 mg of a viscous yellow material. Careful chromatography on a short silica gel column (eluted with 7 : 3 petroleum ether-EtOAc), afforded **21a** (13 mg, identical in all respects with an authentic sample). The second and more polar product (**22**, 26 mg, eluted with 3 : 2 petroleum ether–EtOAc) was found to be a tris-epoxy compound; ^1H NMR (90 MHz) 3.53 dt (J = 8.5, 8.5, 3.5), 3.09 dd (J = 10.3, 3.8), 2.67 d (J = 8.5), 2.64 s (2H), 1.29 s (9H) and 1.04 s (3H).

Acetylation of diepoxide **21a**. This compound (23 mg, *ca* 75% pure) was acetylated with Ac_2O-pyridine. Workup as described above for **10b** gave the desired acetate **21b**. Silica gel-H chromatography afforded, after elution with 7 : 3 petroleum ether–EtOAc, the monoacetate (**21b**, 10 mg) as a viscous oil, $[\alpha]_D$ + 13° (c, 2.7, $CHCl_3$); ^1H NMR 4.91 bs, 4.87 dt (J = 8.5, 8.5, 4.1), 4.81 bs, 2.80 dd (J = 10.9, 3.2), 2.71 d (J = 8.5), 1.97 s (3H), 1.31 s (3H), 1.25 (3H), 1.12 s (3H) and 1.02 s (3H); IR ($CHCl_3$) 3070, 2930, 2860, 1730, 1632, 1455, 1380, 1372, 1240, 1215, 1115, 1000, 960, 910 and 865 cm^{-1}.

Acetylation of diol **23a** to give diacetate **23b**. Acetylation of **23a** (8 mg) with a few drops of Ac_2O–pyridine solution, at room temp overnight, was completed when the mixture was warmed to 70° for an additional 1 hr. The usual workup left an oily product; ^1H NMR 5.71 dd (J = 12.0, 5.6), 5.57 bt (J = 6.2), 5.51 dt (J = 9.7, 7.0), 5.06 bd (J = 9.7), 4.75 bs, 4.49 bs, 2.02 s (3H), 1.99 s (3H), 1.74 bs (3H), 1.70 bs (3H), 1.60 bs (3H) and 1.09 s (3H).

Opening of the epoxide of **20** *to give xeniaphyllenol-C* (**24b**). Compound **20**, (62 mg) was acetylated with Ac_2O–pyridine to give, after evaporation of the reagents, in quantitative yield the monoacetate; ^1H NMR (90 MHz) 5.54 dt (J = 9.4, 6.7), 5.07 bd (J = 9.4), 4.96 bs, 4.86 bs, 2.90 dd (J = 10, 4), 1.97 s (3H), 1.70 bs (6H), 1.18 s (3H), 1.07 s (3H). The acetate (54 mg) in hexane (8 ml) was shaken for 16 hr with activated neutral Al_2O_3 (1.5 g, prepared according to the procedure described by Dev,[17] and warmed to 450° for 4 hr prior to use). The products were then extracted with 10% MeOH in diethyl ether (500 ml) to give a 3 : 2 mixture of **24b** and **32**, which could be separated on a short silica gel column.

Compound **24b**: The less polar (24 mg) was eluted with 9 : 1 petroleum ether–EtOAc, while **32**, the more polar, was eluted with a solvent mixture of 5 : 1.

Compound **24b**: ^1H NMR 5.55 dt (J = 9.1, 6.7), 5.08 bd (J = 9.1), 5.05 bs, 4.95 bs, 4.81 bs, 4.78 bs, 4.10 dd (J = 7, 5), 2.00 s (3H), 1.70 bs (6H), 1.04 s (3H).

Compound **32**: IR ($CHCl_3$) 3590, 3440, 3070, 2930, 2865, 1632, 1445, 1375, 1255, 1005, 972 and 888 cm^{-1}; ^1H NMR 5.60 m (2H), 5.05 bs, 4.95 bs, 4.81 bs, 4.77 bs, 4.10 dd (J = 7, 5), 1.31 s (6H), 1.00 s (3H).

Hydrolysis of acetate **24b** *to give xeniaphyllenol-C* (**24a**). $LiAlH_4$ (0.05 gm) was added to a soln of **24b** (30 mg) in anhyd diethyl ether (10 ml), and the mixture was refluxed for 3 hr. Excess $LiAlH_4$ was destroyed with EtOAc. Dilute (2%) HCl aq and ether were added and the mixture worked up in the usual manner. The organic phase was dried over $MgSO_4$ and evaporated to give a yellow oily residue (24 mg), which was chromatographed on a short silica-gel column. Elution with 4 : 1 petroleum ether–EtOAc afforded a mixture of **24a** and **32** (15 mg, in a ratio of 11 : 9 respectively according to the ^1H NMR integration).

Alumina-induced oxirane opening of **15**. Fresh activated Al_2O_3 (3.5 g) was added to a soln of **15** (103 mg) in CH_2Cl_2. The solvent was evaporated and hexane (8 ml) was added. The mixture has been shaken overnight, then extracted with a 10% MeOH in ether soln to give, after evaporation, a mixture (95 mg) of at least five products, which were separated on a short silica gel H column under suction. The 5 compounds were found to be (in order of polarity): aldehyde **33** (11 mg), epoxy-alcohol **34** (11 mg), diol **35** (25 mg), epoxy-diol **17** (13 mg) and triol **25** (5 mg).

Compound **33**: IR ($CHCl_3$) 3610, 3450 br, 3080, 2940, 2860, 1725, 1640, 1465, 1377, 1260, 1245, 1015 and 895 cm^{-1}; mass spectrum (10 eV), *m/e* (relative intensity) 304 (M^+, $C_{20}H_{32}O_2$, 1), 286(2), 271(3), 268(2), 257(2), 253(4), 247(2), 245(2), 218(6), 205(12), 187(18), 159(24), 147(29), 125(100%), 107(60) and 83(91); ^1H NMR 9.43 s, 4.92 bs, 4.84 bs, 4.70 bs, 4.49 bs, 3.99 t (J = 6), 1.72 bs (3H), 1.01 s (6H).

Compound **34**: IR ($CHCl_3$) 3600, 3450 br, 3070, 2930, 2860, 1630, 1455, 1377, 1255, 1070, 1008, 960, 900 and 860 cm^{-1}; mass spectrum (15 eV), *m/e* (relative intensity) 289 (M^+-CH_3, $C_{19}H_{29}O_2$, 2), 271(2), 229(2), 218(3), 205(5), 187(15), 175(11), 159(19), 149(25), 136(40), 125(47), 121(47), 109(55), 107(77), 93(93) and 43(100%); ^1H NMR 4.97 bs, 4.93 bs, 4.86 bs (2H), 4.01 bt (J = 5.9), 2.88 dd (J = 11, 4), 1.72 bs (3H), 1.19 s (3H), 1.02 s (3H).

Compound **35**: IR ($CHCl_3$) 3610, 3450 br, 3080, 2940, 2865, 1632, 1453, 1380, 1260, 1070, 1015, 905 and 865 cm^{-1}; mass spectrum (15 eV), *m/e* (relative intensity) 304 (M^+, $C_{20}H_{32}O_2$, 0.5), 271(1), 257(1), 243(2), 229(2), 205(5), 187(13), 159(12), 149(16), 147(18), 136(100%), 107(40) and 43(50); ^1H NMR 5.05 bs, 496 bs, 4.93 bs, 4.85 bs, 4.80 bs, 4.77 bs, 4.10 dd (J = 9, 4), 4.01 bt (J = 5–6), 1.73 bs (3H), 1.00 bs (3H).

Compounds **17** *and* **25**. The two have been found to possess indistinguishable spectral data from the natural products.

Epoxidation of caryophyllene. To a soln of caryophyllene (6.3 g, Fluka, puriss, 97% according to GC) in $CHCl_3$ (250 mL) at

0°, was added dropwise with stirring a soln of *m*-chloropenbenzoic acid (6.7 g, 1.07 equiv) in $CHCl_3$ during a 3.5 hr period. Stirring was continued for another 2.5 hr. Then 15% Na_2CO_3 aq (40 ml) was added, the organic phase separated, washed with water, dried over $MgSO_4$ and evaporated to yield 6.81 g of products which were separated on a silica-H column under suction. The products were, in order of polarity, unreacted caryophyllene (0.8%), caryophyllene-oxide (79%), alcohol **26** (8%), epoxy-alcohol **27** (10%) and unidentified more oxygenated products (2%).

Alcohol **26**: IR (neat) 3380, 3058, 2920, 2840, 1620, 1445, 1377, 1352, 1280, 1252, 1048, 1010, 988, 885 and 782 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 220 (M^+, $C_{15}H_{24}O$, 2), 205(5), 202(6), 187(10), 159(13), 149(20), 135(23), 131(24), 109(44), 107(45), 93(56), 81(55) and 43(100%); for ^1H NMR see Table 8 and for ^{13}C NMR Table 7.

Epoxy-alcohol **27**: ^1H NMR 4.79 bs, 4.55 bs, 3.74 dd (J = 10.9, 6.6), 2.92 dd (J = 9.2, 6.3), 1.28 s (3H), 0.99 s (6H); ^{13}C NMR: 153.8 s, 110, 4t, 71.0 d, 63.7 d, 63.7 s; IR (neat) 3420 br, 2940, 1620 and 1440 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 236 (M^+, $C_{15}H_{24}O_2$, 0.5), 221(1.5), 218(1.2), 207(21), 155(30) and 43(100%).

The oxirane opening of caryophyllene-oxide. This Al_2O_3— induced oxirane opening was performed as described by Dev;[17] caryophyllene-oxide (1.7 g) in hexane (52 mL) was shaken for 14 hr over 43.5 g fresh-activated Al_2O_3. The products (1.67 g) obtained after extraction and evaporation, were separated on a silica-H column (under suction) with solvent mixtures of petroleum ether-EtOAc to give, in order of polarity: starting material (1%), alcohol **30** (= caryophyllenol-I,[16] 5%), a rearranged product **29** (2.5%) and alcohol **28** (63%). The rest of the products were not separated.

Alcohol **30**. IR (CCl_4) 3620, 3360 br, 3080, 2960, 2870, 1637, 1455, 1370, 1017, 995 and 890 cm^{-1}; ^1H NMR 5.43 m 4.87 bs, 4.87 bs, 4.84bs, missing 4.61 dd (J = 9, 6), 1.67 bs (3H), 1.00 s (3H), 0.98 s (3H); ^{13}C NMR 153.3 s, 137.0 s, 125.7d, 110.0 t, 69.7 d.

Rearrangement-product **29**. IR (neat) 3350 br, 3070, 2940 br, 2860, 1635, 1465, 1380, 1365, 1285, 1255, 1050, 1035, 1005 and 880 cm^{-1}; ^1H NMR 4.65 bs, 4.46 bs, 3.31 bs (2H), 1.00 s (3H), 0.98 s (3H), 0.88 s (3H).

Alcohol **28**. IR (neat) 3330, 3055, 2920, 2840, 1630, 1455, 1440, 1375, 1360, 1035, 1020, 898, 882 and 865 cm^{-1}; mass spectrum (15 eV), *m/e* (relative intensity) 220 (M^+, $C_{15}H_{24}O$, 1), 205(4), 202(3), 191(7), 187(7), 159(12), 136 (100%); for ^1H NMR see Table 8 and for ^{13}C NMR Table 7.

Acetylation of alcohol **26**. This was acetylated with Ac_2O–pyridine to give an oily material which was chromatographed on a silica-gel column: IR($CHCl_3$) 2930, 2865, 1727, 1632, 1365, 1255, 1018, 965 and 898 cm^{-1}; ^1H NMR 5.74 dd (J = 12, 5.6), 5.62 bt (J = 8), 4.74 bs, 4.50 bs, 2.03 s (3H), 1.60 bs (3H), 1.04 s (3H), 0.97 s (3H).

Jones oxidation of alcohol **26**. To a soln of **26** (100 mg) in acetone (15 ml) at 0° were added a few drops of Jones reagent until the orange colour remained for 10 min. Excess reagent was destroyed with MeOH and the mixture was worked up in the usual manner to give a mixture of products (85 mg). This was separated on a silica-H column to give, after elution with petroleum ether, compound **31** (26 mg). The remaining products, most likely rearrangement products, were not separated. Compound **31**: ^1H NMR (90 MHz) 5.73 dt (J = 1.5, 7.9), 4.83 bs, 4.66 bs, 2.54 m (2H), 1.84 bs (3H) 0.99 s (3H) and 0.97 s (3H).

$LiAlH_4$ *reduction of ketone* **31**. A soln of **31** (18 mg) in anhydiethyl ether (5 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (40 mg) in 5 mL anhyd ether. Stirring at room temp was continued for 2 hr then the excess $LiAlH_4$ was destroyed with EtOAc (0.2 mL). After the usual workup an oily residue (16 mg) was obtained. This oil was found to be composed of 2 epimeric alcohols **26** and **30**, in a ratio of 3 : 7 (GC). The two were separated on a 2% $AgNO_3$ impregnated silica gel column to give after elution with 10% ether in petroleum ether, **30** (8.5 mg) and the more polar **26** (3 mg). These two products were found to be identical in all respects (IR, ^1H NMR, GC) with the corresponding alcohols, obtained in the previous reactions, described above.

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