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Reactions of Dienes with Selenium Dioxide III. Selenolabdanes from Methyl 15-*O*-Acetylisocupressate

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Abstract.- The reaction of methyl 15-*O*-acetylisocupressate with SeO_2/MeOH yielded, in addition to the expected products of allylic oxidation, ≈20% of selenepanes and selenocanes. The formation of cyclic selenium compounds from diolefins in this reaction is similar to that observed from acetyllinalool. The mechanistic proposal through a double electrophilic attack to both double bonds explains the structural variation of the selenium containing products in this and in previous cases.

INTRODUCTION

In a previous report we described the reaction between natural 1,6-diolefins like linalool and linalyl acetate, with SeO_2 in MeOH[1,2]. The reaction with linalyl acetate produced the expected products of allylic oxidation, besides minor amounts of compounds containing selenium in the molecule. Only selenium products were obtained when the reaction was carried out with linalool. These products are structurally different from those obtained from linalyl acetate. Recently[3] we studied the reaction with model 3-hydroxy-1,6-diolefins which was similar to the results obtained with linalool, thus confirming that the formation of 8-oxa-3-selenabicyclo[3,2,1[1,5]]octanes from this substrates is general.

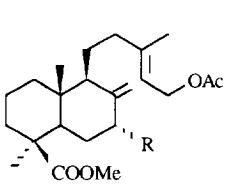
The addition of selenium species to diolefins, during treatment with SeO_2, has also been described for other substrates[4,5]. Besides the "ene" reaction-sigmatropic rearrangement, responsible for the allylic oxidation, the selenium atom in SeO_2 produced electrophilic addition to double bonds yielding selenium containing products, as for example in the SeO_2 treatment of benzyl ether of geraniol. The formation of selenium products has also been observed in the treatment of monoolefins with SeO_2[6-8]. These products showed different structures and were obtained in different yields, depending on the starting material and reaction conditions. In general, an initial electrophilic attack of the Selenium species to the olefin has been proposed for the reaction mechanism [2-5].

In order to check if this special reaction takes place with other 1,6-diolefinic systems, we have studied the products obtained after SeO_2/MeOH treatment of methyl 15-*O*-acetylisocupressate (**1**). Compounds derived from allylic oxidation were isolated as main reaction products, but selenium derivatives are also produced in ~20% yield. The mechanism proposed for the formation of these compounds is also based in the electrophilic attack of SeO_2 or other selenium species produced in the allylic oxidation.

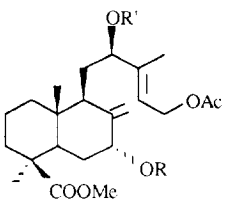
RESULTS AND DISCUSSION

Oxidation with SeO_2/MeOH was performed by the same procedure previously described[1]. Compounds derived from allylic oxidation were the main reaction products: **2** (18.2 %), **3** (16.2%) and **4** (14.8%). Compounds **5-8**, accounting for 22% yield, showed spectroscopic and analytical data that proved the presence of selenium in their molecules.

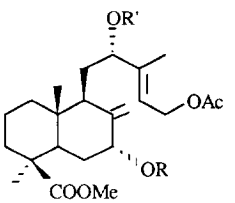
Structure of monooxidation product **2** was deduced from its spectroscopic properties and those of its diacetate **2a** (Tables I and II). Compounds **3** and **4** were identified as double oxidation products at C-7 and C-12. The configuration for each stereoisomer was established on the basis of changes in chemical shifts of H-17 in H^1 NMR induced by the presence of the hydroxyl group at C-12[9]. A deshielding effect (0.15-0.35 ppm) for one of these protons is observed for compounds with *12S* configuration, as a result of spatial proximity to the 12-OH group. Substance **3** and its acetate **3a** showed shielding effects on H-17 higher than those of **4** and its acetate **4a**. In consequence, **3** is the (12*R*) 7,12-dihydroxy derivative and **4** the (12*S*) 7,12-dihydroxy derivative of the starting material.



1 R=H
2 R=OH
2a R=OAc

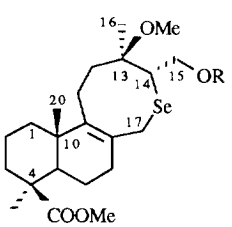


3 R=R'=H
3a R=R'=Ac
3b R=Ac, R'=H

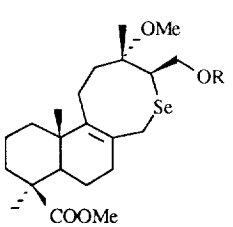


4 R=R'=H
4a R=R'=Ac
4b R=Ac, R'=H

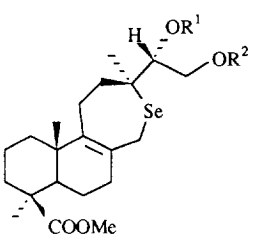
The presence of selenium in compounds **5-8** was deduced from the mass spectra. Products **5** and **6** display two molecular ions, in agreement with formula $C_{24}H_{38}O_5{}^{78}Se$ and $C_{24}H_{38}O_5{}^{80}Se$. Products **7** and **8** also showed two molecular ions, in accordance with formula $C_{23}H_{36}O_5{}^{78}Se$ and $C_{23}H_{36}O_5{}^{80}Se$. In all cases, the relative intensities of both molecular ions correspond with natural abundances of ^{78}Se and ^{80}Se. Furthermore, strong oxidation with H_5IO_6 followed by hydrazine reduction produced characteristic precipitate of selenium[10] from compounds **5-8**.



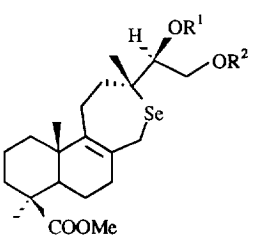
5 R=OAc
5a R=H



6 R=OAc
6a R=H



7 R^1=H, R^2=Ac
7a R^1=R^2=Ac
7b R^1=R^2=H
7c R^1,R^2=$C(CH_3)_2$



8 R^1=H, R^2=Ac
8a R^1=R^2=Ac
8b R^1=R^2=H
8c R^1,R^2=$C(CH_3)_2$

Compounds **5** and **6** showed similar features in their NMR spectra (Tables III and IV), which suggested a close structural relationship between both compounds. Small changes in the decaline system of the diterpenic

skeleton were observed. The main differences from the starting material were: disappearance of $\Delta^{8(17)}$ and Δ^{13} double bonds, presence of a tetrasubstituted double bond, an additional methoxy group on a non protonated carbon atom and one methine and one methylene, as points of attachment of the selenium atom. From this data it was possible to propose a 14,17-episelenolabdane constitution for both compounds. 2D-Heteronuclear H/C correlations supported this structural assignment, particularly for the modified C-12 to C-16 moiety.

The difference between **5** and **6** lay on the configuration at C-13 and C-14. Several nOe difference experiments revealed a *cis* relationship between CH_3-16 and CH_2-15, but due to the lack of significant nOe effects with any protons of the decaline system, we failed to ascertain the absolute stereochemistry at positions 13 and 14. In consequence, stereoisomeric structures **5** and **6** were indistinctly assigned to these products. Basic hydrolysis of **5** and **6** produced alcohols **5a** and **6a**.

Similarly, compounds **7** and **8** were structurally related. The NMR spectra (Tables III and IV) of both compounds, were compared to those of **5**, **6** and to the starting material. The following differences were observed: lack of MeO- group, a -CHOH-CH_2OAc fragment was present at C14-C15 and a Selenium atom was bonded to C-13 and C-17. Consequently, the constitution of 13,17-episelenolabdane was proposed for **7** and **8**, and the difference between both compounds again lay on the stereochemistry at C-13 and C-14.

The hydrolysis of **7** and **8** produced the dihydroxy derivatives **7b** and **8b**, which were converted to the acetonides **7c** and **8c** by treatment with 2,2-dimethoxypropane. Thus, the substructures proposed for the C-13 and C-15 moieties were confirmed, but it was not possible to distinguish between the absolute stereochemistries of **7** and **8** at these carbon atoms. Compound **7c** was crystallized and the X-ray diffraction (Figure 1) allowed

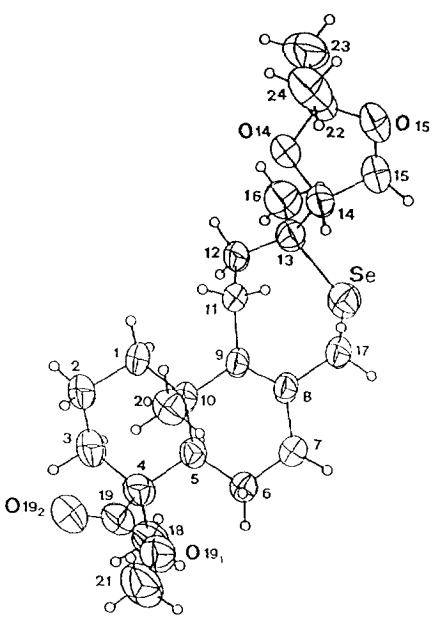


Figure 1. Perspective view of molecule **7c** showing the numbering of atoms.

Table 1. Fractional coordinates for non-hydrogen atoms ($\times 10^4$) and equivalent isotropic parameters[11]

Atoms	x/a (σ)	y/b (σ)	z/c (σ)	B_{eq} (Å^2)
C(1)	3930(4)	5813(11)	12696(3)	4.7(2)
C(2)	4372(5)	5400(15)	13748(3)	5.1(3)
C(3)	3967(5)	6842(12)	14334(4)	5.2(3)
C(4)	2626(4)	6968(10)	14087(3)	4.6(2)
C(5)	2116(4)	7301(8)	1300(8)	4.0(2)
C(6)	808(4)	7662(10)	12621(3)	4.3(2)
C(7)	519(4)	8569(9)	11661(3)	4.2(2)
C(8)	1109(3)	7622(8)	11047(3)	3.5(2)
C(9)	1994(3)	6365(7)	11358(3)	3.3(2)
C(10)	2477(4)	5780(8)	12398(3)	3.5(2)
C(11)	2556(4)	5496(7)	10686(3)	3.9(2)
C(12)	3389(3)	6860(12)	10418(3)	4.2(2)
C(13)	2919(4)	8134(10)	9559(4)	4.3(2)
Se(13)	1695(0)	10003(2)	9656(0)	5.5(0)
C(14)	2402(4)	6914(10)	8665(3)	4.2(2)
O(14)	3303(3)	5711(8)	8538(2)	5.3(2)
C(15)	1949(5)	7979(14)	7737(4)	5.9(3)
O(15)	2151(4)	6545(11)	7095(3)	7.0(3)
C(16)	3885(5)	9472(11)	9476(5)	5.8(3)
C(17)	671(4)	8164(9)	10030(3)	3.9(2)
C(18)	2356(6)	8724(12)	14612(4)	6.3(3)
C(19)	2189(5)	5223(12)	14456(3)	4.9(2)
O(19_1)	1037(3)	5232(10)	14239(3)	6.3(2)
O(19_2)	2774(4)	3958(9)	14930(3)	6.5(2)
C(20)	2055(5)	3701(9)	12496(4)	5.3(2)
C(21)	507(7)	3604(17)	14581(6)	7.9(4)
C(22)	3103(5)	5470(9)	7560(4)	4.8(3)
C(23)	4177(7)	6097(19)	7338(6)	8.0(5)
C(24)	2861(8)	3326(18)	7325(5)	8.1(4)

us to know the definitive structure of this derivative as methyl 15-acetoxy-14*R*-hydroxy-13*S* ,17-episeleno-labd-8-en-19-oate acetonide . In consequence the other stereoisomer **8c** has to be the methyl 15-acetoxy-14*S*-hydroxy-13*R*,17-episeleno-labd-8-en-19-oate acetonide. Taking into account the mechanistic considerations that are discussed below, the most favoured conformation of these compounds and the spectroscopic characteristics of compounds **5-8**, it was possible to assign the absolute stereochemistries depicted for all of these compounds.

In our previous work, we proposed two consecutive electrophilic attacks to double bonds in 1,6-diolefins as a feasible mechanism to explain the formation of cyclic selenides. Selenium (IV) species (as SeO_2 or $SeO(OMe)_2$) or a reduced selenium species, generated from the allylic oxidation, would be responsible for those electrophilic reactions. The structure and fate of intermediates initially produced, would be strongly dependent on the structure of the substrates, as it was observed for linalool and linalyl acetate. From the former, oxa-selena-bicyclic compounds are produced as main reaction products, and from the latter, selenepanes are isolated in a 15% yield besides the expected allylic oxidation products.

The Selenium containing products obtained in the reaction of SeO_2 and 15-*O*-acetylisocupressate (**1**), are comparable with those obtained in the reaction of linalyl acetate, and the mechanisms would be related. A proposal explaining the formation of **5-8** compounds is depicted in Scheme 1. Two common intermediates **I** and **II**, derived from an initial attack to the Δ^{13} double bond by selenium species present in the reaction mixture, are formed depending on the facial approach.

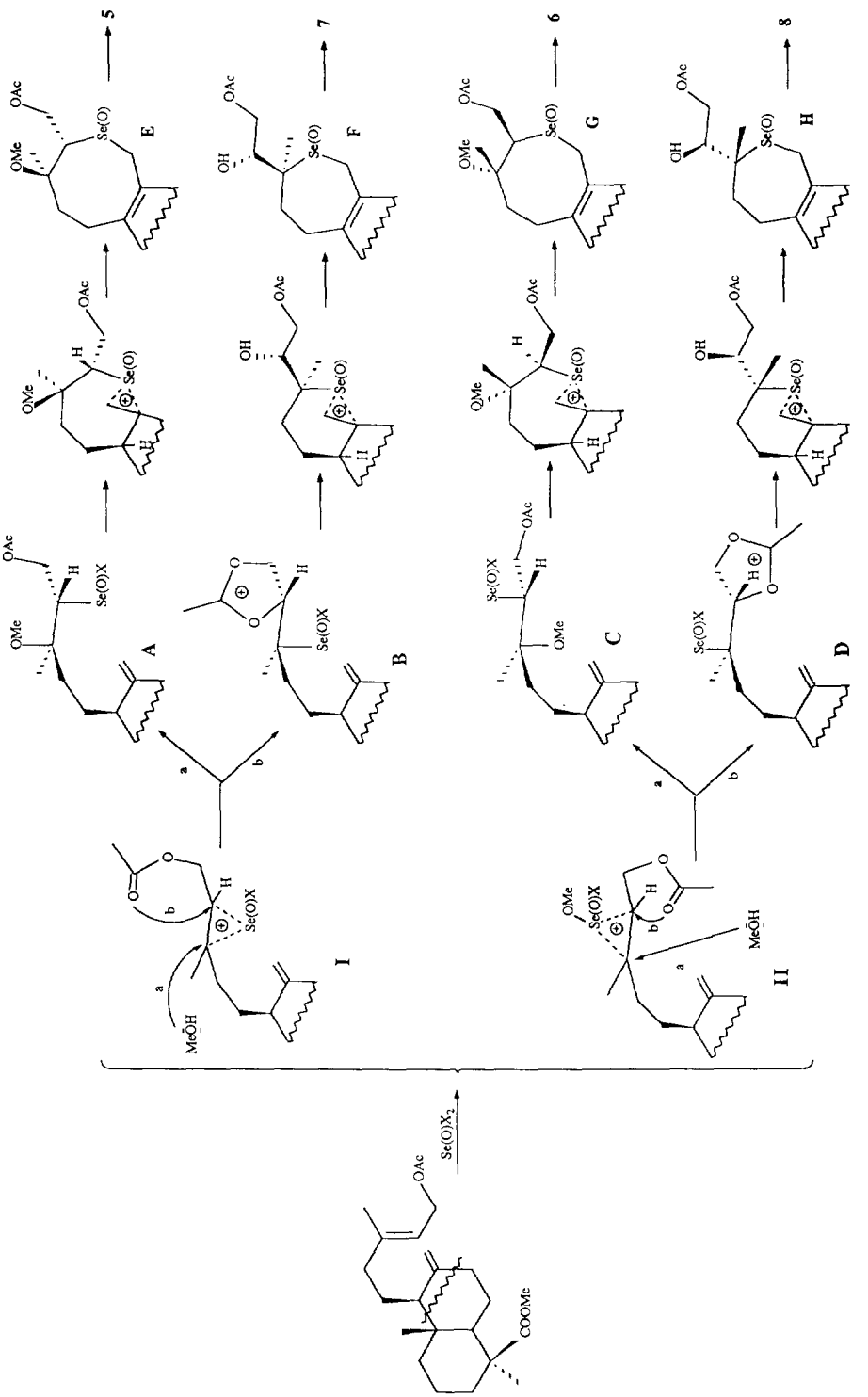
The episelenonio intermediates could be opened by a nucleophile in two different ways: a) external opening by one molecule of solvent, to give the methoxy selenointermediates **A** or **C**, and b) internal opening by the acetate group, to produce **B** or **D**. The second electrophilic attack takes place in an intramolecular fashion, to generate selenocine derivatives **E** or **G** and selenepine derivatives **F** or **H** as a function of the carbon atom attached to Selenium in each intermediate. Finally, if the actual electrophile is a Se (IV) species as SeO_2, reduction of the intermediate selenoxides in the reaction medium would produce compounds **5-8**. The electrophilic character of SeO_2 is responsible of some reactions with olefins and carbonyls[12], and in some instances has also been used to explain the allylic oxidation of olefins. In addition, selenoxides have been observed as products of the reaction of SeO_2 with olefins[13-15]. Furthermore, reduction of selenoxides to selenides by oxygen interchange with Se(II) species has also been described[16-18]. By a parallel mechanism Se(II) species can also produce compounds **5-8**, but in this case the final reduction of selenoxides to selenides is not necessary. Se(II) is produced in the sigmatropic rearrangement during the allylic oxidation, and thus it is possible to propose Se(II) as responsible for the formation of cyclic selenides in this reaction.

This mechanistic proposal also accounts for the stereochemistry of each derivative. The opening of episelenenio intermediates must be produced with "anti" geometry between selenium and the oxygenated nucleophile. Accordingly, only the intermediates **A-D** could be produced from the episelenonio intermediates **I** and **II**.

These reactions open a route to seven and eight members cyclic selenides from diolefins through a double electrophilic attack to the double bonds. The use of different substrates: hydroxylated, oxygenated (esters, ethers,..) and non oxygenated, produce different results. The study of the effect of selenium reagents on the reaction products is now in progress in order to improve the utility of this type of reactions.

EXPERIMENTAL PART

To a stirred solution of 3.0 g of 15-O-acetylisocupressate **1** in MeOH (30 ml), 1.33 g of SeO_2 in MeOH (40 ml) was added at 45°C. The reaction was refluxed for 7 h. The selenium was eliminated by filtration, the



Scheme 1. Mechanistic proposal for the formation of organoselenium compounds from methyl 15-*O*-isocupressate (**I**). $Se(O)X_2$= SeO_2, $SeO(OMe)_2$, $SeO(OH)OMe$ if Se(IV) is the reactive specie, or SeX_2 = $Se(OH)_2$, $Se(OMe)_2$, $Se(OH)OMe$ if Se(II) is the actual electrophile.

TABLE II. ^{1}H NMR Spectral data for 1-4 (200 MHz, $CDCl_3$, δ values in ppm, *J* values in Hz, TMS int. std.)

H	1	2	2a	3	3a	3b	4	4a	4b
7		4.38t (2.9)	5.40t (3.1)	4.37t (2.9)	5.43t (3.0)	5.40t (2.9)	4.34t (2.9)	5.40t (2.7)	5.39t (3.0)
12				4.05d (8.0)	5.15d (8.0)	4.01d (8.2)	4.11dd (7.0;14.4)	5.19dd (6.7;12.3)	4.07dd (4.3;10.2)
14	5.30ta (7.1)	5.30ta (7.2)	5.28ta (7.1)	5.54ta (6.9)	5.55ta (6.6)	5.55ta (6.8)	5.40ta (7.0)	5.46ta (6.6)	5.36ta (7.3)
15	4.57d (7.1)	4.57d (7.2)	4.58d (7.1)	4.62d (6.9)	4.59d (6.6)	4.61d (6.8)	4.61d (5.7)	4.64d (6.6)	4.64d (6.5)
16	1.69s	1.69s	1.69s	1.72s	1.70s	1.71s	1.68s	1.70s	1.69s
17	4.51sa 4.85sa	4.63sa 5.06sa	4.76sa 5.21sa	4.59sa 5.08sa	4.73sa 5.24sa	4.73sa 5.23sa	4.75sa 5.06sa	5.13sa 5.26sa	4.92sa 5.24sa
18	1.18s	1.18s	1.14s	1.19s	1.15s	1.15s	1.17s	1.14s	1.14s
20	0.51s	0.49s	0.54s	0.48s	0.50s	0.50s	0.49s	0.51s	0.51s
19-OMe	3.61s	3.62s	3.62s	3.62s	3.62s	3.62s	3.61s	3.62s	3.61s
7-OAc			2.06s		2.06s	2.06s		2.06s	2.05s
12-OAc					2.04s			2.02s	
15-OAc	2.04s	2.05s	2.05s	2.06s	2.05s	2.05s	2.04s	2.05s	2.04s

TABLE III. ^{13}C NMR Spectral data for 1-4 (50.3 MHz, $CDCl_3$, δ values in ppm, TMS int. std.)

C	1	2	2a	3	3a	3b	4	4a	4b
1	39.2	38.7	38.9	39.7	38.9	38.9	38.8	38.8	38.9
2	20.0	20.0	20.0	19.9	19.9	20.0	19.9	19.8	20.1
3	38.8	38.2	38.2	39.2	38.0	38.2	38.0	37.9	38.2
4	44.3	44.0	43.9	44.0	43.7	44.1	43.9	43.7	44.0
5	55.5	48.6	49.7	48.9	49.7	49.8	48.4	49.5	49.8
6	26.3	32.5	30.5	32.9	30.4	30.7	32.3	30.2	30.6
7	38.7	73.9	76.2	73.6	75.9	76.4	73.5	76.5	76.5
8	148.0	149.4	144.6	149.1	144.5	145.4	149.8	143.6	144.9
9	58.5	48.9	50.0	45.4	46.6	46.6	45.9	46.8	47.1
10	40.2	40.3	39.9	40.0	39.6	39.8	40.0	39.5	39.8
11	21.9	21.1	21.2	29.9	27.7	29.7	28.1	26.0	28.3
12	38.3	37.9	37.7	73.8	75.5	74.3	76.1	78.0	76.4
13	142.6	142.3	142.2	144.1	139.6	144.3	142.1	137.7	142.3
14	118.3	118.6	118.8	118.4	120.7	118.9	121.2	123.5	121.9
15	61.3	61.3	61.3	61.1	60.6	61.0	61.0	60.5	61.0
16	16.4	16.3	16.4	12.5	12.7	12.4	11.7	11.8	12.0
17	106.3	109.1	111.9	109.3	111.6	112.0	109.1	113.0	112.3
18	28.8	28.5	28.5	28.5	28.4	28.6	28.4	28.4	28.6
19	176.5	177.7	177.4	177.7	177.2	177.5	177.7	177.1	177.4
20	12.6	11.7	11.8	11.8	11.8	12.1	10.5	11.6	10.8
19-OMe	50.9	51.0	51.1	51.1	51.1	51.2	51.0	51.0	51.3
15-OAc	20.9	20.9	21.2	20.9	21.2	21.5	20.8	21.1	21.3
15-OAc	170.6	171.0	170.6	171.0	170.7	170.9	171.1	171.3	170.7
7-OAc			20.9		21.0	20.9		21.0	20.9
7-OAc			170.0		169.8	170.2		169.8	170.1
12-OAc					20.8			20.7	
12-OAc					169.7			169.5	

TABLE IV. ^{1}H NMR Spectral data for 5-8 (200 MHz, $CDCl_3$, δ values in ppm, *J* values in Hz, TMS int. std.)

H	5	5a	6	6a	7	7a	7b	7c	8	8b	8c
14	3.27t (5.3)	3.37dd (9.0;6.4)	3.34dd (6.1;4.8)	3.41dd (7.8;7.5)	4.10da (9.1)	5.67dd (2.1;8.8)	4.09dd (5.8;4.3)	4.53t (6.6)	3.95da (8.8)	3.98da (10.4)	4.32t (6.6)
15	4.35m	3.87dd (10.8;9.0) 3.76dd (10.8;6.4)	4.33dd (11.5;6.1) 4.41dd (11.5;4.8)	3.86 m	4.19dd (9.9;9.1) 4.70d (9.9)	4.19dd (8.8;11.7) 5.00dd (2.1;11.7)	3.94dd (8.2;3.1) 3.66dd (8.2;10.7)	3.98dd (6.4;8.8) 4.10dd (6.8;8.8)	4.19dd (8.8;11.4) 4.58dd (2.1;11.4)	3.77da (10.4) 3.66da (10.4)	3.97dd (6.8;8.6) 4.04dd (6.8;8.6)
16	1.14s	1.20s	1.07s	1.14s	1.33s	1.29s	1.34s	1.32s	1.46s	1.47s	1.44s
17	3.06d (12.0) 3.43d (12.0)	3.10d (12.5) 3.45d (12.5)	3.18d (12.6) 3.34d (12.6)	3.14d (12.6) 3.41d (12.6)	2.75d (14.0) 3.52d (14.0)	2.56d (14.2) 3.81d (14.2)	2.81d (13.9) 3.46d (13.9)	2.75d (13.8) 3.47d (13.8)	3.07d (13.7) 3.20d (13.7)	3.00d (13.7) 3.28d (13.7)	3.02d (13.6) 3.21d (13.6)
18	1.21s	1.21s	1.21s	1.21s	1.21s	1.20s	1.21s	1.21s	1.21s	1.21s	1.21s
20	0.86s	0.87s	0.82s	0.82s	0.74s	0.71s	0.75s	0.74s	0.75s	0.75s	0.75s
13-OMe	3.20s	3.24s	3.20s	3.23s							
19-OMe	3.64s	3.64s	3.63s	3.63s	3.63s	3.63s	3.63s	3.62s	3.63s	3.63s	3.62
14-OAc						2.03s					
15-OAc	2.05s		2.06s		2.10s	2.09s			2.11s		
Me								1.35s			1.35s
Me								1.42s			1.42s

TABLE V. ^{13}C NMR Spectral data for 5-8 (50.3 MHz, $CDCl_3$, δ values in ppm, *J* values in Hz, TMS int. std.)

C	5	5a	6	6a	7	7a	7b	7c	8	8b	8c
1	36.9	36.9	37.7	37.6	36.3	36.3	36.3	36.4	36.5	36.5	36.5
2	19.5	19.5	19.7	19.6	19.5	19.5	19.5	19.6	19.6	19.6	19.5
3	37.8	37.7	38.0	38.8	37.7	37.7	37.7	37.8	37.8	37.8	37.8
4	43.8	44.0	44.0	43.9	44.0	44.0	43.9	44.0	44.1	44.0	44.0
5	53.5	53.4	53.5	54.3	53.3	53.2	53.2	53.3	53.3	53.2	53.3
6	20.7	20.8	20.2	21.1	20.9	20.8	20.9	20.9	20.9	21.0	21.0
7	32.8	33.0	33.5	33.8	33.1	33.1	33.0	33.0	33.0	33.0	32.9
8	128.8	127.1	128.4	128.6	133.5	133.9	133.4	133.8	133.9	134.1	134.0
9	144.7	145.5	147.7	145.8	144.0	143.6	144.0	143.7	144.2	144.3	143.8
10	40.4	40.3	40.1	40.2	39.6	39.4	39.6	39.7	39.7	39.7	39.9
11	22.8	22.6	20.9	22.6	21.3	21.5	21.2	21.1	21.2	21.3	21.1
12	29.5	30.0	30.5	30.7	23.4	23.4	23.4	22.6	23.3	23.3	22.6
13	82.0	84.1	82.0	83.6	46.5	44.0	48.9	44.7	47.3	48.0	45.5
14	48.3	49.9	50.6	51.5	74.3	73.7	76.4	79.6	75.6	77.7	80.9
15	63.8	62.6	64.4	63.0	67.0	64.5	63.4	66.3	66.8	63.1	66.0
16	20.6	20.0	21.0	20.2	24.0	24.4	24.3	23.0	24.2	24.4	23.0
17	34.8	35.7	36.2	36.1	35.9	36.2	35.9	36.4	35.6	35.6	36.4
18	28.3	28.4	28.5	28.4	28.3	28.3	28.4	28.4	28.4	28.4	28.4
19	177.6	177.8	178.0	177.8	178.0	177.9	178.1	177.9	178.0	178.0	178.0
20	17.4	17.6	18.3	18.3	17.1	17.2	17.1	17.2	17.2	17.2	17.1
19-OMe	50.9	51.1	51.0	51.6	51.1	51.1	51.2	51.0	51.1	51.1	51.0
15-OAc	20.8		21.1		21.0	21.0			21.0		
15-OAc	170.6		170.8		170.5	170.7			171.4		
13-OMe	50.0	49.9	50.3	50.2		20.8		109.7			109.5
						170.1		26.3			26.3
								25.1			25.1

solvent was evaporated and the residue was solved in ether and washed with $NaHCO_3$. After several chromatographic separations (hexane-EtOAc mixtures) of the reaction product (3.4 g) the following compounds were isolated: Acetylisocupressate (40 mg), complex mixture of Se products (76 mg), **5** (230 mg), **6** (90 mg), **7** (240 mg), **2** (600 mg), **8** (220 mg), **4** (645 mg), **3** (550 mg).

By similar procedure 380 mg of starting material **2** were refluxed with SeO_2 (730 mg) in MeOH for 16 h. By chromatography of the reaction product: **2** (114 mg), a complex mixture of Se products (40 mg), **3b** (85 mg) and **4b** (76 mg), were isolated.

(7R) Methyl 15-O-acetyl-7-hydroxyisocupressate (2) IR (film) cm^{-1}: 3480, 2930, 1720, 1650, 1230, 1150, 1090, 900, 820. ^1H NMR: Table II, ^{13}C NMR: Table III. Acetylation product **2a**. IR (film) cm^{-1}: 2940, 1720, 140, 1375, 1250, 1160. 1025, 920. ^1H NMR: Table II, ^{13}C NMR: Table III.

(7R,12R) Methyl 15-O-acetyl-7,12-dihydroxyisocupressate (3) IR (film) cm^{-1}: 3380, 2920, 1720, 1650, 1380, 1230, 1150, 1040, 900. ^1H NMR: Table II, ^{13}C NMR: Table III. Acetylation product **3a**. IR (film) cm^{-1}: 2940, 1720, 1650, 1470, 1370, 1245, 1155, 1090,1020, 990, 920. ^1H NMR: Table II, ^{13}C NMR: Table III.

(7R,12R) Methyl 15-O-acetyl-7-acetoxy-12-hydroxyisocupressate (3b) IR (film) cm^{-1}: 3600, 2950, 1725, 1650, 1440, 1380, 1250, 1160, 1095, 980, 920. ^1H NMR: Table II, ^{13}C NMR: Table III. By acetylation **3a** was obtained. ^1H NMR: Table I, ^{13}C NMR: Table II.

(7R, 12S) Methyl 15-O-acetyl-7,12-dihydroxyisocupressate (4) IR (film) cm^{-1}:3400, 2925, 1720, 1640, 1370, 1230, 1150, 1040, 900. ^1H NMR: Table II, ^{13}C NMR: Table III. Acetylation product **4a**. IR (film) cm^{-1}: 2940, 1720, 1650, 1370, 1240, 1155, 1090, 990, 920. ^1H NMR: Table II, ^{13}C NMR: Table III.

(7R, 12S) Methyl 15-O-acetyl-7-acetoxy-12-hydroxyisocupressate (4b) IR (film) cm^{-1}: 3600, 2950, 1730, 1650, 1470, 1380, 1340, 1240, 1160, 1100, 925. ^1H NMR: Table II, ^{13}C NMR: Table III.

(13R,14S) Methyl 15-acetoxy-13-methoxy-14,17-episeleno-labd-8-en-19-oate (5) IR (film) cm^{-1}: 2980, 1720, 1480, 1380, 1240, 1165, 1140, 1100, 910. ^1H NMR: Table IV, ^{13}C NMR: Table V. Anal. Calcd. for $C_{24}H_{38}O_5Se$: C, 59.37; H, 7.89; O, 16.48; Se, 16.26. Found: C, 58.94; H, 7.69. By KOH/MeOH saponification 80 mg of **5** afforded 67 mg of **5a**. IR (film) cm^{-1}: 3420, 2940, 1720, 1640, 1470, 1370, 1220, 1160, 1140, 1120. ^1H NMR: Table IV, ^{13}C NMR: Table V.Anal. ($C_{22}H_{22}O_7$) C: calc, 66.32; found, 66.25; H: calc, 5.57; found 5.56.

(13S,14R) Methyl 15-acetoxy-13-methoxy-14,17-episeleno-labd-8-en-19-oate (6) IR (film) cm^{-1}: 2940, 1725, 1250, 1140, 1100, 910. ^1H NMR: Table IV, ^{13}C NMR: Table V. Anal. Calcd. for $C_{24}H_{38}O_5Se$: C, 59.37; H, 7.89; O, 16.48; Se, 16.26. Found: C, 59.00; H, 7.74. By KOH/MeOH saponification 56 mg of **6** afforded 50 mg of **6a**. IR (film) cm^{-1}: 3420, 2940, 1725, 1645, 1475, 1375, 1230, 1160, 1140, 1120. ^1H NMR: Table IV, ^{13}C NMR: Table V.

(13S,14R) Methyl 15-acetoxy-14-hydroxy-13,17-episeleno-labd-8-en-19-oate (7) IR (film) cm^{-1}: 3420, 1720, 1660, 1470, 1380, 1330, 1160, 1090, 1020, 890. ^1H NMR: Table IV, ^{13}C NMR: Table V. Anal. Calcd. for $C_{23}H_{36}O_5Se$: C, 58.59; H, 7.70; O, 16.97; Se, 16.75. Found: C, 58.52; H, 7.70. By acetylation of 87 mg of **7**, 82 mg of acetylated product **7a** were obtained. IR (film) cm^{-1}: 1730, 1650, 1440, 1380, 1330, 1240, 1160,

1020, 990, 965, 870. ^{1}H NMR: Table IV, ^{13}C NMR: Table V. From 35 mg of **7**, 25 mg of saponification product **7b** were obtained. IR (film) cm^{-1}: 3480, 2950, 1720, 1650, 1380, 1330, 1160, 1090, 1030, 990, 965, 920, 870. ^{1}H NMR: Table IV, ^{13}C NMR: Table V. By treatment of 16 mg of the saponification product **7b** with 2,2-dimethoxypropane and catalytic TMSCl in acetone, 18 mg of acetonide **7c** were produced; IR (film) cm^{-1}: 2950, 1720, 1440, 1380, 1240, 1160,1140, 990, 910. 860. ^{1}H NMR: Table IV, ^{13}C NMR: Table V.

X-Ray Analysis of compound 7c. Single crystals of the title compound were grown from ether solution. Compound **7c** crystallized as colorless blocks in the monoclinic space group $P2_1$. Accurate lattice parameters were determined by least squares refinement of 25 reflections measured on a CAD-4 Enraf-Nonius automatic diffractometer.

Intensities for 2100 unique reflections ($\theta<65^\circ$) were measured at room temperature by a $\omega\theta$ scan procedure. No deviations in the intensity of checked reflections were observed during the data collection. Correction for Lorentz and polarization effects were made; absorption was ignored.

Physical and crystal Data of compound 7c

Chemical Formula	$C_{24}H_{38}O_4Se$	Density(Calculated)	1.294 g.cm^{-3}
Formula Weight	468.5	Z	2
Crystal dimensions	0.2x0.2x0.1 mm^3	X-radiation used for data	λ(CuKα) 1.54178Å
Symmetry	Monoclinic		
Space Group	$P2_1$	*Collection*	
Unit Cell dimensions	a=12.173(1)Å	Total number of reflections with $\theta<65^\circ$	2103
	b=6.915(1)Å	Number of reflections with I≥3σ(I)	1873
	c=15.051(2)Å	Linear absorcion coefficient, m	2.57 mm^{-1}
	β=108.38(2)°	Disagreement index, R	0.039
	V=1202.3(3)Å^3		

Determination of the structure of compound 7c

The structure was solved using direct methods and Fourier techniques[19]. Following the refinement of all positional and anisotropic thermal parameters of non hydrogen atoms(R=0.054) a difference Fourier map was calculated from which it was possible locate all the hydrogen atoms; then the positions and isotropic thermal parameters of these atoms were refined. Refinement of 414 parameter based on 1873 reflections having I≥3σ(I) led to a final disagreement index R=0.039.

The scattering factor tables for non-hydrogen atoms and the anomalous dispersion corrections for Se were taken from the International Tables for X-ray Crystallography[20] whereas the scattering factors for hydrogens were taken from ref. 21. This study establishes the 13*S*14*R* configuration for compound **7c**.

A perspective view of the molecule is depicted in Figure 1. Fractional coordinates for non-hydrogen atoms (x10^4) and equivalent isotropic parameters with the estimated standard derivations in parentheses are given in Table 1. The crystalline cohesion is ensured by van der Waals contacts.

(13R,14S) Methyl 15-acetoxy-14-hydroxy-13,17-episeleno-labd-8-en-19-oate (8) IR (film) cm^{-1}: 3620, 296, 3460, 2960, 1740, 1380, 1330, 1250, 1160, 1140, 1050, 980, 920. ^{1}H NMR: Table IV, ^{13}C NMR: Table V. Anal. Calcd. for $C_{23}H_{36}O_5Se$: C, 58.59; H, 7.70; O, 16.97; Se, 16.75. Found: C, 58.58; H, 7.65. From 54 mg of **8**, 41 mg of saponification product **8b** were obtained; IR (film) cm^{-1}: 3600, 2950, 1720, 1380, 1330, 1160, 1140, 1090, 1020, 990, 920, 870. ^{1}H NMR: Table IV, ^{13}C NMR: Table V. By treatment of 15.9 mg of saponification product with 2,2-dimethoxypropane and catalytic TMSCl in acetone, 13.6 mg of acetonide **8c**

were produced, IR (film) cm^{-1}: 2950,1720, 1660, 1470, 1380, 1240, 1160, 1100,990, 920, 860. ^1H NMR: Table IV, ^{13}C NMR: Table V.

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