Photochemical Transformations of Some Neoclerodane and Labdane Diterpene Ketones

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Some neoclerodane (**2–4**) and labdane (**5** and **6**) diterpene ketones having a β- or γ-hydroxy function, an α-epoxy group, or an α-olefinic double bond have been irradiated at λ = 313 nm in dry solvents (benzene or methanol). Fruticolone (**2**) yielded the naturally occurring 5,6-*seco*-neoclerodan-6,1α-olide derivative fruticolide (**1**), while hispanolone (**5**) gave the δ-lactone **8**, both transformations involving a Norrish type I photoreaction. The α,β-unsaturated ketone derivative **4** was transformed into **7** by a stereoselective intramolecular [2+2] cycloaddition reaction involving its furanic 13(16)-double bond. Finally, the α-epoxy ketone **6** was rearranged to the 10(9→8)*abeo*-labda-7,9-dione derivative **10**. Apart from the interest in these reactions for synthetic purposes, the photochemical transformation of fruticolone (**2**) into fruticolide (**1**) suggests that the latter might originate from the former as an artefact during the extraction and isolation procedure, rather than from any biogenetic pathway.

Introduction

In recent years, many plants belonging to the genus *Teucrium* (family Labiatae) have been investigated and a great number of neoclerodane[1] diterpenoids have been isolated from them.[2] Interest in these compounds has been stimulated by their challenging structures, their biological activities, particularly as insect antifeedants against some economically important plant pests,[3] and, more recently, by their hepatotoxicity.[4]

In continuation of our studies on neoclerodanes from *Teucrium*,[5] we have been concerned with the very unusual structure of fruticolide (**1**), a minor constituent of the aerial parts of *T. fruticans*.[6] This diterpene possesses a 5,6-*seco*-neoclerodan-6,1α-olide structural feature, which has not previously been found in the neoclerodanes isolated to date.[2] On comparison of the structure of fruticolide (**1**) with those of the other neoclerodanes isolated from the same plant,[7] it occurred to us that **1** might arise from a photochemical transformation of fruticolone (**2**)[7a] rather than from a biogenetic pathway. We report here the photochemical transformation of fruticolone (**2**) into fruticolide (**1**) and the structure of an interesting photoproduct derived from the neoclerodane 7,8-didehydrofruticolone (**4**),[7b] as well as the results obtained in phototransformations of the labdane diterpene hispanolone (**5**)[8] and its 8α,9α-epoxy derivative **6**.[9]

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Results and Discussion

Solutions of compounds **2**−**6** in benzene or methanol were irradiated at λ = 313 nm under the conditions described in the Experimental Section. After standard workup, the products of the photoreactions were isolated and their structures were established by spectroscopic means.

Photolysis of fruticolone (**2**)[7a] gave a compound identical in all respects (melting point, $[\alpha]_D$, IR, ^{1}H- and ^{13}C-NMR, and mass spectra) to fruticolide (**1**).[6] This identity was also supported by comparison with an authentic sample. The formation of **1** starting from **2** can only be explained in terms of a Norrish type I reaction,[10] generating a ketene intermediate that gives fruticolide (**1**) by intramolecular nucleophilic attack of the C-1α hydroxy group on the C-6 carbon atom. In the photolysis of **2**, the hydrogen transfer step to form the ketene intermediate takes place stereoselectively, as demonstrated by the retention of the stereochemistry at the C-5 stereogenic centre. This behaviour may be attributed to the conformational rigidity of the biradical intermediate.[11]

Photoreaction of 8β-hydroxyfruticolone (**3**)[7b] yielded a very complex mixture of compounds, which were not investigated further. We supposed that **3** could be subjected to both a photolysis and a spontaneous thermal dehydration process to form the α,β-unsaturated ketone derivative **4**, which itself undergoes a photochemical reaction. In fact, it is known that **3** is easily transformed into **4** when a chloroform solution of the former is left to stand at room temperature for 3 days.[7b] The same transformation was achieved by stirring a chloroform solution of **3** in the dark, thus explaining the aforementioned complex outcome of the photoreaction of this compound. In the Experimental Section, we include some physical (m.p., $[\alpha]_D$) and spectroscopic (UV) data of **4** that has not previously been report-

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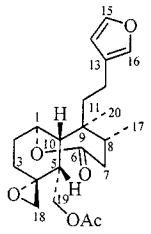

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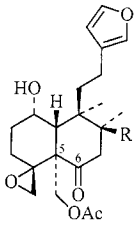

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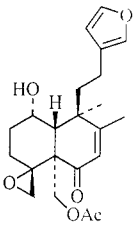
3 R=OH



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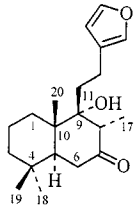

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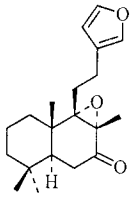

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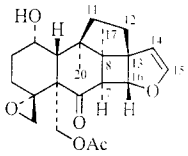

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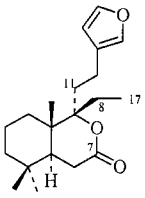

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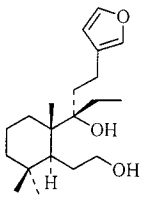

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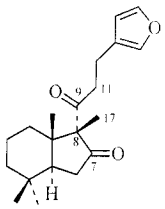

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ed,[7b] as well as the complete assignment of its ^{1}H-NMR spectrum (see Table 1). Furthermore, we give some corrections to the carbon atom assignments published elsewhere[7b] (see Table 2).

Irradiation of compound **4** yielded a substance which was assigned the structure **7** on the basis of the following results. Elemental analysis and low-resolution mass spectrometry indicated a molecular formula of $C_{22}H_{28}O_6$, identical to that of the starting material **4**, while its ^{1}H- and ^{13}C-NMR spectra (Tables 1 and 2, respectively) were in agreement with the presence of a cyclobutane moiety [δ_H = 2.85 (d, J = 3.2 Hz, 1 H, 7α-H) and 4.54 (d, J = 3.2 Hz, 1 H, 16β-H); δ_C = 57.7 (d, C-7), 58.1 (s, C-8), 64.1 (s, C-13), and 85.0 (d, C-16)] instead of the C-7, C-8 olefinic and C-13, C-16 furanic double bonds of **4** [δ_H = 5.88 (q, $J_{7,17}$ = 1.2 Hz, 1 H, 7-H) and 7.18 (ddd, $J_{16,12A}$ = 1.2 Hz, $J_{16,14}$ = 1.0 Hz, $J_{16,15}$ = 1.7 Hz, 1 H, 16-H); δ_C = 128.6 (d, C-7), 163.4 (s, C-8), 124.2 (s, C-13), and 138.5 (d, C-16)]. The ^{1}H-^{1}H COSY spectrum of **7** confirmed the vicinal relationship between the 7α-H and 16β-H protons, while the HMBC spectrum showed connectivities between C-16 [δ = 85.0 (d)] and the 7α-H, 14-H, and 15-H [δ = 2.85 (d), 4.79 (d), and 6.43 (d), respectively], and between C-8 [δ = 58.1 (s)] and 16β-H [δ = 4.54 (d)], among others.

The relative stereochemistry of all the asymmetric centres of **7** was in complete agreement with the results of NOE experiments. In particular, the α-configuration of the C-7 proton was strongly supported by the NOE enhancements observed for the 17-Me [δ = 1.35 (s), 2%] and 19-H_A [δ = 4.63 (d), 3%] protons when the signal of the C-7 proton [δ = 2.85 (d)] was irradiated. Moreover, irradiation at δ = 1.35 (17-Me) caused NOE enhancement in the signals of 7-H, 14-H [δ = 4.79 (d)], 19-H_A, and 20-Me [δ = 1.16 (s)], thus confirming that all these hydrogen atoms possess an α-configuration. Consequently, considering the well-known mechanism of photochemical [2+2] cycloaddition reactions,[10] the hydrogen atom at the C-16 position must be in a β-configuration. This was further supported by the small coupling constant (J = 3.2 Hz) observed between 7α-H and 16β-H.[12] Thus, compound **7** is derived from **4** through a totally selective intramolecular [2+2] cycloaddition, where the α-face of the furan ring can approach only the β-face of the enone system so as to give the *trans*-substituted cyclobutane. Some examples of identical reactions in mono- and sesquiterpenoids possessing an enone function and an olefinic double bond have been reported in the literature.[13]

The above results on the photoreactions of compounds **2**–**4** encouraged us to investigate the behaviour of other available labdane diterpenes, in which the presence of carbonyl groups confers photochemical reactivity. Photolysis of hispanolone (**5**), the major diterpene constituent of *Ballota hispanica*,[8] gave the δ-lactone derivative **8**, the structure of which was supported by its ^{1}H- and ^{13}C-NMR spectra (Tables 1 and 2) and other data (see Experimental Section), as well as by data relating to its lithium aluminium hydride reduction product **9** (Tables 1 and 2, and Experimental Section). In particular, the C-7 and C-9 carbon atom resonances of **8** at δ = 172.3 (s) and 91.2 (s), respectively, and the presence of an ethyl substituent attached at C-9 [δ_H = 1.74 and 1.86 (2 dq, J_{gem} = 14.9 Hz, $J_{8,17}$ = 7.3 Hz for the former, 7.6 Hz for the latter, 1 H each, methylene C-8), and 1.02 (br. t, J = 7.4 Hz, 3 H, 17-Me); long-range ^{1}H-^{13}C correlation between C-9 and the 8-H_A, 8-H_B, and 17-Me protons in the HMBC spectrum] clearly established that the photolysis product of **5** had the structure **8**. Also in this case, a Norrish type I rearrangement of the carbonyl group of **5** led to the δ-lactone **8** through a ketene intermediate. To the best of our knowledge, this is one of the few examples of the photochemical transformation of β-hydroxy ketones into δ-lactones.[11b]

Finally, irradiation of the α-epoxy ketone **6**[9] gave the 10(9→8)*abeo*-labda-7,9-dione derivative **10** in poor yield (20%), together with unchanged material (**6**) and a complex mixture of side-products. The structure of **10** was supported by its spectroscopic data (Tables 1 and 2, and Experimental Section). The presence in **10** of an (8*R*) stereogenic centre and a five-membered ring B was established from NOE experiments {enhancement of the signal of the 20-Me protons [δ = 0.85 (d), $J_{20,1\alpha}$ = 0.7 Hz, 4%] when the 17-Me protons [δ = 1.14 (s)] were irradiated}, and from the HMBC spectrum, which showed, among others, connectivities of both C-8 [δ = 71.7 (s)] and C-10 [δ = 46.9 (s)] with the 17-Me and 20-Me protons, as well as between C-7 [δ = 218.3 (s)] and 5α-H [δ = 1.92 (dd)], 6α-H [δ = 2.32 (dd)], 6β-H [δ = 1.98 (dd)], and 17-Me. The transformation of **6** into **10** occurs through a well-known stereospecific

photorearrangement, which has been exhaustively studied with several triterpene and steroid derivatives.[14]

In summary, we have shown that three naturally occurring diterpenoids (**2**, **3**, and **5**) and two semi-synthetic products (**4** and **6**), possessing carbonyl groups along with other functionalities, can be photochemically transformed into substances with interesting modified hydrocarbon skeletons. The products are potentially useful for synthetic purposes. Moreover, one of these products, fruticolide (**1**), which has previously been found as a minor constituent of the aerial parts of *Teucrium fruticans*,[6] has now been obtained by photolysis of fruticolone (**2**), a major constituent of the same plant.[7a] This result leaves open the question as to whether this photochemical structural modification has been designed by Nature in order to fulfil some biological role, or whether it is formed by an adventitious process that occurs during the extraction and/or isolation procedure.

Experimental Section

General: Melting points: Kofler block apparatus, uncorrected values. − Optical rotations: Perkin−Elmer 241 MC polarimeter. − IR spectra: Perkin−Elmer 681 spectrophotometer. − ^{1}H- and ^{13}C-NMR spectra: In $CDCl_3$ solution using a Varian Unity 500 instrument at 500 MHz (^{1}H) or 125.7 MHz (^{13}C); ^{13}C-NMR assignments were made with the aid of HMQC and HMBC spectra. − MS: Positive EI mode with a Hewlett-Packard HP 5989A instrument; no fragments below *m/z* = 50 are recorded. − Elemental analyses: Carlo Erba EA 1108 apparatus. − Merck silica gel no. 7734 (70−230 mesh) deactivated with 15% H_2O (w/v) was used for column chromatography. − Starting materials (**2**−**6**) were available from previous work.[7−9]

General Procedure for Irradiation of Compounds 2−6: A solution of the compound in anhydrous benzene or anhydrous methanol (ANYDROSCAN®, Delchimica) in a Pyrex tube was purged with N_2 for 15 min. It was then irradiated in a Rayonet RPR-100 photoreactor fitted with 16 Hg lamps irradiating at λ = 313 nm and a merry-go-round apparatus. The progress of the reaction was monitored by TLC. Reaction was stopped when the reactant spot was no longer visible or when it became apparent that the reaction product was decomposing more rapidly than it was being formed. At the end of the reaction, the solvent was removed in vacuo and the residue was chromatographed on silica gel with the solvents indicated in each case.

Fruticolide (1) from Fruticolone (2): A solution of **2** (100 mg, 0.256 mmol) in dry benzene (50 mL) was irradiated for 2 h. The

Table 1. ^{1}H-NMR spectral data of compounds **4** and **7**−**10**[a]

H	**4**	**7**	**8**	**9**	**10**	$J_{H,H}$ [Hz]	**4**	**7**	**8**	**9**	**10**
1α			1.31 td	1.26 td	1.08 dddd	1α,1β			12.7	13.4	12.9
1β	4.43 ddd	4.34 br dd	ca. 1.55[b]	1.44 ddd	ca. 1.58[b]	1α,2α			3.9	3.9	4.2
2α	1.88 dddd	ca. 1.90[b]	ca. 1.50[b]	ca. 1.35[b]	ca. 1.49[b]	1α,2β			12.7	13.4	12.9
2β	1.74 dddd	ca. 1.90[b]	ca. 1.50[b]	ca. 1.35[b]	1.65 ddddd	1α,20			0	0	0.7
3α	2.36 dddd	2.16 dddd	1.14 td	1.07 td	1.06 ddd	1β,2α	3.9	5.0	[b]	5.4	[b]
3β	1.18 ddd	1.34 dt	ca. 1.47[b]	1.34 ddd	ca. 1.49[b]	1β,2β	3.9	1.8	[b]	3.4	3.4
5α			1.88 dd	1.56 dd	1.92 dd	1β,10β	1.8	< 0.4			
6α			2.49 dd	1.66 m	2.32 dd	2α,2β	13.1	[b]	[b]	[b]	13.9
6β			2.32 dd	1.66 m	1.98 dd	2α,3α	4.9	7.1	3.7	3.4	4.2
7A	5.88 q	2.85 d		3.71 td		2α,3β	5.2	6.2	[b]	5.1	[b]
7B				3.83 ddd		2β,3α	11.2	7.7	13.4	13.0	12.9
8A			1.74 dq	1.49 dq		2β,3β	4.6	6.2	[b]	3.2	3.4
8B			1.86 dq	2.26 dq		3α,3β	13.9	14.7	13.4	13.0	12.9
10β	2.23 d	2.08 br s				3α,18B	1.8	0.5			
11A	1.87 ddd	ca. 1.65[b]	1.94 ddd	1.84 ddd	ca. 2.63[b]	5α,6α(A)			6.3	2.9	6.7
11B	2.01 m	ca. 1.65[b]	2.07 ddd	2.07 ddd	ca. 2.63[b]	5α,6β(B)			12.9	4.6	13.7
12A	2.07 dddd	ca. 1.60[b]	ca. 2.54[b]	2.47 ddd	ca. 1.58[b]	6α(A),6β(B)			18.8	[b]	17.2
12B	2.19 ddd	ca. 1.75[b]	ca. 2.54[b]	2.53 ddd	ca. 2.63[b]	6A,7A				5.4	
14	6.22 dd	4.79 d	6.27 dd	6.31 dd	6.23 dd	6A,7B				6.1	
15	7.35 t	6.43 d	7.35 t	7.34 t	7.32 t	6B,7A				9.4	
16	7.18 ddd	4.54 d	7.23 m	7.23 m	7.21 dd	6B,7B				4.6	
Me-17	1.91 d	1.35 s	1.02 br t	0.95 t	1.14 s	7A,7B				9.5	
18A	2.45 d[c]	2.51 d[c]				7α,16β		3.2			
18B	2.98 dd[d]	3.59 dd[d]				7,17	1.2	0			
Me-18			0.87 s	0.84 s	0.88 s	8A,8B			14.9	14.2	
19A	4.79 d	4.63 d				8A(B),17			7.4	7.6	
19B	5.01 d	5.15 d				11A,11B	14.3	[b]	14.2	13.9	[b]
Me-19			0.92 s	0.92 s	0.90 s	11A,12A	3.9	[b]	11.7	11.9	[b]
Me-20	1.45 s	1.16 s	1.07 s	1.02 s	0.85 d	11A,12B	4.2	[b]	5.6	5.2	[b]
OAc	2.01 s	1.98 s				11B,12A	10.0	[b]	5.6	5.2	[b]
						11B,12B	9.5	[b]	11.7	12.3	[b]
						12A,12B	13.2	[b]	[b]	14.4	[b]
						12A,16	1.2	0	<0.4	<0.4	0
						14,15	1.7	2.7	1.7	1.7	1.7
						14,16	1.0	0	1.0	0.9	0.7
						15,16	1.7	0	1.7	1.7	1.7
						18A,18B	5.1	5.4			
						19A,19B	11.5	12.4			

[a] At 500 MHz, in $CDCl_3$ solution. Chemical shifts are reported with respect to the signal of residual $CHCl_3$ (δ = 7.25). − [b] Overlapped signal; approximate δ values were established from HMQC spectra. − [c] *exo* hydrogen atom with respect to ring B. − [d] *endo* hydrogen atom with respect to ring B.

residue was subsequently chromatographed ($MeOH/CH_2Cl_2$, 3:97, as eluent), giving **1** (80 mg, 0.203 mmol, 80% yield) as a less polar component than **2**. Colourless needles (from EtOAc/petroleum ether), m.p. 152−154°C; $[\alpha]_D^{25} = +5.1$ ($c = 0.208$, $CHCl_3$); IR, ^1H and ^{13}C NMR, and MS identical to those of the previously described compound {ref.[6] m.p. 153−155°C; $[\alpha]_D^{25} = +4.7$ ($c = 0.128$, $CHCl_3$)}. Comparison with an authentic sample confirmed the identity.

Preparation of 19-Acetoxy-4α,18;15,16-diepoxy-1α-hydroxyneoclerodа-7,13(16),14-trien-6-one (4) from 8β-Hydroxyfruticolone (3): A solution of **3** (100 mg, 0.246 mmol) in $CHCl_3$ (10 mL) was stirred in the dark for 24 h. Evaporation of the solvent followed by chromatographic purification (EtOAc/petroleum ether, 1:1, as eluent) of the residue and crystallization from EtOAc/petroleum ether gave **4** (76 mg, 0.197 mmol, 85% yield) as colourless needles; m.p. 169−171°C. − $[\alpha]_D^{21} = +20.6$ ($c = 0.189$, $CHCl_3$). − UV: $\lambda_{max} = 239$ nm ($\log \varepsilon = 4.01$). − ^1H NMR: see Table 1. − ^{13}C NMR: see Table 2. − IR and MS identical with those reported previously.[7b]

Table 2. ^{13}C-NMR spectral data of compounds **4** and **7−10**[a]

C	4	7	8	9	10
1	66.1 d	67.4 d	33.4 t	35.0 t	34.4 t
2	34.1 t[b]	33.3 t	18.1 t	18.6 t	18.6 t
3	27.7 t[b]	27.9 t	40.8 t	41.9 t	40.7 t
4	60.3 s	60.4 s	32.6 s	36.1 s	32.3 s
5	50.8 s	52.3 s	41.3 d	46.1 d	48.7 d
6	195.4 s	208.7 s	28.6 t	28.4 t	36.1 t
7	128.6 d	57.7 d	172.3 s	65.5 t	218.3 s
8	163.4 s	58.1 s	27.0 t	30.3 t	71.7 s
9	43.0 s	44.6 s	91.2 s	80.2 s	211.7 s
10	47.2 d	55.2 d	40.2 s	45.6 s	46.9 s
11	38.6 t[b]	45.3 t	34.9 t	36.0 t	42.0 t
12	19.9 t	32.1 t	20.3 t	20.6 t	19.4 t
13	124.2 s	64.1 s	124.6 s	125.8 s	123.5 s
14	110.6 d	104.3 d	110.8 d	111.1 d	111.1 d
15	143.2 d[b]	148.7 d	142.9 d	142.7 d	142.8 d
16	138.5 d[b]	85.0 d	138.7 d	138.5 d	139.3 d
17	19.2 q[b]	20.9 q	9.5 q	9.9 q	14.0 q
18	50.9 t	51.6 t	33.0 q	33.8 q	33.7 q
19	65.1 t	63.9 t	21.3 q	22.4 q	21.2 q
20	24.1 q[b]	21.2 q	15.5 q	16.6 q	16.2 q
OAc	170.4 s	170.5 s			
	21.0 q	21.0 q			

[a] At 125.7 MHz, $CDCl_3$ solution. Chemical shifts are reported with respect to the solvent signal ($\delta_{CDCl3} = 77.00$). All assignments were in agreement with HMQC and HMBC spectra. − [b] Assignments amended with respect to those reported previously (see ref.[7b]).

19-Acetoxy-4α,18;15,16-diepoxy-1α-hydroxy-7β,16α;8β,13α-dicycloneoclerod-14-en-6-one (7) from Compound 4: A solution of **4** (100 mg, 0.257 mmol) in dry methanol (40 mL) was irradiated for 40 min. The residue was subsequently chromatographed using $MeOH/CH_2Cl_2$ (3:97) as eluent, giving **7** (44 mg, 0.113 mmol, 44% yield) as a less polar component than **4**, besides starting material (24 mg, 0.062 mmol, 24% recovered). Colourless needles (EtOAc/petroleum ether), m.p. 168−170°C. − $[\alpha]_D^{21} = -19.9$ ($c = 0.372$, $CHCl_3$). − IR (KBr): $\tilde{\nu} = 3450$ cm^{-1} (OH), 3090, 3080, 1600 (vinyl ether), 3030 (oxirane), 1735, 1250 (OAc), 1715 (ketone). − EI MS; *m/z* (%): 388 $[M]^+$ (1), 373 (2), 328 (3), 315 $[M - CH_2OAc]^+$ (100), 297 (22), 253 (26), 215 (37), 203 (24), 173 (25), 161 (27), 159 (43), 95 (69), 91 (26), 81 (38), 67 (20). − ^1H NMR: see Table 1. − ^{13}C NMR: see Table 2. − $C_{22}H_{28}O_6$ (388.4): calcd. C 68.02, H 7.27; found C 67.93, H 7.19.

(9*S*)-15,16-Epoxy-7,8-*seco*-labda-13(16),14-dien-7,9-olide (8) from Hispanolone (5): A solution of **5** (100 mg, 0.314 mmol) in dry benzene (50 mL) was irradiated for 4 h. The residue was subsequently chromatographed using EtOAc/petroleum ether (1:10) as eluent, giving **8** (60 mg, 0.188 mmol, 60% yield) as a less polar component than **5**, besides starting material (5 mg, 0.016 mmol, 5% recovered). Colourless needles (EtOAc/petroleum ether), m.p. 78−79°C. − $[\alpha]_D^{21} = -3.3$ ($c = 0.457$, $CHCl_3$). − IR (KBr): $\tilde{\nu} = 3130$ cm^{-1}, 3100, 1500, 875 (furan), 1710 (δ-lactone). − EI MS; *m/z* (%): 318 $[M]^+$ (5), 223 (2), 194 (4), 152 (86), 124 (22), 123 (16), 109 (100), 95 (55), 81 (29), 69 (10), 67 (17), 55 (12). − ^1H NMR: see Table 1. − ^{13}C NMR: see Table 2. − $C_{20}H_{30}O_3$ (318.4): calcd. C 75.43, H 9.50; found C 75.51, H 9.43.

Lithium Aluminium Hydride Reduction of Compound 8 to (9*S*)-15,16-Epoxy-7,8-*seco*-labda-13(16),14-diene-7,9-diol (9): To a stirred solution of **8** (100 mg, 0.314 mmol) in THF (10 mL) at room temperature was added an excess of $LiAlH_4$ (60 mg, 1.58 mmol). After 5 h, the reaction mixture was poured into a saturated NH_4Cl solution/crushed ice mixture and extracted with several portions of EtOAc. The combined organic layers were dried (Na_2SO_4). Evaporation of the solvent followed by chromatographic purification of the residue gave **9** (70 mg, 0.217 mmol, 69% yield) as colourless needles (EtOAc/petroleum ether); m.p. 120−121°C. − $[\alpha]_D^{21} = +12.6$ ($c = 0.261$, $CHCl_3$). − IR (KBr): $\tilde{\nu} = 3240$ br. cm^{-1} (OH), 1580, 1500, 870 (furan). − EI MS; *m/z* (%): $[M]^+$ absent, 304 $[M - H_2O]^+$ (1), 169 (6), 153 (80), 152 (30), 125 (12), 109 (49), 95 (54), 81 (100), 69 (27), 57 (28), 55 (18). − ^1H NMR: see Table 1. − ^{13}C NMR: see Table 2. − $C_{20}H_{34}O_3$ (322.4): calcd. C 74.49, H 10.63; found C 74.32, H 10.71.

(8*R*)-15,16-Epoxy-10(9→8)-*abeo*-labda-13(16),14-diene-7,9-dione (10) from Compound 6: A solution of **6** (100 mg, 0.316 mmol) in dry benzene (100 mL) was irradiated for 1.5 h. The residue was subsequently chromatographed using EtOAc/petroleum ether (3:97) as eluent, giving **10** (21 mg, 0.066 mmol, 21% yield) as a more polar component than **6**, besides starting material (14 mg, 0.044 mmol, 14% recovered). Colourless oil. − $[\alpha]_D^{24} = -89.1$ ($c = 0.304$, $CHCl_3$). − IR (NaCl): $\tilde{\nu} = 3140$ cm^{-1}, 1630, 1503, 873 (furan), 1750, 1703, 1688 (diketone). − EI MS; *m/z* (%.): 316 $[M]^+$ (9), 221 (9), 194 (15), 179 (100), 95 (18), 81 (34), 69 (10), 67 (8), 55 (9). − ^1H NMR: see Table 1. − ^{13}C NMR: see Table 2. − $C_{20}H_{28}O_3$ (316.4): calcd. C 75.91, H 8.92; found C 75.96, H 8.72.

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[1] Although the hydrocarbon skeleton of these diterpenes is biogenetically derived from an *ent*-labdane and hence they should be named *ent*-clerodanes, we prefer to use the term neoclerodane proposed by Rogers et al. for defining the absolute configuration (D. Rogers, G. G. Unal, D. J. Williams, S. V. Ley, G. A. Sim, B. S. Joshi, K. R. Ravindranath, *J. Chem. Soc., Chem. Commun.* **1979**, 97−99) since this nomenclature is adopted in the majority of the articles published on this subject since 1979.

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[12] In compound **7**, irradiation at δ = 4.54 (16β-H) under NOE conditions caused enhancements in the 7α-H (δ = 2.85, 3%) and 15-H (δ = 6.43, 1%) protons, but this result does not provide any reliable information about the stereochemistry at C-16. However, a structure with the opposite configuration at the C-13 and C-16 carbon atoms is not possible, because of the presence in **7** of an additional five-membered carbocycle comprising the C-8, C-9, C-11, C-12, and C-13 carbon atoms (see a molecular model of **7**).

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