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New Sesquiterpene Lactones of Eremophilane-Type from *Ligularia Fauriei* (Fr.) Koidz.[1]

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Two new sesquiterpene lactones of eremophilane-type were isolated from *Ligularia Fauriei* (Fr.) Koidz., and their structures including absolute stereochemistry were shown to be 8β-hydroxyeremophil-7(11)-ene-12,8α;14β,6α-diolide (**1**) and eremophil-7(11)-ene-12,8α;14β,6α-diolide (**2**), respectively. The isolation of the two known lactones, 6β,8β-dihydroxyeremophil-7(11)-en-12,8α-olide (**3**) and 6β-hydroxyeremophil-7(11)-en-12,8α-olide (**4**), is also described. The photosensitized autoxidation of the known furanoeremophilan-14β,6α-olide (**5**) gave **1** and 8β-methoxyeremophil-7(11)-ene-12,8α;14β,6α-diolide (**18**).

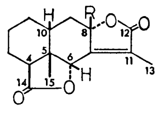
During chemical investigation on plants of the genus *Ligularia* (Compositae) and related plants,[2] two new sesquiterpene lactones were isolated from *Ligularia Fauriei* (Fr.) Koidz. In the present communication, the structure determination leading to 8β-hydroxyeremophil-7(11)-ene-12,8α; 14β,6α-diolide (**1**) and eremophil-7(11)-ene-12,8α; 14β,6α-diolide (**2**) for these sesquiterpenes is described.

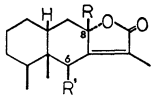
A benzene extract of the roots of the plant was subjected to separation by column chromatography on silica gel to give four sesquiterpene lactones (**1**, **2**, **3**, and **4**) in addition to the previously reported furanoeremophilan-14β,6α-olide (**5**).[3,4]

The lactone (**1**), mp 253.5—254 °C (dec), $[\alpha]_D$ +94° ($CHCl_3$), crystallized from a mixture of benzene and chloroform as colorless needles. The molecular formula of $C_{15}H_{18}O_5$ was determined by elemental analysis and the appearance of the molecular ion peak at *m/e* 278 in the mass spectrum. The IR, UV, and PMR spectra indicated the presence of a tertiary methyl, an olefinic methyl, an α,β-unsaturated γ-lactone,[5,6] a γ-lactone, and a hydroxyl group; signals due to a secondary methyl were absent (*cf.* Experimental). Acetylation of the lactone (**1**) with acetic anhydride in pyridine gave a monoacetate (**6**) showing no hydroxyl absorption in its IR spectrum. Based on these spectral data, the structure (**1**) is suggested for this lactone (**1**), providing that the lactone belongs to a sesquiterpene of eremophilane-type. The following evidence provides support for the proposed structure (**1**).

It has been reported that the autoxidation of atractylon (**7**) gives a lactone (**8**) and a hydroxylactone (**9**), and that the latter compound (**9**) in turn affords an unsaturated enol lactone (**10**) by dehydration.[7] Oxidation of atractylon (**7**) with dichlorodicyanobenzoquinone (DDQ) to yield **10** has also been described.[8] Furanoeremophilan-14β,6α-olide (**5**) with the known absolute stereochemistry[3] was treated with DDQ in dioxane to give an unsaturated enol lactone (**11**). The same compound (**11**) was obtained by dehydration of the lactone (**1**) with phosphorus oxychloride in pyridine. Irradiation of **5** in methanol with a high pressure mercury lamp under an oxygen atmosphere in the presence of Rose Bengal gave a compound identical with the lactone (**1**). The observation described above shows that the lactone (**1**) can be formulated as 8ξ-hydroxyeremophil-7(11)-ene-12,8α; 14β,6α-diolide. The β-configuration of the hydroxyl group at $C_{(8)}$ was suggested by the presence in the lactone (**1**) of a long-range spin-coupling (J=2 Hz) between the olefinic methyl ($C_{(11)}$–CH_3) protons and the allylic proton ($C_{(6\beta)}$–H) at the lactone terminus. An examination of the stereostructure of **1** with 8β-OH by the use of Dreiding model shows that the angle between $C_{(6\beta)}$–H and $C_{(11)}$–CH_3 is around 90°, in agreement with the observed homoallylic spin-coupling constant.[9] In an alternative structure with 8α-OH, the angle lies around 30° and the corresponding homoallylic spin-coupling would be negligible.[9] This received support from the following observation.[10] Naya *et al.*[10] reported the presence of a homoallylic spin-coupling (J=1.0—1.5 Hz) between $C_{(6\alpha)}$–H and $C_{(11)}$–CH_3 in 6β-hydroxy-8α-methoxyeremophil-7(11)-en-12,8β-olide (**12**) and 6β-acetoxy-8α-methoxyeremophil-7(11)-en-12,8β-olide (**13**) whose structures were firmly established, while the absence of this long-range spin-coupling in 6β-hydroxy-8β-methoxyeremophil-7(11)-en-12,8α-olide (**14**) and 6β-acetoxy-8β-methoxyeremophil-7(11)-en-12,8α-olide(**15**). The angles between $C_{(6\alpha)}$–H and $C_{(11)}$–CH_3 were reported to be 90° and 20° for the 8α- (**12** and **13**) and 8β-methoxy (**14** and **15**) derivatives, respectively. Therefore, the structure including absolute stereochemistry of the lactone (**1**) should be represented by 8β-hydroxyeremophil-7(11)-ene-12,8α;14β,6α-diolide (**1**).

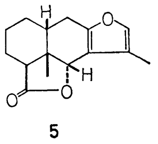
The molecular formula of $C_{15}H_{18}O_4$ was given for the lactone (**2**), mp 186—186.5 °C (dec.), $[\alpha]_D$+93°





1 R = OH
2 R = H
6 R = OAc
18 R = OMe

3 R = OH, R' = OH
4 R = H, R' = OH
16 R = OAc, R' = OAc
17 R = H, R' = H



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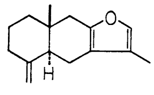

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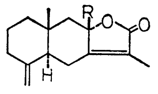
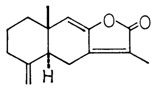


8 R = H
9 R = OH



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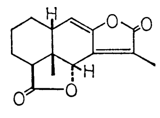

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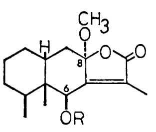
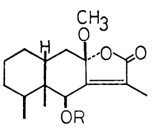


12 R=H
13 R=Ac



14 R=H
15 R=Ac

(CHCl$_3$). The spectral data suggested the presence of a tertiary methyl, an olefinic methyl, an α,β-unsaturated γ-lactone, and a γ-lactone grouping (*cf.* Experimental). No hydroxyl absorption was observed in the IR spectrum. In the PMR spectrum of the lactone (**2**) the signals due to the proton (C$_{(8)}$–H) at the unsaturated lactone terminus appeared at δ 4.75 as a multiplet, while the corresponding signals were absent in the spectrum of the lactone (**1**). Treatment of the lactone (**1**) with sodium borohydride in methanol containing sodium hydroxide gave the lactone (**2**). These results show that the lactone (**1**) contains one hydroxyl group more than the lactone (**2**), and that the hydroxyl group at C$_{(8)}$ of **1** must be replaced by a hydrogen atom in the case of the lactone (**2**). PMDR experiments revealed the presence in the lactone (**2**) of long-range spin-couplings of the olefinic methyl (C$_{(11)}$–CH$_3$) protons to the allylic proton (C$_{(6\beta)}$–H; J=2 Hz) and to the other allylic proton (C$_{(8)}$–H; J=2 Hz). This observation leads to the 8β-H configuration for the lactone (**2**).[9] Thus, the structure including absolute stereochemistry of the lactone (**2**) is shown to be eremophil-7(11)-ene-12,8α; 14β,6α-diolide (**2**).

The lactone (**3**), mp 217—218 °C (dec), $[\alpha]_D$+82° (EtOH), gave a diacetate (**16**), mp 120.5—121 °C, by acetylation with acetic anhydride in pyridine. This lactone (**3**) proved to be identical with 6β,8β-dihydroxy-eremophil-7(11)-en-12,8α-olide (**3**),[10] recently reported by Naya *et al.* The lactone (**4**), mp 207—207.5 °C, $[\alpha]_D$+213° (CHCl$_3$), was found to be identical with 6β-hydroxyeremophil-7(11)-en-12,8α-olide (**4**).[6,10,11] The lactone (**3**) was treated with sodium borohydride in methanol containing sodium hydroxide to yield two products, which were shown to be **4** and eremophil-7(11)-en-12,8α-olide (**17**),[12,13] respectively. The similar treatment of **4** gave **17**.

The photosensitized autoxidation of **5** in methanol gave a compound (**18**), C$_{16}$H$_{20}$O$_5$, mp 184.5—185 °C, besides the lactone (**1**). The PMR spectrum of **18** indicated the presence of a methoxyl group. The multiplet due to 8β-H appeared in the spectrum of **2** is absent in that of **18**. The other spectral data of **2** and **18** were almost identical, showing the presence of the common groupings: a tertiary methyl, an olefinic methyl, an α,β-unsaturated γ-lactone, and a γ-lactone grouping (*cf.* Experimental). The extra methoxyl group of **18** must be located on C$_{(8)}$ of the structure moiety of **2**. The presence of a long-range spin-coupling (J=2 Hz) of the olefinic methyl (C$_{(11)}$–CH$_3$) protons to the allylic proton (C$_{(6\beta)}$–H) at the lactone terminus was observed for **18**.[9] Therefore, the structure of the photoproduct (**18**) should be represented by 8β-methoxyeremophil-7(11)-ene-12,8α; 14β,6α-diolide (**18**).

The two lactones (**1** and **2**)[14] represent the first examples of eremophilane-type sesquiterpenes with two lactone rings in their molecules.

Experimental

All mps were determined on a hot block and reported uncorrected. IR, UV, and mass spectra were recorded on Hitachi EPI-G2, Hitachi EPS-3, and Hitachi RMU-6 spectrometers, respectively. Measurements of optical rotation were carried out using a JASCO DIP-SL polarimeter. PMR spectra were taken on a Hitachi R-20 or a JEOL JNM-PS-100 spectrometer, using TMS as internal standard. Kieselgel G nach Stahl and Kieselgel 60 PF$_{254}$ (Merck) were used for analytical and preparative TLC, respectively. For column chromatography Wakogel C-200 (Wako Pure Chemicals) was used.

Isolation of the Lactones (1, 2, 3, and 4). Dried roots (900 g) of *L. Fauriei* were extracted twice with hot benzene (2 l). The residue obtained after removal of the solvent was chromatographed on a column of silica gel (180 g). Elution with petroleum ether–ether (20: 1, 1 l) gave furanoeremophilan-14β, 6α-olide (**5**)[3,4] (5.40 g). After elution of **5**, more polar constituents were eluted with ether. The residue obtained after evaporation of the solvent was subjected to chromatographic separation on a column of silica gel (100 g).

Elution with benzene (1.2 l) gave, on removal of the solvent, a solid, which was crystallized from ether to afford eremophil-7(11)-ene-12, 8α; 14β, 6α-diolide (**2**; 204 mg) as needles, mp 186—186.5 °C (dec.); $[\alpha]_D$ +93° (c 0.91, CHCl$_3$); UV (EtOH) λ_{max} 217 nm (ε 19300); IR (Nujol) 1786, 1739, and 1684 (sh) cm^{-1}; PMR (CDCl$_3$) δ 1.29 (3H, s; C$_{(5)}$–CH$_3$), δ 2.00 (3H, t, $J_{6\beta,13}$=2 and $J_{8\beta,13}$=2 Hz; C$_{(11)}$–CH$_3$), δ 4.75 (1H, m, $J_{8\beta,13}$=2, $J_{8\beta,9\alpha}$=13, and $J_{8\beta,9\beta}$=5 Hz (by PMDR experiments); C$_{(8\beta)}$–H), and δ 5.05 (1H, q, $J_{6\beta,13}$=2 Hz (confirmed by PMDR experiments); C$_{(6\beta)}$–H); mass spectrum *m/e* 262 (relative intensity 73%; M$^+$), *m/e* 152 (100%). Found: C, 69.13; H, 7.14%. Calcd for C$_{15}$H$_{18}$O$_4$: C, 68.68; H, 6.92%.

Subsequent elution with benzene–ether (10: 1, 400 ml) and evaporation of the solvents gave a residue, which was crystallized from benzene to yield 6β-hydroxyeremophil-7(11)-en-12, 8α-olide[6,10,11] (**4**; 40 mg) as needles, mp 207—207.5 °C (lit, mp 208 °C[6,11] and mp 204—205 °C[10]); $[\alpha]_D$ +213° (c 1.19, CHCl$_3$) (lit, $[\alpha]_D$ +205.8° (CHCl$_3$),[6] $[\alpha]_D$ +203° (CHCl$_3$),[10] and $[\alpha]_D$ −35.4° (CHCl$_3$)[11,15]); UV (EtOH) λ_{max} 218 nm (ε 14400) [lit, λ_{max} 218.5 nm (ε 13700) (EtOH)[6] and λ_{max} 220 nm (log ε 4.12)[11]]; IR (Nujol) 3440, 1739, 1709 (sh), and 1690 cm^{-1}; PMR (CDCl$_3$) δ 0.80 (3H, d-like; C$_{(4)}$–CH$_3$), δ 1.13 (3H, s; C$_{(5)}$–CH$_3$), δ 1.85 (3H, d, $J_{8\beta,13}$=2 Hz; C$_{(11)}$–CH$_3$), δ 4.80 (1H, s; C$_{(6\alpha)}$–H), δ *ca.* 5.1 (1H, m; C$_{(8\beta)}$–H), and

δ 2.23 (1H, s, disappeared on addition of D_2O; $C_{(6\beta)}$-OH); mass spectrum *m/e* 250 (7%, M^+), *m/e* 126 (100%). Found: C, 72.00; H, 8.90%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%. This lactone was found to be identical (mp, mixed mp, $[\alpha]_D$, IR, UV, PMR, and mass spectra) with an authentic specimen of **4**.[6]

Fractions eluted with benzene–ether (5: 1, 400 mg) gave, on removal of the solvents, a solid, which was crystallized from chloroform–benzene to afford 8β-hydroxyeremophil-7(11)-ene-12, 8α; 14β, 6α-diolide (**1**; 250 mg) as needles, mp 253.5—254 °C (dec); $[\alpha]_D$ +94° (*c* 0.88, $CHCl_3$); UV (EtOH) λ_{max} 214 nm (ε 12400); IR (Nujol) 3260, 1787, and 1710 cm^{-1}; PMR (acetone-d_6) δ 1.28 (3H, s; $C_{(5)}$-CH_3), δ 1.86 (3H, d, $J_{6\beta,13}$=2 Hz; $C_{(11)}$-CH_3), δ 5.18 (1H, q, $J_{6\beta,13}$=2 Hz (confirmed by PMDR experiments); $C_{(6\beta)}$-H), and δ 6.51 (1H, s, disappeared on addition of D_2O; $C_{(8\beta)}$-OH); mass spectrum *m/e* 278 (44%, M^+), *m/e* 109 (100%). Found: C, 65.08; H, 6.42%. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52%.

Successive elution with the same solvents [benzene–ether (5: 1), 500 ml] and the evaporation of the solvents gave a residue. This was crystallized from chloroform–benzene to yield 6β,8β-dihydroxyeremophil-7(11)-en-12, 8α-olide (**3**; 567 mg)[10] as plates, mp 217—218 °C (dec) (lit, mp 211—212 °C); $[\alpha]_D$ +82° (*c* 0.98, EtOH) [lit, $[\alpha]_D$ +169° ($CHCl_3$)[10]]; UV (EtOH) λ_{max} 219 nm (ε 11800); IR (Nujol) 3480, 3230, and 1721 cm^{-1}; ($CHCl_3$) 3530, 1761, 998, and 980 (sh) cm^{-1} (lit, ($CHCl_3$) 3525, 3250, 1760, 1005, and 990 cm^{-1} [10]); PMR (acetone-d_6) δ 0.80 (3H, d-like; $C_{(4)}$-CH_3), δ 1.12 (3H, s; $C_{(5)}$-CH_3), δ 1.83 (3H, s, $C_{(11)}$-CH_3), and δ 4.64 (1H, br. s; $C_{(6\alpha)}$-H); ($CDCl_3$) δ 0.82 (3H, unresolved signals; $C_{(4)}$-CH_3), δ 1.13 (3H, s, $C_{(5)}$-CH_3), δ 1.88 (3H, s; $C_{(11)}$-CH_3), δ 2.09 (2H, s; $C_{(9)}$-H_2), δ 2.96 and δ 3.10 (each 1H, s, disappeared on addition of D_2O; $C_{(6\beta)}$-OH and $C_{(8\beta)}$-OH), and δ 4.62 (1H, s; $C_{(6\alpha)}$-H); [lit, ($CDCl_3$) δ 0.78 (3H, unresolved signals; $C_{(4)}$-CH_3), δ 1.11 (3H, s; $C_{(5)}$-CH_3), δ 1.87 (3H, s; $C_{(11)}$-CH_3), δ 2.07 (2H, s; $C_{(9)}$-H_2), δ 2.70 (2H, br. s; $C_{(6\beta)}$-OH and $C_{(8\beta)}$-OH), and δ 4.60 (1H, s; $C_{(6\alpha)}$-H)[10]]; mass spectrum *m/e* 248 [6%, $(M-18)^+$], *m/e* 109 (100%) (no molecular ion peak was observed). Found: C, 67.89; H, 8.53%. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33%. This lactone proved to be identical with **3**, recently reported by Naya *et al.*[10]

Acetylation of the Lactone (1). The lactone (**1**; 36 mg) was acetylated with acetic anhydride (2 ml) in pyridine (3 ml) at room temperature. Treatment as usual gave a residue, which was chromatographed on a column of silica gel (5 g). Fractions eluted with benzene (14 ml) gave an oil, which was purified by preparative TLC. Crystallization of the oil from petroleum ether afforded a monoacetate (**6**; 17 mg) as needles, mp 183—184 °C; IR (Nujol) 1800, 1784, 1773, and 1707 cm^{-1}; PMR ($CDCl_3$) δ 1.32 (3H, s; $C_{(5)}$-CH_3), δ 2.06 (3H, d, $J_{6\beta,13}$=2 Hz; $C_{(11)}$-CH_3), δ 2.13 (3H, s; -$COCH_3$), and δ 5.04 (1H, q, $J_{6\beta,13}$=2 Hz; $C_{(6\beta)}$-H); mass spectrum *m/e* 320 (3%, M^+), *m/e* 278 [100%, $(M-42)^+$]. Found: C, 63.66; H, 6.26%. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29%.

Acetylation of the Lactone (3). To a solution of **3** (30 mg) in pyridine (2 ml) was added acetic anhydride (1 ml), and the solution was left for 3 days at room temperature. After working up in the usual manner, a crystalline product was obtained. Recrystallization from petroleum ether gave a diacetate (**16**; 38 mg), as needles, mp 120.5—121 °C (lit, 119.5—120.5 °C[10]); IR (Nujol) 1770, 1751, 1733, and 1248 cm^{-1}; PMR ($CDCl_3$) δ 0.82 (3H, unresolved signals; $C_{(4)}$-CH_3), δ 1.00 (3H, s; $C_{(5)}$-CH_3), δ 1.96 (3H, s; $C_{(11)}$-CH_3), δ 1.98 (3H, s; -$COCH_3$), δ 2.02 (3H, s; -$COCH_3$), and δ 5.88 (1H, s; $C_{(6\alpha)}$-H); mass spectrum *m/e* 308 [3%, $(M-42)^+$], *m/e* 109 (100%) (no molecular ion peak was observed). Found: C, 65.24; H, 7.45%. Calcd for $C_{19}H_{26}O_6$: C, 65.12; H, 7.48%.

Oxidation of the Lactone (5) with DDQ. A mixture of furanoeremophilan-14β,6α-olide (**5**; 500 mg) and DDQ (1.2 g) in dioxane (10 ml) was heated at 80 °C for 1 h, and then the solvent was evaporated under reduced pressure. The residue was extracted with hot benzene. The reaction mixture obtained after removal of the benzene was chromatographed on a column of silica gel (50 g). Elution with benzene–ether (5: 1, 1 l) gave a mixture of crystalline products (227 mg, recrystallized from benzene), which was subjected to sublimation. From the sublimated material (119 mg), a product (34 mg) with R_f value 0.62 (benzene–ether, 1: 1) on TLC (silica gel) was collected by repeated preparative TLC. Crystallization of the product from ether gave an unsaturated enol lactone (**11**; 23 mg) as an amorphous solid, IR (neat) 1785 and 1665 cm^{-1}; PMR ($CDCl_3$) δ 1.38 (3H, s; $C_{(5)}$-CH_3), δ 2.12 (3H, br. s; $C_{(11)}$-CH_3), δ 2.65 (1H, dd, $J_{3\alpha,4\alpha}$=2 and $J_{3\beta,4\alpha}$=12 Hz; $C_{(4\alpha)}$-H), δ 2.96 (1H, m; $C_{(10\beta)}$-H), δ 5.28 (1H, q, $J_{6\beta,13}$=1.5 Hz; $C_{(6\beta)}$-H), and δ 5.65 (1H, d, $J_{9,10\beta}$=3 Hz; $C_{(9)}$-H) (the presence of these spin-couplings was confirmed by PMDR experiments); mass spectrum *m/e* 260 (9%, M^+ related to a molecular formula of $C_{15}H_{16}O_4$], *m/e* 67 (100%). This compound is very unstable and most of the compound decomposed within 1 day on leaving it in a solution. The purity was checked before and after the measurement of these spectra. The UV (EtOH) spectra showed the absorption maximum at 280 nm.[7,8] However, the ε value could not be determined precisely due to fragility of the compound. Appearance of the maximum at 222 nm during the measurement would be due to the decomposition of the compound. Elemental analysis gave an unsatisfactory result probably due to the unstability of the compound.

Dehydration of the Lactone (1). To a stirred solution of **1** (51 mg) in pyridine (2 ml), phosphorus oxychloride (0.2 ml) was added at 0 °C, and the stirring was continued for 1 h at 0 °C, then for 4 h at room temperature. After addition of crushed ice, the reaction mixture was extracted with chloroform (50 ml). The extract was dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. From the reaction mixture, the unsaturated enol lactone (**11**; 9 mg) was obtained by preparative TLC, which was found to be identical (TLC, IR, PMR, and mass spectra) with the sample (**11**) prepared by oxidation of **5**.

Photosensitized Autoxidation of the Lactone (5) in Methanol. Rose Bengal (53 mg) was added to a solution of **5** (308 mg) in methanol (600 ml), and the resulting solution was irradiated with a high pressure mercury lamp (100W, Rikosha) under oxygen atmosphere at 0 °C for 1 h. The residue obtained after removal of the methanol under reduced pressure, was chromatographed on a column of silica gel (50 g). Elution with benzene–ether (10: 1) gave two principal fractions: the less polar fraction (269 mg) and the more polar fraction (21 mg). From the more polar fraction, a crystalline product (9.5 mg) was obtained after recrystallization from benzene–chloroform, which was found to be identical (mp, TLC, IR, and PMR spectra) with 8β-hydroxyeremophil-7(11)-ene-12, 8α;14β,6α-diolide (**1**).

The less polar fraction was repeatedly chromatographed on a column of silica gel (50 g). Elution with benzene–ether (20: 1, 200 ml) gave 8β-methoxyeremophil-7(11)-ene-12,8α;14β,6α-diolide (**18**; 111 mg, recrystallized from petroleum ether), mp 184.5—185 °C; UV (EtOH) λ_{max} 216 nm (ε 14700); IR(Nujol) 1790, 1765, and 1690 cm^{-1}; PMR ($CDCl_3$) δ 1.29 (3H, s; $C_{(5)}$-CH_3), δ 2.01 (3H, d, $J_{6\beta,13}$=2 Hz; $C_{(11)}$-CH_3), δ 3.21 (3H, s; -OCH_3), and δ 4.88 (1H, q, $J_{6\beta,13}$=2 Hz; $C_{(6\beta)}$-H); mass spectrum *m/e* 292 (35%, M^+), *m/e* 67 (100%). Found: C, 65.67; H, 6.66%. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90%.

When the lactone (**5**) in methanol was either left for 3 days under bubbling of oxygen or irradiated with ultraviolet rays for 5 h under oxygen atmosphere, **5** suffered no change.

Reduction of the Lactone (1) with Sodium Borohydride. To a mixture of **1** (30 mg) and aqueous sodium hydroxide (10%, 0.3 ml) in methanol (3 ml), sodium borohydride (51 mg) was added at 0 °C with stirring, and the stirring was continued for 1 h at 0 °C, then for 2 h at room temperature. After evaporation of the methanol under reduced pressure, the residue was acidified with sulfuric acid (0.5 M), and extracted with ether. The ethereal solution was dried over anhydrous sodium sulfate and the solvent was removed to give a residue, which was chromatographed on a column of silica gel (7 g), using benzene–ether (10:1) as eluent. A crystalline product (5 mg) was obtained, which was purified by crystallization from ether. This compound (2 mg) was found to be identical (mp, TLC, IR, PMR, and mass spectra) with eremophil-7(11)-ene-12,8α; 14β,6α-diolide (**2**).

Reduction of the Lactone (3) with Sodium Borohydride. The lactone (**3**; 30 mg) was treated with sodium borohydride (50 mg) in methanol containing sodium hydroxide according to the procedures described in the reduction of **1**. The residue was chromatographed on a column of silica gel (20 g). Elution with benzene (120 ml) gave an oily product, which then solidified (10 mg). This compound proved to be identical with eremophil-7(11)-en-12,8α-olide (**17**),[12,13] mp 107—111 °C; IR (Nujol) 1740, 1687, and 1035 cm^{-1}; PMR ($CDCl_3$) δ 0.80 (3H, d-like; $C_{(4)}$–CH_3), δ 1.05 (3H, s; $C_{(5)}$–CH_3), δ 1.80 (3H, t, $J_{6\beta,13}=2$ Hz and $J_{8\beta,13}=2$ Hz; $C_{(11)}$–CH_3), δ 2.90 (1H, d, $J_{6\alpha,6\beta}=15$ Hz; $C_{(6\alpha)}$–H) (signals due to $C_{(6\beta)}$–H is overlapped with other signals), and δ 4.61 (1H, m; $C_{(8\beta)}$–H); mass spectrum *m/e* 234 (8%, M^+ related to a molecular formula of $C_{15}H_{22}O_3$), *m/e* 123 (100%).

Successive elution with benzene–ether (5:1, 90 ml) gave a product (3 mg), mp 207—207.5 °C, whose IR, PMR, and mass spectra were found to be identical with those of 6β-hydroxyeremophil-7(11)-en-12,8α-olide (**4**).[6]

Reduction of the Lactone (4) with Sodium Borohydride. Treatment of the lactone (**4**; 13 mg) with sodium borohydride (55 mg) in methanol containing sodium hydroxide, according to the procedures described in the reduction of **3**, gave a residue, which was chromatographed on a column of silica gel (5 g). Elution with benzene (150 ml) gave a crystalline compound (3 mg). This compound was found to be identical (mp, TLC, IR, and PMR spectra) with **17** described above. Further elution with ether (30 ml) afforded the unchanged starting material (**4**; 10 mg).

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14) These lactones might be considered as artifacts produced from **5** during isolation procedures. Although the fresh extract of the plant was examined by thin layer chromatography, no conclusive evidence was obtained due to the complexity of a mixture of the constituents. The subsequent separation led to the isolation of **1** and **2** as described in Experimental.

15) This reported $[\alpha]_D$ value seems to be erroneous.