The Photosensitized Oxygenation of Furanoeremophilanes. II.[1] The Preparation and Stereochemistry of the Isomeric Hydroperoxides and the Corresponding Lactones from Furanofukinin and Furanoeremophilane

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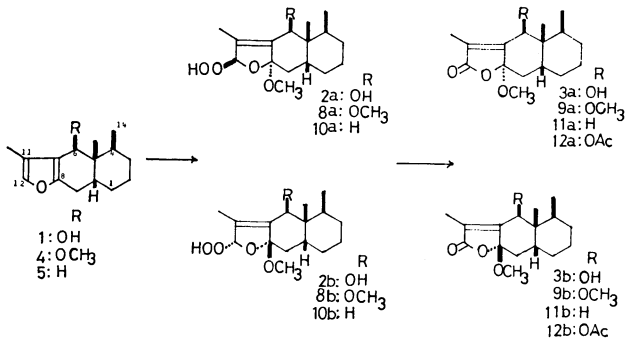
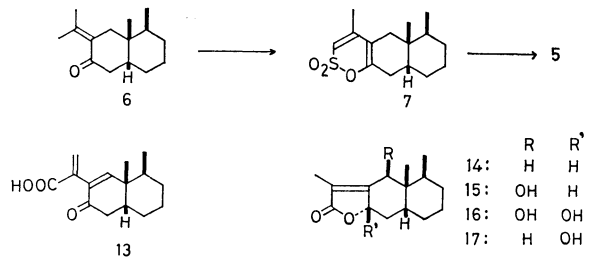
The dye-sensitized oxygenation of furanofukinin, and furanoeremophilane, in methanol gave, quantitatively, crystalline mixtures of two isomeric hydroperoxides each consisting of a pair of 8α-methoxy-12β-hydroperoxy and 8β-methoxy-12α-hydroperoxy derivatives respectively. The hydroperoxides were readily transformed to the corresponding lactones with acetic anhydride–pyridine through dehydration. The stereochemistry of the hydroperoxides and the corresponding lactones has been elucidated by spectral and chemical methods according to a previously outlined generalization. Further, furanofukinin, furanoeremophilane, and 8β-hydroxyeremophilenolide, have been synthesized from petasalbin, fukinone, and an epimeric mixture of 8α- and 8β-methoxy lactones, respectively.

In our previous paper,[1] we reported on the photosensitized oxygenation of petasalbin (**1**) to yield, quantitatively, a mixture of two isomeric hydroperoxides, (**2a**) and (**2b**), both of which were then transformed quantitatively to the corresponding lactones, (**3a**) and (**3b**), by treatment with acetic anhydride–pyridine. Their configurational assignments were ascertained by a comparison of the chemical and spectral properties between sets of the two isomeric substances. In the present paper, we will describe the photosensitized oxygenation of furanofukinin (**4**)[2] and furanoeremophilane (**5**),[3] performed in order to examine the utility of the generalization outlined in the preceding paper[1] for the configurational assignments to hydroperoxides, **2a,b**, and the corresponding lactones, **3a,b**, converted from petasalbin, **1**. Thus, a pair of 8α- and 8β-methoxy isomers have been estimated to exist in non-steroidal and steroidal A/B *cis* chair/chair conformations respectively.



Both furanofukinin, **4**, and furanoeremophilane, **5**, were isolated from the rhizomes of a wild plant,[2] *Petasites japonicus* Maxim. and its subspecies, subsp. *gigantus* Kitam. These substances, **4** and **5**, were also synthesized in good yields by the methylation of petasalbin, **1**, with methanol in the presence of acetic acid, and by Treibs' method[4,5] *via* sultone (**7**) from fukinone (**6**), respectively.

The dye-sensitized oxygenation of furanofukinin, **4**, in methanol gave a crystalline product, which showed



two spots on TLC (R_f, 0.40 and 0.20; benzene–ethyl acetate, 10 : 1) and which was then separated by fractional recrystallization from benzene to afford two hydroperoxides, (**8a**) (mp 116.0—117.0 °C (dec)) and (**8b**) (mp 136.0—137.0 °C (dec)). Both hydroperoxides have the same molecular formula, $C_{17}H_{28}O_5$, and both are positive to a peroxide test (KI–AcOH). They showed similar spectra characteristic of hydrperoxide groups: δ 11.30 (s) and 11.29 (s); IR(KBr): 3380 and 3350 cm^{-1}. Upon treatment with acetic anhydride–pyridine, the mixture of hydroperoxides, **8a,b**, gave, quantitatively, an epimeric mixture of 6β,8α-dimethoxyepieremophilenolide[6] (**9a**) (mp 132.5—133.5 °C) and 6β,8β-dimethoxyeremophilenolide (**9b**) (mp 123.0—123.5 °C) through dehydration. Subsequently each lactone was isolated by fractional recrystallization from benzene.

The stereochemistry of the hydroperoxides, **8a,b**, and the corresponding lactones, **9a,b**, can be readily determined as follows according to the previously outlined generalization.[1] The formation and the stereochemistry of the hydroperoxides, **8a,b**, can be well demonstrated by the use of the approved mechanism on the basis of the known oxygenation mode[1,7] of a furan moiety in methanol. Then, with the aid of the Dreiding model, it is evident that the introduced 8α- and 8β-methoxyl groups force the molecules to adopt exclusively non-steroidal (**A**) and steroidal (**B**) A/B *cis* chair/chair configurations respectively (*cf.* Fig. 1). Therefore, the non-steroidal 8α- (**A**) and steroidal 8β-isomers (**B**) have *cis-anti-cis* and *cis-syn-cis*-type ring-fusion systems, and they will tend to possess *trans* and

Table 1. Comparison of the chemical shifts (δ), specific rotations, and R_f values of the corresponding isomers

Compound [mp]°C	Solvent[a]	15-Me	14-Me	13-Me	6-H	$[\alpha]_D^\circ$ c) MeOH d) CHCl	R_f d) $CHCl_3$
8a [116—117]	A	0.78 s	0.96 d J=7.5	1.87 d J=1.5	4.20 q J=1.5	−54[c]	0.40[b]
8b [136—137]	A	1.02 s	0.78 d J=5.3	1.85 s	3.88 s	+13.4[c]	0.20[b]
9a [132.5—133.5]	B	0.75 s	0.96 d J=7.5	1.90 d J=1.8	4.28 q J=1.8	−185[d]	0.80[b]
9b [123—123.5]	B	0.99 s	0.75 d	1.81 s	3.89 s	+170[d]	0.70[b]
10a [123.5—124]	A	0.80 s	0.98 d J=6.0	1.71 d J=1.2		−15.2[c]	0.40[b]
10b [120.5—121]	A	0.98 s	0.80 d J=6.0	1.74 d J=1.2		+2.9[c]	0.40[b]
11a [110.5—111.5]	B	0.77 s	0.98 d J=7.0	1.76 d J=1.5		−168[d]	0.78[d]
11b [98.5—99.5]	B	0.98 s	0.74 d J=6.0	1.76 d J=1.2		+164[d]	0.70[d]
17 [212—213.5]	A	1.04 s	0.80 d J=5.5	1.73 d J=1.6		+157[d]	

a) A: acetone-d_6; B: CCl_4. b) C_6H_6: AcOEt, 10 : 1. c) MeOH. d) $CHCl_3$.

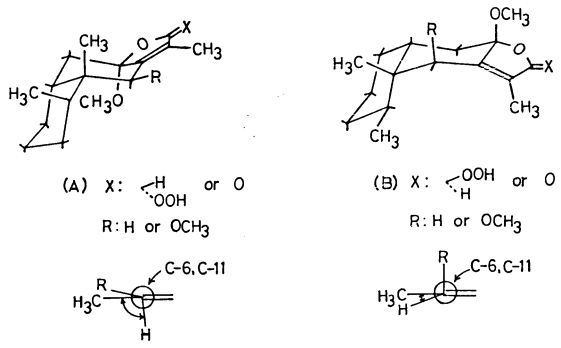


Fig. 1. Conformations of 8α- and 8β-methoxyl isomers, and the angles between 6-H and 13-CH_3.

cis characters respectively, depending on the molecular volume and the symmetric factor.[8]

Next, furanoeremophilane, **5**, lacking a C-6 substituent, was photooxygenated by a method similar to that described above to yield a single spot on TLC; it was nevertheless separated to furnish two hydroperoxides, (**10a**) (mp 123.5—124.0 °C (dec)) and (**10b**) (mp 120.5—121.0 °C (dec)), by careful recrystallization from light petroleum. Subsequently, the correspoding lactones, (**11a**) (mp 110.5—111.5 °C) and (**11b**) (mp 98.5—99.5 °C), were obtained from each hydrperoxide, **10a** or **10b**, by dehydration with acetic anhydride–pyridine, and also from the **10a,b** mixture by lactonization, followed by column chromatography and fractional recrystallization respectively. The stereochemistry of **10a,b** and **11a,b** can be settled in a similar manner; that is, the 8α- and 8β-isomers have non-steroidal (**A**) and steroidal (**B**) conformations (*cf.* Fig. 1).

Finally, the specified assignments to the 8α-(**A**) and 8β-(**B**) configurations between the two isomers were drawn by a comparison of the melting points, solubilities, adsorptive properties, specific rotations, and NMR spectra. In Table 1, the *cis*-like 8β-methoxy derivatives generally have lower melting points, higher solubilities, and stronger adsorptive properties than those of the *trans*-like 8α-isomers, in agreement with the well-known "von Auwers-Skita rule"[8] (*cf.* Experimental). There are, however, a few exceptions in which the 8β-methoxyl isomer, **8b**, has a higher melting point, together with a lower solubility, than the corresponding 8α-isomer, **8a**, much as in the relation between 6β-acetoxy-8α- and 6β-acetoxy-8β-methoxy lactones, **12a** and **12b**, described in the earlier work.[1]

In addition, in the NMR spectra of the hydroperoxides, **8a,b**, and the lactones, **9a,b**, only the 8α-methoxyl derivatives, **8a** and **9a**, exhibit homoallylic couplings[9] (1.0—1.8 Hz) between 6α-H and 13-CH_3, because the dihedral angle between the plane of the double bond—C-6–C-13— and the 6α-H is around 90°, as shown by an inspection of the configuration (**A**) with the Dreiding model (Fig. 1), whereas 8β-isomers do not show these couplings between 6α-H and 13-CH_3, all lying around 20° (*cf.* Fig. 1 and Table 1). Furthermore, the 8α-methoxy compounds showed the chemical shifts due to 14-methyls at a lower field than those due to 15-methyls; this relation of the chemical shifts between 14- and 15-methyls is reversed in the 8β-series (*cf.* Table 1). These variations in the chemical shifts may be explained similarly in terms of the effect due to the alteration in the geometry of the skeleton observed in the steroid field— by bending rings away from the angular methyl group, or by blocking the angular methyl's view over the remaining skeleton the methyl signal may cause a downfield shift.[10] On the other hand, 8β-methoxyl compounds have stronger positive rotations than the corresponding isomers. This can be expected from the helicities[1] derived from dihydrofuran/ring A fusion. The helicity was clarified by ORD-CD study in the 6-oxo derivatives of **3a** and **3b**.

All the derivatives, **10a,b** and **11a,b**, transformed

from furanoeremophilane, **5**, showed the signals due to 13-methyls with homoallylic couplings in their NMR spectra: δ 1.71 and 1.74 (each d, J=1.2 Hz) in **10a** and **10b**, and 1.76 and 1.76 (each d, J=1.2 and 1.5 Hz) in **11a** and **11b**. These couplings are obviously the expected ones between 6α-protons and 13-methyls in 8α-methoxyl compounds, and between 6β-protons and 13-methyls in 8β-isomers, as a consideration of the angles with the Dreiding model shows (Fig. 1).

Thus, summarizing the above results, the generalization outlined in the previous paper[1] was found also to be applicable to the configurational assignments of the hydroperoxides, **8a**,**b** and **10a**,**b**, and the lactones, **9a**,**b** and **11a**,**b**, prepared from furanofukinin, **4**, and furanoeremophilane, **5**.

On alkaline hydrolysis, a mixture of dimethoxy lactones, **9a**,**b**, gave a sole product, $C_{15}H_{20}O_3$ (mp 95.0—96.0 °C), which was identical with the expected unsaturated acid (**13**)[1] previously prepared by alkaline hydrolysis from a mixture of 6β-acetoxy-8(α and β)-methoxy lactones **12a**,**b**. On the other hand, a mixture of **11a**,**b** was treated with 1.5 M potassium hydroxide–methanol to yield also a sole product, $C_{15}H_{22}O_3$ (mp 212.0—213.5 °C), in a good yield: this product showed spectra suggesting the presence of a hydroxyl group and an α,β-unsaturated γ-lactone group: 3565, 3330 (OH), and 1745, 1697 cm^{-1} (unsaturated γ-lactone C=O), and an UV maximum at 222 nm. The structure of this lactone was easily inferred from its NMR spectrum, closely similar to that of the natural eremophilenolide (**14**)[11] except for the absence of the signal due to 8-H. Moreover, the lactone revealed a steroidal character—the chemical shift due to 14-methyl is higher than that due to 15-methyl in the NMR spectrum, and it showed a strong positive rotation (Table 1). The above conclusion can be further supported by the similar feature observed in the known natural eremophilenolides with 8β-substituents (a hydrogen or a hydroxyl) other than a methoxyl group. The specific rotations and the chemical shifts of 15- and 14-methyls in the spectra of eremophilenolide, **14**, 6β-hydroxyeremophilenolide (**15**), and 6β,8β-dihydroxyeremophilenolide (**16**) are as follows; **14**: $[\alpha]_D^{20}$+16.6° (c, 3.67, $CHCl_3$),[12,13] δ 1.01 (s) and 0.78 (br d);[11] **15**: $[\alpha]_D^{24}$+205.8° (c, 1.021, $CHCl_3$), δ 1.11 (s) and 0.78 (non-resolved methyl signal);[14] **16**: $[\alpha]_D^{19}$+169° (c, 0.985, $CHCl_3$), δ 1.11 (s) and 0.78 (non-resolved methyl signal).[1] Thus, the lactone can be represented as in the formula (**17**) with a steroidal configuration (**B**). Compound **17** has previously been derived as the by-product from the autoxidation of furanoeremophilane, **5**, by Šorm *et al.*[15]

Experimental

The IR, UV, and mass spectra were taken with Hitachi EPI-G3, Cary 14, and Hitachi RMU-6 spectrophotometers respectively. The NMR spectra were recorded with a Hitachi R-20B (60 MHz) spectrophotometer, and the chemical shifts are reported in δ-values (with TMS as the internal reference). The optical rotations were measured with a Perkin-Elmer 141 polarimeter. The TLC were run on Kieselgel G (Merck).

Synthesis of Furanofukinin (4). Petasalbin, **1** (492 mg), was dissolved in a solution of methanol (10 ml) and acetic acid (0.5 ml), and then left for three days at room temperature. After the removal of the solvent *in vacuo* and dilution with water, the reaction product was extracted with ether. Subsequent working-up as usual gave a crude product as a yellow oil (477 mg), which was purified by column chromatography on alumina (10 g, grade IV), with light petroleum–ether (100 : 1) as the eluent, and by vacuum-distillation to give furanofukinin (**4**) as a colorless oil; bp 96.0—106.0 °C (bath temperature)/6×10^{-3} mmHg. This was identical in all respects with the natural specimen.[2]

Synthesis of Furanoeremophilane (5) via Sultone (7) from Fukinone (6). *Sultone (7)*: Concentrated sulfuric acid (d= 1.84, 1.91 g) was stirred, drop by drop, into acetic anhydride (5.15 g) under ice-cooling below −10 °C, and then fukinone, **6** (3.34 g) ,was added to the stirred solution over a period of 15 min under continued cooling. After stirring for a further 1.5 h, the mixture was left for 38 h at −8 °C—−4 °C and for 1 h at room temperature. The subsequent addition to the reaction mixture of cracked ice (*ca.* 1 g) and a solution of sodium hydroxide (0.89 g) in water (1.6 ml) deposited yellowish brown crystals, which were filtered and washed with water. The crude product (3.0 g, 70%) was recrystallized from ethyl acetate to afford a sultone (**7**) as colorless prisms; mp 187.5—188.0 °C; UV: λ_{max}^{MeOH} 275.2 nm (ε, 4330); IR (KBr): 1653, 1578, 1195, 1085, 865 cm^{-1}; NMR ($CDCl_3$): 6.24 (m, 12-H), 1.96 (d, J=1.0 Hz, 13-CH_3), 0.89 (s, 15-CH_3), 0.87 (d, J=6.3 Hz, 14-CH_3).

Found: C, 63.59; H, 7.90; S, 11.38%. Calcd for $C_{15}H_{22}O_3S$: C, 63.80; H, 7.85; S, 11.35%.

Furanoeremophilane (5): A mixture of the sultone, **7** (497 mg), and zinc oxide (500 mg) was subjected to pyrolytic distillation. The distillate was collected in a 10% potassium hydroxide aqueous solution (0.3 ml) and then extracted with ether. The ethereal extract was washed with a saturated sodium hydrogencarbonate solution and then with water, and dried over anhydrous sodium sulfate. The subsequent evaporation of the solvent gave crude furanoeremophilane (**5**) as an oil (360 mg, 94%), which was purified by vacuum-distillation (bp 67—100 °C (bath temperature)/0.15 mmHg) to furnish a pure specimen (297 mg, 77%) and subsequently by GLC to obtain an analytical sample (PEG 20 M, 2.6 m; column temperature, 175 °C; H_2-flow rate, 60 ml/min; retention time, 8.8 min); IR (film): 1641, 1560, 1145, 1087, 985 cm^{-1}; $[\alpha]_D^{23}$ −13.2 °C (c, 1.0, $CHCl_3$).

Found: C, 82.35; H, 10.21%. Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.16%. This compound was identical in all respects (IR, NMR, GLC, and specific rotation) with the natural specimen.[2]

Photosensitized Oxygenation of Furanofukinin (4). A solution of furanofukinin, **4** (770 mg), and Rose Bengal (30 mg) in methanol (300 ml) was irradiated with a circular fluorescent lamp (30 watt) for 1 h under the bubbling of air. After the subsequent removal of the solvent *in vacuo*, the residue was taken up with benzene. The benzene extract was washed with water and then passed through a filter filled with anhydrous sodium sulfate for drying and taking off the dye-stuff. The removal of the solvent *in vacuo* gave a colorless solid, which showed two spots on TLC (R_f, 0.40 and 0.20; benzene–ethyl acetate, 10 : 1) and which was separated into two hydroperoxides, (**8a**) and (**8b**), by careful fractional crystallization from benzene. The **8b** compound was less soluble than **8a** in benzene.

Hydroperoxide (8a): Mp 116.0—117.0 °C (dec) as colorless prisms, $[\alpha]_D^{24}$ −54 °C (c, 1.0, MeOH); IR(KBr): 3380, 1300, 1140, 1090, 960 cm^{-1}; NMR (acetone-d_6): 11.30 (s, OOH), 5.68 (s, 12-H), 4.20 (q, J=1.5 Hz, 6-H) 3.43 and 3.17 (each s, 6- and 8-OCH_3), 1.87 (d, J=1.5 Hz, 13-CH_3),

0.96 (d, J=7.5 Hz, 14-CH_3), 0.78 (s, 15-CH_3).

Found: C, 65.43; H, 9.05%. Calcd for $C_{17}H_{28}O_5$: C, 65.36; H, 9.03%.

*Hydroperoxide (**8b**)*: Mp 136.0—137.0 °C (dec) as colorless needles, $[\alpha]_D^{24}$ +13.4° (*c*, 1.12, MeOH); MS: *m/e* 294 (M^+-H_2O), 154 (base peak); IR(KBr): 3350, 1280, 1200, 1080, 1050, 970 cm^{-1}; NMR (acetone-d_6): 11.29 (s, OOH), 5.73 (s, 12-H), 3.88 (s, 6-H), 3.27 and 3.11 (each s, 6- and 8-OCH_3), 1.85 (s, 13-CH_3), 1.02 (s, 15-CH_3), 0.78 (d, J= 5.3 Hz, 14-CH_3).

Found: C, 65.34; H, 8.97%. Calcd for $C_{17}H_{28}O_5$: C, 65.36; H, 9.03%.

*6β,8α-Dimethoxyepieremophilenolide (**9a**) and 6β,8β-Dimethoxyeremophilenolide (**9b**)*. A mixture of hydroperoxides **8a**, **b** (527 mg) was dissolved in pyridine (4 ml) and acetic anhydride (1 ml) and then left overnight at room temperature. Subsequent working-up as usual gave a colorless solid (480 mg), which was subjected to fractional crystallization from light petroleum to deposit a less soluble isomer (**9a**) (143 mg) and then an epimer (**9b**) (48 mg). In addition, the two hydroperoxides, **8a** (9 mg) and **8b** (15 mg), were transformed into the corresponding lactones, **9a** (6 mg) and **9b** (10 mg).

*6β,8α-Dimethoxyepieremophilenolide (**9a**)*: Mp 132.5—133.5 °C, colorless needles, $[\alpha]_D^{25}$ −185° (*c*, 0.80, $CHCl_3$); UV: λ_{max}^{MeOH} 224 nm (ε, 13700); IR ($CHCl_3$): 1750, 1300, 1100, 960, 920, 900 cm^{-1}; NMR (CCl_4): 4.28 (q, J=1.8 Hz, 6-H), 3.40 and 3.13 (each s, 6- and 8-OCH_3), 1.90 (d, J= 1.8 Hz, 13-CH_3), 0.96 (d, J=7.5 Hz, 14-CH_3), 0.75 (s, 15-CH_3).

Found: C, 69.39; H, 8.85%. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90%.

*6β,8β-Dimethoxyeremophilenolide (**9b**)*: Mp 123.0—123.5 °C, colorless prisms, $[\alpha]_D^{25}$ +170° (*c*, 1.0, $CHCl_3$); UV: λ_{max}^{MeOH} 220.5 nm (ε, 7600); IR($CHCl_3$): 1760, 1320, 1100, 1085, 995, 975, 920 cm^{-1}; NMR(CCl_4): 3.89 (s, 6-H), 3.25 and 3.06 (each s, 6- and 8-OCH_3), 1.81 (s, 13-CH_3), 0.99 (s, 15-CH_3), 0.75 (d, J=5.5 Hz, 14-CH_3).

Found: C, 69.44; H, 8.78%. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90%.

*Photosensitized Oxygenation of Furanoeremophilane (**5**)*. A stirred solution of furanoeremophilane, **5** (560 mg), and Rose Bengal (30 mg) in methanol (300 ml) was irradiated with a circular fluorescent lamp (30 watt) for 1 h under the bubbling of air. A subsequent working-up as has been described above gave a colorless crystalline mixture of hydroperoxides, which showed a single spot on TLC (R_f, 0.40, benzene–ethyl acetate, 10 : 1). The mixture was separated by fractional crystallization from benzene to deposit the less soluble 8α-epimer (**10a**) (181 mg) first, and then the 8β-epimer (**10b**) (167 mg) from the mother liquors.

*Hydroperoxide (**10a**)*: Mp 123.5—124.0 °C (dec) as colorless needles, $[\alpha]_D^{24}$ −15.2° (*c*, 1.0, MeOH); MS: *m/e* 264 (M^+-H_2O), 109 (base peak); IR(KBr): 3300, 1700, 1130, 1040, 960, 860 cm^{-1}; NMR (acetone-d_6): 11.20 (s, OOH), 5.70 (s, 12-H), 3.07 (s, OCH_3), 1.71 (d, J=1.2 Hz, 13-CH_3), 0.98 (d, J=6.0 Hz, 14-CH_3), 0.80 (s, 15-CH_3).

Found: C, 68.03; H, 9.24%. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28%.

*Hydroperoxide (**10b**)*: Mp 120.5—121.0 °C (dec) as colorless prisms, $[\alpha]_D^{24}$ +2.9° (*c*, 1.01, MeOH); MS: *m/e* 264 (M^+-H_2O), 109 (base peak); IR(KBr): 3300, 1710, 1160, 1070, 970, 920 cm^{-1} ;NMR (acetone-d_6): 11.21 (s, OOH), 5.73 (s, 12-H), 3.06 (s, OCH_3), 1.74 (d, J=1.2 Hz, 13-CH_3), 0.98 (s, 15-CH_3), 0.80 (d, J=6.0 Hz, 14-CH_3).

Found: C, 68.03; H, 9.30%. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28%.

*8α- and 8β-Methoxy Lactones, (**11a**) and (**11b**)*. A colorless crystalline mixture of hydroperoxides, **10a**,**b**, prepared from furanoeremophilane, **5** (455 mg), was dissolved in pyridine (1 ml) and acetic anhydride (2 ml) and then left overnight at room temperature. A subsequent working-up in the usual manner gave an oil (524 mg) which showed two spots on TLC (R_f, 0.78 and 0.70, $CHCl_3$) and which was then chromatographed over silica gel (12 g). Elution with light petroleum–ether (50 : 1) and subsequent fractional recrystallization from light petroleum gave 8α-methoxy lactone (**11a**) (130 mg) at first, and the 8β-epimer (**11b**) was obtained from the mother liquors.

*8α-Methoxyepieremophilenolide (**11a**)*: Mp 110.5—111.5 °C, colorless prisms, $[\alpha]_D^{24}$ −168° (*c*, 0.95, $CHCl_3$); UV: λ_{max}^{MeOH} 227 nm (ε, 12500); IR(KBr): 1750, 1690, 1310, 940 cm^{-1}; NMR(CCl_4): 3.05 (s, OCH_3), 1.76 (d, J=1.5 Hz, 13-CH_3), 0.98 (d, J=7.0 Hz, 14-CH_3), 0.77 (s, 15-CH_3).

Found: C, 72.59; H, 9.20%. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15%.

*8β-Methoxyeremophilenolide (**11b**)*: Mp 98.5—99.5 °C, colorless needles, $[\alpha]_D^{24}$ +164° (*c*, 1.08, $CHCl_3$); UV: λ_{max}^{MeOH} 225 nm (ε, 11500); IR(KBr): 1750, 1690, 1170, 990 cm^{-1}; NMR (CCl_4): 2.99 (s, OCH_3), 1.76 (d, J=1.2 Hz, 13-CH_3), 0.98 (s, 15-CH_3), 0.74 (d, J=6.0 Hz, 14-CH_3).

Found: C, 72.65; H, 9.27%. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15%.

*Unsaturated Acid (8-Oxo-eremophila-6,11-dien-12-oic Acid) (**13**)*.[1] A mixture of dimethoxy lactones, **9a**,**b** (200 mg), was dissolved in methanol (10 ml) and 1.84 M potassium hydroxide–methanol (8 ml) and then left for 36 h. After the removal of the solvent and dilution with water, the solution was acidified with 10% sulfuric acid and then extracted with ether. A subsequent working-up as usual gave an acid (198 mg) as a colorless oil, which was recrystallized from diisopropyl ether–light petroleum to afford the pure acid (**13**) (mp 95.0—96.0 °C). The acid, **13**, was found by a mixed-melting point determination and a comparison of the IR spectra to be identical with the 8-oxo-eremophila-6,11-dien-12-oic acid prepared from a mixture of 6β-acetoxy-8(α and β)-methoxy lactones, **12a**,**b**.[1]

*8β-Hydroxyeremophilenolide (**17**)*. A mixture of 8α- and 8β-methoxy lactones, **11a**,**b** (53 mg), was dissolved in a 1.5 M potassium hydroxide–methanol solution (1.3 ml) and then left for 3 h at room temperature. After the evaporation of the solvent *in vacuo* and acidification with 10% sulfuric acid, the reaction mixture was extracted with ether, washed with water, and dried. The removal of the solvent gave a semi-crystalline product (59 mg), which was subsequently recrystallized from methanol–diisopropyl ether to afford 8β-hydroxyeremophilenolide (**17**) (25 mg) as colorless prisms; mp 212.0—213.5 °C, $[\alpha]_D^{20}$ +157° (*c*, 0.69, $CHCl_3$); UV: λ_{max}^{MeOH} 222 nm (ε, 9200); MS: *m/e* 250 (M^+), 91 (base peak); IR($CHCl_3$): 3565, 3330, 1745, 1697 cm^{-1}; NMR (acetone-d_6): 5.90 (br s, OH), 2.83 (d, J=13.5 Hz, 6-CH_2), 1.73 (*d*, J=1.6 Hz, 13-CH_3), 1.04 (s, 15-CH_3), 0.80 (d, J=5.5 Hz, 14-CH_3).

Found: C, 71.93; H, 8.70%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%.

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