

SEVEN FURANOEREMOPHILANES FROM THREE *SENECIO* SPECIES*

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Abstract—The investigation of two further *Senecio* species and the re-investigation of *S. inaequidens* afforded, in addition to known compounds, seven new furanoeremophile derivatives. Six of these are closely related to cacalol, a sesquiterpene type which predominates in the species investigated.

INTRODUCTION

The large genus *Senecio* (tribe Senecioneae, Compositae) has been investigated chemically in some detail. A large variety of sesquiterpenes are present in this genus [1]. However, there are still problems concerning the delimitation of species groups within the genus [2]. We, therefore, have studied two further species and re-investigated a third. Again the overall picture is one similar to that of other species within this group. In addition to known compounds seven new ones were isolated, all being derivatives of the widespread furanoeremophilanes.

RESULTS AND DISCUSSION

A re-investigation of a large amount of roots from *S. inaequidens* DC. afforded, in addition to the constituents isolated before [3, 4], α - and β -farnesene, isohumulene (1), curcumene (2), cacalol (13) and four further compounds, which were new. The least polar one most probably is the ketone 12; its structure follows from the spectroscopic data, though the ^1H NMR spectrum (see Experimental) is not very conclusive, as in similar *cis*-fused compounds [4]. The absence of any low field signal except that of 12-H, however, indicates a 10β -position for the isovaleryloxy group, its presence clearly following from the NMR data (2.23 d (br), 2.12 m , 0.94 d). The 9-keto group give a typical IR band at 1685 cm^{-1} and a UV maximum at 275 nm. The relative chemical shifts of 14- and 15-H are characteristic of a *cis*-decalin derivative. A second compound, obviously, is the acetate 29, its ^1H NMR data being very similar to those of the known angelicate 27 [4] (Table 1). A further angelicate is the cacalol derivative 18. The ^1H NMR spectrum (Table 1) clearly indicates the presence of a hydrogen-bonded β -hydroxy ketone (12.97 s). Double resonance experiments allow the assignment of all signals. In agreement with a model, only the α -configuration of the

2-angeloyloxy residue is likely, as the coupling $J_{3,4}$ indicates a conformation with a quasi-axial 4-methyl group. This, however, also leads to an axial orientation of 2β -H, which is needed to explain the large coupling $J_{2,3}$.

The most polar fractions contain an unusual compound, which obviously also is a benzofuran. High resolution mass spectroscopy gives the molecular formula $C_{17}H_{18}O_7$. The IR spectrum only indicates a hydroxyl and a carbonyl group. The frequency of the latter (1755 cm^{-1}) shows that most probably a lactone is present. The ^1H NMR signals indicate two different methoxyl groups, an aliphatic and an aromatic methyl, a β -methylfuran moiety and two doublets at 4.66 and 3.17 ppm ($J = 7\text{ Hz}$), which must be due to a secondary hydroxyl, as shown by deuterium exchange. Acetylation leads to an acetate, its ^1H NMR spectrum being only slightly different from that of the alcohol. However, the chemical shift of the aliphatic methyl indicates a position very near to the acetate group. If a lactone is present, one oxygen function would still be missing. Reduction with lithium aluminium hydride leads to a compound, molecular formula $C_{16}H_{18}O_5$, its ^1H NMR spectrum indicating the structure 34b, which must be formed by reduction of 33a through the intermediate 34a. Careful inspection of the ^1H NMR of 34b (Table 1) in connection with models indicates the stereochemistry given in the conformation 34c. This would explain the high-field shift of 2-H by the shielding effect of the aromatic ring and is in agreement with the observed couplings. Also the mass spectral behaviour supports the proposed structures; both 33a and 33b show a base peak $m/e 245$, which most probably is 35. 33a, which we have named senaequidolide, is surely an oxidation product of a cacalol derivative.

The roots of *Senecio balsapampae* Cuatr., collected in Ecuador, contain 2, β -zingiberene (3), the furanoeremophilanes 10 [5] and 11 [6], cacalol (13) and its oxidation products 15 and 16 [7]. Furthermore, a ketone is present, which turns out to be 17. In the ^1H NMR spectrum (Table 1) the characteristic down-field signal of 9-H is visible. The methyl singlet at 1.60 ppm indicates the hydroxyl function at C-6. Though signals of the protons at C-2 through C-5

* Part 294 in the series "Naturally Occurring Terpene Derivatives". For Part 293 see Bohlmann, F., Jakupovic, J., Ahmed, M., Grenz, M., Suding, H., Robinson, H. and King, R. M. (1980) *Phytochemistry* 19, (in press).

Table 1. ^1H NMR data of **17**, **18**, **24**, **29**, **31**, **32**, **33a**, **33b** and **34b**

	17	18	24	29	31*	32*	33a	33b	34b
1-H	—	—	7.14 d	6.93 dd	8.29 dd 2.93 ddd 2.59 ddd	8.27 dd 2.78 d(br.) 2.5 m	—	—	6.32 s
2-H	2.64 m 2.98 m	6.05 dd	6.15 dd(br.)	5.94 dd	7.31 dd 1.8 m	7.29 dd 1.75 m	—	3.24 dd 2.80 dd	
3-H	2.46 ddd 2.30 ddd	4.11 d(br.)	2.55 dddd 2.24 ddd	7.22 d(br.)	—	7.22 d(br.)	4.66 d	5.61 s	3.99 dd
4-H	1.80 m	3.58 ddq	3.59 q(br.)	3.34 dq(br.)	—	3.21 ddq	—	3.21 ddq	—
9-H	7.53 s	—	—	—	—	—	—	—	—
12-H	7.42 q	7.51 q	7.39 q	7.36 q	7.44 q	7.43 q	7.48 q	7.51 q	7.39 q
13-H	2.25 d	2.41 d	2.34 d	2.33 d	2.29 d	2.12 s	2.30 d	2.04 s	2.40 d
14-H	1.60 s	2.54 s	5.47 d 5.41 d	1.11 d	4.99 s(br.)	2.49 s	4.99 s(br.)	2.51 s	2.65 s
15-H	1.40 d	1.45 d	1.80 d	5.43 d 5.37 d	2.85 s(br.)	1.18 d	2.87 s(br.)	1.17 d	1.85 s
OCOR	—	6.19 qq 2.08 dq 2.00 dq	5.70 qq 2.20 d 1.88 d	—	—	—	—	1.88 s	—
OMe	—	—	4.18 s	4.13 s	4.31 s	—	4.29 s	—	4.35 s 3.86 s
OH(OAc)	—	12.97 s	—	—	4.85 s	—	2.15 s	3.17 d	—

* Values of $1'$ – $15'$.

J (Hz): **17**: 4.15 = 7; 12.13 = 1.3; (5-H 2.80 m); **18**: 2,3 = 13; 2,3' = 5.5; 3,3' = 12.5; 3,4 = 12; 3',4 = 2.5; 4,15 = 7; 12.13 = 1.3; OAng: 3',4' = 7; 3',5' = 4',5' = 1.5; **24**: 1.2 = 9; 2,3 = 6; 3,4 = 1.7; 4,15 = 7; 12.13 = 1; 14,14' = 12; **30**: 1.2 = 10; 1,3 = 3.5; 2,3 = 2; 2,3' = 6.5; 3,3' = 16.5; 3,4 = 7; 3',4 = 1.5; 4,15 = 7; 12.13 = 1.3; 14,14' = 12; **31/32**: 1.2 = 8.5; 1,3 = 1.5; 2,3 = 7.5; 12.13 = 1.3; 1,1',2,1' = 15; 1,1',2,1' = 6; 1,1',2,1' = 2; 1,2',2' = 9; 3',4' = 7; 3,2',4' = 3; 4',15' = 7; **33a/b**: 12.13 = 1; (**33a**; 3,0H = 7); **34**: 2,2' = 11; 2,3 = 5.5; 2',3 = 10; 12.13 = 1.

are not first order, decoupling experiments support the proposed structure. We have named **17** isocacalone. The aerial parts also afforded **2**, **3**, **10**, **11**, **13**, **15** and **16**.

The roots of *S. trichopterygius* Muscher, native in central Africa, however, grown from seeds, afforded the endoperoxide **4** [8], the diterpene **9** [9], the known cacialol derivatives **13** [10], **14** [10], **19** [11], **20** [12], **21** [12], **22** [13], **23** [4], **25** [13], **26** [14], **29** and **30** [1], as well as the senecioylate **24**, its structure clearly following from the ^1H NMR data (Table 1), very similar to those of **23**. Finally, a further dimeric cacialol derivative was isolated, the dihydro compound **31** of a dimer isolated before [13], assignment of which follows from the ^1H NMR data. The position of the free phenolic OH group was established from the ^1H NMR data of the corresponding acetate **32** (Table 1), only the signals of $1'$ -H being shifted when compared with the chemical shifts of **31**. The aerial parts contain germacrene D (**5**), ocimene (**6**), eugenol (**7**), the germacrane derivative **8** [15] and the cacialol derivatives **19**, **23**, **24** and **27** [4]. The overall picture of the three species investigated shows that they are probably closely related.

EXPERIMENTAL

^1H NMR: 270 MHz, TMS as int. standard; MS: 70 eV, direct inlet; optical rotation: CHCl_3 . The plant material was extracted with Et_2O -petrol (1:2) and the resulting extracts were first

separated by column chromatography (SiO_2 , act. grade II) and further by repeated TLC (SiO_2 , GF 254). Known compounds were identified by comparison of the IR and ^1H NMR spectra with those of authentic compounds.

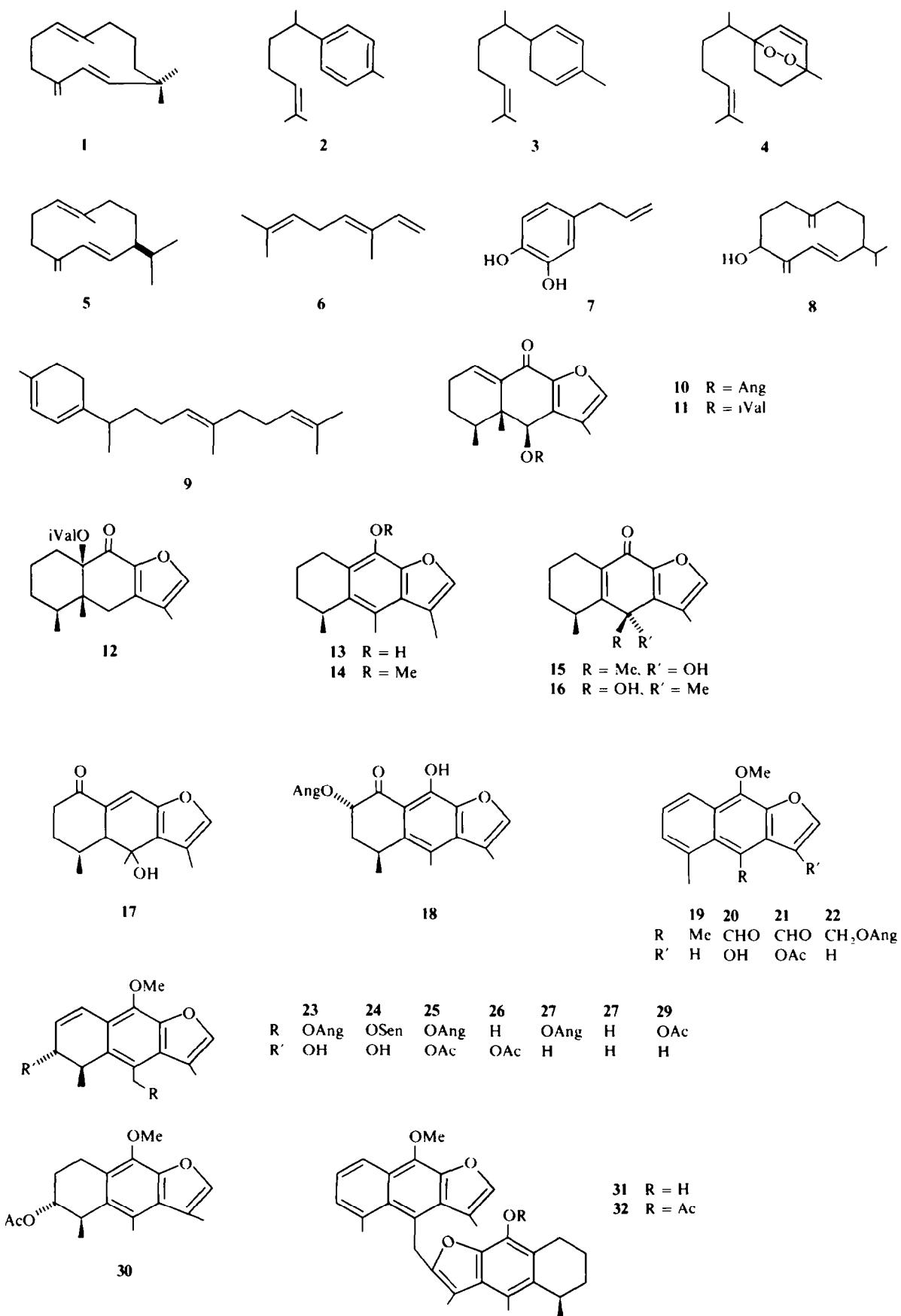
Senecio inaequidens (collected near Bremen). Air-dried roots (2 kg) afforded, in addition to previously isolated compounds, 5 mg α -, 5 mg β -farnesene, 10 mg 1, 5 mg **2**, 10 mg **12** (Et_2O -petrol, 1:4), 15 mg **13**, 20 mg **18** (Et_2O -petrol, 1:1) and 5 mg **33a** (Et_2O).

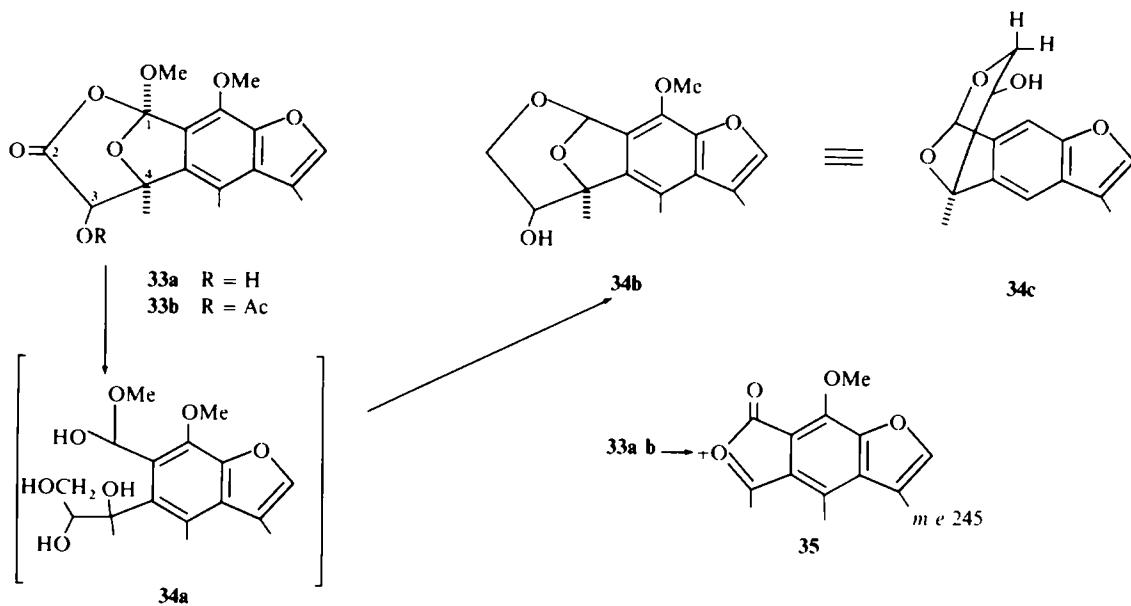
Senecio balsapampae (voucher RMK 7915). The roots (300 g) afforded 2 mg **2**, 2 mg **3**, 15 mg **10**, 25 mg **11**, 40 mg **13**, 6 mg **15**, 5 mg **16** and 5 mg **17** (Et_2O -petrol, 1:3), while the aerial parts (700 g) gave 10 mg **2**, 5 mg **3**, 3 mg **10**, 15 mg **11**, 20 mg **13**, 5 mg **15** and 5 mg **16**.

Senecio trichopterygius (voucher 79/1415, from seeds, Botanical Garden Liège). The roots (1 kg) afforded 10 mg **4**, 120 mg **9**, 10 mg **13**, 3 mg **14**, 200 mg **19**, 20 mg **20**, 30 mg **21**, 3 mg **22**, 60 mg **23**, 10 mg **24** (Et_2O -petrol, 1:1), 3 mg **25**, 10 mg **26**, 10 mg **29**, 10 mg **30** and 5 mg **31** (Et_2O -petrol, 1:1), while the aerial parts (1.5 kg) gave 15 mg **5**, 5 mg **6**, 10 mg **8**, 20 mg **7**, 5 mg **19**, 150 mg **23**, 5 mg **24** and 10 mg **27**.

10 β -Isovaleryloxy-furanoeremophil-9-one (**12**). Colourless oil, IR $\nu_{\text{max}}^{\text{CIR}}$ cm^{-1} : 1735 (CO_2R), 1685 (conj. ketone); MS: M^+ m/e (rel. int.): 332.199 (31) ($\text{C}_{20}\text{H}_{28}\text{O}_4$); 248 (100) ($M - \text{O}=\text{C}=\text{CHCHMe}_2$); 230 (28) ($M - \text{RCO}_2\text{H}$); 85 (72) ($\text{C}_4\text{H}_9\text{CO}^+$).

$$[\alpha]_{D}^{24} = \frac{589}{-48.1} \frac{578}{-49.6} \frac{546}{-57.7} \frac{436 \text{ nm}}{-112.3} (c = 0.26).$$





Isocacalone (17). Colourless oil, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 3600 (OH), 1675 (conj. ketone), 1630, 1600 (C=C); MS: M⁺ m/e (rel. int.): 246.126 (51) (C₁₅H₁₈O₃); 231 (100) (M - Me).

$$[\alpha]_{24}^{\text{d}} = \frac{589}{+48} - \frac{578}{+52} - \frac{546}{+65} - \frac{436 \text{ nm}}{+201} \quad (c = 0.1).$$

2a-Angeloyloxy-1-oxocacalol (18). Colourless oil, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 3500-2800 (OH), 1720 (C=CCO₂R), 1650, 1625, 1590 (hydrogen-bonded PhCO); MS: M⁺ m/e (rel. int.): 342.147 (71) (C₂₀H₂₂O₅); -O=C=C(Me)CH=CH₂; 260 (100); 83 (62) (C₄H₇CO⁺).

$$[\alpha]_{24}^{\text{d}} = \frac{589}{-34.3} - \frac{578}{-36.0} - \frac{546 \text{ nm}}{-44.6} \quad (c = 0.82).$$

3a-Hydroxy-14-senecioyloxy-1,2-dehydrocacalol methyl ether (24). Colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 3590 (OH), 1710 (C=CCO₂R); MS: M⁺ m/e (rel. int.): 356.162 (24) (C₂₁H₂₄O₅); 338 (28) (M - H₂O); 256 (34) (M - RCO₂H); 239 (100) (338 - RCO₂); 83 (31) (C₄H₇CO⁺).

$$[\alpha]_{24}^{\text{d}} = \frac{589}{-33.1} - \frac{578}{-36.2} - \frac{546}{-46.5} - \frac{436 \text{ nm}}{-70.8} \quad (c = 0.13).$$

14-Acetoxy-1,2-dehydrocacalol methyl ether (29). Colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 1740, 1225 (OAc); 1635, 1610, 1570 (C=C, aromatic); MS: M⁺ m/e (rel. int.): 300.136 (80) (C₁₈H₂₀O₄); 258 (100) (M - ketene); 243 (65) (258 - Me).

$$[\alpha]_{24}^{\text{d}} = \frac{589}{+28.5} - \frac{578}{+33.1} - \frac{546}{+40.0} - \frac{436 \text{ nm}}{+88.5} \quad (c = 0.13).$$

12-(Dehydrocacalohastin-14-yl)-cacalol (31). Colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 3590 (OH); 1515 (furan); MS: M⁺ m/e (rel. int.): 468.230 (100) (C₃₁H₃₂O₄); 453 (14) (M - Me)

$$[\alpha]_{24}^{\text{d}} = \frac{589}{+0.8} - \frac{578}{+1.2} - \frac{546 \text{ nm}}{+3.9} \quad (c = 0.26).$$

4 mg 31 were heated 3 hr in 0.1 ml Ac₂O at 70°. TLC (Et₂O-petrol, 1:1) afforded 3 mg 32, colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 1770

(PhOAc), 1515 (furan); MS: M⁺ m/e (rel. int.): 510 (1); 468 (2) (M - ketene); 43 (100) (MeCO⁺).

Senaequidolide (33a). Colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 3600 (OH); 1755 (lactone); MS: M⁺ m/e 334.105 (2) (C₁₇H₁₈O₇); 245.081 (100) (C₁₄H₁₃O₄); (M - Me, OOCCH(OH)). To 2 mg 33a in 1 ml CHCl₃, 5 mg 4-pyrrolidinopyridine [16] and 0.05 ml Ac₂O were added. After 2 hr, usual work-up afforded 2 mg 33b, colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 1750 (OAc, lactone); MS: M⁺ m/e (rel. int.): 376 (6); 332 (20) (M - CO₂); 245.081 (100) (C₁₄H₁₃O₄); (M - Me, O₂CCH(OAc)); Cl(isobutane); M + 1 377 (100%). To 2 mg 33a in 1 ml Et₂O 10 mg LiAlH₄ were added. After reaction for 1 hr, dil H₂SO₄ was added. TLC (Et₂O-petrol 1:1) afforded 1.3 mg 34b, colourless gum, IR $\nu_{\text{max}}^{\text{CCl}_4} \text{cm}^{-1}$: 3600 (OH); MS: M⁺ m/e (rel. int.): 290.000 (59) (C₁₆H₁₈O₅); 246 (95) (M - CH₂CH(OH)); 231 (100) (246 - Me); 203 (51) (231 - CO); 175 (15) (203 - CO).

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