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NEW FURANOEREMOPHILANES FROM SOUTH AFRICAN *SENECIO* SPECIES*

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Key Word Index—*Senecio inornatus*; *S. halimifolius*; *S. medley-woodii*; *S. inaequidens*; Compositae; furanoeremophilanes; benzofuranes; dihydroeuparine derivative.

Abstract—An investigation of South African *Senecio* species afforded in addition to previously known compounds three new furanoeremophilanes, six compounds derived from cacalol and a dihydroeuparin derivative. Structures were elucidated by spectroscopic methods and some chemical transformations. Chemotaxonomical aspects are discussed briefly.

INTRODUCTION

During the last three years we have investigated several representatives of the large genus *Senecio* [1, 2]. As a continuation of our studies of South African species we have now investigated some additional plants, all collected in Natal. The results confirm that furanoeremophilanes are very widespread in this genus.

RESULTS AND DISCUSSION

Senecio medley-woodii Hutch. was collected near St. Michels-on-Sea in Natal. The roots contained as the main constituent 10β-furanoeremophilane (**1**) [3] together with two further compounds, which have not been isolated before. The ^{1}H NMR data of the less polar compound showed it was a diester of **1**. A singlet at δ 2.04 (3H), a doublet at 1.22 (3H) ($J = 7$ Hz), a *tq* at 2.42 (2H) ($J = 7$ and 7) and a triplet at 0.94 (3H) ($J = 7$) clearly indicated the nature of the ester groups. Signals at 5.27 (1H, *ddd*, $J = 9, 4, 4$) and at 6.35 (*br s*) together with those typical for a furanoeremophilane (see Table 1) showed, that the ester groups were located at C-3 and C-6. Partial saponification afforded a compound with a 3β-hydroxyl and a 6β-(2-methylbutyric acid) ester. Therefore the diester had structure **2**. The *cis*-annelation followed from the observed coupling constants (see Table 1). The third compound was identified as the corresponding ketone **4**. As observed earlier [1, 2], it is only at elevated temperature that compounds of this type afford first order NMR spectra while at room temperature broad signals are observed. Partial saponification showed that the ester groups were in the same position as in **2** (Table 1). The aerial parts contained germacrene D (**6**) in addition to **1** and **2**.

The roots of *S. halimifolius* L., one of the succulent

Table 1. ^{1}H NMR signals of compounds **2**–**5** (270 MHz, δ-values, TMS as internal standard)

	2 ($CDCl_3$)	**3** ($CDCl_3$)	**4** (C_6D_6, 75°)	**5** (C_6D_6, 75°)
3α-H	5.27 *ddd*	4.35 *ddd*	5.00 *ddd*	3.63 *m*
4α-H	2.10 *m*	2.04 *m*	1.97 *m*	2.00 *m*
6α-H	6.35 *s*(*br*)	6.36 *s*(*br*)	6.37 *s*(*br*)	6.39 *s*(*br*)
9α-H	2.32 *d*(*br*)	2.26 *d*(*br*)	—	—
9β-H	2.84 *dd*(*br*)	2.87 *dd*(*br*)	—	—
10β-H	1.88 *m*	1.8 *m*	2.63 *dd*	2.62 *dd*
12-H	7.04 *s*(*br*)	7.05 *s*(*br*)	6.85 *s*(*br*)	6.84 *s*(*br*)
13-H	1.87 *d*	1.86 *d*	1.81 *s*(*br*)	1.82 *s*(*br*)
14-H	1.05 *s*	1.06 *s*	1.16 *s*	1.21 *s*
15-H	0.95 *d*	1.01 *d*	0.76 *d*	0.81 *d*
OAc	2.04 *s*	—	1.68 *s*	—
OCOR	2.42 *tq*	2.45 *tq*	2.26 *tq*	2.26 *tq*
	1.22 *d*	1.24 *d*	1.08 *d*	1.05 *d*
	0.94 *t*	1.02 *t*	0.78 *t*	0.80 *t*

J (Hz); **2** and **3**: $2\alpha,3\alpha = 3\alpha,4\alpha = 4$; $2\beta,3\alpha = 9$; $4\alpha,15 = 7$; $9\alpha,9\beta = 17$; $9\beta,10\beta = 6$; $12,13 = 1$; **4** and **5**: $1\alpha,10\beta = 7$, $1\beta,10\beta = 4$; $4\alpha,15 = 7$

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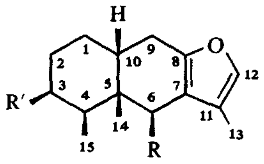
* Part 143 in the series "Naturally Occurring Terpene Derivatives", for part 142 see: Bohlmann, F., Mahanta, P. K., Jakupovic, J., Rastogi, R. C. and Natu, A. A. (1978) *Phytochemistry* **17**, 1165.

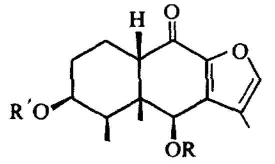
species contained in very minute amounts a furanoeremophilane, whose spectroscopic properties were very similar to those of **7** [4]. However the 6-H signal was shifted to considerably higher field. The only structure which agrees with this observation is **8**, the 6α-epimer of **7** (Table 2).

The aerial parts afforded **6**, **9**, **10** [5] and **13** [6] together with a further euparin derivative, with structure **11**, as shown by saponification of **10**, which yielded an alcohol identical with **11**.

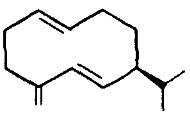
Senecio inaequidens DC has been investigated before [1, 2]. However, the material was grown from seeds. Reinvestigation of material collected from several places in Natal showed that there were some differences in the composition of the constituents. Most of the compounds isolated previously were found again. However, none of the acyl pyrroles reported before could be isolated. The aerial parts yielded in addition to the typical benzofurans **13**, **14**, **16** and **23** [1, 2, 6] three new ones. The structure of **15** was elucidated from the NMR spectral data, which were very similar to those of **14** (Table 2). The two other compounds could be



	1	**2**	**3**
R =	H	OMebu	OMebu
R' =	H	OAc	OH



4 *R* = Mebu, *R'* = Ac
5 *R* = Mebu, *R'* = *H*



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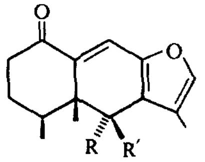
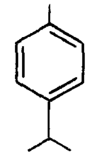


7 *R* = H, *R'* = OAng
8 *R* = OAng, *R'* = H



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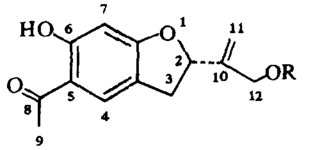
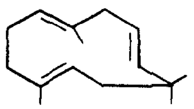


10 *R* = Ac
11 *R* = H



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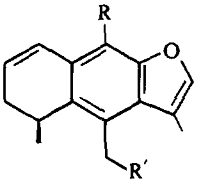
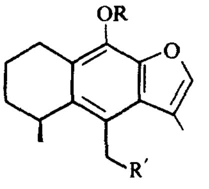
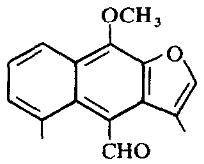


13 *R* = OCH_3, *R'* = H
14 *R* = OCH_3, *R'* = OAng
15 R = OCH_3, *R'* = OiVal
16 *R* = OCH_3, *R'* = OH



17 *R* = *R'* = H
18 *R* = OCOEt, *R'* = H
19 *R* = OCOEt, *R* = OAc
20 *R* = OCOEt, *R* = OH



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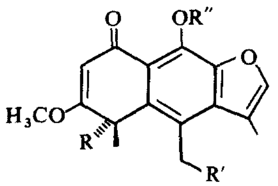
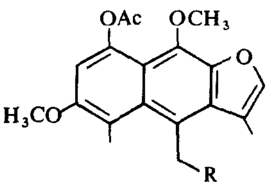


22 *R* = *R'* = *R''* = H
23 *R* = *R'* = H, *R''* = CH_3
24 *R* = OH, *R'* = H, *R''* = CH_3
25 *R* = H, *R'* = OH, *R''* = CH_3



26 *R* = H
27 *R* = OAc

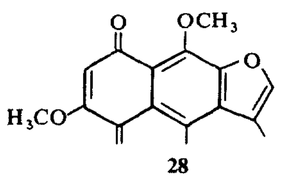


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Table 2. ^1H NMR data for compounds **8**, **15**, **18**, **19** and **20** ($CDCl_3$)

	8	+ $Eu(fod)_3$	**15**	**18**	**19**	**20**
1α-H	—	—	6.94 *dd*	2.83 *dd*(*br*)	2.85 *dd*(*br*)	2.84 *dd*(*br*)
1β-H				2.54 *m*	2.60 *m*	2.60 *m*
2-H	2.64 *m*	7.75 *m*	5.94 *ddd*	1.80 *m*	1.81 *m*	1.81 *m*
3-H		3.72 *m* 3.14 *m*	2.54 *dddd* 2.15 *m*			
4-H	2.29 *ddq*	4.33 *m*	3.33 *dq*(*br*)	3.25 *ddq*	3.41 *ddq*	3.46 *ddq*
6-H	5.93 *s*	7.13 *s*	—	—	—	—
9-H	7.44 *s*	12.28 *s*	—	—	—	—
12-H	7.26 *q*	7.40 *s*(*br*)	7.37 *q*	7.22 *q*	7.30 *q*	7.29 *q*
13-H	2.10 *d*	2.47 *s*(*br*)	2.33 *d*	2.37 *d*	2.29 *d*	2.41 *d*
14-H	1.02 *s*	2.47 *s*(*br*)	4.45 *d* 4.36 *d*	2.57 *s*	5.49 *d* 5.37 *d*	5.01 *d* 4.95 *d*
15-H	1.03 *d*	1.88 *d*	1.12 *d*	1.19 *d*	1.23 *d*	1.27 *d*
OCH_3	—	—	4.13 *s*	—	—	—
OCOR	6.01 *qq*	6.25 *qq*	2.27 *d*(*br*)	2.70 *q*	2.71 *q*	2.71 *q*
	1.85 *dq*	2.32 *d*(*br*)	2.15 *m*	1.33 *t*	1.34 *t*	1.34 *t*
	1.80 *dq*	2.23 *s*(*br*)	0.96 *d*	—	—	—
OAc	—	—	—	—	2.09 *s*	—

J (Hz); **8**: 3α,4α = 6; 3β,4α = 9; 4α,15 = 7; 12,13 = 1; 18,19 = 7; 18,20 = 19,20 = 1.5. **15**: 1.2 = 9; 1,3 = 3; 2,3 = 6.5; 2,3′ = 2.3; 3,4 = 7; 4,15 = 7; 12,13 = 1,4; 14,14 = 13; 17,18 = 8; 18,19 = 18,20 = 7; **18–20**: 1α,1β = 16; 1α,2α = 4; 3α,4α = 5; 3β,4α = 10; 4α,15 = 7. **19** and **20**: 14,14 = 13.

separated from **23** only with difficulty. The structure of **24** followed from the NMR spectral data and the data of the anhydro compound **28**, obtained by heating **24** with acetic anhydride. Compound **25**, however, could not be separated completely from **23**. After acetylation the NMR spectra (Table 3) of the resulting acetates showed that we were dealing with the structures **26** and **27**. As demonstrated earlier, ketones like **23** are acetylated via enolisation [1, 2]. Therefore the presence of **25** seems to be established.

The roots of *Senecio inornatus* DC afforded large quantities of **13**, cacalol (**17**) [7] and **21** together with two further benzofurans (**18** and **19**). The structures clearly followed from the spectroscopic data. The relative position of the acetate group was indicated by the chemical shift of the corresponding NMR signal (Table 2). The aerial parts also contained **17**, **18** and **19** together with **6** and a further benzofuran, which was found to be **20** since acetylation produced compound **19**.

The chemotaxonomical importance of the compounds isolated from the four species is not completely clear. Furanoeremophilanes are definitely typical for the genus *Senecio*. However, they are also present in several related genera. On the other hand there are several *Senecio* species which do not contain these compounds [1, 2]. Furthermore it is an open question whether such compounds are useful when considering the proposed new classification of the whole tribe [9]. The highly dehydrogenated cacalol derivatives, which are not widespread, but are typical of the genus *Cacalia* may be of special interest. Certainly further investigations, both from the chemical as well as from the botanical viewpoint, are necessary to arrive at any final conclusions.

Table 3. ^1H NMR data for compounds **24**, **26**, **27** and **28** ($CDCl_3$)

	24	Δ^+	**26**	**27**	**28**
2-H	6·70 *s*	0·14	7.04 *s*	7.15 *s*	7.02 *s*
12-H	7.33 *q*	0	7.36 *q*	7.45 *q*	7.46 *q*
13-H	2.29 *d*	0	2.44 *d*	2.39 *d*	2.33 *s*(*br*)
14-H	2.73 *s*	0.02	3.09 *s*	5.79 *s*	2.70 *s*
15-H	1.72 *s*	0.06	2.92 *s*	2.89 *s*	5.16 *s* 4.99 *s*
OCH_3	3.75 *s*	0.09	3.96 *s*	3.98 *s*	3.94 *s*
	3.72 *s*	0.42	3.86 *s*	3.88 *s*	3.93 *s*
OAc	—		2.45 *s*	2.47 *s*	—
				2.16 *s*	

J (Hz): 12,13 = 1; $^+\Delta$-values after addition of about 0.05 equivalents of $Eu(fod)_3$.

EXPERIMENTAL

IR spectra were measured in CCl_4 or $CHCl_3$; ^1H NMR employed TMS as internal standard, assignments were established by extensive double resonance experiments; MS were determined at 70 eV; optical rotations were measured in $CHCl_3$. The air dried plant material was extracted with Et_2O–petrol (1:2) and the extracts were first separated by CC (Si gel, act. grade II) and further by repeated TLC (Si gel, GF 254) using Et_2O–petrol mixtures as eluents. Known compounds were identified by comparison of their ^1H NMR and IR spectra with those of authentic material.

Senecio medley-woodii Hutch. (voucher 77/223). 125 g roots afforded 80 mg **1**, 50 mg **2** (Et_2O–petrol, 1:3) and 10 mg **4** (Et_2O–petrol, 1:1), while 860 g aerial parts yielded 5 mg **6**, 10 mg **1** and 3 mg **2**.

Senecio halimifolius L. (voucher 77/345, Botanic Gardens Kirstenbosch). 470 g roots afforded 10 mg **8** (Et_2O–petrol, 1:1) and 410 g aerial parts gave 200 mg **6**, 200 mg **9**, 5 mg **13**, 300 mg **10** and 100 mg **11** (Et_2O–petrol, 2:1).

Senecio inaequidens DC (voucher 77/6, 77/50, 77/66, 77/72, 77/77, 77/288). The different collections were extracted separately and the extracts were compared by TLC. No differences could be detected. 200 g roots afforded 10 mg **13**, 60 mg **14**, 30 mg **22** and 30 mg **23**, while 500 g aerial parts yielded 50 mg **12**, 20 mg **13**, 600 mg **14**, 600 mg **15** (Et_2O–petrol, 1:3), 20 mg **16**, 150 mg **23**, 50 mg **24** (Et_2O–petrol, 3:1 and CH_2Cl_2–Et_2O, 5:1) and *ca* 15 mg **25** (Et_2O–petrol, 3:1).

Senecio inornatus DC (voucher 77/45). 950 g roots afforded 0.3 g **13**, 2.8 g **18** (Et_2O–petrol, 1:3), 5.6 g **17**, 3.1 g **19** (Et_2O–

petrol, 1:1) and 0.25 g **21**, while 740 g aerial parts yielded 1 g **6**, 1.1 g **18**, 1 g **17**, 1.2 g **19** and 0.5 g **20** (Et_2O–petrol, 1:1).

3β - Acetoxy - 6β - (2 - methylbutyryloxy) - 10βH - furanoeremophilane (**2**). Colourless oil, IR ν_{max} cm^{-1}: OAc 1740, 1250; CO_2R 1730. MS *m/e* (rel. int.): 376.225 (M^+, 5) ($C_{22}H_{32}O_5$); 292 (M^+ – O=C=C (Me) Et, 24); 232 (292 – AcOH, 23); 85 ($C_4H_9CO^+$, 47); 43 ($H_3C\,CO^+$, 100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \qquad 578 \qquad 546 \qquad 436\,\text{nm}}{-47.3 \quad -49.6 \quad -57.0 \quad -103.4^\circ} (c = 4.31).$$

10 mg **2** in 2 ml MeOH were heated at 60° for 1 min with 0.5 ml 2N KOH. TLC afforded 5 mg **3**, colourless oil. IR ν_{max} cm^{-1}: OH 3620; CO_2R 1725.

3β - Acetoxy - 6β - (2 - methylbutyryloxy) - 10βH - furanoeremophil-9-one (**4**). Colourless oil, IR ν_{max} cm^{-1}: OAc 1745, 1245; CO_2R 1735; furan ketone 1685, 1535. MS *m/e* (rel. int.): 390.204 (M^+, 5) ($C_{22}H_{30}O_6$); 306 (M^+ – O=C=C (Me) Et, 32); 246 (306 – AcOH, 28); 85 ($C_4H_9CO^+$, 60); 43 (H_3CCO^+, 100). 9 mg **4** were saponified as above. TLC afforded 5 mg **5**, colourless oil, IR ν_{max} cm^{-1}: CO_2R 1740; furan ketone 1688, 1540. MS *m/e* (rel. int.): 348.194 (M^+, 4) ($C_{20}H_{28}O_5$); 330 (M^+ – H_2O, 4); 264 (M^+ – O=C=C (Me) Et, 31); 246 (264 – H_2O, 49); 85 ($C_4H_9CO^+$, 100).

6α - Angeloyloxy - 9, 10 - dehydrofuranoeremophil - 1 - one (**8**). Yellow coloured oil, UV λ_{max}: 346 nm (ether); IR ν_{max} cm^{-1}: C=CCO_2R 1715, 1650; furan ketone 1670, 1610, 1570, 1525. MS *m/e* (rel. int.): 328.167 (M^+, 44) ($C_{20}H_{24}O_4$); 228 (M^+ – $C_4H_7CO_2H$, 100); 83 ($C_4H_7CO^+$, 81); 55 (83 – CO, 57).

12-*Hydroxy*-2, 3-*dihydroeuparine* (**11**). Colourless crystals, mp 77.5° (Et_2O–petrol), UV λ_{max} nm: 325, 273 (ε = 12800, 20300) (ether); IR ν_{max} cm^{-1}: OH 3620; hydrogen bonded ketone 3500–2600, 1640; NMR: 5.42 (*dd(br)*, *J* = 9, 8, 2-H); 3.37 (*dd(br)*, *J* = 16, 9, 3-H); 3.09 (*ddd J* = 16, 8, 1, 3′-H); 6.37 (*s*, 4-H); 7.50 (*t*, *J* = 1, 7-H); 2.54 (*s*, 9-H); 5.29 (*brs*, 11-H); 5.27 (*brs* 11′-H); 4.26 (AB *q*, 12-H), 12.98 (*s*, OH). MS *m/e* (rel int.): 234.089 (M^+, 22) ($C_{13}H_{14}O_4$); 219 (M^+ – Me, 8); 43 ($C_3H_7^+$, 100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \qquad 578 \qquad 546 \qquad 436\,\text{nm}}{-31.6 \quad -33.0 \quad -39.2 \quad -87.3^\circ} (c = 1.16).$$

14-*Isovaleryloxy-O-methyl*-1,2-*dehydrocacalol* (**15**). Colourless oil, IR ν_{max} cm^{-1} CO_2R 1735; C=C 3060, 1610; furane 1570. MS *m/e* (rel. int.): 342.183 (M^+, 46) ($C_{21}H_{26}O_4$); 241 (M^+ – OCOR, 50); 240 (M^+ – RCO_2H, 16); 225(240 – Me, 100); 85 ($C_4H_9CO^+$, 5); 57 (85 – CO, 14).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \qquad 578 \qquad 546 \qquad 436\,\text{nm}}{+51.0 \quad +54.3 \quad +66.0 \quad +174.0} (c = 1.2).$$

4-*Hydroxy*-3-*methoxy*-1-*oxo*-O-*methyl*-2,3-*dehydrocacalol* (**24**). Yellow crystals, mp 176° (CCl_4), UV λ_{max} nm: 303, 225 (ε = 9100, 11900) (ether); IR ν_{max} cm^{-1} OH 3590; C=C – C=O 1665, 1620; benzofurane 1588, 1542. MS *m/e* (rel. int.): 302.115 (M^+, 37) ($C_{17}H_{18}O_5$); 287 (M^+ – ·Me, 100); 284 (M^+ – H_2O, 10); 273 (M^+ – ·CHO, 44); 272 (M^+ – CH_2O, 36); 271 (M^+ – ·OMe, 89); 257 (272 – $·CH_3$, 26)

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \qquad 578 \qquad 546\,\text{nm}}{+7.0 \quad +7.2 \quad +8.1} (c = 0.73).$$

10 mg **24** were refluxed in 2 ml Ac_2O for 1 hr. After TLC (CH_2Cl_2–Et_2O, 5:1) 5 mg **28**, not free from **24**, were obtained, IR ν_{max} cm^{-1} C=C – C=O 1660, 1590; furane 1540. MS *m/e* (rel. int.): 284.105 (M^+, 100) ($C_{17}H_{16}O_4$); 269 (M^+ – ·Me, 28); 255 (M^+ – · CHO, 42).

14-*Hydroxy*-3-*methoxy*-1-*oxo*-O-*methyl*-2,3-*dehydrocacalol* (**25**). Yellow crystals, not free from **23**, IR ν_{max} cm^{-1}: OH 3600; C=C – C=O 1665, 1620. The mixture (8 mg) was heated for 1 hr in 2 ml Ac_2O under reflux. TLC (CH_2Cl_2–Et_2O, 5:1) afford 2 mg **26** and 2 mg **27** (Et_2O–petrol 1:1).

Compound **26**. Yellow crystals, mp 185° (ether), IR ν_{max} cm^{-1}: PhOAc 1775; benzofurane 1610, 1520. MS *m/e* (rel. int.): 328.131 (M^+, 32) ($C_{19}H_{20}O_5$), 286 (M^+ – O=C=CH_2, 100); 271 (286 – $·CH_3$, 63).

Compound **27**. Yellow crystals, mp 168° (ether), IR ν_{max} cm^{-1}: PhOAc 1775; OAc 1735, 1245; benzofurane 1610, 1520. MS *m/e* (rel. int.): 386.136 (M^+, 70) ($C_{21}H_{22}O_7$); 344 (M^+ – O=C=CH_2, 100); 302 (344 – O=C=CH_2, 32).

Calcalolpropionate (**18**). Colourless oil, IR ν_{max} cm^{-1}: PhOCOR 1765. MS *m/e* (rel. int.): 286.157 (M^+) ($C_{18}H_{22}O_3$); 230 (M^+ – O=C=CH Me, 100); 215 (230 – ·Me, 63).

14-*Acetoxy-cacalolpropionate* (**19**). Colourless oil, IR ν_{max} cm^{-1} PhOCOR 1770; OAc 1735, 1230. MS *m/e* (rel. int.): 344.162 (M^+) ($C_{20}H_{24}O_5$); 302 (M^+ – O=C=CH_2, 3); 288 (M^+ – O=C=CH Me, 70); 228 (288 – AcOH, 100).

14-*Hydroxy-cacalolpropionate* (**20**). Colourless oil, IR ν_{max} cm^{-1}: OH 3600; PhOCOR 1770; benzofurane 1670, 1630, 1600. MS *m/e* (rel. int.): 302.152 (M^+) ($C_{18}H_{22}O_4$); 246 (M^+ – O=C=CH Me, 100); 228 (M^+ – $C_2H_5CO_2H$, 49); 231 (246 – ·Me, 25). 15 mg **20** were heated with 1 ml Ac_2O for 30 min at 70°. After TLC 15 mg **19** were obtained, identical with the natural product.

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