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SHORT REPORTS

STRUCTURE OF THE 5,6-DIHYDRO-α-PYRONE, UMURAVUMBOLIDE

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Key Word Index—*Tetradenia riparia*; Lamiaceae; leaves; desacetylumuravumbolide; 5,6-dihydro-α-pyrone.

Abstract—The structure and absolute stereochemisry of umuravumbolide and desacetylumuravumbolide have been elucidated by spectral means.

INTRODUCTION

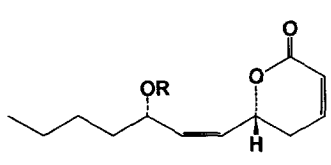
Van Puyvelde *et al.* [1] have ascribed structures **1** and **2** to umuravumbolide and desacetylumuravumbolide, isolated from central African (Rwanda) *Tetradenia* (formerly *Iboza*) *riparia* without specifying the absolute configuration of the two asymmetric centres. The double bond was considered to be *trans* from rather tenuous IR evidence. Soon afterwards, Achenbach and Witzke [2] claimed to have synthesised racemic **1** and **2**, possessing a *trans* double bond, as well as their diastereoisomers.

RESULTS AND DISCUSSION

In order to shed further light on the problem, we have been seeking a suitable source of umuravumbolide or its desacetyl compound from southern African *Tetradenia* species, but have been unsuccessful, until finding an excellent source of desacetylumuravumbolide (the decolourized acetone extract of the dried leaves was virtually pure) in plant material originating from the Pongola valley. Acetylation provided umuravumbolide, which like its desacetyl precursor was optically active, in contradiction to the zero rotations reported previously [1]. The molecular formula of umuravumbolide ($C_{14}H_{20}O_4$) was confirmed by HREI mass spectrometry and the ^{1}H NMR data of **1** and **2**, assigned from extensive ^{1}H decoupling, HMQC and COSY 90 experiments, are in agreement with published values. The ^{13}C NMR data were obtained at much higher field than previously [1] and are therefore repeated in Table 1. The 400 MHz ^{1}H NMR spectra of **1** and **2** clearly showed that the exocyclic double bond was *cis* (J = 11 Hz), while the positive Cotton effect near 260 nm ($\Delta\varepsilon$ = + 0.9 at 255 nm) in **2** indicates a (6*R*)-configuration [3] for these compounds.

Table 1. ^{13}C NMR data for **1** and **2** (100 MHz, $CDCl_3$)

C	1	2
2	163.4	163.7
3	121.7	121.5
4	144.2	144.6
5	30.0	29.9
6	74.0	73.7
1′	130.1	127.6
2′	131.7	137.9
3′	69.4	67.8
4′	34.3	36.8
5′	27.2	27.4
6′	21.1	22.6
7′	13.9	14.0
O$\underline{C}$OCH$_3$	170.1	—
OCO$\underline{C}$H$_3$	22.4	—



1. R = Ac
2. R = H

Finally, the absolute configuration of the secondary alcohol group was determined with the aid of Mosher's method by conversion to the (*S*)- and (*R*)-MTPA esters [4]. Application of the MTPA determination rule [5] to the $\Delta\delta_H$ values ($\delta_{H(S)} - \delta_{H(R)}$) observed for all the signals, which were negative in the left segment and positive in the right segment, clearly shows that **1** and **2** possess a (3′*S*)-configuration. Umuravumbolide and desacetylumuravumbolide accordingly possess the absolute stereochemistry shown in structures **1** and **2**, respectively. The pectinolides from *Hyptis pectinata* are therefore their 5α-hydroxy and 5α-acetoxy derivatives [6].

EXPERIMENTAL

Isolation of desacetylumuravumbolide. Dry leaves (2.2 g) of a form of the polymorphic species, *T. riparia*, grown from cuttings collected in the Pongola valley by Dr E. van Jaarsveld of the National Botanical Institute, Kirstenbosch, were extracted in a Soxhlet with Me_2CO, the extract decolourized with charcoal, filtered through Celite and evapd. The resulting pale yellow gum (0.15 g), which showed one main spot on TLC, was flash chromatographed on silica gel in EtOAc–hexane (1:1) to afford desacetylumuravumbolide (0.10 g). $[\alpha]_D^{24}$ − 5.3° ($CHCl_3$; *c* 1.3). IR ν_{max}^{NaCl} cm^{-1}: 3450, 1055 (α,β-unsaturated sec. alcohol), 1715 (α,β-unsaturated δ-lactone), 1680, 1375, 1240, 940. CD(MeOH): λ_{max} = 255 nm ($\Delta\varepsilon$ = + 0.9). ^{1}H NMR (400 MHz, $CDCl_3$): 0.89 (3H, *t*, $J_{6',7'}$ = 7 Hz, H_3-7'), 1.22–1.30 (2H, *m*, H-5', H-6'), 1.43 (1H, *m*, H-4a'), 1.61 (1H, *m*, H-4b'), 2.02 (1H, *br s*, OH), 2.31–2.47 (2H, *m*, H-5a, H-5e), 4.40 (1H, *dd*, $J_{2',3'}$ = 7.4 Hz, $J_{3',4'}$ = 6.8 Hz, H-3'), 5.32 (1H, *ddd*, $J_{1',6}$ = 7.5 Hz, $J_{5a,6}$ = 17 Hz, $J_{5e,6}$ = 5.5 Hz, H-6), 5.61 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{2',3'}$ = 7.5 Hz, H-2'), 5.66 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{1',6}$ = 7.5 Hz, H-1'), 6.03 (1H, *dd*, $J_{3,4}$ = 9.8 Hz, $J_{3,5ae}$ = 2 Hz, H-3), 6.85 (1H, *ddd*, $J_{3,4}$ = 9.8 Hz, $J_{4,5a}$ = 3 Hz, $J_{4,5e}$ = 5 Hz, H-4).

Umuravumbolide. Acetylation of **2** for 24 hr with Ac_2O and pyridine at room temp. afforded **1**. $[\alpha]_D^{20}$ + 30° ($CDCl_3$; *c* 2.1). IR ν_{max}^{NaCl} cm^{-1}: 1740 (ester carbonyl), 1720 (α,β-unsaturated lactone), 1685, 1240, 1020, 940. ^{1}H NMR (400 MHz, $CDCl_3$): δ0.88 (3H, *t*, $J_{6',7'}$ = 7 Hz, H_3-7'), 1.23 (2H, *m*, H-5'), 1.32 (2H, *m*, H-6'), 1.51 (1H, *m*, H-4a'), 1.68 (1H, *m*, H-4b'), 2.02 (3H, *s*, acetyl), 2.27 (1H, *m*, H-5a), 2.44 (1H, *m*, H-5e), 5.36–5.43 (2H, *m*, H-6, H-3'), 5.52 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{2',3'}$ = 10 Hz, H-2'), 5.71 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{1',6}$ = 8 Hz, H-1'), 6.03 (1H, *dd*, $J_{3,4}$ = 9.8 Hz, $J_{3,5ae}$ = 2 Hz, H-3), 6.85 (1H, *ddd*, $J_{3,4}$ = 9.8 Hz, $J_{4,5a}$ = 3 Hz, $J_{4,5e}$ = 5 Hz, H-4); HREIMS: Observed *m/z* = 252.1338, $C_{14}H_{20}O_4$ requires 252.1361.

(S) and (R)-MPTA esters of desacetylumuravarumbolide. (i) A soln of **1** (10 mg) in CH_2Cl_2 (1 ml) was treated at room temp. with (*S*)-MPTA (26 mg), DCC (73 mg) and DMAP (11 mg) for 30 min. The soln was diluted with EtOAc, worked-up as usual and chromatographed on silica gel in benzene–hexane–EtOAc. The fr. eluted with EtOAc–hexane (1:1) gave the (*S*)-MPTA ester as an oil (14 mg). ^{1}H NMR (400 MHz), $CDCl_3$): δ0.83 (3H, *t*, $J_{6',7}$ = 7 Hz, H_3-7'), 1.18 (2H, *m*, H-6'), 1.25 (2H, *m*, H-5'), 1.56 (1H, *m*, H-4'a), 1.71 (1H, *m*, H-4'b), 2.30 (1H, *m*, H-5a), 2.48 (1H, *m*, H-5e), 3.50 (3H, *s*, OMe), 5.43 (1H, *m*, H-6), 5.60 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{1',6}$ = 9 Hz, H-1'), 5.67 (1H, *m*, H-3'), 5.81 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{2',5'}$ = 8 Hz, H-2'), 6.06 (1H, *dd*, $J_{3,4}$ = 10 Hz, $J_{3,5ae}$ = 2 Hz, H-3), 6.86 (1H, *ddd*, $J_{3,4}$ = 10 Hz, $J_{4,5a}$ = 3 Hz, $J_{4,5e}$ = 5 Hz, H-4), 7.39 (3H, *m*, Ph), 7.48 (2H, *m*, Ph). (ii) Treatment of **1** (8.5 mg) with (*R*)-MPTA as described in (i) gave the (R)-MPTA ester as an oil. ^{1}H NMR (400 MHz, $CDCl_3$: δ0.89 (3H, *t*, $J_{6',7'}$ = 7 Hz, H_3-7'), 1.31 (4H, *m*, H-5', H-6'), 1.63 (1H, *m*, H-4a'), 1.80 (1H, *m*, H-4b'), 2.21 (1H, *m*, H-5a), 2.45 (1H, *m*, H-5e), 3.53 (3H, *s*, OMe), 5.41 (1H, *m*, H-6), 5.46 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{1',6'}$ = 9 Hz, H-1'), 5.63 (1H, *m*, H-3'), 5.76 (1H, *dd*, $J_{1',2'}$ = 11 Hz, $J_{2',3'}$ = 8 Hz, H-2'), 6.05 (1H, *dd*, $J_{3,4}$ = 10 Hz, $J_{3,5ae}$ = 2 Hz, H-3), 6.84 (1H, *ddd*, $J_{3,4}$ = 10 Hz, $J_{4,5a}$ = 3 Hz, $J_{4,5e}$ = 5 Hz, H-4), 7.39 (3H, *m*, Ph), 7.47 (2H, *m*, Ph).

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