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TETRADENOLIDE, AN α-PYRONE FROM *TETRADENIA RIPARIA*

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Key Word Index—*Tetradenia riparia*; Lamiaceae; new α-pyrone; 5,6-dihydro-6-(1,2-dihydroxyhexyl)-2-pyrone.

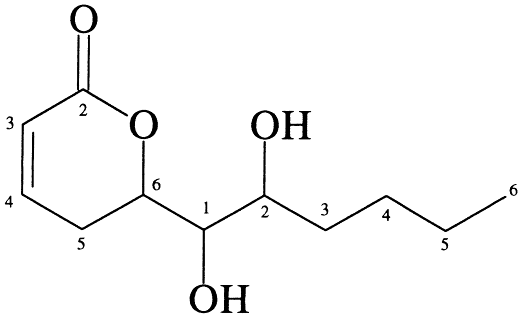
Abstract—A new α-pyrone, tetradenolide, was isolated from the leaves of *Tetradenia riparia*. On the basis of spectroscopic analysis, this compound was identified as 5,6-dihydro-6-(1,2-dihydroxyhexyl)-2-pyrone. © 1998 Published by Elsevier Science Ltd. All rights reserved

INTRODUCTION

Tetradenia riparia (Hochst.) Codd (Lamiaceae) is a widespread shrub throughout oriental and intertropical Africa [1] which is reported to possess several medicinal properties [2, 3]. Previous phytochemical studies of *T. riparia* revealed the presence of diterpenoids [4–6], α-pyrones [7–9] and various terpenes (essential oil) [10]. One compound, a diterpenediol, displayed antimicrobial [3], antispasmodic [11] and antiparasitic activity [12]. In this paper we report on tetradenolide (**1**), a new minor α-pyrone from *T. riparia*. The 6-substituted 5,6-dihydro-α-pyrones are an interesting group of biologically active compounds with antimicrobial, phytotoxic and cytotoxic activity [13–16].

RESULTS AND DISCUSSION

Tetradenolide (**1**) is a new minor α-pyrone isolated in 0.01% yield from the chloroform extract of the leaves of *T. riparia*. The IR (KBr) spectrum ($\nu_{\max}$ 1704 cm^{-1}) is consistent with a six-membered α,β-unsaturated δ-lactone, while the presence of hydroxyl functions was also established (ν_{OH} 3500–3100 cm^{-1}). The 270 MHz ^{1}H NMR spectrum (CDCl$_3$) showed resonances at δ 0.92 (3H, *t*, $J = 7.26$ Hz, Me) and at δ 1.2–1.8 (6H, *m*, $CH_2CH_2CH_2$) which can be attributed to a *n*-butyl group. The signals at δ 6.90–7.10 (1H, *m*, $C\underline{H}{=}CH{-}C{=}O$) and δ 6.02 (1H, $d \times d$, $J = 9.57$ Hz, $J = 1.32$ Hz, $={C\underline{H}}{-}C{=}O$) correspond to the β- and α-protons, respectively, of the lactone double bond and display couplings with the allylic protons (5-position) at δ 2.4–2.8 (2H, *m*, $C\underline{H}_2CH{=}CH$). The ^{13}C NMR spectrum of tetradenolide (**1**) is in full agreement with the proposed structure. The carbonyl region showed a peak at δ 164.02 while the olefinic carbons are situated at δ 146.11 (C-4 ring) and δ 120.95 (C-3 ring). The aliphatic part of the spectrum revealed five resonances, namely the terminal Me at δ 14.00 and four methylene groups at δ 22.62, 25.79, 27.67 and 33.46, attributed to the carbons C-5 alkyl chain, C-5 ring, C-4 alkyl chain and C-3 alkyl chain, respectively. The remaining three carbons connected to oxygen gave resonances in the 70–80 ppm region, but one resonance line was covered by the peaks of CHCl$_3$. The carbons connected to the hydroxyl groups gave rise to peaks at δ 70.20 and 74.36, while the chemical shift at δ 77.10 was attributed to the C-6 carbon of the ring. All assignments in the ^{1}H NMR and ^{13}C NMR spectra were supported by 2D-COSY and 2D-HETCOR experiments. No M$^+$ could be detected in the MS under EI conditions at 70 eV. Tetradenolide (**1**) was then converted into its bis-*O*-trimethylsilyl derivative by treatment with BSTFA, and an EI-MS of this derivative was recorded which gave a M$^+$ at m/z 358 (1%). The diagnostic peaks of the EI-MS are listed in the Experimental.



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EXPERIMENTAL

Plant material

Leaves of *T. riparia* were collected in the prefecture of Butare (South-West of Rwanda) in September 1991 and identified by one of the authors (L. Van Puyvelde). A voucher specimen (LVP no. 1) was deposited in the herbarium of the I.R.S.T. (Institut de Recherche Scientifique et Technologique), Butare, Rwanda.

Extraction and isolation

Air-dried leaves (824 g) of *T. riparia* were successively extracted in a percolator with *n*-hexane and $CHCl_3$. The $CHCl_3$ fraction was extracted with $MeOH–H_2O$ (9:1). The $CHCl_3$ phase was evapd under red. pres. to give a $CHCl_3$-1 extract (43.2 g; 5.2%) and the MeOH was removed from the $MeOH–H_2O$ extract. The H_2O phase was first extracted with $CHCl_3$ to give a $CHCl_3$–2 extract (20.8 g; 2.5%) and then with EtOAc (1.2 g; 0.14%). The EtOAc extract was chromatographed on silica gel (Merck, 230–400 mesh) (100 g) and eluted stepwise with a hexane–EtOAc–MeOH gradient. The frs eluted with MeOH (422 mg) were further chromatographed on silica gel and eluted with a $CHCl_3$–MeOH gradient. The frs eluted with $CHCl_3$–MeOH (19:1) (190 mg) were further sepd by prep. TLC (Merck, Si gel F_{254}, 2 mm) with $CHCl_3$–MeOH (19:1) (4 developments on 18 cm). The TLC band with R_f 0.46 afforded 82.4 mg of tetradenolide (**1**) (0.01%). Crystallization from *n*-hexane-chloroform yielded small colorless needles, mp. 102.8–103°. IR (KBr) $\nu_{\max}$ cm^{-1}: 3500–3100 (*br*, OH), 1704 (α,β-unsatd. δ-lactone). ^1H NMR (270 MHz, $CDCl_3$): δ 0.92 (3H, *t*, $J = 7.26$ Hz, Me) 1.2–1.8 (6H, *m*, $CH_2CH_2CH_2$); 2.4–2.8 (2H, *m*, $C\underline{H}_2{=}C$) 3.6–3.9 (4H, *m*, $C\underline{H}(1){-}O\underline{H}$ and $C\underline{H}(2){-}O\underline{H}$); 4.48–4.62 (1H, *m*, $C\underline{H}(6){-}O$); 6.02 (1H, $d \times d$, $J = 9.57$ Hz, $J = 1.32$ Hz, ${=}C\underline{H}{-}C{=}O$); 6.90–7.10 (1H, *m*, $C\underline{H}{=}CH{-}C{=}O$). ^{13}C NMR (50.29 MHz, $CDCl_3$): δ 14.00 (Me); 22.62 (CH_2); 25.79 ($C{=}C{-}\underline{C}H_2$); 27.67 (CH_2); 33.46 (CH_2); 70.20 ($\underline{C}H{-}O$); 74.36 ($\underline{C}H{-}O$); 77.16 ($\underline{C}H{-}O$); 120.95 (${=}\underline{C}H{-}C{=}O$); 146.11 ($\underline{C}H{=}CH{-}C{=}O$); 164.02 ($C{=}O$). EI-MS, bis-*O*-TMS-derivative, 70 eV, m/z (rel. int.): 358 $[M]^+$ (0.2), 301 (1), 285 (11), 273 (3), 269 (2), 261 (2), 259 (2), 245 (1), 243 (2), 240 (2), 218 (13), 199 (3), 191 (2), 183 (2), 182 (2), 172 (6), 170 (2), 169 (6), 168 (4), 167 (20), 166 (4), 159 (22), 147 (11), 138 (2), 133 (3), 129 (4), 117 (3), 109 (3), 103 (11), 97 (5), 95 (2), 81 (5), 79 (2), 78 (17), 75 (17), 74 (9), 73 (100), 69 (10), 59 (3), 57 (2), 55 (3), 45 (6).

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REFERENCES

1. Troupin, G., *Flore du Rwanda, Spermatophytes*, Vol. III, Institut National de Recherche Scientifique, Butare, Rwanda, 1985, p. 355.
2. Watt, J. M. and Breyer-Brandwijk, M. G., *Medicinal and Poisonous Plants of Southern and Eastern Africa*, E. and S. Livingstone, Edinburgh, 1962, p. 516.
3. Van Puyvelde, L., Nyirankuliza, S., Panebianco, R., Boily, Y., Geizer, I., Sebikali, B., De Kimpe, N. and Schamp, N., *Journal of Ethnopharmacology*, 1986, **17**, 269.
4. Zelnik, R., Rabenhorst, E., Matida, A. K., Gottlieb, H. E., Lavie, D. and Panizza, S., *Phytochemistry*, 1978, **17**, 1795.
5. De Kimpe, N., Schamp, N., Van Puyvelde, L., Dubé, S., Chagnon-Dubé, M., Borremans, F., Antheunis, M. J. O., Declercq, J. P., Germain, G. and Van Meerssche, M., *Journal of Organic Chemistry*, 1982, **47**, 3628.
6. Van Puyvelde, L., De Kimpe, N., Borremans, F., Zhang, W. and Schamp, N., *Phytochemistry*, 1987, **26**, 493.
7. Van Puyvelde, L., Dubé, S., Uwimana, E., Uwera, C., Dommisse, R. A., Esmans, E. L., Van Schoor, O. and Vlietinck, A. J., *Phytochemistry*, 1979, **18**, 1215.
8. Van Puyvelde, L., De Kimpe, N., Dubé, S., Chagnon-Dubé, M., Boily, Y., Borremans, F., Schamp, N. and Anteunis, J. O., *Phytochemistry*, 1981, **20**, 2753.
9. Davies-Coleman, M. T. and Rivett, D. E. A., *Phytochemistry*, 1995, **38**, 791.
10. Campbell, W. E., Gammon, D. W., Smith, P., Abrahams, M. and Purvers, T. D., *Planta Medica*, 1997, **63**, 270.
11. Van Puyvelde, L., Lefebvre, R., Mugabo, P., De Kimpe, N. and Schamp, N., *Planta Medica*, 1987, **53**, 156.
12. Hakizamungu, E., Van Puyvelde, L., Wéry, M., De Kimpe, N. and Schamp, N., *Phytotherapy Research*, 1988, **2**, 207.
13. Pereda-Miranda, R., Hernandez, L., Villavicencio, M. J., Novelo, M. and Ibarra, P., *Journal of Natural Products*, 1993, **56**, 583.
14. Davies-Coleman, M. T. and Rivett, D. E. A., *Phytochemistry*, 1994, **35**, 1590.
15. Matsuda, M., Endo, Y., Fushiya, S., Endo, T. and Nozoe, S., *Heterocycles*, 1994, **38**, 1229.
16. Parker, S. R., Cutler, H. G., Jacyno, J. M. and Hill, R. A., *Journal of Agricultural and Food Chemistry*, 1997, **45**, 2774.