Phytochemistry, Vol. 25, No. 11, pp. 2567–2568, 1986.
Printed in Great Britain.

0031-9422/86 \$3.00 + 0.00
Pergamon Journals Ltd.

OXEPANE DITERPENES FROM *MONTANOA TOMENTOSA**

YOSHITERU OSHIMA†, GEOFFREY A. CORDELL and HARRY H. S. FONG

Program for Collaborative Research in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612, U.S.A.

(*Received* 6 *March* 1986)

Key Word Index—*Montanoa tomentosa* subsp. *tomentosa*; Compositae; oxepane diterpenes; tomentanol; structure elucidation.

Abstract—The leaves of *Montanoa tomentosa* afforded a new oxepane diterpene, tomentanol, and its previously known relatives zoapatanol, montanol, tomexanthin and tomentol. The structure of tomentanol was determined through examination of its spectroscopic properties.

INTRODUCTION

As part of our continuing studies on potential fertility regulating agents from plants, we undertook a phytochemical investigation of the leaves of *Montanoa tomentosa* Cerv. subsp. *tomentosa* for the purpose of re-isolating oxepane diterpene derivatives for further biological evaluation. In a previous communication, we reported on the isolation of the flavonoids nicotiflorin and isoquercitrin [1] from the polar fraction of the methanol extract. Investigation of the non-polar fraction led to the isolation of a new oxepane diterpene, tomentanol (**1**), in addition to the known derivatives zoapatanol (**2**) [2], montanol (**3**) [2], tomexanthin (**4**) [3], and tomentol (**5**) [4]. The pregnancy interruption effect of zoapatanol [5] was confirmed, while tomexanthin was found to be devoid of this activity. Zoapatanol, montanol, tomexanthin and tomentol were found to inhibit the spontaneous contraction of guinea pig uterine strips *in vitro* (Martin, A., Oshima, Y., Cordell, G. A., Waller, D. P. and Fong, H. H. S., unpublished results). Insufficient tomentanol was obtained for biological evaluation. Details and the significance of the biological activities will be reported elsewhere.

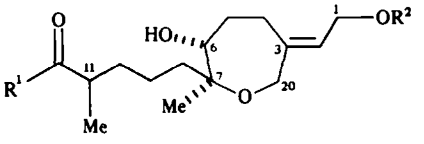
RESULTS AND DISCUSSION

Tomentanol (**1**) was obtained as a colourless oil showing only end absorption in the UV and hydroxyl (3408 cm^{-1}) and alicyclic ketone (1709 cm^{-1}) absorption bands in the IR spectra. With a mass of 352 amu, the compound was isomeric with tomentol (**5**), which we had isolated previously and was currently reported by others [4]. Tomentanol differed from tomentol in that the terminal methyl groups (C-16 and C-17) were now no longer symmetrical (^1H: 1.014 ppm (*d*), ^{13}C: 22.1 ppm). Instead, an olefinic methyl group was observed at δ 1.733, a doublet methyl group at δ 1.022 and a geminal olefin at δ 4.714. In the ^{13}C NMR spectrum a doublet at δ 14.3 (C-15) was replaced by a methine signal at δ 36.2. On this basis, tomentanol was regarded as the $\Delta^{15,16}$-isomer of montanol (**3**) and tomentol (**5**) having the structure **1**. The ^{13}C NMR assignments of montanol (**3**), tomentol (**5**) and tomentanol (**1**) are summarized in Table 1.

EXPERIMENTAL

Plant material. The plant material used in this investigation was cultivated at our Pharmacognosy Field Station, Lisle in the summer of 1982. A herbarium specimen has been deposited at the Field Museum of Natural History, Chicago, IL, U.S.A.

Isolation of oxepane diterpenes. Ground leaves of *M. tomentosa* subsp. *tomentosa* [3] (24.5 kg) were extracted by percolation with EtOAc (2 × 100 L/day/3 days). Removal of the solvent afforded a residue (2.66 kg), which was defatted with hexane. A portion (2.1 kg) of this fraction was chromatographed on a column of silica gel G and subjected to gradient elution with C_6H_6, C_6H_6–EtOAc and EtOAc–MeOH. Chromatography of a portion (15 g) of the C_6H_6–EtOAc (1 : 1) fraction (Fr. 4, 66.7 g) over silica gel G (gradient elution with $CHCl_3$, $CHCl_3$–2-PrOH and 2-PrOH) led to a $CHCl_3$–2-PrOH (49 : 1) eluted fraction (3.67 g), which on further silica gel G chromatography eluting with *n*-hexane–EtOAc led to a tomexanthin-rich fraction. Purification over activated charcoal gave tomexanthin (**4**, 3.0 g) as a colourless



	R^1	R^2
1	$-\overset{13}{C}H_2CH(Me)\overset{\overset{CH_2}{\|}}{C}Me$	H
2	$-CH_2CH{=}CMe_2$	H
3	$-CH{=}C(Me)CHMe_2$	H
4	$-CH{=}CHC(OH)Me_2$	Ac
5	$-CH_2\overset{\overset{CH_2}{\|}}{\underset{15}{C}}CHMe_2$	H

---

*Part IV in the series "Studies on Zoapatle". For Part III see ref. [1].

†Present address: Faculty of Pharmaceutical Sciences, Tohoku University, Aobayama, Sendai, Japan.

Table 1. ^{13}C NMR spectral data for compounds **1**, **3** and **5** (90.54 MHz, $CDCl_3$, TMS as internal standard)

C	Compound Montanol (**3**)*	Tomentol (**5**)	Tomentanol (**1**)
1	58.2	59.1	58.9
2	123.6	123.9	123.5
3	142.4	143.5	143.6
4	23.8	24.1	23.7
5	31.5	32.1	31.9
6	76.6	77.1	76.7
7	80.0	80.5	80.1
8	38.5	38.9	38.4
9	20.9	21.5	21.3
10	33.7	34.0	33.5
11	47.2	46.0	46.9
12	209.7	213.6	214.1
13	120.3	48.2	47.3
14	164.4	149.3	36.2
15	38.3	14.3	149.7
16	20.9	22.1	109.5
17	20.9	22.1	20.6†
18	16.6	17.3	16.7
19	17.6	18.7	18.6
20	68.9	69.7	68.9
21	16.9	112.2	19.8†

*Data are from ref. [6].

†Assignments may be reversed.

oil. Successive chromatography of the third $CHCl_3$–2-PrOH (49:1) soluble fraction (Fr. 6, 120 g from the first column) over silica gel using the gradient elution systems of $CHCl_3$, $CHCl_3$–EtOH and then $CHCl_3$, $CHCl_3$–2-PrOH (monitored by TLC) led to an oxepane diterpene-rich fraction (5.7 g). Repeated HPLC [reverse-phase Whatman Partisil 10, ODS 30, 50 × 2.54 cm i.d., H_2O–MeCN (3:2)] separation of this fraction yielded zoapatanol (**2**, 1.0 g), and a mixture of other oxepane diterpenes. Resolution of the mixture (0.4 g) was achieved by further reverse-phase HPLC using a Beckman Ultrasphere-ODS (5 μm, 250 × 10 mm i.d.) column eluting with H_2O–MeOH (2:3) to yield tomentol (**5**, 15 mg), montanol (**3**, 10 mg) and tomentanol (**1**, 5 mg). The physical and spectroscopic properties of **2**, **3** and **4** have been reported previously.

Tomentanol (**1**). Colourless gum. IR ν_{max}^{film} cm^{-1}: 3408, 1709; UV λ_{max}^{MeOH} nm (ε): 210 (6010); CIMS (CH_4) *m/z* (rel. int.): 353 $[M+H]^+$ (13), 335 $[M+H-H_2O]^+$ (100), 317 $[M+H-2H_2O]^+$ (43), 223 (9), 111 (28); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.022 (3H, *d*, $J = 6.8$ Hz, H_3-17), 1.082 (3H, *d*, $J = 7.0$ Hz, H_3-18), 1.133 (3H, *s*, H_3-19), 1.733 (3H, *br s*, H_3-16), 3.550 (1H, *br s*, H-6), 4.133 (2H, *br s*, H_2-20), 4.213 (2H, *d*, $J = 6.2$ Hz, H_2-1), 4.714 (2H, *br s*, H_2-16), 5.480 (1H, *t*, $J = 6.2$ Hz, H-2); ^{13}C NMR: see Table 1.

Tomentol (**5**). Colourless gum. IR ν_{max}^{film} cm^{-1}: 3431, 1709; UV λ_{max}^{MeOH} nm (ε): 210.5 (5010); CIMS (CH_4) *m/z* (rel. int.): 353 $[M+H]^+$ (8), 335 $[M+H-H_2O]^+$ (100), 317 $[M+H-2H_2O]^+$ (28), 223 (16), 111 (36); ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.014 (6H, *d*, $J = 6.8$ Hz, H_3-16, 17), 1.070 (3H, *d*, $J = 6.8$ Hz, H_3-18), 1.134 (3H, *s*, H_3-19), 2.204 (2H, *m*, H_2-5), 2.490 (1H, *m*, H-15), 2.646 (1H, *m*, H-11), 3.166 (2H, *s*, H_2-13), 3.544 (1H, *br s*, H-6), 4.110 (2H, *br s*, H-20), 4.182 (2H, *d*, $J = 6.5$ Hz, H_2-1), 4.766 (1H, *br s*, H-21), 4.959 (1H, *br s*, H-21), 5.453 (1H, *t*, $J = 6.5$ Hz, H-2); ^{13}C NMR: see Table 1.

Acknowledgements—This study was supported in part by a grant from the Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization (Project 77918C). The helpful discussions and assistance provided by Drs. D. D. Soejarto and D. P. Waller (PCRPS); the technical assistance by Ms. S. Kasnick, Mr. S. Totura and A. Lee (PCRPS); and the assistance of the Research Resources Center, University of Illinois at Chicago, in obtaining the NMR and MS spectral data are gratefully appreciated.

REFERENCES

1. Oshima, Y., Cordell, G. A. and Fong, H. H. S. (1986) *J. Nat. Prod.* (in press).
2. Levine, S. D., Adams, R. E., Chen, R., Cotter, M. L., Hirsch, A. F., Kane, V. V., Kanojia, R. M., Shaw, C., Wachter, M. P., Chin, E., Huettemann, R., Ostrowski, P., Mateos, J. L., Noriega, L., Guzman, A., Mijarez, A. and Tovar, L. (1979) *J. Am. Chem. Soc.* **101**, 3404.
3. Seaman, F. C., Malcolm, A. J. and Fischer, N. H. (1984) *Phytochemistry* **23**, 464.
4. Quijano, L., Calderon, J. S., Gomez, G. F., Rosario, M. V. and Rios, T. (1985) *Phytochemistry* **23**, 464.
5. Hahn, D. W., Ericson, E. W., Lai, M. T. and Probst, A. (1981) *Contraception* **23**, 133.
6. Cotter, M. L. (1981) *Org. Magn. Reson.* **17**, 14.