assignments, respectively. [Found: C, 69.81; H, 8.37. $C_{17}H_{24}O_4$ (292) requires: C, 69.84; H, 8.27%.]

Acknowledgements—The authors thank Mr Sherief I. Khalifa and Mohammed M. Hafez for technical assistance.

REFERENCES

1. Trease, G. E. and Evans, W. C. (1985) *Pharmacognosy* 12th Edn, p. 452. Bailliere Tindall, London.
2. El-Feraly, F. S., McPhail, A. T. and Onan, K. D. (1978) *J. Chem. Soc. Chem. Comm.* 75.
3. Kubo, I., Miura, I., Pettei, M. J., Lee, Y.-W., Pilkiewicz, F. and Nakanishi, K. (1977) *Tetrahedron Letters* 4553.
4. Kioy, D., Gray, A. I. and Waterman, P. (1989) *J. Nat. Prod.* **52**, 174.
5. Al-Said, M. S., Khalifa, S. I. and El-Feraly, F. S. (1989) *Phytochemistry* **28**, 297.
6. Still, W. C., Khan, M. and Mitra, A. (1978) *J. Org. Chem.* **43**, 2923.
7. Kubo, I., Lee, Y.-W., Pettei, M., Pilkiewicz, F. and Nakanishi, K. (1976) *J. Chem. Soc. Chem. Comm.* 1013.
8. Corbet, R. E. and Chee, T. L. (1976) *J. Chem. Soc. Perkin I* 850.
9. El-Feraly, F. S. and Hufford, C. D. (1982) *J. Org. Chem.* **47**, 1527.

Phytochemistry, Vol. 29, No. 3, pp. 977–979, 1990.
Printed in Great Britain.

0031-9422/90 $3.00 + 0.00

OPLOPANES FROM THE LEAVES OF *SENECIO MEXICANUS*

PEDRO JOSEPH-NATHAN, J. ROBERTO VILLAGÓMEZ, LUISA U. ROMÁN* and JUAN D. HERNÁNDEZ*

Departmento de Química del Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Apartado 14-740, México D.F., 07000 México; *Instituto de Invetigaciones Químico Biológicas, Universidad Michoacana de San Nicolas de Hidalgo, Morelia, Michoacán, 58240 México

(*Received* 12 *July* 1989)

Key Word Index—*Senecio mexicanus*; Compositae; oplopane derivatives; structural determination.

Abstract—The leaves of *Senecio mexicanus* afforded three known oplopane derivatives previously found in the roots of the plant and a new oplopane whose structure and stereochemistry followed from X-ray crystallography.

INTRODUCTION

Some species of the genus *Senecio* such as *S. abrotanifolius* L. [1], *S. kleinia* Less [2] and *S. implexus* [3] contain oplopane derivatives. In addition, *Acrisione denticulata* [4], *Juniperus recurva* [5] and *Tussilago* farfara [6, 7] also contain oplopanes. Of special interest is *T. farfara* which gave an oplopane which acts as a cardiovascular respiratory stimulant [6] and which is also a dual receptor antagonist of the platelet activating factor [7]. Recently, we reported the isolation and structural elucidation of the oplopanes **1–3** from the roots of *S. mexicanus* Mc. Vaugh [8, 9]. Now, we describe the isolation of the oplopane derivatives **1–4** from the leaves of *S. mexicanus*. The structure and stereochemistry of the new natural product **4** was determined from a single crystal X-ray analysis of its 2,4-dinitrophenylhydrazone derivative (**5**).

RESULTS AND DISCUSSION

Chromatography of the hexane extracts of *S. mexicanus* gave the four oplopane derivatives **1–4**. Three of these compounds (**1–3**) were previously found in the roots of the plant [8, 9].

Compound **4** is a new oplopane derivative. Its IR spectrum exhibited carbonyl (1735 cm^{-1}) and double bond (1654 cm^{-1}) absorptions. The ^1H NMR spectrum shows two doublets due to the methyl groups of an isopropyl group at δ0.80 and 1.00, a triplet due to a methyl group coupled with a methylene group at δ 1.05 and two broad singlets due to an exocyclic methylene at δ4.55 and 4.70. The ^{13}C NMR spectrum (Table 1) shows 15 signals, one at δ218.0 due to a carbonyl group and two at δ149.9 and 104.0 corresponding to an exocyclic methylene group.

To establish the stereochemistry of **4**, its 2,4-dinitrophenylhydrazone derivative (**5**) was prepared, because crystals of **4** were not suitable for X-ray diffraction analyses. The molecular perspective of **5** (Fig. 1) shows the alpha-orientation of the ethyl group at C-3, while the other chiral centres (C-4, C-5 and C-9) show the same *trans*-arrangement as in compounds **1–3** [8, 9].

When compound **5** was prepared, the acid reaction conditions caused isomerization of the C-8/C-10 double bond in **4** to the C-1/C-9-position, providing compound **6**. The ^1H NMR spectrum shows a singlet at δ5.50 corresponding to H-1. The H-4 and H-8 signals are

Table 1. ^{13}C NMR spectral data of compounds **4**, **6** and **7** (75.4 MHz, $CDCl_3$)

C	4*	6	7
1	40.1	124.2	42.0
2	218.0	212.2	219.4
3	51.8[a]	52.1[c]	55.4
4	50.6[a]	49.8	50.0
5	43.6[b]	51.7[c]	48.8
6	26.1	24.0[d]	26.5
7	35.0	35.7	34.9
8	149.9	36.5	149.7
9	42.1[b]	188.8	46.8
10	104.0	17.9	103.8
11	28.1	28.9	28.4
12	21.3	21.7	21.8
13	15.7	15.7	15.8
14	17.5	23.8[d]	22.3
15	11.9	10.1	10.3

*Measured at 25.2 MHz.
[a–d]Assignments having the same letter may be interchanged.

partially overlapped at δ2.30 as a broad doublet and a septuplet, respectively. The coupling constants of H-8 established the α-orientation of the C-10 methyl group, which gave a doublet at δ1.18. Two doublets due to the isopropyl group and a triplet due to Me-15 were observed at δ0.87, 0.98 and 0.87, respectively. The IR spectrum shows the carbonyl absorption at 1690 cm^{-1}.

Compound **1** was hydrogenated in the presence of Pd/C. Under these conditions both the C-3/C-14 and C-8/C-10 double bonds were hydrogenated. When a small amount of potassium hydroxide was added [10], only the C-3/C-14 double bond was hydrogenated to give **7**, which is an epimer of **4**. Thus the ^1H NMR spectrum of **7** shows, as the most notable change, a triplet due to the Me-15 shifted upfield (δ0.87) with respect to **4** (δ1.05). Two singlets corresponding to the exocyclic methylene at δ4.58 and 4.78 and two doublets due to the isopropyl group at δ0.79 and 0.98 were observed. The IR spectrum shows the carbonyl and double bond absorptions at 1735 and 1650 cm^{-1}, respectively.

EXPERIMENTAL

General. Mps: uncorr. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ with TMS as int. standard. TLC was carried out on 0.25 mm layers of silica gel PF_{254} (Merck).

Plant material. Senecio mexicanus Mc. Vaugh was collected at Km 53 of the Morelia–Zacapu highway, in the State of Michoacán, México, during December 1987. A voucher specimen(JDH 37) is deposited at the Herbarium of Departmento Botánico, ENCB-IPN, Mexico City, where Prof. Jerzy Rzedowski identified the plant material.

Extraction and isolation. Air-dried leaves (2 kg) of *S. mexicanus* were extracted with hexane under reflux and subjected to CC on silica gel 60 (70-230 mesh). Compounds **1** (500 mg), **2** (1 g) and **3** (50 mg) were eluted with non-polar solvents and their spectral data compared with authentic samples [8, 9]. Frs eluted with hexane–$CHCl_3$ (7:3) yielded **4** (150 mg) as crystals, mp 54–56°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (C=O) 1654 (C=C). ^1H NMR (90 MHz): δ0.80 and 1.00 (each 3H, 2*d*, $J_{12,11} = J_{13,11} = 7$ Hz, isopropyl), 1.05 (3H, *t*, $J = 7$ Hz, Me-15), 4.55 (1H, *br s*, H-10) and 4.70 (1H, *br s*, H-10'), ^{13}C NMR: see Table 1;

$$[\alpha]\ \frac{589\quad 578\quad 546\quad 436\quad 365\ nm}{-108\quad -115\quad -140\quad -370\quad -1685}\ (CHCl_3;\ c\ 0.13).$$

2,4-*Dinitrophenylhydrazone of* **4**. To a sample of **4** (100 mg) in 3 ml EtOH was added 1.5 ml 2,4-dinitrophenylhydrazine in EtOH–H_2O–H_2SO_4. After standing at room temp. for 30 min, orange needles mp 144–146° were obtained by recrystallization of the product from $CHCl_3$–EtOH.

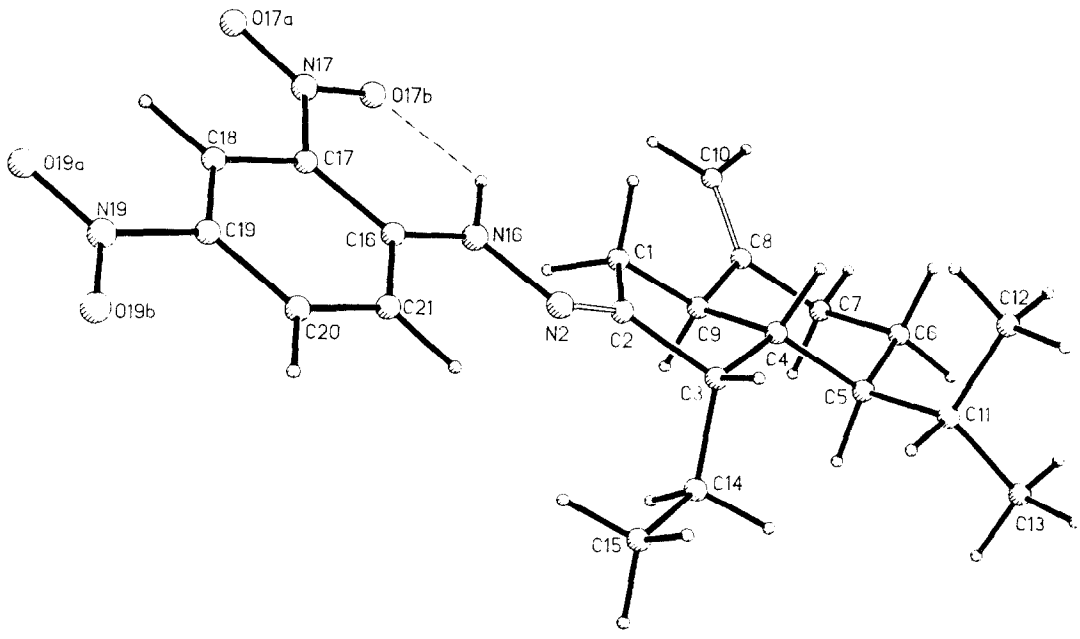
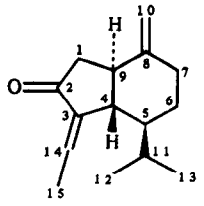
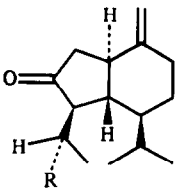


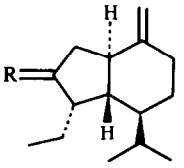
Fig. 1. Molecular perspective of compound **5**.



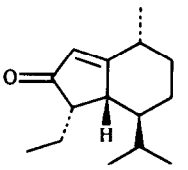
1 Z (3,14)
2 E (3,14)



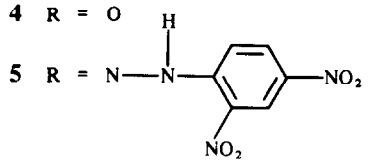
3 R = OH
7 R = H



4 R = O



6



5 R = N—N(H)—C$_6$H$_3$(NO$_2$)$_2$

X-Ray analysis of compound **5**. Single crystals of **5** were grown by slow crystallization from $CHCl_3$–EtOH. They were orthorhombic, space group $P2_12_12_1$ with $a=6.9454(17)$, $b=10.4520(41)$, $c=29.4989(105)$ Å and $d_{calc.}=1.24$ g/cm^3 for $Z=4$ (M, 400). The size of the crystal used for data collection was $0.40\times0.20\times0.02$ mm. No absorption correction was necessary ($\mu=6.7$ cm^{-1}). A total of 1617 reflections were measured for $3°\leqslant\theta\leqslant110°$ of which 1251 reflections were considered to be observed [$I\geqslant2.5\sigma$ (I)]. The final discrepancy indices were $R=5.06\%$ using 1249 reflections in the final refinement. The final difference Fourier map was essentially featureless, the highest residual peaks having densities of 0.15 e/Å^3.

Compound **6**. When compound **5** was prepared, a small amount of **6** was also formed. UV λ_{max}^{EtOH} nm (log ε): 232 (3.64); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1690, 1600 (C=C-C=O). ^{1}H NMR (300 MHz): δ0.87, 0.98 (3H each, 2*d*, $J_{12,11}=J_{13,11}=7$ Hz, isopropyl), 0.87 (3H, *t*, $J=7$ Hz, Me-15), 1.18 (3H, *d*, $J=7$ Hz, Me-10), 2.30 (1H, *m*, $J_{8,10}=J_{8,7\beta}=6$ Hz; $J_{8,7\alpha}=12$ Hz, H-8) and δ5.50 (1H, *br s*, H-1); ^{13}C NMR: see Table 1;

[α]	589	578	546	436	365 nm	
	+59	+63	+77	+207	+854	($CHCl_3$; *c* 0.2).

Compound **7**. To a soln of **1** (243 mg) in 10 ml EtOH (99.5%) was added KOH (250 mg) [10] in 10 ml of EtOH. Then, 24 mg Pd/C (5%) were added. The mixture was stirred for 2 hr at room temp. and 1 atm. pressure in H_2. The product was chromatographed and **7** was obtained as crystals mp 49–51°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1650 (C=C-C=O). ^{1}H NMR (90 MHz): δ0.79. 0.98 (each 3H, 2*d*, $J_{12,11}=J_{13,11}=7$ Hz, isopropyl), 0.87 (3H, *d*, $J=7$ Hz, Me-15), 4.58 (1H, *br s*, H-10) and δ4.78 (1H, *br s*, H-10'); ^{13}C NMR: see Table 1.

Acknowledgements—We are grateful to Prof. J. Rzedowski (ENCB-IPN) for identification of plant material, and to CoSNET, CoNaCyT and Proyectos Estratégicos-SEP (Mexico) for financial support.

REFERENCES

1. Bohlmann, F. and Suwita, A. (1976) *Chem. Ber.* **109**, 2014.
2. Bohlmann, F., Zdero, C. and Gupta, R. K. (1981) *Phytochemistry* **20**, 2024.
3. Bohlmann, F., Ahmed, M., Jakupovic, J. and Jeffrey, C. (1981) *Phytochemistry* **20**, 251.
4. Abdel Aal, M., Bohlmann, F., Sarg, T., El-Domiaty, M. and Nordenstam, B. (1988) *Phytochemistry* **27**, 2599.
5. Weyerstahl, P., Marschall-Weyerstahl, H., Manteuffel, E. and Kaul, V. K. (1988) *Planta Med.* **3**, 259.
6. Yiping, Li and Yunmu, W. (1988) *Gen. Pharmacol.* **19**, 261.
7. L. Huang, San Bao, Chang, M. N., García, M. L., Han, Q. Q., Huang, L., King, V. Kaczorowski, G. S. and Winwuist, R. J. (1987) *Eur. J. Pharmacol.* **141**, 269.
8. Joseph-Nathan, P., Villagómez, J. R., Román, L. U. and Hernández, J. D. (1989) *Phytochemistry* **28**, 1207.
9. Joseph-Nathan, P., Villagómez, J. R., Rojas-Gardida, M., Román, L. U. and Hernández, J. D. (1989) *Phytochemistry* **28**, 2397.
10. Augustine, R. L. (1965) in *Catalytic Hydrogenation, Techniques and Applications in Organic Synthesis*, p. 46. New Jersey.