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# AN OPLOPANE FROM *SENECIO MEXICANUS*

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**Key Word Index**—*Senecio mexicanus*, Compositae, roots, oplopane derivatives, structural determination

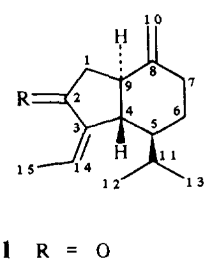
**Abstract**—The roots of *Senecio mexicanus* afforded a new oplopane derivative whose structure was elucidated by spectroscopic methods and by treatment with *p*-toluenesulphonic acid, which yielded three isomeric substances. The stereochemistry of the natural product followed from X-ray crystallography and its absolute configuration from the optical activity.

## INTRODUCTION

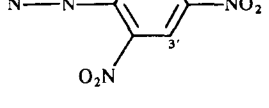
Oplopane [1] derivatives have been isolated mainly from species belonging to the tribe Senecioneae, in particular from the genera *Senecio* [2–4], *Kleinia* [5], *Rugelia* [6] and *Notonia* [7]. Most oplopane derivatives are highly oxygenated, no X-ray diffraction studies have been reported and the $^{13}$C NMR spectra of only two compounds are assigned [8, 9]. We now report the new oplopane derivative **1** from *Senecio mexicanus*, a Mexican plant belonging to the tribe Senecioneae. The relative stereochemistry of **1** has been determined by single crystal X-ray analysis of the 2,4-dinitrophenylhydrazone **2** and the absolute configuration was deduced by comparison of the optical activity of **1** with that of a pregnane derivative [10] having a similar chromophore. We also explored the stability of the oplopane ring system towards acids. Thus, treatment of **1** with *p*-toluenesulphonic acid gave three isomeric derivatives whose structures became evident from their spectral data.

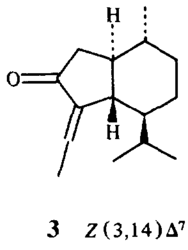
## RESULTS AND DISCUSSION

Chromatography of the hexane extracts of the roots of *S. mexicanus* yielded a crystalline solid, mp 51–53°. The mass spectrum showed a $[M]^+$ at $m/z$ 218 in accordance with the formula $C_{15}H_{22}O$. The presence of a conjugated carbonyl group follows from the IR spectrum and from the sp$^2$ region of the $^{13}$C NMR spectrum, which further shows signals for two exocyclic double bonds (see Table 1). The $^1$H NMR spectrum shows two doublets ($J = 7$ Hz) at $\delta$0.84 and 1.02 corresponding to the non-equivalent methyl groups of an isopropyl group, two broad singlets at $\delta$4.78 and 4.57 of an exocyclic methylene group, and one double quartet at $\delta$6.22 corresponding to H-14, which is coupled to Me-15. The above spectral data are in agreement with structure **1** which is a new sesquiterpene



**1** R = O

**2** R =




**3** $Z(3,14)\Delta^7$
**4** $Z(3,14)\Delta^{1(9)}$
**5** $E(3,14)\Delta^{1(9)}$

Table 1. $^{13}$C NMR spectral data* (75.4 MHz, CDCl$_3$) of compounds **1–5**

| C | **1** | **2** | **3** | **4** | **5** |
|---|---|---|---|---|---|
| 1 | 41.3 | 30.0 | 42.8 | 128.8 | 123.1 |
| 2 | 206.5 | 160.2 | 207.4 | 147.4 | 196.4 |
| 3 | 141.5 | 140.0 | 141.1 | 137.2 | 140.2 |
| 4 | 51.3 | 52.2 | 48.4 | 49.1 | 48.0 |
| 5 | 44.9 | 44.4 | 43.3 | 51.1 | 53.6 |
| 6 | 26.0 | 25.8 | 25.3 | 23.7 | 24.2 |
| 7 | 34.5 | 34.5 | 122.2 | 36.5 | 36.6 |
| 8 | 149.1 | 148.7 | 134.2 | 35.9 | 36.5 |
| 9 | 46.0 | 46.6 | 42.0 | 182.1 | 184.3 |
| 10 | 104.5 | 104.7 | 17.9 | 17.5 | 17.5 |
| 11 | 27.4 | 27.4 | 27.9 | 28.2 | 28.8 |
| 12† | 21.4 | 21.5 | 21.7 | 21.3 | 21.8 |
| 13† | 15.6 | 15.7 | 15.7 | 15.2 | 16.5 |
| 14 | 131.7 | 124.2 | 132.1 | 134.7 | 130.2 |
| 15 | 14.5 | 15.6 | 14.6 | 13.8 | 15.7 |
| 1' |  | 144.8 |  |  |  |
| 2' |  | 129.4 |  |  |  |
| 3' |  | 123.5 |  |  |  |
| 4' |  | 137.9 |  |  |  |
| 5' |  | 130.0 |  |  |  |
| 6' |  | 116.4 |  |  |  |

*In ppm from TMS as the internal standard.
†Assignments may be interchanged.

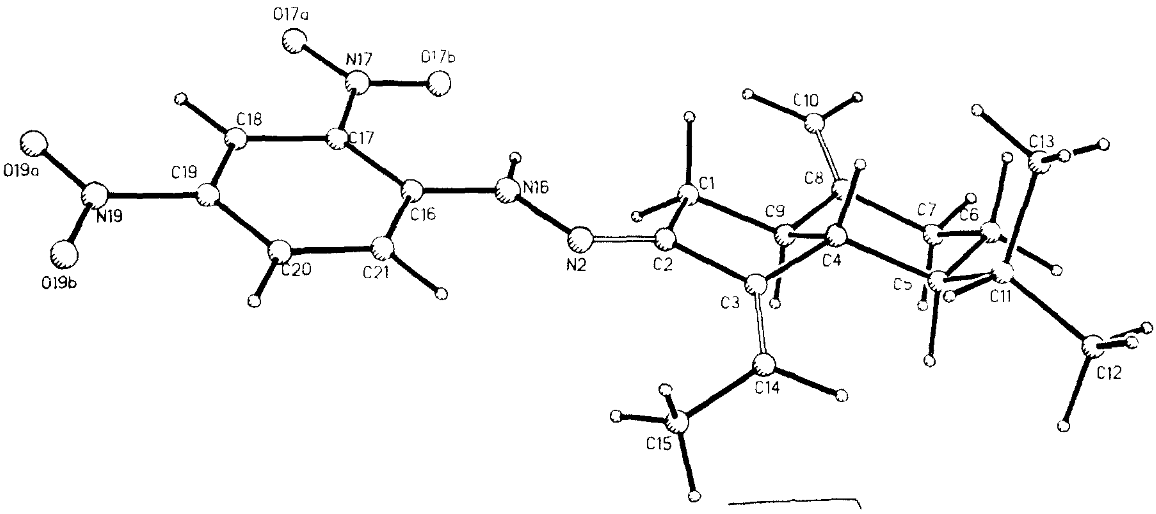


Fig 1 Molecular perspective of compound **1**

closely related to the oplopane derivatives isolated from *S kleinia* [4]

Since crystals of **1** were inadequate for X-ray diffraction studies, the 2,4-dinitrophenylhydrazone **2** was prepared as orange needles, mp 82–84 Its X-ray diffraction analysis provided the molecular perspective (Fig 1) which shows a *trans*-arrangement of C-4, C-5 and C-9, in agreement with all already described oplopane derivatives This analysis also corroborates the *Z*-configuration of the C-3, C-14-double bond and shows that the six-membered ring exists in a chair conformation The coupling constants of H-6α and H-6β, suggest that the conformation in solution is the same The absolute configuration of **1** follows from its negative rotation after comparison with (*Z*)-5,17(20)-pregnadien-3β-ol-16-one acetate [10] In order to explore the chemistry of **1**, it was treated with *p*-toluenesulphonic acid in benzene giving the three isomeric substances **3**–**5** as colourless oils Their structures were elucidated from their spectral data The $^1$H NMR data are given in the Experimental and the $^{13}$C NMR data are summarized in Table 1 The $^1$H NMR assignments were secured by irradiation experiments and the $^{13}$C NMR assignments were confirmed from two-dimensional $^{13}$C-$^1$H chemical shift correlation diagrams of **1**, **3**–**5**

Compound **3** has a double bond at C-7, C-8 while **4** and **5** have a double bond at C-1, C-9 The stereochemistry at C-8 in **4** and **5** is evident from the coupling constants of H-8 and inspection of a Dreiding model Considering that the six-membered ring exists in a chair conformation, the coupling constants of H-8, two of 6 Hz and one of 12 Hz, agree with an alpha-orientation for Me-10 as depicted in **4** The H-14 signal of **5** is shifted downfield and H-15 is shifted upfield with respect to **4**, indicating that the 3,14-double bond has the *E*-configuration Isomers **4** and **5** were interconverted in the presence of catalytic amounts of sulphuric acid in ethanol at room temperature, a *ca* 1 1 ratio is obtained starting with either isomer In contrast, compound **1** is stable under these conditions

## EXPERIMENTAL

*General* Mps uncorr UV spectra were recorded in EtOH and in dioxan and IR spectra from films Specific rotations were measured in CHCl$_3$ $^1$H NMR and $^{13}$C NMR spectra were measured in CDCl$_3$ with TMS as int std EIMS was recorded at 70 eV TLC was carried out on silica gel PF$_{254}$ (Merck)

*Plant material S mexicanus* Mc Vaugh was collected at Km 53 of the Morelia-Zacapu highway, in the State of Michoacan, Mexico, during December 1986 A voucher specimen (JDH37) is deposited at the Herbarium of Departamento Botanico, ENCB-IPN, Mexico City, where Prof Jerzy Rzedowski identified the plant material

*Extraction and isolation* Air-dried roots (700 g) of *S mexicanus* were extracted with hexane and chromatographed by CC on silica gel 60 (70–230 mesh) Frs eluted with hexane yielded **1** (13 g) as colourless crystals Mp 51 53 EIMS *m z* (rel int ) 218 $[M]^+$ ($C_{15}H_{22}O$), 203 $[M-Me]^+$ (10 5), 190 $[M-C_2H_4]^+$ (9 3), 175 $[M-C_3H_7]^+$ (17 9), 161 $[M-C_3H_5O]^+$ (7 5) IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$ 1715, 1640 (C=C-CO) 1440 1386, 1368 (isopropyl), UV $\lambda_{max}^{EtOH}$ nm (log ε) 240 (3 91) $^1$H NMR (300 MHz) δ0 84 and 1 02 (3H each, 2*d*, $J_{12\ 11}=J_{13\ 11}=7$ Hz isopropyl group), 1 26 (1H, *dq*, $J_{6\beta\ 6\alpha}=J_{6\beta\ 5\alpha}=J_{6\beta\ 7\alpha}=13$ Hz, $J_{6\beta\ 7\beta}=4$ 5 Hz H-6β), 1 86 (1H, *qd*, $J_{6\alpha\ 5\alpha}=J_{6\alpha\ 7\alpha}=J_{6\alpha\ 7\beta}=3$ 2 Hz $J_{6\alpha\ 6\beta}=13$ Hz, H-6α), 2 10 (3H, *dd*, $J_{15\ 14}=7$ Hz, $J_{15,4}=2$ 3 Hz, Me-15), 4 78 (1H, *br* s, H-10), 4 57 (1H *br* s, H-10′) and δ6 22 (1H, *dq*, $J_{15\ 14}=7$ Hz, $J_{14\ 4}=2$ Hz, H-14) $^{13}$C NMR, see Table 1 The analytical sample was prepd by recrystallization from hexane (found C, 82 4, H, 10 2, 0, 7 6 $C_{15}H_{22}O$ requires C 82 8, H, 10 2, O 7 4%)

$$[\alpha] = \frac{589}{-194}\ \frac{578}{-208}\ \frac{546}{250}\ \frac{436\ \text{nm}}{-370}\ (\text{CHCl}_3,\ c\ 2)$$

*2,4-Dinitrophenylhydrazone of* **1** Orange needles mp 82–84 IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$ 3314 (N-H), 1618 (C=N), 1591 (C=C) and 1336 (C-N) UV $\lambda_{max}^{dioxane}$ nm (log ε) 371 (4 0), 256 (3 6) $^1$H NMR (300 MHz) δ7 90, 8 35, 9 15 (1H each H-$C_6H_6$), 11 10 (1H, s, N-H), 2 78 (1H, *dd*, $J_{1\alpha,1\beta}=16$ Hz, $J_{1\alpha\ 9\beta}=7$ Hz, H-1α), 2 10 (3H *dd*, $J_{15\ 14}=7$ Hz, $J_{15\ 4}=2$ 5 Hz, Me-15) 6 10 (1H, *dq*, $J_{15\ 14}=7$ Hz, $J_{14\ 4}=2$ 3 Hz, H-14), 1 26 (1H, *dq*, $J_{6\alpha\ 6\beta}=J_{6\beta\ 5\alpha}=J_{6\beta\ 7\alpha}$ $=13$ Hz, $J_{6\beta\ 7\beta}=4$ 5 Hz, H-6β), 1 01 (3H, *d* $J_{11\ 12}=7$ Hz, Me-12) and 0 81 ppm (3H, *d*, $J_{13\ 11}=7$ Hz Me-13)

$$[\alpha] = \frac{589}{+10}\ \frac{578}{+3}\ \frac{546\ \text{nm}}{-34}\ (\text{CHCl}_3,\ c\ 0\ 1)$$

*X-ray analysis* Single crystals of **2** were grown by slow crystallization from CHCl$_3$-EtOH They were orthorhombic, space group $P2_12_12_1$ with $a = 6\ 7295$ (35), $b = 10\ 4381$ (65), $c = 29\ 6848$ (249) Å and $d_{calc} = 1\ 27$ g/cm³ for $Z = 4(M_r\ 398\ 4)$ The intensity data were measured on a Nicolet R3m four-circle diffractometer with $CuK_\alpha$ monochromated radiation in the $\theta$ $2\theta$ scan mode The size of the crystal used for data collection was *ca* 0 50 × 0 10 × 0 20 mm No absorption correction was necessary ($\mu = 7\ 4\ cm^{-1}$) A total of 1508 reflections were measured for $3° \leq \theta \leq 110°$ of which 1352 reflections were considered to be observed ($I \geq 3\sigma(I)$ The structure was solved by direct methods using the software provided by the manufacturer and refined by full matrix least-squares assuming the anisotropic temperature factors for non-hydrogen atoms and the isotropic ones for hydrogen atoms The final discrepancy indices were $R = 4\ 20\%$ using 1348 reflections in the final refinement The final difference Fourier map was essentially featureless, the highest residual peaks having densities of 0 16 e/Å³ Lists containing atomic coordinates and thermal parameters, bond distances, bond angles, anisotropic temperature factors, hydrogen atom coordinates and comparison of the observed and calculated structure factors will be deposited at the Cambridge Crystallographic Data Centre

*Treatment of* **1** *with p-toluenesulphonic acid* A sample of 2 6 g of **1** was dissolved in 15 ml of $C_6H_6$ and 10 mg of *p*-TsOH acid added The soln was refluxed for 78 hr and then washed with $H_2O$ The solvent was removed and the residue chromatographed on a silica gel column Three isomers were sepd, **3** (219 mg), **4** (330 mg) and **5** (150 mg)

*Isomer* **3** Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm⁻¹ 1709 (C=O), 1639 (C=C). UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$) 242 (3 67) $^1$H NMR (300 MHz) 0 85 and 0 93 (3H each, 2*d*, $J = 7$ Hz, isopropyl group), 2 0 (1H, *dd*, $J_{1\beta,9} = 13$ Hz, H-1$\beta$), 1 66 (3H, *br* s, Me-10), 2 12 (3H, *dd*, $J_{15,4} = 2$ Hz, Me-15), 2 47 (1H, *dd*, $J_{1\beta,1\alpha} = 16$ Hz, $J_{1\alpha,9} = 6$ Hz, H-1$\alpha$), 5 40 (1H, *br s*, H-7) and $\delta$6 25 (1H, *dq*, $J_{14,15} = 7\ 3$, $J_{14,4} = 2\ 3$ Hz, H-14) $^{13}$C NMR see Table 1

$$[\alpha] = \frac{589 \quad 578 \quad 546 \quad 436\ \text{nm}}{-216 \quad -227 \quad -270 \quad -633}\ (CHCl_3,\ c\ 0\ 17)$$

*Isomer* **4** Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm⁻¹ 1610, 1681 (C=O), unsatd, 1465, 1440, 1386 (isopropyl group) UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$) 254 (3 90) $^1$H NMR (300 MHz) $\delta$0 92 6H, *d*, $J = 7$ Hz, Me-12, 13), 1 16 (3H, *d*, $J = 7$ Hz, Me-10), 1 27 (1H, *qd*, $J_{6\beta,6\alpha} = J_{6\alpha,5} = 3\ 3$ Hz, H-6$\alpha$), 2 22 (3H, *d*, $J = 7$ Hz, Me-15), 2 35 (1H, *m*, $J_{8,10} = J_{8,7\beta} = 6$ Hz, $J_{8,7\alpha} = 12$ Hz, H-8), 2 87 (1H, *d*, $J = 11$ Hz, H-4), 5 89 (1H, *br* s, H-1) and 6 04 ppm (1H, *q*, $J = 7$ Hz, H-14) $^{13}$C NMR see Table 1

$$[\alpha] = \frac{589 \quad 578 \quad 546 \quad 436\ \text{nm}}{+30 \quad +33 \quad +39 \quad +71}\ (CHCl_3,\ c\ 1\ 64)$$

*Isomer* **5** Colourless oil IR $\nu_{max}^{CHCl_3}$ cm⁻¹ 1690 (C=O), 1645, 1605 (C=C), 1368, 1387, 1440, 1459 (isopropyl group) UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$), 252 (3 90) $^1$H NMR (300 MHz) $\delta$0 89 (3H, *d*, $J = 7$ Hz, Me-12), 0 98 (3H, *d*, $J = 7$ Hz, Me-13), 1 19 (3H, *d*, $J = 7$ Hz, Me-10), 1 36 (1H, *dq*, $J_{6\beta\ 6\alpha} = J_{6\beta,7\alpha} = J_{6\beta,5\alpha} = 13$ Hz, H-6$\beta$), 1 76 (1H, *qd*, $J_{6\alpha,6\beta} = 13$ Hz, $J_{6\alpha\ 5} = J_{6\alpha,7\beta} = J_{6\alpha\ 7\alpha} = 3\ 3$ Hz, H-6$\alpha$), 1 86 (3H, *d*, $J = 7$ Hz, Me-15), 2 11 (1H, *tdd*, $J_{7\beta,6\alpha} = J_{7\beta,6\beta} = 3\ 3$ Hz, $J_{7\beta\ 7\alpha} = 12$ Hz, H-7$\beta$), 2 37 (1H, *m*, $J_{8,10} = J_{8,7\beta} = 6$ Hz, $J_{8,7\alpha} = 12$ Hz, H-8), 3 04 (1H, *d*, $J = 11$ Hz, H-4), 5 90 (1H, *br s*, H-1) and 6 60 ppm (1H, *dq*, $J_{15\ 14} = 7\ 3$ Hz, $J_{14,4} = 1\ 3$ Hz, H-14) $^{13}$C NMR see Table 1

$$[\alpha] = \frac{589 \quad 578 \quad 546 \quad 436\ \text{nm}}{+12 \quad +26 \quad +30 \quad +41}\ (CHCl_3,\ c\ 0\ 36)$$

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