

A THYMOL DERIVATIVE FROM *CALEA NELSONII**

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Key Word Index.—*Calea nelsonii*; Compositae; Heliantheae; thymol derivatives.

Abstract—One new and three previously described thymol derivatives were isolated from the aerial parts of *Calea nelsonii*. Transesterification products of these compounds were obtained under treatment with bentonitic earth.

INTRODUCTION

As a result of our research on *Calea nelsonii* Rob. and Greenm. (Compositae), we have isolated the previously described compounds 10-acetoxy-8,9-epoxy-7-isobutyryloxythymol isobutyrate (1) [1], 8,9-epoxy-7-isobutyryloxythymol isobutyrate (2) [2], 10-acetoxy-8,9-epoxythymol isobutyrate (3) [3] and the new compound 10-acetoxy-8,9-dehydrothymol isobutyrate (4). In a previous work on this species [1], two types of thymol derivatives 8,9-epoxyphenolic esters and 8-hydroxy-9-acyloxy phenols were described. In our case no free phenolic compounds were detected as natural constituents of *C. nelsonii*, but they were produced from compounds 1–3 by bentonitic earth during the isolation process.

RESULTS AND DISCUSSION

Aerial parts of *C. nelsonii* gave four thymol derivatives. The first isolated compounds were identified as 1–3 by comparison of their spectral data with those described in the literature [1–3].

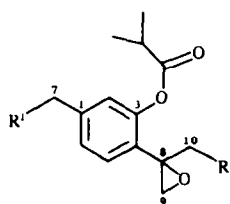
The ¹H NMR spectrum of the new compound 4 (Table 1) resembled that of the known compound 3, but it exhibited signals for two vinylic protons at δ 5.37 and 5.17, showing that 4 possesses an 8,9-double bond instead of the epoxide of 3, which is confirmed by the molecular ion at *m/z* 276, in accordance with the proposed molecular formula (C₁₆H₂₀O₄).

The derivatives 5–8 were obtained when a fraction containing the epoxy thymols 1–3 was chromatographed on bentonitic earth [4] using chloroform–methanol as eluent. These transformations were accompanied by the appearance of phenolic signals, as well as a downfield shift of the C-9 protons in the ¹H NMR spectrum. A similar rearrangement was described earlier for compounds 2 and 3, which gave the transesterified compounds 6 and 8, respectively [1, 2]. In our hands compounds 6 and 7 were presumably obtained from 2, since methanol was present. Nevertheless, compounds 1

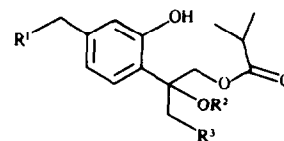
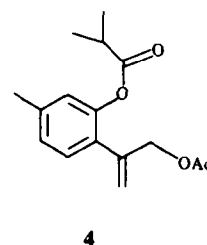
and 3 only gave compounds 5 and 8, in which methanol incorporation was not observed.

EXPERIMENTAL

Isolation of compounds. Ground, dried aerial parts of *C. nelsonii* (1 kg) collected near Tapanatepec, Oaxaca, México (voucher deposited at the Herbarium of the Instituto de Biología, UNAM, AOH-104) were extd with hexane, CHCl₃ and Me₂CO, affording 110, 10 and 16 g of exts, respectively. The hexane ext. (80 g) was fractionated through Celite with hexane, hexane–EtOAc (3:1) and EtOAc, yielding after solvent evapn 52.4, 15.1 and 7.2 g of residues, respectively. The hexane residue (30.2 g) was fractionated by CC (silica gel, Merck G, hexane–EtOAc gradient elution). Frs eluted with hexane (3.6 g) contained compound 4, which was first purified by CC (silica gel, Merck G, hexane) and finally by HPLC (Micropak Si-10; 8 mm × 50 cm; 200 ml hr^{−1}; hexane–EtOAc, 4:1; refractive index);



	R ¹	R ²
1	OiBu	OAc
2	OiBu	H
3	H	OAc



	R ¹	R ²	R ³
5	OiBu	H	OAc
6	OiBu	H	H
7	OiBu	Me	H
8	H	H	OAc

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Table 1. ^1H NMR of compounds 3–5 and 7 (80 MHz, CDCl_3 , TMS as internal standard)

H	3	4	5*	7
2	6.77 <i>br s</i>	7.02 <i>d</i> (1.5)	6.97 <i>br s</i>	6.82 <i>br s</i>
5	7.28 <i>d</i> (8)	7.13 <i>d</i> (8)	7.16 <i>br d</i> (8)	6.99 <i>d</i> (8)
6	6.93 <i>br d</i> (8)	6.87 <i>dd</i> (8, 1.5)	6.88 <i>br d</i> (8)	6.77 <i>br d</i> (8)
7	2.30 <i>s</i> †	2.34 <i>s</i> †	5.11 <i>s</i> †	5.04 <i>s</i> †
9	2.84 <i>d</i> (6)	5.37 <i>dt</i> (2, 1.5)	4.53 <i>s</i> †	4.36 <i>d</i> (12)
9'	2.58 <i>d</i> (6)	5.17 <i>br d</i> (1.5)		4.18 <i>d</i> (12)
10	4.40 <i>d</i> (12)			
		4.76 <i>t</i> (1.5)†	4.53 <i>s</i> †	1.65 <i>s</i> ‡
10'	4.08 <i>d</i> (12)			
3 or 9-Oiso-Bu	2.76 <i>hept</i> (7)	2.75 <i>hept</i> (7)	2.58 <i>hept</i> (7)	2.54 <i>hept</i> (7)
	1.25 <i>d</i> (7)§	1.28 <i>d</i> (7)§	1.12 <i>d</i> (7)§	1.13 <i>d</i> (7) §
7-Oiso-Bu	—	—	2.64 <i>hept</i> (7)	2.60 <i>hept</i> (7)
			1.19 <i>d</i> (7)§	1.21 <i>d</i> (7)§
10-OAc	1.91 <i>s</i> ‡	2.05 <i>s</i> ‡	2.08 <i>s</i> ‡	—
3-OH	—	—	8.97 <i>s</i>	8.56 <i>s</i>
8-OMe	—	—	—	3.28 <i>s</i>

Coupling constants in Hz are in parentheses.

*Determined at 60 MHz.

†Intensity two protons.

‡Intensity three protons.

§Intensity six protons.

236 mg of 4 were obtained. Frs eluted with hexane–EtOAc (19:1) gave 7.13 g of 1, 5.35 g of 2 and 10.63 g of 3.

10-Acetoxy-8,9-dehydrothymol isobutyrate (4). Colourless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1742, 1619, 1506, 1469, 1387, 1239, 1155. EIMS (probe) 70 eV, m/z (rel. int.): 276 $[\text{M}]^+$ ($\text{C}_{16}\text{H}_{20}\text{O}_4$; 6), 233 $[\text{M} - \text{Ac}]^+$ (2), 216 $[\text{M} - \text{HOAc}]^+$ (3), 206 $[\text{M} - \text{C}_4\text{H}_8\text{O}]^+$ (14), 146 $[\text{206} - \text{HOAc}]^+$ (95), 145 $[\text{216} - \text{iso-Bu}]^+$ (94), 131 $[\text{145} - \text{CH}_2]^+$, 71 $[\text{iso-Bu}]^+$ (59), 43 $[\text{Ac}]^+$ (100).

Formation of compounds 5–8. The original hexane ext. (10 g) containing a mixt. of thymols 1–3 was percolated through a column of bentonitic earth ('Tonsil' [4]) with CHCl_3 –MeOH (9:1) as eluent. TLC of the resulting frs revealed the presence of compounds 5–8. Thymols 1–3 were not observed. Compounds 5–8 were purified by CC (silica gel Merck G, hexane–EtOAc, 17:3) and 1.91 g of 5, 1.04 g of 6, 0.82 g of 7 and 3.20 g of 8 were obtained. In a separate reaction, 1 g of bentonitic earth was added to a soln of 2 (100 mg) in CHCl_3 (10 ml). The reaction mixt. was stirred for 2 hr and filtered off to yield quantitatively compound 6 after evapn. of solvent. Under the same conditions compounds 1 and 3 were also quantitatively transformed into 5 and 8, respectively.

10-Acetoxy-8-hydroxy-7,9-di-isobutyryloxythymol (5). Colourless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3366, 1734, 1631, 1578, 1512, 1468, 1389, 1370, 1155. EIMS (probe) 70 eV, m/z (rel. int.): 396 $[\text{M}]^+$ ($\text{C}_{20}\text{H}_{28}\text{O}_8$; 5), 378 $[\text{M} - \text{H}_2\text{O}]^+$ (3), 323 $[\text{M} - \text{AcCH}_2]^+$ (12),

305 $[\text{323} - \text{H}_2\text{O}]^+$ (2), 295 $[\text{M} - \text{iso-BuCH}_2]^+$ (20), 277 $[\text{295} - \text{H}_2\text{O}]^+$ (3), 253 $[\text{295} - \text{C}_2\text{H}_5\text{O}]^+$ (13), 235 $[\text{295} - \text{HOAc}]^+$ (100), 207 $[\text{295} - \text{HO-iso-Bu}]^+$ (81), 71 $[\text{iso-Bu}]^+$ (75), 43 $[\text{Ac}]^+$ (73).

7,9-Di-isobutyryloxy-8-methoxythymol (7). Yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3325, 1738, 1732, 1625, 1577, 1510, 1471, 1391, 1370, 1157. EIMS (probe) 70 eV, m/z (rel. int.): 352 $[\text{M}]^+$ ($\text{C}_{19}\text{H}_{22}\text{O}_6$; 2), 321 $[\text{M} - \text{MeO}]^+$ (1), 265 $[\text{M} - \text{O-iso-Bu}]^+$ (13), 251 $[\text{M} - \text{iso-BuCH}_2]^+$ (100), 233 $[\text{321} - \text{HO-iso-Bu}]^+$ (18), 162 $[\text{233} - \text{iso-Bu}]^+$ (42), 145 $[\text{321} - \text{HO-iso-Bu}]^+$ (25), 71 $[\text{iso-Bu}]^+$ (35).

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