(3H, *s*, $H_1$), 2.42 (2H, *t*, $J_{3,4} = 7.3$, $H_3$), 4.17 (1H, *m*, $J_{8,7} = 5.9$, $H_8$), 5.72 (1H, *ddd*, $J_{10,9} = 15.9$, $J_{10,8} = 1.2$, $H_{10}$), 6.25 (1H, *dd*, $H_9$); $^{13}$C NMR: Table 1.

8-*Hydroxypentadeca*-9E,13Z-*diene*-11-*yn*-2-*one* (2). MS *m/z* (rel. int.): 234 $[M]^+$ (70), 219 $[M - Me]^+$ (45), 193 (35), 176 (32), 159 (40), 149 (45) 135 (60), 121 (72), 95 (73), 83 (100), 71 (75), 55 (98); $^1$H NMR (400 MHz, $CDCl_3$, TMS int. std.) $\delta$: the signals for protons $H_{1-8}$ were the same as for 1, 1.89 (3H, *d*, $J_{15,14} = 6.8$, $H_{15}$), 5.59 (1H, *ddd*, $J_{10,9} = 15.9$, $J_{10,8} = 1.6$, $H_{10}$), 5.99 (1H, *dq*, $H_{14}$), 6.12 (1H, *dd*, $H_9$); $^{13}$C NMR: Table 1.

## REFERENCES

1. Wagner, H., Proksch, A., Riess-Maurer, I., Vollmar, A., Odenthal, S., Stuppner, H., Jurcic, K., LeTurdu, M. and Fang, J. N. (1985) *Arzneim.-Forsch.* **35**, 1069.
2. Bauer, R. F. X., Khan, I. A., Lotter, H., Wagner, H. and Wray, V. (1985) *Helv. Chim. Acta* **68**, 2355.
3. Bauer, R., Khan, I. and Wagner, H. (1986) *Dtsch. Apoth. Ztg.* **126**, 1065.
4. Bauer, R., Khan, I. and Wagner H. (1985) *Acta Agron. Hung.* **34**, Suppl., 88.
5. Bauer, R., Khan, I. and Wagner, H. Poster at the 34th Annual Congress of the Society for Medicinal Plant Research in Hamburg (22–27 Sept. 1986).
6. Foster, S. (1985) *Herbalgram* 3.
7. Schulte, K. E., Rücker, G. and Perlick, J. (1967) *Arzneim.-Forsch.* **17**, 82.
8. Bohlmann, F. and Grenz, M. (1966) *Chem. Ber.* **99**, 3197.
9. Bauer, R., Khan, I. A., Wray, V. and Wagner, H. (1986) *Planta Med.* 424.

---

*Phytochemistry*, Vol. 26, No. 4, pp. 1200–1202, 1987.
Printed in Great Britain.

0031-9422/87 \$3.00 + 0.00

# (7*R*)-*TRANS,TRANS*-NEPETALACTONE FROM *NEPETA ELLIPTICA*

Albert T. Bottini, Vasu Dev,* David J. Garfagnoli, H. Lohani,† C. S. Mathela† and A. K. Pant†

Department of Chemistry, University of California, Davis, CA 95616, U.S.A.; *Department of Chemistry, California State Polytechnic University, Pomona, CA 91768, U.S.A.; †Department of Chemistry, Kumaun University, Nainital 263002, India

(*Received* 9 *June* 1986)

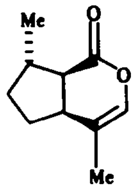
**Key Word Index**—*Nepeta elliptica*; Labiatae; nepetalactone; cyclopentanoid monoterpene; $^{13}$C NMR spectra.

**Abstract**—The major component of the essential oil from the aerial parts of *Nepeta elliptica*, gathered in the Kumaun Region of India, has been identified as (7*R*)-*trans,trans*-nepetalactone primarily by comparison of its IR spectrum with those of its four (7*S*)-stereoisomers and its mass spectrum and $^1$H and $^{13}$C NMR spectra with those of its three diastereomers.

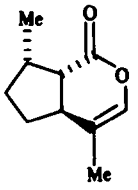
## INTRODUCTION

Several members of the genus *Nepeta* produce one or more diastereomers of (7*S*)-nepetalactone [1–4]. *Nepeta cataria* [1–3] and *N. mussini* [3], the two most thoroughly studied species, give essential oils that contain, respectively, (7*S*)-*cis,trans*- and (7*S*)-*cis,cis*-nepetalactone **1a** and **1b** as the major components and (7*S*)-*trans,cis*-nepetalactone **1c** and **1a** as minor components. significantly, the $^1$H and $^{13}$C NMR spectra of **1a–c** have been described [3], and all four (7*S*)-nepetalactones **1a–d** have been synthesized [5].

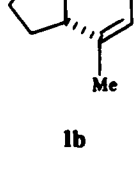
We describe here the isolation and characterization of the fourth naturally occurring diastereomer of nepetalactone and the first with the (*R*)-configuration at $C_7$. (7*R*)-*trans,trans*-Nepetalactone **1d′** was obtained as the major component (80%) of the essential oil from the aerial parts of *Nepeta elliptica* Royle ex Benth., which grows at altitudes of 1500–3000 m in the Kumaun region of India [6].



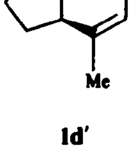
**1a**



**1**



**1b**



**1d′**

## RESULTS AND DISCUSSION

Examination of the steam-volatile oil by GC/MS and comparison of the mass spectrum of the major component with those of **1a–c** [3] indicated that it was a nepetalactone. The required molecular formula $C_{10}H_{14}O_2$ was confirmed by the high resolution electron impact mass spectrum and elemental analysis of the purified product, mp 36–37°. Although the mp is close to that reported for **1c** [3], the specific rotation and the IR and $^1$H NMR spectra were inconsistent with those of **1c** while clearly consistent with those expected for the (7*R*)-*trans,trans*-stereoisomer **1d′** [3, 5].

That the *N. elliptica* product is indeed **1d′** was confirmed by comparison of its $^{13}$C NMR spectrum with those of **1a–c**, which have been thoroughly analysed by Eisenbraun *et al.* [3]. They noted that the chemical shifts of C-3, C-4, C-5, C-7 and C-8 are sensitive to the nature of the ring fusion, and that the chemical shifts of C-1 and C-9 are sensitive to their relative orientation. Examination of Table 1 shows that the chemical shifts assigned to the former five carbons in the *N. elliptica* product are the same to within 0.4 ppm as those of the corresponding carbons in the other *trans*-fused diastereomer **1c**, and the chemical shifts of the latter two carbons are much closer to those for the corresponding carbons in **1a**, the other diastereomer in which C-1 and C-9 are *trans*, than those in **1b** or **1c**. Extension and elaboration of arguments given by Eisenbraun *et al.* [3] also provide explanations for the relative chemical shifts of C-4a and C-7a in **1d′**. They noted that the *trans*-fusion of the rings leads to appreciable puckering of the five-membered ring, which in turn causes the C-9 methyl group in **1c** to occupy an axial-like position. Among the consequences is an upfield-shifting effect at C-4a, which of course is not present in **1d′** wherein the C-9 methyl group is in an equatorial-like position. With regard to the chemical shift of C-7a in **1d′**, note that the substituent on the five-membered ring is *trans–trans* to the five-membered ring substituents at C-4a and C-7. By analogy with the *cis* and *trans*-1,2-dimethyclopentanes, 2-methycyclopentanols and 2-methylcyclopentyl acetates [7], wherein the substituted ring carbons of the *trans* isomers are less shielded than the corresponding ring carbons of the *cis* isomers, it is to be expected, as observed, that the chemical shift for C-7a in **1d′** will be farther downfield than that for C-7a in the other diastereomers. Our finding of **1d′** adds another dimension to the problem of elucidating the biosynthetic pathway to **1a** and related cyclopentanoid monoterpenes [8, 9].

Table 1. $^{13}$C NMR data for diastereomeric nepetalactones, CDCl$_3$*

| Carbon | 1a | 1b | 1c | 1d′ |
|---|---|---|---|---|
| 1 | 170.5 | 169.8 | 169.9 | 170.9 |
| 3 | 133.4 | 134.0 | 135.7 | 135.8 |
| 4 | 115.1 | 115.4 | 120.4 | 120.3 |
| 4a | (40.7) | (39.4) | (37.3) | 41.8 |
| 5 | (30.9) | (30.4) | (26.1) | 25.7 |
| 6 | (33.0) | (32.7) | (30.0) | 31.7 |
| 7 | (39.7) | (38.3) | (32.1) | 32.5 |
| 7a | 49.3 | 46.2 | 49.0 | 52.4 |
| 8 | 15.4 | 14.7 | 14.3 | 14.2 |
| 9 | 20.3 | 17.2 | 17.6 | 20.5 |

*Data for **1a–c** at 25.2 MHz is from [3]; data for **1d′** obtained at 50.3 MHz. Parentheses indicate uncertain assignments, as between C-4a and C-7 and as between C-5 and C-6.

## EXPERIMENTAL

*Plant material. Nepeta elliptica* Royle ex Benth. was collected from Cheena Peak, elevation 2600 m, near Nainital in October 1984. Voucher specimens have been deposited at the Botany Department Herbarium (herbarium collection no. 1322), Kumaun University, and the Forest Research Institute (accession no. 153825), Dehra Dun. Identification was confirmed by Y. P. S. Pangtey, Kumaun University, and P. P. Muyal, Forest Research Institute.

*Isolation of* **1d′**. The aerial parts (2.0 kg) of the freshly collected plants were finely chopped and steam distilled. The distillate was satd. with NaCl and extracted successively with petrol, bp 40–60°, and $CH_2Cl_2$. The organic solns were combined, dried ($Na_2SO_4$) and concd. Removal of the last traces of solvent at red. pres. left 6.0 g (0.3%) of pale yellow essential oil, which deposited a significant amount of crystalline material on cooling to 4°.

The crude oil was analysed using a 50 m x 0.24 mm fused silica capillary column, liquid phase Carbowax 20 M, with He as the carrier gas in a Hewlett-Packard 5880A GC. The column temp, initially 60°, was programmed at 2°/min for 60 min and held at 180° for 30 min. The single major component, subsequently identified as **1d′**, had a retention time of 64.16 min and was estimated on the basis of its GC response to make up 80% of the oil. At least five minor components (1.1–6.4%) with retention times of 43.4–51.2 min and at least one (0.7%) with retention time 66.4 min were noted but not identified. The major component was obtained as a white crystalline solid, mp 36–37°, in > 99.5% GC purity by trituration of the crude solid with small amounts of cold hexane followed by column chromatography ($SiO_2$–hexane–ether).

(7R)-trans,trans-*Nepetalactone* (**1d′**). HREIMS (probe) 70 eV, *m/z* 166.0989 [$C_{10}H_{14}O_2$ requires 166.0994]. LREIMS (GC/MS [10]) 70 eV, *m/z* (rel. int.): 166 $[M]^+$ (80), 151 $[M-CH_3]^+$ (15), 137 [M – CHO) (20), 123 $[M-C_2H_3O]^+$ (82), 109 $[C_8H_{13}]^+$ (54), 95 $[C_6H_7O]^+$ (85), 81 $[C_6H_9]^+$ (100), 69 $[C_5H_9]^+$ (87). IR (KBr pellet) $\nu$, cm$^{-1}$ (% trans.): 930 (38), 950 (41), 970 (42), 990 (40), 1070 (13), 1100 (13), 1140 (25), 1170 (35), 1260 (58), 1290 (53), 1322 (33), 1375 (32), 1445 (44), 1650 (52), 1755 (9). $^1$H NMR (360 MHz, CDCl$_3$): $\delta$6.26 (narrow *m*, $C_3$–H), 2.57–1.34 (7H, CH and $CH_2$), 1.67 (narrow *m*, $C_4$–$CH_3$), 1.17 ppm (*d*, *J* = 7.1 Hz, $C_7$–$CH_3$). $^{13}$C NMR: Table 1.

$$[\alpha]^{\lambda}_{25^\circ} = \frac{578 \qquad 546}{-222^\circ \quad -256^\circ}\ (\mathrm{CHCl_3},\ c\ 0.8)$$

(lit. [5] $[\alpha]^{D}_{20^\circ}$ + 222° for **1d**). (Found: C, 71.97; H, 8.61. $C_{10}H_{14}O_2$ requires: C, 72.26; H, 8.49%.)

*Acknowledgements*—This work was supported in part by a grant from the University Grants Commission, India, to C.S.M. NMR spectra were obtained at the University of California, Davis, NMR Facility; the NT-200 spectrometer used for determination of the $^{13}$C NMR spectra was purchased in part by NSF grant CHE 79-04832 to the Department of Chemistry. High resolution mass spectra were obtained at the Mass Spectrometry Laboratory, Facility for Advanced Instrumentation, A.D. Jones, Director, University of California, Davis; the ZAB-HS mass spectrometer, VG Analytical, used for determination of the spectra was purchased in part by NIH Division of Research

Resources Grant RR 01460. We are grateful to Professor David Forkey, California State University, Sacramento, for assistance in obtaining the GC/MS data and the Council of Scientific and Industrial Research, India, for a fellowship to H.L.

## REFERENCES

1. Bates, R. B., Eisenbraun, E. J. and McElvain, S. M. (1958) *J. Am. Chem. Soc.* **80**, 3240.
2. Bates, R. B. and Sigel, C. W. (1963) *Experientia* **19**, 564.
3. Eisenbraun, E. J., Browne, C. E., Irvin-Willis, R. L., McGurk, D. J., Elliel, E. L. and Harris, D. L. (1980) *J. Org. Chem.* **45**, 3811.
4. Kubrak, M. N. and Popa, D. P. (1980) *Khim. Prir. Soedin.* 420.
5. Trave, R., Marchesini, A. and Garanti, L. (1968) *Gazz. Chim. Ital.* **98**, 1132.
6. Chopra, R. N., Nayar, S. L. and Chopra, I. C. (1956) *Glossary of Indian Medicinal Plants*, p. 175. CSIR, New Delhi.
7. Christl, M., Reich, H. J. and Roberts, J. D. (1971) *J. Am. Chem. Soc.* **93**, 3463.
8. Bellesia, F., Grandi, R., Pagnoni, U. M., Pinetti, A. and Trave, R. (1984) *Phytochemistry* **23**, 83.
9. Bellesia, F., Pagnoni, U. M., Pinetti, A. and Trave, R. (1983) *Phytochemistry* **22**, 2197.
10. Bottini, A. T., Dev, V., Garfagnoli, D. J., Mathela, C. S., Melkani, A. B., Miller, A. A. and Sturm, N. S. (1986) *Phytochemistry* **25**, 207.

---

*Phytochemistry*, Vol. 26, No. 4, pp. 1202–1203, 1987.
Printed in Great Britain.

0031-9422/87 $3.00 + 0.00

# (−)-EPINGAIONE FROM *BONTIA DAPHNOIDES*

ROBERT J. CHINNOCK,* EMILIO L. GHISALBERTI† and PHILLIP R. JEFFERIES†

*The Botanic Gardens of Adelaide and State Herbarium, Adelaide, 5000, South Australia, Australia; †Department of Organic Chemistry, University of Western Australia, Nedlands, 6009, Western Australia, Australia

(*Revised received* 28 *July* 1986)

**Key Word Index**—*Bontia daphnoides*; Myoporaceae; sesquiterpene furan; (−)-epingaione.

**Abstract**—(−)-Epingaione has been isolated as the major lipophilic metabolite of *Bontia daphnoides*, the only member of the Myoporaceae found in the West Indies.

## INTRODUCTION

The Myoporaceae is a small family restricted largely to Australia except for species of *Myoporum*, extending north to China and Japan and to the islands of the Indian and Pacific Oceans, and *Bontia*, a monotypic genus, restricted to the West Indies. *Bontia* appears to be closely related to the Australian genera, differing mainly in the structure of the corolla and minor features of the fruit. Vegetatively, it is indistinguishable from species of *Myoporum*. Biochemical compatability has been established between *Myoporum* and *Bontia* as the latter has been successfully grafted onto *M. insularia* R. Br. Like other genera of the family, *Bontia* is salt-tolerant and is widely used in the Carribean as a windbreak. We have had the opportunity of examining a sample of *Bontia daphnoides* L. and now report on the isolation and identification of the sesquiterpene furan (−)-epingaione from this plant.

## RESULTS AND DISCUSSION

Extraction of the leaves of a sample of *B. daphnoides* with methanol gave a dark-green extract, most of which redissolved in hot ethyl acetate. The water-soluble portion of the remaining extract crystallized from methanol and was identified as D-mannitol. $^1$H NMR and TLC analysis of the ethyl acetate-soluble portion showed the presence of one major component, which was isolated by alumina chromatography. The compound thus obtained was essentially homogeneous, GC analysis indicating that 98% eluted as a single peak, and was shown to be (−)-epingaione (**1**) on the following evidence. Interpretation of the $^1$H NMR and $^{13}$C NMR spectra of **1** (see Table 1 and Experimental) allowed the compound to be formulated as a furanoid sesquiterpene with the constitution shown in **1**. Two diastereoisomers with this constitution are known to occur naturally in Myoporaceae. (−)-Epingaione (**1**) has the *2′S,5′S*-configuration and (−)-ngaione (**2**) the *2′S,5′R*-configuration [1]. A distinction between the two is not easily made on spectroscopic grounds and even the optical rotation in solution can be disturbingly similar, e.g. in benzene, (−)-ngaione has $[\alpha]_D$ $-13.0°$ [2] compared with $-14.8°$ for (−)-epingaione [3]. The crystalline 2,4-dinitrophenyl semicarbazone from (−)-epingaione has mp 166°, $[\alpha]_D^{CHCl_3}$ $-68°$ and that from (−)-ngaione, mp 133–133.5°, $[\alpha]_D^{CHCl_3}$ $-58°$ [3]. The same derivative formed from the sesquiterpene ketone from *B. daphnoides* showed mp 165–165.5° and $[\alpha]_D^{CHCl_3}$ $-70°$ and thus the ketone must be assigned the