J. Org. Chem. 1980, 45, 3811-3814 3811

Structure and Stereochemistry of 4aβ,7α,7aβ-Nepetalactone from *Nepeta mussini* and Its Relationship to the 4aα,7α,7aα- and 4aα,7α,7aβ-Nepetalactones from *N. cataria*

Edmund J. Eisenbraun,*[1a,b] Clinton E. Browne,[1b] Rebecca L. Irvin-Willis,[1b,c]
Donald J. McGurk,[1b,d] Ernest L. Eliel,*[1e] and David L. Harris[1e]

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078, and the William Rand Kenan, Jr. Laboratories of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514

Received January 30, 1980

The structure of the major constituent of the steam-volatile oil from *Nepeta mussini* has been established, through NMR spectroscopy and chemical correlation, to be that of a methylcyclopentane monoterpenoid diastereomeric with the two nepetalactones from *N. cataria*, all having the same absolute configuration at C-7. Stereochemical assignments to the four nepetolactones derived from these nepetalactones are also reported.

4aα,7α,7aα-Nepetalactone (**1a**), isolated from *Nepeta cataria*,[2] was the first methylcyclopentane monoterpenoid to be fully characterized.[3] Subsequently, numerous such monoterpenoids of plant and animal origin were identified, many by correlation with **1a** and its degradation products.[4] In addition to **1a**, *N. cataria* produces, as a minor component, a second diastereomeric enol lactone, 4aα,7α,7aβ-nepetalactone (**1b**),[5a] which has been purified[5b] to the crystalline state, mp 37–39 °C, in the current work by high-pressure liquid chromatography (high-pressure LC). This paper describes the isolation, structure proof, physical properties, and spectral data of a third diastereomeric enol lactone, 4aβ,7α,7aβ-nepetalactone (**1c**), from *N. mussini*.[6] A comparison of these three nepetalactones and their respective degradation products is made.

The major constituent of the steam-volatile oil from the foliage of *N. mussini* was previously reported to be lactone **1b**.[7] However, subsequent chemical degradation of this lactone[1c,d] showed that this assignment was incorrect and should be that of **1c**. The spectra of **1a–c** and their degradation products were examined to confirm the nonequivalence of these enol lactones and to establish the structure of **1c** from *N. mussini.*

The steam-volatile oil obtained from *N. mussini* contains approximately 95% **1c** and only minor amounts of **1a** as indicated by high-pressure LC and ^{13}C NMR. Chloroform extracts of macerated fresh *N. mussini* foliage that had not been steam distilled or even heated showed the same ratio of **1c** to **1a** when examined by high-pressure LC. Preparative high-pressure LC of the steam-volatile oil gave pure **1c**. Lactones **1a** and **1b** were similarly isolated by high-pressure LC from the steam-volatile oil of *N. cataria*.

Table I. ^{13}C NMR Chemical Shifts for Nepetalactones 1a–c[a,b]

carbon	1a	1b	1c
1	170.5	169.9	169.8
3	133.4	135.7	134.0
4	115.1	120.4	115.4
4a	(40.7)	(37.3)	(39.4)
5	(30.9)	(26.1)	(30.4)
6	(33.0)	(30.0)	(32.7)
7	(39.7)	(32.1)	(38.3)
7a	49.3	49.0	46.2
8	15.4	14.3	14.7
9	20.3	17.6	17.2

[a] Spectra were recorded as 0.6 M solutions in $CDCl_3$; chemical shifts are reported in parts per million downfield from internal Me_4Si. [b] Parentheses indicate uncertain assignments, as between C-4a and C-7 and as between C-5 and C-6.

Table II. Selected ^{1}H NMR Chemical Shifts for Nepetalactones 1a–c[a]

proton	1a	1b	1c
3 (vinyl)	6.15 (nm)[b]	6.23 (nm)	6.18 (nm)
8 (allylic CH_3)	1.64 (nm)	1.71 (nm)	1.70 (nm)
9 (CH_3)	1.19 (d, 6)[b]	1.11 (d, 6)	0.99 (d, 7)

[a] Spectral conditions same as in Table I; values in parts per million downfield from internal Me_4Si. [b] Abbreviations in parentheses indicate narrow multiplet (nm) or doublet (d) followed by coupling constant in hertz.

The assignment of configuration of **1c** is based on its ^{13}C and ^{1}H NMR spectra. Chemical shifts (^{13}C and ^{1}H) for **1a**, **1b**, and **1c** are listed in Tables I and II. Assignments of peaks in the ^{13}C spectra are from off-resonance decoupled ^{13}C spectra of **1a** and **1c** (peaks for **1b** assigned by analogy), distinguishing C-5/C-6 from C-4a/C-7 and C-7a as well as C-8/C-9 and based on known chemical-shift effects (C-1, -3, and -4). The C-7a signal is downfield from peaks for the other methine carbons, owing to the adjacent carbonyl group; C-4a and C-7 cannot readily be distinguished, nor can C-5 and C-6. The assignment of signals for C-8 and C-9 is discussed below.

The ^{13}C spectrum of **1c** (Table I) closely resembles that of **1a** (cis ring junction) but not that of **1b** (trans ring junction). Thus, **1c** must be the other cis diastereomer. The only sizeable differences between **1a** and **1c** appear at C-9 and C-7a.[8] The carbonyl (C-1 group) is cis to C-9 in **1c** and trans in **1a**, and accordingly its signal is upfield

---

[1] (a) I am grateful to the chemistry faculty at Chapel Hill for their hospitality during a 1977 sabbatical visit. (b) Oklahoma State University, Stillwater. (c) Ph.D. Dissertation, Oklahoma State University, Stillwater, OK, 1974. (d) Ph.D. Dissertation, Oklahoma State University, Stillwater, OK, 1968. (e) University of North Carolina, Chapel Hill.

[2] (a) S. M. McElvain, P. M. Walters, and R. D. Bright, *J. Am. Chem. Soc.*, **64**, 1828 (1942); (b) J. Meinwald, *ibid.*, **76**, 4571 (1954).

[3] (a) S. M. McElvain and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **77**, 1599 (1955); (b) E. J. Eisenbraun and S. M. McElvain, *ibid.*, **77**, 3383 (1955); (c) S. M. McElvain and E. J. Eisenbraun, *J. Org. Chem.*, **22**, 976 (1957); (d) R. B. Bates, E. J. Eisenbraun, and S. M. McElvain, *J. Am. Chem. Soc.*, **80**, 3420 (1958).

[4] W. I. Taylor and A. R. Battersby, Eds., "Cyclopentanoid Terpene Derivatives", Marcel Dekker, Inc., New York, 1969.

[5] (a) R. B. Bates and C. W. Sigel, *Experientia*, **19**, 564 (1963). (b) Since the specific rotation of **1b** from the earlier purification[5a] was reported as +20.2° and calculated as +21.9° for a pure sample, in contrast to $[\alpha]^{21}_D$ −24.4° (*c* 6.15, $CHCl_3$) for our crystalline sample, we conclude that a typographical error resulted or that the current preparation is the first description of pure **1b**.

[6] R. Trave, A. Marchesini, and L. Garanti, *Gazz. Chim. Ital.*, **98**, 1132 (1968).

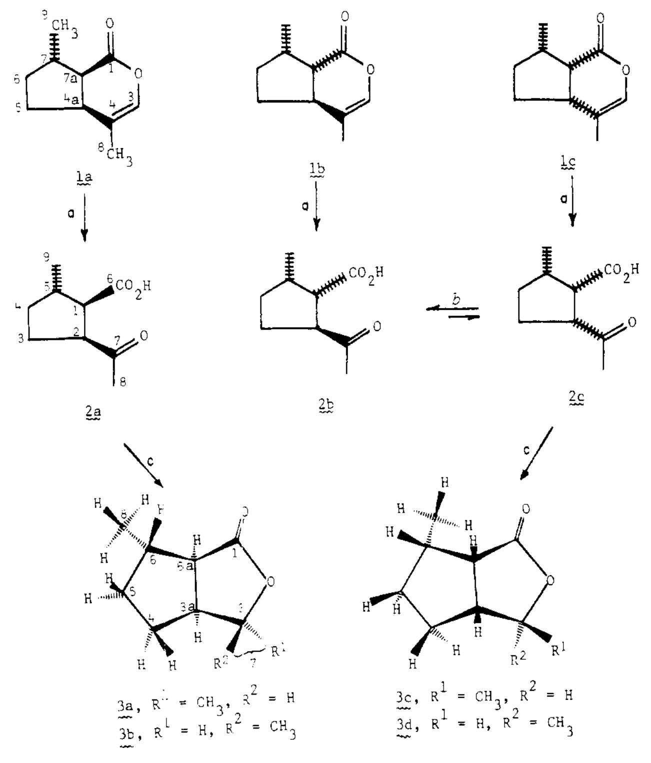
[7] F. E. Regnier, G. R. Waller, and E. J. Eisenbraun, *Phytochemistry*, **6**, 1281 (1967).

[8] One might have expected differences at C-1 and C-7 also. Shifts due to cis–trans isomerism of carbonyl substituents often tend to be attenuated.[9] The shift at C-7 is present but small.

[9] E. L. Eliel and K. M. Pietrusiewicz, *Org. Magn. Reson.*, **13**, 193 (1980).

0022-3263/80/1945-3811$01.00/0

Scheme I[a]



[a] a, O_3, CH_3OH, pyridine; b, OH^-, H_3O^+; c, $NaBH_4$.

in **1c** and downfield in **1a** (the methyl shift in *cis*-1,2-dimethylcyclopentane is 16.1, that in the trans isomer 19.7 ppm).[10] The assignments of C-8 (nearly constant for the three diastereomers) and C-9 were made accordingly. Substitution at C-7a is cis–cis to that at C-7 and C-4a in **1c** but trans–cis in **1a** and **1b**; since the signals of the substituted ring carbons in *cis*-1,2-dimethylcyclopentane (38.6 ppm) are upfield from those in the trans isomer (43.7 ppm), it is reasonable that the C-7a signal in **1c** (46.2 ppm) is upfield from that for **1a** (49.3 ppm) as well as that for **1b** (49.0 ppm).

The ^{13}C spectrum of **1b** differs notably from the other two at C-4, C-4a, C-5, C-6, and C-7, whereas, for reasons already mentioned, it resembles **1a** at C-7a, **1c** at C-9, and both diastereomers at C-8. The downfield shift at C-4 stems from its being trans to C-1—vide supra. The upfield shifts at the other four positions (4a, 5, 6, 7) may be explained as follows: the trans junction of the five-membered ring to the six-membered ring leads to appreciable puckering of the former. The C-9 methyl group in **1b** thus occupies an "axial-like" position unlike those in **1a** and **1c**. This will bring into effect upfield-shifting γ_a effects (at C-5 and C-4a) and differentially upfield-shifting[11] α_a (at C-7) and β_a effects (at C-6; it is not clear why this differential β effect is not also seen at C-7a).

The cis arrangement of the protons of the ring junction of **1c** is also evident from the ^1H NMR spectrum (Table II). The C-9 methyl proton signals in **1c** are shifted markedly upfield relative to those in **1a** because the methyl group in **1c** extends over the face (shielding region) of the carbonyl group; to a much lesser degree this is also true for **1b**.

In view of the suspected stereochemical relationship of **1c** to **1a** or **1b**, the obvious chemical proof should come from correlation of structure through degradation to a common intermediate of established structure and configuration. We proceeded as shown in Scheme I with degradation of **1c** through ozonolysis to nepetonic acid (**2c**). Nepetonic acid (**2c**) displays tautomeric behavior (lactol formation) as evidenced by line broadening in the ^1H NMR spectrum and hydroxyl group absorption[3d] in the IR spectrum. Treatment of **2c** with diazomethane yields a single oxo ester which readily forms a yellow 2,4-dinitrophenylhydrazone (2,4-DNP), mp 122–123 °C.

Table III. ^{13}C NMR Chemical Shifts for Nepetolactones 3a–d[a]

carbon	3a	3b	3c	3d
1	179.8	179.2	177.6	177.2
3	82.4	76.8	82.4	77.1
3a	47.0	44.5	47.9	43.5
4	31.4	25.7	31.6	25.2
5	34.3	35.1	33.9	34.4
6	39.0	38.3	38.1	38.2
6a	52.6	54.2	48.6	49.9
7	22.2	16.4	22.2	16.6
8	20.5	21.2	15.8	15.3

[a] Conditions same as in Table I; shifts are in parts per million downfield from internal Me_4Si.

As expected, nepetonic acid (**2c**) is unstable relative to *trans*-nepetonic acid (**2b**), to which it is readily epimerized. Treatment of the epimerization product with CH_2N_2 gave two methyl esters which were shown by GC analysis to be **2b** and **2c** in a 94:6 ratio. This ester mixture was identical with one similarly prepared from **1b**, as shown by their ^1H NMR and IR spectra and the specific rotation of the parent esters as well as their 2,4-DNP derivatives, mp 75–77 °C and 76–78 °C, undepressed by admixture. This correlation clearly relates **1b** and **1c** as being diastereomers epimeric at C-4a but having identical absolute configuration at C-7 and C-7a. The absolute configuration of C-7 of **1b** is known through its relationship to **1a**, which in turn had been degraded[3a] to (−)-3-methylcyclopentanone and (−)-methylsuccinic acid of known absolute configuration.[3b] Further, **1a** has been chemically related to isoiridomyrmecin,[3c] for which the structure was established through X-ray crystallography.[12]

The nepetolactones **3a** and **3b** have been known ever since the structure of nepetalactone **1a** was established.[3a] they were originally obtained as coproducts in the preparation of nepetonic acid **2a** from nepetalactone **1a** through alkaline hydrogen peroxide oxidation. Their skeletal system demands a cis ring junction;[13] consequently the isolation of the new pair of nepetolactones **3c** and **3d** as degradation products of **1c** points to a cis ring junction for **1c** also. This argument is compelling when it is considered that these new nepetolactones are derived from alkali-labile nepetonic acid **2c**, as shown in Scheme I.

The ^{13}C NMR spectra of **3a–d** (Table III)[14] are in ex-

---

[10] M. Christl, H. J. Reich, and J. D. Roberts, *J. Am. Chem. Soc.*, **93**, 3463 (1971).

[11] In the sense that the α_a and β_a effects are less downfield shifting than α_e and β_e.

[12] J. F. McConnell, A. McL. Mathieson, and B. P. Schoenborn, *Tetrahedron Lett.*, 445 (1962).

[13] The γ-hydroxy acids obtained through $NaBH_4$ reduction of **2a** or **2c** spontaneously lactonize at pH 7–8, whereas the γ-hydroxy acids obtained from **2b** or other *trans*-nepetonic acids do not lactonize on treatment with acid or distillation.[3a]

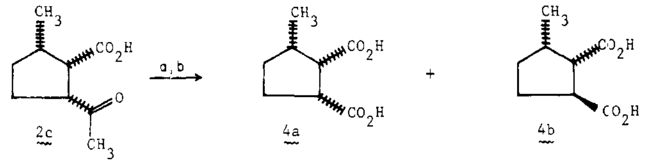
[14] Off-resonance decoupling distinguished carbons 3/3a/6/6a, 4/5, and 7/8. Shifts for C-1 and C-3 are assigned by chemical-shift analogy. The signal for C-6a is downfield from those of C-6 and C-3a because of the adjacent carbonyl group, and the C-3a peak is downfield from that for C-6 because of the larger number of β substituents. The C-5 signal is identified from its expected and observed constancy among the four diastereomers. The C-7 and C-8 signals are assigned to maintain constancy of the C-8 shift between **3a** and **3b** (as well as **3c** and **3d**) and of the C-7 shift between **3a** and **3c** (or **3b** and **3d**).

Table IV. Selected ^{1}H NMR Chemical Shifts for Nepetolactones 3a–d[a]

proton	3a	3b	3c	3d
3	4.31 (m)[b]	4.60 (m)	4.15 (m)	4.69 (m)
7	1.36 (J = 6)[b]	1.30 (J = 6)	1.37 (J = 6)	1.37 (J = 6)
8	1.11 (J = 6)	1.07 (J = 6)	1.17 (J = 7)	1.24 (J = 7)

[a] Spectral conditions same in Table I; values in parts per million downfield from internal Me_4Si. [b] (m) refers to multiplet; coupling constants are in hertz.

Scheme II[a]



[a] a, Br_2, OH^-; b, H_3O^+.

cellent agreement with the assigned structures based on the fact[10] (vide supra) that methyl and α carbon signals in *cis*-1,2-dimethylcyclopentanes are upfield of corresponding signals in the trans isomers. As one proceeds from **3a** to **3b**, the C-7/C-4 relationship changes from trans to cis. This should give upfield shifts for C-7, C-3, C-3a, and C-4 in **3b** relative to **3a**, and indeed these shifts are observed, whereas the remaining carbon signals show very little shift. An entirely analogous situation (and for analogous reasons) is seen in the comparison of **3c** (C-7/C-4 trans) and **3d** (C-7/C-4 cis). On the other hand, **3a** and **3c** are "enantiomer-like" in the lactone region of the molecule and differ only in the C-8/C-1 relationship (trans in **3a**, cis in **3c**). Hence, this pair should be spectrally similar except at C-1, C-8, and the juncture points C-6 and C-6a; signals for three of these carbons are notably upfield in **3c** (the effect at C-6 is very small), whereas the remaining carbons show very similar shifts for **3a** and **3c**. Indeed, the shifts for C-3 and C-7 are exactly the same in these two diastereomers! An exactly analogous situation applies to **3b** compared to **3d**.

The proton spectra (Table IV) are in accord with the assigned configurations. Isomers **3a** and **3c** differ markedly at H-3a from **3b** and **3d**, with the shift of this proton being relatively upfield when it is cis to Me-7 (**3a**, **3c**) and downfield when it is trans (**3b**, **3d**). Similar sizable shift differences have been reported[10] between the CHOAc protons in *cis*- and *trans*-2-methylcyclopentyl acetates. Also, the protons on the Me-8 group are at higher field when the methyl is trans to the adjoining C=O (**3a**, **3b**) and at lower field when it is cis (**3c**, **3d**). This is probably a consequence of the well-known maximum in deshielding by the C=O moiety which occurs in the plane of the carbonyl function.

Further information about the structure, stereochemistry, and configuration of nepetonic acid (**2c**) was gained through hypohalite degradation to the known nepetic acids **4a** and **4b**, as shown in Scheme II. In the haloform reaction, some **2c** is epimerized at C-2 to **2b** at a rate competitive with halogenation α to the oxo group. Methyl esters of these acids **4a** and **4b** were compared with the corresponding synthesized methyl nepetates[15] through use of GC, optical rotation, and melting point of appropriately constituted mixtures.[1c]

Experimental Section

Proton and ^{13}C NMR spectra (fully decoupled and single-frequency off-resonance proton-decoupled) were recorded with a Varian XL-100-15 interfaced with a 32K Nicolet 1080 computer at 100.1 and 25.2 MHz, respectively; some ^{13}C spectra were recorded with a Varian XL-100-12 instrument at 25.16 MHz. Chemical shifts are reported in parts per million downfield from internal Me_4Si, with coupling constants in hertz. Pulsed FT carbon spectra were obtained from approximately 1.5 M solutions in $CDCl_3$ containing 5% Me_4Si (δ $CDCl_3$ = 76.9 ppm), using a 6000-Hz sweepwidth and 8K data points. The majority of the NMR studies were carried out at Chapel Hill.[1a] However, we thank the National Science Foundation for Grants GP 17641 and CHE76-5571 which enabled purchase of NMR instrumentation at Stillwater. IR spectra were recorded with a Beckman IR-8 spectrometer. Mass spectra were recorded with a CEC-21-110B spectrometer at 70 eV. Optical rotations were measured with a Rudolph Model 80 polarimeter. Melting and boiling points are uncorrected. Gas chromatographic analyses were conducted with a Hewlett-Packard 5750 instrument equipped with dual flame-ionization detectors and an 8 ft × 0.25 in. copper tube packed with 6% UC W-98 coated on 80–100-mesh AW DMCS-treated Chromosorb G. Analytical and preparative high-pressure LC were conducted on a Waters Associates Micro-Porasil (silica gel) column with a Waters Associates analytical or Prep-500 LC system equipped with UV and index of refraction detectors.

4aβ,7α,7aβ-Nepetalactone (1c). *N. mussini* plants (674 g) grown from seed were harvested, immediately shredded in a 1-gal. Waring Blendor with 1 L of water, and subjected to steam distillation. The steam distillate was saturated with NaCl and extracted with CH_2Cl_2 (3x). The CH_2Cl_2 extracts were combined, dried (Na_2SO_4), and evaporated under vacuum. Distillation of the residue [40–80 °C (0.3 mm)] gave 4.0 g (0.6% yield) of oil. High-pressure LC analysis using $CHCl_3$ extracts of fresh plants indicated an identical ratio of **1a** to **1c**. Preparative high-pressure LC of the steam-volatile oil followed by bulb-to-bulb (Kugelrohr) distillation gave pure **1c**: bp 60 °C (0.1 mm); $[\alpha]^{23}_D$ +81.0° (c 0.038, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.18 (narrow m, 1 H, H-2), 3.20–1.00 (7 H, CH and CH_2), 1.70 (narrow m, 3 H, H-8), 0.99 (d, J = 7 Hz, 3 H, H-9); IR (neat) 1765, 1140 cm^{-1}; mass spectrum, m/e (relative intensity) 166 (M^+, 55), 123 (98), 95 (60), 81 (100), 68 (64).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.66; H, 8.49. Found: C, 72.32; H, 8.43.

4aα,7α,7aα-Nepetalactone (1a) and 4aα,7α,7aβ-Nepetalactone (1b). Preparative high-pressure LC of the steam-volatile oil obtained from *N. cataria* (same conditions as described for *N. mussini* oil) gave **1a** and **1b**. Lactone **1a**: $[\alpha]^{21}_D$ +3.7° (c 27, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.15 (narrow m, 1 H, H-2), 2.90–1.20 (7 H, CH and CH_2), 1.64 (narrow m, 3 H, H-8), 1.19 (d, J = 6 Hz, 3 H, H-9); IR (neat) 1765, 1140 cm^{-1}; mass spectrum, m/e (relative intensity) 166 (M^+, 33), 123 (88), 109 (38), 95 (100), 81 (39), 69 (51). Lactone **1b**: mp 37–39 °C; $[\alpha]^{21}_D$ −24.4° (c 6.15, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.23 (narrow m, 1 H, H-2), 2.80–1.20 (7 H, CH and CH_2), 1.71 (narrow m, 3 H, H-8), 1.11 (d, J = 6 Hz, 3 H, H-9); IR (neat) 1765, 1140 cm^{-1}; mass spectrum, m/e (relative intensity) 166 (M^+, 66), 123 (79), 109 (52), 94 (70), 81 (100), 69 (100).

1α,2β,5α-Nepetonic Acid (2b) and Methyl Ester. A solution of 300 mg (1.81 mmol) of **1b** in 40 mL of methanol containing 1 mL of pyridine was cooled to −70 °C. Ozone was bubbled through the solution until a blue color persisted. Excess O_3 was flushed from the system with N_2 and then dimethyl sulfide (5 mL) was added. The mixture was allowed to warm to room temperature (1 h), the solvent was removed under reduced pressure, and the residue was dissolved in $NaHCO_3$ solution and then extracted with ether. The aqueous solution was acidified with 10% HCl and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated under vacuum to give 200 mg (98% yield) of **2b**; ^{1}H NMR ($CDCl_3$) δ 9.1 (br hump, 1 H, acidic H), 3.60–3.10 (overlapping m, 2 H, H-1 and H-2), 2.60–1.00 (5 H, H-3, H-4, and H-5), 2.20 (s, 3 H, H-8 methyl), 0.98 (d, J = 7 Hz, 3 H, H-9 methyl).

---

(15) K. S. Schorno, G. H. Adolphen, and E. J. Eisenbraun, *J. Org. Chem.*, **34**, 2801 (1969); (b) E. J. Eisenbraun, G. H. Adolphen, K. S. Schorno, and R. N. Morris, *J. Org. Chem.*, **36**, 414 (1971).

Treatment of **2b** with excess CH_2N_2 in ether and Kugelrohr distillation gave 295 mg (89% yield based on **1b**) of the methyl ester, bp 40-60 °C (0.4 mm). Gas chromatographic analysis indicated the product is a mixture of esters, arising 99% from **2b** and 1% from **2c**: $[\alpha]^{22}{}_D$ +38° (*c* 3.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 3.68 (s, 3 H, CO_2CH_3), 3.50–3.10 (overlapping m, 2 H, H-1 and H-2), 2.18 (s, 3 H, H-8 methyl), 0.88 (d, *J* = 6 Hz, 3 H, H-9 methyl); IR (neat) 1745, 1725 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 184 (M^+, 3), 141 (12), 124 (20), 109 (28), 82 (14), 81 (100). The 2,4-DNP derivative of the methyl ester of **2b** was prepared: mp 75–77 °C; $[\alpha]_D$ +160° (*c* 5.1, $CHCl_3$).

Anal. Calcd for $C_{16}H_{20}N_4O_6$: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.46; H, 5.50; N, 15.16.

1α,2α,5α-Nepetonic Acid (2c) and Methyl Ester. Treatment of 420 mg (2.62 mmol) of **1c** with ozone and workup in the manner described above gave 360 mg (91% yield) of **2c**; ^1H NMR ($CDCl_3$) lactol forms present, δ 7.50 (br hump, 1 H, acidic H), 3.20–2.80 (overlapping m, 2 H, H-1 and H-2), 2.40–1.00 (5 H, H-3, H-4, and H-5), 2.00 (br humps, 3 H, H-8 methyl), 1.09 (d, *J* = 7 Hz, 3 H, H-9 methyl).

A portion of this **2c** was treated with CH_2N_2 to give the methyl ester. Gas chromatographic analysis indicated 94% **2c** and 6% **2b**: ^1H NMR ($CDCl_3$) δ 3.65 (s, 3 H, CO_2CH_3), 3.20–2.85 (overlapping m, 2 H, H-1 and H-2), 2.80–1.25 (5 H, H-3, H-4, and H-5), 2.14 (s, 3 H, H-8 methyl), 1.98 (d, *J* = 7 Hz, 3 H, H-6 methyl); IR (neat) 1745 and 1725 (C=O) cm^{-1}; mass spectrum, *m/e* (relative intensity) 184 (M^+, 4), 129 (45), 127 (23), 109 (26), 100 (35), 81 (89), 43 (100). The 2,4-DNP derivative of **2c** methyl ester melted at 122–123 °C.

Anal. Calcd for $C_{16}H_{20}N_4O_6$: C, 52.73; H, 5.53; N, 15.38. Found: C, 52.63; H, 5.47; N, 15.40.

1α,2β,5α-Nepetonic Acid (2b) from 2c. To 30 mL of aqueous 10% NaOH under N_2 was added 320 mg (1.88 mmol) of **2c**. The solution was magnetically stirred for 2.5 h and then acidified with 10% HCl. The acidified mixture was extracted with ether and the ether extract was dried (Na_2SO_4) and evaporated under vacuum to give **2b** (^1H NMR identical with that described above). Treatment of **2b** with CH_2N_2 and Kugelrohr distillation gave 300 mg (87% yield) of the methyl ester: $[\alpha]^{22}{}_D$ +35.2° (*c* 3.4, $CHCl_3$); ^1H NMR and IR identical with those described above. The 2,4-DNP derivative of **2b** methyl ester was obtained in 60% yield: mp 78–80 °C; mixed with the 2,4-DNP methyl ester of **2b** obtained from **1b**, mp 76–78 °C; $[\alpha]_D$ +172° (*c* 5.0, $CHCl_3$).

3β,3aβ,6aβ-Nepetolactone (3c) and 3α,3aβ,6α,6aβ-Nepetolactone (3d). A solution of 1.5 g (0.97 mmol) of **1c** in 75 mL of CH_3OH and 1.5 mL of pyridine was ozonized and freed of excess ozone as described for **1b**. The mixture was transferred to an ice bath and 1.5-g portions of $NaBH_4$, each in 15 mL of H_2O, were added to the stirred mixture, one immediately and others after 0.5, 1, 2, and 4 h. The mixture was then acidified with 10% HCl and extracted with ether. The ether extract was washed with $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated to yield 500 mg (36% yield) of a mixture consisting of 65% **3c** and 35% **3d**, as indicated by GC analysis. Lactones **3c** and **3d** were separated by preparative GC. Lactone **3c**: bp 60–65 °C (0.05 mm); $[\alpha]^{24}{}_D$ +15.1° (*c* 2.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.15 (m, 1 H, H-3), 3.08–1.40 (7 H, CH and CH_2), 1.37 (d, *J* = 6 Hz, 3 H, H-7), 1.17 (d, *J* = 7 Hz, 3 H, H-8); mass spectrum, *m/e* (relative intensity) 154 (M^+, 23), 99 (70), 94 (40), 82 (76), 81 (93), 67 (100).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.90; H, 9.26.

Lactone **3d**: bp 60–65 °C (0.05 mm); $[\alpha]^{24}{}_D$ +78.9° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.69 (m, 1 H, H-3), 3.12–1.40 (7 H, CH and CH_2), 1.37 (d, *J* = 6 Hz, 3 H, H-7), 1.24 (d, *J* = 7 Hz, 3 H, H-8); mass spectrum, *m/e* (relative intensity) 154 (M^+, 16), 99 (48), 95 (45), 82 (75), 81 (100), 67 (99).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.25; H, 9.15.

3α,3aα,6α,6aα-Nepetolactone (3a) and 3β,3aα,6α,6aα-Nepetolactone (3b). Lactones **3a** and **3b** were prepared from **1a** by the above procedure in 55% yield. Gas chromatographic analysis indicated the mixture to consist of 42% **3a** and 58% **3b**. Preparative GC gave the pure individual lactones. Lactone **3a**: ^1H NMR ($CDCl_3$) δ 4.31 (m, 1 H, H-3), 2.70–1.30 (7 H, CH and CH_2), 1.36 (d, *J* = 6 Hz, 3 H, H-7), 1.11 (d, *J* = 6 Hz, 3 H, H-8); mass spectrum, *m/e* (relative intensity) 154 (M^+, 2), 139 (17), 95 (44), 82 (50), 81 (100), 67 (69). Lactone **3b**: ^1H NMR ($CDCl_3$) δ 4.60 (m, 1 H, H-3), 2.90–1.30 (7 H, CH and CH_2), 1.30 (d, *J* = 6 Hz, 3 H, H-7), 1.07 (d, *J* = 6 Hz, 3 H, H-9); mass spectrum, *m/e* (relative intensity) 154 (M^+, 1), 99 (70), 95 (30), 94 (40), 82 (40), 81 (100), 67 (53).

Acknowledgment. The part of the work performed at the University of North Carolina was supported by National Science Foundation Grant CHE 75-20052. We thank Dr. J. J. Blackwood, Chemical Abstracts Service, for advice on nomenclature.

Registry No. 1a, 21651-62-7; **1b**, 17257-15-7; **1c**, 21651-53-6; **2b**, 21651-52-5; **2b** methyl ester, 6890-02-4; **2b** methyl ester 2,4-DNP derivative, 74366-00-0; **2c**, 58801-35-7; **2c** methyl ester, 74410-38-1; **2c** methyl ester 2,4-DNP derivative, 74410-39-2; **3a**, 74410-40-5; **3b**, 74410-41-6; **3c**, 58845-57-1; **3d**, 58845-58-2.

New Diterpenoids from the Soft Corals *Xenia macrospiculata* and *Xenia obscuronata*

Yoel Kashman* and Amiram Groweiss

Department of Chemistry, Tel-Aviv University, Ramat-Aviv, Israel

Received December 28, 1979

Sixteen diterpenoids have been isolated from two soft corals of the Red Sea, *Xenia macrospiculata* and *X. obscuronata*. These xenia diterpenoids, many of them novel and reported for the first time, are divided into three subgroups: the xenicins [xeniculin (**2**), 9-deacetoxy-14,15-deepoxyxeniculin (**3**), and 9-deacetoxy-14,15-deepoxyxeniculin 7,8-epoxide (**4**)], the xeniolides [xeniolide-A (**6**), xeniolide-B (**7a**), xeniolide-B 9-acetate (**7b**), 7,8-epoxyxeniolide-B (**8**), and xenialactol (**9a**)], and the xeniaphyllanes [xeniaphyllenol (**11**), 4,5-epoxyxeniaphyllenol (**12**), isoxeniaphyllenol (**13**), 4,5-epoxyisoxeniaphyllenol (**14**), 14,15-xeniaphyllandiol (**15a**), xeniaphyllandiol 14-acetate (**15b**), and 4,5-epoxy-14,15-xeniaphyllandiol (**16**)]. The structures were elucidated from spectral data and chemical transformations. The ^{13}C NMR spectra are fully assigned, and their application to the determination of the xenia diterpenoids is discussed. In addition to the above compounds, another diterpenoid, obscuronatin (**23**), was isolated and its structure elucidated.

The soft corals are known to be a source of many different diterpenoids.[1] Many of these diterpenoids belong to a single chemical class, the cembranoids.[2,3] This report deals with a new group of compounds, the xenia di-

0022-3263/80/1945-3814$01.00/0 © 1980 American Chemical Society