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COLEON U 12-METHYL ETHER FROM *NEPETA LEUCOPHYLLA*

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ABSTRACT.—Coleon U 12-methyl ether [**1**] [(*R*)-2,3,4,4a-tetrahydro-5,8,10-trihydroxy-6-methoxy-1,1,4a-trimethyl-7-(1-methylethyl)-9(1*H*)-phenanthrenone] was isolated from roots of *Nepeta leucophylla*, and its structure and absolute configuration were determined by X-ray analysis.

In a continuation of our work on constituents of *Nepeta* species native to the Kumaun region of India (1,2), we examined extracts of the roots of *Nepeta leucophylla* Benth. (Labiatae). Workup of the cold EtOH extract of the freshly collected roots gave a reddish orange crystalline material **1** with mp 172–173°. The mass spectrum of **1** indicated that its molecular formula is C₂₁H₂₈O₅ (*m/z* 360.1915; C₂₁H₂₈O₅ requires 360.1937). Its ¹³C-nmr spectrum indicated the presence of nine sp² carbons, including a carbonyl, with no bonds to hydrogen, six methyls, including an ether methyl, three methylenes, one methine, and two quaternary carbons. Further interpretation of spectral properties was simplified because the crystals were suitable for X-ray analysis, which also allowed direct determination of absolute configuration by analysis of observed Bijvoet differences due to the anomalous scattering effect of oxygen for CuKα radiation (3,4).

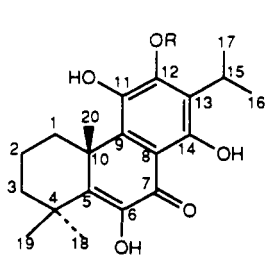
Figure 1 is a computer-generated perspective drawing of **1**. Bond angles and bond lengths for **1** are normal.

A literature search revealed that **1** was first reported in 1977 by Miyase *et al.* (5), who called it coleon U 12-methyl ether. They prepared **1** from CH₂N₂ and naturally occurring coleon U [**2**] which they had isolated together with its tautomer coleon V [**3**] and related compounds from leaf glands of *Plectranthus myrianthus* Brig. (Labiatae) gathered in South Africa. In 1979, Matsumoto and Takeda described multi-step syntheses of **1–3** from (+)-ferruginol (6,7).

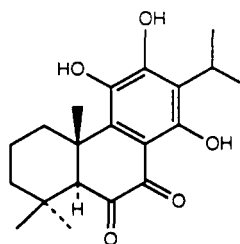
As demethylation of **1** to **2** is likely to be a high yield reaction and as **2** and **3** are easy to interconvert (7), naturally occurring **1** from *N. leucophylla*, because of its ease of isolation in good yield, is a potential source of coleon U, coleon V, and their derivatives.

EXPERIMENTAL

PLANT MATERIAL.—*N. leucophylla* was col-



1 R = Me
2 R = H



3

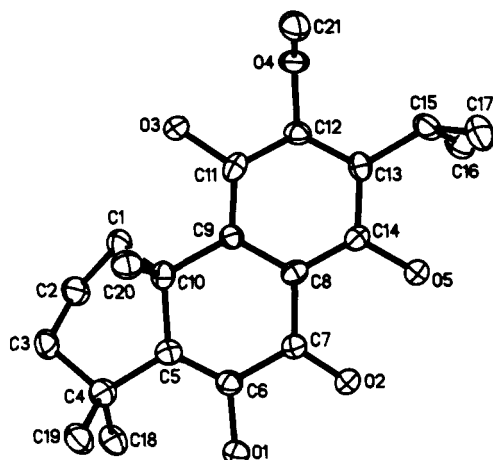


FIGURE 1. Computer-generated perspective drawing of compound 1.

lected from Nainital during June. Identification had been confirmed earlier (2) by Y.P.S. Pangtey, Kumaun University (Herbarium No. 1808), and P.P. Moyal, Forest Research Inst., Dehradun (Accession No. 153826).

ISOLATION OF 1.—The fresh roots (1.77 kg) were cut into pieces, which were crushed and extracted repeatedly with cold EtOH, total volume 20 liters. The extract was concentrated under reduced pressure to 25 ml and extracted (3×25 ml) with CHCl_3 . The viscous residue (1.5 g) from concentration of the CHCl_3 extract was subjected to cc (50 g Si gel, *n*-hexane/ Et_2O), and the residue from concentration of the red colored fractions was subjected to preparative tlc [Si gel *n*-hexane- CHCl_3 (4:1)] to give 180 mg of 1, R_f 0.40, and three minor fractions. The mp, $[\alpha]_D$, ms and ^1H -nmr spectrum of 1 were in satisfactory agreement with literature values (5,6). ^{13}C nmr (CDCl_3 , 125.8 MHz) δ 17.65 (C-2), 20.30 (C-16, C-17), 25.99 (C-15), 27.00, 27.31, and 27.91 (C-18, C-19, C-20), 29.81 (C-1), 36.28 (C-3), 36.58 (C-4), 41.48 (C-10), 62.14 (C-21), 109.01 (C-8), 125.65 (C-13), 135.69 (C-11), 138.37 (C-5), 141.88 (C-6), 145.51 (C-9), 151.18 (C-14), 156.07 (C-12), and 183.64 (C-7).

CRYSTAL DATA.—A crystal of dimensions $0.12 \times 0.30 \times 0.30$ mm was used for collection of X-ray data. Determination of cell dimensions and data collection were carried out with the crystal cooled to 130 K on a Siemens R3 diffractometer with graphite monochromated $\text{CuK}\alpha$ radiation ($\lambda = 1.54184 \text{ \AA}$). Crystal data: trigonal, space group $P3_2$ (no. 145); $a = b = 8.538$ (2), $c = 21.756$ (5) \AA , $Z = 3$, $V = 1373.6$ (7) \AA^3 ,

$\mu = 7.1 \text{ cm}^{-1}$ and $D(130 \text{ K}) = 1.307 \text{ g}\cdot\text{cm}^{-3}$. A total of 1431 reflections with $2\theta \leq 115^\circ$ were measured in ω -scan mode at $4^\circ/\text{min}$, with a 1.0° scan range and a $\pm 1.0^\circ$ background offset; index ranges $b, -9$ to 9 ; $k, 0$ to 9 ; $l, 0$ to 23 . Three standard reflections, monitored every 197 measurements, showed only random variations during the experiment. The structure was solved with direct methods routines of SHELXTL PLUS (8). A total of 1259 independent reflections $I \geq 2\sigma(I)$ were used in the refinement of 234 least squares parameters by full matrix least squares. Refinement converged with $R = 0.045$ and $R_w = 0.048$. Each CH_n group was treated as a rigid group with C-H distances of 0.96 \AA and thermal parameters of H fixed at 0.02 \AA^2 . Five reflections with readily observable Bijvoet differences for $\text{CuK}\alpha$ radiation were found with the program ABSCON (4) based on f'' for C and O. All three forms of their corresponding Friedel pairs were measured. The equivalent intensities were added. Each sum was treated as a single observation and compared with values calculated for the two enantiomers. The results, give in Table 1, are consistent with the R absolute configuration shown in Figure 1.¹

¹Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK.

TABLE 1. Observed and Calculated Bijvoet Ratios.

h, k, l	Equivalent Pairs in Set	% Ratio Observed ^a	% Ratio Calculated ^b
1,2,5	3	-1.1	-2.3
-3,4,3	3	2.5	2.1
-1,1,4	3	-1.0	-1.4
-2,2,5	3	-1.6	-1.6
1,3,12	3	4.4	3.2

^a $200 \{ \sum I(h, k, l) - \sum I(\bar{h}, \bar{k}, \bar{l}) / \sum I(h, k, l) + \sum I(\bar{h}, \bar{k}, \bar{l}) \}$.

^b $200 [(F_+)^2 - (F_-)^2] / [(F_+)^2 + (F_-)^2]$.

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voet difference measurements was purchased under NSF grant CHE-88-2721 to the University of California, Davis. The Ω -500 nmr spectrometer was purchased in part by NIH Division of Research Resources grant RRO4795 and NSF grant BBS88-04739.

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