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DIARYLHEPTANOIDS OF *CENTROLOBIUM* SPECIES*[1]

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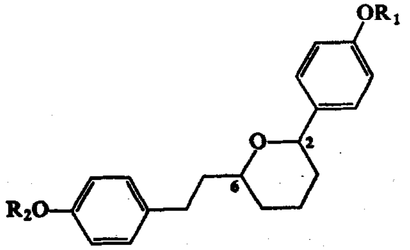
Abstract—The heartwoods of two *Centrolobium* species (Leguminosae) were examined. *C. robustum* Mart. was found to contain piceatannol, (−)-centrolobine (VIIa), (−)-de-*O*-methylcentrolobine (VIIb) and (−)-centrolobol (VI). *C. tomentosum* Benth. was found to contain (+)-centrolobine (IXa), (+)-de-*O*-methylcentrolobine (IXb) and (+)-centrolobol (VIII).

THE TRUNK wood of *Centrolobium robustum* Mart. contains the antibiotic, centrolobine.[2] Its structure (Ia) is known through the work of Marini-Bettòlo and associates,[3] who synthesized the racemates of *O*-methylcentrolobine (Ib)[3] and of centrolobine.[4] The absolute configuration of the two asymmetric centres of centrolobine, however, remained to be established. In the quest for a sample of centrolobine, needed to accomplish this objective, the heartwood of *C. robustum* was re-examined.



(Ia) $R_1 = Me, R_2 = H$
(Ib) $R_1 = R_2 = Me$
(Ic) $R_1 = R_2 = H$

The plant material was secured in the State of Espirito Santo. Fractionation of the ethanol extract of its heartwood by column chromatography, led to four substances. One

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Cq * Part XX of the series *The Chemistry of Brazilian Leguminosae*. For part XIX see R. M. VIEGAS ASSUMPCÃO, S. M. KOPP SILVA and O. R. GOTTLIEB, *Anais Acad. Brasil. Cienc.* **40**, 297 (1968).

[1] Preliminary communications: A. ARAGÃO CRAVEIRO and O. R. GOTTLIEB, *Anais Acad. Brasil. Cienc.* **40**, 39 (1968); *Anais Acad. Brasil. Cienc.* **41**, Supplement, in press (1969); A. ARAGÃO CRAVEIRO, A. DA COSTA PRADO, O. R. GOTTLIEB and P. C. WELERSON DE ALBUQUERQUE, *Anais Acad. Brasil. Cienc.* **41**, Supplement, in press (1969.) Taken, in part, from the M.Sc. Thesis presented by A. ARAGÃO CRAVEIRO to the Universidade Federal Rural do Rio de Janeiro (1969).

[2] O. GONÇALVES DE LIMA, M. MACHADO DE ALBUQUERQUE and M. H. DALIA MAIA, *Rev. Inst. Antibiot. Univ. Recife* **2**, 19 (1959); O. GONÇALVES DE LIMA and L. G. DE PRADO FILHO, personal communication cited in Ref. 3.

[3] I. L. DE ALBUQUERQUE, C. GALEFFI, C. G. CASINOVI and G. B. MARINI-BETTÒLO, *Gazz. Chim. Ital.* **94**, 287 (1964).

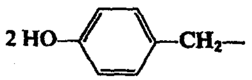
[4] C. GALEFFI, C. G. CASINOVI and G. B. MARINI-BETTÒLO, *Gazz. Chim. Ital.* **95**, 95 (1965).

was identified with piceatannol (3,3′,4,5′-tetrahydroxy-*trans*-stilbene) by direct comparison with an authentic sample. Piceatannol was isolated previously from the heartwood of *Vouacapoua macropetala* Aubl. and *V. americana* Aubl.,[5] other South American species of the Leguminosae.

The i.r. and NMR spectra of a second substance were identical to the corresponding spectra which had been published for centrolobine.[3] Co-chromatography with a sample of centrolobine, obtained during the previous study of *C. robustum*, using a number of solvents for development, led to a single spot in all cases. Nevertheless, whereas the m.ps of the old and the new isolates were identical, the mixed m.p. was considerably depressed. This fact suggested immediately examination of the optical rotation of both samples, and, indeed, the sample of centrolobine isolated in the previous study ($[\alpha]_D^{20^\circ}$ +97°)[3] gives rise, in the 600–400 nm region in MeOH solution, to a plain positive o.r.d. curve, whereas the sample isolated in the present study ($[\alpha]_D^{25^\circ}$ −97·6) gives rise to a plain negative o.r.d. curve. The optical activity of the centrolobines is caused by two asymmetric centres, including one directly attached to an aromatic ring. An examination of the c.d. data showed that the expected Cotton effects,[6] associated with the two electronic transitions in the 300–200 nm region of this aromatic chromophore, are both negative in (−)-centrolobine.

Upon comparison with the analogous spectra of (−)-centrolobine, the i.r., u.v., NMR and o.r.d. curves indicated the structure of (−)-de-*O*-methylcentrolobine (Ic) for the third substance isolated. This proposal was confirmed by conversion of both compounds (Ia and Ic) to the common derivative (−)-*O*-methylcentrolobine (Ib).

More interesting was the fourth compound, designated centrolobol. Its close structural relation to the centrolobines was revealed by the u.v. spectrum, practically superimposable on the analogous spectrum of Ic. The mass spectrum, however, showed the molecular ion peak at two more mass units than would be expected for de-*O*-methylcentrolobine (Ic), and the facile loss of a water molecule. This suggested the structural derivation of centrolobol by hydrogenolytic opening of the pyran-ring of the centrolobine system. Indeed, i.r. as well as NMR evidence, obtained on centrolobol triacetate, pointed to the presence of one alcoholic and two phenolic hydroxyls in centrolobol itself. The aromatic region of this NMR spectrum contained signals related to two symmetrical AA″BB″ systems. The signals of the aliphatic region were attributed to two benzylic and four unconjugated methylenes, besides one carbinolic proton.



(a)

4—CH_2—

(b)

1—CHOH—

(c)

(II)

The structural moieties (IIa, b, c) which became evident through this analysis could be linked in three different ways. The symmetrical alternative (IIIa) cannot represent the optically active centrolobol ($[\alpha]_D^{25^\circ}$ −8·6°). A compound of structure IIIb should be easily dehydrated. Formation of the styryl chromophore was, however, not observed when a benzene solution of centrolobol was heated under reflux with p-toluenesulfonic acid.

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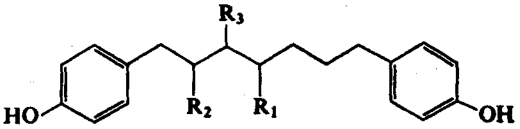
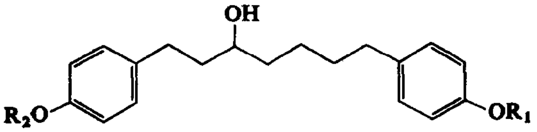
[5] F. E. King, T. J. King, D. H. Godson and L. C. Manning, *J. Chem. Soc.* 4477 (1956).

[6] L. Verbit, A. S. Rao and J. W. Clark-Lewis, *Tetrahedron* **24**, 5839 (1968).



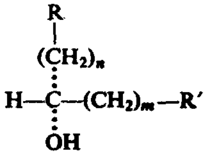
(IIIa) $R_1 = OH, R_2 = R_3 = H$
(IIIb) $R_2 = OH, R_1 = R_3 = H$
(IIIc) $R_3 = OH, R_1 = R_2 = H$

Centrolobol must thus correspond to IIIc. Indeed, only a 3-heptanol should be derivable through the hydrogenolysis of the benzyl ether linkage of a centrolobine. Hydrogenation of (–)-centrolobine (Ia) in presence of a Pd/C catalyst was carried out, and afforded the expected (–)-*O*-methylcentrolobol (IVa). Conversion of this derivative to (–)-di-*O*-methylcentrolobol (IVb), equally accessible from (–)-centrolobol (IVc = IIIc) itself, was achieved by diazomethane methylation.



(IVa) $R_1 = Me, R_2 = H$
(IVb) $R_1 = R_2 = Me$
(IVc) $R_1 = R_2 = H$

The asymmetry of centrolobol is caused by the substituents of the secondary carbinol: two flexible chains which differ by two methylenes. Its absolute configuration could, consequently, be derived by comparison with analogous compounds, the correlation of whose molecular rotation and absolute configuration had been established by Brewster.[7] According to this treatment, an alcohol of absolute configuration (V), in which $m - n = 2$, should have the molecular rotation of –24 which characterizes (–)-centrolobol. The definition of the compound as 3S-1,7-di-(p-hydroxyphenyl)-heptan-3-ol (Newman formulation VI) followed.



$$\begin{array}{c} R \\ | \\ (CH_2)_n \\ \vdots \\ H—C—(CH_2)_m—R' \\ \vdots \\ OH \end{array}$$

(V)

The absolute configuration of (–)-centrolobine (Ia) could now be deduced. The spatial arrangement of the substituents at C-6 cannot suffer alteration during hydrogenolysis to (–)-*O*-methylcentrolobol (IVa), and thus it clearly also occurs in the S-configuration. Marini-Bettòlo *et al.* already stated that the two α-hydrogens of the pyran ring of (+)-centrolobine (Ia) are probably in the axial conformation. The arguments presented in favour of this deduction were the appearance of the corresponding NMR signals at relatively low field,[3] and the synthesis of (±)-centrolobine. For reasons of stability, it was assumed that the acid catalysed

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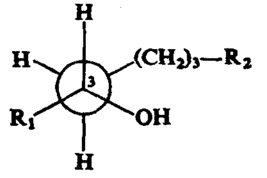
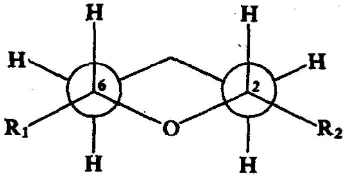
[7] J. H. Brewster, *J. Am. Chem. Soc.* **81**, 5481 (1959).

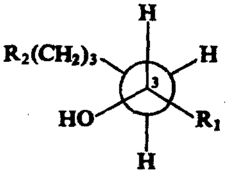
etherification of 1,5-dihydroxy-7-(4-hydroxyphenyl)-1-(4-methoxyphenyl)-heptane should lead to a bisequatorially substituted pyran derivative.[4] The authors did not use the arguments based on magnitude of coupling constants which are usually employed for the assignment of conformation to protons on a cyclic system. The signal due to the proton at C-6 is not sufficiently resolved at 60 MHz to allow the direct determination of these constants. A dramatic improvement of this situation is apparent upon inspection of the 220 MHz spectrum (Fig. 1). The multiplets due to the protons at C-2 and C-6 clearly show that these protons have an axial conformation. This is particularly evident in the pair of doublets which represent H-2 (τ 5·70, $J_{ax-ax} = 10{\cdot}5$ Hz, $J_{ax-eq} = 2{\cdot}0$ Hz) and may be inferred from the pattern width of 25 Hz for the signal due to H-6 (τ 6·56). This width is in accord with the summation of one axial–axial coupling, one axial–equatorial coupling and two vicinal couplings to the non-equivalent methylene protons of the freely rotating side-chain. Detailed analysis of the splitting pattern shown by the H-6 signal gave $J_{ax-ax} = 10{\cdot}5$ Hz, $J_{ax-eq} = 2{\cdot}0$ Hz, $J_{vic} = 5{\cdot}0$ and $= 7{\cdot}5$ Hz (Fig. 1).



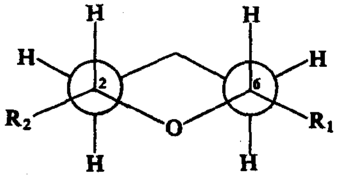
(VI) (–)-Centrolobol, G = H



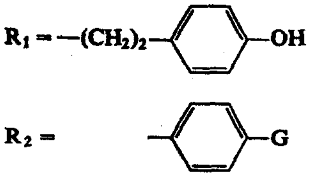
(VIIa) (–)-Centrolobine, G = Me
(VIIb) (–)-De-*O*-methylc., G = H



(VIII) (+)-Centrolobol, G = $\mathrm{H_O}$



(IXa) (+)-Centrolobine, G = Me
(IXb) (+)-De-*O*-methylc., G = H



These configurational and conformational facts are portrayed in the Newman formulation (VIIa) which establishes (–)-centrolobine as 2R-(p-methoxyphenyl)-6S-[β-(p-hydroxyphenyl)-ethyl]-tetrahydropyran.

The alternative presence of (+) and (–)-centrolobine in what is apparently the same species merits attention. The botanical literature[8,9] mentions *C. robustum* var. *macrochaete* Mart. and *C. robustum* var. *microchaete* Mart. whose major morphological difference is the size of a thorn on the seed. *A posteriori* it is impossible to state the variety either of the specimen from which Gonçalves de Lima and Marini-Bettòlo isolated (+)-centrolobine[2,3]

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[8] C. F. P. de Martius, *Flora Brasiliensis*, Vol. XX, Part 1, p. 263, F. Fleischer, Leipzig (1866–1868).
[9] A. Ducke, *Anais Acad. Brasil. Cienc.* 31, 211 (1959).

or of the specimen which we used to give (−)-centrolobine. The questions, whether different stereoisomers are produced by different varieties, different geographical forms, or even if one of the two specimens was incorrectly classified as *C. robustum*, must, at present, be considered unsolved.

However this may be, the configurational identity of C-6 in (−)-centrolobine (VIIa) and (−)-de-*O*-methylcentrolobine (VIIb) and of C-3 in (−)-centrolobol (VI) extracted from our specimen of *C. robustum* suggested the biosynthetic interconnexion of these compounds. It was anticipated on these grounds that in specimens which produce (+)-centrolobine as the most abundant metabolite, dextrorotatory companion substances should occur. We were fortunate to be able to demonstrate the correctness of this prediction analysing *C. tomentosum* Benth. from the Rio Doce region of the State of Espirito Santo. The ethanol extract of its heartwood yielded (+)-centrolobine, (+)-de-*O*-methylcentrolobine and (+)-centrolobol. The NMR data for (+)-centrolobine were identical in all details, including the coupling constants of the two doublets which represent the proton at C-2 and the pattern width of the C-6 proton signal, with the analogous data for (−)-centrolobine. The structure of 2S-(p-methoxyphenyl)-6R-[β-(p-hydroxyphenyl)-ethyl]-tetrahydropyran (IXa) was consequently assigned to (+)-centrolobine, while 3R-1,7-di-(p-hydroxyphenyl)-heptan-3-ol (VIII) was considered to represent (+)-centrolobol.

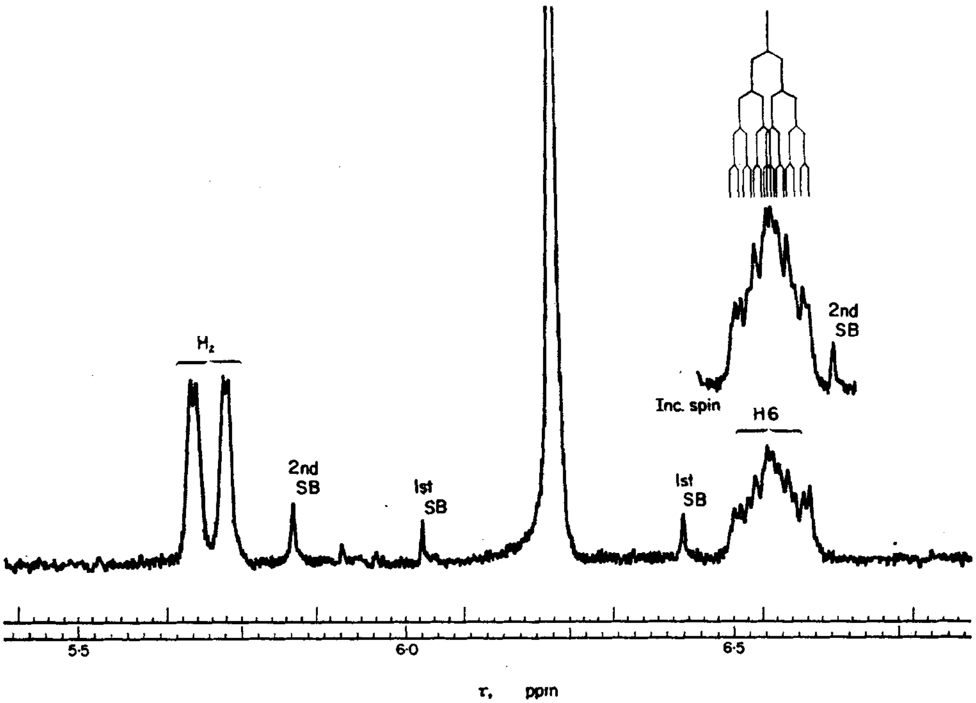

Fig. 1. Portion of the 220 MHz nmr spectrum of (−)-centrolobine in acetone-D_6.

The centrolobines and di-(p-hydroxycinnamoyl)-methane, constituent of *Curcuma longa* L. (family Zingiberaceae),[10] have identical carbon skeletons and aromatic oxygenation patterns. The biosynthesis of this and other curcuminoids seems to involve coupling of 2

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[10] K. R. Srinivasan, *J. Pharm. Pharmacol.* 5, 448 (1953).

cinnamate units with the carbon atom of a precursor of unknown nature. This hypothesis was extrapolated to the biosynthesis of centrolobine.[3] Alternatively, chain extension of 1 cinnamate unit by 5 acetate units could also represent a possible route to the natural diarylheptanoids.

EXPERIMENTAL

Materials and Equipment

M.ps.: Kofler hot stage microscope. Column chromatography: Merck Kieselgel 0·05–0·20 mm. TLC: Merck Kieselgel G. I.r. spectra: Perkin–Elmer Infracord 137. U.v. spectra: Beckman DB-G. NMR spectra: Varian A-60 and Perkin–Elmer R-10, unless otherwise stated, s—singlet, d—doublet, t—triplet, q—quartet, m—multiplet. Mass spectra: A.E.I. MS9. O.r.d. and c.d. curves: Jasco ORD/UV-5. Absorbances were maintained below 2. Direct comparison between samples employed mixture m.p., co-chromatography, i.r., u.v., NMR and o.r.d. curves.

Extraction of Centrolobium robustum. *Isolation of* (–)-*Centrolobine, Piceatannol,* (–)-*Centrolobol and* (–)-*De-O-methylcentrolobine*

The powdered heartwood (2·5 kg) was extracted at room temp. successively with benzene, acetone and EtOH. Evaporation of the benzene solution gave a residue (80 g) which was chromatographed on SiO_2 (500 g) giving a sole crystalline fraction (A_1) upon elution with benzene. Evaporation of the acetone solution gave a residue (20 g) which was chromatographed on SiO_2 (200 g) giving a sole solid fraction (B_1) upon elution with benzene–acetone, 8:2. Evaporation of the EtOH solution gave a residue (20 g) which was chromatographed on SiO_2 (200 g) giving various fractions with the indicated solvents: benzene and benzene–$CHCl_3$, 9:1 (C_1), benzene–$CHCl_3$, 1:1 and $CHCl_3$ (C_2), $CHCl_3$–MeOH, 99:1 (C_3), $CHCl_3$–MeOH, 95:5 (C_4), $CHCl_3$–MeOH, 85:15 (C_5).

A_1 (6·5 g) was recrystallized from light petroleum–benzene yielding (–)-centrolobine (1·5 g). B_1 (0·6g) in MeOH solution was passed through a column of Sephadex LH-20 swelled in the same solvent. The first fractions consisted of a brown resin and were discarded. The crystalline fractions were recrystallized from benzene–acetone yielding piceatannol (100 mg). C_1 (0·2 g) was recrystallized successively from light petroleum–benzene yielding (–)-centrolobine (160 mg). C_2 (0·1 g) was recrystallized from benzene–$CHCl_3$ yielding (–)-de-*O*-methylcentrolobine (30 mg). C_3 (0·2 g) was a brown mass from which nothing useful could be isolated. C_4 (0·5 g) in MeOH solution was purified by filtration through a column of Sephadex-LH-20 swelled in the same solvent. The first fractions were discarded. The crystalline fractions were recrystallized from benzene–acetone yielding (–)-centrolobol (200 mg). C_5 (0·2 g) was treated in the same way as C_4. The crystalline fractions were recrystallized from benzene–acetone yielding piceatannol (50 mg).

Extraction of Centrolobium tomentosum. *Isolation of* (+)-*Centrolobine,* (+)-*Centrolobol and* (+)-*De-O-methylcentrolobine*

The powdered heartwood (1·8 kg) was treated in the same way described for *C. robustum* yielding (+)-centrolobine (300 mg), (+)-centrolobol (60 mg) and (+)-de-*O*-methylcentrolobine (30 mg).

Piceatannol. Slightly yellow crystals, m.p. 225° dec. (m.p. lit.[11] 229° dec.). Identified by direct comparison with an authentic sample.

Piceatannol tetra-acetate. Piceatannol (50 mg) was acetylated with the acetic anhydride–pyridine reagent in the usual manner yielding the tetra-acetate which was recrystallized from light petroleum and benzene. White crystals (60 g), m.p. 119–121° (m.p. lit.[12] 120°). NMR spectrum ($CDCl_3$) τ: 2·32–2·80 (m, 3 arom. *H*), 2·92 (d, $J = 2$ Hz, 2 arom. *H*), 3·05 (s, C*H*=C*H*), 3·17 (d, $J = 2$ Hz, 1 arom. *H*), 7·71 (s, 4 CH_3CO—). Mass spectrum: *m/e* (%) 412 (20), 370 (30), 328 (100), 286 (50), 244 (50), 100 (50).

(–)-*Centrolobine.* Colourless needles, m.p. 84–86°. ν_{max}^{KBr} 3322, 2899, 1600, 1497, 1445, 1361, 1295, 1221, 1168, 1106, 1081, 1047, 1030, 835, 816, 804 cm^{-1}. λ_{max}^{MeOH} 218sh., 225, 282, 285sh. nm (ϵ resp. 13,000, 17,400, 3900, 3500). $\lambda_{max}^{MeOH+NaOH}$ 214, 234, 242, 290 nm (ϵ resp. 19,800, 15,900, 15,900, 4000). NMR spectrum $(CD_3)_2CO$, 220 Mhz] τ: 2·70 (d, $J = 9$ Hz, 2*H*) and 3·13 (d, $J = 9$ Hz, 2*H*), 2·98 (d, $J = 9$ Hz, 2*H*) and 3·26 (d, $J = 9$ Hz, 2*H*), 5·70 (q, $J = 10·5$ and $= 2·0$ Hz, Ar—C*H*OR), 6·24 (s, Ar—OCH_3), 6·52–6·64 (m, R—C*H*OR—), 7·23–7·41 (m, Ar—CH_2—), 8·06–8·43 (m, 3 —CH_2—), 8·50–8·81 (m, —CH_2—). $[\alpha]_D^{25°}$ −97·6° (*c*. 0·10, MeOH). O.r.d. (*c*. 0·10, MeOH): $[\phi]_{589}$ −299, $[\phi]_{550}$ −352, $[\phi]_{500}$ −459, $[\phi]_{450}$ −600, $[\phi]_{400}$ −713. C.d. (*c*. 0·014, MeOH), 22°: $[\theta]_{280}$ 0, $[\theta]_{272}$ −13,500, $[\theta]_{260}$ 0, $[\theta]_{225}$ −17,750.

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[11] G. BILLEK, in *Progress in the Chemistry of Organic Natural Products* (edited by L. ZECHMEISTER), p. 115, Springer-Verlag, Wien (1964).

[12] J. CUNNINGHAM, E. HASLAM and R. D. HAWORTH, *J. Chem. Soc.* 2875 (1963).

(+)-*Centrolobine*. Colourless needles, m.p. 84–86°. I.r., u.v. and NMR spectra identical with the analogous spectra quoted for (–)-centrolobine. $[\alpha]_D^{25°}$ +97·0° (*c*. 0·10, MeOH). O.r.d. (*c*. 0·10, MeOH): $[\phi]_{589}$ +299, $[\phi]_{550}$ +352, $[\phi]_{500}$ +459, $[\phi]_{450}$ +600, $[\phi]_{400}$ +713.

(–)-*De*-O-*methylcentrolobine*. Colourless crystals, m.p. 246–248°. ν_{max}^{KBr} 3448, 2985, 2857, 1613, 1511, 1443, 1366, 1311, 1274, 1227, 1175, 1096, 1087, 1026, 1015, 985, 961, 905, 869, 844, 828, 810, 763, 752 cm^{-1}. λ_{max}^{MeOH} 222sh., 228, 280, 286 sh. nm (ϵ resp. 13,000, 17,400, 3900, 3500).

(+)-*De*-O-*methylcentrolobine*. Colourless crystals, m.p. 246–248°. I.r. spectrum identical with the analogous spectrum quoted for (–)-de-*O*-methylcentrolobine.

(–)-*De*-O-*methylcentrolobine diacetate*. (–)-De-*O*-methylcentrolobine (20 mg) was acetylated with the acetic anhydride–pyridine reagent in the usual manner yielding the diacetate (20 mg) as a viscous oil. NMR spectrum (CCl_4) τ: 2·28–2·95 (m, 2AA″BB″ systems of arom. *H*), 5·55 (q, 8 and 3 Hz, Ar—C*H*.OR—), 6·05–6·65 (m, R—C*H*.OR—), 7·17 (t, 7·5 Hz, Ar—CH_2—), 7·72 (s, 2Ar—O.CO.CH_3), 7·87–8·73 (m, 4 —CH_2—).

(–)-*Centrolobol*. Colourless crystals, m.p. 128–130°. ν_{max}^{KBr} 3425, 2941, 2717, 1587, 1502, 1439, 1348, 1222, 1163, 1101, 1085, 1064, 1026, 913, 864, 850, 825, 772 cm^{-1}. λ_{max}^{MeOH} 218sh., 225, 282, 285sh. nm (ϵ resp. 13,100, 17,500, 3900, 3500); $\lambda_{max}^{MeOH+NaOH}$ 218, 240, 298 nm (ϵ resp. 25,000, 25,000, 4800). NMR spectrum [$(CD_3)_2CO$] τ: 2·86–3·40 (m, 2AA″BB″ systems of arom. *H*), 6·23–6·68 (m, R—C*H*.OH—R), 7·00 (s, R—CH.O*H*—R), 7·21–7·67 (m, 2Ar—CH_2—), 8·15–8·75 (m, 4 —CH_2—). $[\alpha]_D^{25°}$ –8·6° (*c*. 0·10, MeOH). O.r.d. (*c*. 0·17, MeOH): $[\phi]_{589}$ –25·5, $[\phi]_{550}$ –27·6, $[\phi]_{500}$ –34·8, $[\phi]_{450}$ –49·2, $[\phi]_{400}$ –70·2. Mass spectrum: *m*/*e* (%) 300 (13), 282 (25), 175 (7), 161 (2), 160 (2), 133 (80), 120 (68), 107 (100).

(+)-*Centrolobol*. Colourless crystals, m.p. 128–130°. I.r., u.v. and NMR spectra identical with the analogous spectra quoted for (–)-centrolobol. $[\alpha]_D^{25°}$ +8·3° (*c*. 0·10, MeOH).

(–)-*Centrolobol triacetate*. (–)-Centrolobol (100 mg) was acetylated with the acetic anhydride–pyridine reagent at room temp. in the usual manner yielding the triacetate as a viscous oil (40 mg). ν_{max}^{film} 2941, 1770, 1730, 1603, 1504. 1366, 1238, 1215, 1190, 1163, 1015, 909, 847, 810 cm^{-1}. NMR spectrum (CCl_4) τ: 2·80–3·24 (m, 2AA″BB″ systems of arom. *H*), 5·02–5·32 (m, —C*H*.OAc—), 7·25–7·65 (m, 2Ar—CH_2—), 7·85 (s, 2ArO.CO.CH_3), 8·10 (s, RO.CO.CH_3), 8·25–8·80 (m, 4 —CH_2—).

(–)-O-*Methylcentrolobols and* (–)-*di*-O-*methylcentrolobol by methylation of* (–)-*centrolobol*. (–)-Centrolobol (50 mg) was dissolved in MeOH and treated with excess CH_2N_2 in Et_2O at room temp. for 24 hr. Residual CH_2N_2 was destroyed by addition of acetic acid and the solution was evaporated to dryness under vacuum. A $CHCl_3$ solution of the residue was washed exhaustively with 0·5% aq. NaOH, dried and evaporated, yielding, after crystallization from light petroleum, white crystals of (–)-di-*O*-methylcentrolobol (35 mg), m.p. 53–55°. ν_{max}^{KBr} 3175, 2857, 1613, 1515, 1460, 1290, 1242, 1176, 1099, 1064, 1036, 909, 866, 820, 806, 749 cm^{-1}. NMR spectrum (CCl_4) τ: 2·90–3·40 (m, 2AA″BB″ systems of arom. *H*), 6·20 (s, ArOCH_3), 6·24–6·62 (m, —C*H*.OH—), 6·90 (s, —CH.O*H*—), 7·20–7·70 (m, 2Ar—CH_2—), 8·15–8·80 (m, 4 —CH_2—).

The aq. alkaline solution was acidified and extracted with $CHCl_3$. The $CHCl_3$ solution was dried and evaporated yielding the (–)-*O*-methylcentrolobols as an oil. TLC (silica, benzene–acetone, 8:2) produced a single spot. Co-chromatography with the (–)-*O*-methylcentrolobol obtained by hydrogenolysis of (–)-centrolobine also produced a single spot.

(–)-O-*Methylcentrolobol and* (–)-*di*-O-*methylcentrolobol by hydrogenolysis of* (–)-*centrolobine*. (–)-Centrolobine (100 mg) in MeOH (10 ml) was hydrogenated in presence of 30% Pd/C catalyst at room temp. for 24 hr. The reaction mixture was filtered and evaporated. The residue was chromatographed on a SiO_2 column. Elution with benzene gave in the last fractions starting material (20 mg), and in the first fractions (–)-*O*-methylcentrolobol (60 mg) which was crystallized from light petroleum to colourless crystals, m.p. 73–75°. ν_{max}^{KBr} 3226, 2857, 1600, 1515, 1449, 1342, 1266, 1235, 1205, 1176, 1099, 1058, 1031, 909, 870, 830, 820, 810, 752 cm^{-1}. λ_{max}^{MeOH} 225, 279, 284sh. nm (ϵ resp. 17,100, 4800, 3000). NMR spectrum ($CDCl_3$) τ: 2·80–3·50 (m, 2AA″BB″ systems of arom. *H*), 6·20 (s, ArOCH_3), 6·50 (m, —C*H*.OH—), 6·90 (s, —CH.O*H*—), 7·25–7·65 (m, 2Ar—CH_2—), 8·00–8·70 (m, 4 —CH_2—). $[\alpha]_D^{25°}$ –8·6° (*c*. 0·16, MeOH). O.r.d. (*c*. 0·15, MeOH): $[\phi]_{589}$ –27·0, $[\phi]_{550}$ –29·5, $[\phi]_{500}$ –36·7, $[\phi]_{450}$ –51·4, $[\phi]_{400}$ –68·7. Treatment of this product (10 mg) in MeOH solution with excess CH_2N_2 in ether for 24 hr, destruction of residual reagent with acetic acid and evaporation to dryness under vacuum gave (–)-di-*O*-methylcentrolobol (5 mg) identified by direct comparison with the sample obtained by direct methylation of (–)-centrolobol.

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