10.1071/CH04047_AC

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Electronic Supporting Information

Concerning the Proposed Structure of (+)-Laurobtusol: Spectral Discrepancies with the Synthetic, Racemic Stereoisomers

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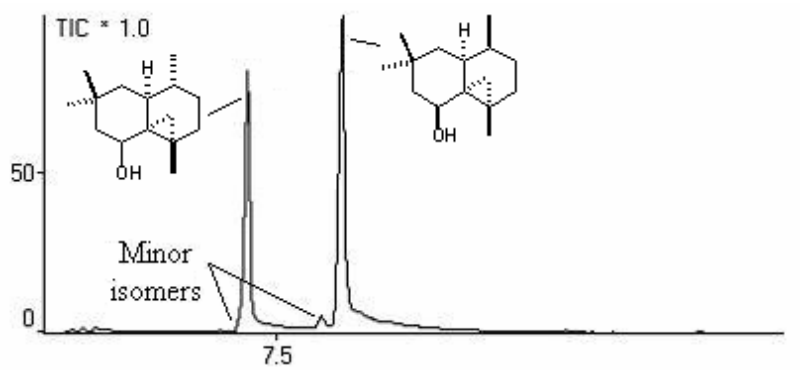
General experimental Procedures

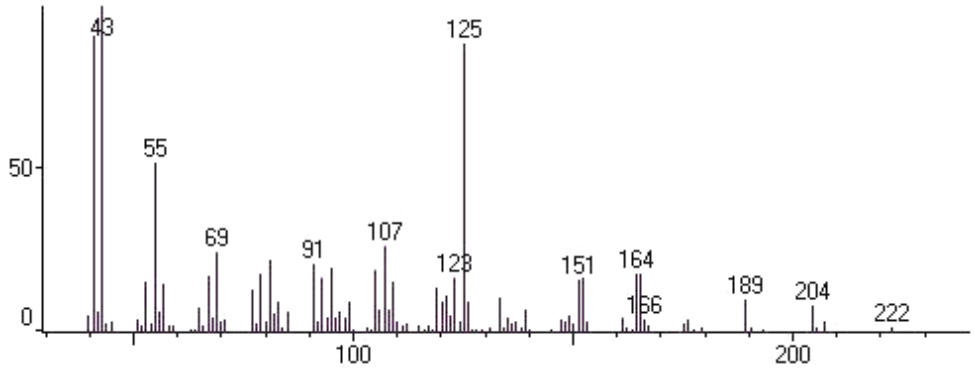
NMR spectra were obtained with Bruker AV400, DRX500 and DRX750 spectrometers, using $CDCl_3$ as solvent, and referenced to residual solvents at δ_H 7.24 and δ_C 77.0. The GCMS were recorded on a Shimadzu QP5100 gas chromatography mass spectrometer at 70eV, using a J & W Scientific DB-5 column. The spectrometer was programmed as 100^{o}C for 2 minutes, then with temperature increased at a rate of 16^{o}C/minute until 250^{o}C. Microanalyses were performed on the Elemental Analyzer Model 1106 from Elemental Microanalysis Limited. Melting points were recorded with a Buchi Schmelzpunktbestimmungs apparatus, and were uncorrected. HPLC separations were performed using either an analytical or a preparative conventional silica column with solvent systems indicated in the relevant sections of the text. Solvents were degassed by vacuum filtering prior usage. A Gilson (Model 131) refractive index detector was used. Flash chromatography was carried out using Merck Kieselgel 60 (230-400 mesh) or Scharlau silica gel (200-400 mesh) under positive pressure from a compressed air line.

GC trace of the synthetic mixture (**15**, **16**, **26** and **27**) from the cyclopropanation

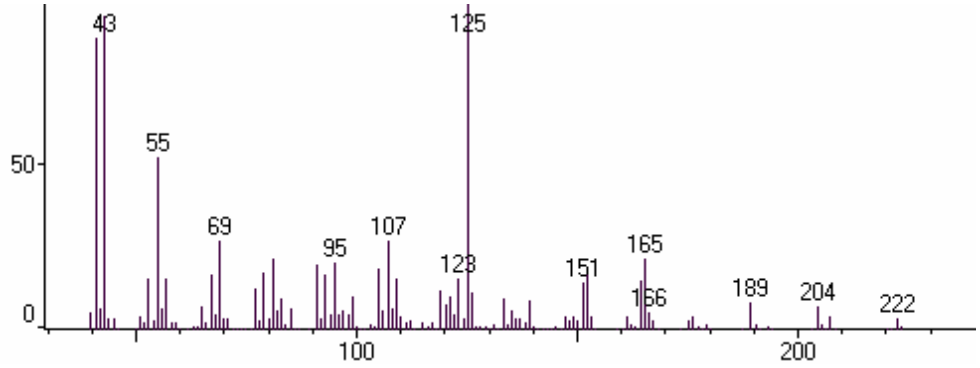


EIMS

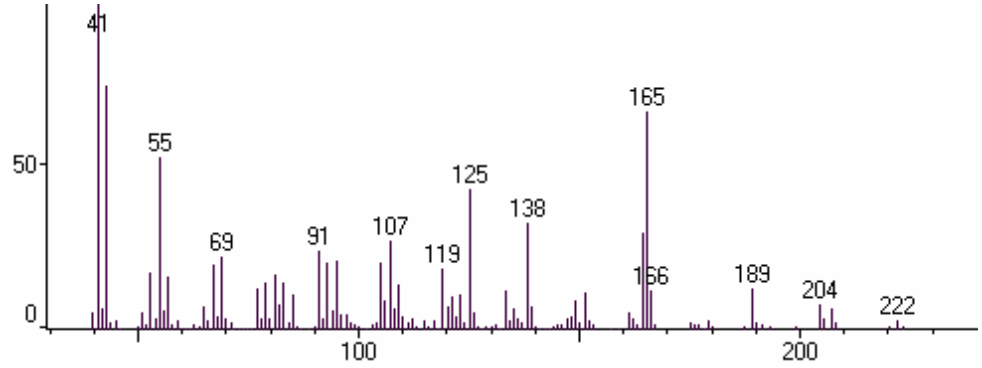
Mass spectrum of **15** (major isomer).



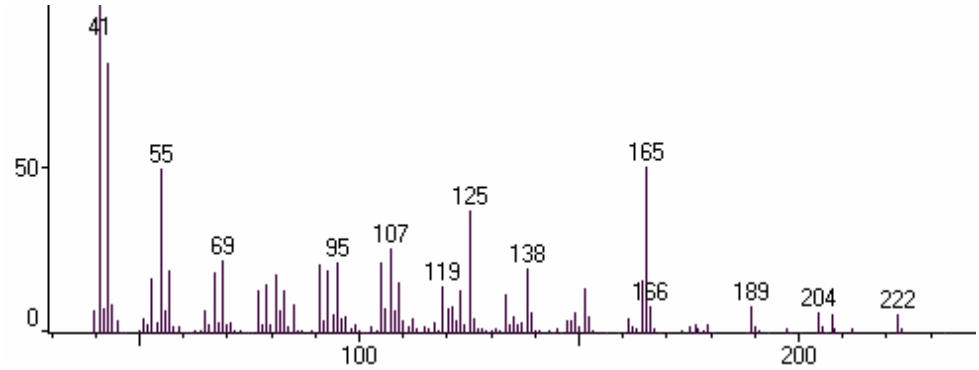
Mass spectrum of **16** (major isomer).



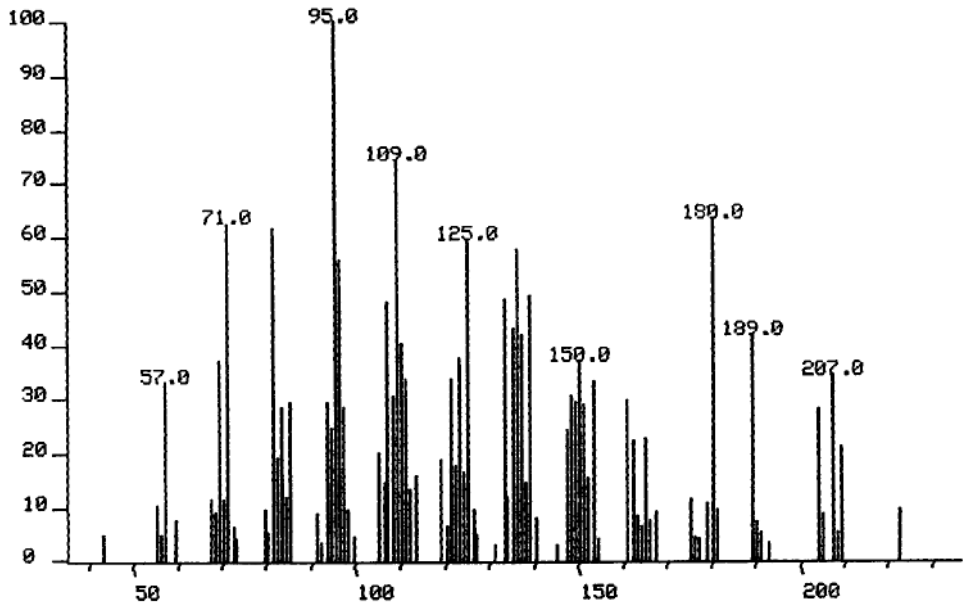
Mass spectrum of **26**/**27** (minor isomer).



Mass spectrum of **27**/**26** (minor isomer).



<u>Mass spectrum of natural laurobtusol</u>. Courtesy of Professor S. Caccamese.



Crystal Data

1a,4,6,6-Tetramethyl-octahydro-cyclopropa[d]naphthalen-8-one **13**: $C_{16}H_{24}O_3$, *M* 264.35, *T* 296 K, triclinic, space group $P2_1/c$ (No. 14), *a* 10.125(4) Å, 16.365(2) Å, *c* 15.575(5) Å, β 90.41(2)º, *V* 2581(1) X^3, D_c (Z = 8) 1.134 g cm^{-3}, *F*(000) 976, μ(Mo Kα) 0.68 cm^{-1}, 4382 unique data ($2\theta_{max}$ 50E), 711 with $I > 2\sigma(I)$; *R* 0.1068 (obs. data), wR_2 0.3762 (all data), goodness of fit 0.911 (CCDC number 237188**)**.

4,7,7-trimethyl-5-oxo-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid ethyl ester (*cis* (1,8a) isomer) **20**: $C_{16}H_{24}O_3$, *M* 264.35, *T* 296 K, triclinic, space group $P\bar{1}$ (No. 2), *a* 6.1785(9) Å, *b* 8.919(2) Å, *c* 14.228(2) X, α 77.44(1)º, β 81.83(1)º, γ 82.13(1)º, *V* 752.9(2) X^3, D_c (Z = 2) 1.166 g cm^{-3}, *F*(000) 288, μ(Mo Kα) 0.79 cm^{-1}, 2621 unique data ($2\theta_{max}$ 50E), 796 with $I > 2\sigma(I)$; *R* 0.0964 (obs. data), wR_2 0.4065 (all data), goodness of fit 1.043 (CCDC number 235971).

4,7,7-trimethyl-5-oxo-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid ethyl ester (*trans* (1,8a) isomer) **21**: $C_{16}H_{24}O_3$, *M* 264.35, *T* 296 K, orthorhombic, space group *Pbca* (No. 61), *a* 9.5928(5) Å, *b* 16.996(2) Å, *c* 19.915(2) X, *V* 3246.9(5) X^3, D_c (Z = 8) 1.082 g cm^{-3}, *F*(000) 1152, μ(Mo Kα) 0.73 cm^{-1}, 2651 unique data ($2\theta_{max}$ 50E), 709 with $I > 2\sigma(I)$; *R* 0.0659 (obs. data), wR_2 0.2789 (all data), goodness of fit 0.948 (CCDC number 235970).

1a,6,6-Trimethyl-8-oxo-decahydro-cyclopropa[d]naphthalene-4-carboxylic acid ethyl ester (*trans* (1a,4) isomer) **23**: $C_{17}H_{26}O_3$, *M* 278.38, *T* 296 K, monoclinic, space group *C*2/*c* (No. 15), *a* 16.237(7) Å, *b* 9.6564(8) Å, *c* 22.98(1) X, β 114.72(2)º, *V* 3273(2) X^3, D_c (Z = 8) 1.130 g cm^{-3}, *F*(000) 1216, μ(Mo Kα) 0.76 cm^{-1}, 2879 unique data ($2\theta_{max}$ 50E), 1159 with $I > 2\sigma(I)$; *R* 0.0569 (obs. data), wR_2 0.2004 (all data), goodness of fit 1.027 (CCDC number 235975).

3,3,5,8-Tetramethyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol (*cis* (1,4a), *trans* (1,5) isomer) **12**: $C_{14}H_{24}O$, *M* 208.33, *T* 153 K, triclinic, space group $P\bar{1}$ (No. 2), *a* 10.108(2) Å, *b* 11.933(3) Å, *c* 12.159(2) X, α 82.57(2)º, β 66.74(1)º, γ 77.36(2)º, *V* 1303.4(5) X^3,

D_c (Z = 4) 1.062 g cm^{-3}, F(000) 464, μ(Mo Kα) 0.64 cm^{-1}, 4579 unique data ($2\theta_{max}$ 50E), 3374 with $I > 2\sigma(I)$; R 0.0555 (obs. data), wR_2 0.1681 (all data), goodness of fit 1.031 (CCDC number 235974).

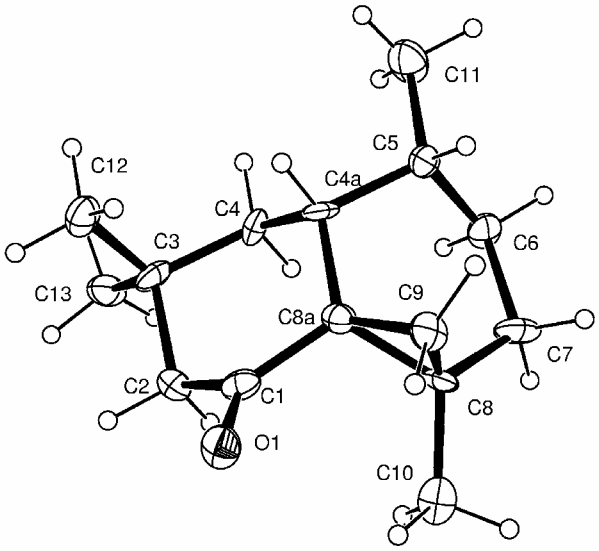
Intensity data were collected on an Enraf-Nonius CAD4 four-circle diffractometer using graphite monochromated Mo-Kα radiation (λ 0.71073 Å) in the ω-2θ scan mode. Lattice dimensions were determined by a least squares fit of the setting parameters of 25 independent reflections. For the structure of 3,3,5,8-tetramethyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol, crystal instability necessitated data collection at 153 K, employing an Oxford Cryostream Cooler. All other data sets were acquired at room temperature. Data reduction, decay correction and empirical absorption corrections (ψ-scans) were performed with the WINGX package.[1] Structures were solved by direct methods with SHELXS and refined by full matrix least squares analysis with SHELXL97.[2] All non-H atoms were refined with anisotropic thermal parameters, except disordered ethoxyl group C-atoms in the structures of 4,7,7-trimethyl-5-oxo-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid ethyl ester (*trans* isomer) and 1a,6,6-trimethyl-8-oxo-decahydro-cyclopropa[d]naphthalene-4-carboxylic acid ethyl ester. All H-atoms were constrained at estimated positions using a riding model. Molecular structures were drawn with non-H atoms at the 30% probability level with ORTEP3.[3] Crystallographic data in CIF format are available from the Cambridge Crystallographic Data Base and the Australian Jounal of Chemistry, PO Box 1139, Collingwood, Vic, 3006 (until 31 December 2005).

References

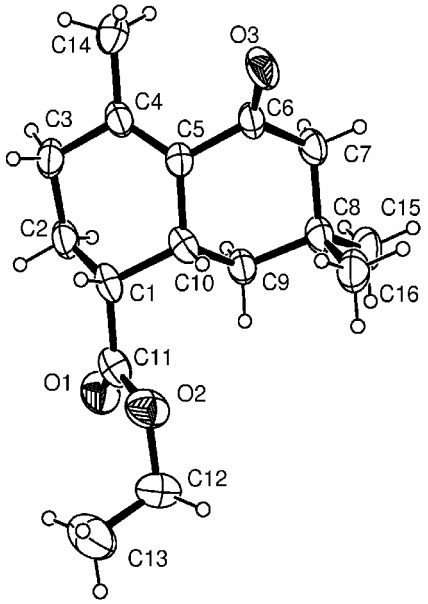
[1] L. J. Farrugia, *J. Appl. Cryst.* **1999**, *32*, 837.

[2] G. M. Sheldrick "SHELX97. Programs for Crystal Structure Analysis," University of Göttingen, Germany, 1997.

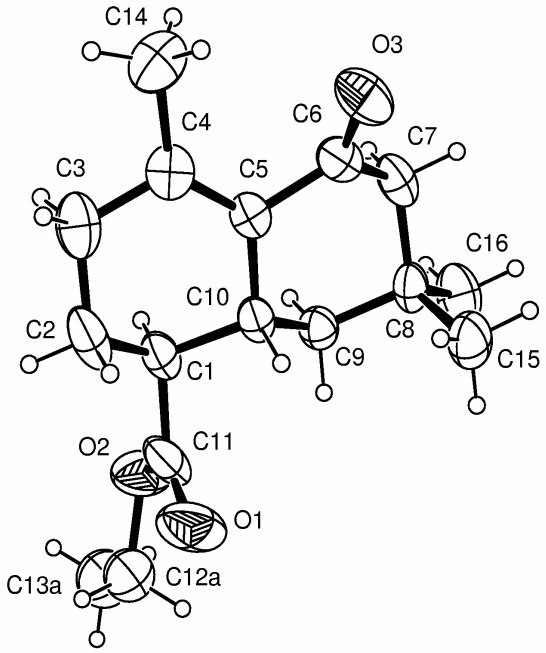
[3] L. J. Farrugia, *J. Appl. Cryst.* **1997**, *30*, 565.



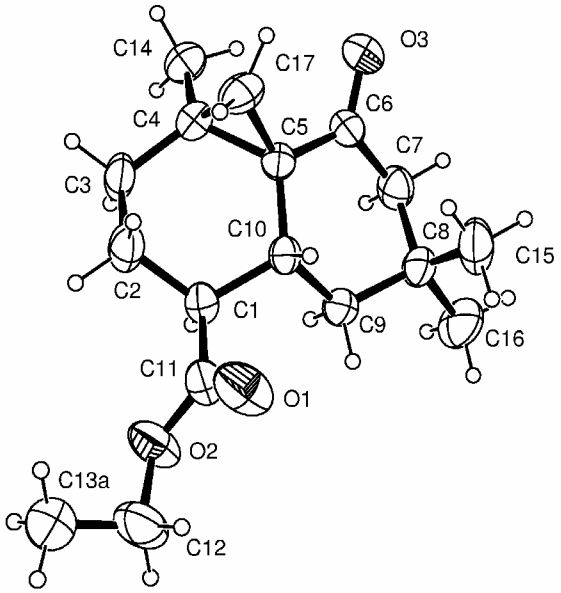
ORTEP plot of compound **13** (one of two crystallographically independent molecules shown, 30% probability ellipsoids shown).



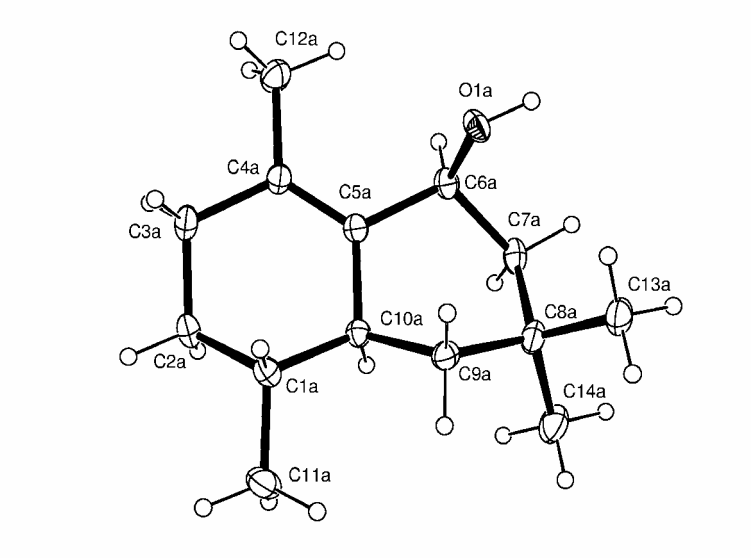
ORTEP plot of compound **20** (30% probability ellipsoids).



ORTEP plot of compound **21** (30% probability ellipsoids).

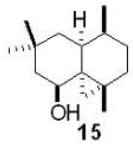


ORTEP plot of compound **23** (30% probability ellipsoids).



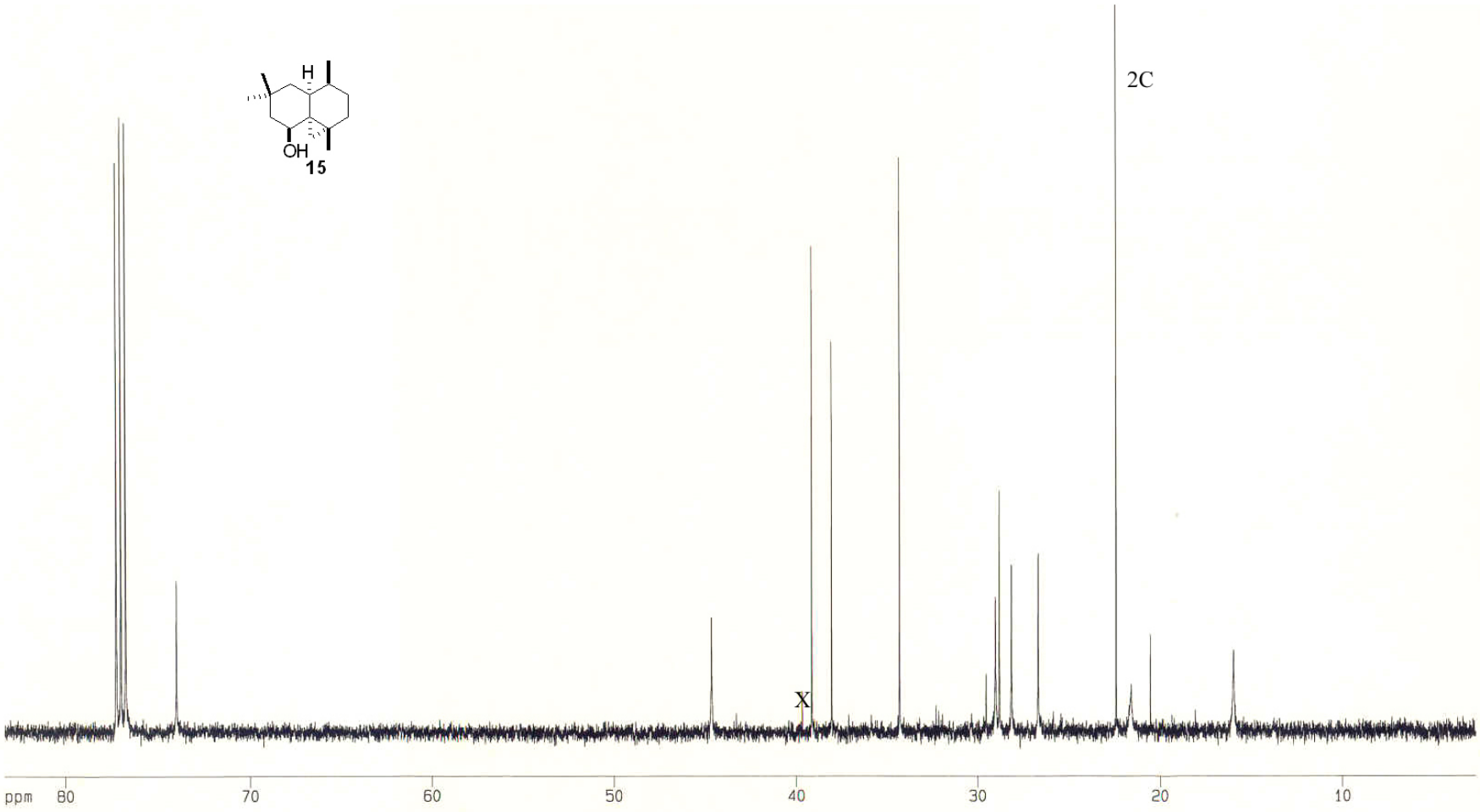
ORTEP plot of compound **12** (one of two crystallographically independent molecules shown, 30% probability ellipsoids).

500 MHz Proton NMR spectrum of the major isomer 15

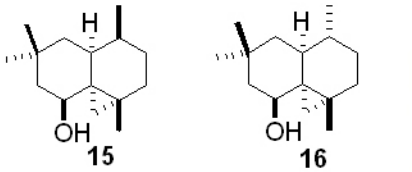


15

125 MHz Carbon-13 NMR spectrum of major isomer 15

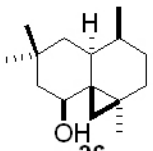


100 MHz Carbon-13 NMR spectrum of the cyclopropyl product mixture 15, 16, 26 and 27 in CDCl3

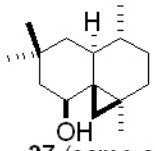


15

16

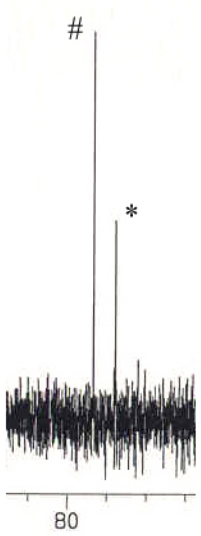


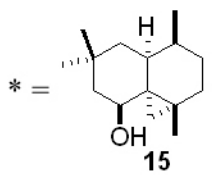
26



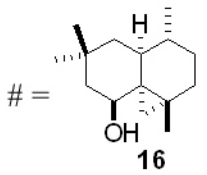
27 (same as **2**)

Expansion of the 100 MHz carbon-13 NMR spectrum of mixture 15, 16, 26 and 27 in CDCl3
(Note broadening of some signals of 15)

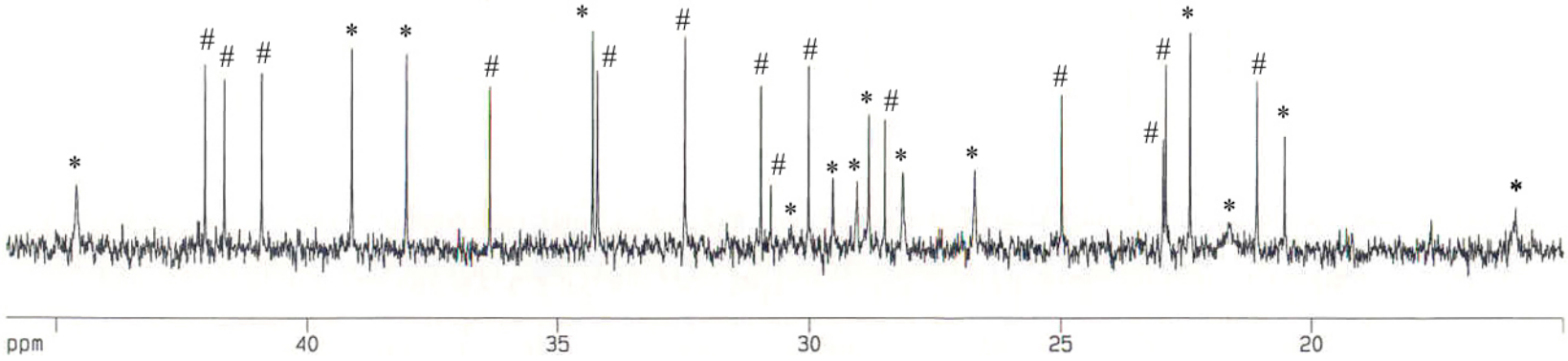




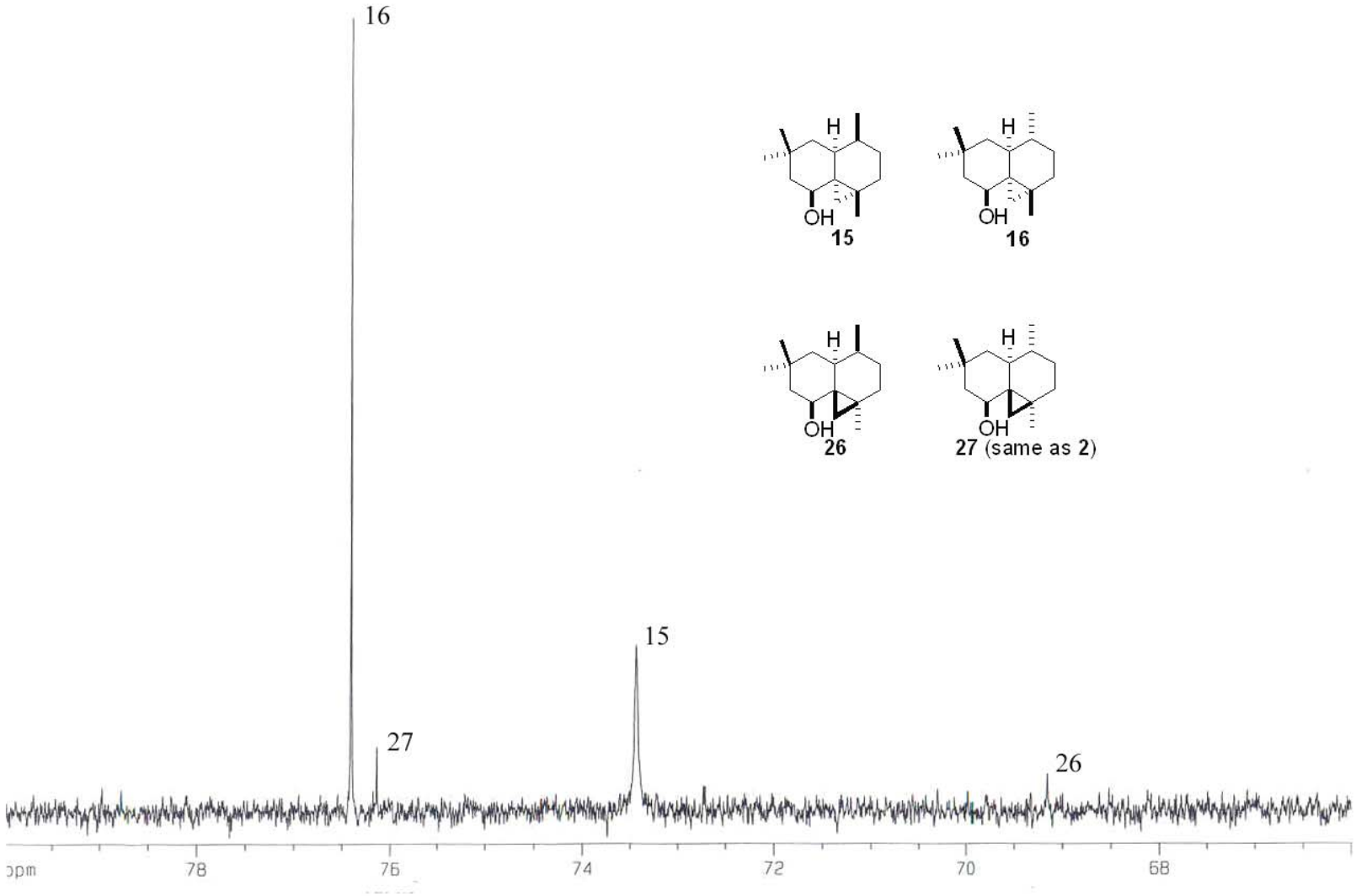
15



16



Expansion of 125 MHz Carbon-13 NMR spectrum of the cyclopropyl product mixture 15, 16, 26 and 27 (benzene-d6)



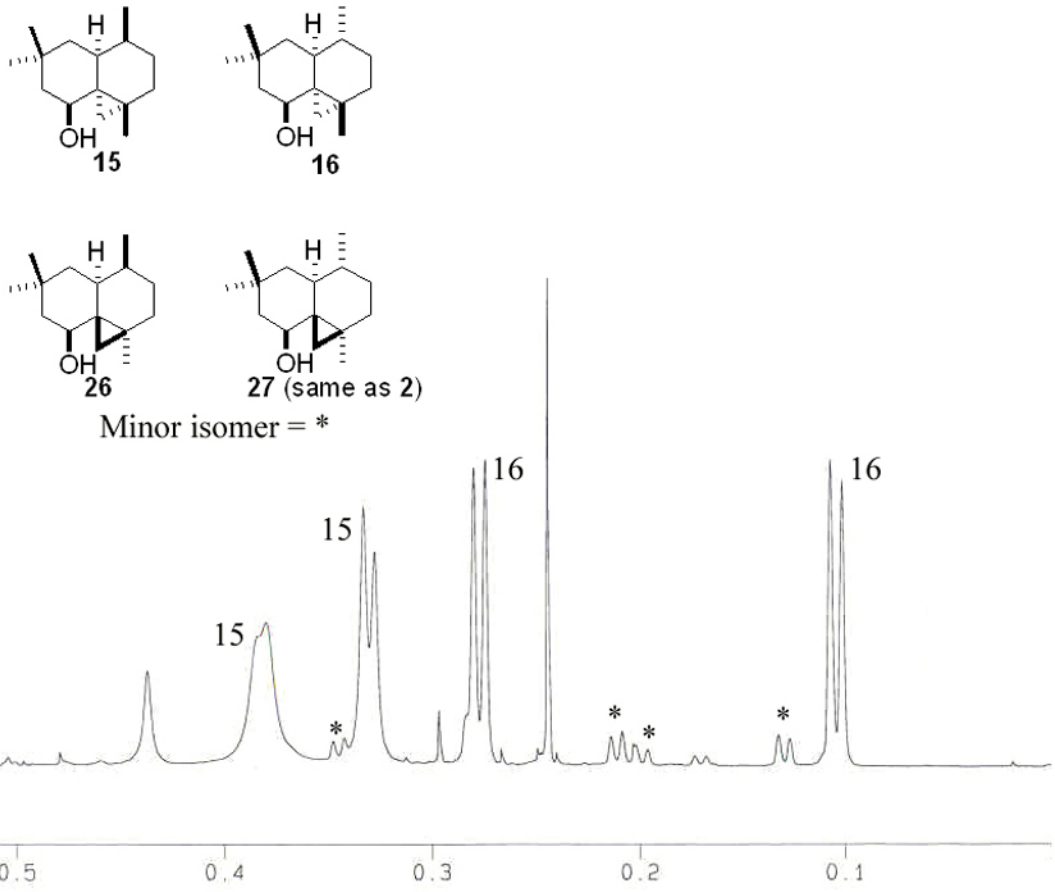
15

16

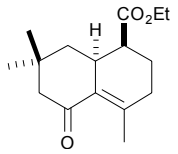
26

27 (same as **2**)

Expansion of the 750 MHz proton NMR spectrum of the mixture of 15, 16, 26 and 27 in benzene-d6 (Note broadening of one of the signals for 15)



Spectral, analytical and physical data of some key intermediates



20

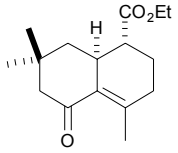
Mp: 66.5 - 68.0°C

Found C 72.36, H 9.31. $C_{16}H_{24}O_3$ requires C 72.69, H 9.15%.

^{1}H NMR (400MHz): δ 4.15 (2H, dq, J 10.8, 7.1), 2.76 (1H, m), 2.24 (1H, dd, J 14.2, 2.5), 2.17 (4H, m), 1.90 (1H, ddd, J 12.9, 6.88, 3.9), 1.83 (3H, d, J 2.1), 1.65 (2H, m), 1.27 (1H, t, J 12.7), 1.24 (3H, t, J 7.2), 0.97 (3H, s), 0.94 (3H, s).

^{13}C NMR (100MHz): δ 203.8, 175.3, 142.1, 132.2, 60.4, 56.1, 46.3, 44.1, 36.6, 32.9, 32.7, 31.7, 25.72, 25.67, 21.3, 14.2.

EIMS (m/z, (%)): 264 (M^+, 67), 249 (31), 191 (32), 175 (100), 149 (23), 134 (24), 107 (27), 91 (43), 79 (23), 77 (29), 41 (22).



21

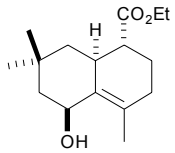
Mp: 41.5 - 44°C

Found: C 72.86, H 9.42. $C_{16}H_{24}O_3$ requires C 72.69, H 9.15%.

^{1}H NMR (400MHz): δ 4.13 (2H, 2 × dq, J 10.8, 7.1), 2.79 (1H, m), 2.71 (1H, m), 2.26 (1H, dd, J 14.5, 2.1), 2.15 (3H, m), 1.87 (3H, dd, J 1.1, 1.0), 1.80 (2H, m), 1.59 (1H, t, J 12.8), 1.40 (1H, ddd, J 12.6, 4.68, 2.0), 1.24 (3H, t, J 7.2), 0.97 (3H, s), 0.96 (3H, s).

^{13}C NMR (100MHz): δ 204.0, 173.7, 141.3, 132.0, 60.1, 55.7, 42.3, 41.2, 35.4, 32.7, 31.8, 31.6, 26.7, 22.1, 21.0, 14.3.

EIMS (m/z, (%)): 264 (M^+, 24), 249 (5), 191 (19), 175 (100), 147 (10), 135 (10), 107 (22), 105 (17), 91 (33), 77 (19), 55 (15), 41 (20).



24

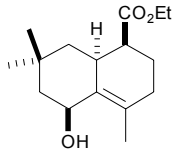
Mp: 93.5 - 95.0°C

Found: C 73.19, H 10.04. $C_{16}H_{26}O_3$ requires C 73.14, H 9.84%.

^{1}H NMR (400MHz): δ 4.61 (1H, br t, J 3.0), 4.14 (2H, 2 × dq, J 10.8, 7.1), 2.36 (1H, br m), 2.20 - 1.82 (5H, m), 1.76 (3H, d, J 1.9), 1.40 - 1.25 (3H, m), 1.24 (3H, t, J 7.2), 1.07 (3H, s), 0.94 (3H, s).

^{13}C NMR (100MHz): δ 176.0, 133.8, 129.8, 68.1, 60.2, 47.2, 42.6, 41.8, 34.6, 33.1, 31.9, 30.6, 28.9, 26.4, 18.5, 14.3.

EIMS (m/z, (%)): 266 (M^+, 17), 192 (100), 177 (29), 175 (34), 159 (48), 107 (30), 105 (45), 93 (37), 91 (54), 79 (30), 55 (39), 43 (44), 41 (53).

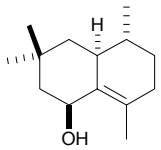


Epi-**24**

^{1}H NMR (400MHz): δ 4.46 (1H, br t, J 5.9), 4.10 (2H, 2 × dq, J 10.8, 7.2), 2.60 (1H, dt, J 10.3, 5.4), 2.34 (1H, m), 2.01 (2H, br dd, J 7.0, 3.9), 1.83 (3H, d, J 0.7), 1.74 (2H, m), 1.51 (2H, d, J 6.2), 1.41 (1H, t, J 12.9), 1.22 (3H, t, J 7.1), 1.03 (1H, dd, J 12.8, 3.1), 0.98 (3H, s), 0.97 (3H, s).

^{13}C NMR (100MHz): δ 174.5, 133.4, 126.3, 70.9, 59.9, 47.7, 43.2, 34.5, 33.0, 32.2, 30.5, 28.4, 22.0, 18.9, 14.3.

EIMS (m/z, (%)): 248 (M^+ - 18, 51), 175 (69), 174 (67), 159 (58), 133 (41), 119 (67), 118 (30), 105 (100), 93 (22), 91 (29), 55 (22), 41 (28).



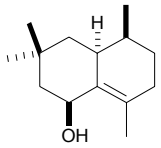
11

^{1}H NMR (400MHz, J in Hz): δ 4.57 (1H, br s), 2.07 (1H, m), 1.90 (1H, dd, J 17.7, 5.4), 1.75 (3H, s), 1.64 (2H, m), 1.58 (1H, dd, J 13.6, 2.5), 1.56 (1H, t, J 11.6), 1.34 (1H, dd, J 14.8, 2.7), 1.24 (1H, dq, J 12.1, 5.6), 1.16 (1H, m), 1.10 (1H, t, J 13.0), 1.08 (3H, s), 0.94 (3H, d, J 6.2), 0.93 (3H, s).

^{13}C NMR (100MHz): δ 135.0, 130.0, 68.6, 42.8, 41.4, 39.8, 34.3, 33.3, 32.5, 31.5, 30.7, 29.0, 20.2, 18.8.

EIMS (m/z, (%)): 208 (M^{+}, 44), 193 (70), 165 (40), 152 (56), 133 (31), 119 (50), 109 (70), 91 (59), 79 (45), 67 (37), 55 (42), 41 (100).

HREIMS for $C_{14}H_{24}O$: calculated 208.1827; found 208.1828.



12

^{1}H NMR (400MHz, J in Hz): δ 4.57 (1H, br s), 2.05 (2H, m), 1.74 (3H, dd, J 1.1, 0.9), 1.63 (2H, m), 1.52 (2H, m), 1.35 – 1.05 (5H, m), 0.94 (3H, s), 0.89 (3H, s), 0.77 (3H, d, J 7.0).

^{13}C NMR (100MHz): δ 133.5, 128.7, 68.8, 43.6, 40.0, 35.7, 33.6, 30.8, 30.5, 29.5, 29.1, 29.0, 18.4, 13.7.

EIMS (m/z, (%)):208 (M^{+}, 49), 193 (81), 165 (41), 152 (48), 133 (34), 119 (58), 109 (72), 91 (69), 79 (42), 67 (33), 55 (49), 41 (100).