SUPPORTING INFORMATION

Total Synthesis of (±)-Cordypyridone A, B and Related Epimers

Ian L. Jones, Felicity K. Moore, Christina L. L. Chai*

Institute of Chemical and Engineering Sciences, 1 Pesek Road, Jurong Island, Singapore, 627833.

Tel: +65 6796 3902 Fax: +65 6316 6184

christina_chai@ices.a-star.edu.sg

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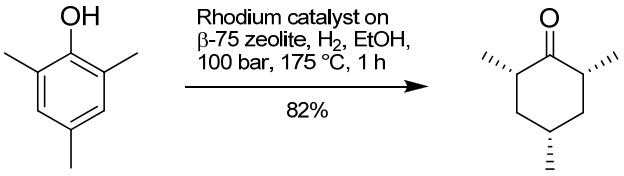
General Experimental Procedures

Melting points were recorded on Buchi Melting Point B-540 apparatus. Infrared spectra were recorded on a Bio-Rad Excalibur Series TFS 3000MX Fourier Transform Infrared Spectrometer. Samples were analysed as thin liquid films or from the specified solvents on NaCl plates or as KBr discs. Infrared spectral data are reported as wavenumber (cm^{-1}). Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on a Bruker NMR spectrometer, operating at 400 MHz for proton and 100 MHz for carbon spectroscopy. The chemical shifts (δ) are reported as the shift in parts per million (ppm) from tetramethylsilane (TMS, 0.00 ppm). Proton and carbon spectra recorded were referenced to their central residual solvent peak; 7.26 and 77.16 ppm for $CDCl_3$, 3.31 and 49.00 ppm for CD_3OD and 2.05 and 29.84 ppm for $(CD_3)_2CO$. Proton spectral data are reported as follows: chemical shift (δ), number of protons, multiplicity (s: singlet, d: doublet, t: triplet, m: multiplet, dd: doublet of doublets etc., b: broad), coupling constant (*J*) in Hz with signals being assigned where possible. Carbon spectral data are reported as follows: chemical shift (δ) and assignment. Low electron impact mass spectra were recorded on a Waters Quattro micro API™ using positive ion electron impact (EI) or electrospray (ESI) techniques (negative and positive ionisation modes). Mass spectral data are listed as mass-to-charge ratios (*m*/z) and relative intensity (% of base peak). High-resolution electron-impact mass spectra (HREIMS) were determined on a Thermo Finnigan MAT XP95 spectrometer. High-resolution electrospray (HRESIMS) techniques were carried out on an Agilent Technologies 6210 Time-of-Flight LC/MS (negative and positive ionisation modes). Microanalyses were performed by the ICES Microanalytical Service on a EuroEA3000 Series CHNS analyser. Analytical thin layer chromatography (TLC) was conducted on aluminium sheets with silica gel 60 F_{254} (Merck). The chromatograms were analysed under a 254 nm UV lamp and developed using a reagent 'dipping' solution [ammonium molybdate/ceric ammonium sulfate/sulfuric acid/water (10g: 0.4g: 5.6 mL: 200 mL)] or potassium permanganate solution [$KMnO_4$/potassium carbonate/5% aqueous sodium hydroxide/water (3g: 20g: 5mL: 300mL)] followed by heating. Flash column chromatography was conducted according to the method of Still and co-workers using Merck silica gel 60 (40-63μm) and analytical reagent (AR) grade solvents indicated.[1] All solvents used were of AR grade, purified by literature procedures and where appropriate, stored over freshly activated molecular sieves. All reactions were carried out under an atmosphere of dry, oxygen-free argon unless otherwise specified. Reactions that involved moisture sensitive compounds were carried out using oven-dried apparatus and with dry solvents.

[1] Still, W. C.; Kahn, M.; Mitra, A. J. Org. Chem. 1978, 43, 2923.

Experimental Section

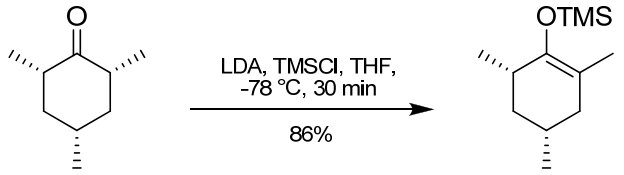
Synthesis of 2,4,6-trimethylcyclohexanone (9)



5 **9**

The β-H 75 Zeolite supported ruthenium catalyst (200 mg) was added to solution of 2,4,6-trimethylphenol **(5)** (10.0 g, 73.4 mmol) in ethanol (100 mL) in a 300 mL Parr reaction vessel. The system was purged three times with nitrogen (16 bar) and subsequently three times with hydrogen (35 bar). The system was then placed under a atmosphere of hydrogen (80 bar) and heated to 170 °C for one hour; a pressure increase (to 100 bar) was observed during this period. The reaction vessel was allowed to cool to room temperature and the pressure released. The reaction mixture was filtered through celite and the volume reduced. The product mixture was purified by column chromatography eluting with ethyl acetate in hexane (1:19) which afforded the *title compound* as a clear colourless mobile and highly volatile liquid (8.45 g, 82%); ν_{max} (CH_2Cl_2)/cm^{-1} 2965, 2931, 2871, 2846, 1714, 1458, 1177, 1130, 996; ^{1}H NMR (400 MHz; $CDCl_3$) δ 2.38-2.48 (2H, m, C<u>H</u>CH$_3$), 1.97-2.05 (3H, m, 2 × CH<u>H</u>, C<u>H</u>Me), 1.03-1.13 (2H, m, 2 × C<u>H</u>H), 0.96 (6H, d, *J* = 6, C<u>H</u>$_3$), 0.93 (3H, d, *J* = 6, C<u>H</u>$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 215.0 (C), 45.4 (2 × CH_2), 44.3 (2 × CH), 32.1 (CH), 21.3 (CH_3), 14.6 (2 × CH_3); EIMS (negative) *m/z* 140 (63%, M^-); 125 (9%); 112 (17%); 97 (39%); 82 (60%); 68 (100%); 55 (41%); 41 (27%); HRESIMS (positive) found 163.10973 $[M+Na]^+$ calculated $(C_9H_{16}ONa)^+$ requires 163.10934.

Synthesis of trimethyl(2,4,6-trimethylcyclohex-1-enyloxy)silane (10)

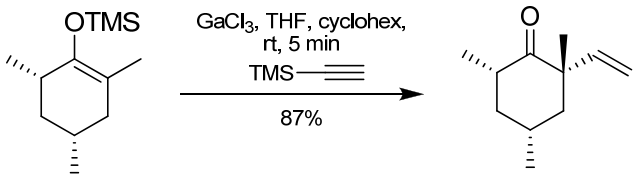


9 **10**

2,4,6-Trimethylcyclohexanone **(9)** (2.00 g, 16.26 mmol) was added dropwise over five minutes to a freshly prepared solution of LDA (17.12 mmol) in THF (20 mL) at -78 °C. The reaction was allowed to stir at this temperature for 20 minutes. Chlorotrimethylsilane (2.32 g, 21.4 mmol, 2.71 mL) was added dropwise, and the reaction was allowed to warm to ambient temperature. Aqueous saturated ammonium chloride solution (10 mL) was added and the reaction

mixture was extracted with ether (3 × 10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the reaction mixture was purified by column chromatography eluting with petrol (100%) which afforded the *title compound* as a clear colourless volatile liquid (2.61 g, 86%); ν_{max} (liquid film)/cm^{-1} 2957, 2929, 2912, 2873, 1714, 1679, 1458, 1377, 1336, 1252, 1187, 1171, 919, 878, 844; ^{1}H NMR (400 MHz; $CDCl_3$) δ 2.17-2.26 (1H, m), 1.88-1.93 (1H, m), 1.72-1.78 (1H, m), 1.66-1.72 (1H, m), 1.59-1.67 (1H, m), 1.54 (3H, s, C$\underline{H}_3$), 1.01 (3H, d, *J* = 7, C$\underline{H}_3$), 0.95-0.99 (1H, m), 0.92 (3H, d, *J* = 7, C$\underline{H}_3$), 0.16 (9H, s, Si(C$\underline{H}_3$)$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) 146.9 (C), 112.2 (C), 42.5 (CH_2), 39.8 (CH_2), 35.2 (CH), 29.2 (CH), 21.9 (CH_3), 19.4 (CH_3), 17.0 (CH_3), 0.65 (3 × CH_3); EIMS (negative) 212 (75 %, $[M]^-$), 197 (100%, $[M\text{-}CH_3]^-$), 170 (66%), 155 (88%), 141 (69%); HREIMS (negative) found 212.1594 $[M]^-$ calculated $(C_{12}H_{24}OSi)^-$ requires 212.1596.

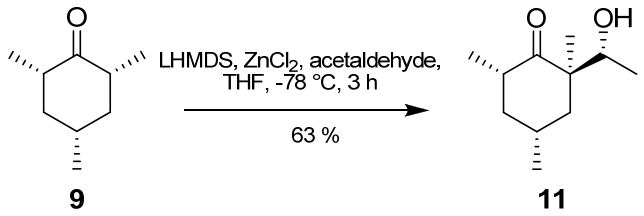
Synthesis of 2,4,6-trimethyl-2-vinylcyclohexanone (7)



10 **7**

Gallium trichloride (8.29 g, 47.0 mmol) was dissolved in dry methylcyclohexane (45 mL) and added dropwise to a stirred solution of (2,4,6-trimethylcyclohex-1-enyloxy)trimethylsilane **(10)** (2.50 g, 11.80 mmol) and trimethylsilylacetylene (2.31 g, 23.80 mmol, 3.32 mL) in dry methylcyclohexane (45 mL). The reaction was stirred at ambient temperature for five minutes during which time a brown precipitate was formed. THF (90 mL) was added to homogenise the reaction mixture after which the reaction was cooled to 0 °C. Sulfuric acid (6M, 50 mL) was added dropwise at 0 °C. The reaction was stirred at 0 °C for a further five minutes and then allowed to warm to ambient temperature. The mixture was extracted with ether (3 × 50 mL) and the combined organics were washed with brine (30 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the resulting mixture was purified by column chromatography eluting with ethyl acetate in petrol (1:9) affording the *title compound* as the predominate diastereoisomer (>9:1) in a clear colourless mobile and highly volatile oil (1.70 g, 87%); ν_{max} (liquid film)/cm^{-1} 2962, 2928, 2872, 1708, 1458, 1378, 1126, 1205, 913; ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.19 (1H, dd, *J* = 18, 11, C$\underline{H}$=CH_2), 5.08 (1H, dd, *J* = 11, 2, CH=C$\underline{H}$H), 4.99 (1H, dd, *J* = 18, 2, CH=H$\underline{H}$), 2.70-2.79 (1H, m, C$\underline{H}$), 2.17-2.23 (1H, m, C$\underline{H}$), 1.97-2.02 (1H, m, C$\underline{H}$H), 1.73-1.78 (1H, m, CH$\underline{H}$), 1.42-1.52 (1H, m, C$\underline{H}$), 1.33 (3H, s, C$\underline{H}_3$), 1.08-1.11 (1H, m, C$\underline{H}$), 0.99 (3H, d, *J* = 6, C$\underline{H}_3$), 0.97 (3H, d, *J* = 6, C$\underline{H}_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 215.7 (C), 143.5 (CH), 112.0 (CH_2), 50.5 (C), 47.5 (CH_2), 44.7 (CH_2), 40.3 (CH), 27.6 (CH), 23.3 (CH_3), 21.7 (CH_3), 15.1 (CH_3); EIMS (negative) *m/z* 165.95 (53%, M^-) 130.83 (38%) 122.93 (100%); HRESIMS (positive) found 189.12511 $[M+Na]^+$ calculated $(C_{11}H_{18}ONa)^+$ requires 189.12499.

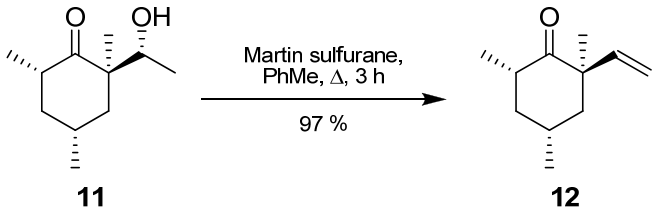
Synthesis of 2-(1-hydroxyethyl)-2,4,6-trimethylcyclohexanone (11)



9 **11**

Freshly prepared LHMDS (2.58 mmol) in THF (5 mL) was added dropwise to a solution of the *meso*-ketone **9** (300 mg, 2.14 mmol) in THF (5 mL) at -78 °C. The reaction was warmed to 0 °C where it was stirred for one hour before being allowed to reach ambient temperature. The reaction mixture was subsequently cooled to -78 °C prior to the addition of zinc chloride (2.57 mL, 1M solution in THF). The reaction mixture was stirred for one hour at 0 °C prior to the addition of acetaldehyde (189 mg, 4.3 mmol, 0.24 mL). It was then stirred at 0 °C for a further one hour. The reaction mixture was allowed to warm to ambient temperature and then quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The solution was extracted with ether (3 × 15 mL) and the combined organics were washed with brine (5 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the product was purified by column chromatography eluting with ethyl acetate in hexane (1:4) affording the *title compound* as a colourless crystalline solid (248 mg, 63%); mp 90.3-91.0 °C; ν_{max} (liquid film)/cm^{-1} 3426, 2955, 2926, 1797, 1450, 1377, 1289, 1204, 1113; ^{1}H NMR (400 MHz; $CDCl_3$) δ 4.38-4.44 (1H, m, C<u>H</u>OH), 2.76-2.86 (1H, m, C<u>H</u>C(O)), 2.09-2.20 (1H, m, $CH_2C\underline{H}CH_2$), 1.99-2.05 (1H, m, C<u>H</u>H), 1.81-1.86 (1H, m, CH<u>H</u>), 1.33-1.35 (1H, m, C<u>H</u>H), 1.18 (3H, d, *J* = 6, C<u>H</u>$_3$), 1.06-1.09 (1H m, CH<u>H</u>), 1.01 (3H, d, *J* = 6, C<u>H</u>$_3$), 0.93 (3H, s, C<u>H</u>$_3$), 0.91 (3H, d, *J* = 6, C<u>H</u>$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 216.4 (C), 70.6 (CH), 53.3 (C), 47.0 (CH_2), 45.0 (CH_2), 40.8 (CH), 27.3 (CH), 21.8 (CH_3), 17.7 (CH_2), 16.2 (CH_3), 15.1 (CH_3); ESIMS (positive) *m/z* 207.14 (100%, $[M+Na]^+$); HRESIMS (positive) found 207.13652 $[M+Na]^+$ calculated $(C_{11}H_{20}O_2Na)^+$ requires 207.13555; HREIMS (negative) found 184.1469 $[M^-]^-$ calculated $(C_{11}H_{20}O_2)^-$ requires 184.1463.

Synthesis of 2,4,6-trimethyl-2-vinylcyclohexanone (12)

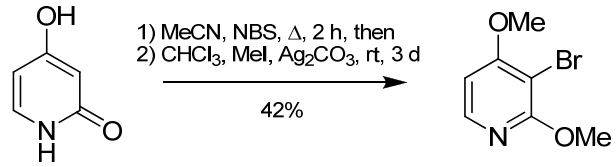


11 **12**

Martin Sulfurane (2.19 g, 3.26 mmol) was added in one portion to a solution of **11** (500 mg, 2.72 mmol) in toluene (30 mL) at ambient temperature. The reaction was heated at reflux for two hours after which the solvent was removed under reduced pressure. The crude reaction mixture was purified by column chromatography eluting with

ethyl acetate in petrol (1:9) affording the *title compound* as a clear colourless mobile and highly volatile liquid (438 mg, 97%); ν_{max} (CH_2Cl_2) 2966, 2928, 2872, 2845, 1771, 1629, 1456, 1375, 1126, 991, 918, 867, 673; ^{1}H NMR (400 MHz; $CDCl_3$) δ 5.96 (1H, dd, *J* = 11, 18, C<u>H</u>=CH_2), 5.11 (1H, dd, *J* = 11, 1, CH=C<u>H</u>H), 4.94 (1H, dd, *J* = 18, 1, CH=CH<u>H</u>), 2.71-2.77 (1H, m, C<u>H</u>C(O)), 2.11-2.24 (1H, m, CH_2C<u>H</u>CH_2), 1.92-2.19 (2H, m, C<u>H_2</u>), 1.26-1.33 (1H, m, C<u>H</u>H), 1.05-1.14 (1H, m, CH<u>H</u>), 1.10 (3H, s, C<u>H_3</u>), 0.97 (3H, d, *J* = 8, C(O)CHC<u>H_3</u>), 0.93 (3H, d, *J* = 8, CH_2CH(C<u>H_3</u>)CH_2); ^{13}C NMR (100 MHz; $CDCl_3$) δ 214.8 (C), 143.4 (CH), 115.2 (CH_2), 52.0 (C), 49.4 (CH_2), 45.2 (CH_2), 41.3 (CH), 28.2 (CH), 24.6 (CH_3), 21.6 (CH_3), 14.9 (CH_3); EIMS (negative) *m/z* 166 (48%, $[M]^-$) 151 (7%, $[M\text{-}Me]^-$); HRESIMS (positive) found 189.12559 $[M+Na]^+$ calculated ($C_{11}H_{18}ONa$) requires 189.12499.

Synthesis of 3-bromo-2,4-dimethoxypyridine (13)

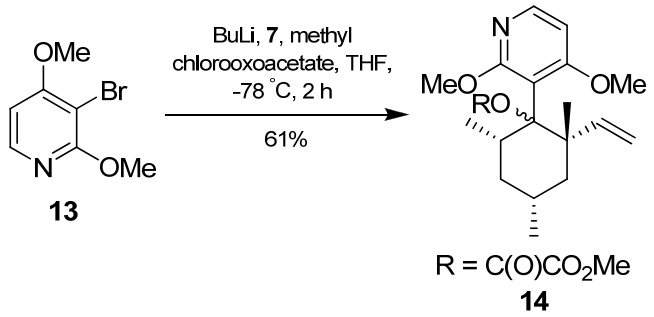


6 **13**

N-Bromosuccinimide (7.62 g, 42.8 mmol) was added to a solution of 2,4-dihydroxypyridine **(6)** (5.00 g,45.0 mmol) in acetonitrile (100 mL). The reaction mixture was stirred at ambient temperature for three hours after which the solvent was removed under reduced pressure. The crude intermediate was suspended in chloroform (90 mL) to which silver carbonate (49.60 g, 180.0 mmol) and iodomethane (11.2 mL, 180.0 mmol) were added. The suspension was stirred at ambient temperature for 72 hours. The reaction mixture was filtered through celite and the solvent was removed from the filtrate under reduced pressure. The product was purified by column chromatography eluting with ethyl acetate in hexane (1:9) to give the *title compound* as a colourless amorphous solid (4.12 g, 42%); 84.6-87.4 °C (Lit.[2] 84-86 °C); ν_{max} (CH_2Cl_2)/cm^{-1} 2948, 2891, 2840, 1588, 1548, 1466, 1392, 1283, 1107, 1033, 795; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.99 (1H, d, *J* = 6, Ar-<u>H</u>), 6.52 (1H, d, *J* = 6, Ar-<u>H</u>), 4.00 (3H, s, OC<u>H_3</u>), 3.94 (3H, s, OC<u>H_3</u>); ^{13}C NMR (100 MHz; $CDCl_3$) δ 163.8 (Ar-C), 161.9 (Ar-C), 146.3 (Ar-CH), 102.5 (Ar-CH), 94.6 (Ar-C), 56.7 (CH_3), 54.8 (CH_3); HRESIMS (positive) found 217.98139 $[M+H]^+$ calculated $(C_7H_9{}^{79}BrNO_2)^+$ requires 217.98112; Elemental analysis calculated for $C_7H_8BrNO_2$: C 38.56, H 3.70, N 6.42. Found: C 38.69, H 3.58, N 6.40%.

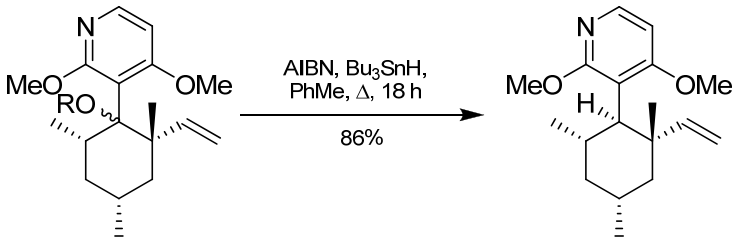
[2] Gibson K. J.; D'Alarcao M.; Leonard N. J. *J. Org. Chem.* **1985**, *50*, 2462.

Synthesis of 1-(2,4-dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate (14)



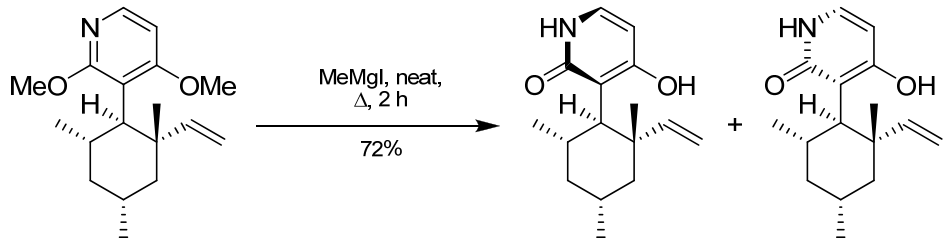
3-Bromo-2,4-dimethoxypyridine **(13)** (1.00 g, 4.59 mmol) was dissolved in THF (10 mL) and cooled to -78 °C. *n*-Butyl lithium (1.49 M, 5.50 mmol, 3.44 mL) was added dropwise after which the solution was stirred for 10 minutes. 2,4,6-Trimethyl-2-vinylcyclohexanone **(7)** (839 mg, 5.04 mmol) was added dropwise over five minutes and the reaction was allowed to stir at -78 °C for 30 minutes. Methyl chlorooxoacetate (856 mg, 6.99 mmol, 644 µL) was added to quench the reaction which was subsequently allowed to warm to ambient temperature. Aqueous ammonium chloride solution (5 mL) was added and the reaction mixture was extracted with ether (3 × 10 mL). The combined organics were washed with brine (5 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the reaction mixture was purified by column chromatography eluting with ethyl acetate in petrol (1:4) which afforded the *title compound* as a clear colourless highly viscous gum (1.10 g, 61%; ratio major:minor atropisomers 3:1); ν_{max} (CH_2Cl_2)/cm^{-1} 2998, 2950, 2928, 1770, 1747, 1584, 1474, 1454, 1383, 1323, 1273, 1206, 1161, 1122, 1096, 1077, 1029, 985, 944, 906, 802, 760; ^{1}H NMR (400 MHz; $CDCl_3$) (major atropisomer) δ 8.00 (1H, d, *J* = 6, Ar-H), 6.57 (1H, d, *J* = 6, Ar-H), 6.20 (1H, dd, *J* = 18, 11, CH=CH_2), 4.71 (1H, dd, *J* = 11, 2, CH=CHH), 4.49 (1H, dd, *J* = 18, 2, CH=CHH), 3.93 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3.36-3.44 (1H, m, CH), 1.82-1.88 (1H, m, CHH), 1.48-1.52 (1H, m, CH), 1.15-1.29 (3H, m), 0.98 (3H, s, CH_3), 0.93 (3H, d, *J* = 7, CH_3), 0.92 (3H, d, *J* = 7, CH_3); (minor atropisomer) 8.01 (1H, d, *J* = 6, Ar-H), 6.43 (1H, d, *J* = 6, Ar-H), 6.16 (1H, dd, *J* = 18, 11, CH=CH_2), 4.70 (1H, dd, *J* = 11, 2, CH=CHH), 4.51 (1H, dd, *J* = 18, 2, CH=CHH), 3.93 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 3.61 (3H, s, OCH_3), 3.46-3.53 (1H, m, CH), 1.82-1.88 (1H, m, CHH), 1.48-1.52 (1H, m, CH), 1.15-1.29 (3H, m), 1.00 (3H, s, CH_3), 0.93 (3H, d, *J* = 7, CH_3), 0.92 (3H, d, *J* = 7, CH_3); ^{13}C NMR (100 MHz; $CDCl_3$) (both atropisomers) δ 166.2 (C), 164.5 (C), 162.6 (C), 161.4 (C), 159.9 (C), 159.8 (C), 155.9 (C), 155.8 (C), 146.1 (CH), 146.0 (CH), 146.0 (CH), 145.9 (CH), 109.3 (CH_2), 109.2 (CH_2), 107.9 (C), 107.6 (C), 103.0 (CH), 102.6 (CH), 95.4 (C), 94.4 (C), 55.8 (CH_3), 55.2 (CH_3), 54.0 (CH_3), 53.4 (CH_3), 53.2 (CH_3), 53.2 (CH_3), 49.3 (C), 49.0 (C), 43.71 (CH_2), 43.67 (CH_2), 39.3 (CH_2), 39.2 (CH_2), 37.60 (CH), 37.56 (CH), 27.7 (CH), 27.6 (2 × CH), 22.4 (CH_3), 20.6 (CH_3), 20.5 (CH_3), 19.2 (CH_3), 19.1 (CH_3); ESIMS (positive) *m*/*z* 392.2 (100%, $[M+H]^+$); HRESIMS (positive) found 392.20725 $[M+H]^+$ calculated ($C_{21}H_{30}NO_6$) requires 392.20676.

Synthesis of 2,4-dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridine (15)



1-(2,4-Dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate **(14)** (150 mg, 0.383 mmol) was dissolved in toluene (7 mL) containing tributyltin hydride (333 mg, 1.15 mmol, 307 µL) and AIBN (cat.). The reaction was heated at reflux for 18 hours. After cooling to ambient temperature the solvent was removed under reduced pressure and the crude reaction material was purified by column chromatography eluting with ethyl acetate in petrol (1:4) affording the *title compound* as a colourless oil of a mixture of atropisomers (95.4 mg, 86%; ratio major:minor atropisomers 2:1); ν_{max} (CH_2Cl_2)/cm^{-1} 2949, 2905, 2867, 1573, 1456, 1397, 1379, 1359, 1319, 1292, 1250, 1191, 1174, 1158, 1136, 1096, 1071, 1047, 1011, 919, 899, 830, 688; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.91 (1H, d, *J* = 6, Ar-H), 6.44 (1H, d, *J* = 6, Ar-H), 5.73 (1H, dd, *J* = 18, 11, CH=CH_2), 4.52-4.62 (2H, m, CH=CH_2), 3.86 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 2.77 (1H, d, *J* = 11, Ar-CH), 2.54-2.69 (1H, m, CHCH_3), 1.74-1.82 (2H, m), 1.10-1.45 (2H, m), 0.98 (3H, s, CH_3), 0.90 (3H, d, *J* = 6, CH_3), 0.66-0.81 (1H, m, CHCH_3), 0.59 (3H, d, *J* = 6, CH_3); (minor atropisomer) 7.90 (1H, d, *J* = 6, Ar-H), 6.45 (1H, d, *J* = 6, Ar-H), 5.80 (1H, dd, *J* = 18, 11, CH=CH_2), 4.52-4.62 (2H, m, CH=CH_2), 3.85 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 2.78 (1H, d, *J* = 12, Ar-CH), 2.54-2.69 (1H, m, CHCH_3), 1.74-1.82 (2H, m), 1.10-1.45 (2H, m), 0.96 (3H, s, CH_3), 0.90 (3H, d, *J* = 6, CH_3), 0.66-0.81 (1H, m, CHCH_3), 0.62 (3H, d, *J* = 6, CH_3); ^{13}C NMR (100 MHz; $CDCl_3$) (both atropisomers) δ 166.2 (C), 165.8 (C), 164.8 (C), 164.0 (C), 150.0 (CH), 149.9 (CH), 145.10 (CH), 145.08 (CH), 111.4 (C), 111.2 (C), 108.7 (2 × CH_2) 102.1 (CH), 101.6 (CH), 55.6 (CH_3), 55.0 (CH_3), 53.6 (CH_3), 52.9 (CH_3), 49.7 (CH), 49.4 (CH_2), 49.3 (CH_2), 47.9 (CH), 45.60 (CH_2), 45.58 (CH_2), 43.6 (C), 43.5 (C), 29.5 (CH), 29.2 (CH), 28.1 (CH), 28.0 (CH), 23.1 (CH_3), 23.0 (CH_3), 21.40 (CH_3), 21.35 (CH_3), 19.0 (CH_3), 18.9 (CH_3); ESIMS (positive) *m*/*z* 290.22 (100%, $[M+H]^+$); HRESIMS (positive) found 290.21084 $[M+H]^+$ calculated ($C_{18}H_{28}NO_2$) requires 290.21146.

Synthesis of 1-dehydroxycordypyridone A and B; 4-hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one (3)



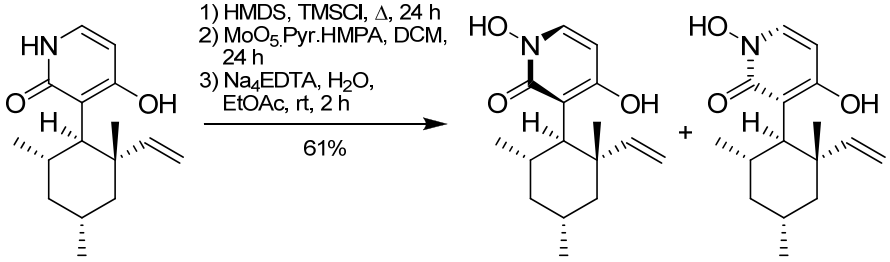
15 **3a** **3b**

Methyl iodide (486 mg, 3.42 mmol, 213 μL) was added dropwise over a period of 15 minutes to ether (7 mL) containing magnesium turnings (77.6 mg, 3.19 mmol) and a small crystal of iodine at 0 °C. The reaction was allowed to warm to ambient temperature over a period of one hour maintaining an internal temperature below that of 30 °C during which time the magnesium was consumed. 2,4-Dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)-pyridine **(15)** (60 mg, 0.297 mmol) was dissolved in a small amount of ether and added to the reaction mixture. The solvent was evaporated and the reaction was heated to 165 °C at which it remained for three hours. The reaction mixture was allowed to cool to ambient temperature. Ether (10 mL) was added and the reaction was quenched with aqueous saturated ammonium chloride solution (10 mL). The mixture was extracted with ethyl acetate (3 × 10 mL). The combined organics were washed with brine (5 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude reaction mixture was purified by column chromatography eluting with methanol in dichloromethane (1:9) affording the *title compounds* as a colourless amorphous solid (39.0 mg, 72%; ratio major:minor atropisomers 12:7); spectral assignments for **3a** and **3b** were made from comparison with literature values of known compound **3a**;[3] ν_{max} (nujol)/cm^{-1} 3260, 2953, 2854, 1611, 1551, 1463, 1377, 1334, 1319, 1302, 1267, 1192, 1166, 1127, 1083, 1033, 905, 801, 721; ^{1}H NMR (400 MHz; $(CD_3)_2CO$) (1-dehydroxycordypyridone A) δ 8.50-10.50 (2H, s br, XH), 7.13 (1H, d, *J* = 7, Ar-H), 5.97 (1H, dd, *J* = 11, 18, CH=CH_2), 5.90 (1H, d, *J* = 7, Ar-H), 4.72 (1H, dd, *J* = 18, 2, CH=CHH), 4.65 (1H, dd, *J* = 11, 2, CH=CHH), 2.89-3.10 (1H, m, $CHCH_3$), 2.58 (1H, d, *J* = 11, Ar-CH), 1.72-1.85 (2H, m, $CHHCH(CH_3)CH_2$), 1.27-1.35 (1H, m, (C)CHH), 1.08-1.21 (1H, m, (C)CHH), 1.11 (3H, s, CH_3), 0.88 (3H, d, *J* = 6, CH_3), 0.59-0.76 (1H, m, CHH), 0.67 (3H, d, *J* = 6, CH_3); ^{13}C NMR (100 MHz; $(CD_3)_2CO$) δ 165.1 (2 × C), 151.7 (CH), 133.3 (CH), 112.4 (C), 109.0 (CH_2), 99.7 (CH), 50.3 (CH_2), 49.6 (CH), 46.3 (CH), 44.7 (C), 28.8 (CH_2), 28.7 (CH), 23.4 (CH_3), 22.0 (CH_3), 20.3 (CH_3); ^{1}H NMR (400 MHz; $(CD_3)_2CO$) (1-dehydroxycordypyridone B) δ 8.50-10.50 (2H, s br, XH), 7.10 (1H, d, *J* = 7, Ar-H), 6.09 (1H, dd, *J* = 11, 18, CH=CH_2), 5.89 (1H, d, *J* = 7, Ar-H), 4.67 (1H, dd, *J* = 18, 2, CH=CHH), 4.58 (1H, dd, *J* = 11, 2, CH=CHH), 2.95 (1H, d, *J* = 11, Ar-CH) 2.58-2.69 (1H, m, $CHCH_3$), 1.72-1.85 (2H, m, $CHHCH(CH_3)CH_2$), 1.27-1.35 (1H, m, (C)CHH), 1.08-1.21 (1H, m, (C)CHH), 1.11 (3H, s, CH_3), 0.88 (3H, d, *J* = 6, CH_3), 0.59-0.76 (1H, m, CHH), 0.70 (3H, d, *J* = 6, CH_3); ^{13}C NMR (100 MHz; $(CD_3)_2CO$) δ 163.94 (C), 163.92 (C), 151.6 (CH), 132.5 (CH), 113.0 (C), 108.6 (CH_2), 99.7 (CH), 50.6 (CH_2), 49.8 (CH), 46.4 (CH), 44.8 (C), 28.8 (CH_2), 28.7 (CH), 23.3 (CH_3), 21.6 (CH_3),

[3] Isaka, M.; Tanticharoen, M.; Kongsaeree, P.; Thebtaranonth, Y. *J. Org. Chem*. **2001**, *66*, 4803.

19.5 (CH_3); ESIMS (positive) *m*/*z* 262.20 (100%, $[M+H]^+$); ESIMS (negative) 260.23 (100%, $[M-H]^-$); HRESIMS (positive) found 262.18005 $[M+H]^+$ calculated ($C_{16}H_{24}NO_2$) requires 262.18016; HRESIMS (positive) found 260.16478 $[M-H]^-$ calculated ($C_{16}H_{22}NO_2$) requires 260.16560.

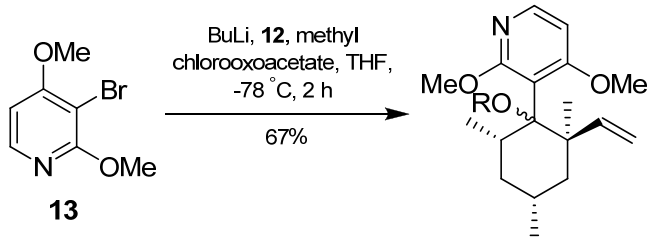
Synthesis of cordypyridone A (1a) and B (1b)



4-Hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one **(3)** (91 mg, 348 μmol) was dissolved in dry HMPA (10 mL) containing one drop of dry chlorotrimethylsilane. The mixture was heated at reflux for 24 hours after which it was cooled to ambient temperature and the solvent was removed under reduced pressure. The crude intermediate was dissolved in dry dichloromethane (10 mL) and freshly prepared Vedej's reagent (183.3 mg, 348 μmol) was added in one portion and the reaction was allowed to stir at ambient temperature for a further 24 hours. The solvent was removed under reduced pressure and the resulting molybdenum complex was partitioned between ethyl acetate (10 mL) and aqueous tetrasodium ethylenediaminetetraacetic acid (10 mL). The biphasic solution was stirred for two hours after which the aqueous phase was neutralised. The organics were separated and the aqueous layer was extracted with ethyl acetate (2 × 5 mL). The volume of ethyl acetate was reduced and the extraction with aqueous tetrasodium ethylenediaminetetraacetic acid was repeated until the molybdenum was completely removed. The organic layer was then washed with brine (5 mL) and dried ($MgSO_4$). The crude reaction mixture was purified by preparative HPLC using a reverse-phase column (Phenomenex Gemini C-18, 250 mm × 21.30 mm × 10 μm; MeCN:H_2O = 45:55 isocratic; 20 mL/min.) forming cordypyridone B **(1b)** (t_R = 18.8 min., 26.7 mg, 28%) and cordypyridone A **(1a)** (t_R = 27.0 min., 31.6 mg, 33%) as colourless amorphous solids in a combined yield of 61%; spectra data corresponded with literature values; cordypyridone A **(1a)** mp 260-262 °C (dec); ν_{max} (nujol)/cm^{-1} 3091, 2951, 1633, 1546, 1435, 1266, 1212, 1126, 1043, 1001, 912, 796, 683, 625; ^{1}H NMR (400 MHz; $(CD_3)_2CO$) δ 8.35-10.75 (2H, s br, 2 × OH), 7.70 (1H, d, *J* =8, Ar-H), 6.01 (1H, d, *J* = 8, Ar-H), 5.93 (1H, dd, *J* = 18, 11, CH=CH_2), 4.69 (1H, dd, *J* = 18, 2, CH=CHH), 4.64 (1H, dd, *J* = 11, 2, CH=CHH), 2.93-3.03 (1H, m, CH), 2.63 (1H, d, *J* = 11, Ar-CH), 1.74-1.84 (2H, m, CH-CHH), 1.31-1.36 (1H, m, CHH), 1.09-1.15 (1H, m, CHH), 1.07 (3H, s, CH_3), 0.89 (3H, d, *J* = 6, CH_3), 0.64-0.71 (1H, m, CHH), 0.63 (3H, d, *J* = 6, CH_3); ^{13}C NMR (100 MHz; $(CD_3)_2CO$) δ 163.0 (C), 159.1 (C), 151.1 (CH), 129.7 (CH), 111.7 (C), 109.4 (CH_2), 97.4 (CH), 50.1 (CH), 50.1 (CH_2), 46.1 (CH_2), 44.8 (C), 28.7 (CH), 28.6 (CH), 23.3 (CH_3), 21.8 (CH_3), 20.0 (CH_3); ESIMS (negative) *m*/*z* 276.16 (100%, $[M-H]^-$); HRESIMS (negative) found 276.16050 $[M-H]^-$ calculated ($C_{16}H_{22}NO_3$) requires 276.16052;

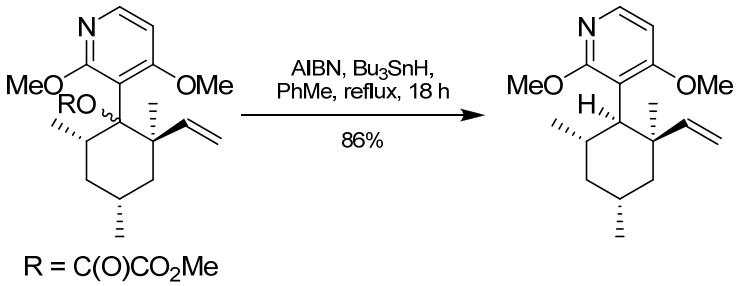
HRESIMS (positive) found 300.15751 $[M+Na]^+$ calculated ($C_{16}H_{23}NO_2Na$) requires 300.15701; cordypyridone B **(1b)** mp 250-253 °C (dec); ν_{max} (nujol)/cm^{-1} 3086, 2950, 2906, 1636, 1538, 1440, 1334, 1266, 1234, 1169, 1055, 906, 802, 548; ^{1}H NMR (400 MHz; $(CD_3)_2CO$) δ 8.40-10.20 (2H, s br, 2 × OH), 7.63 (1H, d, *J* = 8, Ar-H), 6.02 (1H, dd, *J* = 17, 11, CH=CH_2), 6.01 (1H, d, *J* = 8, Ar-H), 4.65 (1H, dd, *J* = 17, 2, CH=CHH), 4.55 (1H, d, *J* = 11, 2, CH=HH), 2.91 (1H, d, *J* = 12, Ar-CH), 2.63-2.71 (1H, m, CH), 1.74-1.81 (1H, m, CHH), 1.74-1.79 (1H, m, CH), 1.29-1.36 (1H, m), 1.10-1.18 (1H, m, CHH), 1.10 (3H, s, CH_3), 0.89 (3H, d, *J* = 6, CH_3), 0.65-0.74 (1H, m, CHH), 0.69 (3H, d, *J* = 6, CH_3); ^{13}C NMR (100 MHz; $(CD_3)_2CO$) δ 162.0 (C), 160.8 (C), 151.3 (CH), 129.1 (CH), 112.2 (C), 109.0 (CH_2), 98.0 (CH), 51.2 (CH), 50.4 (CH_2), 46.2 (CH_2), 44.9 (C), 29.5 (CH), 28.7 (CH), 23.2 (CH_3), 21.6 (CH_3), 19.4 (CH_3); ESIMS (negative) *m*/*z* 276.16 (100%, $[M-H]^-$); HREIMS (negative) found 276.16096 $[M-H]^-$ calculated ($C_{16}H_{22}NO_3$) requires 276.16052.

Synthesis of 1-(2,4-dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate (14B)



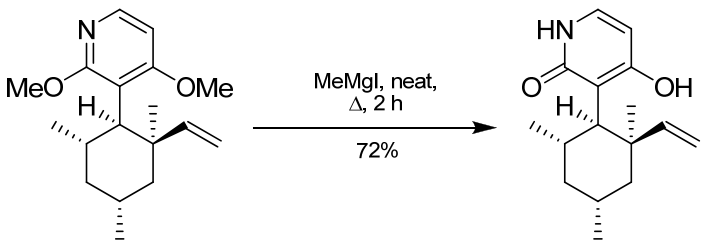
Method used was analogous to the synthesis of **14** in which the *title compound* was formed as a clear colourless highly viscous gum (860 mg, 67%; ratio major:minor atropisomers 7:4); ν_{max} (CH_2Cl_2)/cm^{-1} 3437, 2949, 2928, 1771, 1748, 1636, 1584, 1475, 1456, 1383, 1323, 1272, 1203, 1171, 1121, 1094, 799, 759; ^{1}H NMR (400 MHz; $CDCl_3$) (major atropisomeric) δ 8.00 (1H, d, *J* = 6, Ar-H), 6.54 (1H, d, *J* = 6, Ar-H), 6.07 (1H, dd, *J* = 17, 11, CH=CH_2), 4.87 (1H, dd, *J* = 11, 1, CH=CHH), 4.78 (1H, dd, *J* = 17, 1, CH=CHH), 3.93 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 3.20-3.29 (1H, m, CH), 1.88-1.99 (1H, m, CH), 1.73-1.82 (1H, m, CHH), 1.45-1.52 (2H, m, CHHCHCHH), 1.16-1.27 (1H, m, CHH), 0.97 (3H, s, CH_3), 0.89-0.91 (6H, s br, 2 × CH_3); (minor atropisomer) 8.01 (1H, d, *J* = 6, Ar-H), 6.49 (1H, d, *J* = 6, Ar-H), 6.12 (1H, dd, *J* = 17, 11, CH=CH_2), 4.88 (1H, dd, *J* = 11, 1, CH=CHH), 4.78 (1H, dd, *J* = 17, 1, CH=CHH), 3.92 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 3.32-3.41 (1H, m, CH), 1.88-1.99 (1H, m, CH), 1.73-1.82 (1H, m, CHH), 1.45-1.52 (2H, m, CHHCHCHH), 1.16-1.27 (1H, m, CHH), 0.95 (3H, s, CH_3), 0.89-0.91 (6H, s br, 2 × CH_3); ^{13}C NMR (100 MHz; $CDCl_3$) (both atropisomers) δ 166.1 (C), 164.4 (C), 163.0 (C), 161.8 (C), 160.0 (C), 159.9 (C), 156.0 (C), 155.9 (C), 146.7 (CH), 146.5 (CH), 142.5 (2 × CH), 112.6 (CH_2), 112.5 (CH_2), 107.2 (C), 107.0 (C), 102.9 (CH), 102.6 (CH), 95.0 (C), 94.3 (C), 55.61 (CH_3), 55.58 (CH_3), 53.5 (CH_3), 53.4 (CH_3), 53.2 (2 × CH_3), 49.8 (2 × C), 43.19 (CH_2), 43.17 (CH_2), 39.15 (CH_2), 39.09 (CH_2), 38.4 (CH), 38.3 (CH), 27.49 (CH), 27.47 (CH), 24.5 (CH_3), 24.4 (CH_3), 22.4 (2 × CH_3), 20.4 (CH_3), 20.3 (CH_3); ESIMS (positive) *m*/*z* 414.55 (32%, $[M+Na]^+$), 392.56 (100%, $[M+H]^+$), 310.53 (65%), 288.54 (31%, $[M-OC(O)CO_2Me]^+$); HRESIMS (positive) found 392.20619 $[M+H]^+$ calculated ($C_{21}H_{30}NO_6$) requires 392.20676.

Synthesis of 2,4-dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridine



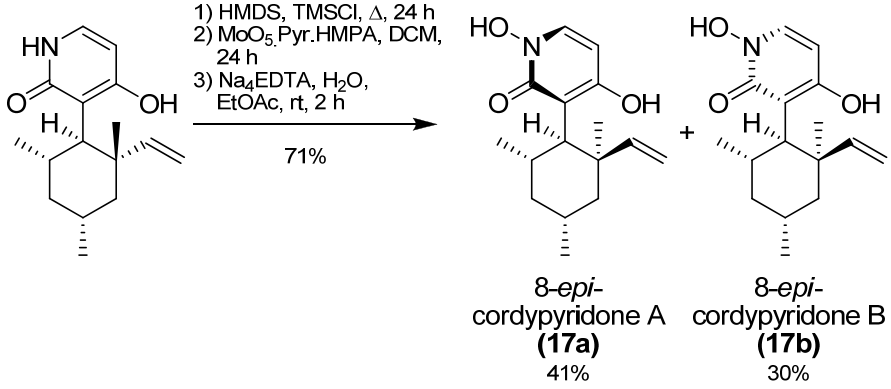
Method used was analogous to the synthesis of **15** in which the *title compound* was formed as a clear colourless viscous oil (517 mg, 82%; ratio major:minor atropisomers 6:5); ν_{max} (CH_2Cl_2)/cm^{-1} 2950, 2907, 2868, 2837, 1584, 1456, 1399, 1358, 1273, 1257, 1179, 1142, 1107, 1032, 906, 804; ^{1}H NMR (400 MHz; $CDCl_3$) (major atropisomer) δ 7.93 (1H, d, *J* = 6, Ar-H), 6.48 (1H, d, *J* = 6, Ar-H), 6.39 (1H, dd, *J* = 18, 11, CH=CH_2), 4.80 (1H, dd, *J* = 11, 2, CH=CHH), 4.59 (1H, dd, *J* = 18, 2, CH=CHH), 3.80 (3H, s, OCH_3), 3.69 (3H, s, OCH_3), 2.79 (1H, d, *J* = 12, Ar-CH), 2.52-2.66 (1H, m, CH), 1.76-1.90 (2H, m), 1.58-1.63 (1H, m), 1.08-1.17 (1H, m, CHH), 0.89 (3H, d, *J* = 6, CH_3), 0.79 (3H, s, CH_3), 0.65-0.76 (1H, m, CH), 0.59 (3H, d, *J* = 6, CH_3); (minor atropisomer) 7.91 (1H, d, *J* = 6, Ar-H), 6.43 (1H, d, *J* = 6, Ar-H), 6.35 (1H, dd, *J* = 18, 11, CH=CH_2), 4.78 (1H, dd, *J* = 11, 2, CH=CHH), 4.60 (1H, dd, *J* = 18, 2, CH=CHH), 3.89 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 2.79 (1H, d, *J* = 12, Ar-CH), 2.52-2.66 (1H, m, CH), 1.76-1.9 (2H, m), 1.58-1.63 (1H, m), 1.08-1.17 (1H, m, CHH), 0.89 (3H, d, *J* = 6, CH_3), 0.82 (3H, s, CH_3), 0.65-0.76 (1H, m, CH), 0.61 (3H, d, *J* = 7, CH_3); ^{13}C NMR (100 MHz; $CDCl_3$) (both atropisomers) δ 166.4 (C), 165.8 (C), 165.0 (C), 164.4 (C), 145.3 (CH), 145.2 (CH), 145.08 (CH), 145.05 (CH), 111.1 (C), 110.9 (C), 109.0 (CH_2), 108.9 (CH_2), 102.6 (CH), 101.3 (CH), 55.7 (CH_3), 54.8 (CH_3), 53.7 (CH_3), 52.6 (CH_3), 51.7 (CH), 50.4 (CH_2), 50.3 (CH_2), 49.7 (CH), 45.71 (CH_2), 45.68 (CH_2), 42.8 (C), 42.5 (C), 29.9 (CH), 29.7 (CH), 28.04 (CH), 28.01 (CH), 26.4 (CH_3), 26.3 (CH_3), 23.04 (CH_3), 23.02 (CH_3), 21.23 (CH_3), 21.19 (CH_3); ESIMS (positive) *m*/*z* 290.55 (100%, $[M+H]^+$); HRESIMS (positive) found 290.21091 $[M+H]^+$ calculated ($C_{18}H_{28}NO_2$) requires 290.21146.

Synthesis of (4-hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one)



Method used was analogous to the synthesis of **3** in which the *title compounds* was formed as a colourless amorphous solid (143 mg, 72%; ratio major:minor atropisomers 7:4); ν_{max} (nujol)/cm^{-1} 3254, 3109, 2947, 1611, 1551, 1462, 1443, 1320, 1266, 1164, 1026, 895, 795, 671, 609, 538, 439; ^{1}H NMR (400 MHz; CD_3OD) δ (major atropisomer) 7.12 (1H, d, *J* = 8, C<u>H</u>), 6.51 (1H, dd, *J* = 18, 11, C<u>H</u>=CH$_2$), 5.98 (1H, d, *J* = 8, C<u>H</u>), 4.81 (1H, dd, *J* = 11, 2, CH=C<u>H</u>H), 4.76 (1H, dd, *J* = 18, 2, CH=CH<u>H</u>), 2.78 (1H, d, *J* = 12, C<u>H</u>), 2.67-2.59 (1H, m, C<u>H</u>), 1.80-1.90 (1H, m, C<u>H</u>), 1.75-1.80 (1H, m, C<u>H</u>H), 1.60-1.65 (1H, m, CH<u>H</u>), 1.08-1.14 (1H, m, C<u>H</u>H), 0.92 (3H, s, C<u>H</u>$_3$), 0.87 (3H, d, *J* = 6, C<u>H</u>$_3$), 0.69-0.77 (1H, m, CH<u>H</u>), 0.68 (3H, d, *J* = 6, C<u>H</u>$_3$); ^{13}C NMR (100 MHz; CD_3OD) δ 168.5 (C), 167.0 (C), 147.1 (CH), 133.0 (CH), 113.1 (C), 110.2 (CH_2), 102.9 (CH), 52.5 (CH), 51.1 (CH_2), 46.9 (CH_2), 44.3 (C), 30.7 (CH), 29.2 (CH), 27.8 (CH_3), 23.3 (CH_3), 21.4 (CH_3); ^{1}H NMR (400 MHz; CD_3OD) δ (minor atropisomer) 7.11 (1H, d, *J* = 8, C<u>H</u>), 6.63 (1H, dd, *J* = 18, 12, C<u>H</u>=CH$_2$), 6.01 (1H, d, *J* = 8, C<u>H</u>), 4.80 (1H, dd, *J* = 12, 2, CH=C<u>H</u>H), 4.75 (1H, dd, *J* = 18, 2, CH=CH<u>H</u>), 2.84-2.92 (1H, m, C<u>H</u>), 2.58 (1H, d, *J* = 12, C<u>H</u>), 1.77-1.86 (1H, m, C<u>H</u>), 1.75-1.78 (1H, m, C<u>H</u>H), 1.62-1.66 (1H, m, CH<u>H</u>), 1.02-1.08 (1H, m, C<u>H</u>H), 0.92 (3H, s, C<u>H</u>$_3$), 0.86 (3H, d, *J* = 6, C<u>H</u>$_3$), 0.62-0.68 (1H, m, CH<u>H</u>), 0.66 (3H, d, *J* = 6, C<u>H</u>$_3$); ^{13}C NMR (100 MHz; CD_3OD) δ 168.5 (C), 167.0 (C), 147.1 (CH), 133.0 (CH), 113.2 (C), 110.2 (CH_2), 102.9 (CH), 52.5 (CH), 51.2 (CH_2), 46.9 (CH_2), 44.4 (C), 30.7 (CH), 29.2 (CH), 27.8 (CH_3), 23.3 (CH_3), 21.4 (CH_3); ESIMS (positive) *m/z* 284.38 (100%, $[M+Na]^+$), 262.38 (66%, $[M+H]^+$); HRESIMS (positive) found 262.17951 $[M+H]^+$ calculated ($C_{16}H_{24}NO_2$) requires 262.18016; HRESIMS (negative) found 260.16504 $[M-H]^-$ calculated ($C_{16}H_{22}NO_2$) requires 260.16560.

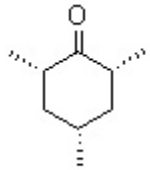
Synthesis of 8-*epi*-cordypyridone A (17a) and B (17b)



Method used was analogous to the synthesis of **1**. The *title compounds* were isolated by preparative HPLC using a reverse-phase column (Phenomenex Gemini C-18, 250 mm × 21.30 mm × 10 µm; MeCN:H_2O = 45:55 isocratic; 20 mL/min.) giving 8-*epi*-cordypyridone B **(17b)** (t_R = 18.9 min., 30.2 mg, 30%) and 8-*epi*-cordypyridone A **(17a)** (t_R = 27.3 min., 41.3 mg, 41%) as colourless amorphous solids in a combined yield of 71%; 8-*epi*-cordypyridone A **(17a)** mp 230-231.2 °C (dec); ν_{max} (nujol)/cm^{-1} 3085, 2955, 2905, 1628, 1541, 1443, 1358, 1304, 1258, 1135, 1034, 903, 798, 679, 631; ^{1}H NMR (400 MHz; $(CD_3)_2CO$) δ 9.82-10.30 (2H, s br, 2 × O<u>H</u>), 7.73 (1H, d, *J* = 8, Ar-<u>H</u>), 6.71 (1H, dd, *J* = 18, 11, C<u>H</u>=CH$_2$), 6.07 (1H, d, *J* = 8, Ar-<u>H</u>), 4.74-4.82 (2H, m, CH=C<u>H</u>$_2$), 2.94-3.02 (1H, m, C<u>H</u>), 2.62 (1H,

d, *J* = 11, Ar-C<u>H</u>), 1.57-1.81 (3H, m), 1.04-1.10 (1H, m, C<u>H</u>H), 0.96 (3H, s, C<u>H</u>$_3$), 0.86 (3H, d, *J* = 6, C<u>H</u>$_3$), 0.66-0.73 (1H, m, CH<u>H</u>), 0.64 (3H, d, *J* = 6, C<u>H</u>$_3$); ^{13}C NMR (100 MHz; $(CD_3)_2CO$) δ 162.2 (C), 161.8 (C), 146.7 (CH), 130.6 (CH) 111.8 (C), 110.4 (CH_2), 98.6 (CH), 52.9 (CH_2), 50.4 (CH), 46.4 (CH_2), 44.1 (C), 28.7 (CH_3), 28.0 (CH), 23.2 (CH_3), 21.5 (CH_3); ESIMS (negative) *m*/*z* 276.22 (100%, $[M-H]^-$); HRESIMS (negative) found 276.16024 $[M-H]^-$ calculated ($C_{16}H_{22}NO_3$) requires 276.16052; HRESIMS (positive) found 300.15750 $[M+Na]^+$ calculated ($C_{16}H_{23}NO_3Na$) requires 300.15701; 8-*epi*-cordypyridone B **(17b)** mp 226.1-227.6 °C (dec); ν_{max} (nujol)/cm^{-1} 3087, 2952, 2907, 1636, 1537, 1440, 1269, 1060, 802, 667; ^{1}H NMR (400 MHz; $(CD_3)_2CO$) δ 8.20-10.40 (2H, s br, 2 × O<u>H</u>), 7.67 (2H, d, *J* = 8, Ar-<u>H</u>), 6.51 (1H, dd, *J* = 18, 11, C<u>H</u>=CH_2), 5.98 (1H, d, *J* = 8, Ar-<u>H</u>), 4.82 (1H, dd, *J* = 16, 2, CH=C<u>H</u>H), 4.77 (1H, dd, *J* = 11, 2, CH=CH<u>H</u>), 2.87 (1H, d, *J* = 11, Ar-C<u>H</u>), 2.57-2.68 (1H, m, C<u>H</u>), 1.74-1.90 (2H, m), 1.62-1.66 (1H, m), 1.07-1.13 (1H, m, C<u>H</u>H), 0.89 (3H, s, C<u>H</u>$_3$), 0.87 (3H, d, *J* = 6, C<u>H</u>$_3$), 0.68-0.76 (1H, m, CH<u>H</u>), 0.68 (3H, d, *J* = 6, C<u>H</u>$_3$); ^{13}C NMR (100 MHz; $(CD_3)_2CO$) δ 163.58 (C), 163.56 (C), 147.2 (CH), 129.9 (CH), 110.4 (C), 110.2 (CH_2), 97.3 (CH), 51.9 (CH_2), 50.9 (CH), 46.3 (CH_2), 44.1 (C), 28.6 (CH), 28.4 (CH), 23.2 (CH_3), 21.7 (CH_3), 21.5 (CH_3); ESIMS (negative) *m*/*z* 276.22 (100%, $[M-H]^-$); HRESIMS (negative) found 276.15940 $[M-H]^-$ calculated ($C_{16}H_{22}NO_3$) requires 276.16052; HRESIMS (positive) found 300.15661 $[M+Na]^+$ calculated ($C_{16}H_{23}NO_3Na$) requires 300.15701.

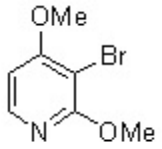
400 MHz, solvent $CDCl_3$



2,4,6-Trimethylcyclohexanone

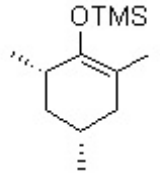
9

100 MHz, solvent $CDCl_3$



3-Bromo-2,4-dimethoxypyridine
13

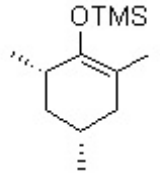
400 MHz, solvent $CDCl_3$



Trimethyl(2,4,6-trimethylcyclohex-1-enyloxy)silane

10

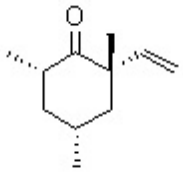
100 MHz, solvent $CDCl_3$



Trimethyl(2,4,6-trimethylcyclohex-1-enyloxy)silane

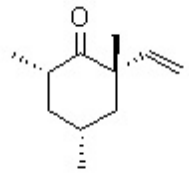
10

400 MHz, solvent $CDCl_3$



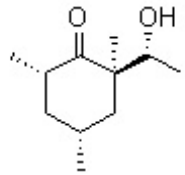
2,4,6-Trimethyl-2-vinylcyclohexanone
7

100 MHz, solvent $CDCl_3$



2,4,6-Trimethyl-2-vinylcyclohexanone
7

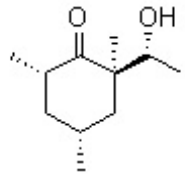
400 MHz, solvent $CDCl_3$



2-(1-Hydroxyethyl)-2,4,6-trimethylcyclohexanone

11

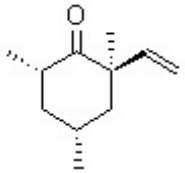
100 MHz, solvent $CDCl_3$



2-(1-Hydroxyethyl)-2,4,6-trimethylcyclohexanone

11

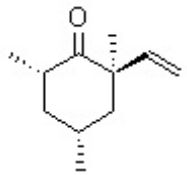
400 MHz, solvent $CDCl_3$



2,4,6-Trimethyl-2-vinylcyclohexanone

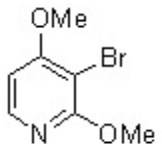
12

100 MHz, solvent $CDCl_3$



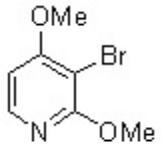
2,4,6-Trimethyl-2-vinylcyclohexanone
12

400 MHz, solvent $CDCl_3$



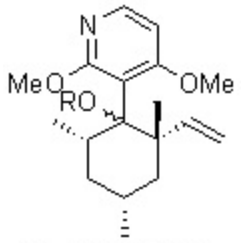
3-Bromo-2,4-dimethoxypyridine
13

100 MHz, solvent $CDCl_3$



3-Bromo-2,4-dimethoxypyridine
13

400 MHz, solvent $CDCl_3$

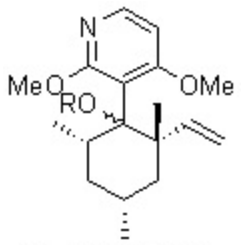


R = $C(O)CO_2Me$

1-(2,4-dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate

14

100 MHz, solvent $CDCl_3$



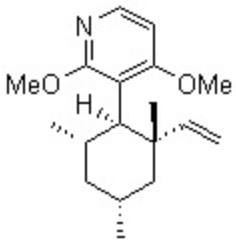
R = $C(O)CO_2Me$

1-(2,4-dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate

14

166.2 164.5 162.6 161.4 159.9 159.8 155.9 155.8 146.0 145.9 109.3 109.2 107.8 107.6 103.0 102.6 95.4 94.4 55.8 55.2 54.0 53.4 53.2 49.0 43.7 43.7 39.3 37.6 37.6 27.7 27.6 22.4 20.6 20.5 19.2 19.1

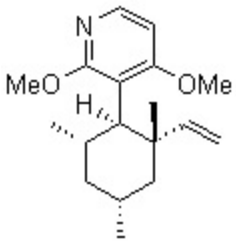
400 MHz, solvent $CDCl_3$



2,4-dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridine

15

100 MHz, solvent $CDCl_3$



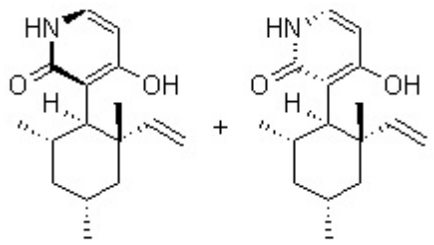
2,4-dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridine
15

166.2 165.8 164.8 164.0 150.0 149.9 145.1 145.1 111.4 111.2 108.7 102.1 101.6 55.6 55.0 53.6 52.9 49.4 47.9 45.6 43.5 29.4 29.2 28.1 28.0 23.1 23.0 21.4 21.4 19.0 18.9

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

400 MHz, solvent $(CD_3)_2CO$

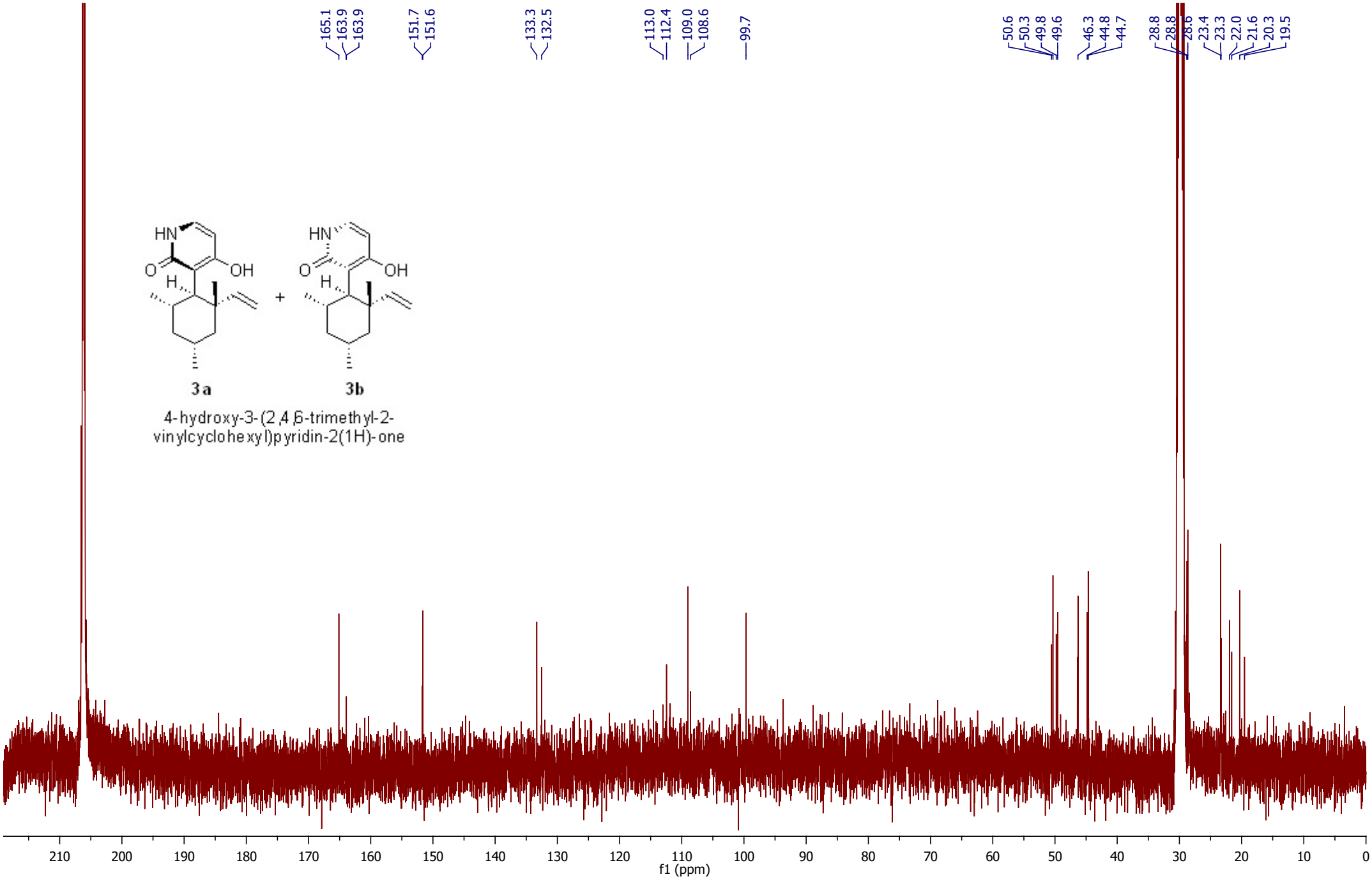


3a **3b**

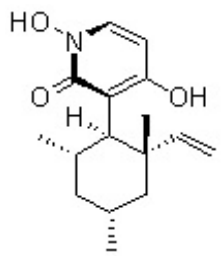
4-hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one

f1 (ppm)

100 MHz, solvent $(CD_3)_2CO$

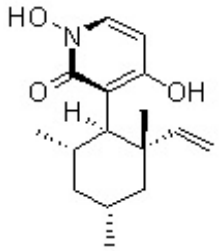


400 MHz, solvent $(CD_3)_2CO$



Cordypyridone A
(1a)

100 MHz, solvent $(CD_3)_2CO$



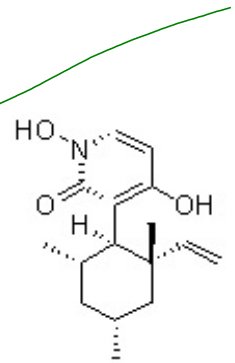
Cordypyridone A
(1a)

163.0
159.1
151.1
129.7
111.7
109.4
97.4
50.1
50.1
46.1
44.8
28.7
28.6
23.3
21.8
20.0

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

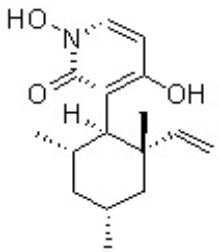
f1 (ppm)

400 MHz, solvent $(CD_3)_2CO$



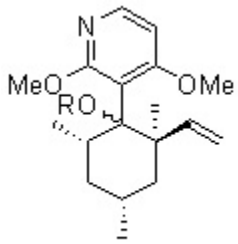
Cordypyridone B
(1 b)

100 MHz, solvent $(CD_3)_2CO$



Cordypyridone B
(1 b)

400 MHz, solvent $CDCl_3$

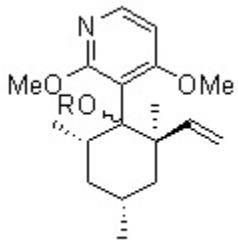


R = $C(O)CO_2Me$

1-(2,4-dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate

16

100 MHz, solvent $CDCl_3$



R = $C(O)CO_2Me$

1-(2,4-dimethoxypyridin-3-yl)-2,4,6-trimethyl-2-vinylcyclohexyl methyl oxalate

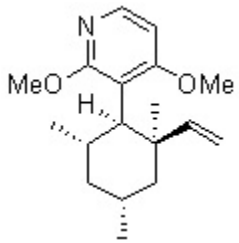
16

166.1 164.4 163.0 161.8 160.0 159.9 156.0 155.9 146.7 146.5 142.5 112.6 112.5 107.2 107.0 102.9 102.6 95.0 94.3 55.6 55.6 53.5 53.4 53.2 49.8 43.2 43.2 39.1 38.3 27.5 27.5 24.5 24.4 22.4 20.4 20.3

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

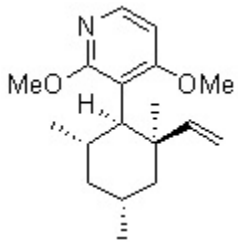
f1 (ppm)

400 MHz, solvent $CDCl_3$



2,4-Dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridine

100 MHz, solvent $CDCl_3$



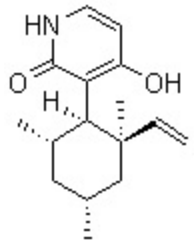
2,4-Dimethoxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridine

166.3 165.8 165.0 164.0 145.3 145.2 145.1 145.1 111.1 110.9 109.0 108.9 102.6 101.3 55.7 54.8 53.7 52.6 51.7 50.4 50.3 49.7 45.7 45.7 42.5 28.0 26.4 26.3 23.0 23.0 21.2 21.2

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

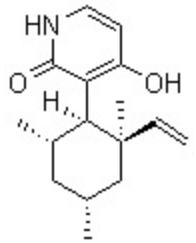
f1 (ppm)

400 MHz, solvent CD_3OD



(4-hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one)
major

100 MHz, solvent CD_3OD

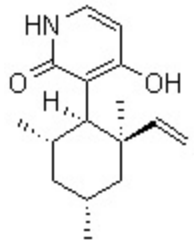


(4-hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one)
major

168.5
167.0
147.1
133.0
113.2
110.2
102.9
52.5
51.1
46.9
44.4
30.7
29.2
27.8
23.3
21.4

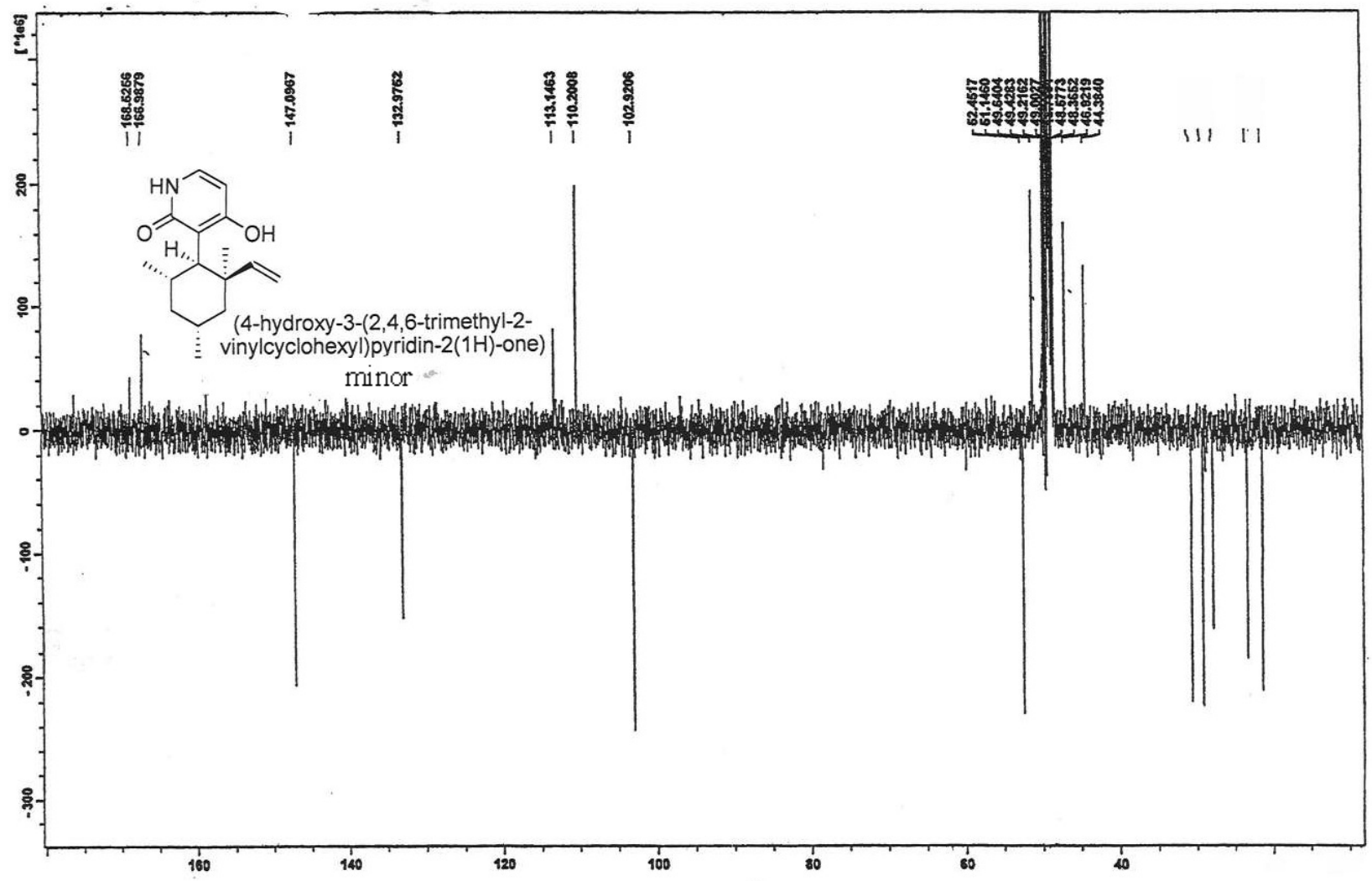
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

400 MHz, solvent CD_3OD

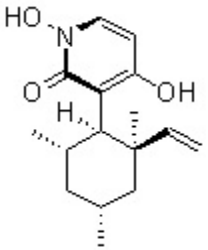


(4-hydroxy-3-(2,4,6-trimethyl-2-vinylcyclohexyl)pyridin-2(1H)-one)
minor

100 MHz, solvent CD_3OD

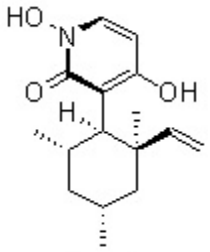


400 MHz, solvent $(CD_3)_2CO$



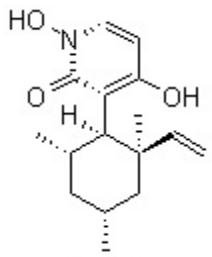
8-*epi*-
cordypyridone A
(17 a)

100 MHz, solvent $(CD_3)_2CO$



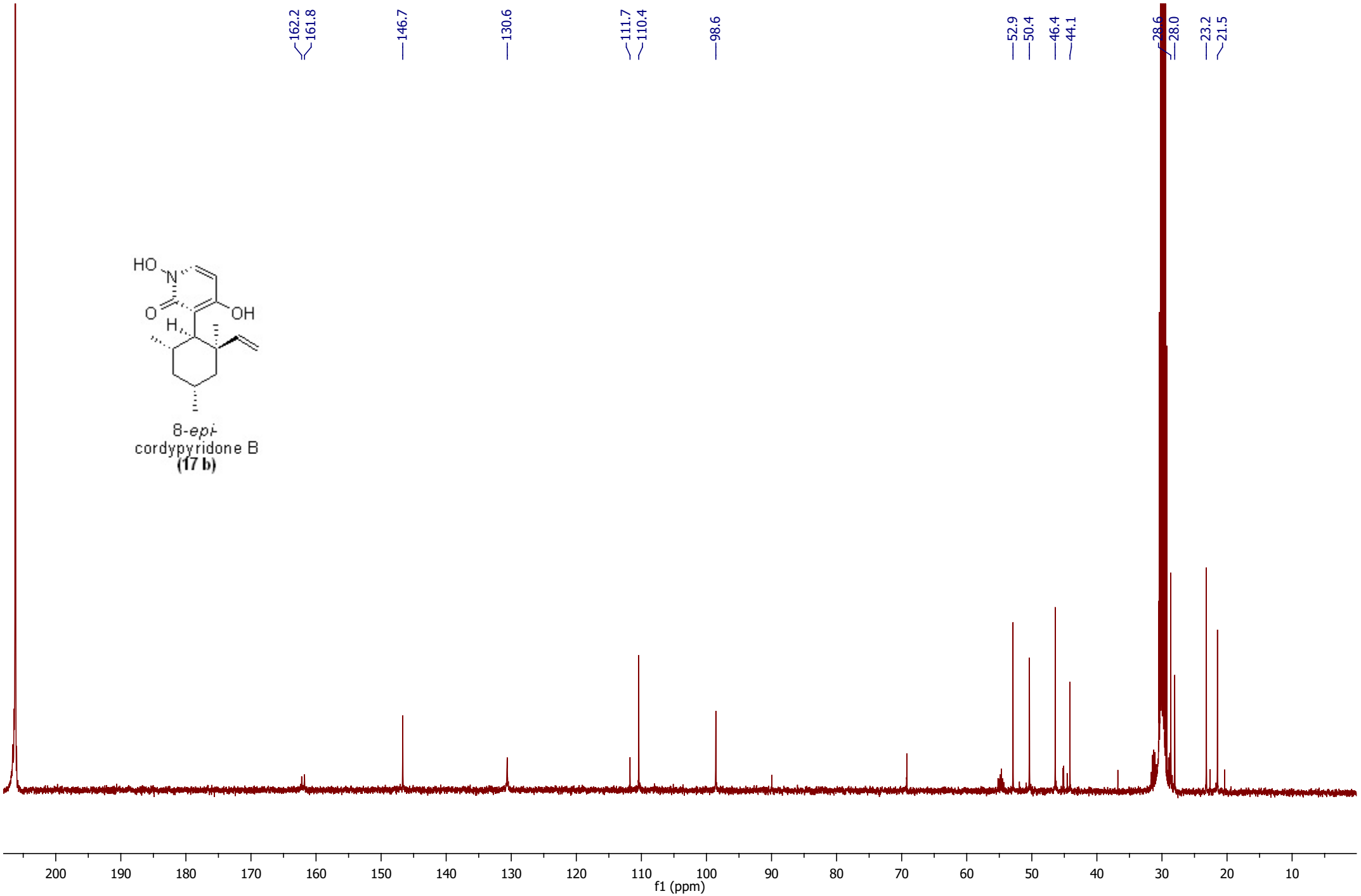
8-*epi*-
cordypyridone A
(17 a)

400 MHz, solvent $(CD_3)_2CO$



8-*epi*-
cordypyridone B
(17 b)

100 MHz, solvent $(CD_3)_2CO$



8-*epi*-
cordypyridone B
(17 b)