Total Synthesis of Amaminol A: Establishment of the Absolute Stereochemistry

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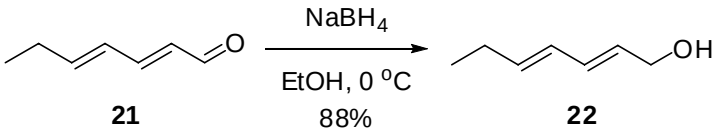
Supporting Information

General Methods. All reactions were carried out under an argon atmosphere in flame-dried glassware, unless otherwise noted. Nonaqueous reagents were transferred under argon *via* syringe or cannula and dried prior to use. THF and ether were distilled from Na/benzophenone, toluene from Na, MeOH from $Mg(OMe)_2$ and CH_2Cl_2 from CaH_2. The concentration of butyl lithium was determined by double titration method using 1,3-diphenyl acetone-*p*-tosyl hydrazone (200 mg) in dry THF (4 ml). Other solvents and reagents were used as obtained from supplier, unless otherwise noted. Analytical TLC was performed using Merck silica gel F_{254} (10-12 μm) plates and analyzed by UV light or by staining upon heating either with ninhydrin solution (1 g ninhydrin, 100 mL ethanol, 5 drops glacial acetic acid), PMA solution (2.5 g phosphomolybdic acid, 100 mL EtOH, 5 mL conc. H_2SO_4, 1.5 mL

[#] X-ray crystallography.

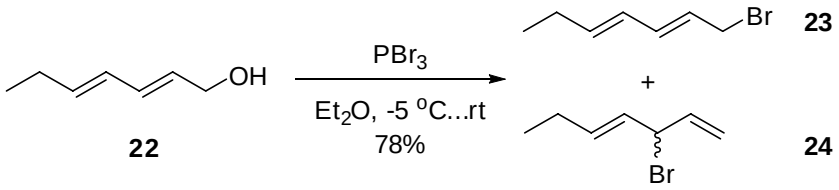
85% H_3PO_4) or $KMnO_4$ solution (1 g $KMnO_4$, 2 g Na_2CO_3, 100 mL H_2O). For silica gel chromatography, the flash chromatography technique was used, with Merck silica gel 60 (40-63 μm) and p.a. grade solvents unless otherwise noted.

IR spectra were recorded on a Perkin-Elmer Spectrum One spectrometer. Optical rotations were obtained with a Perkin-Elmer 343 polarimeter. The ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or in *d4*-MeOD on a Bruker Avance 400 (^{1}H 399.98 MHz; ^{13}C 100.59 MHz) spectrometer. The chemical shifts are reported in ppm relative to residual $CHCl_3$ (δ 7.26) or residual MeOH (δ 3.31) for ^{1}H NMR. For the ^{13}C NMR spectra, the solvent peaks $CDCl_3$ (δ 77.0) and *d4*-MeOD (δ 49.0) were used as the internal standard. HRMS-spectra were recorded on Waters LCT Premier –spectrometer. The enantiomeric excess (ee) of the IMDA products were determined by GC in comparison to the corresponding racemic samples using a Hewlett Packard HP 5890 instrument, Supelco β-Dex™ 120 column (30 m x 0.25 mm, 0.25 μm film) in isotherm (130 °C), helium as carrier gas (34 cm/s), with Hewlett Packard 5971 MS detector (270 °C) for ee analysis and isotherm (145 °C), helium as carrier gas (33 cm/s) for de analysis.



(*2E,4E*)-heptadien-1-ol (22).[1] Heptadienal **21** (14.2 mL, 100 mmol, 100 mol %, Kosher grade >88%) was dissolved in EtOH (200 mL) and cooled to 0 °C. Sodium borohydride (3.9 g, 100 mmol, 100 mol %) was added and the mixture was stirred for 15 min. The solution was concentrated and the residue partitioned between ether (200 mL) and aqueous 1 M NaOH (200 mL). The aqueous phase was back-extracted with ether (100 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous sodium sulfate and evaporated to give a yellow oil. The product was purified by distillation under reduced pressure (18 mmHg) to give alcohol **13** (9.90 g, 88%) as a clear liquid. B.p.

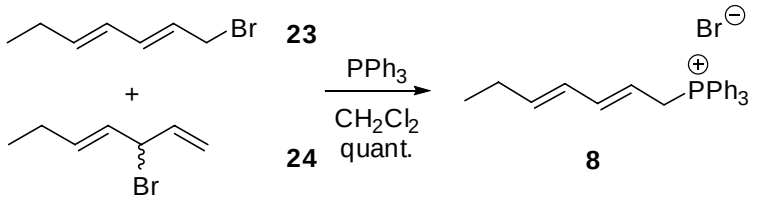
96-98 °C (18 mmHg). R_f = 0.19 (20% EtOAc / hexanes); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.22 (dd, *J* = 10.1, 15.1 Hz, 1H), 6.04 (dd, *J* = 10.2, 15.0 Hz, 1H), 5.68-5.80 (m, 2H), 4.16 (t, *J* = 5.6 Hz, 2H), 2.10 (dq, *J* = 6.4, 7.1 Hz, 2H), 1.34 (t, *J* = 5.8 Hz, 1H), 1.01 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 137.2, 132.1, 129.3, 128.3, 63.5, 25.6, 13.4.



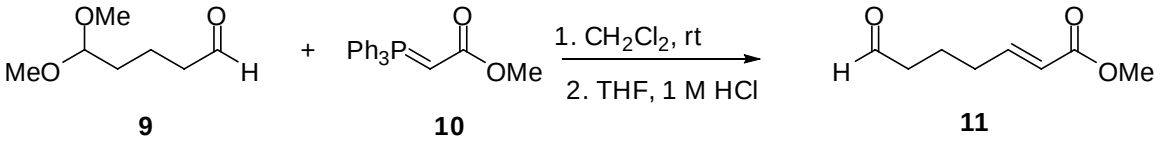
(*2E,4E*)-1-Bromohepta-2,4-diene (23) and (*E*)-3-bromohepta-1,4-diene (24). A slurry of (*2E,4E*)-hepta-2,4-dienol **22** (3.20 mL, 25 mmol, 100 mol %) and calcium hydride (1.57 g, 37.5 mmol, 150 mol %) in dry ether (20 mL) was stirred for 60 minutes. The reaction mixture was cooled to 0ºC and phosphorous tribromide (0.87 mL, 9.3 mmol, 37.3 mol %) in dry ether (5 mL) was added. After 40 minutes the reaction was quenched by addition of methanol (0.15 mL, 3.7 mmol, 15 mol %) after which the mixture was allowed to warm to room temperature. The mixture was filtered through celite followed by ether washings. The solvent was evaporated and the crude product purified by Kugelrohr distillation (15 mmHg, air bath 80 ºC) to afford a 2:1 mixture of bromides **23** and **24** (3.44 g, 78%) as a slightly yellow oil. The product decomposes at room temperature but it was found to be only slightly decomposed when kept four months in a freezer (-18 ºC). R_f = 0.67 (20% EtOAc / hexanes).

For **23:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.16-6.37 (m, 1H), 6.03 (dd, *J* = 10.4, 15.2 Hz, 1H), 5.71-5.89 (m, 2H), 4.03 (d, *J* = 7.8 Hz, 2H), 2.12 (dq, *J* = 6.3, 7.0 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.1, 135.3, 127.8, 126.1, 33.8, 25.6, 13.2.

For **24:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.26 (dd, *J* = 1.2 Hz, 16.5 Hz, 1H), 5.15 (dd, *J* = 1.2, 9.7 Hz, 1H), 4.51 (dt, *J* = 6.8, 9.4 Hz, 1H), 1.86-2.05 (m, 2H), 1.00 (t, *J* = 7.3 Hz). Other proton signals were obscured; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 135.6, 134.3, 132.4, 119.0, 57.5, 32.3, 12.3.

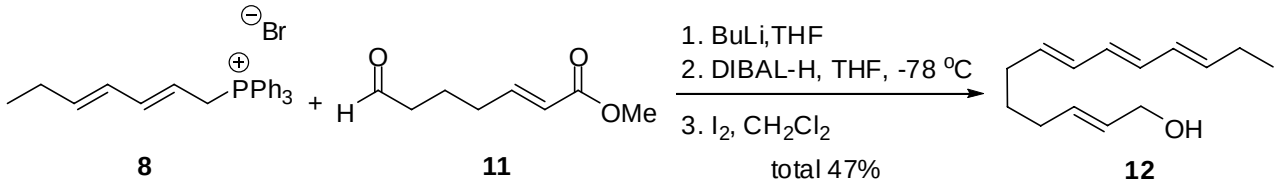


(*2E,4E*)-Hepta-2,4-dienyltriphenylphosphonium bromide (8).[2] Triphenyl phosphine (8.66 g, 33.0 mmol, 100 mol %) was dissolved in dry dichloromethane (85 mL) and a mixture of bromides **23** and **24** (6.07 g, 34.7 mmol, 105 mol %) was added at room temperature. The mixture was stirred for 20 hours and the solvent was evaporated and the residue dried in vacuo for 14 hours to give 14.78 g (quant.) of phosphonium salt **6** as white foam. The product is highly hygroscopic, light sensitive and decomposes at room temperature and therefore it was used as such. It was found to be stable in a freezer (-18 °C). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.64-7.89 (m, 15H), 6.37 (ddd, *J* = 5.1, 10.2, 15.1 Hz, 1H), 5.89 (dd, *J* = 10.8, 14.7 Hz, 1H), 5.69 (ddt, *J* = 2.4, 4.8, 11.9 Hz, 1H), 5.27-5.38 (m, 1H), 4.75 (dd, *J* = 7.4, 15.2 Hz, 2H), 2.03 (dq, *J* = 7.5, 7.7 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ [140.9, 140.7], [139.5, 139.4], [134.9, 134.9], [133.9, 133.8], [130.2, 130.1], [127.5, 127.4], [118.4, 117.6], [113.3, 113.1], [28.4, 28.9], [25.8, 25.4], [13.0, 13.0].



(*E*)-Methyl-7-oxo-hept-2-enoate (11). Aldehyde **9**[3] (20.5 g, 122.0 mmol, 100 mol %, purity ~87%) was dissolved in dry dichloromethane (280 mL) at room temperature and methyl (triphenylphosphoranylidene)acetate **10** was added. The mixture was stirred overnight and the solvent was removed by evaporation. The residual white solid containing oil was treated with hexane (100 mL). The solids were filtered off and washed with hexane (2 x 50 mL). The combined solvents were evaporated to give 29.76 g of crude acetal as a clear oil.

This crude acetal was dissolved in THF (10 mL) and aqueous 1 M HCl (150 mL). The mixture was strirred for 30 min and ether (150 mL) was added. The aqueous phase was extracted with ether (3 x 100 mL). The combined organic extracts were washed with brine (200 mL), dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was purified by distillation under reduced pressure (0.2 mbar, 70-71 °C) to afford aldehyde **11** as a clear liquid (16.9 g, 88% over two steps). Geometrical isomer-ratio was found to be 20:1 (*E:Z*). R_f = 0.42 (50% EtOAc / hexanes); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.4 Hz, 1H), 6.92 (dt, *J* = 6.9, 15.6 Hz, 1H), 5.85 (dt, *J* = 1.5, 15.6 Hz, 1H), 3.73 (s, 3H), 2.49 (dt, *J* = 1.3, 7.2 Hz, 2H), 2.25 (ddt, *J* = 1.3, 7.2 Hz, 7.3 Hz, 2H), 1.81 (ddt, *J* = 7.3, 7.3, 7.3 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.5, 166.8, 147.8, 121.8, 51.4, 42.9, 31.2, 20.3. These data match those reported in the literature.[4]

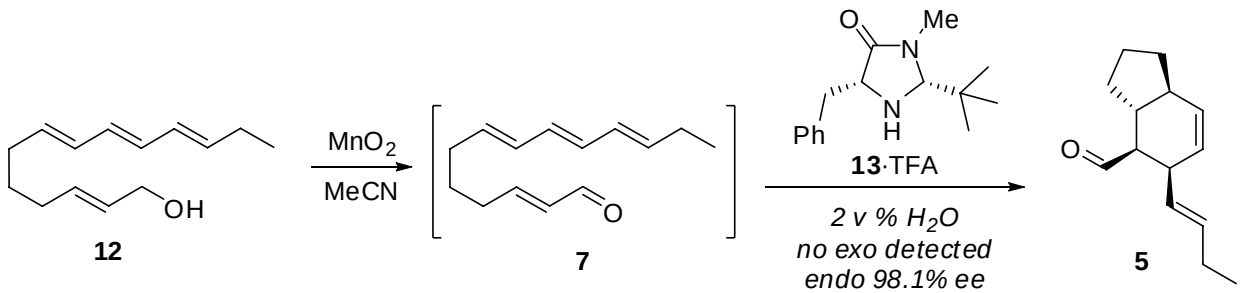


(*2E,7E,9E,11E*)-Tetradeca-2,7,9,11-tetraen-1-ol (12). Phosphonium salt **8** (14.4 g, 30.0 mmol, 120 mol %, purity estimated to be ~90%) in dry CH_2Cl_2 (20 mL) and THF (80 mL) was cooled to -30 °C. To this slurry was added 2.3 M butyl lithium in hexanes during 15 minutes (13.0 mL, 30.0 mmol, 120 mol %) resulting in a red slurry. The mixture was stirred for 1 h and aldehyde **11** (3.9 g, 25.0 mmol, 100 mol %) in dry THF (25 mL) was cannulated into reaction mixture. The mixture was allowed to warm to room temperature and stirring was continued for 1 h. The reaction was quenched by addition of saturated ammonium chloride solution (80 mL). Also CH_2Cl_2 (80 mL) was added and phases were separated. The aqueous phase was extracted with CH_2Cl_2 (50 mL). The combined organic extracts were washed with brine (150 mL), dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was dissolved in a small amount of CH_2Cl_2 and filtered through a 3 cm pad of silica using 20% ethyl acetate in hexanes. The solvents were evaporated and residual solids containing oil was treated

with hexanes (100 mL). The solids were filtered off and rinsed with hexanes (2 x 50 mL). Evaporation of solvents gave 5.1 g of crude ester as a yellow oil. Geometrical isomer-ratio was found to be 2:1 (*E:Z*).

The crude ester was dissolved in dry THF (100 mL) and cooled to -78ºC. To this solution was added 1.0 M diisobutyl aluminium hydride in toluene (75.0 mL, 75.0 mmol, 300 mol %) and the mixture was stirred for 1 h. The reaction was quenched by addition of aqueous saturated solution of Rochelle's salt (100 mL) and the mixture was allowed to warm to room temperature. After 18 h the phases were separated and the aqueous phase was extracted with ether (100 mL). The combined organic extracts were dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was purified by flash chromatography using 20% ethyl acetate in hexanes to give 2.51 g of alcohol **12** as a clear oil.

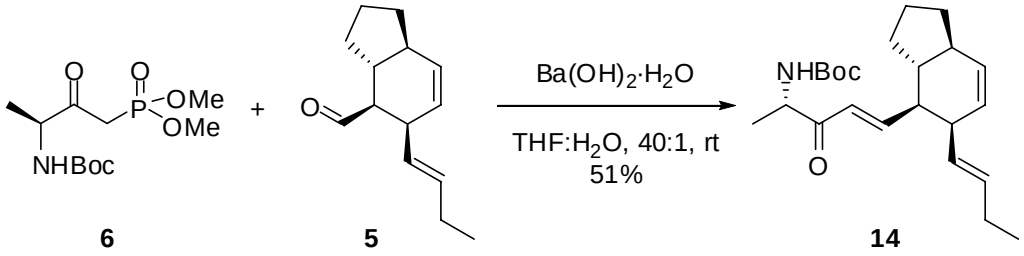
Alcohol **12** was dissolved in dichloromethane (50 mL) and treated with iodine (0.15 g, 0.60 mmol, 5 mol %). The mixture was stirred for 30 minutes and saturated solution of sodium thiosulphate (50 mL) was added. The biphasic mixture was stirred vigorously for 30 minutes. The phases were separated and the aqueous phase was extracted with dichloromethane (25 mL). The combined organic extracts were dried over anhydrous sodium sulfate and evaporated to dryness to give alcohol **12** (2.46 g, 47% over two steps) in 4:1 (*E:Z*) ratio as a yellow oil. R_f = 0.20 (20% EtOAc / hexanes); IR (thin film, cm^{-1}) 3338, 3012, 2962, 2929, 2855, 1455, 1437, 1088, 993, 968. For major isomer **12**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.92-6.22 (m, 4H), 5.57-5.79 (m, 4H), 4.08 (br s, 2H), 2.01-2.26 (m, 6H), 1.48 [dq, *J* = 7.5 Hz, (d), 2H], 1.28 (br s, 1H), 1.00 (t, *J* = 7.54 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 136.0, 133.6, 132.8, 131.0, 130.8, 130.6, 129.4, 129.2, 32.1, 31.5, 28.6, 25.7, 13.5; HRMS (ESI) calc. for [M+Na] $C_{14}H_{22}ONa$ 229.1568, found 229.1517, Δ = 1.3 ppm.



(*3aR,4S,5R,7aS*)-5-[(*E*)-But-1-enyl]-2,3,3a,4,5,7a-hexahydro-*1H*-indene-4-carbaldehyde (5).

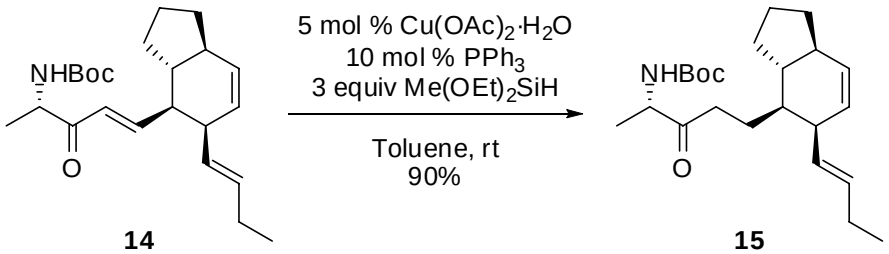
Alcohol **12** (1.03 g, 5.0 mmol, 100 mol %) was dissolved in acetonitrile (40 mL) and manganese oxide (4.35 g, 50.0 mmol, 1000 mol %) was added. The mixture was stirred for 1 hour at room temperature. A second portion of manganese oxide (3.44 g, 39.5 mmol, 790 mol %) was added. After 5 hours, the mixture was filtered through celite followed by MeCN rinsing (2 x 10 mL). The resulting yellow solution containing aldehyde **7** was cooled to -20 ºC and distilled water (1 mL) was added. Catalyst **13** (0.25 g, 1.0 mmol, 20 mol %) and trifluoroacetic acid (77 μL, 1.0 mmol, 20 mol %) were added and the mixture was stirred at -18 ºC for 18 hours. The reaction was quenched by addition of 1% aq. $NaHCO_3$ (100 mL). Pentane (60 mL) was added and the mixture was allowed to warm to room temperature. The aqueous phase was extracted with pentane (2 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous sodium sulfate and evaporated carefully (> 300 mmHg, water bath 25 ºC) to dryness to give 0.90 g of a yellow oil. The crude product was purified by flash chromatography using 5% ether in pentane to afford aldehyde **5** (0.36 g, 35% over two steps) as a clear oil. GC-MS analysis showed >308:1 endo:exo (no exo detected) and 98.1% ee selectivities. The product is highly volatile. R_f = 0.54 (20% EtOAc / hexanes); IR (thin film, cm^{-1}) 3018, 2959, 2871, 1723, 1455, 1066, 968; $[\alpha]^{20}$ = -223.8 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.64 (d, *J* = 2.9 Hz, 1H), 5.90 (d, *J* = 9.8 Hz, 1H), 5.55 (dt, *J* = 6.3, 15.1 Hz, 1H), 5.43 (ddd, *J* = 2.6, 4.1, 9.7 Hz, 1H), 5.33 (ddt, *J* = 1.4, 8.7, 15.2 Hz, 1H), 3.28-3.38 (m, 1H), 2.53 (ddd, *J* = 2.9, 6.3, 11.4 Hz, 1H), 1.95-2.04 (m, 3H), 1.61-1.92 (m, 5H), 1.06-1.24 (m, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 204.8, 135.3,

129.7, 129.3, 127.6, 56.1, 44.9, 41.1, 39.5, 28.4, 27.5, 25.4, 22.3, 13.6; HRMS (ESI) calc. for [M+Na] $C_{14}H_{20}ONa$ 227.1412, found 227.1410, Δ = 0.9 ppm.



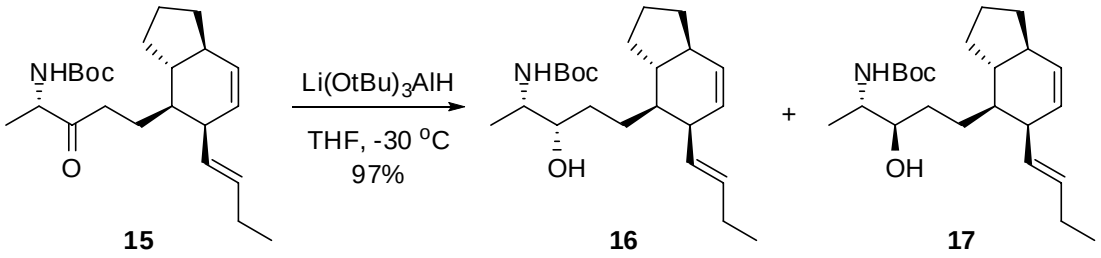
6 **5** **14**

***tert*-Butyl (*S,E*)-5-{(*3aR,4S,5R,7aS*)-5-[(*E*)-but-1-enyl]-2,3,3a,4,5,7a-hexahydro-*1H*-inden-4-yl}-3-oxopent-4-en-2-ylcarbamate (14)**. Activated (kept 1 hour under high vacuo at 130-140 ºC) barium hydroxide monohydrate (0.156 g, 0.91 mmol, 55 mol %) was mixed with phosphonate **6**[5] (0.537 g, 1.82 mmol, 110 mol %) in THF (10 mL) for 10 minutes. To this mixture was added aldehyde **5** (0.338, 1.65 mmol, 100 mol %) in 40:1 THF:H_2O (10 mL) and the mixture was stirred at room temperature for 24 hours. The reaction mixture was diluted with ether (20 mL) and 0.5 M phosphoric acid (20 mL) was added. The mixture was stirred vigorously until clear. Phases were separated and the aqueous phase was extracted with ether (20 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was purified by flash chromatography using 20% ether in hexanes to give enone **14** (0.317 g, 51%) as a clear oil. R_f = 0.47 (20% EtOAc / hexanes); IR (thin film, cm^{-1}) 3426, 2962, 2871, 1716, 1695, 1627, 1492, 1446, 1366, 1167, 1044, 1019; $[\alpha]^{20}$ = -151.6 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.87 (dd, *J* = 9.9, 15.8 Hz, 1H), 6.09 (d, *J* = 15.9 Hz, 1H), 5.88 (d, *J* = 9.7 Hz, 1H), 5.21-5.53 (m, 4H), 4.65 (dq, *J* = 9.9, 15.8 Hz, 1H), 2.49 [ddd, *J* = 6.5, 10.5 Hz (d), 1H], 1.96-2.06 (m, 2H), 1.79-1.92 (m, 2H), 1.47-1.77 (m, 3H), 1.44 (s, 9H), 1.32 (d, *J* = 7.1 Hz, 3H), 1.12-1.30 (m, 1H), 0.99-1.10 (m, 1H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.5, 155.0, 152.4, 134.9, 129.9, 129.5, 128.1, 126.4, 79.4, 52.5, 48.1, 45.2, 45.1, 42.8, 28.9, 28.3, 27.9, 25.5, 22.0, 19.5, 13.7; HRMS (ESI) calc. for [M+Na] $C_{23}H_{35}NO_3Na$ 396.2515, found 396.2516, Δ = 0.3 ppm.



14 **15**

***tert*-Butyl (*S*)-5-{(*3aR,4S,5R,7aS*)-5-[(*E*)-but-1-enyl]-2,3,3a,4,5,7a-hexahydro-*1H*-inden-4-yl}-3-oxopentan-2-ylcarbamate (15)**. A flask was charged with $Cu(OAc)_2 \cdot H_2O$ (1.3 mg, 6.7 μmol, 5 mol %, kept 1 h under high vacuum at 90 ºC), dry toluene (1 mL) and $Me(OEt)_2SiH$ (0.056 g, 0.40 mmol, 300 mol %) under argon. The mixture was stirred for 2 h while the color of the reaction mixture turned from blue to green and gradually orange. Enone **14** (0.050 g, 0.13 mmol, 100 mol %) dissolved in dry toluene (1 mL) was added and mixture was stirred for 16 h. The reaction was quenched with addition of acetic acid (38 μL, 0.67 mmol, 500 mol %) and 1 M TBAF solution in THF (0.20 mL, 0.20 mmol, 150 mol %). After 20 minutes the solvents were evaporated. The crude product was purified by flash chromatography using 10-15% ether in hexanes to afford ketone **15** (0.045 g, 90%) as a clear oil. R_f = 0.42 (20% EtOAc / hexanes); IR (thin film, cm^{-1}) 3359, 2958, 2928, 2869, 1711, 1494, 1454, 1366, 1247, 1170; $[\alpha]^{20}$ = -137.6 (*c* 0.9, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.80 (d, *J* = 9.6 Hz, 1H), 5.47 (dt, *J* = 6.3, 15.1 Hz, 1H), 5.38 (ddd, *J* = 2.6, 4.3, 9.7 Hz, 1H), 5.20-5.32 (m, 2H), 4.23-4.36 (m, 1H), 2.78-2.87 (m, 1H), 2.57 (ddd, *J* = 5.1, 10.7, 16.3 Hz, 1H), 2.39 (ddd, *J* = 6.0, 9.7, 15.9 Hz, 1H), 2.00 (ddq, *J* = 1.4, 7.5, 13.7 Hz, 2H), 1.61-1.86 (m, 5H), 1.45-1.60 (m, 2H), 1.42 (s, 9H), 1.20-1.33 (obs m, 2H), 1.30 (obs d, *J* = 7.1 Hz, 3H), 1.07-1.20 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 209.8, 155.1, 133.8, 130.7, 129.4, 128.3, 79.5, 54.7, 46.1, 44.6, 43.2, 42.0, 36.5, 29.2, 28.3, 27.8, 25.6, 25.0, 22.1, 18.1, 13.9; HRMS (ESI) calc. for [M+Na] $C_{23}H_{37}NO_3Na$ 398.2671, found 398.2672, Δ = 0.3 ppm.

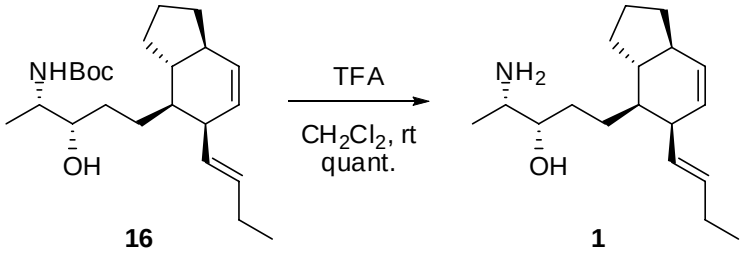


15 **16** **17**

***N*-Boc (*2S,3R*)-epi-amaminol A (30) and *N*-Boc amaminol A (29)**. Ketone **15** (0.045 g, 0.12 mmol, 100 mol %) was dissolved in dry THF (2 mL). The solution was cooled to -30 °C and lithium tri-*tert*-butoxy aluminium hydride was added. The mixture was stirred for 1 h, then diluted with ether (5 mL) and 0.5 M H_3PO_4 –solution (5 mL) was added. The mixture was allowed to warm to room temperature. Phases were separated and the aqueous phase was extracted with ether. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was purified by flash chromatography using 10-20% ethyl acetate in hexanes to give in elution order fraction A of alcohol **16** (0.028 g, 62%) as light yellow crystals and fraction B 0.016 g (35%) of a mixture of **16** and **17** as white solids. Total yield was 0.044 g (97%). Selectivity was found to be *syn:anti* 3:1 based on crude NMR data. Alcohol **17** can be purified by another flash chromatography followed by recrystallization from ethyl acetate hexanes. Alternatively by chancing the reductant to L-Selectride, alcohol **17** can be obtained in 1:2 *syn:anti*-ratio.

For **16:** R_f = 0.25 (20% EtOAc / hexanes); IR (thin film, cm^{-1}) 3436, 2959, 2869, 1687, 1504, 1454, 1366, 1247, 1170; $[\alpha]^{20}$ = -203.8 (*c* 1.0, $CHCl_3$ ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.80 (d, *J* = 9.6 Hz, 1H), 5.46 (dt, *J* = 6.3, 15.1 Hz, 1H), 5.39 (ddd, *J* = 2.5, 4.2, 9.5 Hz, 1H), 5.28 (dd, *J* = 9.0, 15.2 Hz, 1H), 4.65 (br s, 1H), 3.61 (br s, 1H), 3.38-3.49 (m, 1H), 2.79-2.91 (m, 1H), 2.01 [dq, *J* = 7.4 Hz (d), 2H], 1.62-1.92 (m, 6H), 1.50-1.62 (m, 2H), 1.20-1.49 (obs m, 4H), 1.44 (obs s, 9H), 1.07-1.20 (obs m, 2H), 1.15 (obs d, *J* = 6.7 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.1, 133.5, 131.0, 129.4, 128.6, 79.3, 75.1, 50.4, 46.2, 44.7, 43.1, 42.4, 31.1, 29.3, 28.3, 27.9, 26.3, 25.6, 22.1, 18.3, 13.9; HRMS (ESI) calc. for [M+Na] $C_{23}H_{39}NO_3Na$ 400.2828, found 400.2833, Δ = 1.2 ppm. These data match those obtained from the orginal spectra.

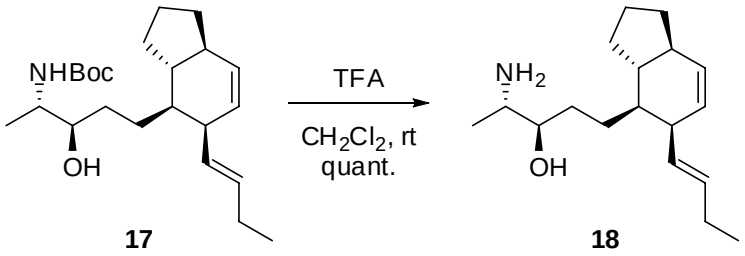
For **17:** R_f = 0.20 (20% EtOAc / hexanes); IR (thin film, cm^{-1}) 3365, 2955, 2868, 1683, 1527, 1453, 1367, 1176, 1042; $[\alpha]^{20}$ = -217.9 (*c* 0.7, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.81 (d, *J* = 9.7 Hz, 1H), 5.46 (dt, *J* = 6.3, 15.1 Hz, 1H), 5.39 (ddd, *J* = 2.6, 4.4, 9.6 Hz, 1H), 5.26 (dd, *J* = 9.1, 15.1 Hz, 1H), 4.77 (br s, 1H), 3.67 (br s, 1H), 3.52-3.61 (m, 1H), 2.82-2.92 (m, 1H), 2.05-2.28 (m, 1H), 1.95-2.05 (m, 2H), 1.63-1.88 (m, 5H), 1.50-1.63 (m, 3H), 1.44 (s, 9H), 1.09-1.35 (m, 5H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.8, 133.4, 131.1, 129.3, 128.6, 79.4, 75.0, 50.3, 46.2, 44.7, 43.3, 43.1, 30.8, 29.3, 28.4, 27.9, 27.3, 25.6, 22.1, 14.3, 13.9; HRMS (ESI) calc. for [M+Na] $C_{23}H_{39}NO_3Na$ 400.28,28 found 400.2824, Δ = 1.0 ppm.



16 **1**

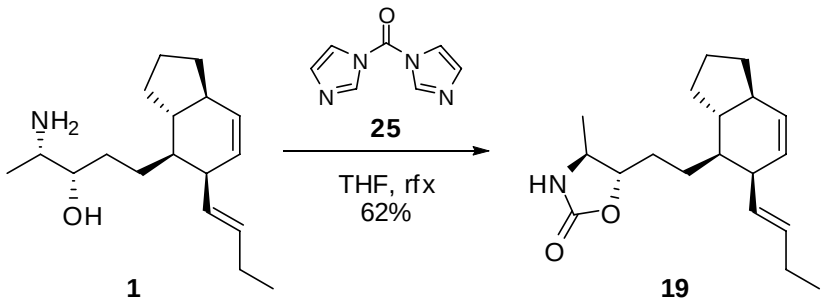
Amaminol A (1). Alcohol **16** (0.017 g, 0.045 mmol, 100 mol %) was dissolved in dichloromethane (1 mL) and trifluoroacetic acid (0.1 mL) was added. After 3 h the mixture was diluted with dichloromethane (2 mL) and 1 M NaOH (2 mL) was added. The organic phase was washed with 1 M NaOH (2 mL). The combined aqueous phases were extracted with dichloromethane (2 mL). The combined organic extracts were dried over anhydrous sodium sulfate and evaporated to give amaminol A **1** (0.013 g, quant.) as an oil. IR (thin film, cm^{-1}) 3262, 2958, 2870, 1739, 1601, 1454, 1077, 974; $[\alpha]^{20}$ = -214.8 (*c* 0.7, $CHCl_3$); ^{1}H-NMR (400 MHz, *d4*-MeOD) δ 5.79 (d, *J* = 9.87 Hz, 1H), 5.48 (dt, *J* = 5.9, 15.7 Hz, 1H), 5.29-5.43 (m, 2H), 3.16-3.27 (m, 1H), 2.84-2.93 (m, 1H), 2.69 (dq, *J* = 6.5 Hz (d), 1H), 2.03 [ddq, *J* = 1.1, 7.4 Hz (d), 2H], 1.66-1.88 (m, 5H), 1.56-1.66 (m, 1H), 1.34-1.55 (m, 4H), 1.10-1.25 (m, 2H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, *d4*-MeOD) δ 134.7, 132.2, 130.1, 130.0, 77.2, 52.1, 47.7, 46.0, 44.2, 44.0, 31.7, 30.4, 28.9, 27.3, 26.7, 23.1, 19.3, 14.3; HRMS (ESI) calc. for [M+H] $C_{18}H_{32}NO$ 278.2484, found 278.2479, Δ = 1.8 ppm.

Amaminol A **1** was converted to its corresponding TFA salt for comparison with the original spectral data. For **1·TFA**: $[\alpha]^{20}$ = -88.3 (*c* 1.0, MeOH); ^{1}H-NMR (400 MHz, *d4*-MeOD) δ 5.80 (d, *J* = 9.7 Hz, 1H), 5.50 (dt, *J* = 6.2, 14.9 Hz, 1H), 5.29-5.43 (m, 2H), 3.46 (dt, *J* = 2.9, 7.6 Hz, 1H), 3.09 (dq, *J* = 6.6, 6.8 Hz, 1H), 2.85-2.94 (m, 1H), 1.98-2.08 (m, 2H), 1.67-1.89 (m, 5H), 1.36-1.66 (m, 5H), 1.25 (d, *J* = 6.7 Hz, 3H), 1.10-1.23 (m, 2H), 0.98 (t, *J* = 7.2 Hz); ^{13}C-NMR (100 MHz, *d4*-MeOD) δ 134.8, 132.0, 130.2, 129.9, 73.1, 53.1, 47.6, 45.9, 44.2, 44.0, 31.8, 30.4, 28.9, 26.8, 26.7, 23.1, 15.9, 14.3. These data match those reported in the literature.[6]

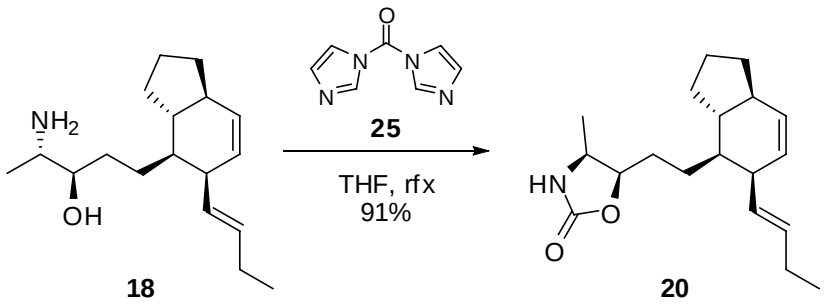


17 **18**

(*2S,3R*)-epi-Amaminol A (18). The compound was prepared as described for **1** starting from **17** (7 mg, 18 μmol, 100 mol %) giving **18** (5 mg, quant.) as an oil. IR (thin film, cm^{-1}) 3330, 2956, 2869, 1729, 1695, 1454, 1375, 1297,1181, 998, 969; $[\alpha]^{20}$ = -213.4 (*c* 0.5, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.79 (d, *J* = 9.6 Hz, 1H), 5.50 (dt, *J* = 6.3, 15.2 Hz, 1H), 5.38 (ddd, *J* = 2.5, 4.4, 9.7 Hz, 1H), 5.30 (ddt, *J* = 1.3, 9.0, 15.1 Hz, 1H), 3.33-3.94 (m, 1H), 2.86-2.96 (m, 1H), 2.73-2.83 (m, 1H), 2.02 [ddq, *J* = 1.2, 7.4 Hz (d), 2H], 1.50-1.89 (m, 8H), 1.09-1.39 (m, 5H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 134.5, 132.2, 130.1 (d), 77.0, 51.8, 47.6, 46.1, 44.6, 31.2, 30.4, 29.0, 28.8, 26.7, 23.1, 16.8, 14.4; HRMS (ESI) calc. for [M+H] $C_{18}H_{32}NO$ 278.2484, found 278.2495, Δ = 4.0 ppm.



(4S,5S)-5-(2-((3aR,4S,5R,7aS)-5-((E)-but-1-enyl)-2,3,3a,4,5,7a-hexahydro-1H-inden-4-yl)ethyl)-4-methyloxazolidin-2-one (19). To a solution of aminoalcohol **1** (7 mg, 26 μmol, 100 mol %) in dry THF (2 mL) under argon was added carbonyl di-imidazole (6.4 mg, 40 μmol, 150 mol %). The mixture was refluxed for 19 h. The solvent was evaporated and the crude product was purified by flash chromatography using 50% ethyl acetate in hexanes as eluent to give of carbamate **19** (5 mg, 62%) as white crystals. Needle shape crystals for x-ray crystallography were obtained by recrystallization from EtOAc (30 μL) / hexanes (0.3 mL). R_f = 0.50 (EtOAc); IR (thin film, cm^{-1}) 3256, 2956, 2927, 2868, 1752, 1454, 1393, 1239; $[\alpha]^{20}$ = -190.2 (*c* 0.5, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.82 (d, *J* = 9.6 Hz, 1H), 5.46 (dt, *J* = 6.3, 15.2 Hz, 1H), 5.40 (ddd, *J* = 2.6, 4.2, 9.6 Hz, 1H), 5.18-5.30 (m, 2H), 4.08 [ddd, *J* = 4.8, 6.8 Hz (d), 1H], 3.57 [dq, *J* = 6.3 Hz (d), 1H], 2.80-2.90 (m, 1H), 2.01 [ddq, *J* = 1.1, 7.3 Hz (d), 2H], 1.76-1.88 (m, 3H), 1.64-1.76 (m, 3H), 1.52-1.63 (m, 2H), 1.31-1.52 (m, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.06-1.21 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.8, 133.8, 130.8, 129.4, 128.2, 84.3, 53.2, 46.2, 44.6, 43.2, 42.2, 30.9, 29.9, 27.9, 25.7, 25.6, 22.1, 20.6, 14.0; HRMS (ESI) calc. for [M+Na] $C_{19}H_{29}NO_2Na$ 326.2096, found 326.2089, Δ = 2.1 ppm. These data match those obtained from the original spectra.



(4S,5R)-5-(2-((3aR,4S,5R,7aS)-5-((E)-but-1-enyl)-2,3,3a,4,5,7a-hexahydro-1H-inden-4-yl)ethyl)-4-methyloxazolidin-2-one (20). The compound was prepared as described for **19** starting from **18** (9 mg, 32 μmol) giving **20** (9 mg, 91%) as a clear oil. R_f = 0.42 (EtOAc); IR (thin film, cm^{-1}) 3270, 2955, 2926, 2869, 1751, 1455, 1389, 1232, 1107, 970; $[\alpha]^{20}$ = -111.8 (*c* 0.8, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.81 (d, *J* = 9.7 Hz, 1H), 5.46 (dt, *J* = 6.2, 15.2 Hz, 1H), 5.39 (ddd, *J* = 2.5, 4.4, 9.7 Hz, 1H), 5.22-5.32 (m, 2H), 4.41-4.51 (m, 1H), 3.85 (dq, *J* = 6.5, 6.7 Hz, 1H), 2.83-2.91 (m, 1H), 1.96-2.05 (m, 2H), 1.46-1.88 (m, 10H), 1.17-1.36 (m, 2H), 1.05-1.19 (obs m, 1H), 1.15 (obs d, *J* = 6.6 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.3, 133.6, 130.8, 129.4, 128.5, 80.9, 51.1, 46.2, 44.6, 43.3, 42.7, 29.2, 27.9, 27.3, 26.5, 25.6, 22.1, 16.0, 13.9; HRMS (ESI) calc. for [M+Na] $C_{19}H_{29}NO_2Na$ 326.2096, found 326.2112, Δ = 4.9 ppm.

Relative stereochemistry analysis. To verify the relative stereochemistries, the aminoalcohols **1** and **18** were converted to the cyclic carbamate analogues **19** and **20**. Coupling constants between H2-H3 were and 6.3 Hz (for **19**) and 6.7 Hz (for **20**) and therefore we could not rely on this data for accurate determination of the relative stereochemistry. However, NOE experiments combined with molecular modeling obtained with Hyperchem software v. 7.51 with MM+ theory suggested the stereochemical assignments to be *2S,3S* for **19** and *2S,3R* for **20** (Figure 1).

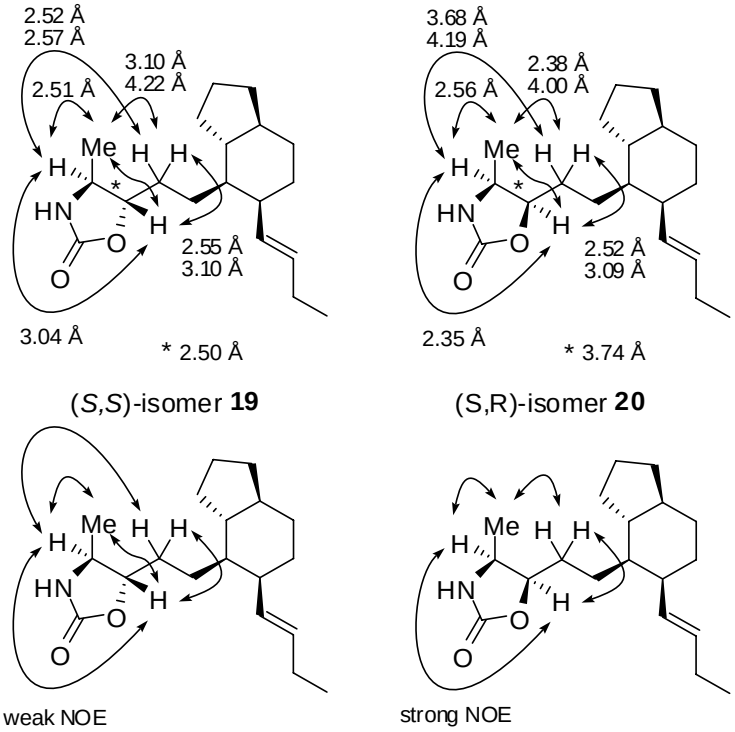


Figure 1. NOE-study of absolute stereochemistries of **19** and **20**. Measured distances from molecular modeling are shown on top and found NOE's are presented at the bottom.

X-ray crystallography. The absolute stereochemistry was assigned based on the synthesis procedure and confirmed qualitatively by the weak anomalous dispersion effects during the refinements. Crystal data for **19** (Figure 2): formula $C_{19}H_{29}NO_2$, crystal size 0.2 × 0.3 × 0.3 mm, monoclinic, space group $P2_1$ (no. 4), a = 11.886(1) Å, b = 5.3996(4) Å, c = 14.772(1) Å, β = 104.433(4)°, V = 918.1(1) Å^3 , Z = 2, ρ_{calcd} = 1.098 cm^{-3}, MoK$_\alpha$ radiation, λ = 0.71069 Å, μ = 0.070 mm^{-1}, T = 173.0(1) K, Bruker-Nonius Kappa CCD diffractometer, 16295 reflections measured, 3220 independent, 2597 with I >2s(I) (2.85 < 2θ < 50°), 201 parameters, R_{int}= 0.0369, $R1$ = 0.0595 [I >2s(I)], $wR2$ = 0.1451, GOF = 1.107. Minimum and maximum peaks in the difference map -0.172 and 0.317 eÅ^{-3}. Crystallographic data (excluding structure factors) for **19** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 648016. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road Cambridge CB21EZ UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

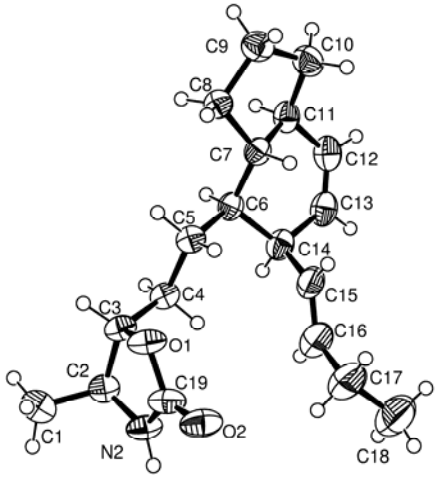


Figure 2. A plot of the X-ray crystal structure of carbamate **19** with atom labels and thermal displacement parameters at 50% probability level.

References

[1] This material is commercially available.

[2] Gunatilaka, A. A. L.; Hirai, N.; Kingston, D. G. I. *Tetrahedron Lett.* **1983**, *24*, 5457-5460. No NMR data available.

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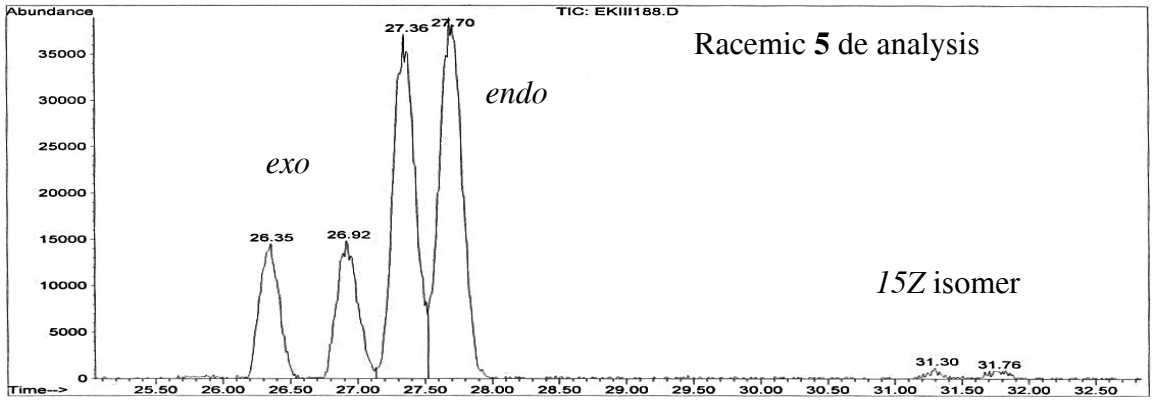
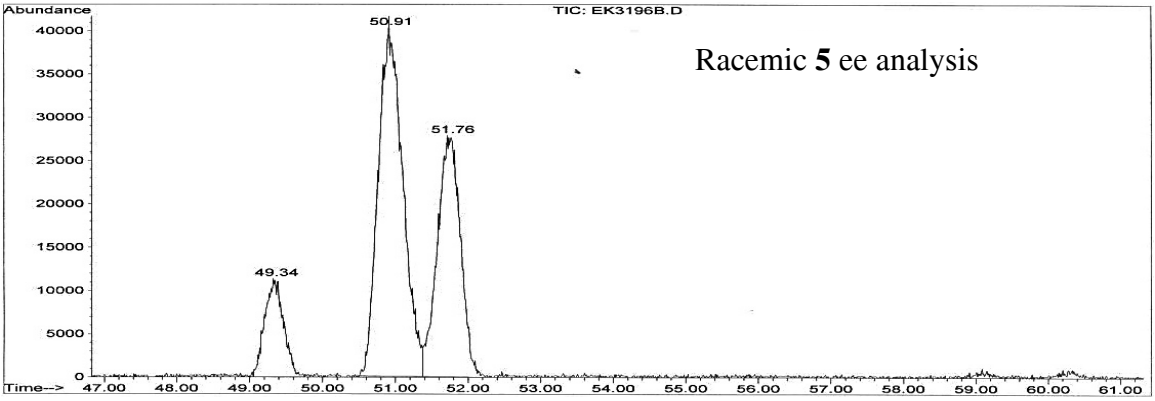
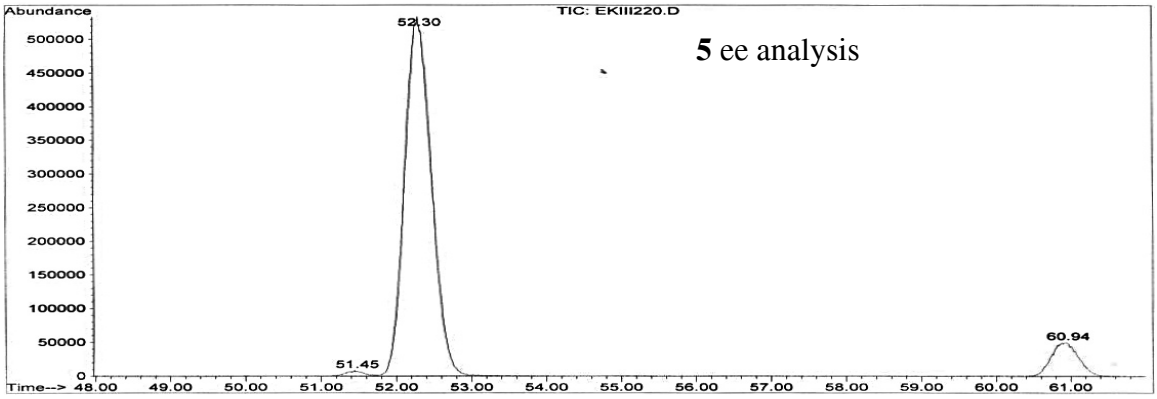
[6] N. U. Sata, N. Fusetani, *Tetrahedron Lett.* **2000**, *41*, 489-492. Original spectra for **1**, **16**, **19** were provided by professor Shigeki Matsunaga, University of Tokyo.

Aldehyde 5 de and ee analysis





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Title     :

Signal    : TIC

peak  R.T. first  max last  PK   peak      peak      peak    % of
  #   min   scan scan scan  TY  height     area     % max.  total
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 2  52.296  4356 4406 4507 VV 9   528592 131789265 100.00%  90.453%
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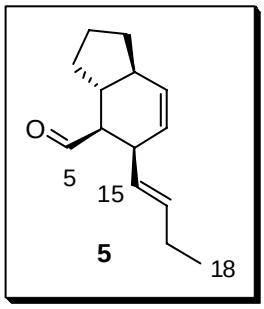

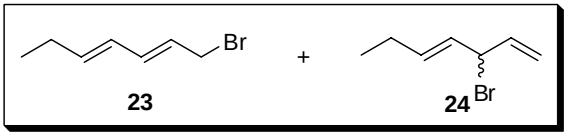

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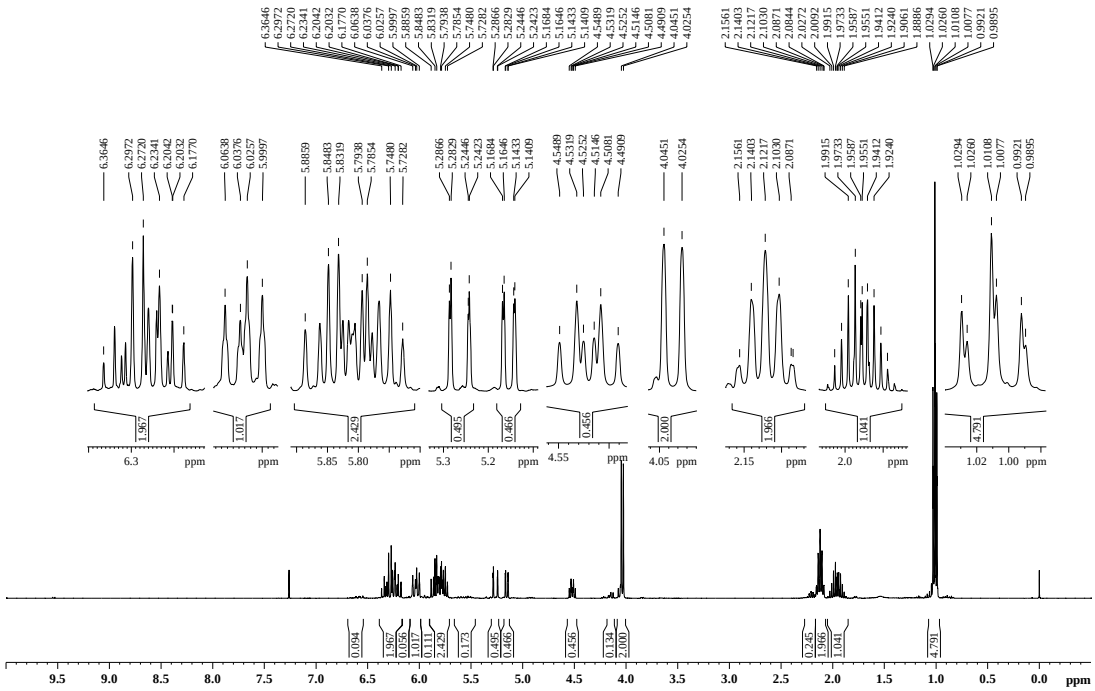

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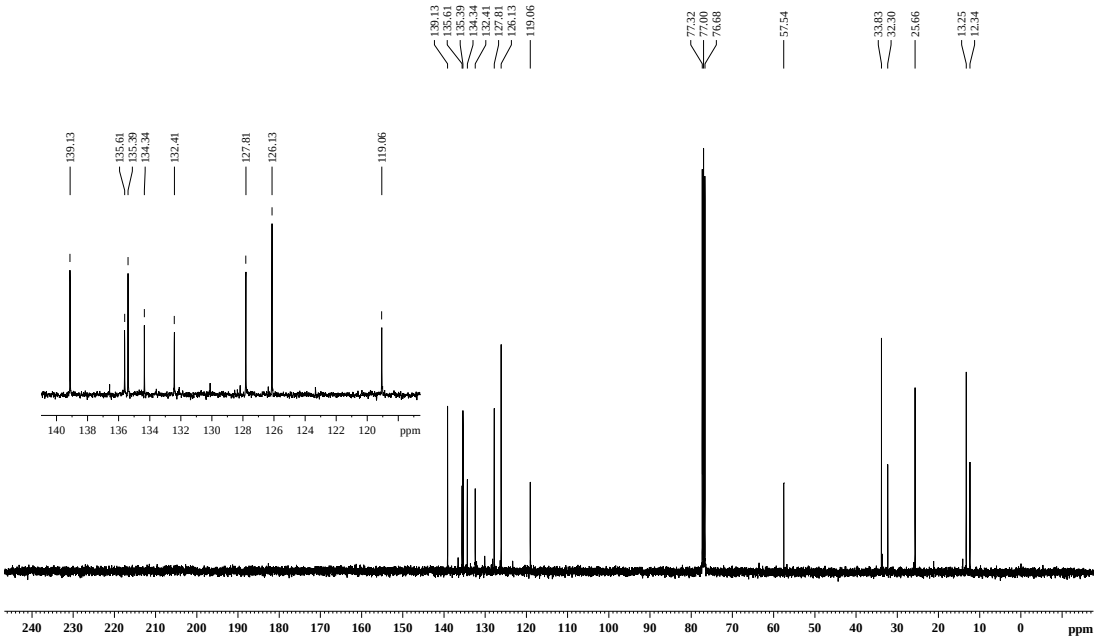

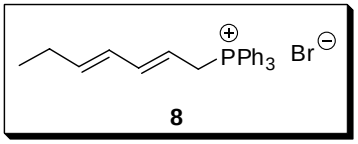

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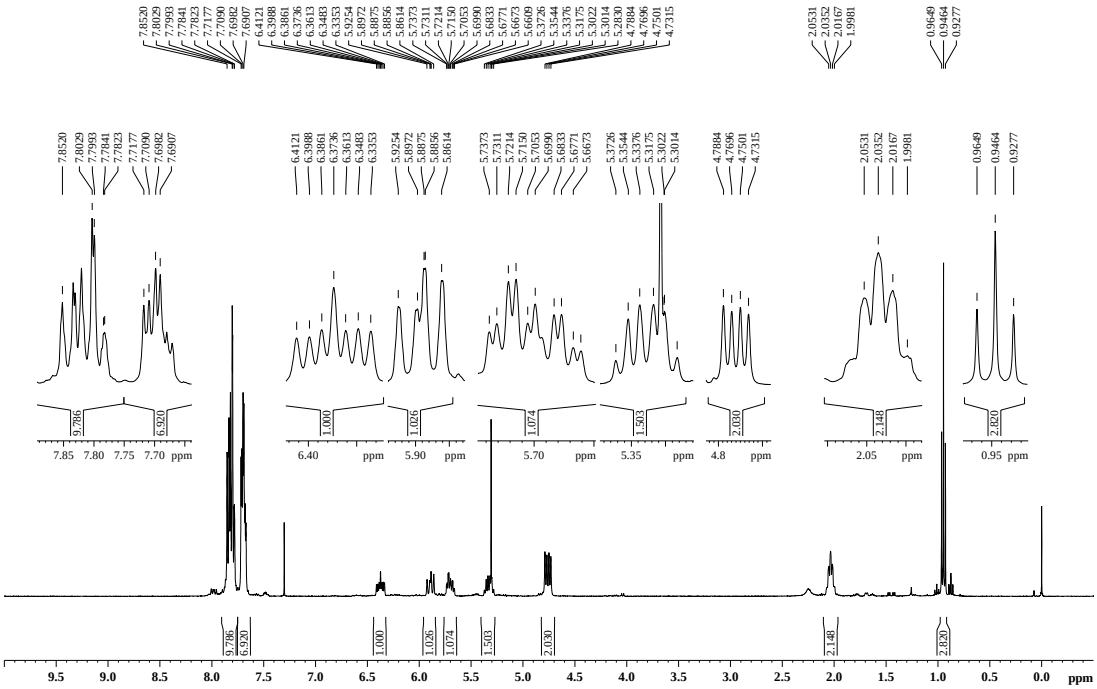

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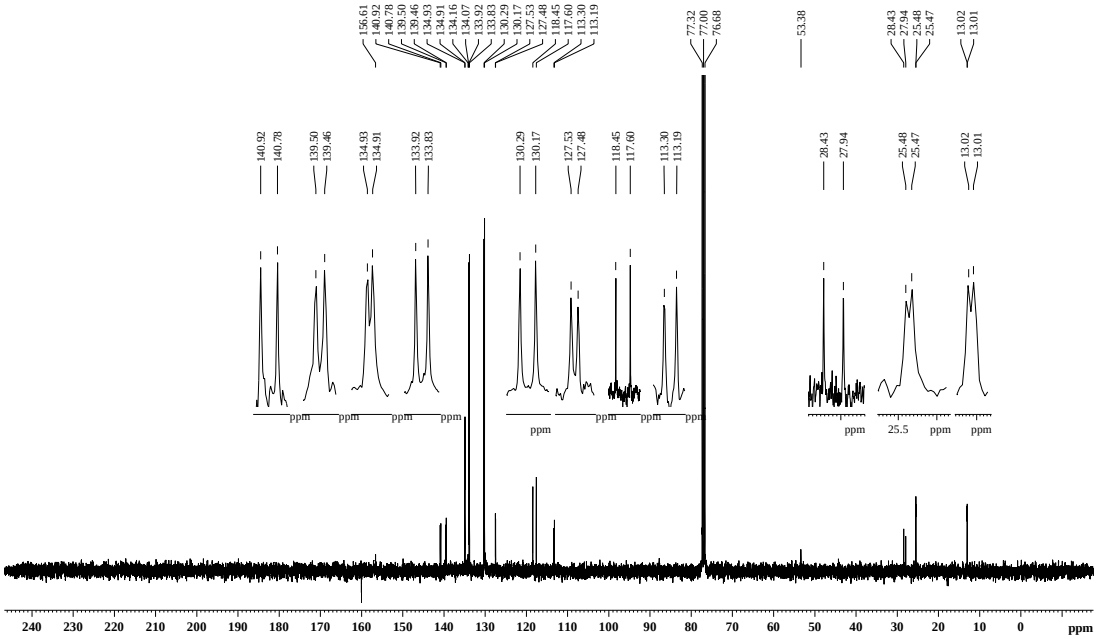

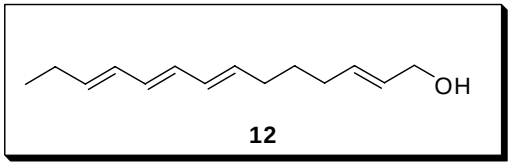

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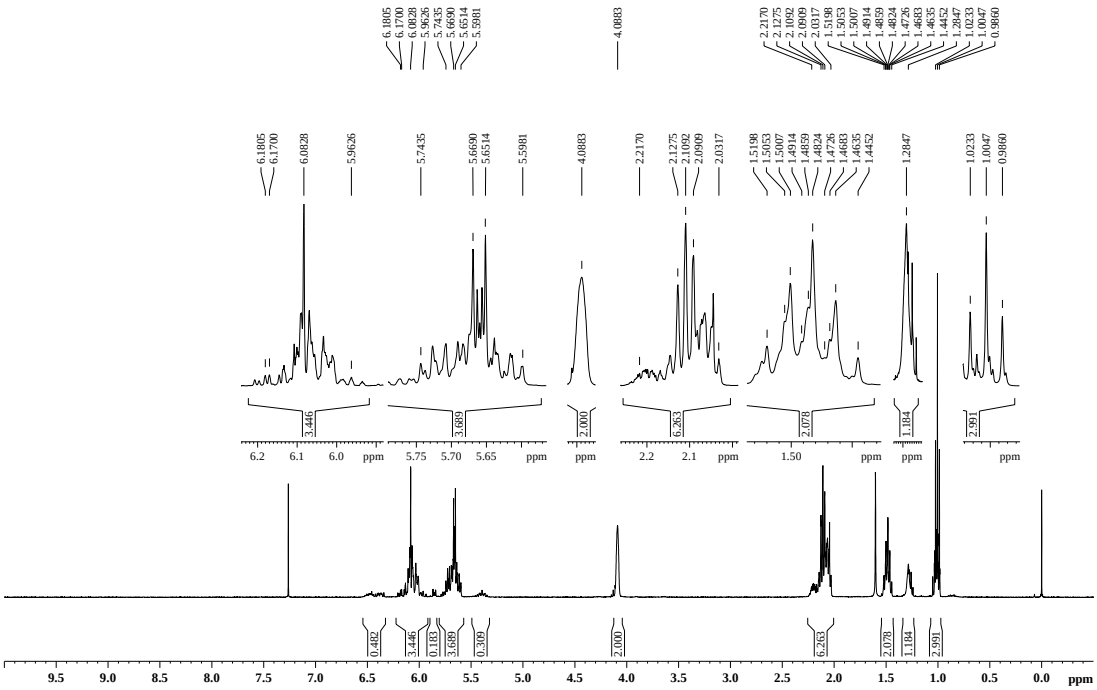

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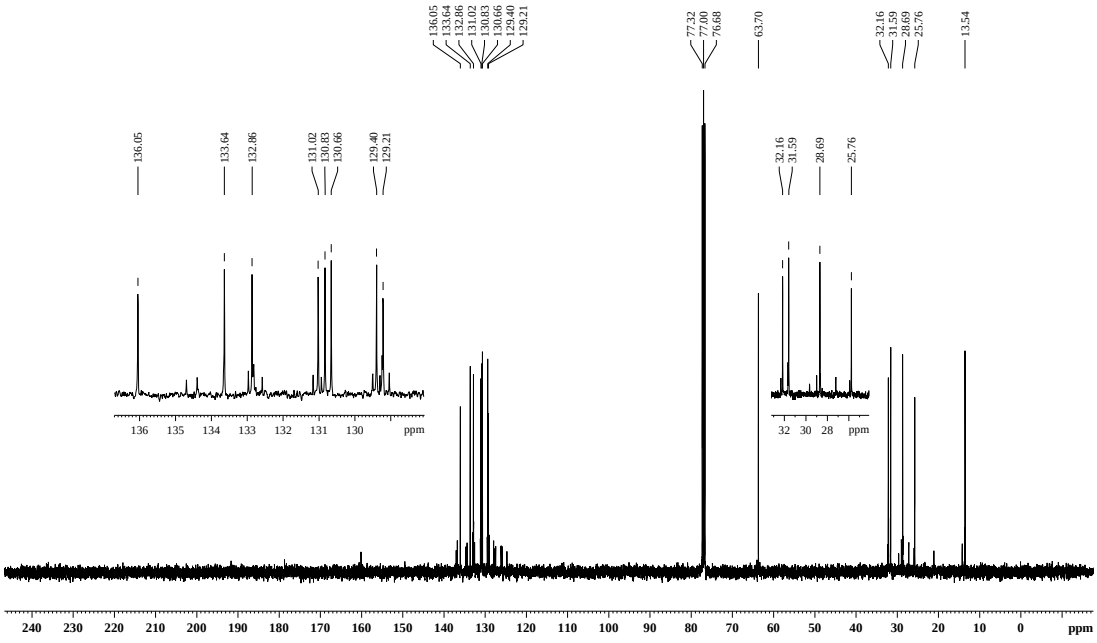
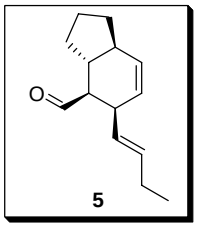
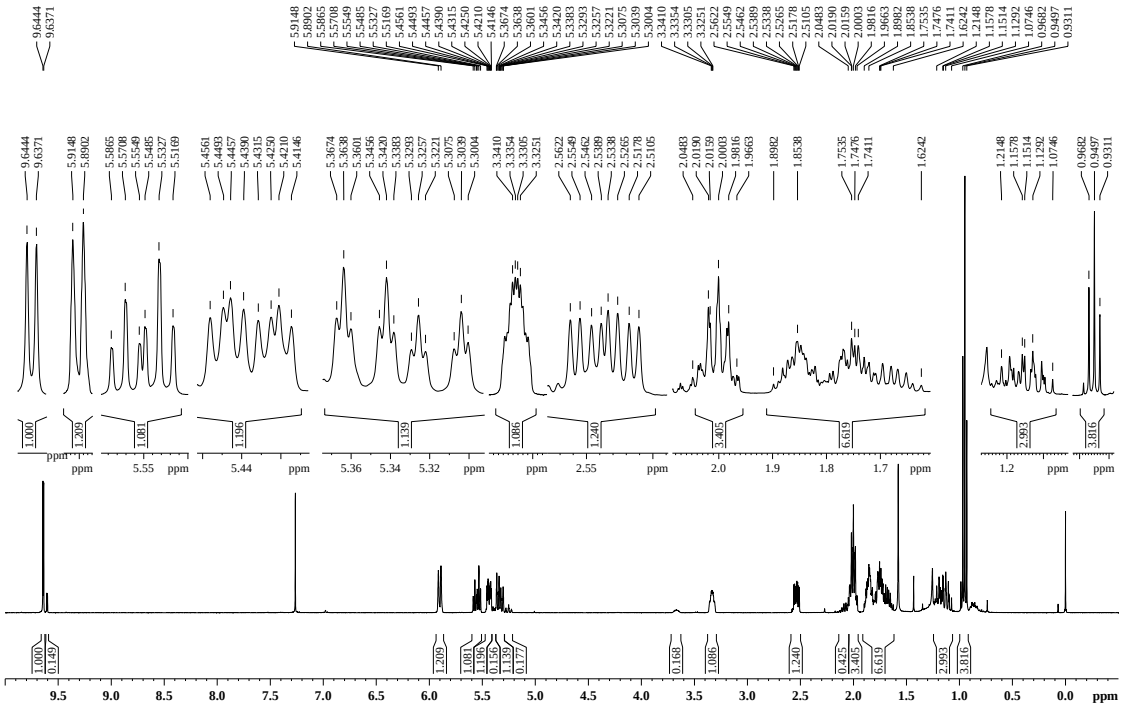
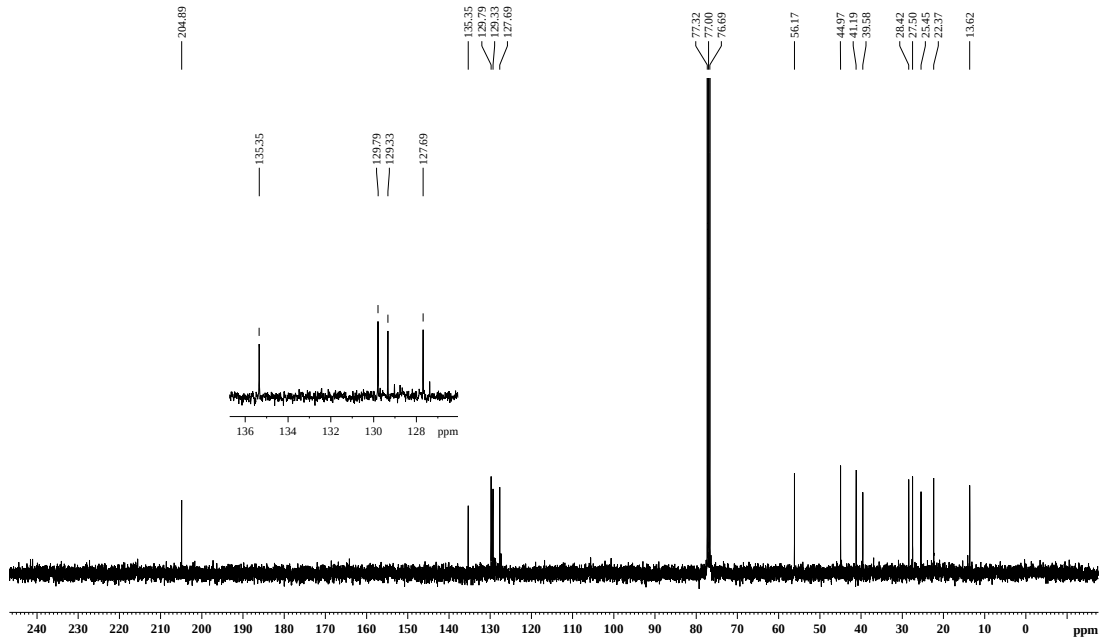


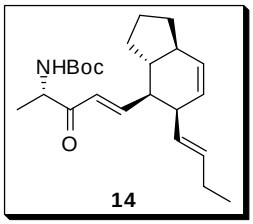


EKIII220 f8-15
25.08.2006 CDCl3

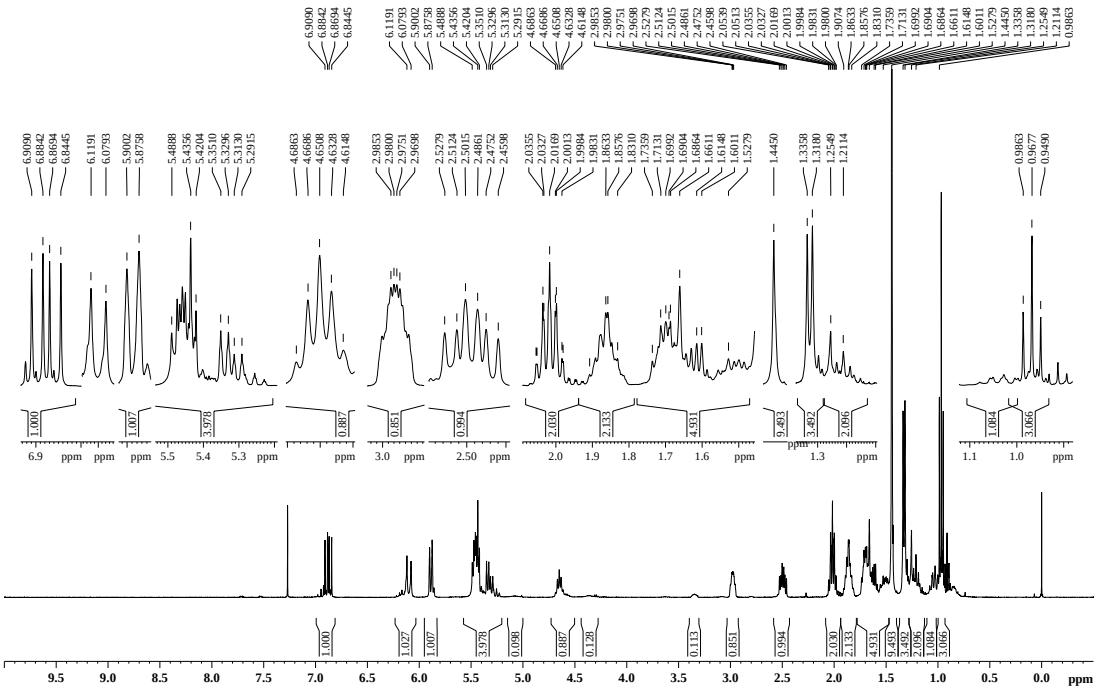


EKIII220 f8-15
25.08.2006 CDCl3

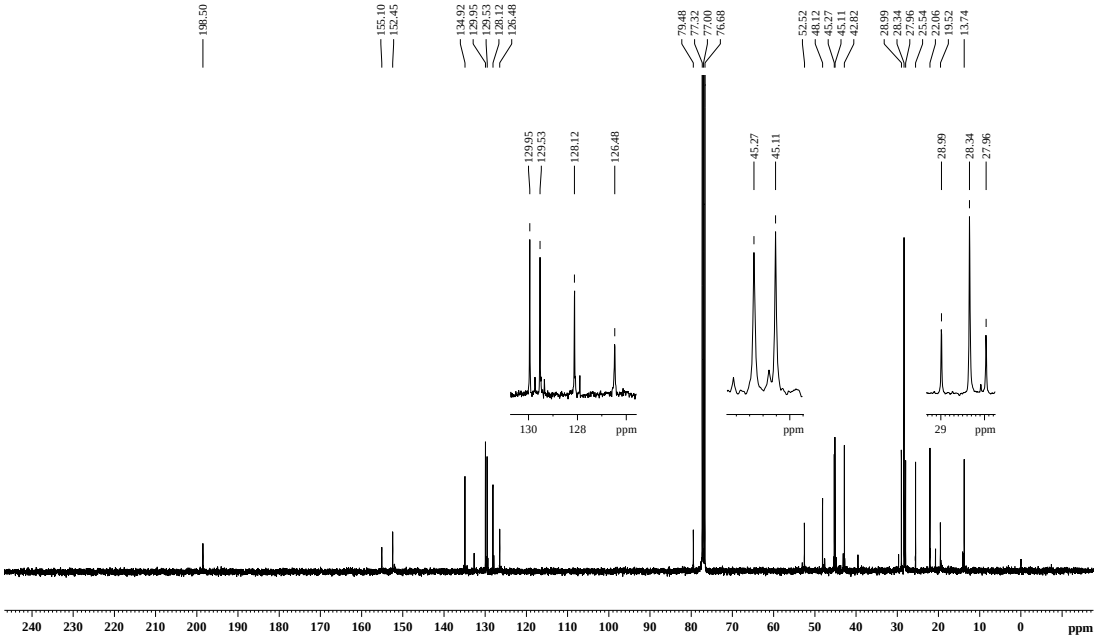


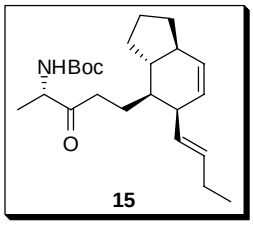


EKIII238 f7-16
22.09.2006 CDCl3

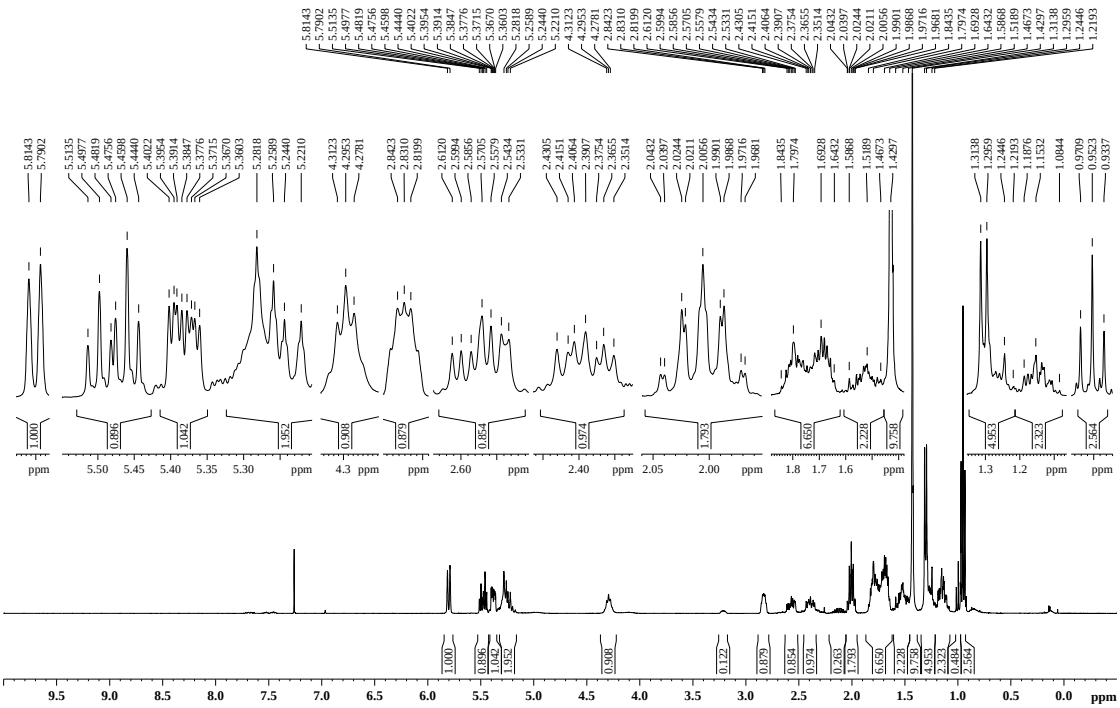


EKIII238 f7-16
22.09.2006 CDCl3

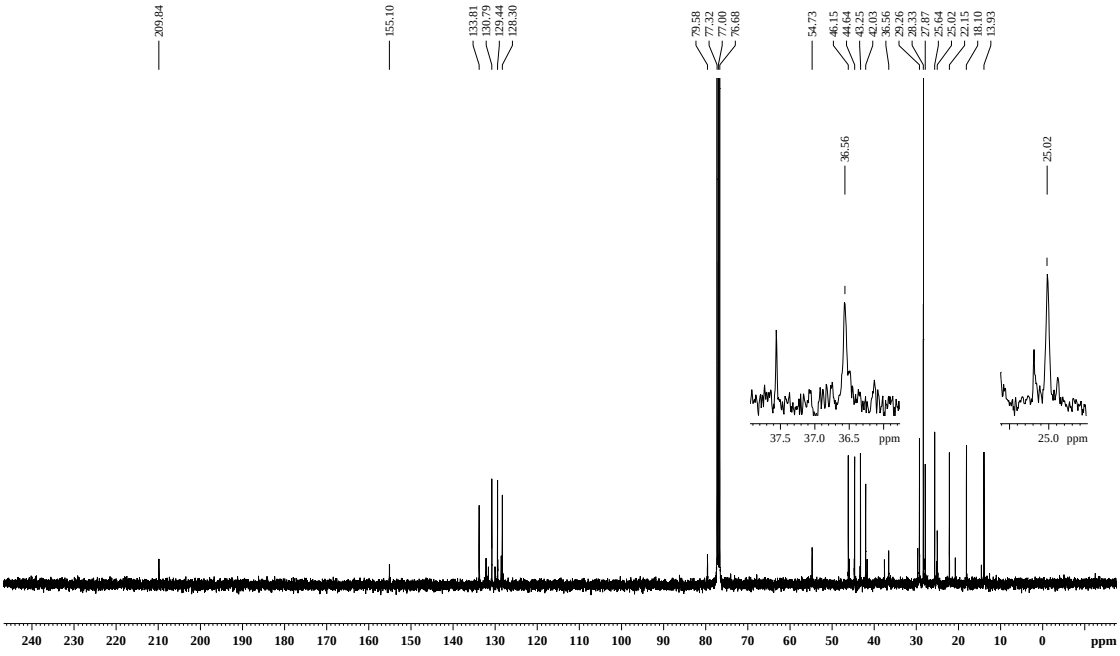


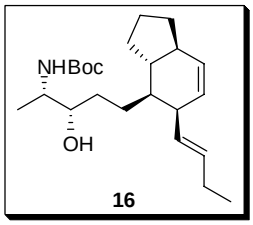


EKIV116 f11-37
18.05.2007 CDCl3

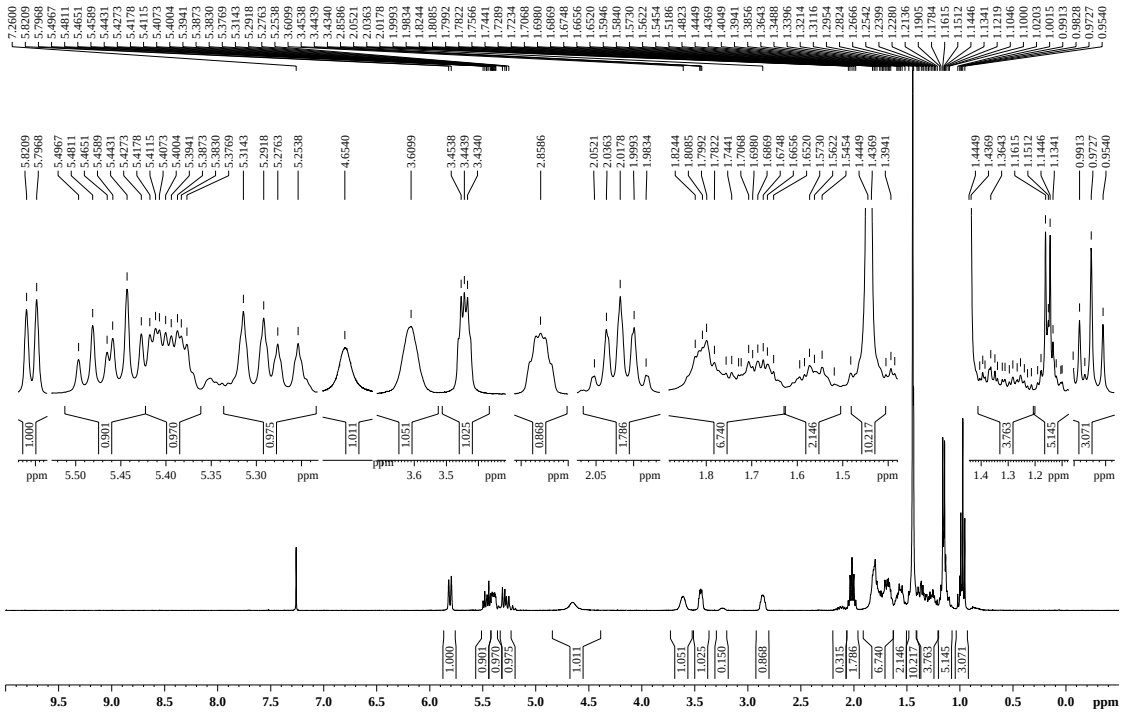


EKIV110 f9-26
05.05.2007 CDCl3

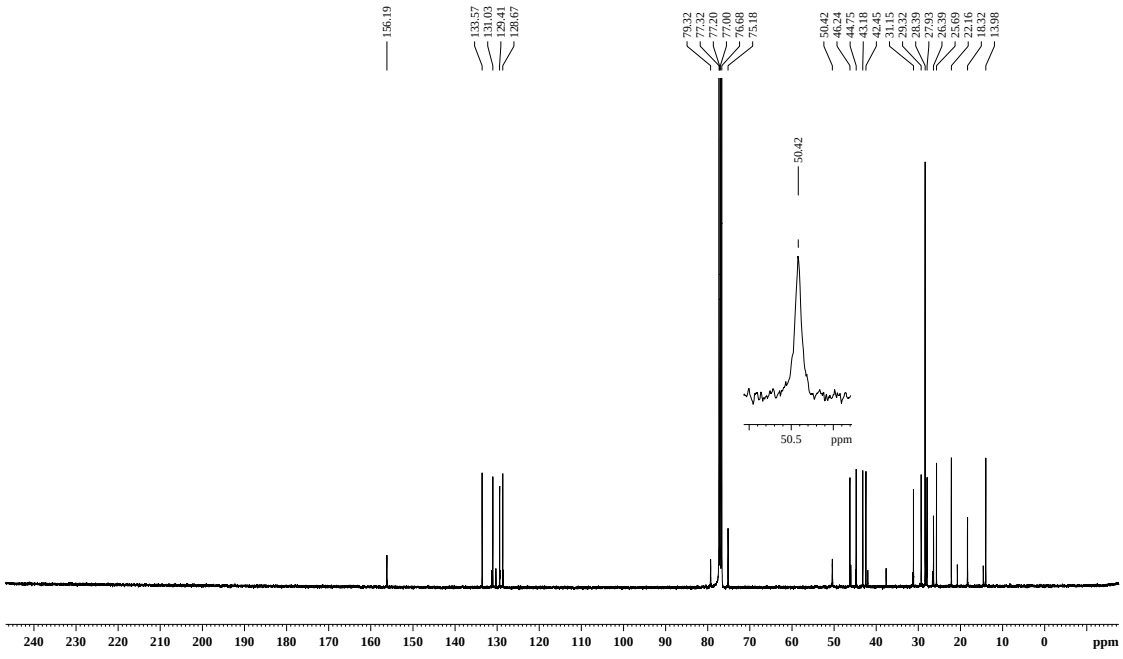


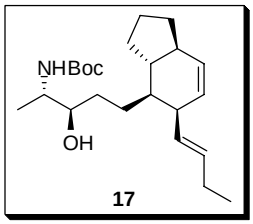


EKIV118 f26-41 recryst.
24.05.2007 CDCl3

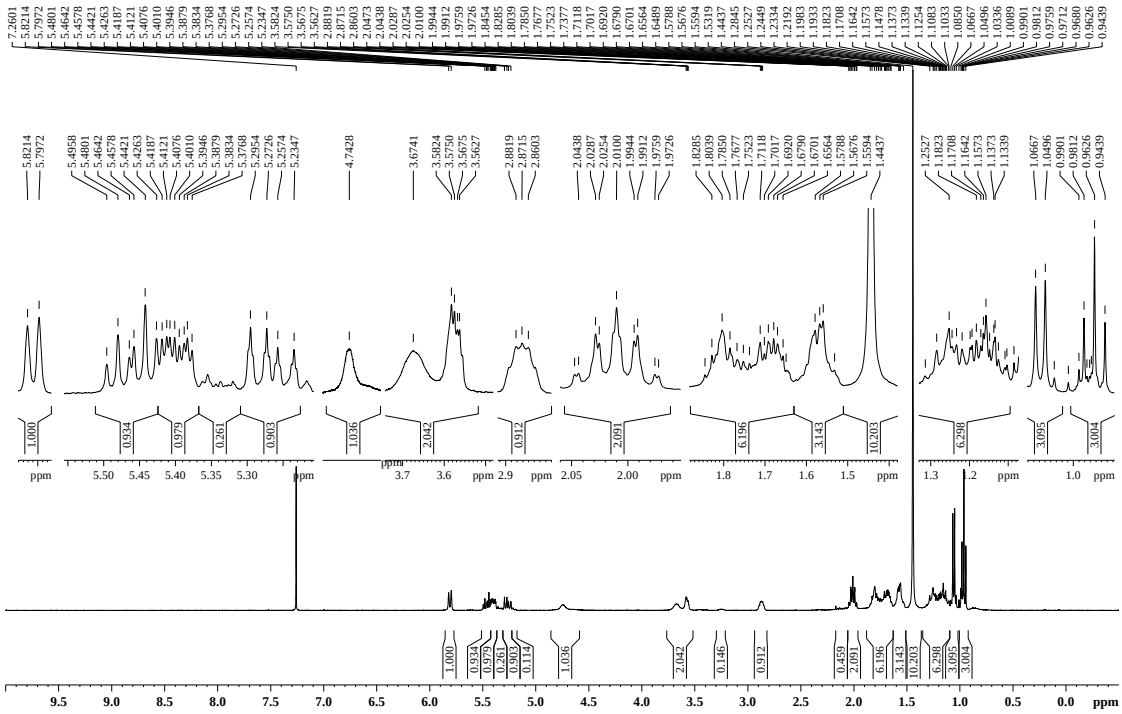


EKIV118 f26-41 recryst.
24.05.2007 CDCl3

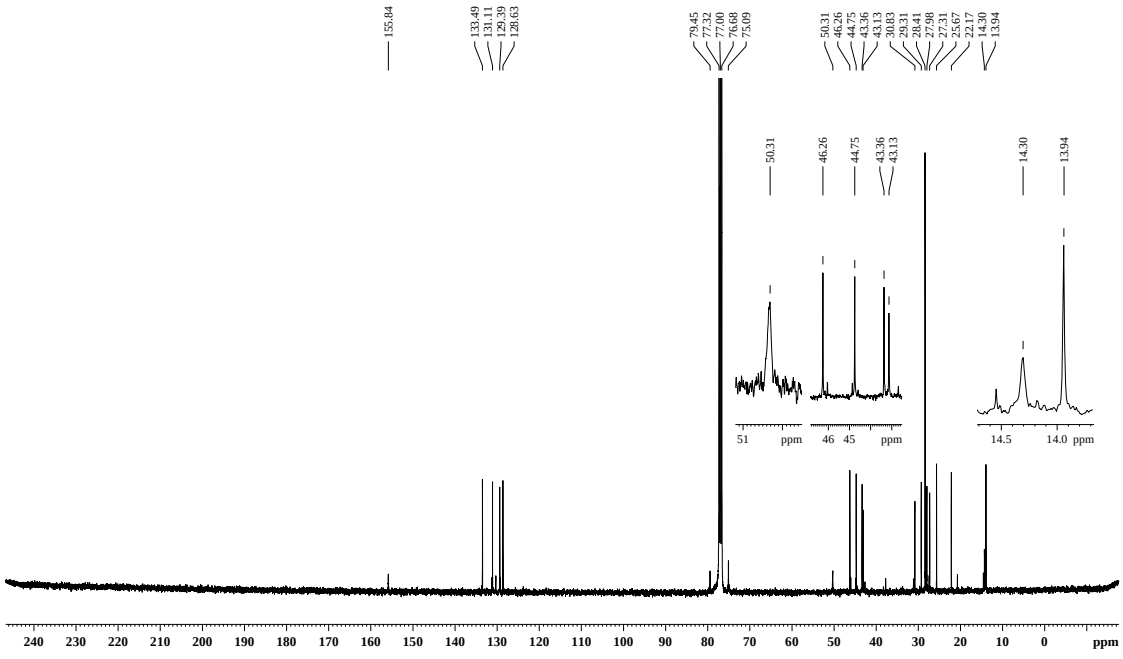


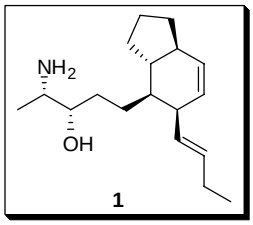


EKIV82B recryst.
26.03.2007 CDCl3

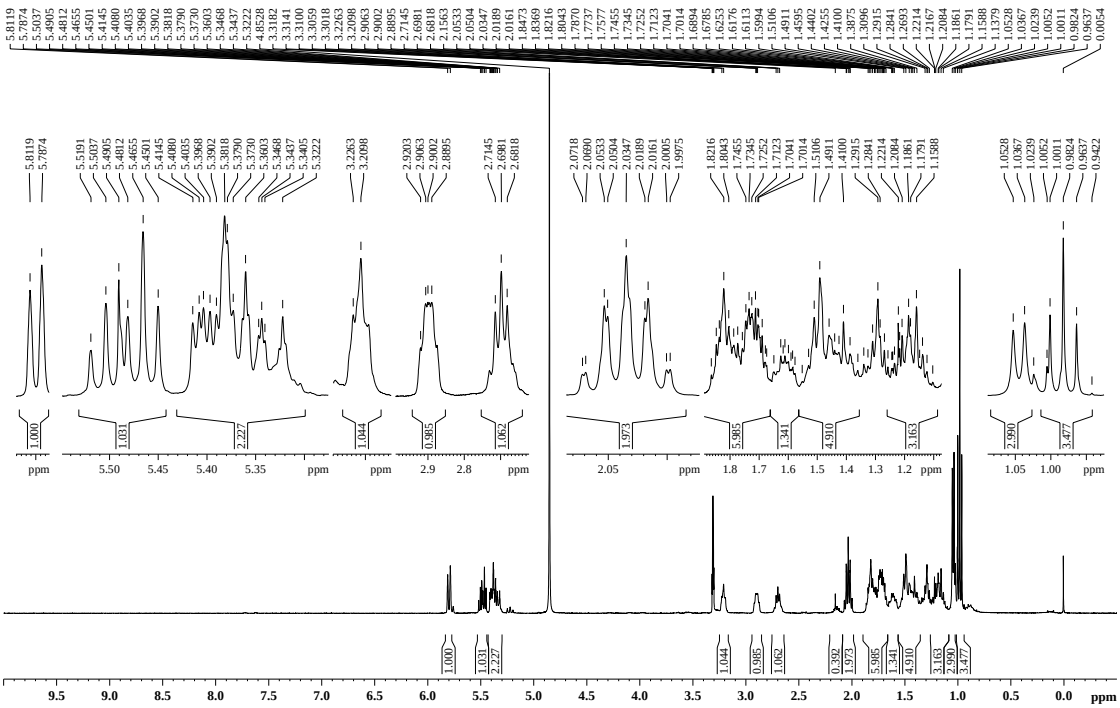


EKIV82B recryst.
05.05.2007 CDCl3

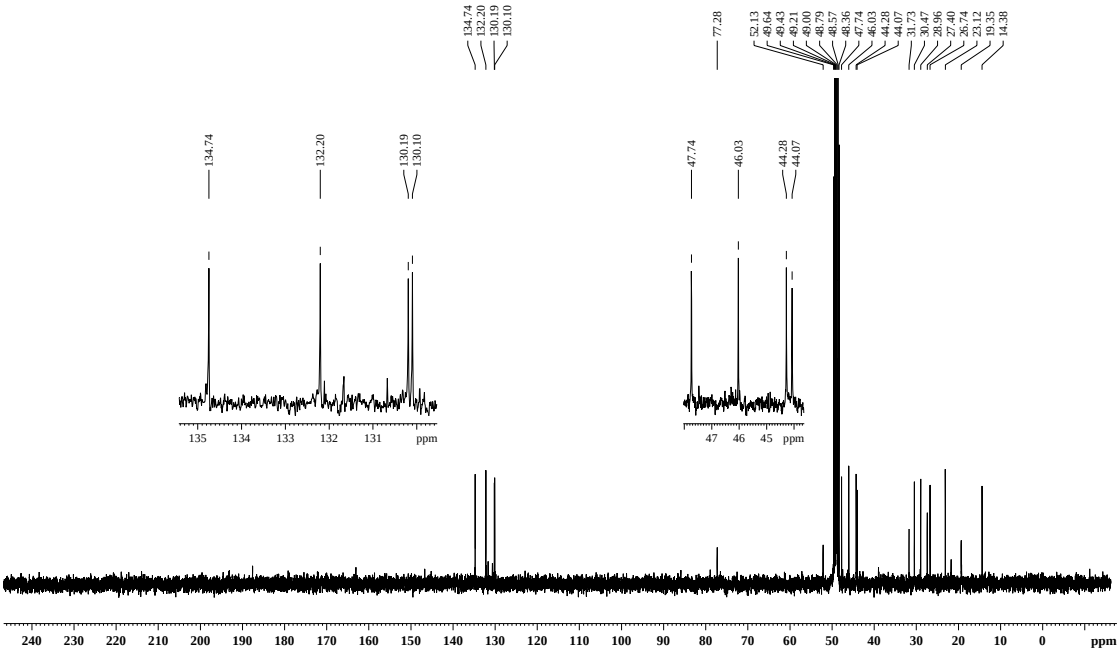


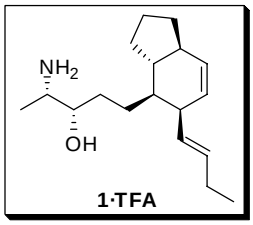


EKIV128 crude
30.05.2007 MeOD

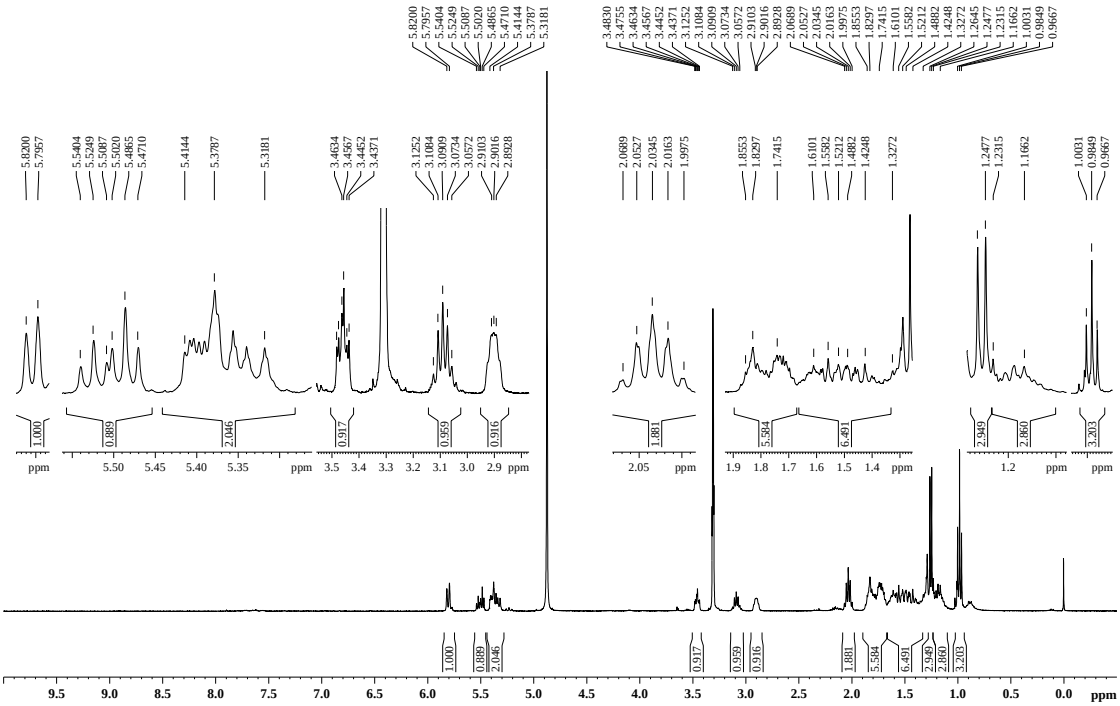


EKIV128 crude
30.05.2007 MeOD

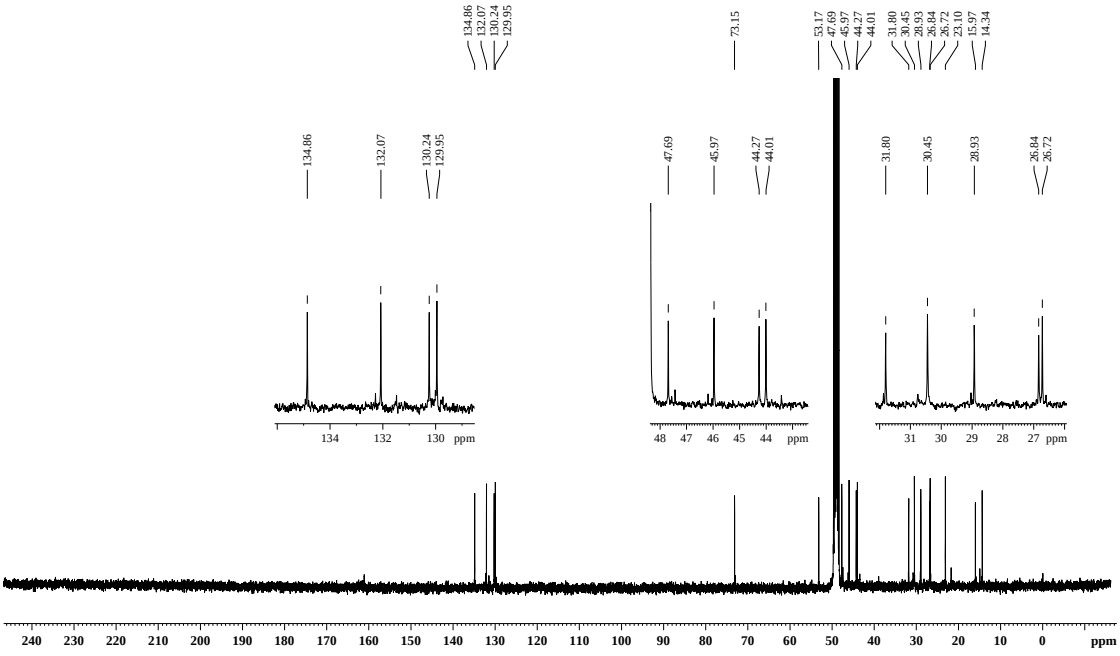


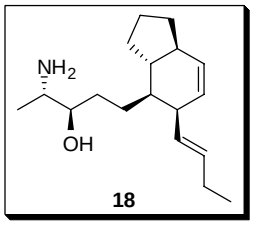


EKIV128 rescued +TFA
07.06.2007 MeOD

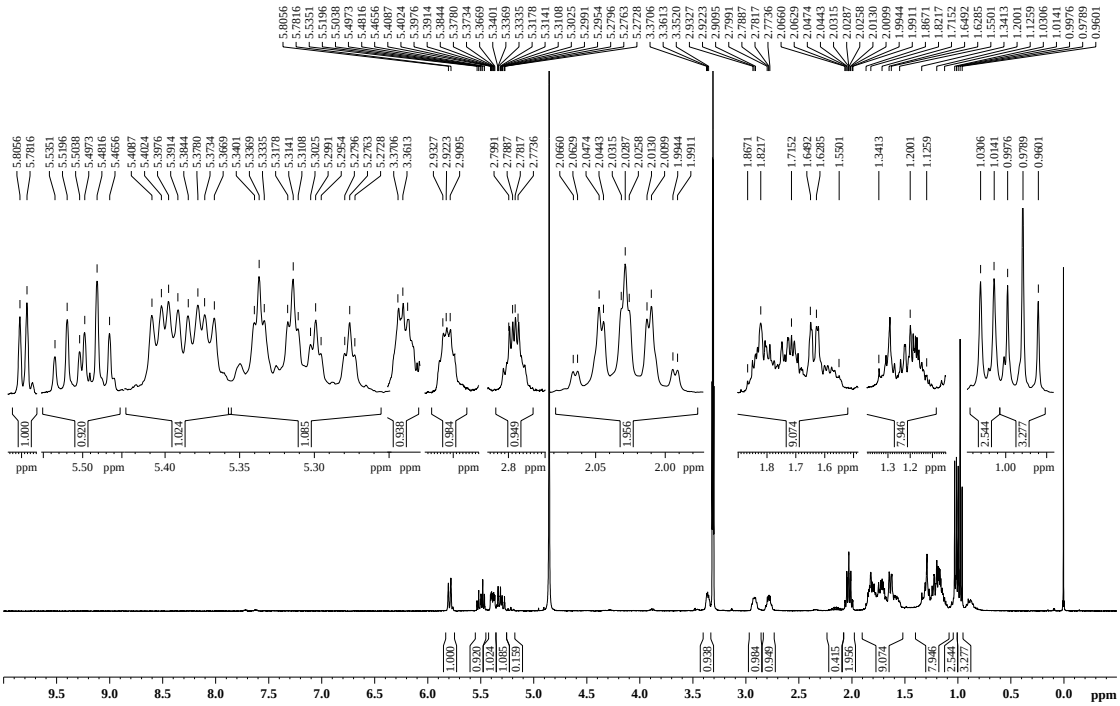


EKIV128 rescued +TFA
07.06.2007 MeOD

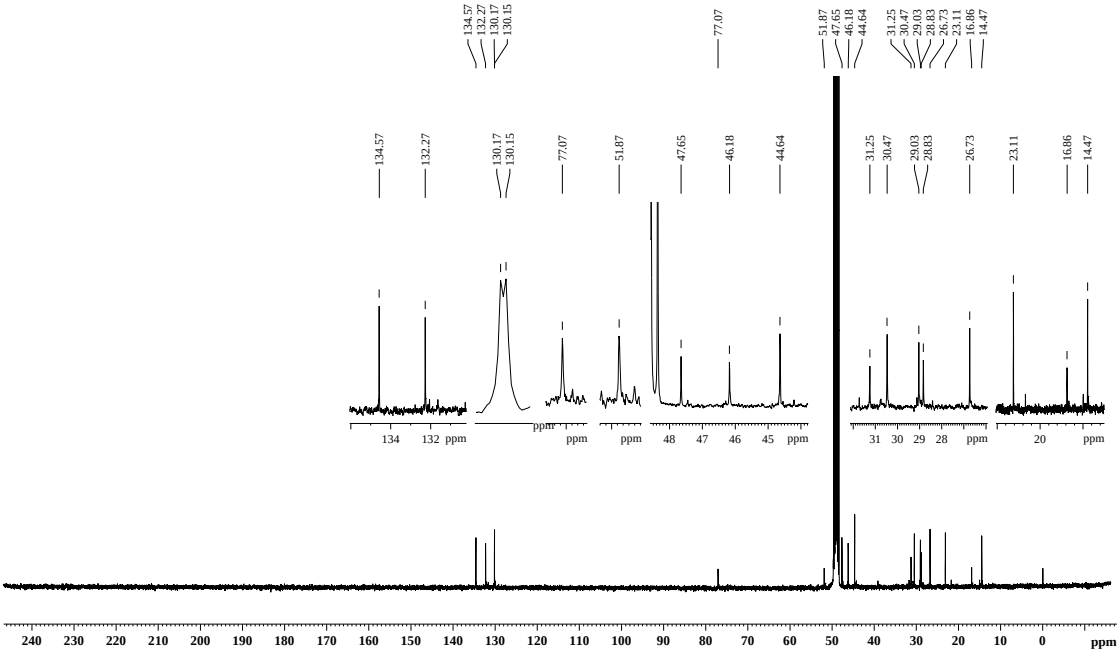


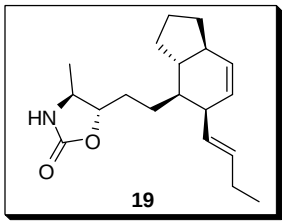


EKIV180 crude
04.09.2007 MeOD



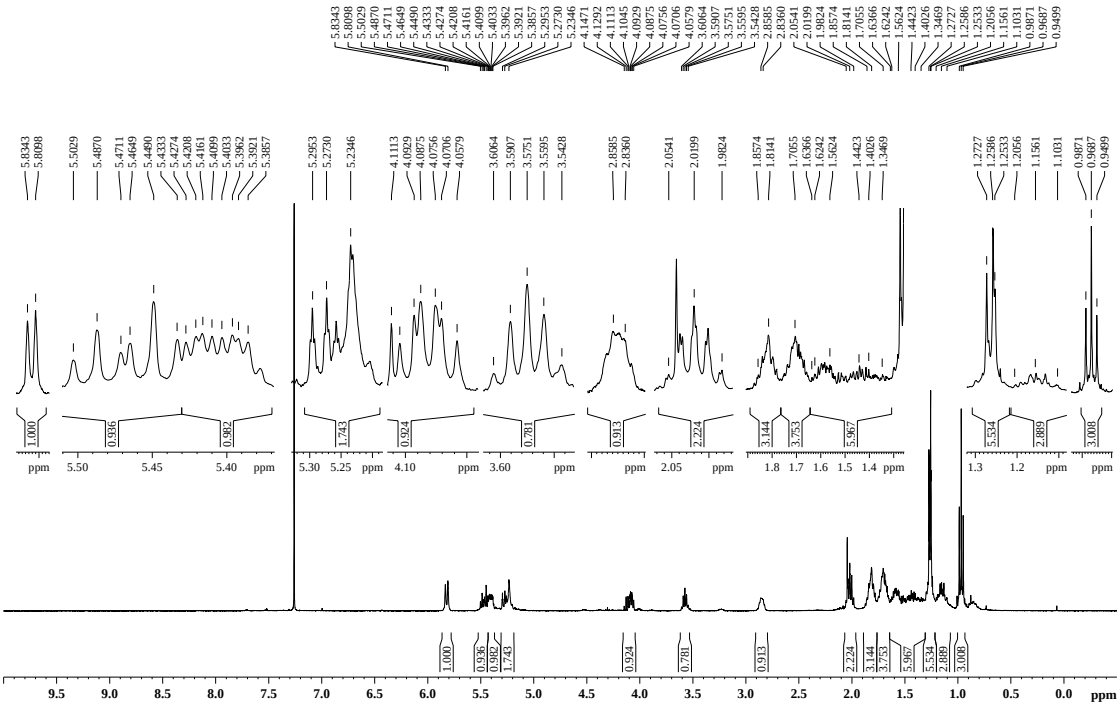
EKIV180 crude
04.09.2007 MeOD



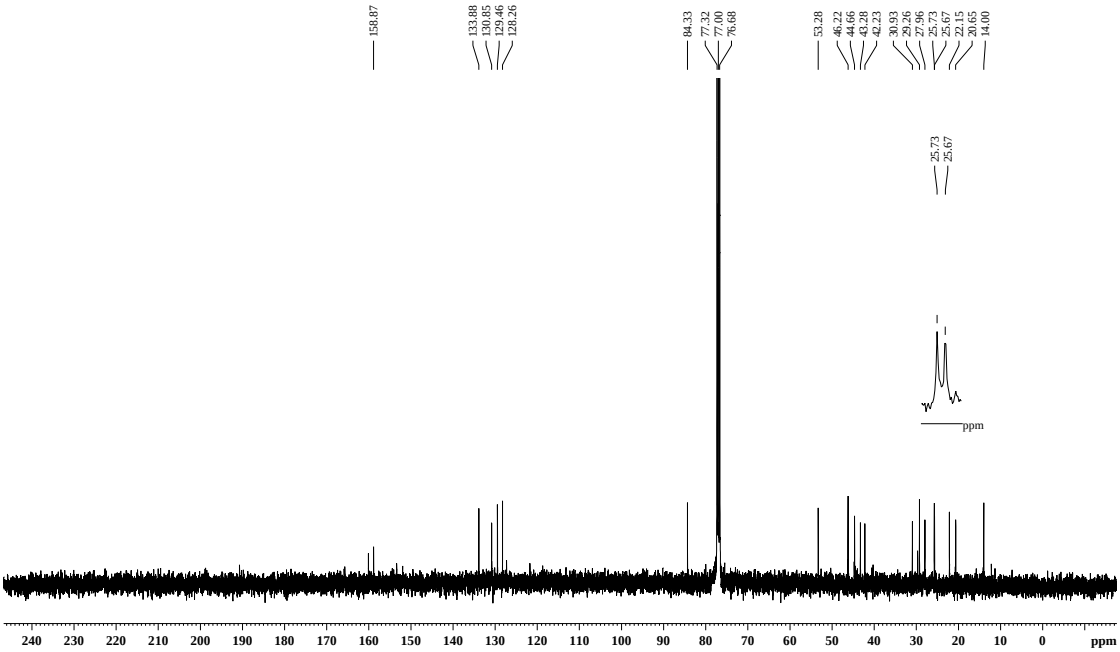


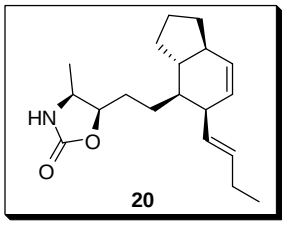
19

EKIV94 f8-11
03.04.2007 CDCl3

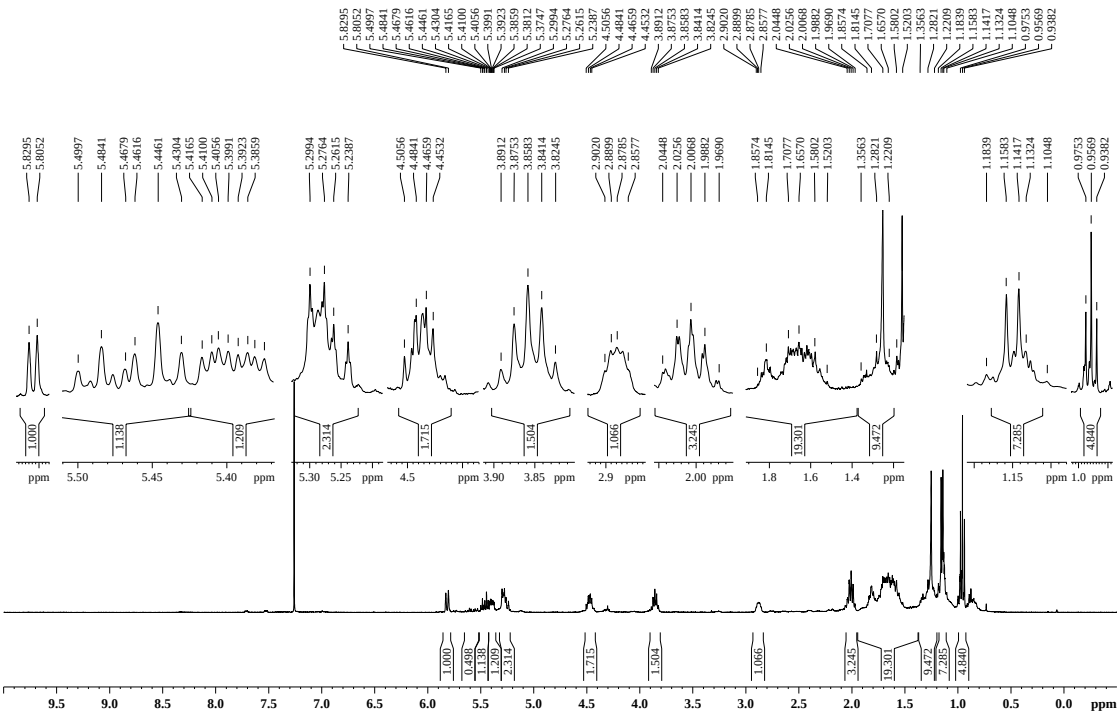


EKIV94 f8-11
11.04.2007 CDCl3





EKIV92 f5-15
29.03.2007 CDCl3



EKIV92 f5-15
29.03.2007 CDCl3