A Convergent and Stereodivergent Synthesis of Complex 1-Aza-7-Oxabicyclo[2.2.1]heptanes

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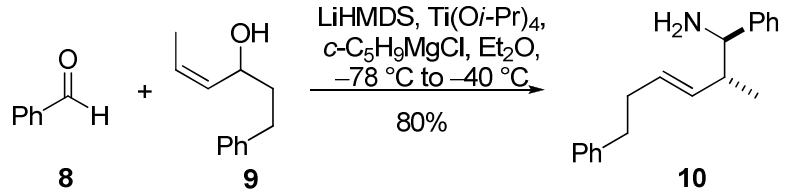
Supporting Information

General Information: All reactions were carried out in flame-dried flasks under an atmosphere of dry argon unless otherwise specified. Toluene and dichloromethane were dried over activated alumina columns and sparged with argon prior to use. Diethyl ether and tetrahydrofuran were dried and distilled from sodium-benzophenone. Ti(O*i*-Pr)$_4$ (Aldrich, 97%) was distilled prior to use (69-70 °C, < 1 Torr). Butyllithium and *c*-C_5H_9MgCl (Aldrich) were titrated by the method of Love *et al.*[1] Chiral allylic alcohols **(–)-9** and **(+)-11** were prepared according to the literature procedures for similar compounds.[2,3] Enantiomeric excess of chiral alcohols **(–)-9** and **(+)-11** was determined by using Mosher's ester analysis.[4] Enantiomeric excess of homoallylic amines **52** and **56** was determined by using Mosher's amide analysis.[5] All other solvents and reagents were used as received from commercial suppliers. Thin-layer chromatography was performed on 250 μm E. Merck silica gel plates (60F-254). Flash column chromatography was performed using Silicycle SiliaFlash P60 silica gel, 40-63 μm particle size. ^{1}H NMR data were recorded at 400 MHz on a Bruker AM-400 in CD_3Cl or CD_2Cl_2. ^{13}C NMR data were recorded at 100 MHz on a Bruker AM-400. ^{13}C NMR data are reported by listing the chemical shift along with a parenthetical description of the substitution (q = three attached protons, t = two attached protons, d = one attached proton, s = no attached proton). Infrared spectra were recorded on a PerkinElmer SpectrumOne FT-IR instrument. LRMS spectra were acquired on a Varian 500-MS mass spectrometer under soft ionization mode. HRMS (ESI-TOF-MS) was performed on Thermo LTQ Orbitrap Mass Spectrometry at Scripps Florida. Optical rotations were measured using a quartz cell with a 0.5 mL capacity and a 10 cm path length.

Procedure for the preparation of primary amines listed in *Table 1*:

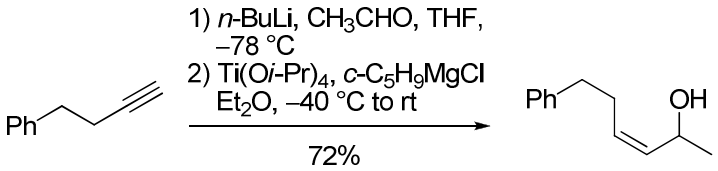


8 **9** **10**

Preparation of (±)-(1*S*,2*S*,*E*)-2-methyl-1,6-diphenylhex-3-en-1-amine (10): To a solution of 530 mg (5.0 mmol) of benzaldehyde in 10 mL of anhydrous ether was added 5.0 mL (5.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.56 mL (1.42 g, 5.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 5.0 mL (10.0 mmol) of 2.0 M *c*-C$_5$H$_9$MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to –40 °C over 30 min, then the mixture was stirred at –40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **9** in 4 mL of THF, prepared by deprotonation of 440 mg (2.5 mmol) of alcohol **9** at –78 °C with 1.1 mL (2.75 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula.[6] The mixture was warmed to room temperature over 2 h, then stirred for 12 h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of sat. aq. NaHCO$_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried (MgSO$_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH$_2$Cl$_2$:MeOH:NH$_4$OH = 400:10:1) to give 534 mg (80%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **10** as a colorless oil.

Data for amine **10**: IR (neat) 3584, 3366, 2958, 1603, 1495, 1454 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.79 (d, *J* = 6.8 Hz, 3H, CH$_3$), 1.70 (br, 2H, NH$_2$), 2.31 (qd, *J* = 8.0, 6.8 Hz, 1H, CHCH$_3$), 2.42 (m, 2H, PhCH$_2$C<u>H</u>$_2$-), 2.75 (m, 2H, PhC<u>H</u>$_2$), 3.53 (d, *J* = 8.8 Hz, 1H, C<u>H</u>NH), 5.32 (m, 1H, -CH$_2$CH=C<u>H</u>-), 5.53 (td, *J* = 13.6, 6.4 Hz, 1H, CH$_2$C<u>H</u>=CH)), 7.21-

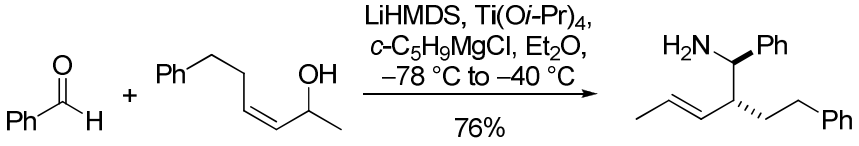
7.29 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.13 (q), 34.44 (t), 35.87 (t), 45.24 (d), 60.96 (d), 125.83 (d), 126.99 (d), 127.37 (d), 128.27 (d), 128.32 (d), 128.58 (d), 131.00 (d), 134.13 (d), 141.87 (s), 144.67 (s); LRMS $C_{19}H_{23}N + H^+$ calcd *m*/*z* 266.2, found *m*/*z* 266.5.



11

Preparation of (*Z*)-6-phenylhex-3-en-2-ol (11): To a solution of 5.0 g (38.5 mmol) of 4-phenyl-1-butyne in 40 mL of anhydrous THF at –78 °C was added 16.9 mL of *n*-BuLi (2.5 M in hexanes) dropwise via a syringe under argon. The mixture was stirred for 30 min before introduction of a cold (–78 °C) solution of acetaldehyde in 20 mL of THF via cannula. After stirring for 30 min, 25 mL of sat. aq. NH_4Cl was added. The aqueous phase was extracted with 50 mL of diethyl ether (2×). The combined organic extract was washed with 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by flash chromatography over 100 g of silica gel (10% ethyl acetate in hexanes) to afford 7.0 g (>99%) of 6-phenylhex-3-yn-2-ol as a colorless oil. 3.1 g (17.8 mmol) of 6-phenylhex-3-yn-2-ol was immediately added to a solution of 10.1 g (35.8 mmol) of Ti(O*i*-Pr)$_4$ in 60 mL of anhydrous ether under argon at –78 °C, followed by dropwise addition of 44.5 mL (89.0 mmol) of *c*-C_5H_9MgCl (2.0 M in Et_2O) over 20 min under argon. The mixture was stirred at –40 °C for 2 h, then was slowly raised to 0 °C over 1 h before adding 30 mL of sat. aq. $NaHCO_3$. The resulting slurry was stirred rapidly for overnight and resulted in a biphasic mixture. The aqueous layer was extracted with 50 mL of diethyl ether (2×). The combined organic extract was dried ($MgSO_4$) and concentrated *in vacuo.* The residue was purified by chromatography over 50 g of silica gel (10% ethyl acetate in hexanes) to give 2.26 g (72%, d.r. ≥ 20:1, *Z*:*E* ≥ 20:1) of alcohol **11** as a water white oil.

Data for alcohol **11**: IR (neat) 3368, 2968, 1709, 1603, 1496, 1368, 1257, 1058 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.12 (d, *J* = 6.4 Hz, 3H, CH_3), 1.59 (br, 1H, OH), 2.47 (m, 2H, CH_2), 2.71 (m, 2H, CH_2), 4.46 (qd, *J* = 8.0, 6.4 Hz, 1H, C<u>H</u>OH), 5.46 (m, 2H, -C<u>H</u>=C<u>H</u>-), 7.19-7.33 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.09 (q), 29.54 (t), 35.71 (t), 63.61 (d), 126.07 (d), 128.34 (d), 128.68 (d), 129.70 (d), 134.71 (d), 141.54 (s); LRMS $C_{12}H_{16}O + Na^+$ calcd *m*/*z* 199.1, found *m*/*z* 199.3.

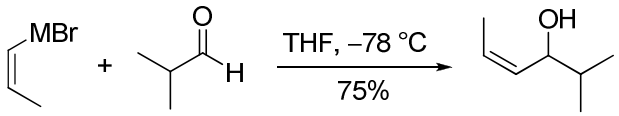


8 **11** **12**

Preparation of (±)-(1*R*,2*R*,*E*)-2-phenethyl-1-phenylpent-3-en-1-amine (12): To a solution of 424 mg (4.0 mmol) of benzaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to –40 °C over 30 min, then the mixture was stirred at –40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **11** in 4 mL of THF, prepared by deprotonation of 352 mg (2.0 mmol) of alcohol **11** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred for 12 h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of saturated aqueous $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH =

400:10:1) to give 404 mg (76%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **12** as a colorless oil.

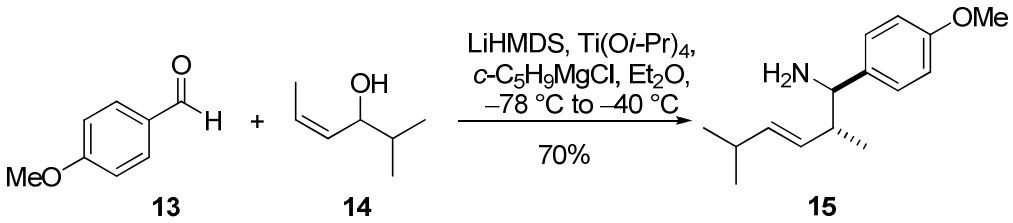
Data for amine **12**: IR (neat) 3584, 3233, 2918, 1584, 1495 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30 and 1.38 (m, 2H, $PhCH_2C\underline{H}_2$-), 1.50 (br, 2H, NH_2), 1.69 (dd, *J* = 6.4, 1.6 Hz, 3H, CH_3), 2.08 (tdd, *J* = 8.8, 8.8, 3.6 Hz, 1H, $C\underline{H}CH_2$), 2.25 and 2.54 (m, 2H, $PhC\underline{H}_2$), 3.57 (d, *J* = 8.8 Hz, 1H, $C\underline{H}NH$), 5.20 (m, 1H, $CH_3CH{=}C\underline{H}$-), 5.53 (qd, *J* = 12.4, 6.4 Hz, 1H, $CH_3C\underline{H}{=}CH$)), 7.10-7.23 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.16 (q), 33.18 (t), 35.53 (t), 50.79 (d), 59.88 (d), 125.53 (d), 127.05 (d), 127.48 (d), 128.15 (d), 128.28 (d), 128.38 (d), 128.97 (d), 132.57 (d), 142.45 (s), 144.71 (s); LRMS $C_{19}H_{23}N$ + H^+ calcd *m*/*z* 266.2, found *m*/*z* 266.4.



14

Preparation of (*Z*)-2-methylhex-4-en-3-ol (14): To a flame-dried 50 mL 3-neck round bottom flask was charged 600 mg (25.0 mmol) of magnesium turnings and 2 mg of iodine under argon. After introduction of 10 mL of anhydrous THF, the mixture was refluxed at 60 °C until it changed from brown to water white. A solution of 0.62 g (5.0 mmol) of (*Z*)-1-bromopropene in 20 mL of anhydrous THF was added via a syringe at a rate to maintain reflux. After stirring for an additional 2 h at 60 °C, the Grignard solution prepared was cooled to rt, and then was cannulated into a solution of 288 mg (4.0 mmol) of isobutyraldehyde in 10 mL of anhydrous THF at –78 °C under argon. After stirring for 2 h, 10 mL of sat. aq. NH_4Cl was added. The aqueous phase was extracted with 20 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (10% ethyl acetate in hexanes) to give 342 mg (75%, d.r. ≥ 20:1, *Z*:*E* ≥ 20:1) of alcohol **14** as a water white oil.

Data for alcohol **14**: IR (neat) 3367, 2958, 2874, 1659, 1469, 1381, 1006 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.80 (d, *J* = 6.8 Hz, 3H, CH_3), 0.89 (d, *J* = 6.8 Hz, 3H, CH_3), 1.46 (br, 1H, OH), 1.61 (dd, *J* = 7.2, 2.0 Hz, 3H, CH_3), 4.10 (m, 1H, C<u>H</u>OH), 5.36 (m, 1H, C<u>H</u>=CHCH$_3$), 5.76 (qd, *J* = 12.8, 6.8 Hz, 1H, CH=C<u>H</u>CH$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.42 (q), 17.91 (q), 18.20 (q), 34.21 (d), 72.25 (d), 126.96 (d), 131.79 (d); LRMS $C_7H_{14}O + Na^+$ calcd *m*/*z* 137.1, found *m*/*z* 137.3.

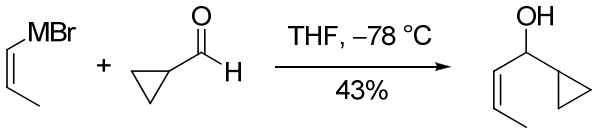


13 **14** **15**

Preparation of (±)-(1*R*,2*R*,*E*)-1-(4-methoxyphenyl)-2,5-dimethylhex-3-en-1-amine (15): To a stirred solution of 544 mg (4.0 mmol) of 4-methoxybenzaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to –40 °C over 30 min, then the mixture was stirred at –40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **14** in 4 mL of THF, prepared by deprotonation of 228 mg (2.0 mmol) of alcohol **14** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then stirred for 16 h. Finally, sequential addition of 10 mL of diethyl ether and 10 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 30 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH =

400:10:1) to give 326 mg (70%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **15** as a colorless oil.

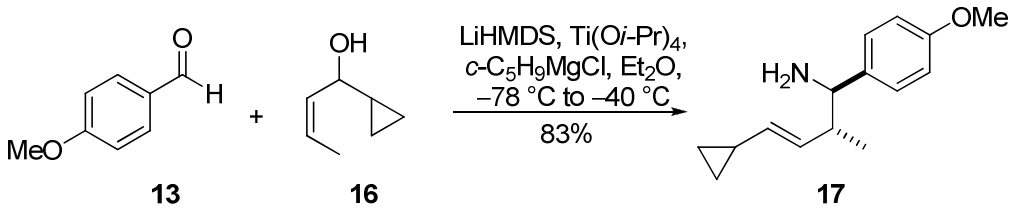
Data for amine **15**: IR (neat) 3246, 2958, 2869, 1611, 1585, 1512, 1463 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.58 (d, *J* = 6.8 Hz, 3H, CH_3), 0.81 (d, *J* = 3.2 Hz, 3H, $CH(C\underline{H}_3)_2$), 0.83 (d, *J* = 3.2 Hz, 3H, $CH(C\underline{H}_3)_2$), 1.41 (br, 2H, NH_2), 2.06 (qd, *J* = 8.0, 7.2 Hz, 1H, $C\underline{H}CH_3$), 2.12 (m, 1H, $C\underline{H}(CH_3)_2$), 3.36 (d, *J* = 8.8 Hz, 1H, $C\underline{H}NH$), 3.63 (s, 3H, OMe), 5.07 (dd, *J* = 15.6, 8.8 Hz, 1H, $CH{=}C\underline{H}CHCH_3$), 5.39 (dd, *J* = 15.6, 6.8 Hz, 1H, *i*-$PrC\underline{H}{=}CH$), 6.68 (dd, *J* = 6.4, 2.0 Hz, 2H, Ph-), 7.07 (d, *J* = 8.8 Hz, 2H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.23 (q), 22.69 (q), 22.73 (q), 31.14 (d), 45.36 (d), 55.25 (q), 60.42 (d), 113.56 (d), 128.36 (d), 130.18 (d), 136.89 (s), 139.38 (d), 158.59 (s); LRMS ($C_{17}H_{23}NO + H^+ - NH_3$) calcd *m*/*z* 217.2, found *m*/*z* 217.4.



16

Preparation of (*Z*)-1-cyclopropylbut-2-en-1-ol (16): To a flame-dried 50 ml 3-neck round bottom flask was charged 0.72 g (30.0 mmol) of magnesium turnings and 2 mg of iodine under argon. After introduction of 10 mL of anhydrous THF, the mixture was refluxed at 60 °C until it changed from brown to water white. A solution of 1.68 g (12.0 mmol) of (*Z*)-1-bromopropene in 20 mL of anhydrous THF was added via a syringe at a rate to maintain reflux. After stirring for an additional 2 h at 60 °C, the Grignard solution prepared was cooled to rt, and was cannulated into a solution of 0.7 g (10.0 mmol) of cyclopropanecarbaldehyde in 10 mL of anhydrous THF at –78 °C under argon. After stirring for 2 h, 10 mL of sat. aq. NH_4Cl was added. The aqueous phase was extracted with 20 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (20% ethyl acetate in hexanes) to give 480 mg (43%, d.r. ≥ 20:1, *Z*:*E* ≥ 20:1) of alcohol **16** as a water white oil.

Data for alcohol **16**: IR (neat) 3367, 3081, 3011, 2919, 1660, 1431, 1021 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.25 and 0.32 (m, 2H, $CH(C\underline{H}_2)_2$), 0.47 and 0.52 (m, 2H, $CH(C\underline{H}_2)_2$), 1.03 (m, 1H, $C\underline{H}(CH_2)_2$), 1.66 (dd, *J* = 6.8, 1.6 Hz, 3H, CH_3), 1.73 (br, 1H, OH), 3.95 (t, *J* = 8.0 Hz, 1H, $C\underline{H}OH$), 5.51 (m, 1H, $C\underline{H}$=$CHCH_3$), 5.61 (qd, *J* = 12.8, 6.8 Hz, 1H, CH=$C\underline{H}CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.00 (t), 1.15 (t), 11.73 (d), 16.05 (q), 69.53 (d), 124.64 (d), 130.23 (d); LRMS $C_7H_{12}O$ + Na^+ calcd *m*/*z* 135.1, found *m*/*z* 135.2.

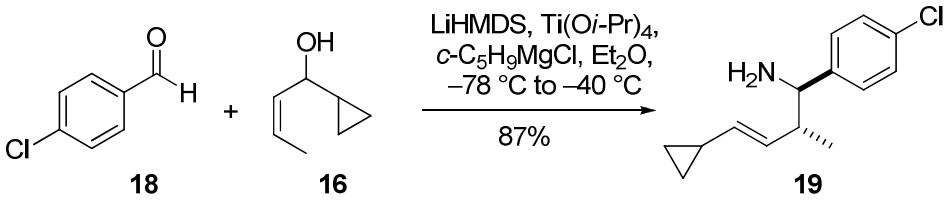


13 **16** **17**

Preparation of (±)-(1*R*,2*R*,*E*)-4-cyclopropyl-1-(4-methoxyphenyl)-2-methylbut-3-en-1-amine (17): To a solution of 544 mg (4.0 mmol) of 4-methoxybenzaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to –40 °C over 30 min, then was stirred at –40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **16** in 4 mL of THF, prepared by deprotonation of 224 mg (2.0 mmol) of alcohol **16** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred for 16 h. Finally, sequential addition of 10 mL of diethyl ether and 10 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 30 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH =

400:10:1) to give 384 mg (83%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **17** as a colorless oil.

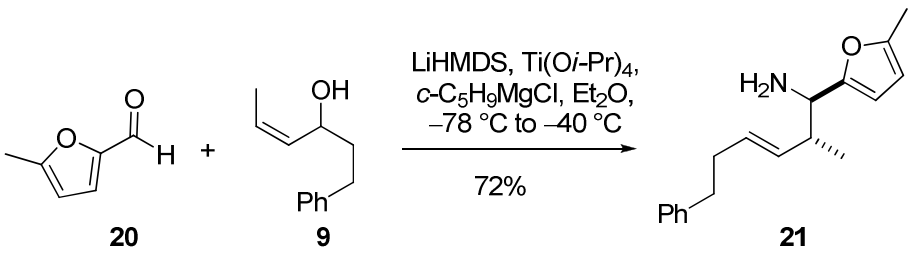
Data for amine **17**: IR (neat) 3585, 3247, 2958, 2838, 1614, 1594, 1515, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.20 (m, 2H, CH(C<u>H</u>$_2$)$_2$), 0.53 (m, 2H, CH(C<u>H</u>$_2$)$_2$), 0.61 (d, *J* = 6.8 Hz, 3H, CH_3), 1.23 (m, 1H, C<u>H</u>(CH$_2$)$_2$), 1.42 (br, 2H, NH_2), 2.08 (qd, *J* = 8.0, 6.8 Hz, 1H, C<u>H</u>CH$_3$), 3.38 (d, *J* = 8.0 Hz, 1H, C<u>H</u>NH), 3.65 (s, 3H, OMe), 4.96 (dd, *J* = 15.2, 8.8 Hz, 1H, CH=C<u>H</u>CH(CH$_2$)$_2$), 5.24 (dd, *J* = 15.2, 8.8 Hz, 1H, CH$_3$C<u>H</u>=CH), 6.70 (d, *J* = 8.8 Hz, 2H, Ph-), 7.07 (d, *J* = 8.8 Hz, 2H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.58 (t), 6.61 (t), 13.67 (d), 18.24 (q), 45.37 (d), 55.26 (q), 60.53 (d), 113.57 (d), 128.33 (d), 130.60 (d), 135.60 (d), 136.95 (s), 158.60 (s); LRMS ($C_{15}H_{17}NO$ + H^+ - NH_3) calcd *m*/*z* 215.1, found *m*/*z* 215.3.



Preparation of (±)-(1*R*,2*R*,*E*)-1-(4-chlorophenyl)-4-cyclopropyl-2-methylbut-3-en-1-amine (19): To a stirred solution of 564 mg (4.0 mmol) of 4-chlorobenzaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to –40 °C over 30 min, then the mixture was stirred at –40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **16** in 4 mL of THF, prepared by deprotonation of 224 mg (2.0 mmol) of alcohol **16** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min

stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred for 16 h. Finally, sequential addition of 10 mL of diethyl ether and 10 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 30 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 400:10:1) to give 410 mg (87%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **19** as a colorless oil.

Data for amine **19**: IR (neat) 3711, 3368, 2962, 1662, 1594, 1489, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.21 (m, 2H, CH($C\underline{H}_2$)$_2$), 0.54 (m, 2H, CH($C\underline{H}_2$)$_2$), 0.63 (d, *J* = 6.8 Hz, 3H, CH_3), 1.22 (m, 1H, C$\underline{H}$(CH_2)$_2$), 1.42 (br, 2H, NH_2), 2.06 (qd, *J* = 8.0, 6.8 Hz, 1H, C$\underline{H}CH_3$), 3.42 (d, *J* = 8.0 Hz, 1H, C$\underline{H}$NH), 4.95 (dd, *J* = 15.2, 8.8 Hz, 1H, CH=C$\underline{H}$CH(CH_2)$_2$), 5.21 (dd, *J* = 15.2, 8.8 Hz, 1H, $CH_3C\underline{H}$=CH), 7.12 (m, 4H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.61 (t), 6.65 (t), 13.67 (d), 18.09 (q), 45.17 (d), 60.53 (d), 128.30 (d), 128.75 (d), 130.27 (d), 132.54 (s), 136.08 (d), 143.31 (s); LRMS $C_{14}H_{18}ClN$ + H^+ calcd *m*/*z* 236.1, found *m*/*z* 236.3.

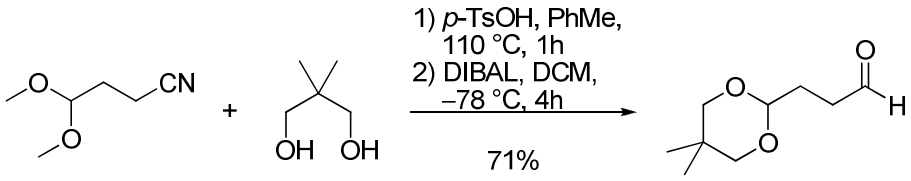


20 **9** **21**

Preparation of (±)-(1*R*,2*R*,*E*)-1-(5-methylfuran-2-yl)-2-phenethylpent-3-en-1-amine (21): To a solution of 440 mg (4.0 mmol) of 5-methylfuran-2-carbaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the

solution was cooled to −78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to −40 °C over 30 min, then the mixture was stirred at −40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **11** in 4 mL of THF, prepared by deprotonation of 352 mg (2.0 mmol) of alcohol **11** at −78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred for 12 h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 200:10:1) to give 388 mg (72%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **21** as a colorless oil.

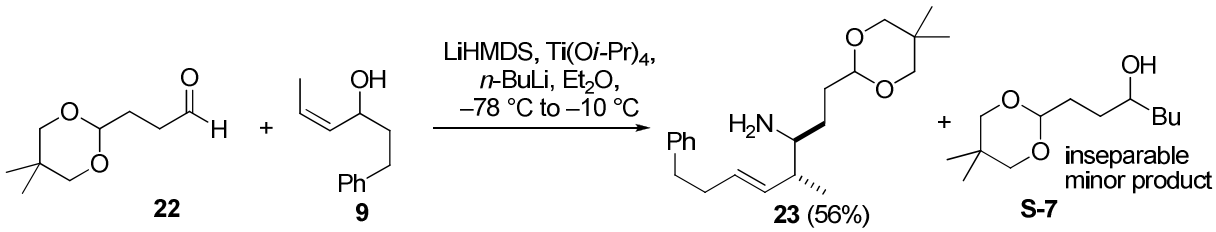
Data for amine **21**: IR (neat) 3300, 2953, 1714, 1248, 824 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30 and 1.44 (m, 2H, $PhCH_2C\underline{H}_2$-), 1.50 (br, 2H, NH_2), 1.62 (dd, *J* = 6.4, 1.6 Hz, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.18 (m, 1H, C<u>H</u>CH_2Bn), 2.31 and 2.49 (m, 2H, $PhC\underline{H}_2$), 3.51 (d, *J* = 8.4 Hz, 1H, C<u>H</u>NH_2), 5.11 (m, 1H, $CH_3CH{=}C\underline{H}$-), 5.45 (qd, *J* = 12.4, 6.4 Hz, 1H, $CH_3C\underline{H}{=}CH$)), 5.70 (s, 1H, furan), 5.82 (s, 1H, furan), 7.10-7.23 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.56 (q), 18.17 (q), 33.33 (t), 33.42 (t), 48.70 (d), 53.50 (d), 105.70 (d), 106.68 (d), 125.56 (d), 128.18 (d), 128.27 (d), 128.40 (d), 128.96 (d), 132.10 (d), 142.51 (s), 150.87 (s), 155.43 (s); LRMS $C_{18}H_{23}NO + H^+$ calcd *m*/*z* 270.2, found *m*/*z* 270.4.



22

Preparation of 3-(5,5-dimethyl-1,3-dioxan-2-yl)propanal (22): To a solution of 6.4 g (50 mmol) of 4,4-dimethoxybutanenitrile (from TCI) in 50 mL of toluene was added 5.5 g (52.5 mmol) of 2,2-dimethylpropane-1,3-diol and 0.2 g (1.2 mmol) of *p*-TsOH. The mixture was refluxed at 110 °C for 1 h. The solution was concentrated, then was diluted with 50 mL of dichloromethane. The resulting solution was washed with 20 mL of sat. aq. $NaHCO_3$, dried ($MgSO_4$), and concentrated *in vacuo*. 3.4 g of the crude product was dissolved in 100 mL of dichloromethane. To the resulting solution was added 34 mL (34 mmol) of 1.0 M DIBAL in hexanes at −78 °C under argon. After stirring for 2 h, 2 mL of MeOH and 20 mL of sat. aq. Rochelle's salt were sequentially added. The resulting white suspension was stirred overnight. The aquesous phase was extracted with 50 mL of dichloromethane (2×). The combined organic phases were dried ($MgSO_4$), concentrated, and chromatographed over 100 g of silica gel with 20% ethyl acetate-hexanes as eluent. 2.4 g (71%) of aldehyde **22** was isolated as a water white oil.

Data for aldehyde **22**: IR (neat) 2955, 2848, 1724, 1472, 1394, 1139 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.71 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.99 (td, *J* = 7.2, 4.4 Hz, 2H, CH_2), 2.59 (td, *J* = 7.2, 1.6 Hz, 2H, $C\underline{H}_2CHO$), 3.42 and 3.58 (ABq, *J* = 10.8 Hz, 4H, 2× OCH_2), 4.51 (t, *J* = 4.4 Hz, 1H, $C\underline{H}(OR)_2$), 9.77 (t, *J* = 1.6 Hz, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.77 (q), 22.92 (q), 27.41 (t), 30.05 (s), 38.04 (t), 77.20 (t), 100.41 (d), 202.10 (d); LRMS $C_9H_{16}O_3 + H^+$ calcd *m*/*z* 173.1, found *m*/*z* 173.3.



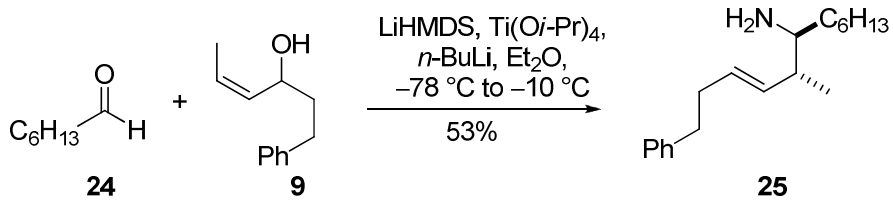
Preparation of (±)-(3*S*,4*R*,*E*)-1-(5,5-dimethyl-1,3-dioxan-2-yl)-4-methyl-8-phenyloct-5-en-3-amine (23):

Flask A**:** To a solution of 688 mg (4.0 mmol) of aldehyde **22** in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –78 °C under argon. The resulting pale yellow solution was stirred for 20 min, then was cannulated into flask B. (see below)

Flask B: To a solution of 1.22 mL (1.14 g, 4.0 mmol) of Ti(O*i*-Pr)$_4$ in 16 mL of anhydrous ether was added 3.2 mL (8.0 mmol) of 2.5 M *n*-BuLi in hexanes at –78 °C under argon. The temperature of the reaction was allowed to raise to –40 °C over 20 min, resulting in an organge solution. To the reaction mixture was introduced *N*-TMS imine prepared in flask A (described above) via cannula. The temperature of the reaction was raised to –10 °C over 1 h, then was kept at –10 °C for 20 min, resulting in a wine-red solution. Next, a solution of lithium alkoxide of alcohol **9** in 4 mL of THF, prepared by deprotonation of 352 mg (2.0 mmol) of alcohol **9** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the wine-red solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred at room temperature for 12 h. Finally, 10 mL of diethyl ether and 5 mL of sat. aq. $NaHCO_3$ were added sequentially and the resulting solution was stirred vigorously for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 100:10:1) to give an inseparable mixture containing 370 mg (56%) of homoallylic amine **23** and 64 mg of amine **S-7** as a colorless oil.

Data for amine **23**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.72 (s, 3H, CH_3), 0.99 (d, *J* = 6.8 Hz, 3H, $CHCH_3$), 1.19 (s, 3H, CH_3), 1.68 (m, 4H, $(CH_2)_2$), 2.03 (m, 1H, C<u>H</u>CH_3), 2.34 (td, *J* = 8.0, 7.2 Hz, 2H, $BnCH_2$), 2.44 (m, 1H, C<u>H</u>NH_2), 2.68 (t, *J* = 7.2 Hz, 2H, $PhC\underline{H}_2$), 3.42 and 3.50 (ABq, *J* = 10.4 Hz, 4H, 2 x OCH_2), 4.41 (t, *J* = 4.8 Hz, 1H, C<u>H</u>$(OR)_2$), 5.27 (m, 1H, -CH_2CH=C<u>H</u>), 5.84 (td, *J* = 13.2, 6.8 Hz, 1H, -CH_2C<u>H</u>=CH), 7.15 - 7.26 (m, 5H, Ph-).

Data for the minor product **S-7**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.72 (s, 3H, CH_3), 0.90 (t, *J* = 7.2 Hz, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.57 (m, 8H, $(C\underline{H}_2)_4CH_3$), 1.71 (m, 4H, $(CH_2)_2$), 2.69 (m, 1H, C<u>H</u>NH), 3.42 and 3.50 (ABq, *J* = 10.4 Hz, 4H, OCH_2), 4.30 (t, *J* = 4.8 Hz, C<u>H</u>$(OR)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.10 (q), 21.85 (q), 22.84 (t), 23.00 (q), 28.33 (t), 30.15 (s), 31.54 (t), 32.31 (t), 37.76 (t), 51.06 (d), 77.23 (t), 102.27 (d); LRMS $C_{13}H_{27}NO_2$ + H^+ calcd m/z 230.2 found m/z 230.4.



24 **9** **25**

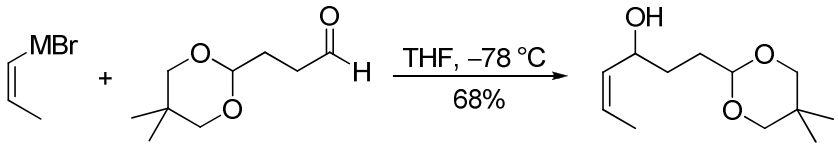
Preparation of (±)-(5*R*,6*S*,*E*)-5-methyl-1-phenyldodec-3-en-6-amine (25):

Flask A**:** To a solution of 456 mg (4.0 mmol) of heptaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –78 °C under argon. The resulting pale yellow solution was stirred for 20 min, then was cannulated into flask B. (see below)

Flask B: To a solution of 1.22 mL (1.14 g, 4.0 mmol) of Ti(O*i*-Pr)$_4$ in 16 mL of anhydrous ether was added 3.2 mL (8.0 mmol) of 2.5 M *n*-BuLi in hexanes at –78 °C under argon. The temperature of the reaction was allowed to rise to –50 °C over 20 min, resulting in an orange solution. To the reaction mixture was introduced the *N*-TMS imine prepared in flask A (described above) via cannula. The temperature of the reaction was raised to –10 °C over 1 h, and then was kept at –10 °C for 20 min, resulting in a wine-red solution.

Next, a solution of lithium alkoxide of alcohol **9** in 4 mL of THF, prepared by deprotonation of 352 mg (2.0 mmol) of alcohol **9** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the wine-red solution via cannula. The mixture was warmed to room temperature over 2 h, then stirred for 12 h. Finally, 10 mL of diethyl ether and 5 mL of sat. aq. $NaHCO_3$ were added and the resulting solution was stirred vigorously for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 200:10:1) to give 270 mg (53%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **25** as a colorless oil.

Data for amine **25**: IR (neat) 3027, 2927, 1603, 1497, 1455, 1377 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74 (t, *J* = 6.8 Hz, 3H, $C\underline{H}_3(CH_2)_5$), 0.81 (dd, *J* = 6.4, 1.2 Hz, 3H, CH_3), 1.13 (br, 10 H, $CH_3(C\underline{H}_2)_5$), 1.24 (br, 2H, NH_2), 1.88 (m, 1H, $C\underline{H}CH_3$), 2.20 (td, *J* = 7.2, 6.8 Hz, 2H, $BnC\underline{H}_2$), 2.30 (m, 1H, $C_6H_{13}C\underline{H}$-), 2.55 (t, *J* = 7.6 Hz, 2H, $PhC\underline{H}_2$), 5.12 (dd, *J* = 14.4, 7.2 Hz, 1H, -CH_2CH=C$\underline{H}$-), 5.32 (td, *J* = 15.2, 6.8 Hz, 1H, -$CH_2C\underline{H}$=CH)), 7.03-7.12 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.11 (q), 17.35 (q), 22.66 (t), 26.27 (t), 29.51 (t), 31.88 (t), 34.47 (t), 34.79 (t), 35.99 (t), 42.68 (d), 55.55 (d), 125.75 (d), 128.25 (d), 128.53 (d), 130.38 (d), 133.33 (d), 141.91 (s); LRMS $C_{19}H_{31}N + H^+$ calcd *m*/*z* 274.3, found *m*/*z* 274.5.

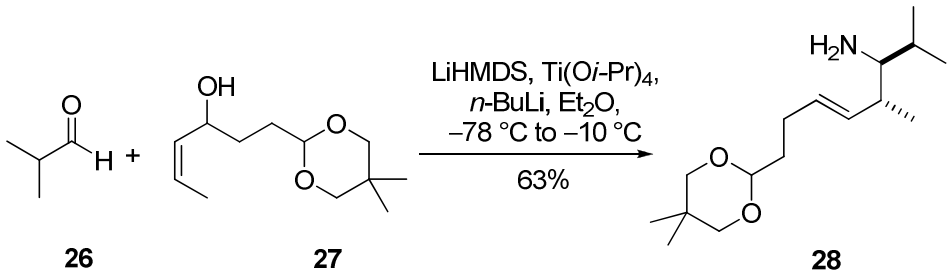


22 **27**

Preparation of (*Z*)-1-(5,5-dimethyl-1,3-dioxan-2-yl)hex-4-en-3-ol (27): To a flame-dried 50 mL 3-neck round bottom flask was charged 600 mg (25.0 mmol) of magnesium turnings and 2 mg of iodine under argon. After introduction of 10 mL of anhydrous THF, the mixture was heated with a heat gun until the color changed from brown to water white. A solution of 0.62 g (5.0 mmol) of (*Z*)-1-bromopropene in 20 mL of anhydrous

THF was added via a syringe at a rate to maintain reflux. After stirring for an additional 2 h at 60 °C, the Grignard solution prepared was cooled to rt, and then was cannulated into a solution of 688 mg (4.0 mmol) of aldehyde **22** in 10 mL of anhydrous THF at –78 °C under argon. After stirring for 2 h, 10 mL of sat. aq. NH_4Cl was added. The aqueous phase was extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (10% ethyl acetate in hexanes) to give 580 mg (68%, d.r. ≥ 20:1, *Z*:*E* ≥ 20:1) of alcohol **27** as a water white oil.

Data for alcohol **27**: IR (neat) 3418, 2593, 2849, 1659, 1471, 1394 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.72 (m, 4H, $(CH_2)_2$), 1.73 (d, *J* = 6.8 Hz, 3H, CH_3), 2.01 (d, *J* = 4.0 Hz, 1H, OH), 3.44 and 3.63 (ABq, *J* = 10.4 Hz, 4H, 2× OCH_2), 4.51 (t, *J* = 4.4 Hz, 1H, C<u>H</u>$(OR)_2$), 4.53 (m, 1H, C<u>H</u>OH), 5.43 (m, 1H, C<u>H</u>=CHCH_3), 5.59 (qd, 1H, CH=C<u>H</u>CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.31 (q), 21.83 (q), 23.01 (q), 30.12 (s), 30.82 (t), 31.66 (t), 67.22 (d), 101.99 (d), 126.16 (d), 133.31 (d); LRMS $C_{12}H_{22}O_3 + H^+$ calcd *m*/*z* 215.2, found *m*/*z* 215.4.



26 **27** **28**

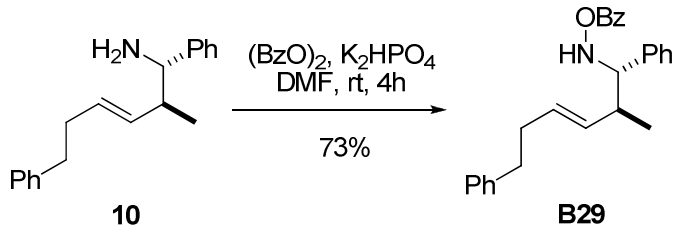
Preparation of (±)-(3*S*,4*R*,*E*)-8-(5,5-dimethyl-1,3-dioxan-2-yl)-2,4-dimethyloct-5-en-3-amine (28):

Flask A**:** To a solution of 288 mg (4.0 mmol) of isobutaldehyde in 10 mL of anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at –78 °C under argon. The resulting pale yellow solution was stirred for 20 min, then was cannulated into flask B. (see below)

Flask B: To a solution of 1.22 mL (1.14 g, 4.0 mmol) of Ti(O*i*-Pr)$_4$ in 16 mL of anhydrous ether was added 3.2 mL (8.0 mmol) of 2.5 M *n*-BuLi in hexanes at –78 °C under argon. The temperature of the reaction was allowed to rise to –40 °C over 20 min, resulting in an orange solution. To the reaction mixture was introduced the *N*-TMS imine prepared in flask A (discussed above) via cannula. The temperature of the reaction was raised to –10 °C over 1 h, and then was kept at –10 °C for 20 min, resulting in a wine-red solution. Next, a solution of lithium alkoxide of alcohol **27** in 4 mL of THF, prepared by deprotonation of 428 mg (2.0 mmol) of alcohol **27** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the wine-red solution via cannula. The mixture was warmed to room temperature over 2 h, and then was stirred for 12 h. Finally, 10 mL of diethyl ether and 5 mL of saturated aqueous $NaHCO_3$ were added and the resulting solution was stirred vigorously for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 200:10:1) to give 343 mg (63%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **28** as a colorless oil.

Data for amine **28**: IR (neat) 3391, 2956, 2847, 1615, 1471 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.65 (s, 3H, CH_3), 0.79 (d, *J* = 6.8 Hz, 3H, CH_3), 0.87 (d, *J* = 6.8 Hz, 3H, $CH(C\underline{H}_3)_2$), 0.90 (d, *J* = 6.8 Hz, 3H, $CH(C\underline{H}_3)_2$), 1.05 (br, 2H, NH_2), 1.12 (s, 3H, CH_3), 1.62 (m, 1H, $C\underline{H}CH_3$), 1.65 (m, 2H, $C\underline{H}_2CH(OR)_2$), 2.08 (m, 2H, $=CHC\underline{H}_2$), 2.09 (m, 1H, $C\underline{H}(CH_3)_2$), 2.18 (d, *J* = 8.8 Hz, 1H, $C\underline{H}NH$), 3.34 and 3.53 (ABq, *J* = 12.8 Hz, 4H, $(-OCH_2)_2$), 4.35 (t, *J* = 4.8 Hz, 1H, $CH(OR)_2$), 5.26 (dd, *J* = 15.2, 8.4 Hz, 1H, $-CH=C\underline{H}CHCH_3$), 5.39 (td, *J* = 15.2, 6.4 Hz, 1H, $CH_2C\underline{H}=CH$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.31 (q), 18.22 (q), 20.74 (q), 21.86 (q), 22.98 (q), 27.14 (t), 29.92 (d), 30.17 (s), 34.70 (t), 40.59 (d), 60.72 (d), 77.24 (t), 101.67 (d), 130.32 (d), 133.52 (d); LRMS $C_{16}H_{31}NO_2 + H^+$ calcd *m*/*z* 270.4, found *m*/*z* 270.4.

Procedure for the preparation of nitrone cyclization products in *Figure 3*:

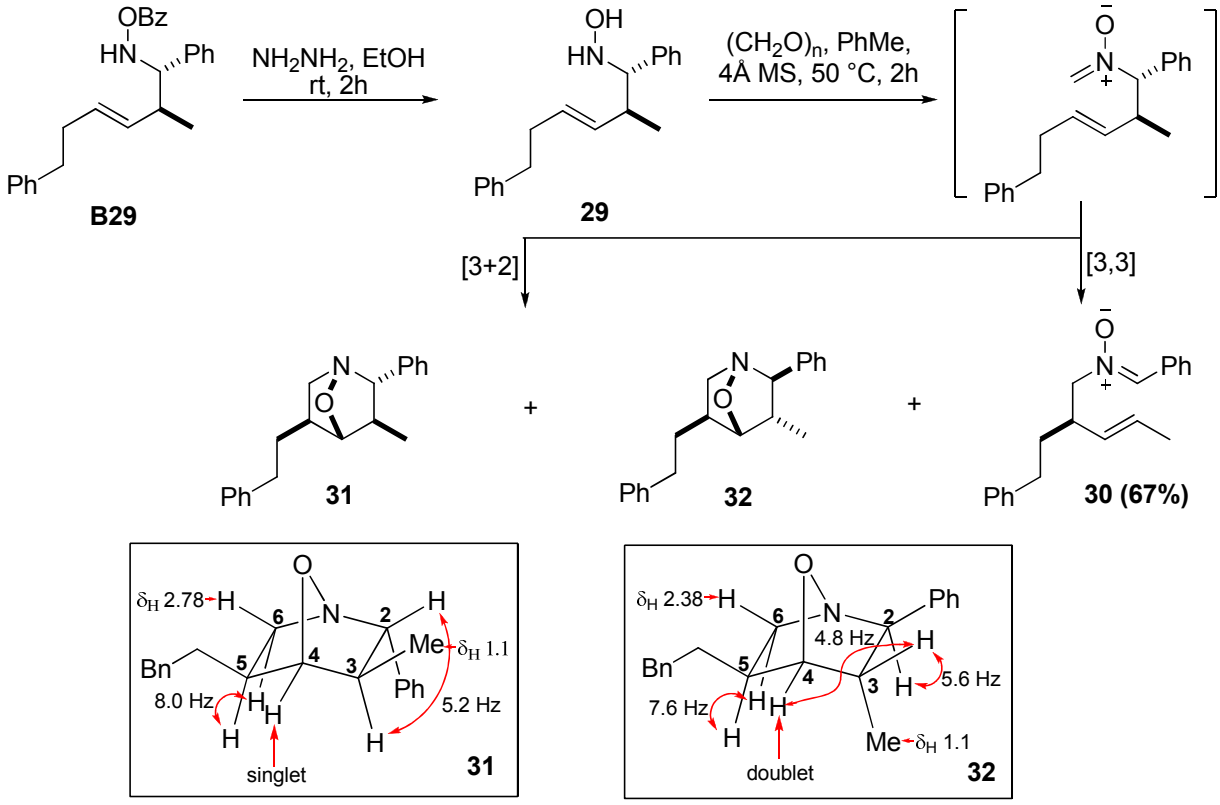


10 **B29**

Preparation of (±)-*O*-benzoyl-*N*-((1*S*,2*S*,*E*)-2-methyl-1,6-diphenylhex-3-enyl)-hydroxylamine (B29): The general procedure of *N*-oxidation was based on work reported by Johnson *et al*.[7] To a suspension of 309 mg (1.28 mmol) of dibenzoyl peroxide and 277 mg (1.59 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 282 mg (1.14 mmol) of amine **10** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. When the reaction appeared complete by TLC, 21 mg (0.26 mmol) of piperidine was added and stirred for 10 min to remove excess dibenzoyl peroxide. (Note: Dibenzoyl peroxide and benzoylamine **B29** are inseparable via column chromatography.) The mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography over 50 g of silica gel, eluting with 5% ethyl acetate in hexanes to give 299 mg (73%) of benzyolamine **B29** as a colorless oil.

Data for benzoylamine **B29**: IR (neat) 3233, 3028, 1721, 1602, 1495, 1453 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.73 (d, *J* = 6.8 Hz, 3H, CH_3), 2.36 (m, 2H, -C<u>H</u>$_2$CH_2Ph), 1.51 (br, 1H, NH), 2.45 (qd, *J* = 9.2, 7.2 Hz, 1H, CH_3C<u>H</u>), 2.69 (t, *J* = 7.6 Hz, 2H, -C<u>H</u>$_2$Ph), 3.70 (dd, *J* = 9.2, 2.8 Hz, 1H, C<u>H</u>NH), 5.38 (m, 1H, CH_2CH=C<u>H</u>-), 5.65 (td, *J* = 15.6, 6.4 Hz, 1H, CH_2C<u>H</u>=CH)), 7.07-7.29 (m, 10H, Ph-), 7.43, 7.74 and 7.95 (m, 5H, C_6<u>H</u>$_5$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.13 (q), 34.38 (t), 35.81 (t), 41.14 (d), 70.13 (d), 125.79 (d), 127.59 (d), 128.10 (d), 128.26 (d), 128.30 (s), 128.40 (d), 128.54 (d), 129.26 (d), 132.11 (d), 132.89 (d), 133.14 (d), 139.91 (s), 141.83 (s), 166.75 (s); LRMS $C_{26}H_{27}NO_2$ + H^+ calcd *m*/*z* 386.2, found *m*/*z* 386.4.

Note: All benzoylamines prepared in this paper could be quantitatively hydrolyzed to their corresponding hydroxylamines (monitored by ^{1}H NMR) upon treatment with hydrazine hydrate in ethanol at ambient temperature for 2-12 h.[8] However, as hydroxylamines were easily oxidized to oximes by air, or decomposed on silica gel, all of them were prepared and used immediately without purification. Each benzoylamine of corresponding hydroxylamine # is labeled as **B#**.



Preparation of (*R,3E,NZ*)-*N*-benzylidene-2-phenethylpent-3-en-1-amine oxide (30), (±)-(2*S*,3*R*,4*S*,5*S*)-3-methyl-5-phenethyl-2-phenyl-7-oxa-1-azabicyclo[2.2.1]-heptanes (31) and (±)-(2*R*,3*S*,4*S*,5*S*)-3-methyl-5-phenethyl-2-phenyl-7-oxa-1-azabicyclo[2.2.1]heptanes (32): To a solution of 100 mg (0.27 mmol) of benzoylamine **B29** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was

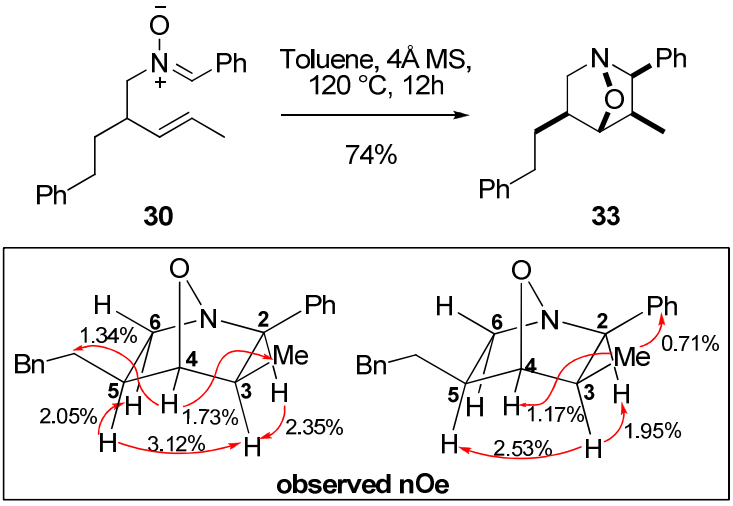
concentrated *in vacuo* again, then was dissolved in 10 mL of anhydrous toluene under argon. The prepared solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves and 42 mg (1.4 mmol) of paraformaldehyde. The reaction was heated at 50 °C for 2 h before cooling down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (20% ethyl acetate in hexanes) to give 53 mg (67%, *E*:*Z* ≥ 20:1) of **30** together with 13 mg (17%) of an inseparable mixture of **31** and **32** (**31** : **32** = 2.5 : 1).

Data for nitrone **(30)**: IR (neat) 3060, 2935, 2855, 1670, 1566, 1494, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.59 and 1.83 (m, 2H, $PhCH_2C\underline{H}_2$), 1.58 (dd, *J* = 6.4, 1.6 Hz, 3H, CH_3), 2.59 and 2.75 (m, 2H, $PhC\underline{H}_2$), 2.99 (m, 1H, $C\underline{H}CH_3$), 3.67 (ABq, *J* = 12.0, 8.0 Hz, 1H, $C\underline{H}_2NO$), 3.87 (ABq, *J* = 12.0, 6.4 Hz, 1H, $C\underline{H}_2NO$), 5.27 (m, 1H, $CH=C\underline{H}CHR$), 5.65 (qd, *J* = 15.2, 6.4 Hz, 1H, $CH_3C\underline{H}=CH$)), 7.17 (s, 1H, $ClC_6H_4C\underline{H}=N$), 7.19-7.28 (m, 5H, Ph-), 7.43 and 8.22 (m, 5H, $C_6\underline{H}_5CH=N$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.06 (q), 33.42 (t), 34.18 (t), 40.95 (d), 72.01 (t), 125.85 (d), 128.38 (d), 128.40 (s), 128.46 (d), 128.54 (d), 129.15 (d), 130.26 (d), 130.39 (s), 130.43 (d), 134.72 (d), 142.04 (s); LRMS $C_{20}H_{23}NO + H^+$ calcd *m*/*z* 294.2, found *m*/*z* 294.5.

Data for oxazabicyclo[2.2.1]heptanes **31**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.10 (d, *J* = 7.2 Hz, 3H, CH_3), 1.51 and 1.74 (m, 2H, $PhCH_2C\underline{H}_2$), 1.78 (m, 1H, C(5)H), 2.02 (dq, *J* = 7.2, 5.2 Hz, 1H, C(3)$\underline{H}CH_3$), 2.38 (ABq, *J* = 12.0, 3.2 Hz, 1H, C(6)$\underline{H}_2$), 2.52 (t, *J* = 8.0 Hz, 2H, $PhC\underline{H}_2$), 2.92 (ABq, *J* = 11.6, 7.6 Hz, 1H, C(6)$\underline{H}_2$), 4.04 (d, *J* = 5.2 Hz, 1H, C(2)$\underline{H}$), 4.14 (s, 1H, C(4)$\underline{H}$), 7.10-7.23 (m, 10H, Ph-).

Data for oxazabicyclo[2.2.1]heptanes **32**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.10 (d, *J* = 7.2 Hz, 3H, CH_3), 1.62 and 1.82 (m, 2H, $PhCH_2C\underline{H}_2$), 2.23 (dq, *J* = 7.2, 5.2 Hz, 1H, C(3)$\underline{H}CH_3$), 2.27 (m, 1H, C(5)H), 2.59 (m, 2H, $PhC\underline{H}_2$), 2.76 (ABq, *J* = 11.6, 4.8 Hz, 1H, C(6)$\underline{H}_2$), 3.00 (ABq, *J* = 11.2, 8.0 Hz, 1H, C(6)$\underline{H}_2$), 3.06 (d, *J* = 5.6 Hz, 1H, C(2)$\underline{H}$), 4.39 (d, *J* = 4.8 Hz, 1H, C(4)$\underline{H}$), 7.10-7.23 (m, 10H, Ph-).

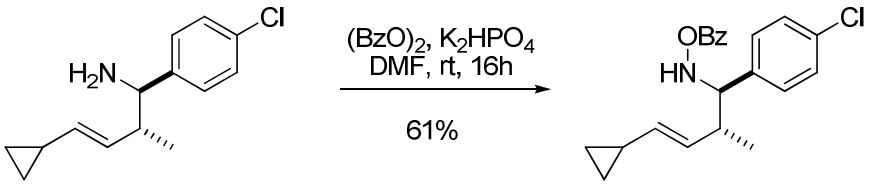
Note: As the minor products **31** and **32** were inseparable, only ^1H NMR and ^1H-^1H COSY were conducted. The structures were assigned based on their coupling constants and comparison with similar compounds.



Preparation of (±)-(2*S*,3*S*,4*R*,5*R*)-3-methyl-5-phenethyl-2-phenyl-7-oxa-1-azabicyclo-[2.2.1]-heptanes (33): To a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves was added a solution of 50 mg (0.19 mmol) of nitrone **30** in 10 mL of anhydrous toluene. The reaction was heated at 120 °C for 12 h before cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 37 mg (74%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptane **33** as a colorless oil. No evidence were found for the production of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **33**: IR (neat) 3061, 2929, 1657, 1494, 1452 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.45 (d, *J* = 7.2 Hz, 3H, CH_3), 1.57 and 1.82 (m, 2H, $PhCH_2C\underline{H}_2$), 1.93 (m, 1H, C(5)H), 2.26 (dq, *J* = 8.0, 7.2 Hz, 1H, C(3)$\underline{H}CH_3$), 2.58 (m, 2H, $PhC\underline{H}_2$), 2.74 (ABq, *J* = 11.6, 4.8 Hz, 1H, C(6)$\underline{H}_2NO$), 3.00 (ABq, *J* = 11.6, 8.0 Hz, 1H, C(6)$\underline{H}_2NO$), 3.88 (d, *J* = 8.0 Hz, 1H, C(2)$\underline{H}NO$), 4.08 (s, 1H, C(4)$\underline{H}$), 7.10-7.23 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.13 (q), 34.13 (t), 35.63 (t), 45.27 (d), 45.27 (d), 63.37 (t), 74.13 (d), 89.03 (d), 125.97 (d), 126.48 (d), 127.60 (d), 127.82 (d), 128.44 (d), 128.46 (s), 139.44 (s), 141.70 (s); HRMS $C_{20}H_{23}NO + H^+$ calcd *m*/*z* 294.1858, found *m*/*z* 294.1856.

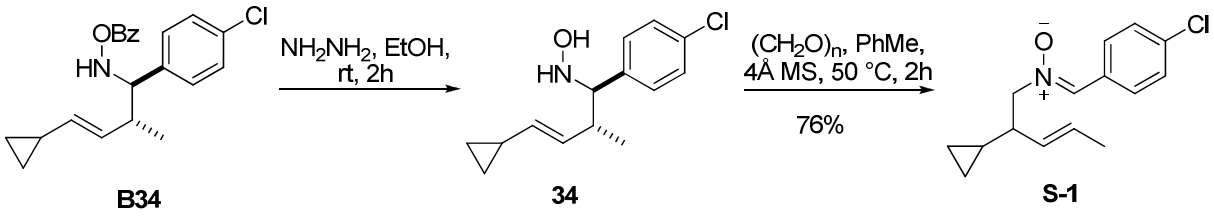
Procedure for the preparation of substituted 1-aza-7-oxabicyclo[2.2.1]heptanes listed in *Table 2*:



19 **B34**

Preparation of (±)-*O*-benzoyl-*N*-((1*R*,2*R*,*E*)-1-(4-chlorophenyl)-4-cyclopropyl-2-methylbut-3-enyl)hydroxylamine (B34): To a suspension of 510 mg (2.1 mmol) of dibenzoyl peroxide and 454 mg (2.61 mmol) of dipotassium hydrogen phosphate in 15 mL of DMF was added a solution of 350 mg (1.48 mmol) of amine **19** in 3 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. When the reaction was judged complete by TLC, 26 mg (0.3 mmol) of piperidine was added and the resulting solution was stirred for 10 min to remove excess dibenzoyl peroxide. (Note: Dibenzoyl peroxide benzoylamine **B34** are inseparable via column chromatography.) The mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 2.5% ethyl acetate in hexanes to give 320 mg (61%) of benzyolamine **B34** as a colorless oil.

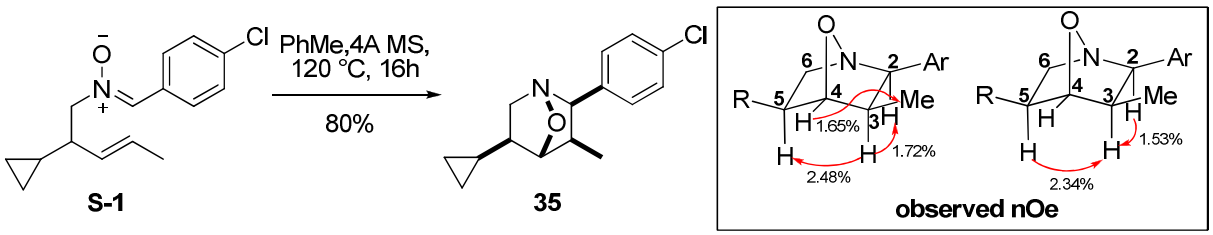
Data for benzoylamine **B34**: IR (neat) 3229, 3063, 2858, 1720, 1585, 1451 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.34 (m, 2H, $CH(C\underline{H}_2)_2$), 0.66 (m, 2H, $CH(C\underline{H}_2)_2$), 0.74 (d, J = 6.8 Hz, 3H, CH_3), 1.37 (m, 1H, $C\underline{H}(CH_2)_2$), 1.50 (s, 1H, NH), 2.39 (qd, J = 8.0, 6.0 Hz, 1H, $C\underline{H}CH_3$), 3.69 (dd, J = 13.2, 3.6 Hz, 1H, $C\underline{H}NH$), 5.14 (dd, J = 15.2, 8.4 Hz, 1H, $CH{=}C\underline{H}CH(CH_2)_2$), 5.41 (dd, J = 15.2, 8.8 Hz, 1H, $CH_3C\underline{H}{=}CH$), 7.12 (m, 4H, Ph-), 7.46, 7.74 and 8.04 (m, 5H, $C_6\underline{H}_5CO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.73 (t), 6.77 (t), 13.59 (d), 18.16 (q), 41.14 (d), 69.63 (d), 128.36 (d), 128.45 (s), 128.46 (d), 128.98 (d), 129.25 (d), 129.41 (d), 133.26 (d), 137.14 (d), 138.70 (s), 166.76 (s); LRMS $C_{21}H_{23}ClNO_2 + H^+$ calcd *m*/*z* 356.1, found *m*/*z* 356.4.



B34 **34** **S-1**

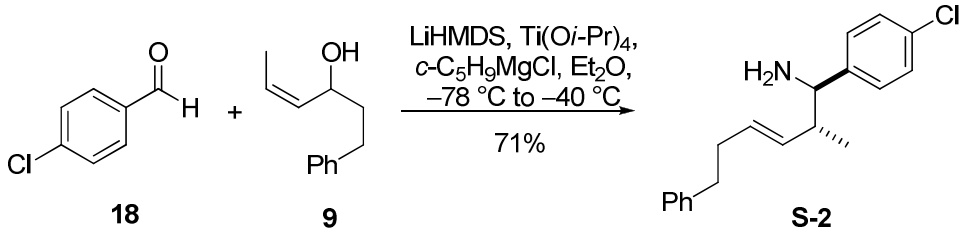
Preparation of (3*E*,*NZ*)-*N*-(4-chlorobenzylidene)-2-cyclopropylpent-3-en-1-amine oxide (S-1): To a solution of 114 mg (0.32 mmol) of benzoylamine **B34** in 10 mL of degassed anhydrous ethanol was added 0.2 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, then was diluted by 10 mL of anhydrous toluene under argon. The solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves and 45 mg (1.6 mmol) of paraformaldehyde. The reaction was heated at 50 °C for 2 h, then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (20% ethyl acetate in hexanes) to give 64 mg (76%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of nitrone **S-1** as a colorless oil.

Data for nitrone **S-1**: IR (neat) 3584, 3401, 2940, 1669, 1588, 1487 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.13 (m, 1H, CH(C$\underline{H}_2$)$_2$), 0.35 (m, 3H, CH(C$\underline{H}_2$)$_2$), 0.48 (m, 1H, C$\underline{H}$(CH$_2$)$_2$), 1.56 (d, *J* = 6.4 Hz, 3H, CH_3), 2.44 (m, 1H, C$\underline{H}CH_3$), 3.52 (ABq, *J* = 11.6, 7.6 Hz, 1H, C$\underline{H}_2$NO), 3.63 (ABq, *J* = 11.6, 7.6 Hz, 1H, C$\underline{H}_2$NO), 5.29 (dd, *J* = 15.6, 7.6 Hz, 1H, CH=C$\underline{H}$CHR), 5.51 (qd, *J* = 15.2, 6.4 Hz, 1H, $CH_3C\underline{H}$=CH)), 6.76 (s, 1H, CH=NO), 7.21 (d, *J* = 8.4 Hz, 2H, ClC$_6\underline{H}_4$CH=NO), 8.23 (d, *J* = 8.8 Hz, 2H, ClC$_6\underline{H}_4$CH=N); ^{13}C NMR (C_6D_6, 100 MHz) δ 2.83 (t), 3.42 (t), 13.45 (d), 17.82 (q), 44.75 (d), 71.70 (t), 127.00 (d), 128.57 (d), 129.24 (d), 129.86 (s), 130.29 (d), 131.85 (d), 134.82 (s); LRMS $C_{15}H_{18}ClNO + H^+$ calcd *m*/*z* 264.1, found *m*/*z* 264.5.



Preparation of (±)-(2*R*,3*R*,4*S*,5*S*)-2-(4-chlorophenyl)-5-cyclopropyl-3-methyl-7-oxa-1-azabicyclo[2.2.1]heptane (35): To a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves was added a solution of 30 mg (0.11 mmol) of nitrone (**S-1**) in 10 mL of anhydrous toluene. The reaction was heated at 120 °C for 12 h, then was cooled down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 24 mg (80%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptane **35** as a colorless oil. No evidence were found for the presence of other isomeric product.

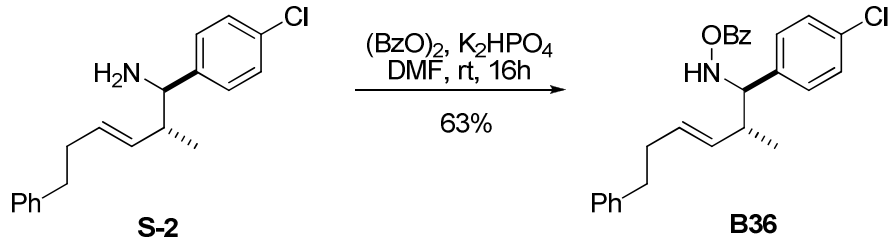
Data for oxazabicyclo[2.2.1]heptane **35**: IR (neat) 3585, 3084, 2980, 1596, 1493, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.05 (m, 1H, CH(C<u>H</u>$_2$)$_2$), 0.15 (m, 1H, CH(C<u>H</u>$_2$)$_2$), 0.44 (m, 2H, CH(C<u>H</u>$_2$)$_2$), 0.46 (d, *J* = 7.2 Hz, 3H, CH_3), 0.76 (m, 1H, C<u>H</u>(CH$_2$)$_2$), 1.32 (m, 1H, C(5)H), 2.21 (dq, *J* = 8.0, 7.2 Hz, 1H, C(3)<u>H</u>CH$_3$), 2.91 (ABq, *J* = 11.6, 4.8 Hz, 1H, C(6)<u>H</u>$_2$NO), 3.01 (ABq, *J* = 11.2, 7.6 Hz, 1H, C(6)<u>H</u>$_2$NO), 3.82 (d, *J* = 8.0 Hz, 1H, C(2)<u>H</u>NO), 4.23 (s, 1H, C(4)<u>H</u>), 7.18 (s, 4H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 3.43 (t), 4.21 (t), 14.92 (d), 16.12 (q), 45.31 (d), 51.43 (d), 63.22 (t), 73.64 (d), 89.75 (d), 127.96 (d), 129.02 (d), 132.20 (s), 138.09 (s); HRMS $C_{15}H_{18}ClNO$ + H^+ calcd *m*/*z* 264.1155, found *m*/*z* 264.1154.



Preparation of (±)-(1*R*,2*R*,*E*)-1-(4-chlorophenyl)-2-methyl-6-phenylhex-3-en-1-amine (S-2): To a solution of 563 mg (4.0 mmol) of 4-chlorobenzaldehyde in 10 mL of

anhydrous ether was added 4.0 mL (4.0 mmol) of 1.0 M LiHMDS in THF at −10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to −78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to −40 °C over 30 min, then stirred at −40 °C for an additional 1.5 h, resulting in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **9** in 4 mL of THF, prepared by deprotonation of 352 mg (2.0 mmol) of alcohol **9** at −78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, and then was stirred for an additional 12 h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 400:10:1) to give 425 mg (71%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **S-2** as a colorless oil.

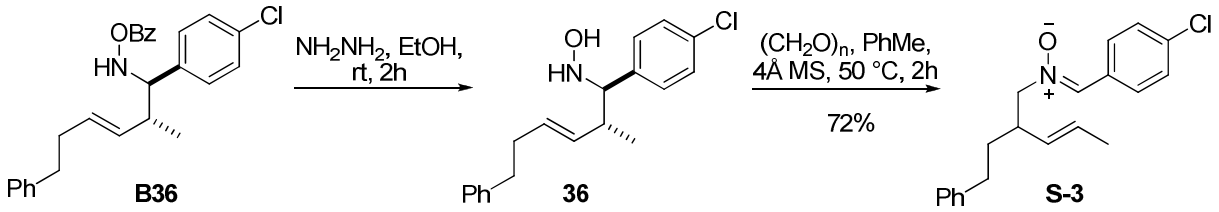
Data for amine **S-2**: IR (neat) 3367, 3026, 2926, 1602, 1487, 1454 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.68 (d, *J* = 6.8 Hz, 3H, CH_3), 1.34 (br, 2H, NH_2), 2.16 (qd, *J* = 8.0, 7.2 Hz, 1H, $CHCH_3$), 2.31 (m, 2H, CH_2), 2.62 (m, 2H, CH_2), 3.43 (d, *J* = 8.0 Hz, 1H, C<u>H</u>NH), 5.17 (m, 1H, CH=C<u>H</u>CH(CH_3)), 5.50 (td, *J* = 15.2, 6.8 Hz, 1H, CH_2C<u>H</u>=CH)), 7.10-7.22 (m, 9H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.96 (q), 34.37 (t), 35.79 (t), 45.20 (d), 60.30 (d), 125.84 (d), 128.29 (d), 128.31 (d), 128.57 (d), 128.72 (d), 131.25 (d), 132.52 (s), 133.74 (d), 141.78(s), 143.21 (s); LRMS $C_{19}H_{22}ClN + H^+$ calcd *m*/*z* 300.2, found *m*/*z* 300.5.



S-2 **B36**

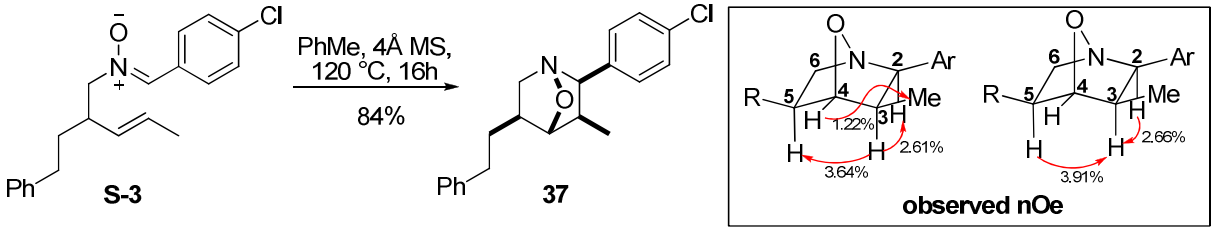
Preparation of (±)-*O*-benzoyl-*N*-((1*R*,2*R*,*E*)-1-(4-chlorophenyl)-2-methyl-6-phenylhex-3-enyl)-hydroxylamine (B36): To a suspension of 290 mg (1.2 mmol) of dibenzoyl peroxide and 261 mg (1.5 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 300 mg (1.0 mmol) of amine **S-2** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. When the reaction was judged complete by TLC, 17 mg (0.2 mmol) of piperidine was added and the resulting solution was stirred for 10 min to remove excess dibenzoyl peroxide. (Note: Dibenzoyl peroxide and benzoylamine **B36** are inseparable via column chromatography.) The mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 2.5% ethyl acetate in hexanes to give 265 mg (63%) of benzyolamine **B36** as a water white oil.

Data for amine **B36**: IR (neat) 3230, 3026, 2929, 1718, 1601, 1490, 1451 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.72 (d, *J* = 6.8 Hz, 3H, CH_3), 1.49 (br, 1H, NH), 2.35 (m, 2H, CH_2), 2.36 (m, 1H, C<u>H</u>CH_3), 2.68 (t, *J* = 7.6 Hz, 2H, PhC<u>H</u>$_2$), 3.67 (dd, *J* = 9.2, 3.6 Hz, 1H, C<u>H</u>NH), 5.34 (m, 1H, CH=C<u>H</u>CH(CH_3)), 5.63 (td, *J* = 15.2, 6.8 Hz, 1H, CH_2C<u>H</u>=CH)), 7.10-7.44 (m, 9H, Ph-), 7.32, 7.74 and 7.91 (m, 5H, C_6<u>H</u>$_5$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.98 (q), 34.32 (t), 35.74 (t), 41.15 (d), 69.41 (d), 125.82 (d), 128.32 (d), 128.38 (d), 128.46 (d), 128.53 (d), 129.25 (d), 129.41 (d), 132.49 (d), 133.25 (s), 133.26 (d), 138.56 (s), 141.73 (s), 166.69 (s); LRMS $C_{26}H_{26}ClNO_2$ + H^+ calcd m/z 420.2 found m/z 420.4.



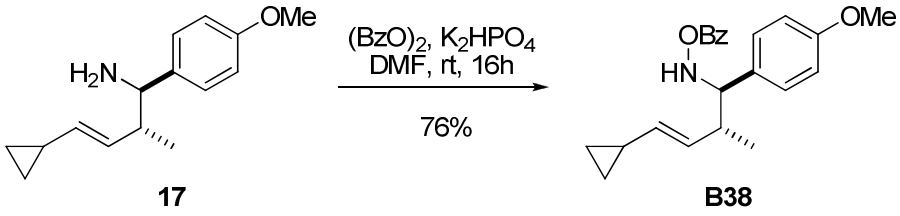
Preparation of (3*E*,*NZ*)-*N*-(4-chlorobenzylidene)-2-phenethylpent-3-en-1-amine oxide (S-3): To a solution of 91 mg (0.21 mmol) of benzoylamine **B36** in 10 mL of degassed anhydrous ethanol was added 0.2 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, and then was dissolved in 10 mL of anhydrous toluene under argon. The solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves and 31.5 mg (1.05 mmol) of paraformaldehyde. The reaction was heated at 50 °C for 2 h, then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (20% ethyl acetate in hexanes) to give 51 mg (72%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of nitrone **S-3** as a colorless oil.

Data for nitrone **S-3**: IR (neat) 3026, 2935, 1587, 1486, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.53 and 1.71 (m, 2H, $PhCH_2C\underline{H}_2$), 1.58 (dd, *J* = 6.4, 1.6 Hz, 3H, CH_3), 2.52 and 2.65 (m, 2H, $PhC\underline{H}_2$), 2.87 (m, 1H, $C\underline{H}CH_3$), 3.67 (ABq, *J* = 12.0, 8.0 Hz, 1H, $C\underline{H}_2NO$), 3.78 (ABq, *J* = 12.0, 6.4 Hz, 1H, $C\underline{H}_2NO$), 5.17 (m, 1H, CH=C<u>H</u>CHR), 5.51 (qd, *J* = 15.2, 6.4 Hz, 1H, $CH_3C\underline{H}$=CH)), 7.09 (s, 1H, $ClC_6H_4C\underline{H}$=N), 7.09-7.21 (m, 5H, Ph-), 7.29 (d, *J* = 8.8 Hz, 2H, $ClC_6\underline{H}_4CH$=N), 8.09 (d, *J* = 8.8 Hz, 2H, $ClC_6\underline{H}_4CH$=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.05 (q), 33.40 (t), 34.16 (t), 41.00 (d), 72.07 (d), 125.89 (d), 128.39 (d), 128.72 (s), 128.83 (s), 129.27 (d), 129.66 (d), 130.30 (d), 133.56 (d), 135.66 (s), 141.96 (s); LRMS $C_{20}H_{22}ClNO + H^+$ calcd *m*/*z* 328.1, found *m*/*z* 328.5.



Preparation of (±)-(2*R*,3*R*,4*S*,5*S*)-2-(4-chlorophenyl)-3-methyl-5-phenethyl-7-oxa-1-azabicyclo-[2.2.1]heptane (37): To a 25 mL sealed tube loaded with 0.5 g of activated 4 Å molecular sieves was added a solution of 25 mg of nitrone **S-3** in 10 mL of anhydrous toluene. The reaction was heated at 120 °C for 12 h, then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5 % ethyl acetate in hexanes) to give 21 mg (84%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptane **37** as a colorless oil. No evidence was found for the presence of other isomeric product.

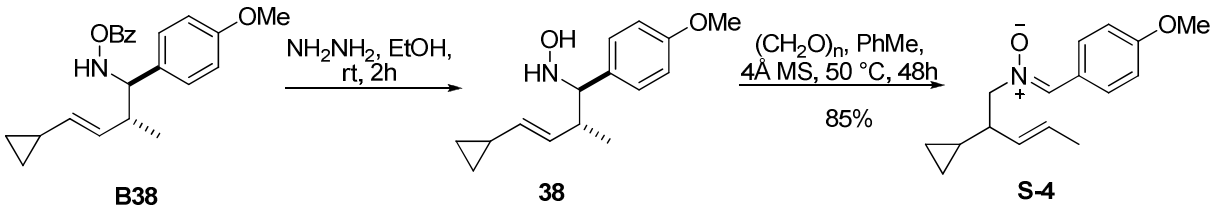
Data for oxazabicyclo[2.2.1]heptane **37**: IR (neat) 3085, 2968, 2930, 1602, 1493, 1454, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.44 (d, *J* = 7.2 Hz, 3H, CH_3), 1.58 and 1.79 (m, 2H, $PhCH_2C\underline{H}_2$), 1.92 (m, 1H, C(5)H), 2.25 (dq, *J* = 8.0, 7.2 Hz, 1H, C(3)$\underline{H}CH_3$), 2.57 (m, 2H, $PhC\underline{H}_2$), 2.73 (ABq, *J* = 11.2, 5.2 Hz, 1H, C(6)$\underline{H}_2NO$), 3.00 (ABq, *J* = 11.2, 7.6 Hz, 1H, C(6)$\underline{H}_2NO$), 3.84 (d, *J* = 8.4 Hz, 1H, C(2)$\underline{H}NO$), 4.07 (s, 1H, C(4)$\underline{H}$), 7.10-7.23 (m, 9H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.16 (q), 34.09 (t), 35.59 (t), 45.25 (d), 45.48 (d), 63.26 (t), 73.52 (d), 89.03 (d), 126.00 (d), 127.97 (d), 128.43 (d), 128.48 (d), 129.00 (d), 132.22 (s), 138.02 (s), 141.61 (s); HRMS $C_{20}H_{22}ClNO + H^+$ calcd *m*/*z* 328.1468, found *m*/*z* 328.1468.



Preparation of (±)-*O*-benzoyl-*N*-((1*R*,2*R*,*E*)-4-cyclopropyl-1-(4-methoxyphenyl)-2-methylbut-3-enyl)hydroxylamine (B38): To a suspension of 484 mg (2.0 mmol) of dibenzoyl peroxide and 436 mg (2.5 mmol) of dipotassium hydrogen phosphate in 10

mL of DMF was added a solution of 384 mg (1.67 mmol) of amine **17** in 5 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. When the reaction was judged complete by TLC, 28 mg (0.33 mmol) of piperidine was added and the resulting solution was stirred for 10 min to remove excess dibenzoyl peroxide. (Note: Dibenzoyl peroxide and benzoylamine **B38** are inseparable via column chromatography.) The mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 2.5% ethyl acetate in hexanes to give 445 mg (76%) of benzyolamine **B38** as a colorless oil.

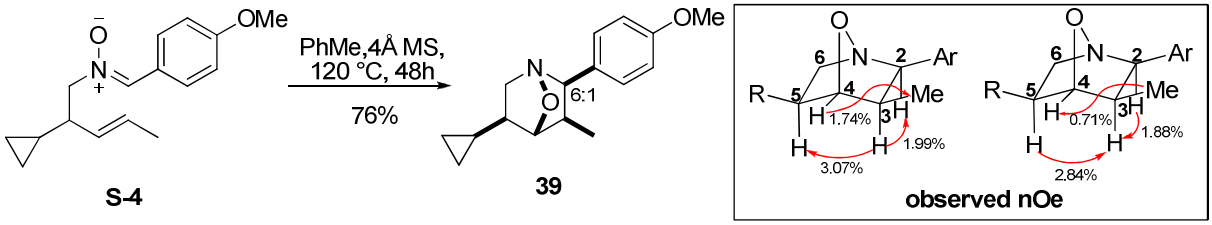
Data for benzoylamine **B38**: IR (neat) 3233, 3069, 2962, 1721, 1612, 1513, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.34 (m, 2H, $CH(C\underline{H}_2)_2$), 0.64 (m, 2H, $CH(C\underline{H}_2)_2$), 0.74 (d, J = 6.8 Hz, 3H, CH_3), 1.35 (m, 1H, $C\underline{H}(CH_2)_2$), 1.60 (br, 1H, NH), 2.41 (m, 1H, $C\underline{H}CH_3$), 3.67 (dd, J = 9.2, 2.8 Hz, 1H, $C\underline{H}NH$), 3.73 (s, 3H, OMe), 5.15 (dd, J = 15.2, 8.4 Hz, 1H, $CH{=}C\underline{H}CH(CH_2)_2$), 5.43 (dd, J = 15.2, 8.8 Hz, 1H, $CH_3C\underline{H}{=}CH$), 6.80 and 7.22 (m, 4H,-$C_6\underline{H}_4OMe$), 7.43, 7.76 and 8.01 (m, 5H, $C_6\underline{H}_5CO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.69 (t), 6.73 (t), 13.62 (d), 18.28 (q), 41.18 (d), 55.22 (q), 69.75 (d), 113.66 (d), 128.38 (d), 129.10 (d), 129.28 (d), 129.68 (d), 132.04 (s), 133.11 (d), 136.48 (d), 159.02 (s), 166.81 (s); LRMS $C_{22}H_{25}NO_3 + Na^+$ calcd m/z 374.2, found m/z 374.3.



Preparation of (3*E*,*NZ*)-2-cyclopropyl-*N*-(4-methoxybenzylidene)pent-3-en-1-amine oxide (S-4): To a solution of 176 mg (0.50 mmol) of benzoylamine **B38** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of

dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, then was dissolved in 10 mL of anhydrous toluene under argon. The solution of hydroxylamine in toluene was added into a 25 mL sealed tube loaded with 0.5 g of activated 4 Å molecular sieves and 30 mg (1.0 mmol) of paraformaldehyde. The reaction was heated at 50 °C for 48 h, then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (20% ethyl acetate in hexanes) to give 110 mg (85%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of nitrone **S-4** as a colorless oil.

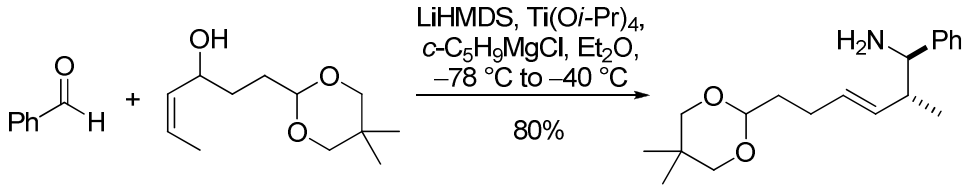
Data for nitrone **S-4**: IR (neat) 3400, 3077, 3001, 2937, 1737, 1603, 1507, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.09 and 0.14 (m, 2H, CH(C<u>H</u>$_2$)$_2$), 0.28 (m, 2H, CH(C<u>H</u>$_2$)$_2$), 0.51 (m, 1H, C<u>H</u>(CH$_2$)$_2$), 1.47 (d, *J* = 6.4 Hz, 3H, CH_3), 2.11 (qd, *J* = 7.6 Hz, 1H, C<u>H</u>CH$_3$), 3.65 (ABq, *J* = 12.0, 8.0 Hz, 1H, C<u>H</u>$_2$NO), 3.76 (ABq, *J* = 11.6, 6.8 Hz, 1H, C<u>H</u>$_2$NO), 3.68 (s, 3H, OMe), 5.19 (dd, *J* = 15.2, 7.6 Hz, 1H, CH=C<u>H</u>CHR), 5.40 (qd, *J* = 15.2, 6.4 Hz, 1H, CH$_3$C<u>H</u>=CH)), 6.76 (d, *J* = 9.2 Hz, 2H, MeOC$_6$<u>H</u>$_4$), 7.10 (s, 1H, C<u>H</u>=NO), 8.05 (d, *J* = 9.2 Hz, 2H, MeOC$_6$<u>H</u>$_4$-); ^{13}C NMR (C_6D_6, 100 MHz) δ 2.80 (t), 3.45 (t), 13.51 (d), 18.09 (q), 44.70 (d), 55.34 (q), 71.62 (t), 113.82 (d), 123.57 (s), 127.52 (d), 129.97 (d), 130.46 (d), 134.44 (d), 160.91 (s); LRMS $C_{16}H_{21}NO_2$ + H^+ calcd *m*/*z* 260.2, found *m*/*z* 260.4.



Preparation of (±)-(2*R*,3*R*,4*S*,5*S*)-5-cyclopropyl-2-(4-methoxyphenyl)-3-methyl-7-oxa-1-azabicyclo[2.2.1]heptane (39): To a 25 mL sealed tube loaded with 0.5 g of activated 4 Å molecular sieves was added a solution of 46 mg (0.18 mmol) of nitrone **S-4** in 10 mL of anhydrous toluene. The reaction was heated at 120 °C for 48 h, then was cooled down to room temperature. The crude solution was concentrated *in vacuo*. The

residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 35 mg (76%, d.r. = 6:1) of oxazabicyclo[2.2.1]heptane **39** as a colorless oil.

Data for oxazabicyclo[2.2.1]heptane **39**: IR (neat) 3583, 3077, 2965, 1614, 1583, 1514, 1463 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.11 (m, 1H, CH(C$\underline{H}_2$)$_2$), 0.23 (m, 1H, CH(C$\underline{H}_2$)$_2$), 0.52 (m, 2H, CH(C$\underline{H}_2$)$_2$), 0.56 (d, *J* = 7.2 Hz, 3H, CH_3), 0.85 (m, 1H, C$\underline{H}$(CH$_2$)$_2$), 1.39 (m, 1H, C(5)H), 2.28 (dq, *J* = 8.0, 7.6 Hz, 1H, C(3)$\underline{H}CH_3$), 3.00 (ABq, *J* = 11.6, 4.8 Hz, 1H, C(6)$\underline{H}_2$NO), 3.10 (ABq, *J* = 11.6, 8.0 Hz, 1H, C(6)$\underline{H}_2$NO), 3.81 (s, 3H, OMe), 3.91 (d, *J* = 8.4 Hz, 1H, C(2)$\underline{H}$NO), 4.31 (s, 1H, C(4)$\underline{H}$), 6.84 (d, *J* = 8.8 Hz, 2H, MeOC$_6\underline{H}_4$-), 7.25 (d, *J* = 8.4 Hz, 2H, MeOC$_6H_4$-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 3.42 (t), 4.20 (t), 14.96 (d), 16.14 (q), 45.51 (d), 51.45 (d), 55.21 (q), 63.31 (t), 73.82 (d), 89.73 (d), 113.20 (d), 128.66 (d), 131.78 (s), 158.17 (s); HRMS $C_{16}H_{21}NO_2$ + H^+ calcd *m*/*z* 260.1651, found *m*/*z* 260.1648.

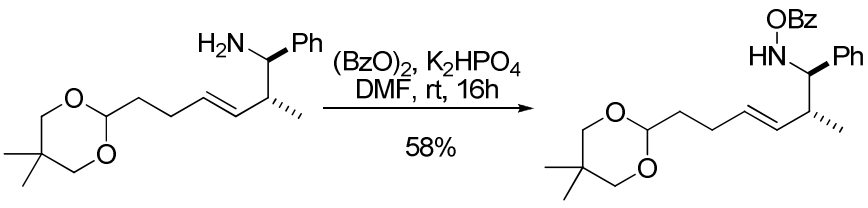


8 **27** **S-5**

Preparation of (±)-(1*R*,2*R*,*E*)-6-(5,5-dimethyl-1,3-dioxan-2-yl)-2-methyl-1-phenylhex-3-en-1-amine (S-5): To a solution of 201 mg (1.9 mmol) of benzaldehyde in 10 mL of anhydrous ether was added 1.9 mL (1.9 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 0.88 mL (0.81 g, 2.85 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 2.95 mL (5.7 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the reaction was raised to –40 °C over 30 min, then was stirred at –40 °C for an additional 1.5 h, resulted in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **27** in 4 mL of

THF, prepared by deprotonation of 203 mg (0.95 mmol) of alcohol **27** at −78 °C with 0.42 mL (1.05 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred for 12 h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 400:10:1) to give 230 mg (80%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of homoallylic amine **S-5** as a colorless oil.

Data for amine **S-5**: IR (neat) 3379, 2953, 1603, 1493, 1470, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.61 (s, 3H, CH_3), 0.66 (d, *J* = 6.8 Hz, 3H, CH_3), 1.08 (s, 3H, CH_3), 1.43 (br, 2H, NH_2), 1.63 (m, 2H, $=CHCH_2$), 2.06 (td, *J* = 7.6, 6.8 Hz, 2H, $C\underline{H}_2CH(OR)_2$), 2.19 (m, 1H, $CH_3C\underline{H}$), 3.30 and 3.49 (ABq, *J* = 10.4 Hz, 4H, $(OCH_2\text{-})_2$), 3.46 (d, *J* = 8.4 Hz, 1H, $PhC\underline{H}$-), 4.32 (t, *J* = 5.2 Hz, 1H, $C\underline{H}(OR)_2$), 5.22 (m, 1H, $CH_3CH=C\underline{H}$-), 5.47 (td, *J* = 14.8, 6.4 Hz, 1H, $CH_2C\underline{H}$=CH)), 7.12-7.21 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.17 (q), 21.85 (q), 23.00 (q), 27.09 (t), 30.17 (s), 34.63 (t), 45.30 (d), 61.01 (d), 77.34 (d), 101.67 (d), 126.97 (d), 127.38 (d), 128.20 (d), 131.21 (d), 133.64 (d), 144.76 (s); LRMS $C_{19}H_{29}NO_2$ + H^+ calcd *m*/*z* 304.2, found *m*/*z* 304.3.

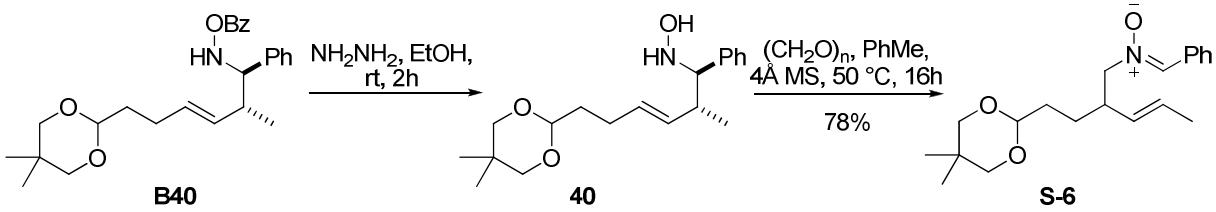


S-5 **B40**

Preparation of (±)-*O*-benzoyl-*N*-((1*R*,2*R*,*E*)-6-(5,5-dimethyl-1,3-dioxan-2-yl)-2-methyl-1-phenylhex-3-enyl)hydroxylamine (B40): To a suspension of 152 mg (0.63 mmol) of dibenzoyl peroxide and 138 mg (0.80 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 160 mg (0.53 mmol) of amine **S-5**

in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. The mixture was poured into 50 mL of deionized water and stirred for 30 min until it turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 20% ethyl acetate in hexanes to give 130 mg (58%) of benzyolamine **B40** as a colorless oil.

Data for benzoylamine **B40**: IR (neat) 3228, 2954, 2848, 1718, 1602, 1494, 1452, 1266 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.64 (s, 3H, CH_3), 0.75 (d, *J* = 6.8 Hz, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.70 (m, 2H, =CHC$\underline{H}_2$), 2.17 (td, *J* = 7.6, 6.8 Hz, 2H, C$\underline{H}_2$CH$(OR)_2$), 2.48 (m, 1H, $CH_3C\underline{H}$), 3.38 (dd, *J* = 10.4, 6.8 Hz, 2H, (OC$\underline{H}_2$-)$_2$), 3.52 (d, *J* = 10.4 Hz, 2H, (OC$\underline{H}_2$-)$_2$), 3.72 (dd, *J* = 9.2, 3.6 Hz, 1H, PhC$\underline{H}$-), 4.42 (t, *J* = 5.2 Hz, 1H, C$\underline{H}(OR)_2$), 5.41 (m, 1H, CH_3CH=C$\underline{H}$-), 5.62 (td, *J* = 15.2, 6.8 Hz, 1H, $CH_2C\underline{H}$=CH)), 7.10-7.29 (m, 5H, Ph-), 7.43, 7.72 and 8.07 (m, 5H, $C_6\underline{H}_5CO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.16 (q), 21.85 (q), 23.03 (q), 27.01 (t), 30.17 (s), 34.32 (t), 41.16 (d), 70.16 (d), 77.17 (d), 101.49 (d), 127.58 (d), 128.09 (d), 128.26 (d), 128.39 (d), 128.51 (s), 129.25 (d), 132.23 (d), 132.57 (d), 133.12 (d), 139.96 (s), 166.71 (s); LRMS $C_{26}H_{33}NO_2$ + H^+ calcd *m*/*z* 424.2, found *m*/*z* 424.2.

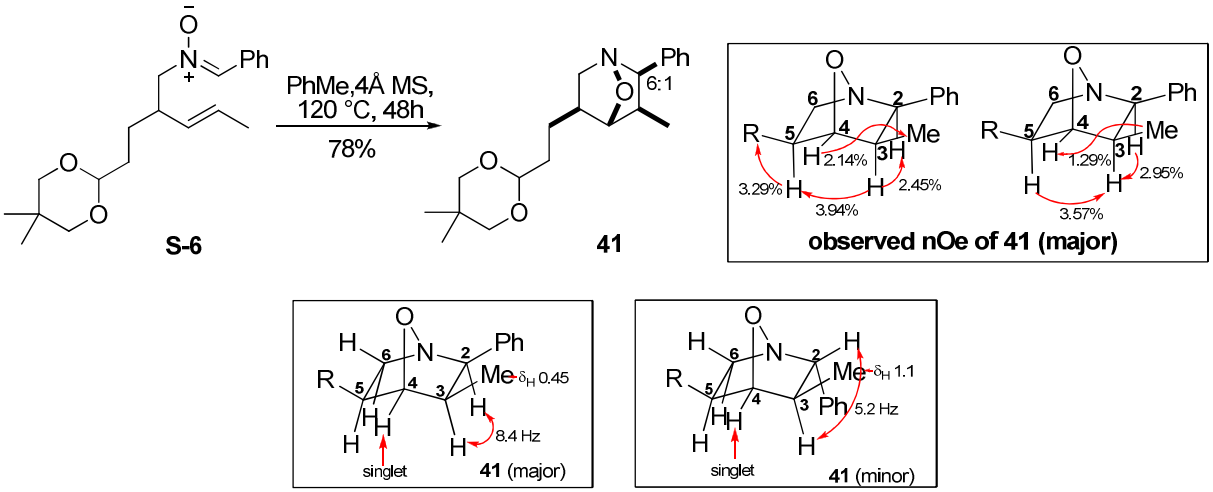


B40 **40** **S-6**

Preparation of (±)-(3*E*,*NZ*)-*N*-benzylidene-2-(2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl)pent-3-en-1-amine oxide (S-6): To a solution of 130 mg (0.31 mmol) of benzoylamine **B40** in 10 mL of degassed anhydrous ethanol was added 0.3 mL of hydrazine hydrate under argon. After stirring for 8 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, then dissolved in 10 mL of anhydrous toluene under argon. The solution of hydroxylamine in toluene was added

into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves and 30 mg (1.0 mmol) of paraformaldehyde. The reaction was heated at 50 °C for 16 h, and then was cooled down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by flash chromatography over 10 g of silica gel (20% to 50% ethyl acetate in hexanes) to give 80 mg (78%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of nitrone **S-6** as a colorless oil.

Data for nitrone **S-6**: IR (neat) 3060, 2936, 1670, 1582, 1567, 1495, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.63 (s, 3H, CH_3), 1.10 (d, *J* = 6.8 Hz, 3H, CH_3), 1.53 (d, *J* = 6.4 Hz, 3H, CH_3), 1.31, 1.53 and 1.67 (m, 4H, =CHCH(CH_2)$_2$-), 2.82 (m, 1H, C(2)HCH=), 3.33 and 3.50 (ABq, *J* = 10.8 Hz, 4H, (OCH_2-)$_2$), 3.66 (ABq, *J* = 11.6, 8.4 Hz, 1H, CH_2NO), 3.77 (ABq, *J* = 11.6, 6.4 Hz, 1H, CH_2NO), 4.34 (t, *J* = 5.6 Hz, 1H, CH(OR)$_2$), 5.11 (m, 1H, CH_3CH=CH-), 5.51 (qd, *J* = 15.2, 6.8 Hz, 1H, CH_2CH=CH-), 7.33 and 8.15 (m, 5H, C_6H_5-), 8.14 (m, 1H, CH=NO); ^{13}C NMR (C_6D_6, 100 MHz) δ 17.99 (q), 21.83 (q), 22.98 (q), 26.42 (t), 32.45 (t), 40.99 (d), 72.00 (t), 77.22 (t), 101.86 (d), 128.43 (d), 128.54 (d), 129.01 (d), 130.20 (d), 130.28 (d), 130.45 (d), 134.68 (s); LRMS: $C_{20}H_{29}NO_3$ + H^+ calcd *m*/*z* 332.2, found *m*/*z* 332.4.

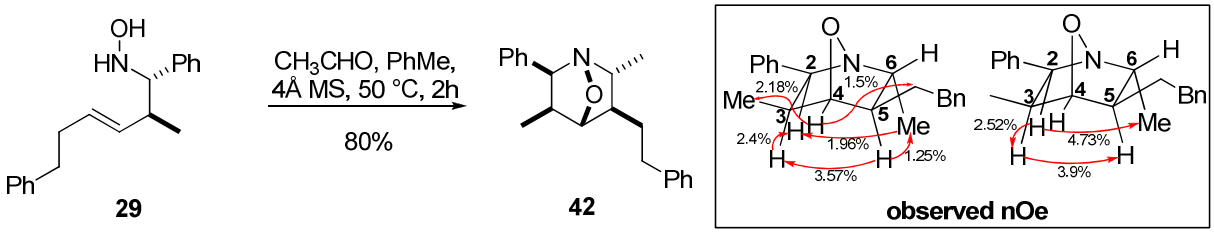


Preparation of (±)-(2*R*,3*R*,4*S*,5*S*)-5-(2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl)-3-methyl-2-phenyl-7-oxa-1-azabicyclo[2.2.1]heptane (41): To a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves was added a solution of 80 mg (0.24 mmol) of nitrone **S-**

6 in 10 mL of anhydrous toluene. The reaction was heated at 120 °C for 48 h, then was cooled down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 62 mg (78%, d.r. = 6:1) of an inseparable mixture of oxazabicyclo[2.2.1]heptane **41** and its diastereomer in a ratio of 6:1 as a colorless oil.

Data for the major product oxazabicyclo[2.2.1]heptane **41**: IR (neat) 3584, 2953, 2850, 1603, 1495, 1471 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.45 (d, *J* = 7.2 Hz, 3H, CH_3), 0.65 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.59 (m, 4H, $(CH_2)_2$), 1.93 (m, 1H, C(5)H), 2.30 (qd, *J* = 8.4, 7.6 Hz, 1H, C(3)$\underline{H}CH_3$), 2.69 (dd, *J* = 11.6, 4.8 Hz, 1H, C(6)$\underline{H}_2$), 3.00 (dd, *J* = 11.6, 7.6 Hz, 1H, C(6)$\underline{H}_2$), 3.35 and 3.53 (ABq, *J* = 10.4 Hz, 4H, $(OCH_2\text{-})_2$), 3.89 (d, *J* = 8.4 Hz, 1H, C(2)H), 4.09 (s, 1H, C(4)H), 4.36 (t, *J* = 4.8 Hz, 1H, $CH(OR)_2$), 7.11-7.29 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.14 (q), 21.85 (q), 23.00 (q), 28.16 (t), 30.15 (s), 33.20 (t), 45.62 (d), 45.80 (d), 63.41 (t), 74.13 (d), 77.35 (t), 89.00 (d), 101.82 (d), 126.45 (d), 127.62 (d), 127.80 (d), 128.58 (d), 139.49 (s); HRMS $C_{20}H_{29}NO_3 + H^+$ calcd *m*/*z* 332.2226, found *m*/*z* 332.2223.

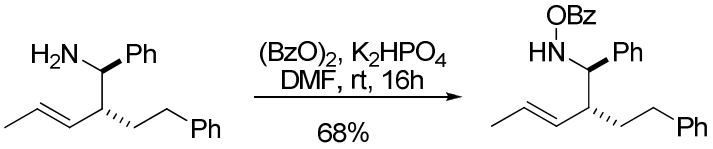
Data for the minor product: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.64 (s, 3H, CH_3), 1.10 (d, *J* = 7.2 Hz, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.53 (m, 4H, $(CH_2)_2$), 1.68 (m, 1H, C(5)H), 2.04 (qd, *J* = 6.8, 5.6 Hz, 1H, C(3)$\underline{H}CH_3$), 2.33 (dd, *J* = 11.6, 4.8 Hz, 1H, C(6)$\underline{H}_2$), 2.89 (dd, *J* = 11.6, 7.6 Hz, 1H, C(6)$\underline{H}_2$), 3.32 and 3.51 (ABq, *J* = 10.4 Hz, 4H, $(OCH_2\text{-})_2$), 4.05 (d, *J* = 5.2 Hz, 1H, C(2)H), 4.14 (s, 1H, C(4)H), 4.31 (t, *J* = 4.8 Hz, 1H, $CH(OR)_2$), 7.11-7.29 (m, 5H, Ph). (Note: Since the major product and minor product were inseparable, this data was based ^1H NMR and COSY of the mixture. The structure of the minor was based on coupling constants of C(2)H, C(3)H, C(4)H and C(5)H as well as chemical shifts of C(6)H_2 and methyl group on C(3)H).



Preparation of (±)-(2*R*,3*R*,4*S*,5*S*,6*S*)-3,6-dimethyl-5-phenethyl-2-phenyl-7-oxa-1-azabicyclo-[2.2.1]heptane (42): To a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves was added a solution of 79 mg (0.25 mmol) of hydroxylamine **29** in 10 mL of anhydrous toluene, followed by addition of 0.1 mL (1.8 mmol) of acetaldehyde via syringe. The reaction was heated at 120 °C for 72 h, then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 65 mg (80%, d.r. = 4:1) of an inseparable mixture of oxazabicyclo[2.2.1]heptane **42** and its diastereomer as a colorless oil.

Data for oxazabicyclo[2.2.1]heptane **42**: IR (neat) 3583, 3077, 2965, 1614, 1583, 1514, 1463 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.45 (d, *J* = 7.2 Hz, 3H, C(3)HC$\underline{H}_3$), 1.22 (d, *J* = 7.2 Hz, 3H, C(6)HC$\underline{H}_3$), 1.35 (m, 1H, C(5)H), 1.64 and 1.75 (m, 2H, C$\underline{H}_2$Bn), 2.19 (qd, *J* = 8.6, 7.2 Hz, 1H, C(3)H), 2.60 (m, 2H, PhC$\underline{H}_2$-), 3.09 (qd, *J* = 8.6, 7.2 Hz, 1H, C(6)$\underline{H}$CH$_3$), 3.98 (s, 1H, C(4)H), 4.33 (d, *J* = 8.4 Hz, 1H, C(2)H), 7.11-7.29 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.58 (q), 16.46 (q), 34.41 (t), 35.39 (t), 46.29 (d), 53.02 (d), 65.06 (d), 68.58 (d), 91.37 (d), 125.96 (d), 126.02 (d), 126.43 (d), 126.46 (d), 126.83 (d), 128.50 (d), 139.63 (s), 141.79 (s); HRMS $C_{21}H_{26}NO + H^+$ calcd *m*/*z* 308.2014, found *m*/*z* 308.2013.

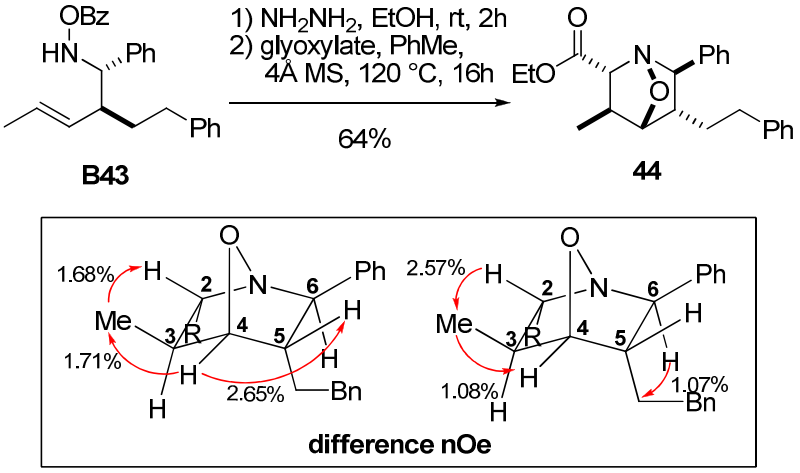
Procedure for the preparation of nitrone cyclization products listed in *Table 3*:



12 **B43**

Preparation of (±)-*O*-benzoyl-*N*-((1*R*,2*R*,*E*)-2-phenethyl-1-phenylpent-3-enyl)-hydroxylamine (B43): To a suspension of 331 mg (1.4 mmol) of dibenzoyl peroxide and 298 mg (1.71 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 301 mg (1.14 mmol) of amine **12** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. When the reaction was judged complete by TLC, 18 mg (0.23 mmol) of piperidine was added and the resulting solution was stirred for 10 min to remove excess dibenzoyl peroxide. (Note: Dibenzoyl peroxide and benzoylamine **B43** are inseparable via column chromatrgraphy.) The mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 2.5% ethyl acetate in hexanes to give 297 mg (68%) of benzyolamine **B43** as a colorless oil.

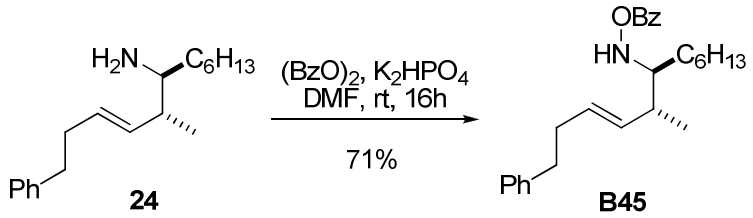
Data for benzoylamine **B43**: IR (neat) 3226, 2919, 1719, 1602, 1585, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.42 and 1.56 (m, 2H, -C<u>H</u>$_2$CH$_2$Ph), 1.58 (br, 1H, NH), 1.86 (dd, *J* = 6.4, 1.6 Hz, 3H, CH_3), 2.38 and 2.66 (m, 2H, -C<u>H</u>$_2$Ph), 2.46 (m, 1H, C<u>H</u>CH$_2$Bn), 3.90 (dd, *J* = 9.6, 3.6 Hz, 1H, C<u>H</u>NH), 5.43 (m, 1H, CH$_3$CH=C<u>H</u>-), 5.74 (qd, *J* = 13.2, 6.8 Hz, 1H, CH$_3$C<u>H</u>=CH)), 7.01-7.40 (m, 10H, Ph-), 7.52, 7.82 and 8.18 (m, 5H, C$_6$<u>H</u>$_5$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.16 (q), 32.69 (t), 33.02 (t), 46.18 (d), 69.15 (d), 125.67 (d), 127.67 (d), 128.21 (d), 128.22 (d), 128.33 (s), 128.40 (d), 129.25 (d), 130.20 (d), 131.30 (d), 133.15 (s), 139.90 (s), 141.97 (s), 166.82 (s); LRMS $C_{26}H_{27}NO_2 + H^+$ calcd *m*/*z* 386.2, found *m*/*z* 386.4.



Preparation of (±)-(2*R*,3*S*,4*S*,5*S*,6*R*)- ethyl 3-methyl-5-phenethyl-6-phenyl-7-oxa-1-azabicyclo-[2.2.1]heptane-2-carboxylate (44): To a solution of 100 mg (0.26 mmol) of benzoylamine **B43** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 6 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, and then was dissolved in 10 mL of anhydrous toluene under argon. The resulting solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 60 µL (60 mg, 0.29 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The temperature of the reaction was heated at 100 °C for 12 h, and then was cooled down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 61 mg (64%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptanes **44** as the a water white oil. No evidence was found for the presence of other isomeric product.

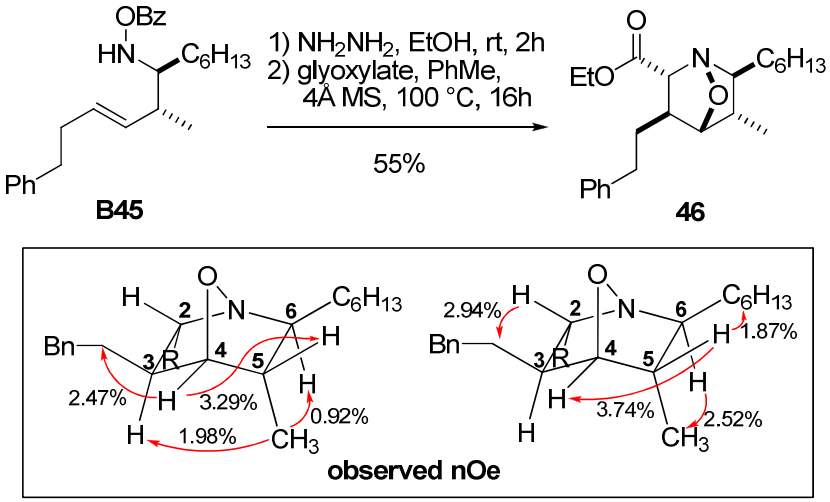
Data for oxazabicyclo[2.2.1]heptane **44**: IR (neat) 3436, 2931, 1732, 1455, 1031 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.02 (d, *J* = 6.8 Hz, 3H, CH_3), 1.22 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$), 1.88 and 2.01 (m, 2H, $PhC\underline{H}_2$-), 2.37 (m, 1H, C(5)$\underline{H}CH_2$-), 2.42 and 2.62 (m, 2H, -$C\underline{H}_2Bn$), 2.58 (m, 1H, C(3)$\underline{H}$), 3.56 (d, *J* = 6.0 Hz, 1H, C(6)$\underline{H}NO$), 3.60 (d, *J* = 6.5 Hz, 1H, C(2)$\underline{H}$), 4.16 (m, 2H, $OC\underline{H}_2CH_3$), 4.23 (d, *J* = 7.2 Hz, 1H, C(4)$\underline{H}$), 7.02-7.31 (m,

10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.21 (q), 18.96 (q), 30.37 (t), 35.57 (t), 35.68 (d), 54.80 (d), 61.44 (t), 71.49 (d), 77.81 (d), 90.12 (d), 126.13 (d), 126.84 (d), 127.17 (d), 128.33 (d), 128.51 (d), 128.52 (d), 141.27 (s), 143.30 (s), 169.26 (s); HRMS $C_{23}H_{27}NO_3$ + H^+ calcd *m*/*z* 366.2069, found *m*/*z* 366.2068.



Preparation of (±)-*O*-benzoyl-*N*-((5*R*,6*S*,*E*)-5-methyl-1-phenyldodec-3-en-6-yl)-hydroxylamine (B45): To a suspension of 160 mg (0.66 mmol) of dibenzoyl peroxide and 144 mg (0.83 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 150 mg (0.55 mmol) of amine **24** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h, and then was poured into 50 mL of deionized water with stirring. After 30 min, the mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 2.5% ethyl acetate in hexanes to give 152 mg (71%) of benzyolamine **B45** as a colorless oil.

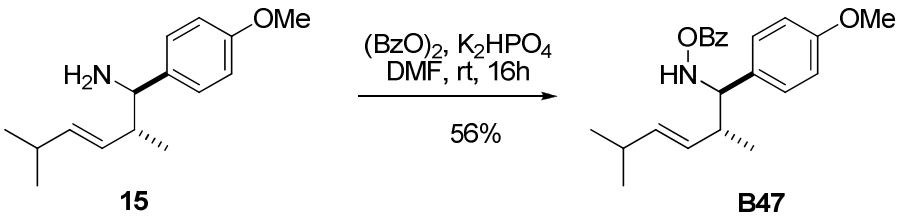
Data for amine **B45**: IR (neat) 3229, 3028, 2919, 1720, 1496, 1452 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (t, *J* = 6.8 Hz, 3H, $C\underline{H}_3(CH_2)_5$), 0.99 (d, *J* = 6.8 Hz, 3H, CH_3), 1.22 and 1.37 (m, 10 H, $CH_3(C\underline{H}_2)_5$), 1.50 (br, 2H, NH), 2.26 (td, *J* = 7.2, 6.8 Hz, 2H, $BnC\underline{H}_2$), 2.35 (qd, *J* = 7.2 Hz, 1H, $C\underline{H}CH_3$), 2.63 (t, *J* = 7.2 Hz, 2H, $PhC\underline{H}_2$), 2.80 (m, 1H, $C_6H_{13}C\underline{H}$-), 5.33 (dd, *J* = 15.2, 7.2 Hz, 1H, -CH_2CH=C$\underline{H}$-), 5.43 (td, *J* = 15.2, 6.8 Hz, 1H, -$CH_2C\underline{H}$=CH)), 7.09-7.40 (m, 5H, Ph-), 7.49, 7.79 and 7.92 (m, 5H, $C_6\underline{H}_5CO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.09 (q), 16.67 (q), 22.63 (t), 26.09 (t), 29.03 (t), 29.52 (t), 31.75 (t), 34.41 (t), 35.90 (t), 38.52 (d), 65.18 (d), 125.73 (d), 128.24 (d), 128.48 (d), 128.51 (d), 129.26 (d), 130.85 (d), 132.78 (d), 133.15 (d), 141.91 (s), 167.0 (s); LRMS $C_{26}H_{35}NO_2$ + H^+ calcd *m*/*z* 394.3, found *m*/*z* 394.5.



Preparation of (±)-(2R,3S,4R,5S,6S)-ethyl 6-hexyl-5-methyl-3-phenethyl-7-oxa-1-azabicyclo-[2.2.1]heptane-2-carboxylate (46): To a solution of 67 mg (0.17 mmol) of benzoylamine **B45** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, and then was dissolved in 10 mL of anhydrous toluene under argon. The prepared solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 36 µL (36 mg, 0.18 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The reaction was heated at 100 °C for 2 h, and then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (10% ethyl acetate in hexanes) to give 35 mg (55%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptanes **46** as a water white oil. No evidence was found for the presence of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **46**: IR (neat) 3438, 3063, 2957, 2928, 1733, 1496, 1455, 1207 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.82 (t, *J* = 7.2 Hz, 3H, CH3), 0.97 (d, *J* = 7.2 Hz, 3H, CH_3), 1.21 (m, 10H, $(CH_2)_5$), 1.68 and 1.78 (m, 2H, BnCH_2-), 1.90 (m, 1H, C(5)HCH_3), 2.23 (td, *J* = 8.4, 5.2 Hz, 1H, C(6)HNO), 2.50 (m, 1H, C(3)H), 2.54 (m, 2H, -CH_2Ph), 3.62 (d, *J* = 5.2 Hz, 1H, C(2)H), 4.15 (m, 2H, OCH_2CH_3), 4.26 (d, *J* = 4.8 Hz, 1H, C(4)H), 7.10-7.22 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.39 (q), 14.09 (q),

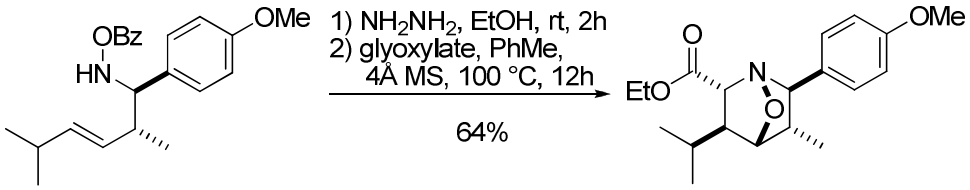
14.12 (q), 22.63 (t), 26.97 (t), 29.23 (t), 31.82 (t), 34.18 (t), 35.30 (t), 35.93 (t), 40.31 (d), 45.52 (d), 61.32 (t), 70.02 (d), 76.51 (d), 89.75 (d), 125.98 (d), 128.36 (d), 128.42 (d), 141.51 (s), 169.12 (s); HRMS $C_{23}H_{35}NO_3$ + H^+ calcd *m*/*z* 374.2695, found *m*/*z* 374.2692.



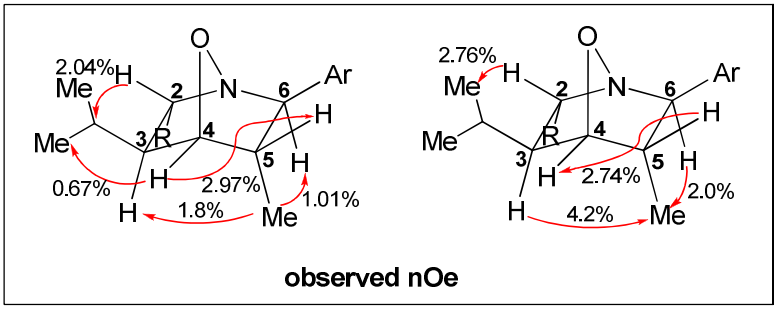
15 **B47**

Preparation of (±)-*O*-benzoyl-*N*-((1*R*,2*R*,*E*)-4-cyclopropyl-1-(4-methoxyphenyl)-2-methylbut-3-enyl)hydroxylamine (B47): To a suspension of 145 mg (0.60 mmol) of dibenzoyl peroxide and 131 mg (0.75 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 120 mg (0.51 mmol) of amine **15** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h, then was poured into 50 mL of deionized water and stirred for 30 min until it turned clear. The reaction mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 5% ethyl acetate in hexanes to give 102 mg (56%) of benzyolamine **B47** as a colorless oil.

Data for benzoylamine **B47**: IR (neat) 3232, 2959, 2869, 1721, 1612, 1512, 1453 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74 (d, *J* = 6.8 Hz, 3H, CH_3), 0.96 (d, *J* = 6.8 Hz, 3H, $CH(C\underline{H}_3)_2$), 0.99 (d, *J* = 6.8 Hz, 3H, $CH(C\underline{H}_3)_2$), 1.50 (br, 1H, NH), 2.26 (m, 1H, $C\underline{H}(CH_3)_2$), 2.42 (m, 1H, $C\underline{H}CH_3$), 3.65 (dd, *J* = 9.2, 3.6 Hz, 1H, $C\underline{H}NH$), 3.75 (s, 3H, OMe), 5.29 (dd, *J* = 15.2, 8.8 Hz, 1H, -CH=$C\underline{H}CHCH_3$), 5.58 (dd, *J* = 15.2, 6.4 Hz, 1H, $(CH_3)_2CHC\underline{H}$=CH), 6.81 and 7.21 (m, 4H, -$C_6\underline{H}_4$OMe), 7.44, 7.75 and 8.12 (m, 5H, $C_6\underline{H}_5CO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.18 (q), 22.52 (q), 22.57 (q), 31.16 (d), 41.20 (d), 55.23 (q), 69.67 (d), 113.64 (d), 128.38 (d), 128.59 (s), 129.10 (d), 129.12 (d), 129.27 (d), 132.15 (s), 133.10 (d), 140.31 (d), 159.00 (s), 166.83 (s); LRMS $C_{22}H_{26}NO_3$ + H^+ calcd *m*/*z* 352.2, found *m*/*z* 352.4.



B47 **48**

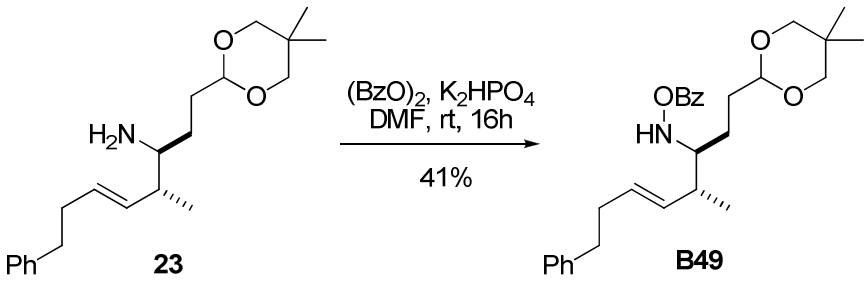


observed nOe

Preparation of (±)-(2*R*,3*S*,4*R*,5*S*,6*R*)-ethyl-3-isopropyl-6-(4-methoxyphenyl)-5-methyl-7-oxa-1-azabicyclo[2.2.1]heptane-2-carboxylate (48): To a solution of 60 mg (0.17 mmol) of benzoylamine **B47** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, and then was dissolved in 10 mL of anhydrous toluene under argon. The resulting solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 40 µL (40 mg, 0.20 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The reaction was heated at 100 °C for 12 h, and then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 36 mg (64%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptanes **48** as a water white oil. No evidence was found for the presence of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **48**: IR (neat) 3435, 2961, 1732, 1612, 1585, 1464 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.92 (d, *J* = 6.8 Hz, 3H, CH_3), 1.02 (d, *J* = 6.4 Hz, 3H, CH_3), 1.23 (d, *J* = 7.2 Hz, 3H, CH_3), 1.30 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$), 1.71 (m, 1H, $C\underline{H}(CH_3)_2$), 2.41 (dd, *J* = 8.8, 6.0 Hz, 1H, C(3)H*i*-Pr), 2.49 (m, 1H, $CH_3C(5)\underline{H}$-), 3.48 (d,

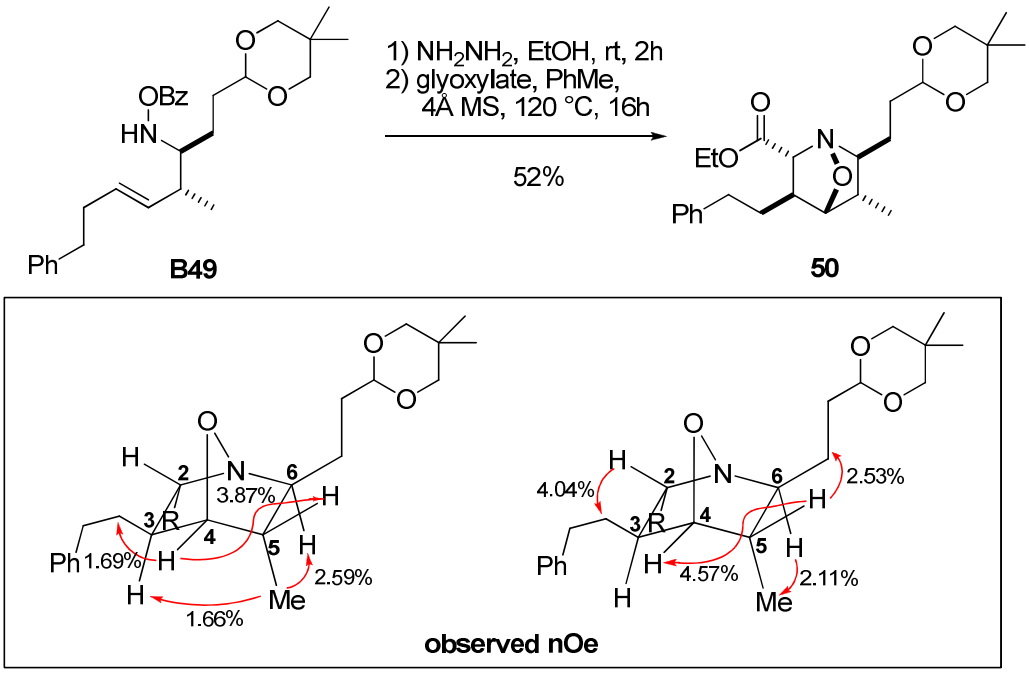
J = 6.4 Hz, 1H, C(6)H), 3.80 (s, 3H, OMe), 3.87 (d, *J* = 5.6 Hz, 1H, C(2)HCO$_2$Et), 4.25 (m, 2H, OC$\underline{H}_2$CH$_3$), 4.65 (d, *J* = 4.4 Hz, 1H, C(4)$\underline{H}$), 6.86 (dd, *J* = 6.8, 2.0 Hz, 2H, C$_6\underline{H}_4$OMe), 7.31 (dd, *J* = 6.8, 2.0 Hz, 2H, C$_6\underline{H}_4$OMe); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 12.19 (q), 14.16 (q), 19.91 (q), 21.26 (d), 30.19 (d), 47.71 (d), 54.30 (q), 61.47 (t), 71.98 (d), 74.70 (d), 88.35 (d), 113.6 (d), 127.66 (d), 135.42 (s), 158.70 (s), 169.49 (s); HRMS C$_{19}$H$_{27}$NO$_4$ + H$^+$ calcd *m*/*z* 334.2018, found *m*/*z* 334.2017.



Preparation of (±)-*O*-benzoyl-*N*-((3*S*,4*R*,*E*)-8-(5,5-dimethyl-1,3-dioxan-2-yl)-2,4-dimethyloct-5-en-3-yl)hydroxylamine (B49): To a suspension of 324 mg (1.34 mmol) of dibenzoyl peroxide and 287 mg (1.65 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 370 mg (1.1 mmol) of amine **23** (contaminated by 64 mg of **S-7**) in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h before pouring into 50 mL of deionized water with stirring. After 30 min, the mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. NaHCO$_3$ solution and 50 mL of brine, dried (MgSO$_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 10% ethyl acetate in hexanes to give 190 mg (41%) of benzyolamine **B49** as a colorless oil (contaminated by inseparable benzoylamine DY-3-38A as noted on ^{1}H NMR spectrum).

Data for benzoylamine **B49**: IR (neat) 3234, 2956, 1721, 1602, 1495, 1452 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.65 (s, 3H, CH$_3$), 0.99 (d, *J* = 6.8 Hz, 3H, CHC$\underline{H}_3$), 1.11 (s, 3H, CH$_3$), 1.74 (m, 4H, (CH$_2$)$_2$), 2.25 (td, *J* = 8.0, 7.2 Hz, 2H, BnCH$_2$), 2.30 (m, 1H, C$\underline{H}$CH$_3$), 2.60 (t, *J* = 7.2 Hz, 2H, PhC$\underline{H}_2$), 2.81 (m, 1H, C$\underline{H}$NH$_2$), 3.33 and 3.50 (ABq, *J* = 10.4 Hz, 4H, OCH$_2$), 4.38 (t, *J* = 4.8 Hz, 1H, C$\underline{H}$(OR)$_2$), 5.31 (m, 1H, -CH$_2$CH=C$\underline{H}$), 5.45

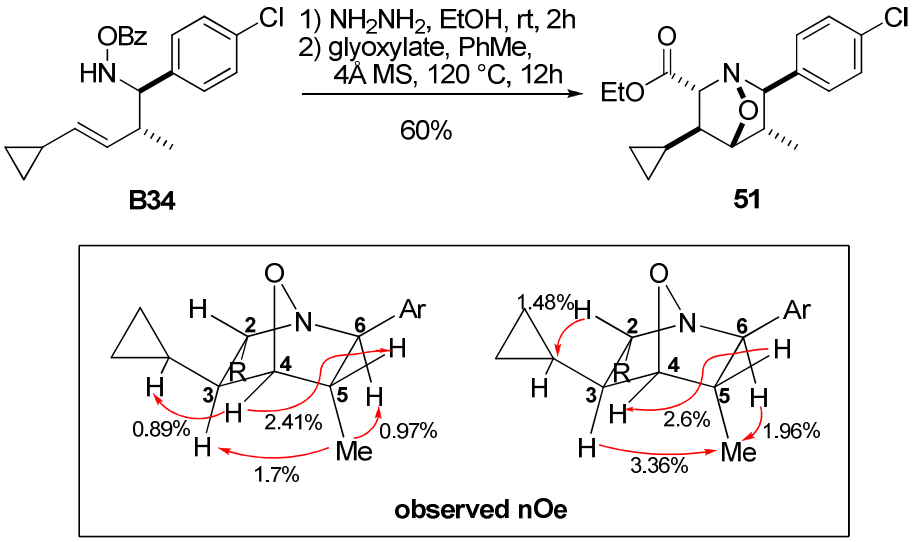
(td, *J* = 13.2, 6.8 Hz, 1H, -CH_2C<u>H</u>=CH), 7.10-7.26 (m, 5H, Ph-), 7.50, 7.82 and 7.95 (m, 5H, C_6<u>H_5</u>CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.87 (q), 21.86 (q), 23.03 (q), 23.45 (t), 30.13 (s), 31.26 (t), 34.42 (t), 35.88 (t), 38.67 (d), 64.85 (d), 77.20 (t), 102.05 (d), 125.73 (d), 128.24 (d), 128.48 (d), 18.78 (s), 129.29 (d), 129.32 (d), 131.11 (d), 132.66 (d), 133.10 (d), 141.93 (s), 166.44 (s); LRMS $C_{28}H_{27}NO_2$ + H^+ calcd *m*/*z* 452.3, found *m*/*z* 452.6.



Preparation of (±)-(2R,3S,4R,5S,6S)-ethyl-6-(2-(5,5-dimethyl-1,3-dioxan-2-yl)ethyl)-5-methyl-3-phenethyl-7-oxa-1-azabicyclo[2.2.1]heptane-2-carboxylate (50): To a solution of 60 mg (0.14 mmol) of benzoylamine **B49** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, and then was dissolved in 10 mL of anhydrous toluene under argon. The prepared solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 40 µL (40 mg, 0.20 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The reaction was heated at

120 °C for 16 h, then was cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 30 mg (52%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptanes **50** as the a water white oil. No evidence was found for the presence of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **50**: IR (neat) 2955, 2850, 1732, 1603, 1496, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.63 (s, 3H, CH_3), 0.96 (d, *J* = 7.2 Hz, 3H, C(5)HC$\underline{H}_3$), 1.10 (s, 3H, CH_3), 1.22 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$)), 1.56 and 1.74 (m, 4H, $(CH_2)_2$), 1.75 (m, 2H, BnC$\underline{H}_2$), 1.92 (qd, *J* = 7.2, 5.2 Hz, 1H, C(5)H), 2.28 (td, *J* = 8.0, 5.2 Hz, 1H, C(6)H), 2.50 (m, 1H, C(3)H), 2.56 (m, 2H, PhC$\underline{H}_2$), 3.32 and 3.51 (ABq, *J* = 11.2 Hz, 4H, -OCH_2), 3.61 (d, *J* = 5.6 Hz, 1H, C(2)H), 4.14 (m, 2H, $OC\underline{H}_2CH_3$), 4.26 (d, *J* = 4.8 Hz, 1H, C(4)H), 4.34 (t, *J* = 4.8 Hz, 1H, C$\underline{H}(OR)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.27 (q), 14.14 (q), 21.84 (q), 23.00 (q), 30.01 (t), 30.12 (s), 32.10 (t), 34.16 (t), 35.28 (t), 40.35 (d), 45.51 (d), 61.35 (t), 69.75 (d), 76.40 (d), 77.18 (t), 89.76 (d), 102.09 (d), 125.97 (d), 128.36 (d), 128.41 (d), 141.51 (s), 169.08 (s); HRMS $C_{25}H_{37}NO_5$ + H^+ calcd *m*/*z* 432.2750, found *m*/*z* 432.2746.

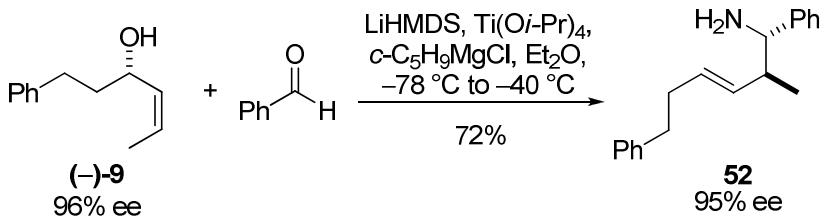


Preparation of (±)-(2*R*,3*S*,4*R*,5*S*,6*R*)-ethyl-6-(4-chlorophenyl)-3-cyclopropyl-5-methyl-7-oxa-1-azabicyclo[2.2.1]heptane-2-carboxylate (51): To a solution of 60 mg (0.17 mmol) of benzoylamine **B34** in 10 mL of degassed anhydrous ethanol was added

0.25 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, and then was dissolved in 10 mL of anhydrous toluene under argon. The prepared solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 50 µL (50 mg, 0.24 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The reaction was heated at 120 °C for 12 h, then cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (10% ethyl acetate in hexanes) to give 32 mg (60%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptanes **51** as a water white oil. No evidence was found for the presence of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **51**: IR (neat) 3435, 3080, 2966, 1645, 1738, 1597, 1493, 1463, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.17 (m, 1H, CH(C$\underline{H}_2$)$_2$), 0.25 (m, 1H, CH(C$\underline{H}_2$)$_2$), 0.48 (m, 2H, CH(C$\underline{H}_2$)$_2$), 0.88 (m, 1H, C$\underline{H}$(CH$_2$)$_2$), 1.10 (d, *J* = 7.2 Hz, 3H, CH_3), 1.21 (t, *J* = 7.2 Hz, 3H, OCH$_2$C$\underline{H}_3$), 1.89 (dd, *J* = 9.6, 5.6 Hz, 1H, C(3)H), 2.34 (m, 1H, C(5)$\underline{H}$CH$_3$), 3.39 (d, *J* = 6.0 Hz, 1H, C(6)$\underline{H}$NO), 3.95 (d, *J* = 4.2 Hz, 1H, C(2)$\underline{H}$), 4.15 (m, 2H, OC$\underline{H}_2$CH$_3$), 4.58 (d, *J* = 4.8 Hz, 1H, C(4)$\underline{H}$), 7.22 (m, 4H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 3.49 (t), 4.59 (t), 12.43 (d), 14.17 (q), 14.67 (q), 46.43 (d), 48.94 (d), 61.52 (t), 71.74 (d), 76.63 (d), 90.72 (d), 127.81 (d), 128.52 (d), 132.81 (s), 141.64 (s), 169.22 (s); HRMS $C_{18}H_{22}ClNO_3$ + H^+ calcd *m*/*z* 336.1366, found *m*/*z* 336.1366.

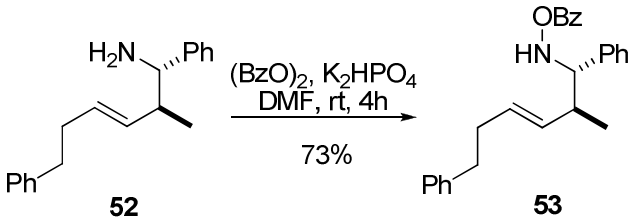
Procedure for the preparation of molecules listed in *Figure 6*:



Preparation of (1*S*,2*S*,*E*)-2-methyl-1,6-diphenylhex-3-en-1-amine (52): To a solution of 424 mg (4.0 mmol) of benzaldehyde in 10 mL of anhydrous ether was added 4.0 mL

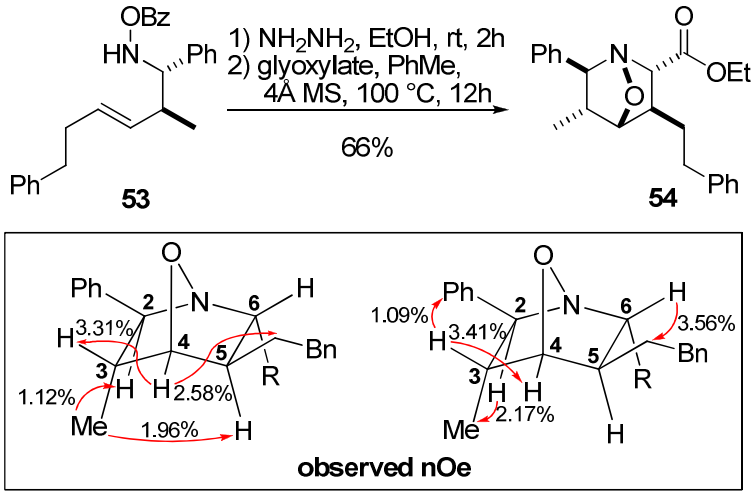
(4.0 mmol) of 1.0 M LiHMDS in THF at –10 °C under argon. The reaction mixture initially appeared milky, then quickly became a clear pale yellow solution. After 20 min, a solution of 1.83 mL (1.70 g, 6.0 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added via a syringe. After stirring for 5 min, the solution was cooled to –78 °C, and 6.0 mL (12.0 mmol) of 2.0 M *c*-C_5H_9MgCl in diethyl ether was added via a syringe over 2 min. The temperature of the solution was raised to –40 °C over 30 min, then the reaction was stirred at –40 °C for an additional 1.5 h, resulted in a dark brown suspension. Next, a solution of lithium alkoxide of alcohol **(–)-9** in 4 mL of THF, prepared by deprotonation of 352 mg (2.0 mmol, 96% ee by Mosher's ester) of alcohol **(–)-9** at –78 °C with 0.88 mL (2.2 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the brown solution via cannula. The mixture was warmed to room temperature over 2 h, then was stirred for 12 h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of saturated aqueous $NaHCO_3$ was followed by vigorous stirring for 1 h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 400:10:1) to give 382 mg (72%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1, 95% ee by Mosher's amide,) of homoallylic amine **52** as a colorless oil.

Data for amine **52**: IR (neat) 3584, 3366, 2958, 1603, 1495, 1454 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.79 (d, *J* = 6.8 Hz, 3H, CH_3), 1.70 (br, 2H, NH_2), 2.31 (qd, *J* = 8.0, 6.8 Hz, 1H, $CHCH_3$), 2.42 (m, 2H, $PhCH_2C\underline{H}_2$-), 2.75 (m, 2H, $PhC\underline{H}_2$), 3.53 (d, *J* = 8.8 Hz, 1H, C<u>H</u>NH), 5.32 (m, 1H, -CH_2CH=C<u>H</u>-), 5.53 (td, *J* = 13.6, 6.4 Hz, 1H, $CH_2C\underline{H}$=CH)), 7.21-7.29 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.13 (q), 34.44 (t), 35.87 (t), 45.24 (d), 60.96 (d), 125.83 (d), 126.99 (d), 127.37 (d), 128.27 (d), 128.32 (d), 128.58 (d), 131.00 (d), 134.13 (d), 141.87 (s), 144.67 (s); LRMS $C_{19}H_{23}N$ + H^+ calcd *m*/*z* 266.2, found *m*/*z* 266.5; $[\alpha]_D^{25}$ = – 57.7° (*c* 0.10, $CHCl_3$).



***O*-benzoyl-*N*-((1*S*,2*S*,*E*)-2-methyl-1,6-diphenylhex-3-enyl)hydroxylamine (53):** To a suspension of 309 mg (1.28 mmol) of dibenzoyl peroxide and 277 mg (1.59 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 282 mg (1.14 mmol) of amine **52** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h. When the reaction was judged complete by TLC, 21 mg (0.26 mmol) of piperidine was added and the resulting solution was stirred for 10 min to remove excess dibenzoyl peroxide. (Note: Dibenzoyl peroxide and benzoylamine **53** are inseparable via column chromatography.) The mixture was poured into 50 mL of deionized water and stirred for 30 min until the suspension turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 5% ethyl acetate in hexanes to give 299 mg (73%) of benzyolamine **53** as a colorless oil.

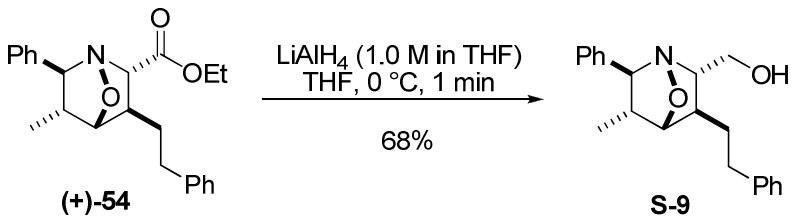
Data for amine **53**: IR (neat) 3233, 3028, 1721, 1602, 1495, 1453 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.73 (d, *J* = 6.8 Hz, 3H, CH_3), 2.36 (m, 2H, -C<u>H</u>$_2$CH_2Ph), 1.51 (br, 1H, NH), 2.45 (qd, *J* = 9.2, 7.2 Hz, 1H, CH_3C<u>H</u>), 2.69 (t, *J* = 7.6 Hz, 2H, -C<u>H</u>$_2$Ph), 3.70 (dd, *J* = 9.2, 2.8 Hz, 1H, C<u>H</u>NH), 5.38 (m, 1H, CH_2CH=C<u>H</u>-), 5.65 (td, *J* = 15.6, 6.4 Hz, 1H, CH_2C<u>H</u>=CH)), 7.07-7.29 (m, 10H, Ph-), 7.43, 7.74 and 7.95 (m, 5H, C_6<u>H</u>$_5$CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.13 (q), 34.38 (t), 35.81 (t), 41.14 (d), 70.13 (d), 125.79 (d), 127.59 (d), 128.10 (d), 128.26 (d), 128.30 (s), 128.40 (d), 128.54 (d), 129.26 (d), 132.11 (d), 132.89 (d), 133.14 (d), 139.91 (s), 141.83(s), 166.75 (s); LRMS $C_{26}H_{27}NO_2$ + H^+ calcd *m*/*z* 386.2, found *m*/*z* 386.4; $[\alpha]_D^{25}$ = + 64.5° (*c* 0.10, $CHCl_3$).



Preparation of (2*S*,3*R*,4*S*,5*R*,6*S*)-ethyl 5-methyl-3-phenethyl-6-phenyl-7-oxa-1-azabicyclo[2.2.1]-heptane-2-carboxylate (54): To a solution of 110 mg (0.28 mmol) of benzoylamine **53** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, then was dissolved in 10 mL of anhydrous toluene under argon. The solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 60 µL (60 mg, 0.29 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The reaction was heated at 100 °C for 12 h, then cooled down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 68 mg (66%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptanes **54** as a water white oil. No evidence was found for the presence of other isomeric product.

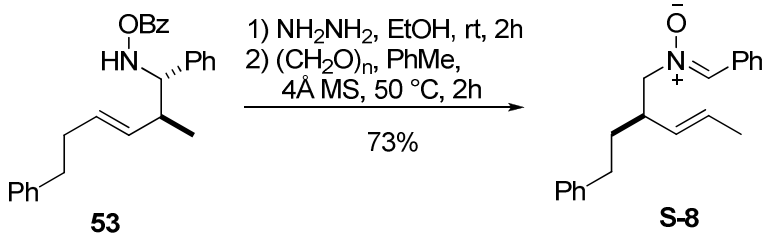
Data for oxazabicyclo[2.2.1]heptane **54**: IR (neat) 3027, 2932, 1733, 1454, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (d, *J* = 6.8 Hz, 3H, CH_3), 1.30 (t, *J* = 6.8 Hz, 3H, $OCH_2C\underline{H}_3$), 1.91 (m, 2H, $BnC\underline{H}_2$-), 2.51 (m, 1H, C(5)$\underline{H}CH_3$), 2.71 (m, 2H, -$C\underline{H}_2Ph$), 2.72 (m, 1H, C(3)$\underline{H}$), 3.57 (d, *J* = 6.0 Hz, 1H, C(6)$\underline{H}$NO), 3.84 (d, *J* = 5.6 Hz, 1H, C(2)$\underline{H}$), 4.24 (m, 2H, $OC\underline{H}_2CH_3$), 4.52 (d, *J* = 4.4 Hz, 1H, C(4)$\underline{H}$), 7.22-7.42 (m, 10H, Ph-); ^{13}C NMR

($CDCl_3$, 100 MHz) δ 12.39 (q), 14.16 (q), 34.21 (t), 35.26 (t), 40.80 (d), 49.11 (d), 61.50 (t), 72.32 (d), 76.58 (d), 89.66 (d), 126.07 (d), 126.45 (d), 127.04 (d), 128.39 (d), 128.48 (d), 141.37 (s), 143.01 (s), 169.22 (s); HRMS $C_{23}H_{27}NO_3$ + H^+ calcd *m*/*z* 366.2069, found *m*/*z* 366.2065; $[\alpha]_D^{25}$ = + 17.7° (*c* 0.10, $CHCl_3$).



(*R*)- and (*S*)-MTPA derivatives for the determination of the absolute configuration of oxazabicyclo[2.2.1]heptane (+)-54: To a solution of 10 mg (0.03 mmol) of oxazabicyclo[2.2.1]heptane **(+)-54** in 1 mL of anhydrous THF was added 0.03 mL (0.03 mmol) of 1.0 M $LiAlH_4$ in THF via a syringe at 0 °C under argon. After 1 min, sequential addition of 0.03 mL of water, 0.03 mL of 1.0 N NaOH and 0.1 mL of water was followed by vigorous stirring for 10 min. The organic phase was concentrated with 0.5 g of silica gel *in vacuo*, and the residue was chromatographed over 2 g of silica gel (Hexanes : EtOAc = 20:1) to give 6 mg (68%, 94% ee by Mosher's ester) of alcohol **S-9** as a colorless oil.

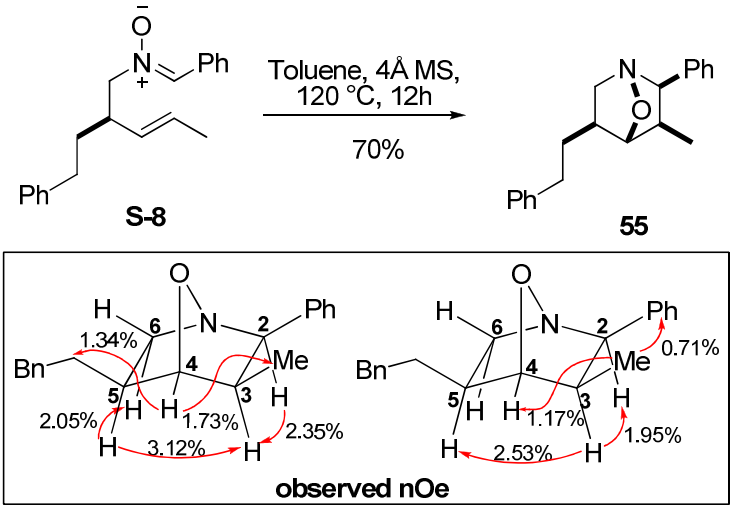
Data for alcohol **S-9**: IR (neat) 3400, 3026, 2926, 1603, 1495, 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.10 (d, *J* = 7.2 Hz, 3H, CH_3), 1.71 and 1.82 (m, 2H, BnC$\underline{H}_2$-), 1.90 (m, 1H, C(5)$\underline{H}CH_3$), 2.37 (m, 1H, C(3)$\underline{H}$), 2.71 (t, *J* = 8.0 Hz, 2H, -C$\underline{H}_2$Ph), 3.26 (m, 1H, C(6)$\underline{H}$NO), 3.66 (d, *J* = 5.6 Hz, 1H, C(2)$\underline{H}$), 3.81 (ABq, *J* = 12.0, 8.4 Hz, 1H, C$\underline{H}_2$OH), 3.86 (ABq, *J* = 12.0, 4.8 Hz, 1H, C$\underline{H}_2$OH), 4.39 (d, *J* = 4.8 Hz, 1H, C(4)$\underline{H}$), 7.22-7.42 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.19 (q), 34.38 (t), 35.18 (t), 39.83 (d), 49.67 (d), 60.96 (t), 69.04 (d), 75.61 (d), 89.26 (d), 126.07 (d), 126.48 (d), 126.90 (d), 128.35 (d), 128.49 (d), 128.51 (d), 141.45 (s), 143.67 (s); LRMS $C_{21}H_{26}NO_2$ + H^+ calcd *m*/*z* 324.2, found *m*/*z* 324.4.



53 **S-8**

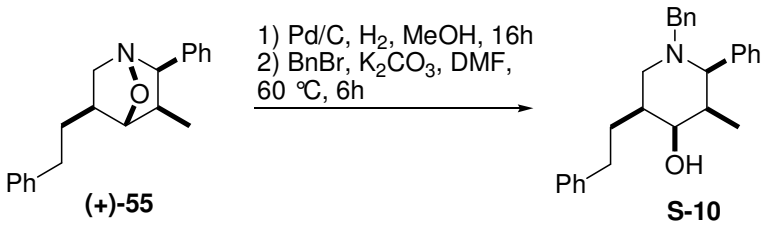
Preparation of (*R,3E,NZ*)-*N*-benzylidene-2-phenethylpent-3-en-1-amine oxide (S-8): To a solution of 110 mg (0.28 mmol) of benzoylamine **53** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, then was dissolved in 10 mL of anhydrous toluene under argon. The prepared solution of hydroxylamine in toluene was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves and 42 mg (1.4 mmol) of paraformaldehyde. The reaction was heated at 50 °C for 2 h before cooling down to room temperature. The crude solution was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (20% ethyl acetate in hexanes) to give 60 mg (73%, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1) of nitrone **S-8** as a colorless oil.

Data for nitrone **S-8**: IR (neat) 3060, 2935, 2855, 1670, 1566, 1494, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.59 and 1.83 (m, 2H, $PhCH_2C\underline{H}_2$), 1.58 (dd, *J* = 6.4, 1.6 Hz, 3H, CH_3), 2.59 and 2.75 (m, 2H, $PhC\underline{H}_2$), 2.99 (m, 1H, $C\underline{H}CH_3$), 3.67 (ABq, *J* = 12.0, 8.0 Hz, 1H, $C\underline{H}_2NO$), 3.87 (ABq, *J* = 12.0, 6.4 Hz, 1H, $C\underline{H}_2NO$), 5.27 (m, 1H, CH=C<u>H</u>CHR), 5.65 (qd, *J* = 15.2, 6.4 Hz, 1H, $CH_3C\underline{H}$=CH), 7.17 (s, 1H, $ClC_6H_4C\underline{H}$=N), 7.19-7.28 (m, 5H, Ph-), 7.43 and 8.22 (m, 5H, $C_6\underline{H}_5CH$=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.06 (q), 33.42 (t), 34.18 (t), 40.95 (d), 72.01 (t), 125.85 (d), 128.38 (d), 128.40 (s), 128.46 (d), 128.54 (d), 129.15(d), 130.26 (d), 130.39 (s), 130.43 (d), 134.72 (d), 142.04 (s); LRMS $C_{20}H_{23}NO + H^+$ calcd *m*/*z* 294.2, found *m*/*z* 294.5.



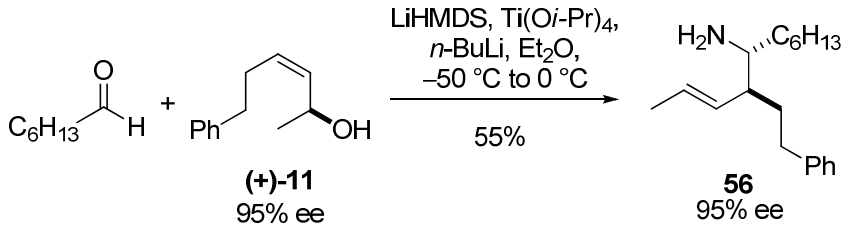
Preparation of (2*S*,3*S*,4*R*,5*R*)-3-methyl-5-phenethyl-2-phenyl-7-oxa-1-azabicyclo-[2.2.1]heptane (55): To a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves was added a solution of 60 mg of nitrone **S-8** in 10 mL of anhydrous toluene. The reaction was heated at 120 °C for 12 h before cooled down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (5% ethyl acetate in hexanes) to give 42 mg (70%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptane **55** as a colorless oil. No evidence was found for the presence of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **55**: IR (neat) 3061, 2929, 1657, 1494, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.45 (d, *J* = 7.2 Hz, 3H, CH_3), 1.57 and 1.82 (m, 2H, $PhCH_2C\underline{H}_2$), 1.93 (m, 1H, C(5)H), 2.26 (dq, *J* = 8.0, 7.2 Hz, 1H, C(3)$\underline{H}CH_3$), 2.58 (m, 2H, $PhC\underline{H}_2$), 2.74 (ABq, *J* = 11.6, 4.8 Hz, 1H, C(6)$\underline{H}_2NO$), 3.00 (ABq, *J* = 11.6, 8.0 Hz, 1H, C(6)$\underline{H}_2NO$), 3.88 (d, *J* = 8.0 Hz, 1H, C(2)$\underline{H}NO$), 4.08 (s, 1H, C(4)$\underline{H}$), 7.10-7.23 (m, 10H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.13 (q), 34.13 (t), 35.63 (t), 45.27 (d), 45.27 (d), 63.37 (t), 74.13 (d), 89.03 (d), 125.97 (d), 126.48 (d), 127.60 (d), 127.82 (d), 128.44 (d), 128.46 (s), 139.44 (s), 141.70 (s); HRMS $C_{20}H_{23}NO + H^+$ calcd *m*/*z* 294.1858, found *m*/*z* 294.1856; $[\alpha]_D^{25}$ = + 30.3° (*c* 0.10, $CHCl_3$).



(*R*)- and (*S*)-MTPA derivatives for the determination of the absolute configuration of oxazabicyclo[2.2.1]heptane (+)-55: To a suspension of 6 mg of Pd/C (5 wt.%) in 2 mL of methanol was added a solution of 10 mg (0.03 mmol) of oxazabicyclo[2.2.1]heptane **(+)-55** in 1 mL of methanol under H_2 at room temperature. After stirring for 16 h, the black suspension was filtered through a celite pad. The filtrate was concentrated *in vacuo*, and the resulting residue was dissolved in 1 mL of anhydrous DMF. To the solution was added sequentially 5 mg (0.03 mmol) of benzyl bromide and 4 mg (0.03 mmol) of K_2CO_3 under argon. The white suspension was stirred at 60 °C for 6 h before pouring into 5 mL of H_2O. After a vigorous stirring for an additional 30 min, the mixture was extracted with 10 mL of EtOAc. The organic phase was dried ($MgSO_4$), concentrated, and chromatographed over 2 g of silica gel (Hexanes : EtOAc = 20 : 1) to give 4 mg (40%, 93% ee by Mosher's ester) of alcohol **S-10** as a colorless oil.

Data for alcohol **S-10**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.62 (d, *J* = 7.2 Hz, 3H, CH_3), 1.29 (d, *J* = 3.6 Hz, 1H, OH), 1.46 and 1.65 (m, 2H, $PhCH_2C\underline{H}_2$), 1.79 (m, 1H, C(5)H), 1.81 (m, 1H, C(3)$\underline{H}CH_3$), 2.08 (ABq, *J* = 12.0 Hz, 1H, C(6)$\underline{H}_2$), 2.53 (m, 2H, $PhC\underline{H}_2CH_2$), 2.62 (ABq, *J* = 12.0, 4.0 Hz, 1H, C(6)$\underline{H}_2NO$), 2.74 and 3.60 (ABq, *J* = 13.6 Hz, 2H, $PhC\underline{H}_2N$), 3.10 (d, *J* = 10.4 Hz, 1H, C(2)$\underline{H}NO$), 3.73 (m, 1H, C(4)$\underline{H}$), 7.10-7.23 (m, 15H, Ph-), LRMS $C_{27}H_{31}NO + H^+$ calcd *m*/*z* 386.2, found *m*/*z* 386.4.



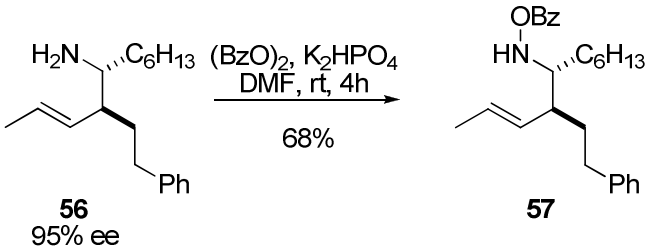
Preparation of (4*S*,5*R*,*E*)-4-phenethylundec-2-en-5-amine (56):

Flask A**:** To a solution of 272 mg (4.0 mmol) of benzaldehyde in 5 mL of anhydrous ether was added 2.4 mL (2.4 mmol) of 1.0 M LiHMDS in THF at –78 °C under argon. The resulting pale yellow solution was stirred for 20 min, then was cannulated into flask B. (see below)

Flask B: To a solution of 0.74 mL (676 mg, 2.38 mmol) of Ti(O*i*-Pr)$_4$ in 10 mL of anhydrous ether was added 1.9 mL (4.76 mmol) of 2.5 M *n*-BuLi in hexanes at –78 ^{o}C under argon. The reaction was allowed to rise to –50 °C over 20 min, resulting in an orange solution. To the reaction mixture was introduced *N*-TMS imine prepared in flask A. The temperature of the reaction was raised to –10 °C over 1 h, then was kept at –10 °C for 20 min, resulted in a wine-red solution. Next, a solution of lithium alkoxide of alcohol **(+)-11** in 2 mL of THF, prepared by deprotonation of 210 mg (1.19 mmol, 95% ee by Mosher's ester) of alcohol **(+)-11** at –78 ^{o}C with 0.52 mL (1.31 mmol) of 2.5 M *n*-BuLi in hexanes followed by 10 min stirring, was added to the wine-red solution at –78 ^{o}C via cannula. The mixture was warmed to room temperature over 2h, then was stirred for an additional 12h. Finally, sequential addition of 10 mL of diethyl ether and 5 mL of sat. aq. $NaHCO_3$ was followed by vigorous stirring for 1h. The aqueous phase was separated and extracted with 10 mL of diethyl ether (2×). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo* to afford a pale yellow oil. The residue was purified by chromatography over 50 g of silica gel (CH_2Cl_2:MeOH:NH_4OH = 400:10:1) to give 180 mg (55% yield, d.r. ≥ 20:1, *E*:*Z* ≥ 20:1, 95% ee by Mosher's amide) of homoallylic amine **56** as a colorless oil.

Data for amine **56**: IR (neat) 3295, 2925, 1603, 1495, 1454, 1377 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (t, *J* = 6.8 Hz, 3H, C$\underline{H}_3$(CH$_2$)$_5$), 1.13-1.40 (br, 10H, CH$_3$(C$\underline{H}_2$)$_5$), 1.66

(dd, J = 6.4, 1.6 Hz, 3H, CH_3), 1.55 and 1.68 (m, Bn$C\underline{H}_2$), 1.85 (m, 1H, $C\underline{H}CH_3$), 2.51 (m, 1H, $C_6H_{13}C\underline{H}$-), 2.38 and 2.60 (m, 2H, Ph$C\underline{H}_2$), 5.20 (dd, J = 13.6, 7.6 Hz, 1H, $CH_3CH{=}C\underline{H}$-), 5.32 (qd, J = 13.6, 6.4 Hz, 1H, $CH_3C\underline{H}{=}CH$)), 7.03-7.16 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.08 (q), 18.18 (q), 22.63 (t), 26.23 (t), 29.48 (t), 31.86 (t), 33.66 (t), 33.90 (t), 35.41 (t), 48.45 (d), 54.57 (d), 125.62 (d), 128.03 (d), 128.26 (d), 128.41 (d), 131.46 (d), 142.79 (s); LRMS $C_{19}H_{31}N + H^+$ calcd m/z 274.3, found m/z 274.4; $[\alpha]_D^{25}$ = + 5.6° (c 0.10, $CHCl_3$).



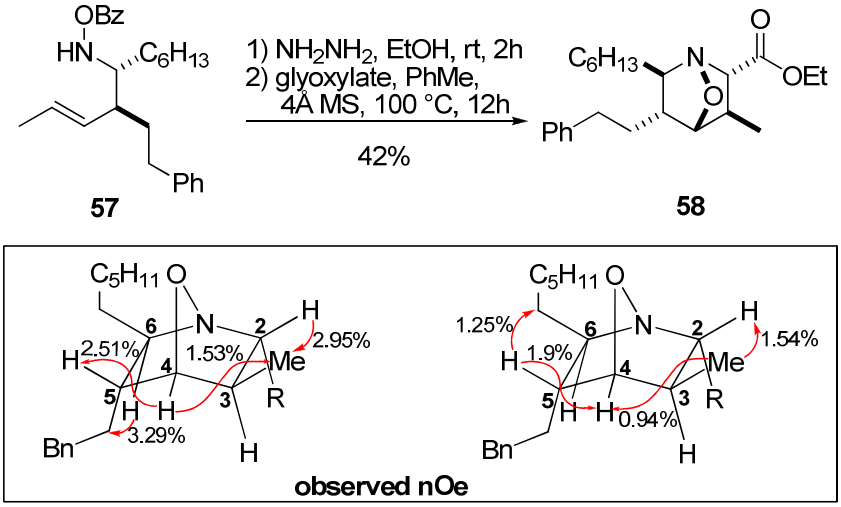
56
95% ee

57

Preparation of *O*-benzoyl-*N*-((4*S*,5*R*,*E*)-4-phenethylundec-2-en-5-yl)hydroxylamine (57): To a suspension of 119 mg (0.49 mmol) of dibenzoyl peroxide and 108 mg (0.62 mmol) of dipotassium hydrogen phosphate in 10 mL of DMF was added a solution of 112 mg (0.41 mmol) of amine **56** in 2 mL of DMF under argon. The suspension was stirred at room temperature for 16 h before pouring into 50 mL of deionized water and stirred for 30 min until it turned clear. The mixture was extracted with 50 mL of ethyl acetate (2×). The organic phase was washed with 50 mL of sat. aq. $NaHCO_3$ solution and 50 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography with 50 g of silica gel, eluting with 5% ethyl acetate in hexanes to give 110 mg (68%) of benzyolamine **57** as a colorless oil.

Data for benzoylamine **57**: IR (neat) 2929, 2857, 1719, 1602, 1452, 1270 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (t, J = 6.8 Hz, 3H, $C\underline{H}_3(CH_2)_5$), 1.21 and 1.32 (m, 10 H, $CH_3(C\underline{H}_2)_5$), 1.50 (br, 1H, NH), 1.60 and 1.84 (m, 2H, Bn$C\underline{H}_2$), 1.67 (dd, J = 6.4, 1.2 Hz, 3H, CH_3), 2.18 (m, 1H, $C\underline{H}CH_2$Bn), 2.41 and 2.63 (m, 2H, Ph$C\underline{H}_2$), 2.87 (m, 1H, $C_6H_{13}C\underline{H}$-), 5.28 (dd, J = 16.8, 9.2 Hz, 1H, $CH_3CH{=}C\underline{H}$-), 5.44 (qd, J = 16.8, 6.4 Hz, 1H, $CH_3C\underline{H}{=}CH$)), 7.16-7.30 (m, 5H, Ph-), 7.50, 7.84 and 7.92 (m, 5H, $C_6\underline{H}_5CO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.07 (q), 18.13 (q), 22.60 (t), 25.96 (t), 29.47 (t), 29.62 (t), 31.71 (t),

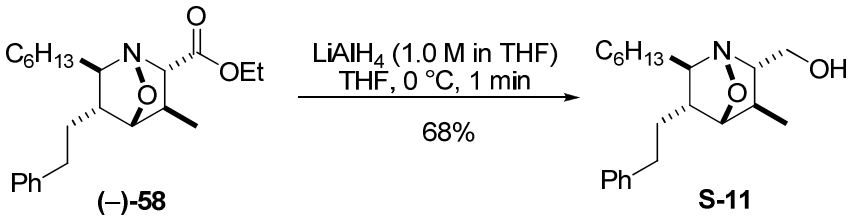
32.91 (t), 33.76 (t), 44.44 (d), 64.42 (d), 125.68 (d), 128.27 (d), 128.46 (d), 128.49 (d), 128.68 (s), 128.77 (d), 129.26 (d), 131.12 (d), 133.15 (d), 142.42 (s), 166.63 (s); LRMS $C_{26}H_{35}NO_2 + H^+$ calcd *m*/*z* 394.3, found *m*/*z* 394.4; $[\alpha]_D^{25} = -13.9°$ (*c* 0.10, $CHCl_3$).



Preparation of (2*S*,3*R*,4*R*,5*R*,6*R*)-ethyl 6-hexyl-3-methyl-5-phenethyl-7-oxa-1-azabicyclo[2.2.1]-heptane-2-carboxylate (58): To a solution of 80 mg (0.20 mmol) of benzoylamine **57** in 10 mL of degassed anhydrous ethanol was added 0.5 mL of hydrazine hydrate under argon. After stirring for 4 h, the crude solution was concentrated *in vacuo*, then dissolved in 10 mL of dichloromethane under argon. The dichloromethane solution was concentrated *in vacuo* again, then was dissolved in 10 mL of anhydrous toluene under argon. The prepared toluene solution of hydroxylamine was added into a 25 mL sealed tube with 0.5 g of activated 4 Å molecular sieves. A solution of 42 µL (42 mg, 0.21 mmol) of ethyl glyoxylate (50% wt in H_2O) was added to the reaction mixture via a syringe. The reaction was heated at 100 °C for 12 h before cooling down to room temperature. The crude was concentrated *in vacuo*. The residue was purified by chromatography over 10 g of silica gel (10% ethyl acetate in hexanes) to give 32 mg (42%, d.r. ≥ 20:1) of oxazabicyclo[2.2.1]heptane **58** as a water white oil. No evidence was found for the presence of other isomeric product.

Data for oxazabicyclo[2.2.1]heptane **58**: IR (neat) 3437, 2930, 2858, 1733, 1454, 1377, 1202 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.80 (t, *J* = 7.2 Hz, 3H, CH3), 0.96 (d, *J* = 7.2

Hz, 3H, CH_3), 1.19 and 1.45 (m, 10H, $(CH_2)_5$), 1.22 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$), 1.75 (m, 2H, $BnC\underline{H}_2$-), 1.83 (m, 1H, C(5)$\underline{H}CH_3$), 2.32 (td, *J* = 8.4, 5.2 Hz, 1H, C(6)$\underline{H}$NO), 2.49 (m, 1H, C(3)$\underline{H}$), 2.51 (m, 2H, -$C\underline{H}_2$Ph), 3.50 (d, *J* = 5.2 Hz, 1H, C(2)$\underline{H}$), 4.15 (m, 2H, $OC\underline{H}_2CH_3$), 4.16 (d, *J* = 4.0 Hz, 1H, C(4)$\underline{H}$), 7.11-7.23 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.10 (q), 14.14 (q), 18.98 (q), 22.63 (t), 27.20 (t), 29.22 (t), 30.14 (t), 31.82 (t), 35.18 (d), 35.71 (t), 36.42 (t), 51.57 (d), 61.27 (t), 68.80 (d), 77.73 (d), 90.24 (d), 126.10 (d), 128.31 (d), 128.50 (d), 141.45 (s), 169.13 (s); HRMS $C_{23}H_{35}NO_3 + H^+$ calcd *m*/*z* 374.2695, found *m*/*z* 374.2694; $[\alpha]_D^{25} = -39.0°$ (*c* 0.10, $CHCl_3$).



(–)-58 **S-11**

(*R*)- and (*S*)-MTPA derivatives for the determination of the absolute configuration of oxazabicyclo[2.2.1]heptane (–)-58: To a solution of 10 mg (0.03 mmol) of oxazabicyclo[2.2.1]heptane **(–)-58** in 1 mL of anhydrous THF was added 0.03 mL (0.03 mmol) of 1.0 M $LiAlH_4$ in THF at 0 °C under argon. After 1 min, sequential addition of 0.03 mL of water, 0.03 mL of 1.0 N NaOH and 0.1 mL of water was followed by vigorous stirring for 10 min. The organic phase was concentrated with 0.5 g of silica gel *in vacuo*, and the residue was chromatographed over 2 g of silica gel (Hexanes : EtOAc = 40:1) to give 6 mg (68%, 93% ee by Mosher's ester) of alcohol **S-11** as a colorless oil.

Data for alcohol **S-11**: IR (neat) 3400, 3027, 2926, 2856, 145a, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.80 (t, *J* = 7.2 Hz, 3H, CH_3), 0.92 (d, *J* = 7.2 Hz, 3H, CH_3), 1.20 and 1.50 (m, 10H, $(CH_2)_5$), 1.69 (m, 2H, $BnC\underline{H}_2$-), 1.75 (m, 1H, C(5)$\underline{H}CH_3$), 2.49 (m, 1H, C(3)$\underline{H}$), 2.52 (m, 1H, C(2)H), 2.54 (m, 2H, -$C\underline{H}_2$Ph), 3.03 (td, *J* = 8.4, 5.6 Hz, 1H, C(6)$\underline{H}$NO), 3.74 (ABq, m, 2H, $C\underline{H}_2$OH), 4.14 (d, *J* = 4.4 Hz, 1H, C(4)$\underline{H}$), 7.11-7.23 (m, 5H, Ph-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.10 (q), 18.98 (q), 22.61 (t), 27.25 (t), 29.27 (t), 30.28 (t), 31.81 (t), 35.10 (d), 35.80 (t), 36.44 (t), 51.91 (d), 61.06 (t), 65.03 (d),

76.58 (d), 89.86 (d), 126.14 (d), 128.25 (d), 128.53 (d), 141.50 (s); LRMS $C_{21}H_{33}NO_2$ + H^+ calcd *m*/*z* 332.3, found *m*/*z* 332.4.

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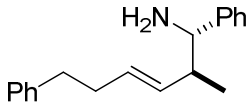
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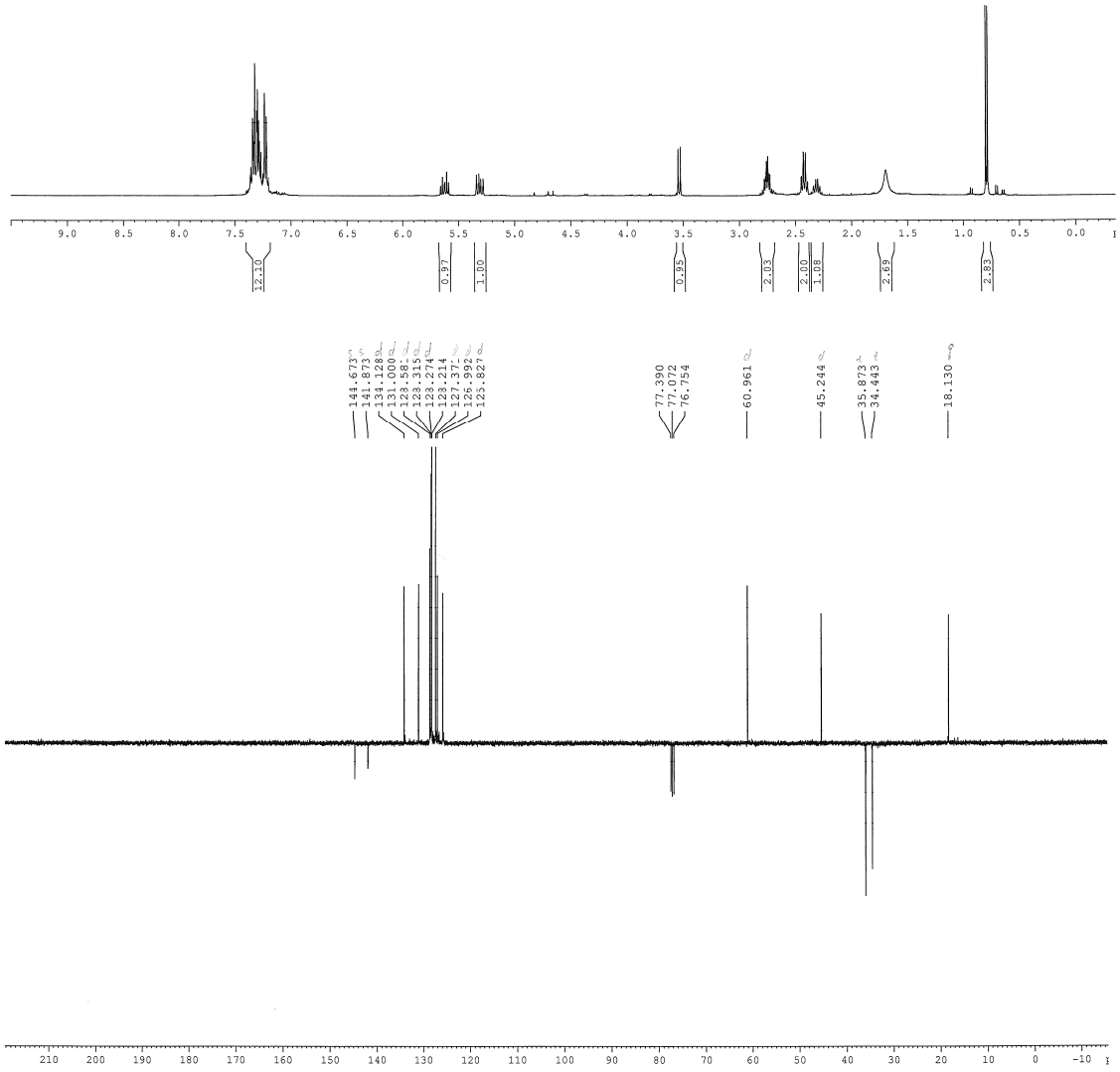
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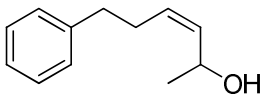
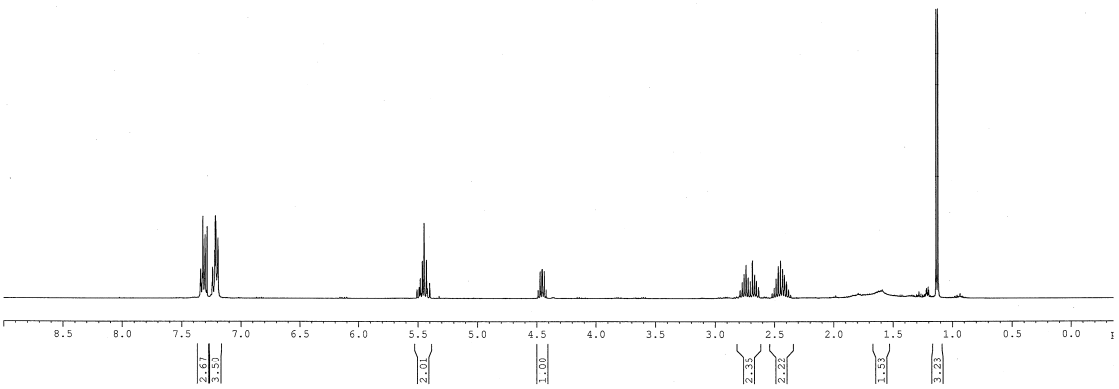
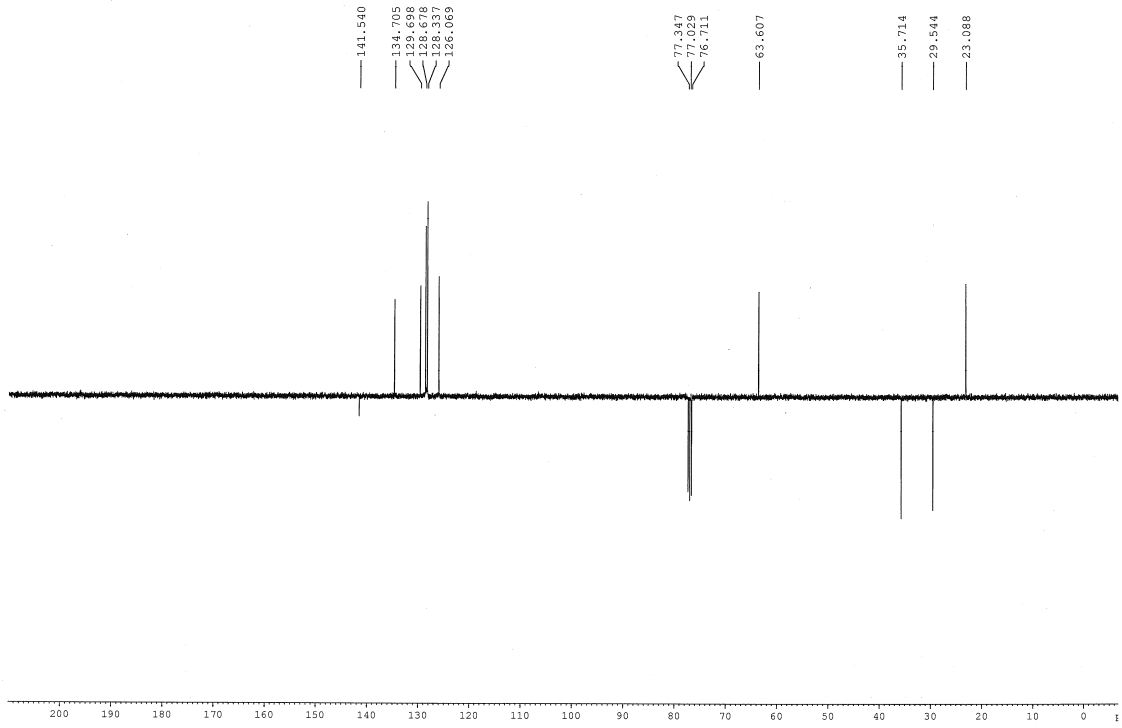
18.130

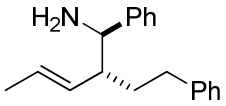


11 (DY-2-255)

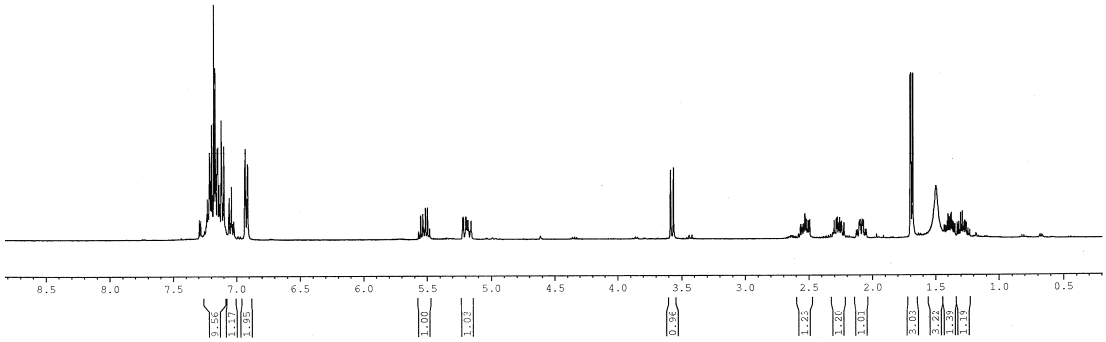


DY-2-255-2(AP

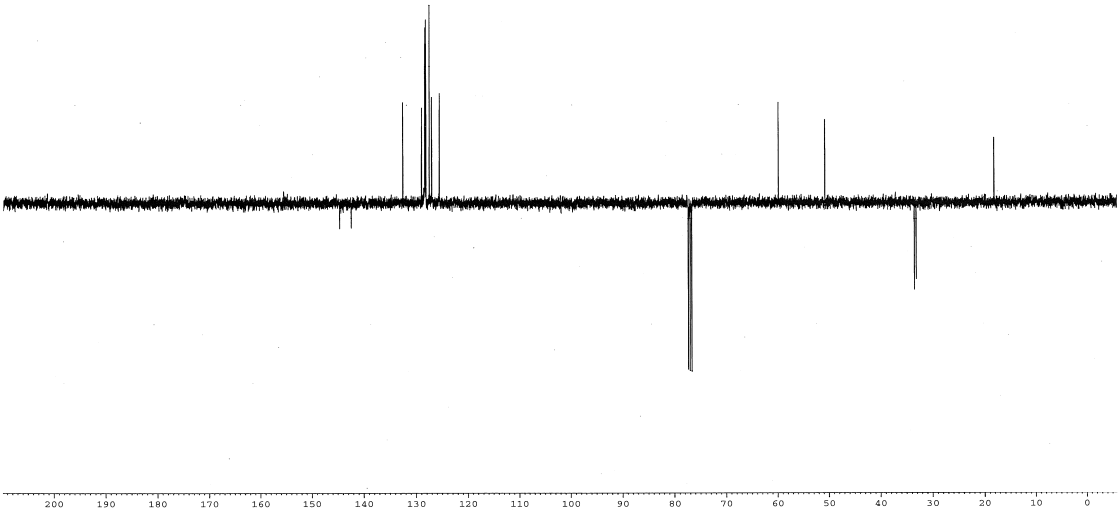


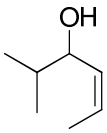


12 (DY-3-21)

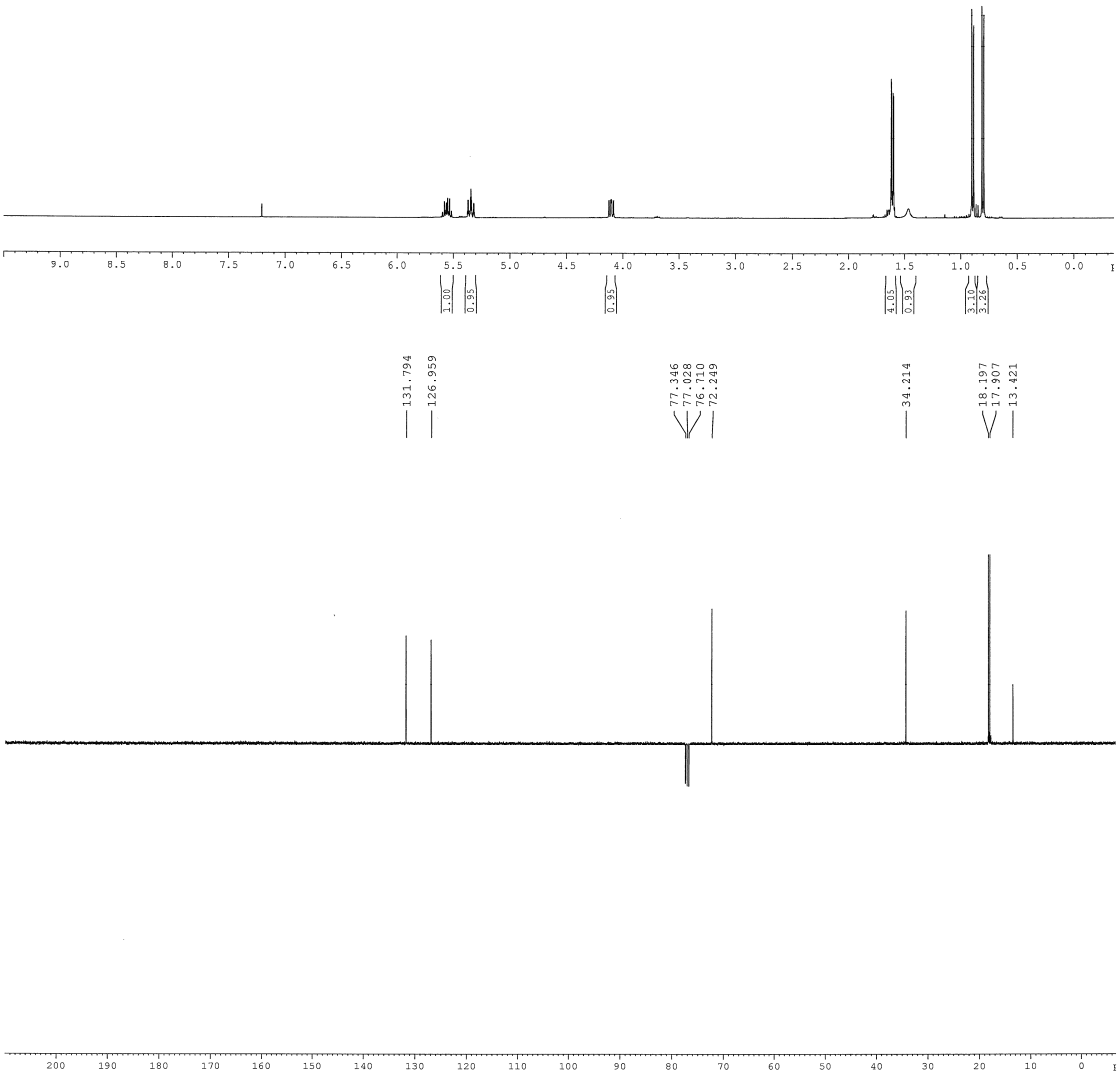


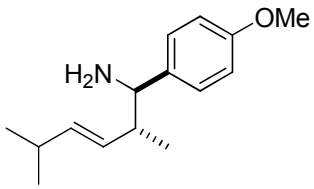
DY-3-21-3(apt)
C13APT



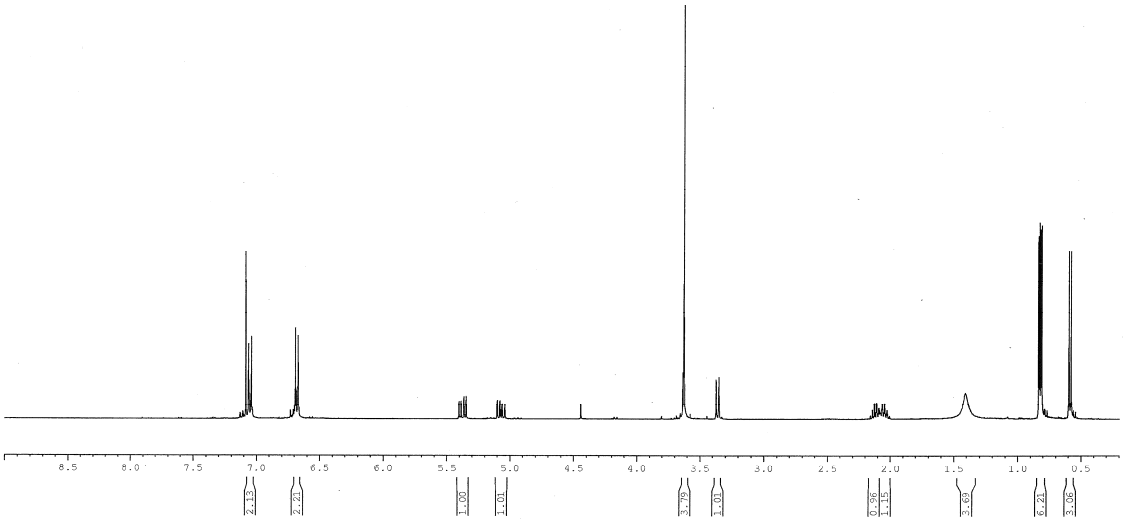

OH

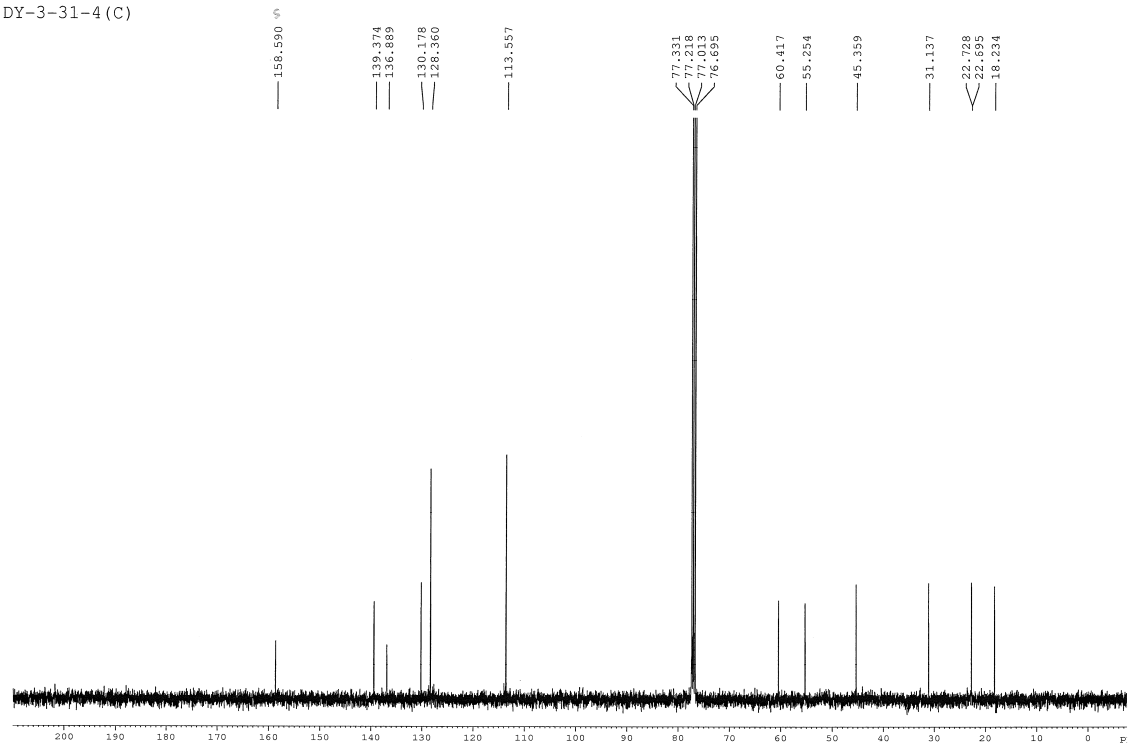
14

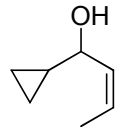

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.00
0.95
0.95
4.05
0.93
3.10
3.26
131.794
126.959
77.346
77.028
76.710
72.249
34.214
18.197
17.907
13.421
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


OMe
H2N

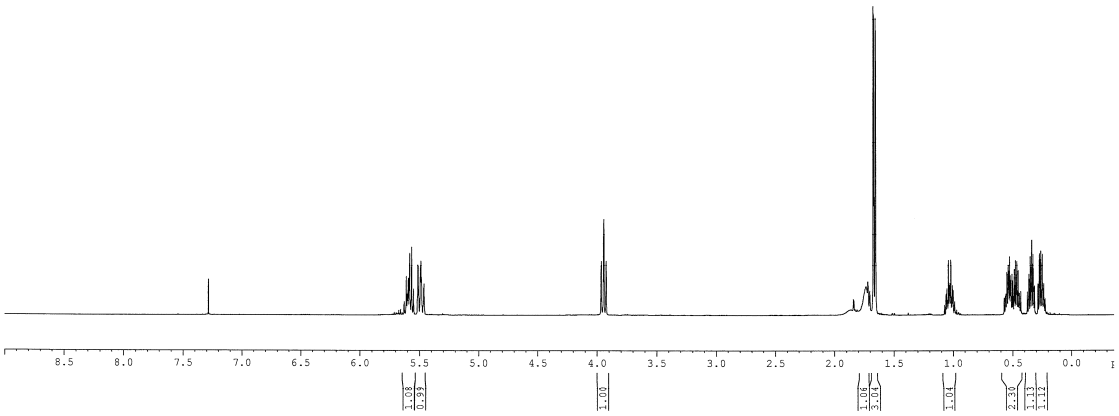
15 (DY-3-31)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
2.15
2.21
1.00
1.01
3.79
1.01
0.96
1.15
3.66
6.21
3.06

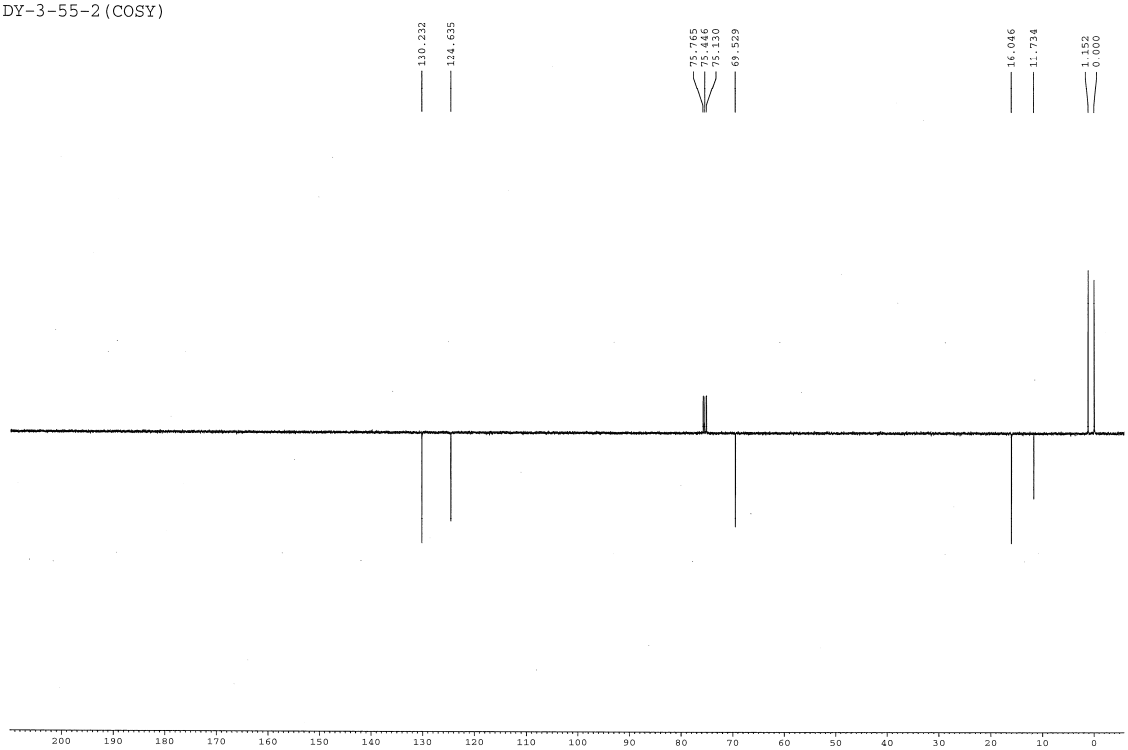

DY-3-31-4(C)
158.590
139.374
136.889
130.178
128.360
113.557
77.331
77.218
77.013
76.695
60.417
55.254
45.359
31.137
22.728
22.695
18.234
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

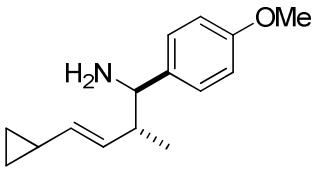


16 (DY-3-55)

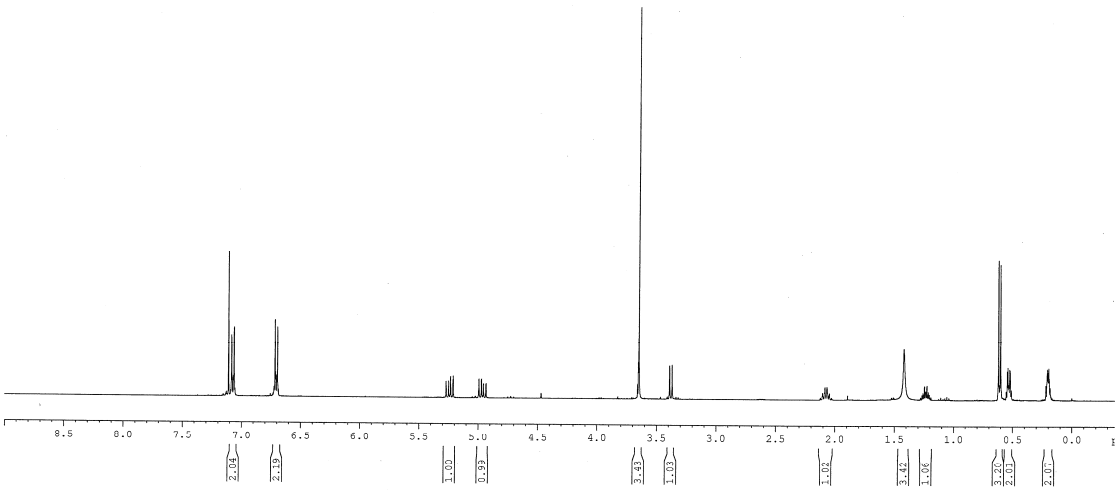


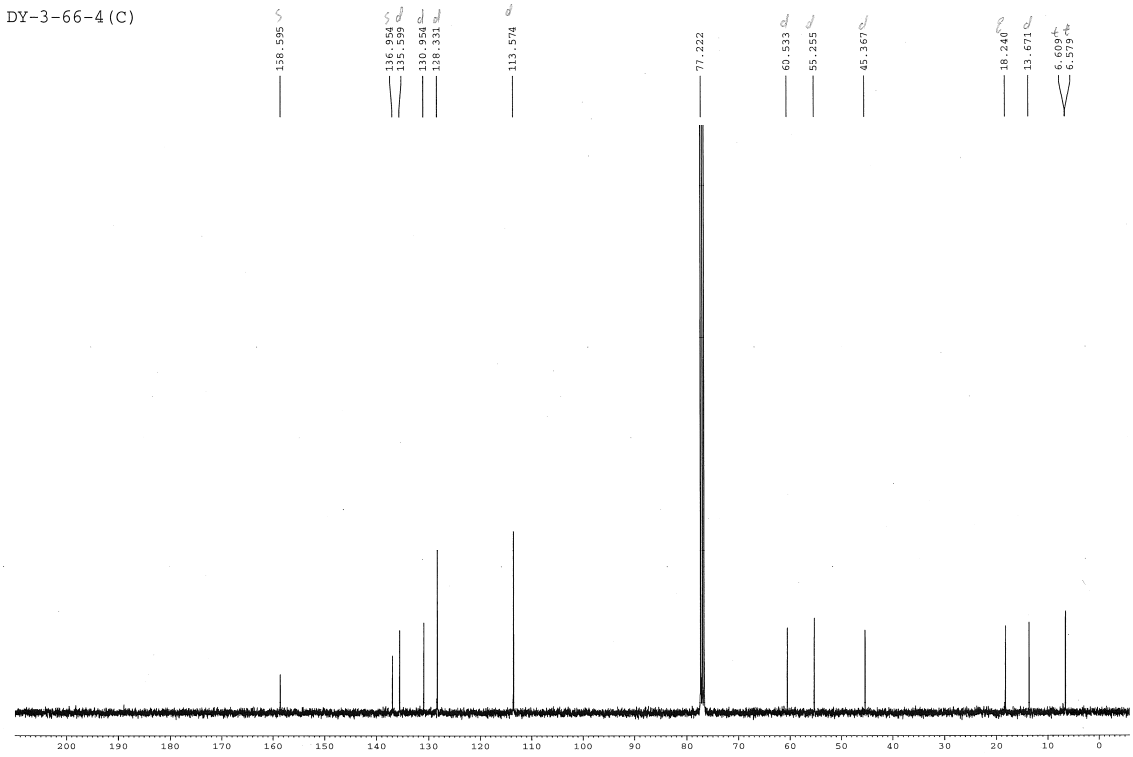
DY-3-55-2(COSY)

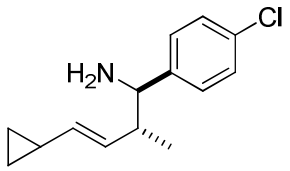



OMe
H2N

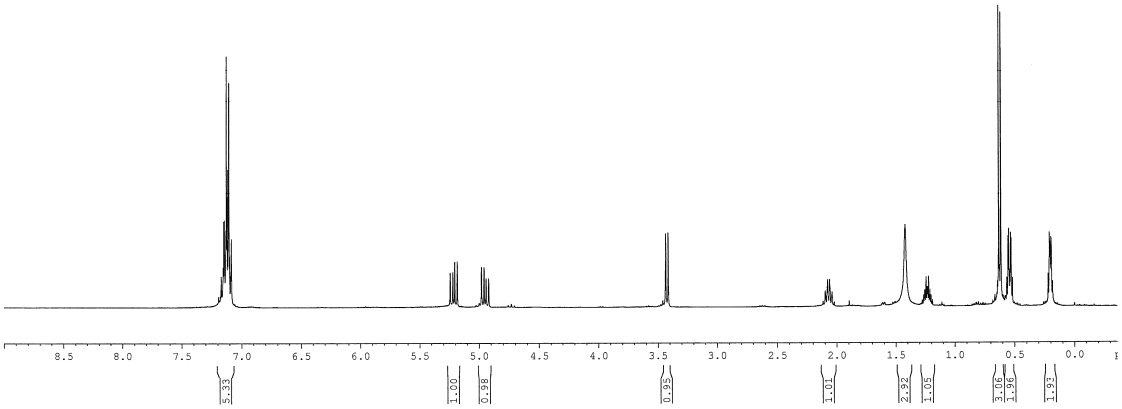
17 (DY-3-66)

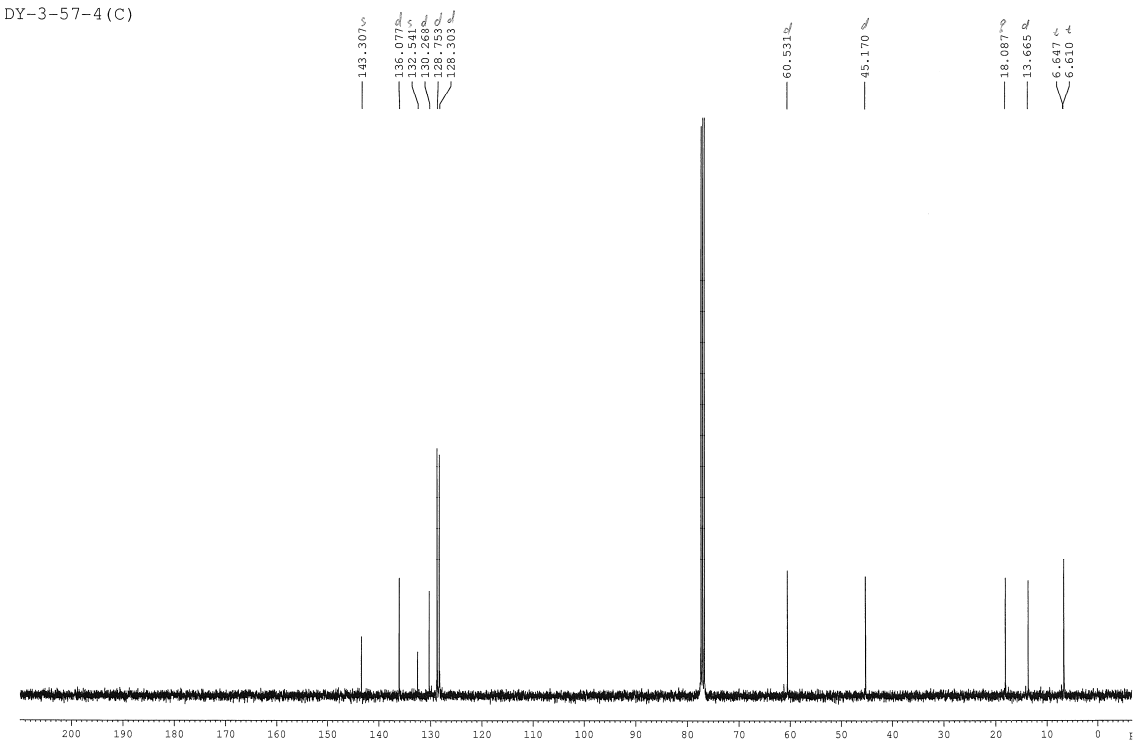

9.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.04
2.19
1.00
0.99
3.43
1.03
1.02
3.42
1.08
3.20
2.03
2.01

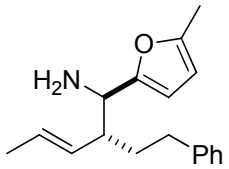

DY-3-66-4(C)
158.595
136.954
135.599
130.954
128.331
113.574
77.222
60.533
55.255
45.367
18.240
13.671
6.609
6.579
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Cl
H2N

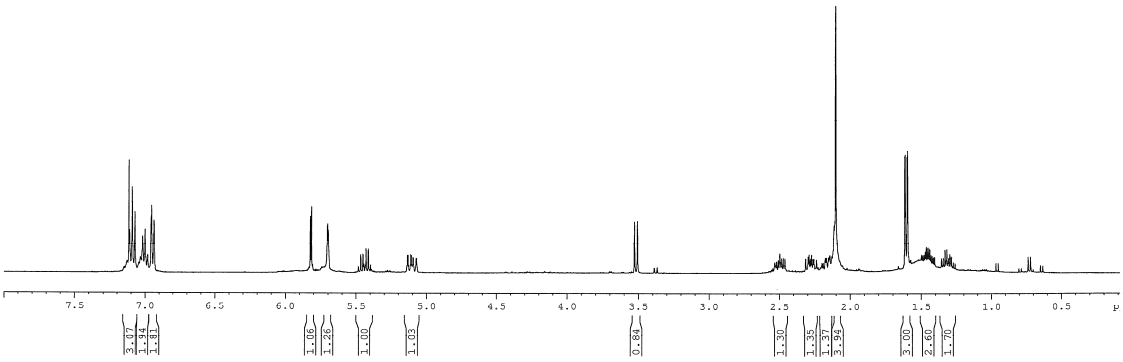
19 (DY-3-56)

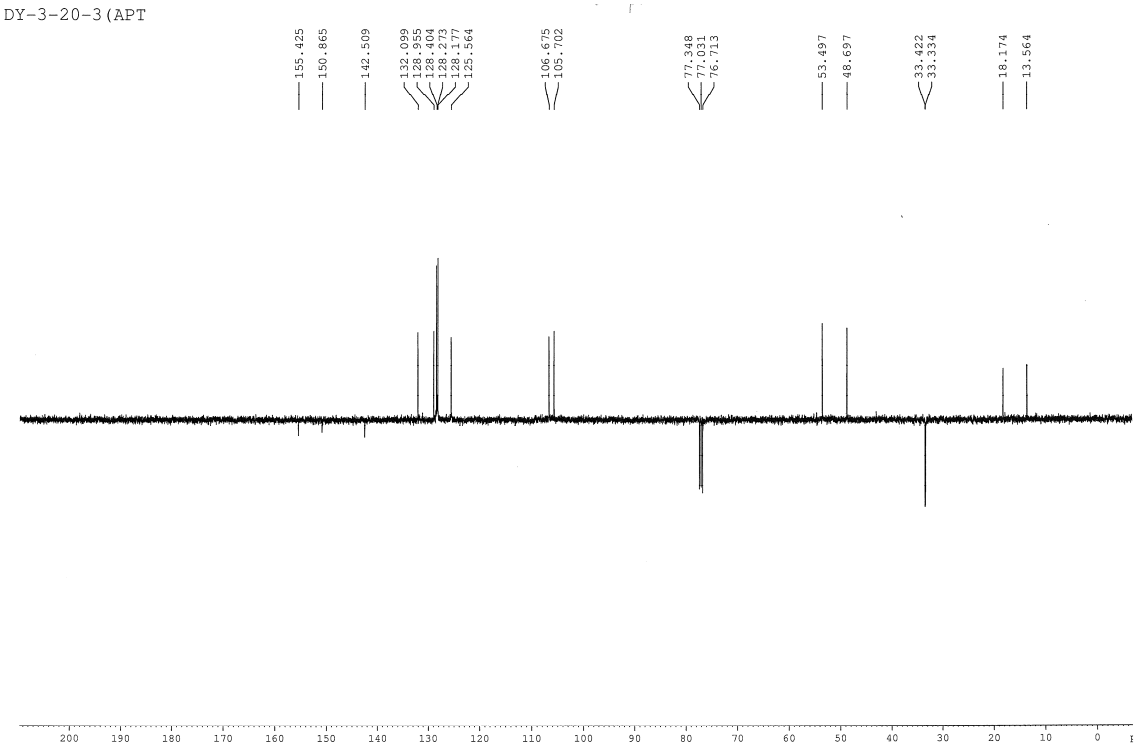

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.33
1.00
0.98
0.95
1.01
2.92
1.05
3.06
1.90
1.93

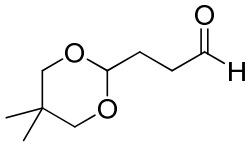

DY-3-57-4(C)
143.307
136.077
132.541
130.268
128.753
128.303
60.531
45.170
18.087
13.665
6.647
6.610
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


O
H2N
Ph

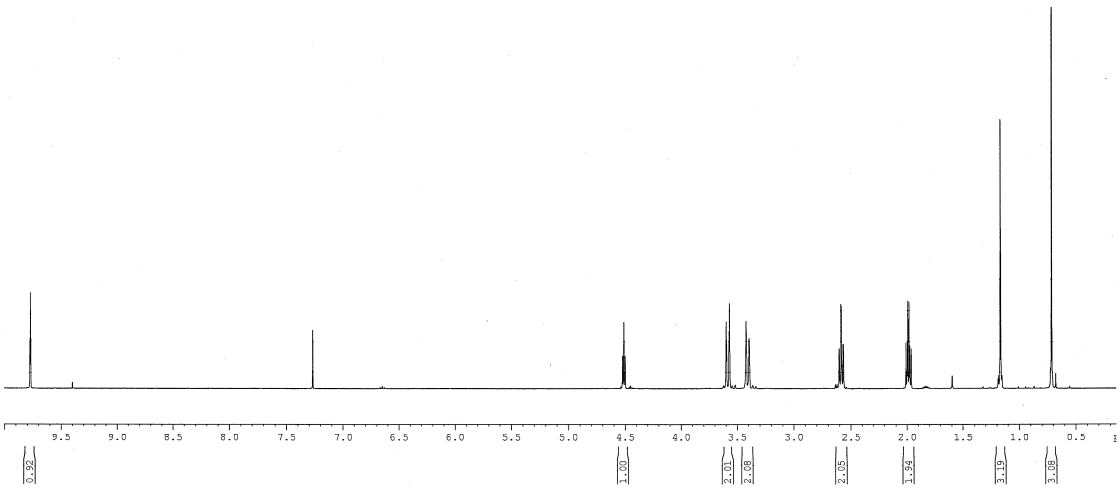
21 (DY-3-20)

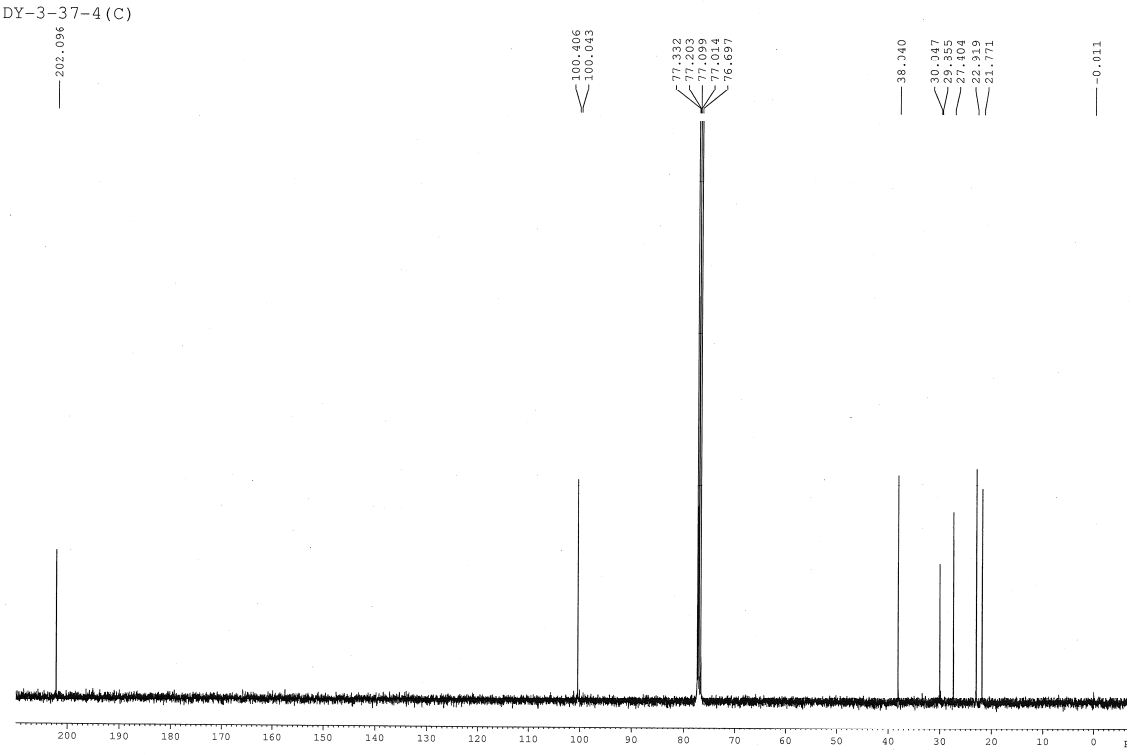

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
3.07
1.44
1.81
1.06
1.26
1.00
1.03
0.84
1.30
1.35
1.37
3.94
3.00
2.60
1.70

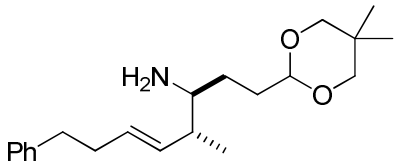

DY-3-20-3(APT
155.425
150.865
142.509
132.099
128.955
128.404
128.273
128.177
125.564
106.675
105.702
77.348
77.031
76.713
53.497
48.697
33.422
33.334
18.174
13.564
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


O
O
O
H

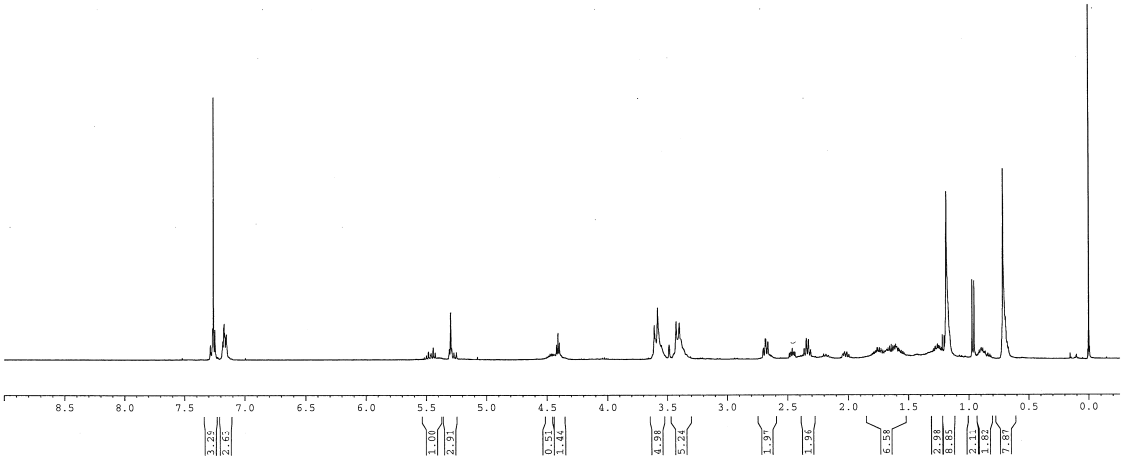
22 (DY-3-37)


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
0.92
1.00
2.01
2.08
2.05
1.94
3.19
3.08

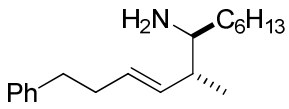

DY-3-37-4(C)
202.096
100.406
100.043
77.332
77.203
77.099
77.014
76.697
38.340
30.047
29.355
27.404
22.319
21.771
-0.011
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0



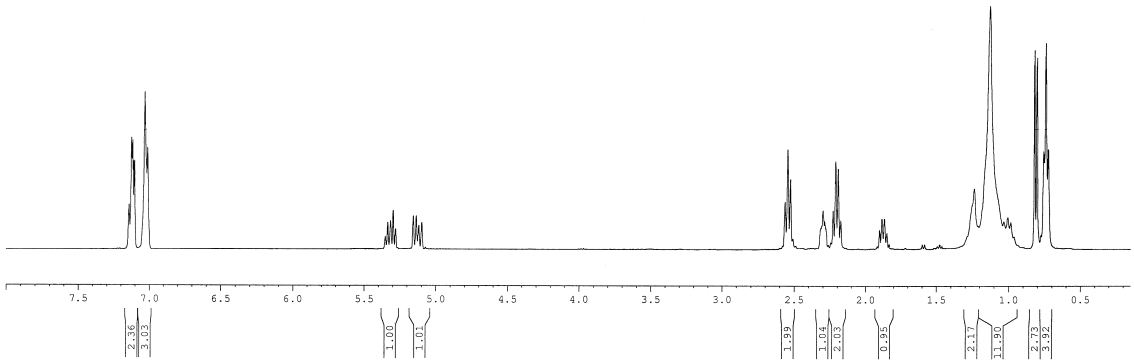
23 (DY-3-38B)

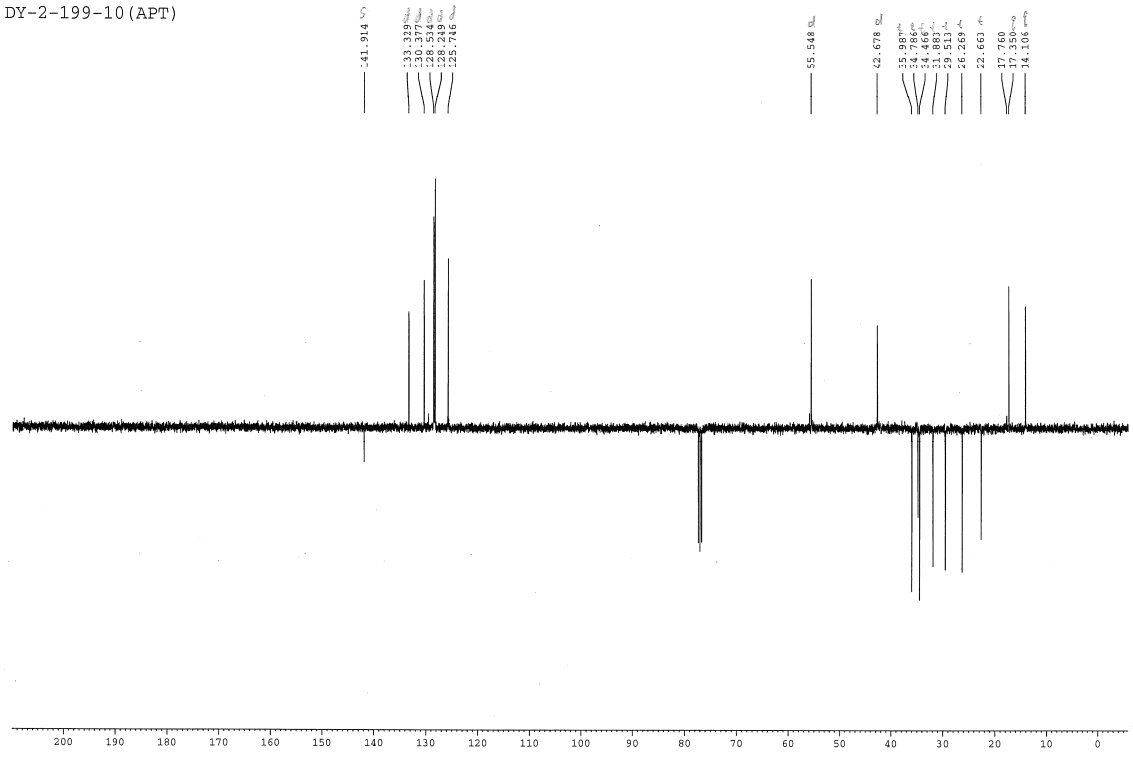


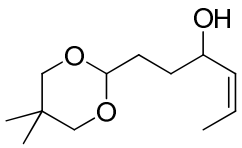
Note: Efforts toward obtaining pure **23** was failed due to its extremely high polarity.Instead, highly concentrated **23** (>90% purity as shown in ^{1}H NMR) was used in the following step.


H2N
C6H13
Ph

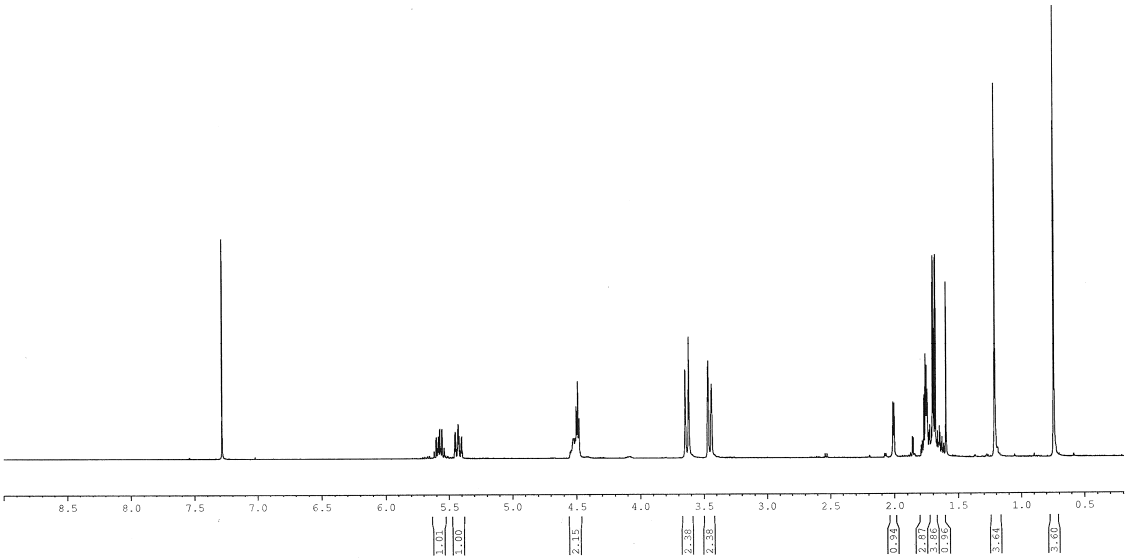
25 (DY-3-1)

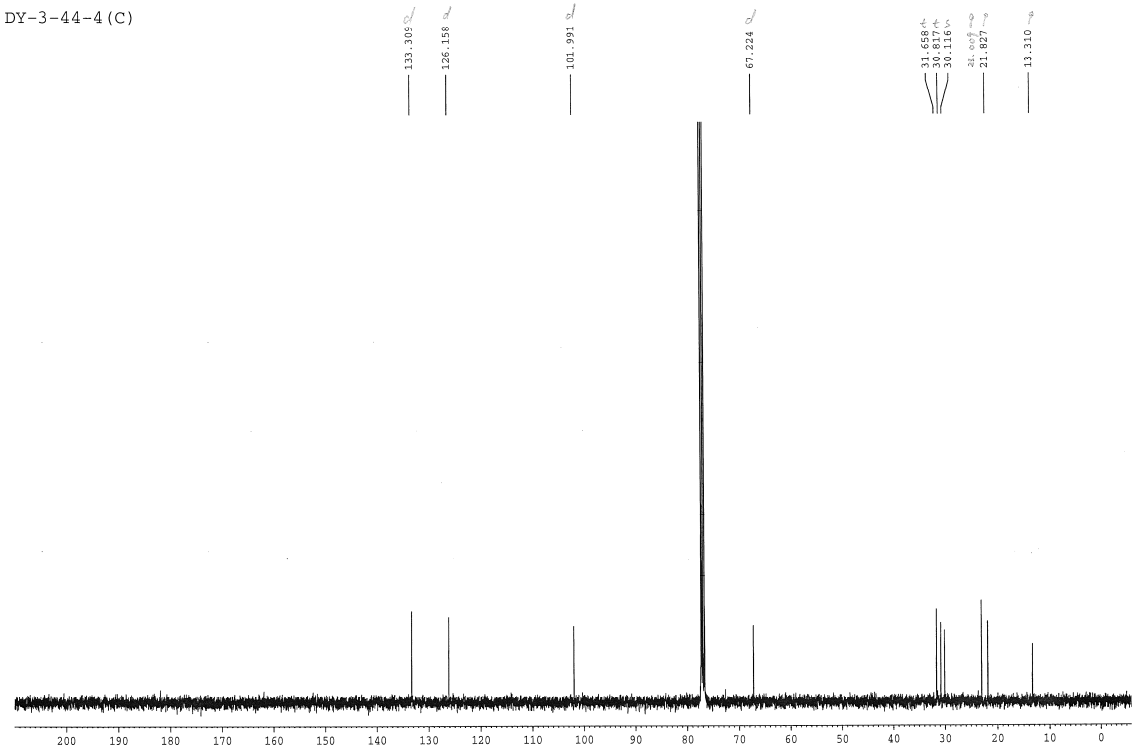

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
2.36
3.03
1.00
1.01
1.99
1.04
2.03
0.95
2.17
11.90
2.73
3.92

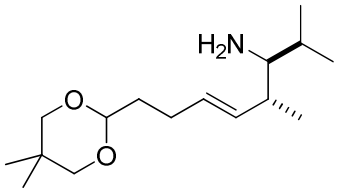

DY-2-199-10(APT)
141.914
133.329
129.274
128.534
128.249
125.746
55.548
42.678
35.987
34.786
34.466
31.883
29.513
26.269
22.663
17.760
17.350
14.106
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


OH
O
O

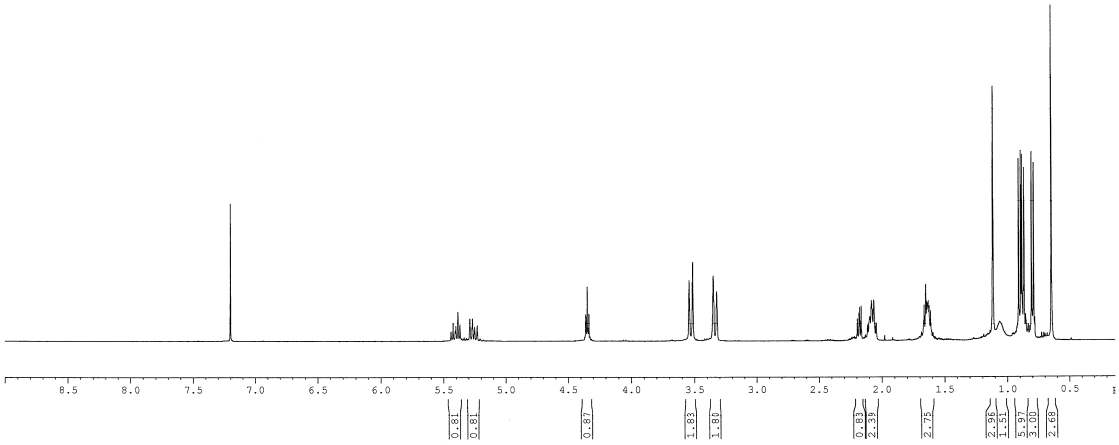
27 (DY-3-44)

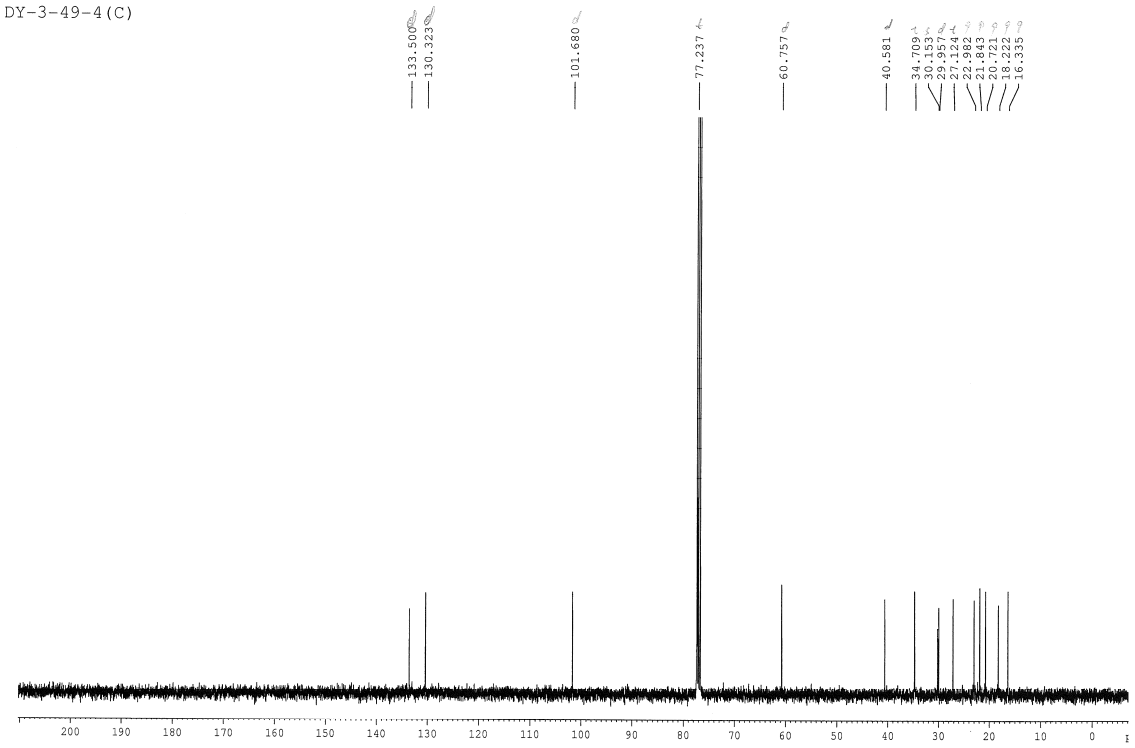

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.01
1.00
2.15
2.38
2.38
0.94
2.87
3.86
0.96
3.64
3.60

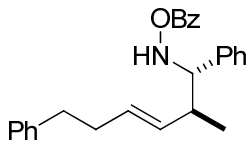

DY-3-44-4(C)
133.309
126.158
101.991
67.224
31.658
30.877
30.116
21.827
13.310
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


H2N
O
O

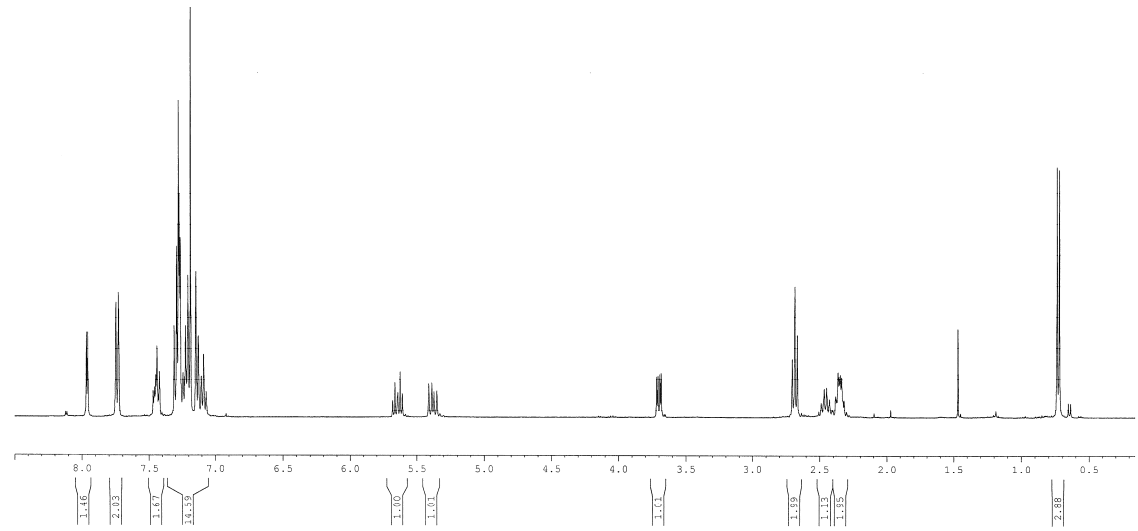
28 (DY-3-49)

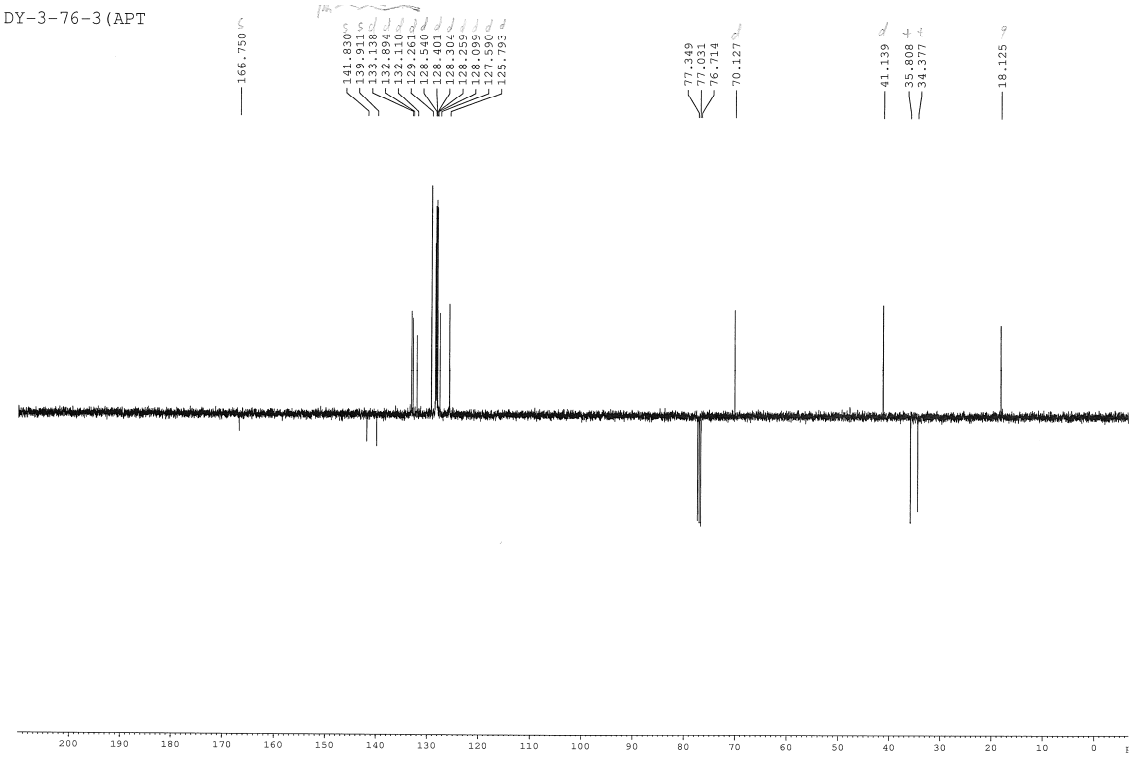

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.81
0.81
0.87
1.83
1.80
0.83
2.39
2.75
2.96
1.91
5.97
3.09
2.68


DY-3-49-4(C)
133.500
130.323
101.680
77.237
60.757
40.581
34.709
30.153
29.957
27.124
22.982
21.843
20.722
18.232
16.335
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

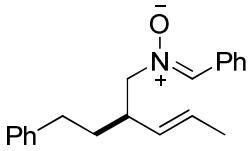

OBz
HN
Ph
Ph

B29

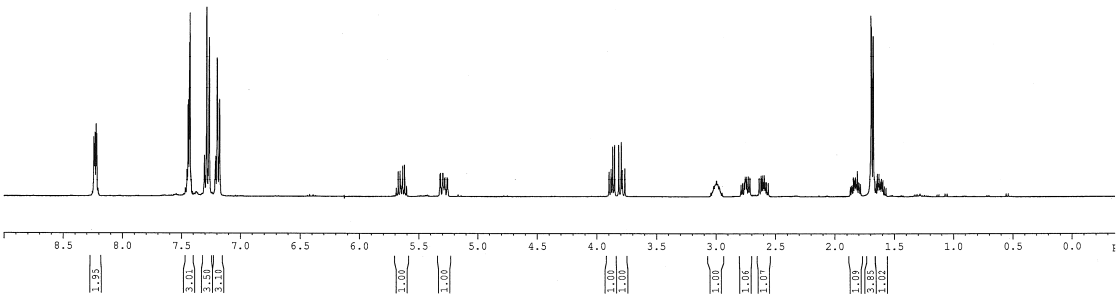

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.46
2.03
3.67
14.59
1.40
1.01
1.14
1.59
1.13
1.35
2.88

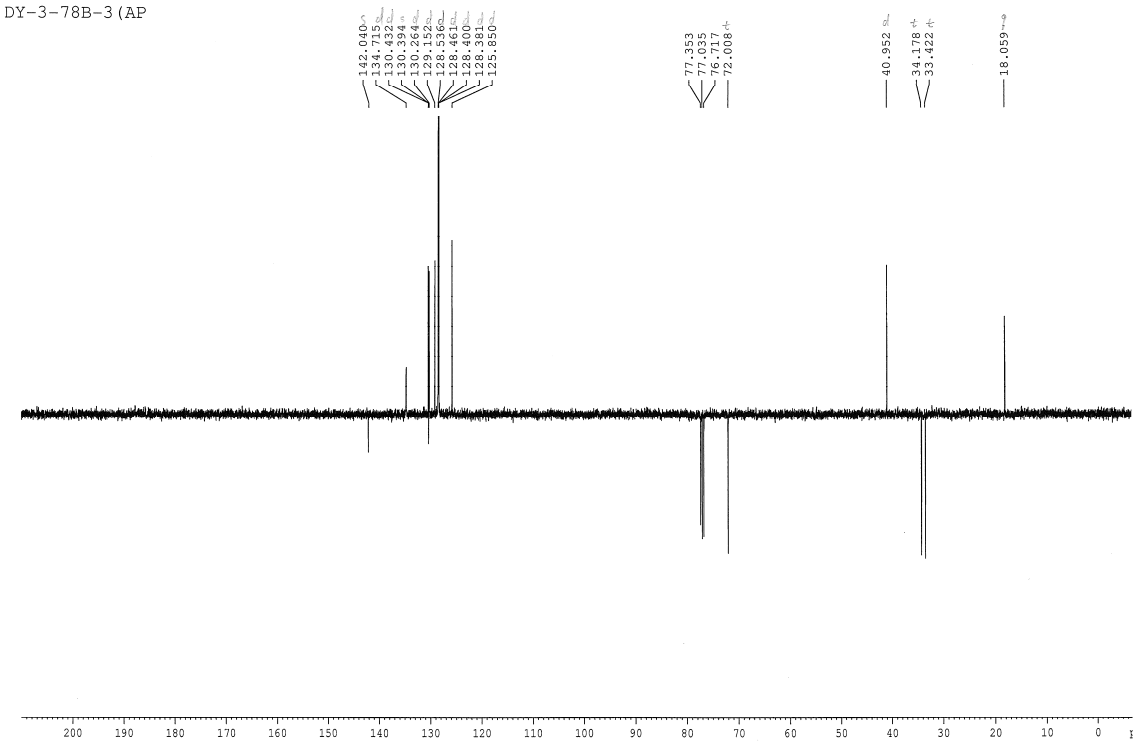

DY-3-76-3(APT
166.750
141.830
139.911
133.138
132.894
132.110
129.261
128.540
128.401
128.302
128.259
128.095
127.790
127.792
125.792
77.349
77.031
76.714
70.127
41.139
35.808
34.377
18.125

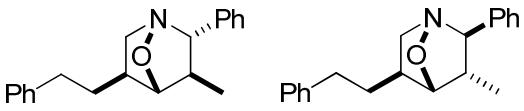
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



30

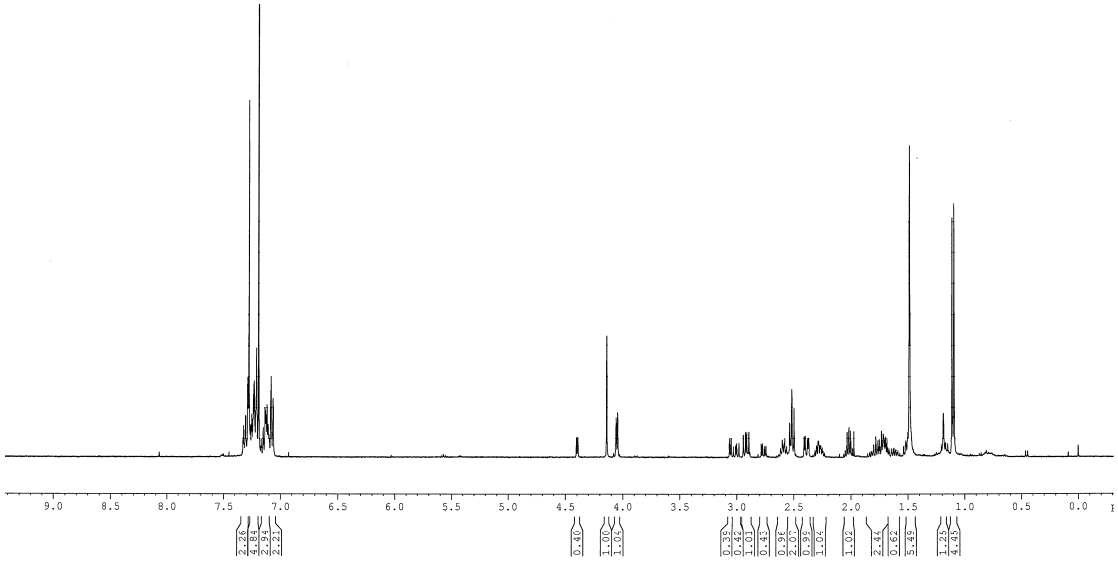


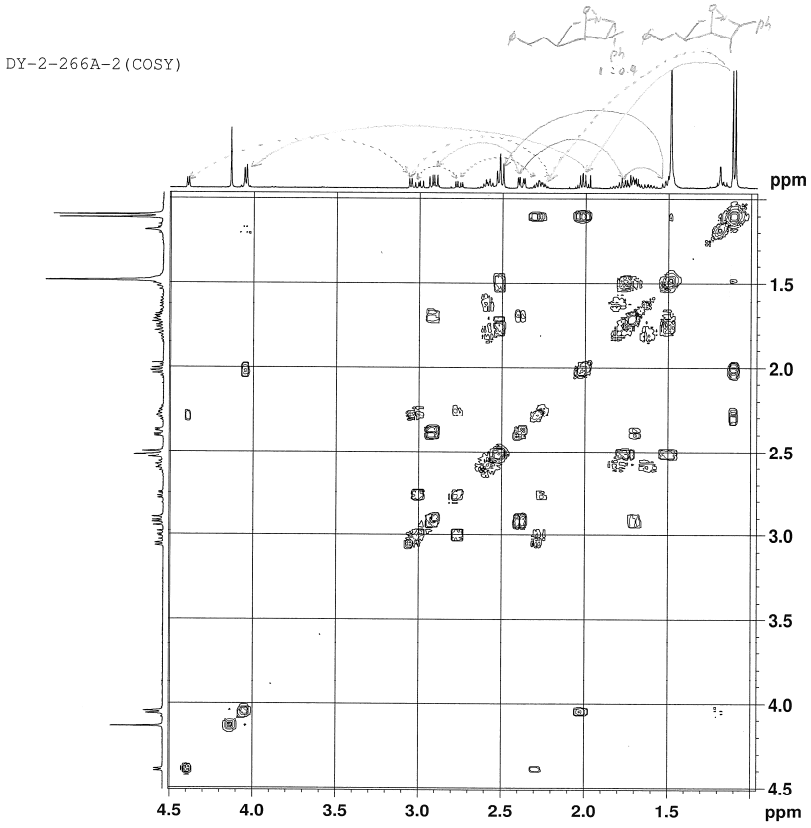

DY-3-78B-3(AP
142.040
134.715
130.432
130.394
130.264
129.152
128.536
128.461
128.400
128.381
125.850
77.353
77.035
76.717
72.008
40.952
34.178
33.422
18.059

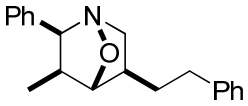


31 **32**

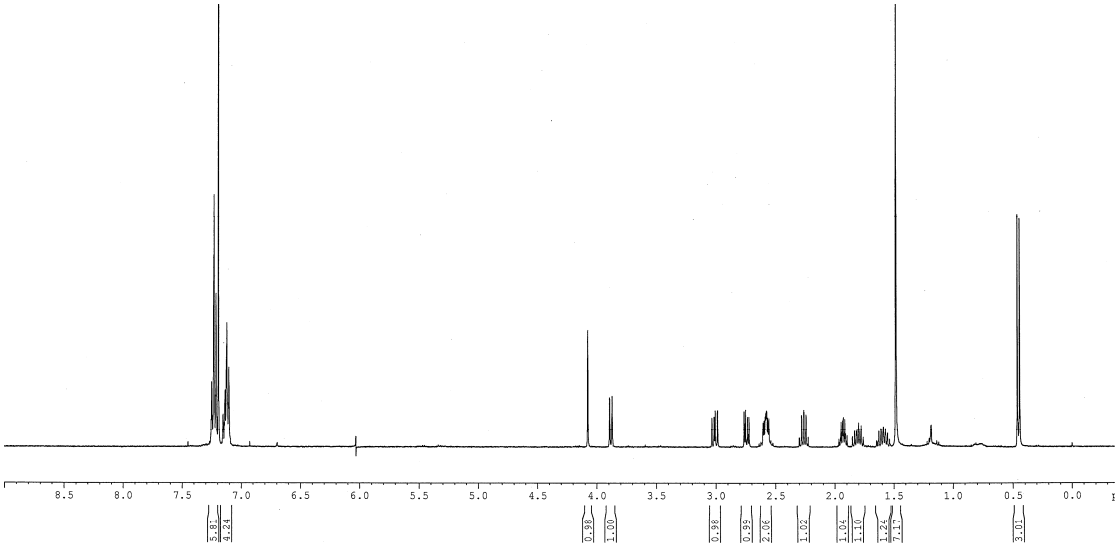
(**31**:**32** = 2.5:1)

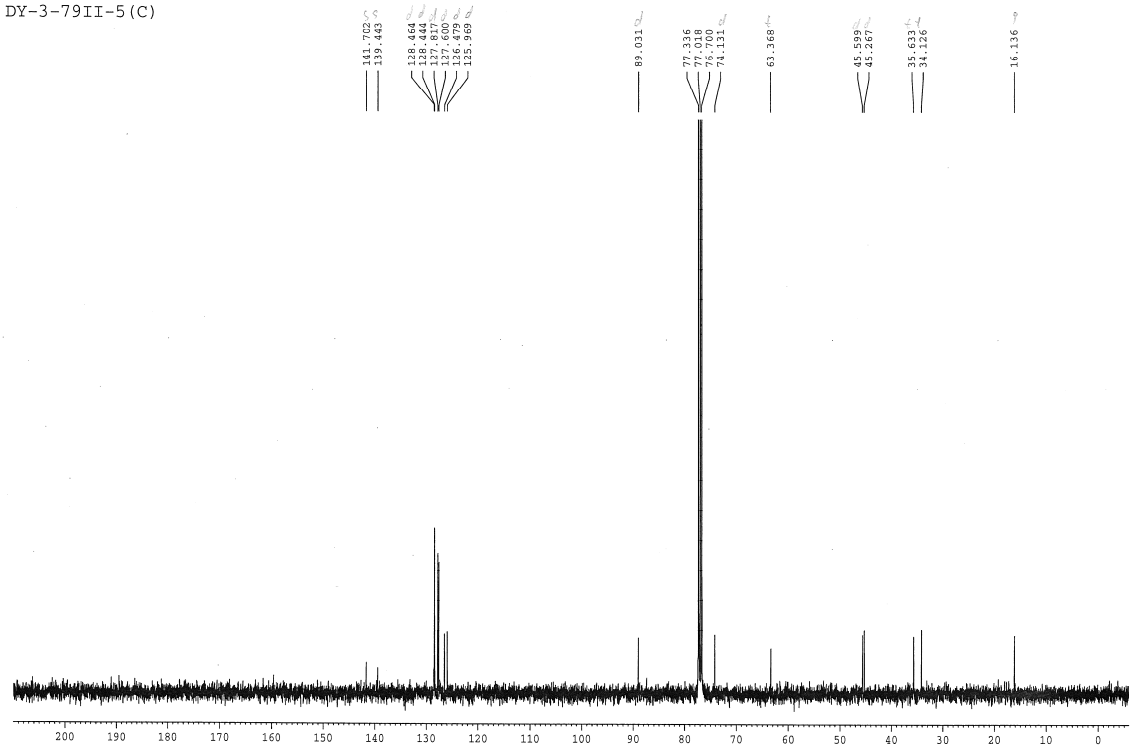




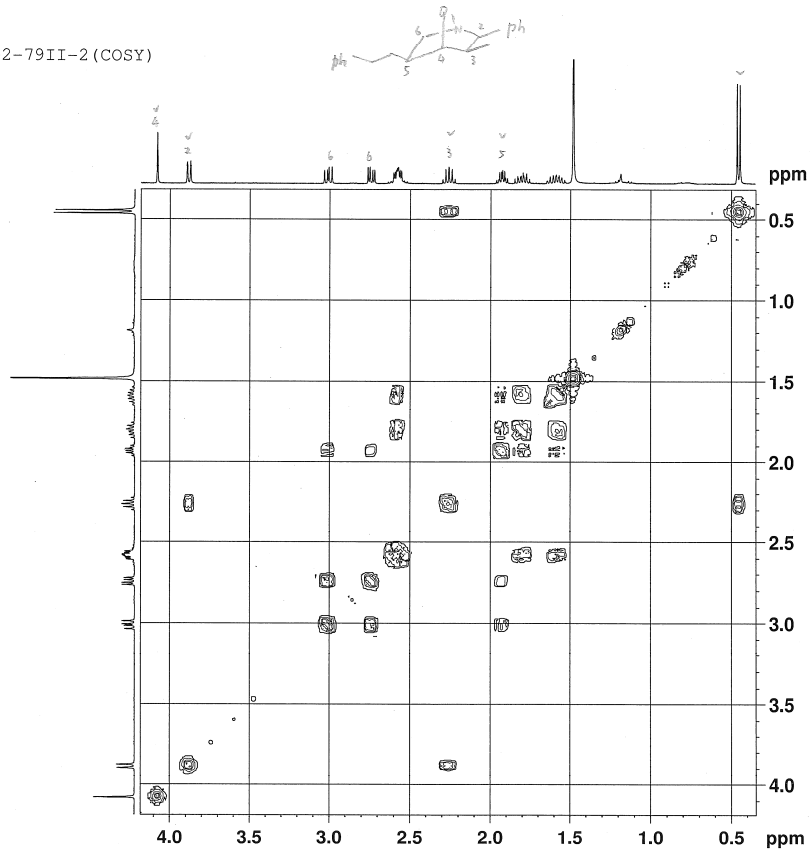

Ph
N
O
Ph

33

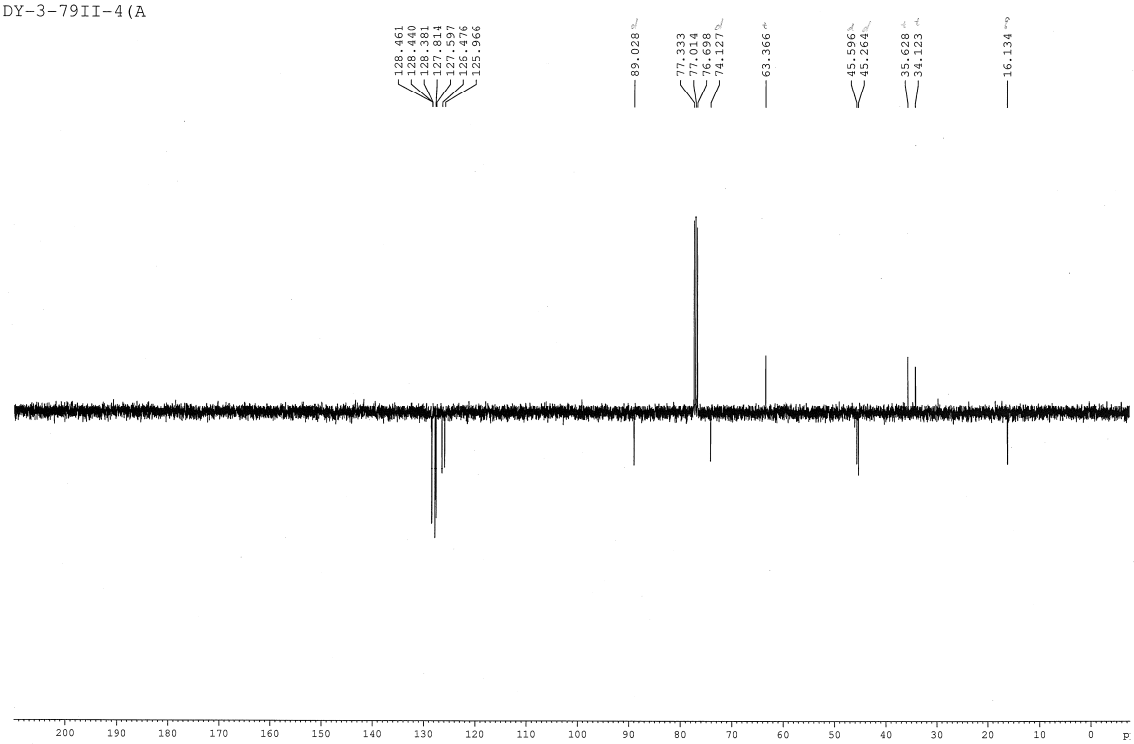

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.88
4.24
0.98
1.00
0.98
0.99
2.06
1.02
1.04
1.10
1.24
2.13
3.01

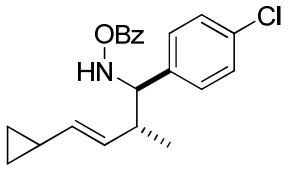

DY-3-79II-5(C)
141.702
139.443
128.464
128.444
127.817
127.600
126.478
125.969
89.031
77.336
77.018
76.700
74.131
63.368
45.599
45.267
35.633
34.126
16.136
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

DY-2-79II-2(COSY)

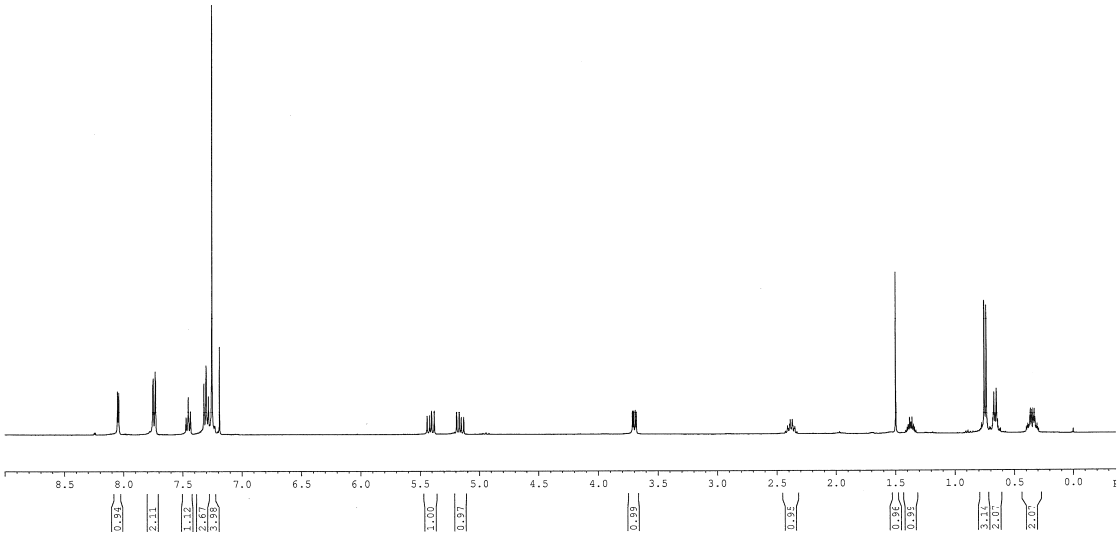


DY-3-79II-4(A

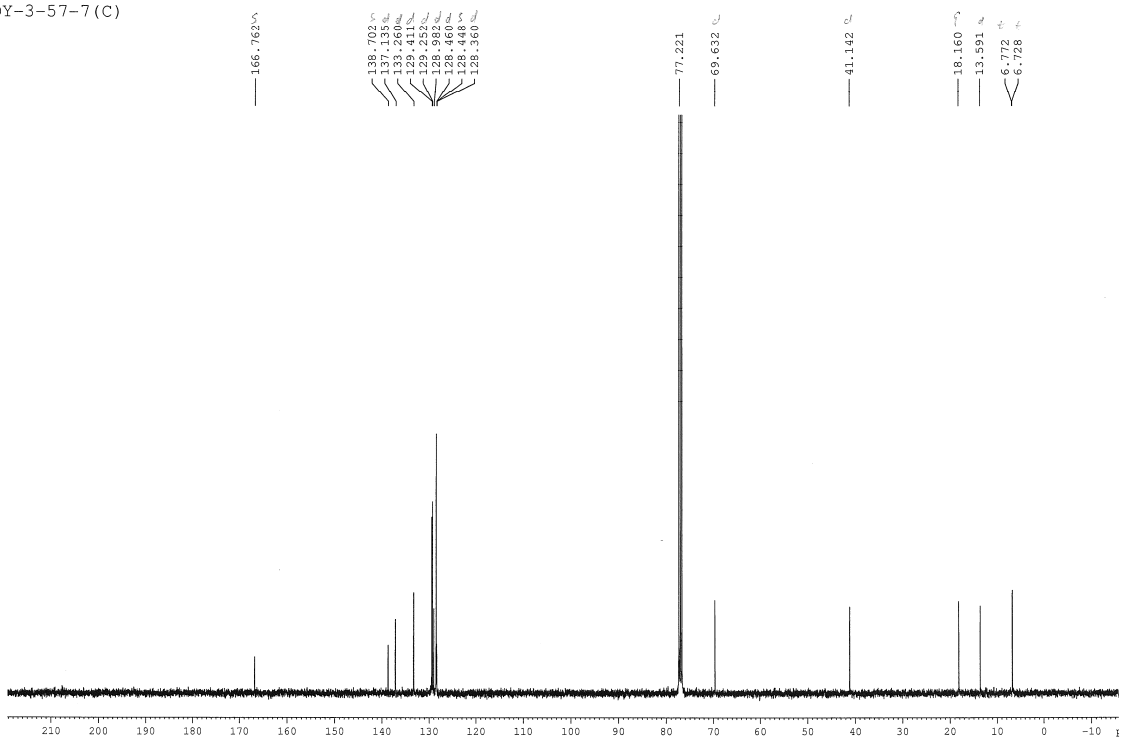


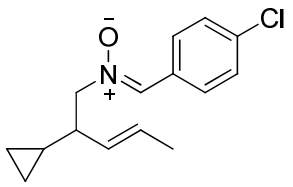


B34 (DY-3-57)

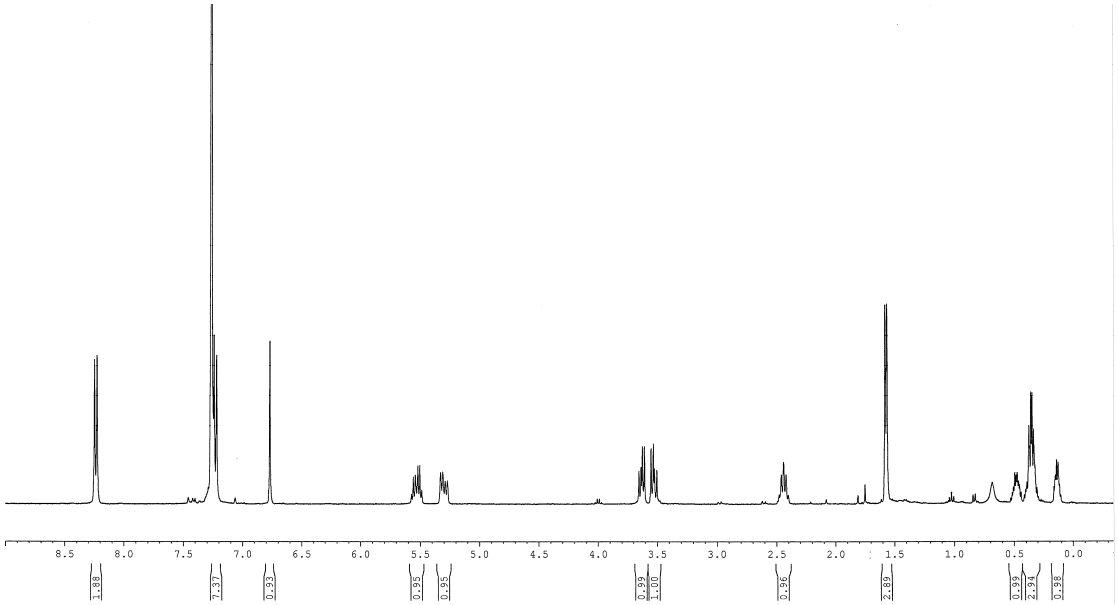


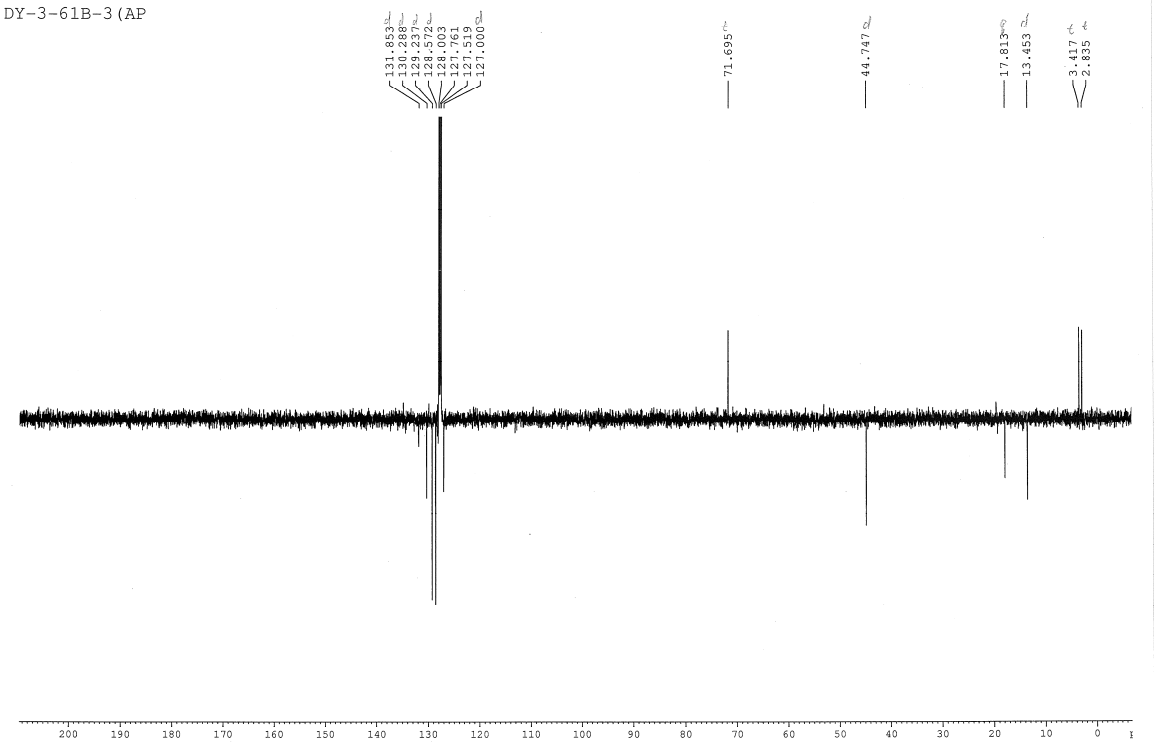
DY-3-57-7(C)

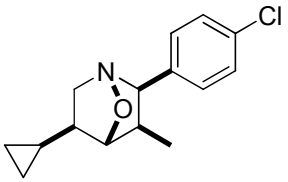



Cl
O
N
+

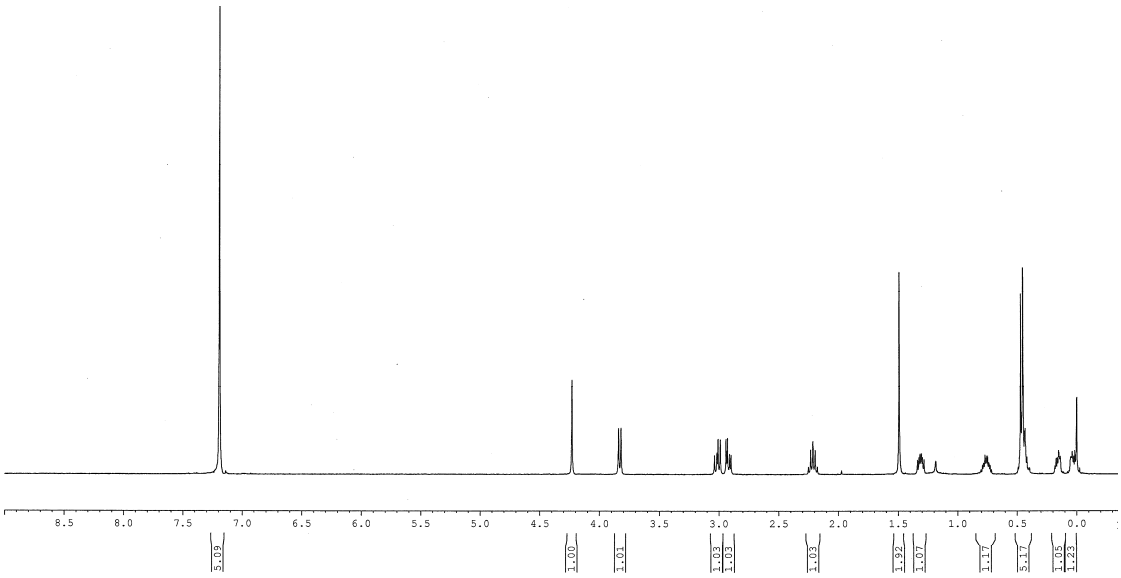
S-1 (DY-3-61B)

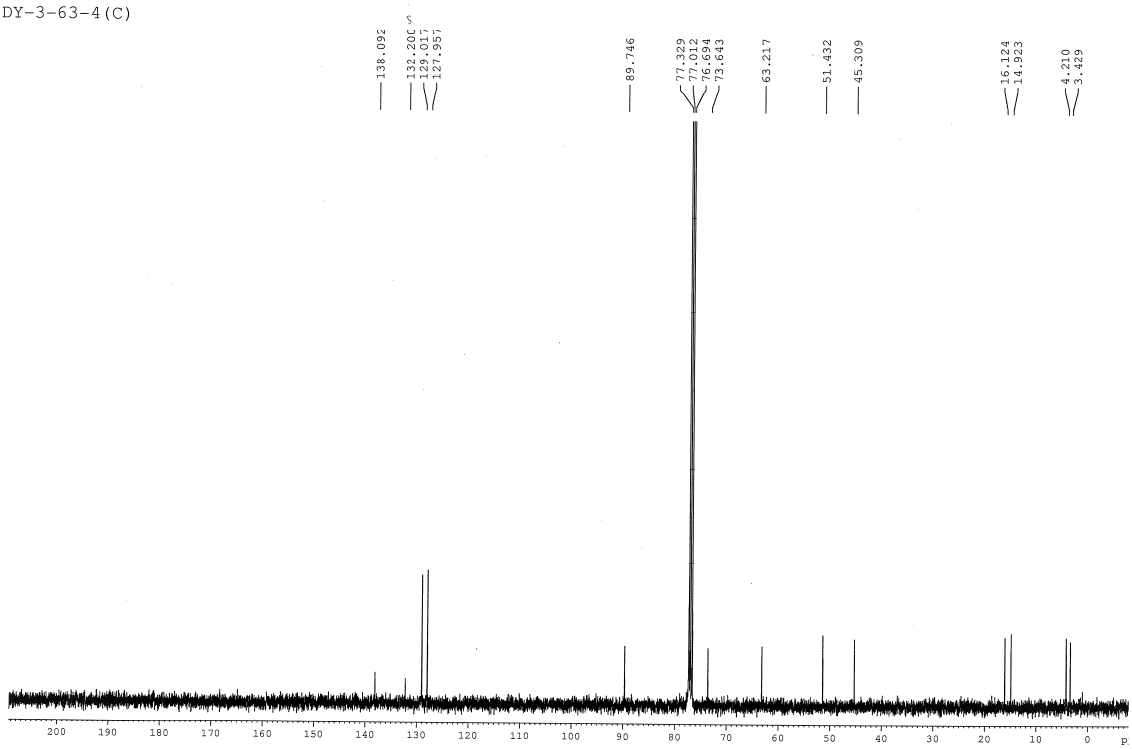

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.88
7.37
0.93
0.95
0.95
0.99
1.00
0.96
2.89
0.99
2.94
0.98

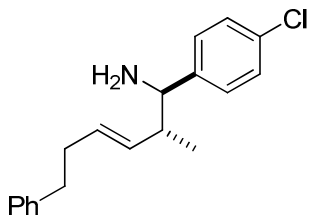

DY-3-61B-3(AP
131.853
130.288
129.237
128.572
128.003
121.761
121.518
127.008
71.695
44.747
17.813
13.453
3.417
2.835
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Cl
N
O

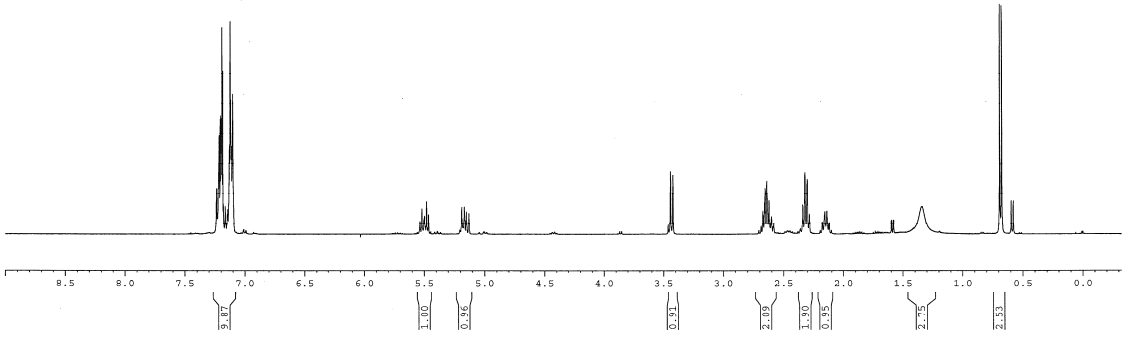
35 (DY-3-63)

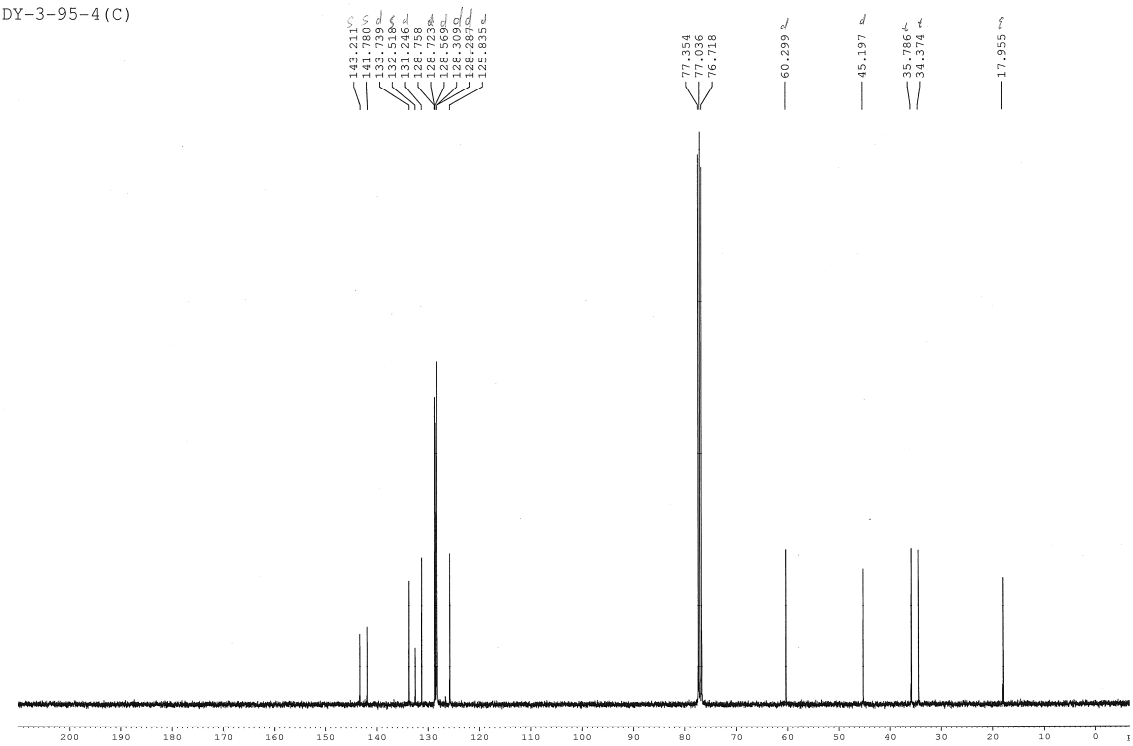

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.09
1.00
1.01
1.03
1.03
1.03
1.92
1.07
1.17
5.17
1.05
1.23

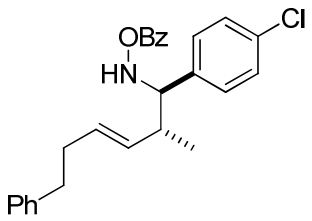

DY-3-63-4(C)
138.092
132.200
129.011
127.957
89.746
77.329
77.012
76.694
73.643
63.217
51.432
45.309
16.124
14.923
4.210
3.429
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Cl
H2N
Ph

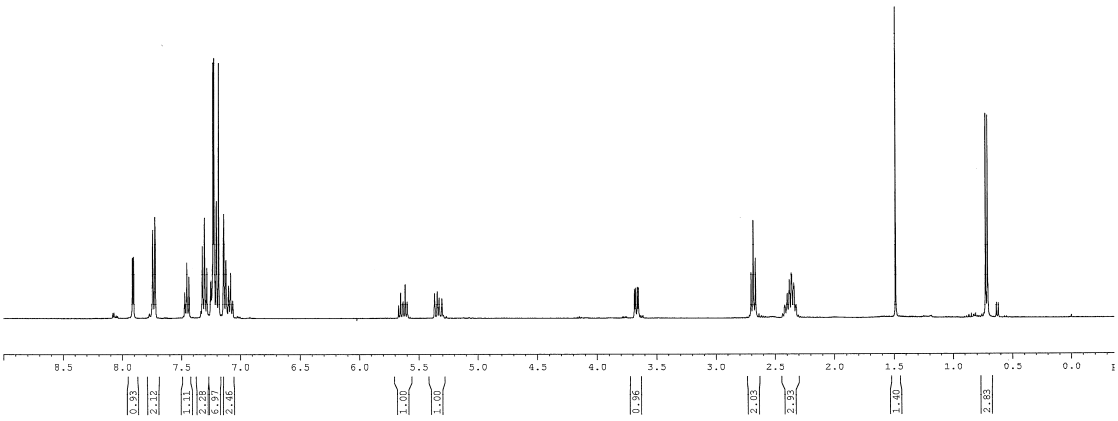
S-2 (DY-3-95)

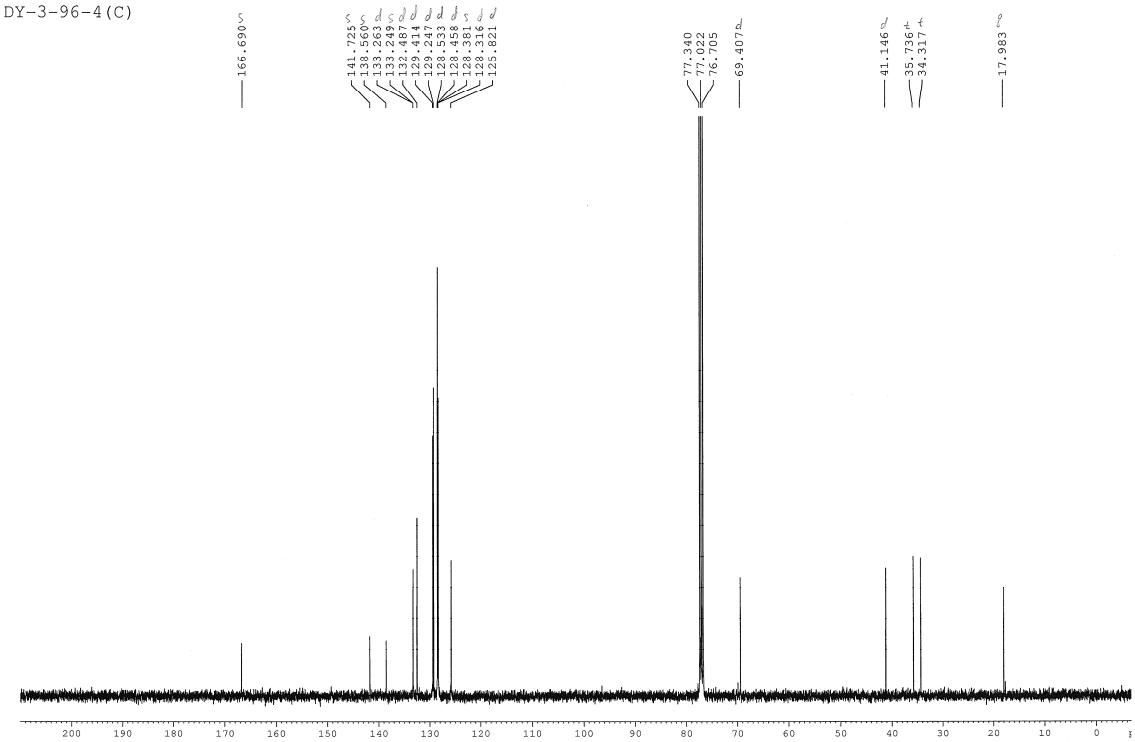

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
9.87
1.00
0.96
0.91
2.09
1.90
0.95
2.75
2.53

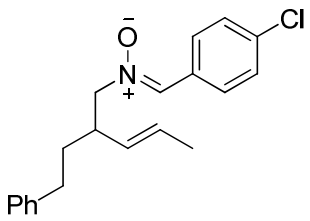

DY-3-95-4(C)
143.211
141.780
133.739
132.518
131.146
128.723
128.569
128.309
128.287
125.835
77.354
77.036
76.718
60.299
45.197
35.786
34.374
17.955
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


OBz
HN
Cl
Ph

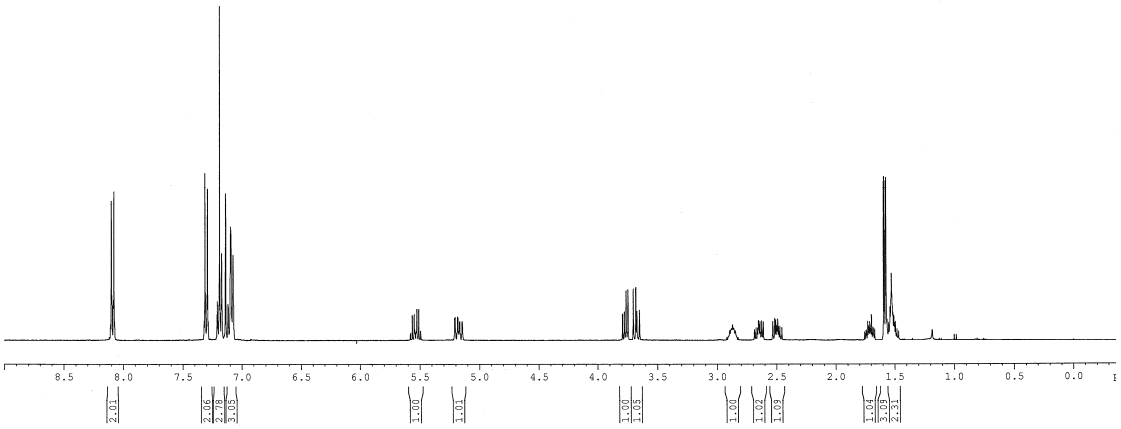
B36 (DY-3-96)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.93
2.12
1.11
2.28
6.97
2.46
1.00
1.00
0.96
2.03
2.93
1.40
2.83

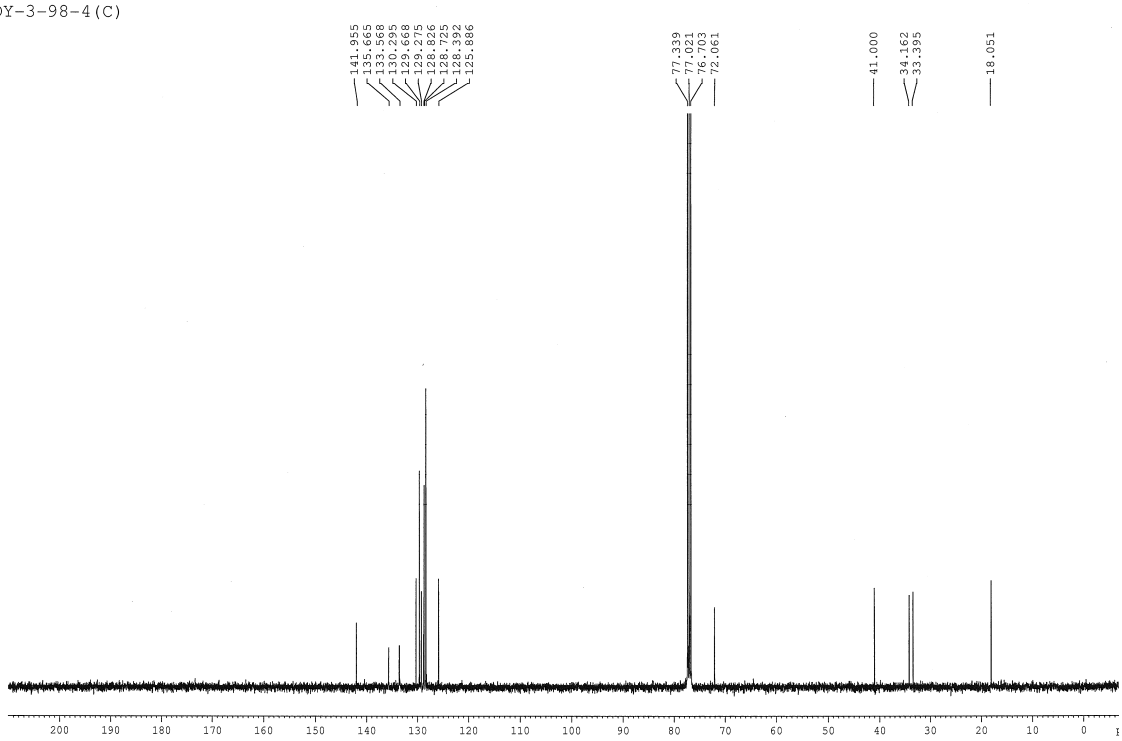

DY-3-96-4(C)
166.690
141.725
138.560
133.263
133.249
132.487
129.414
129.247
128.533
128.458
128.381
128.316
125.821
77.340
77.022
76.705
69.407
41.146
35.736
34.317
17.983
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

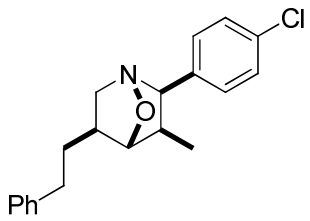


S-3 (DY-3-98)

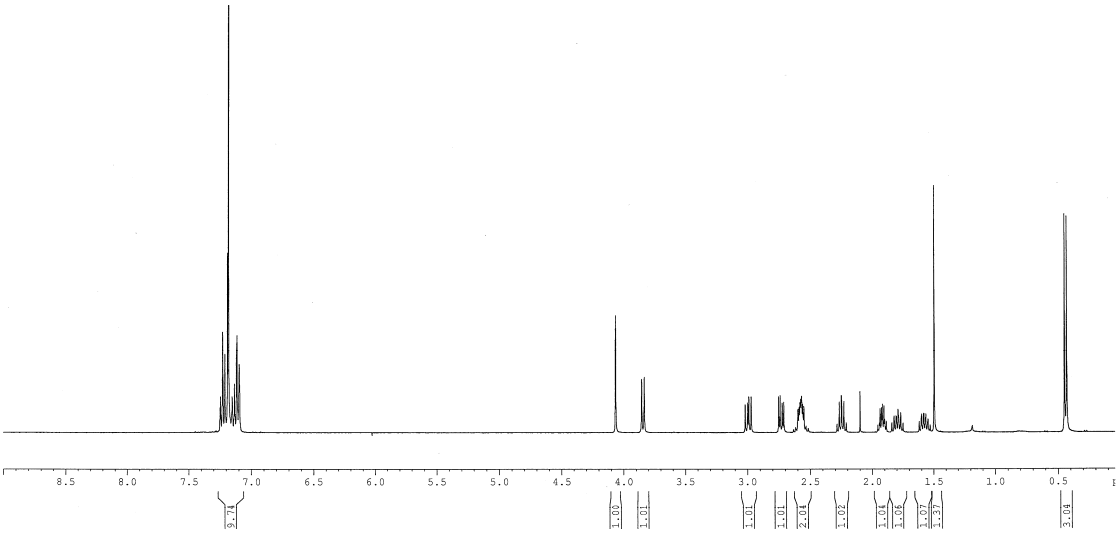


DY-3-98-4(C)

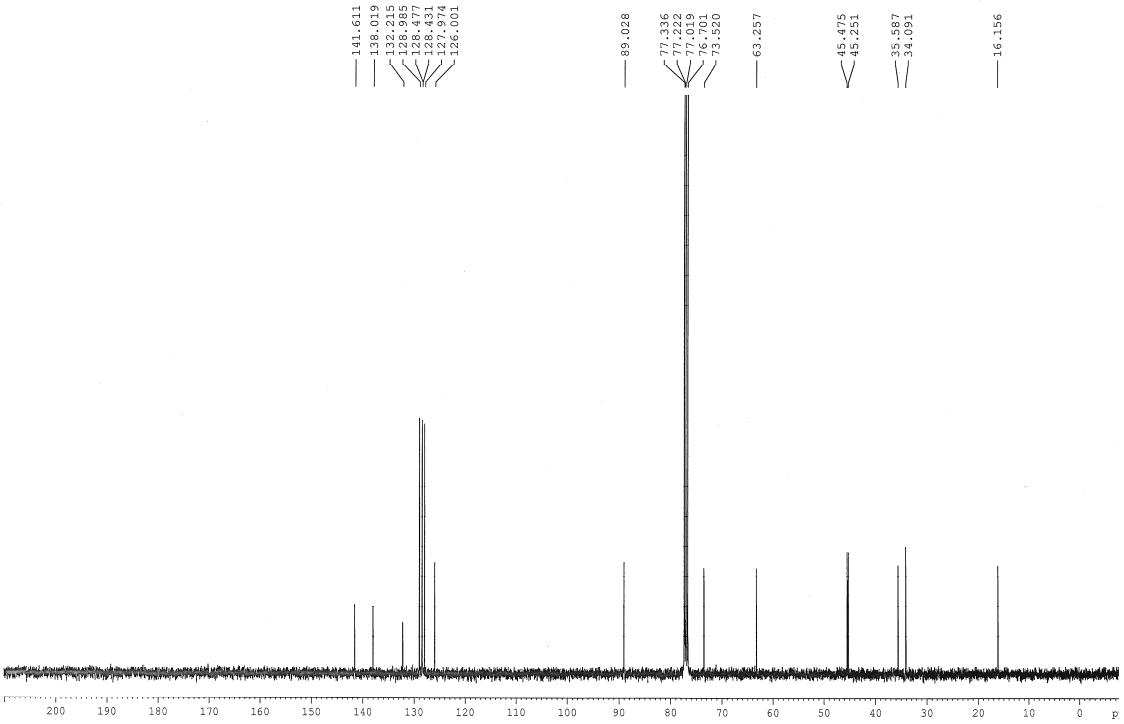


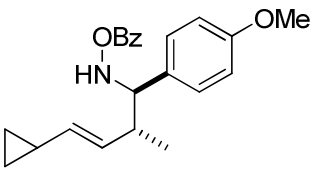


37 (DY-3-99)

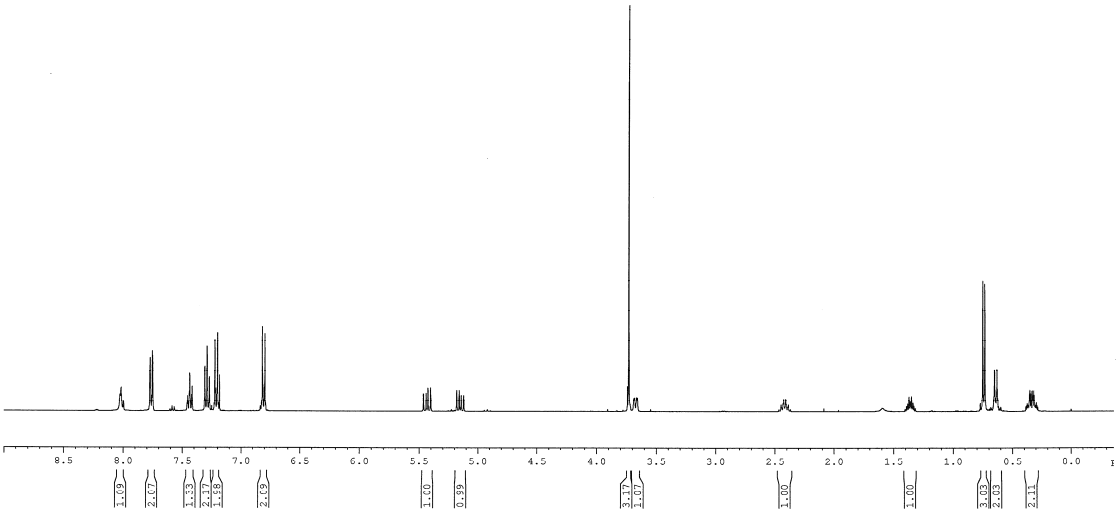


DY-3-99-4(C)

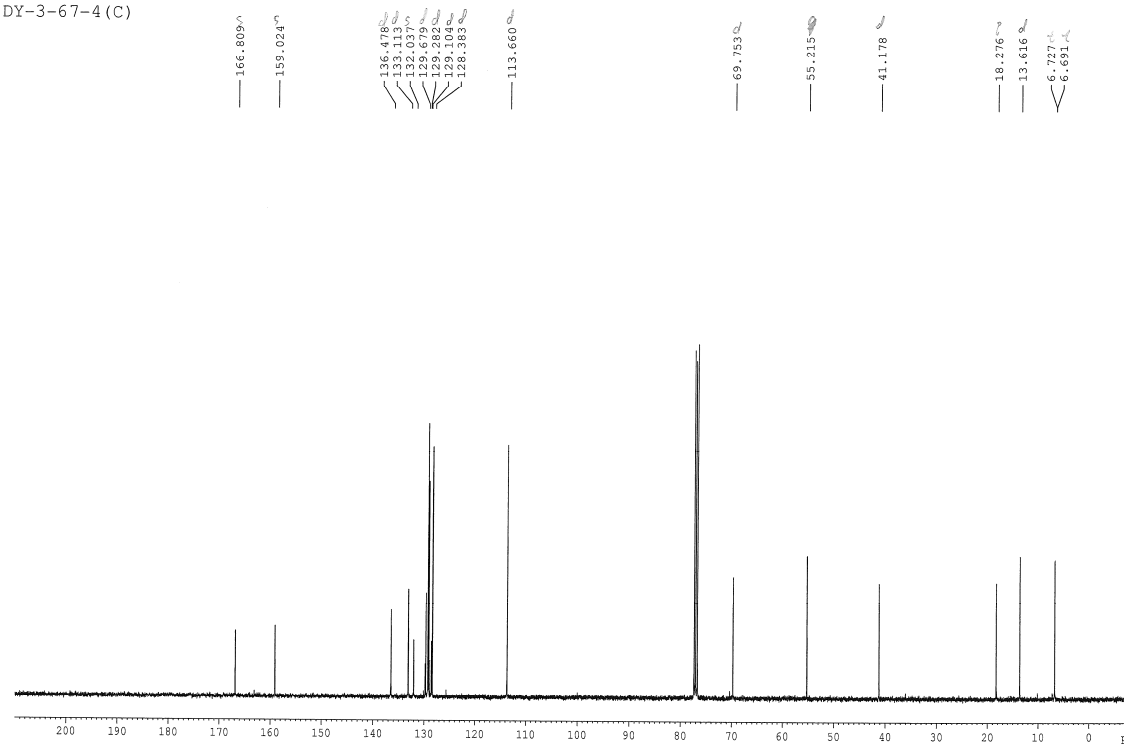


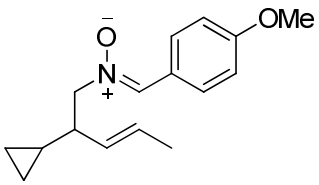


B38 (DY-3-67)

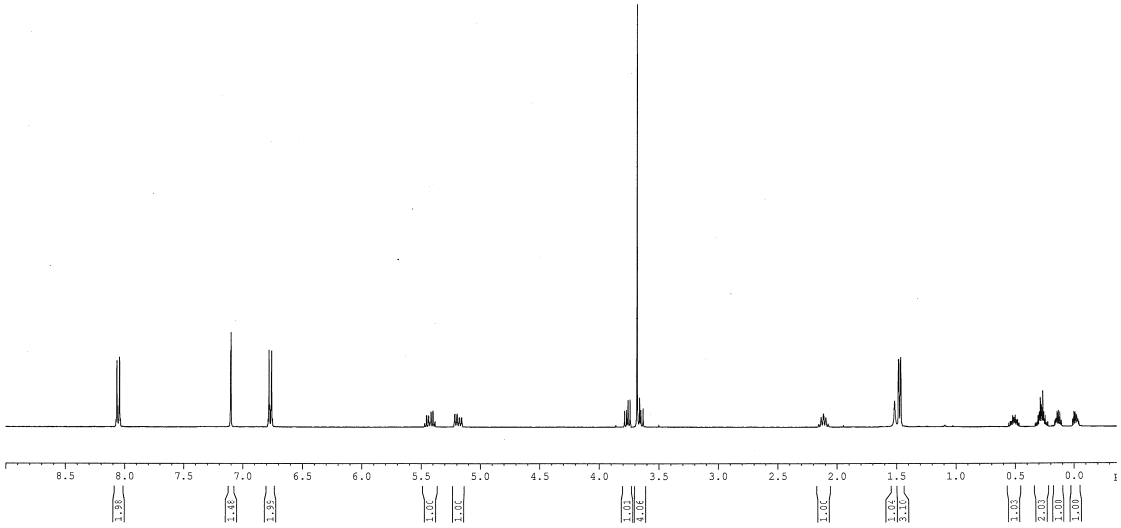


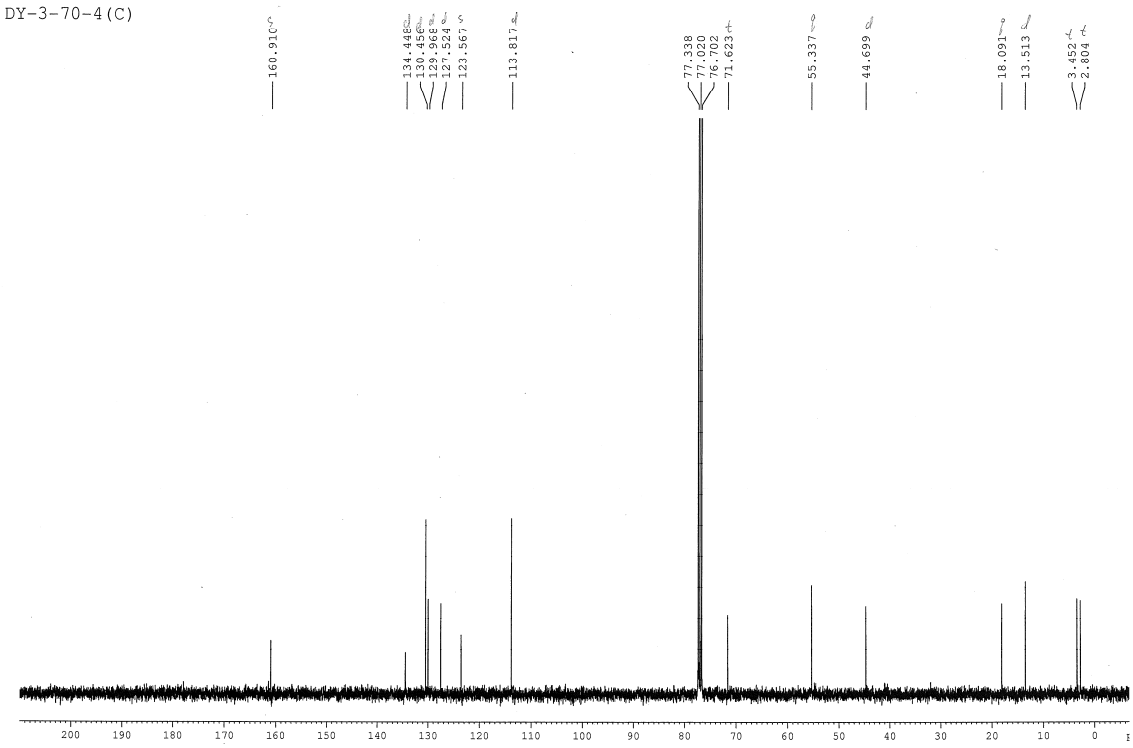
DY-3-67-4(C)

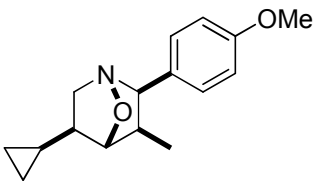



OMe
O
N
+

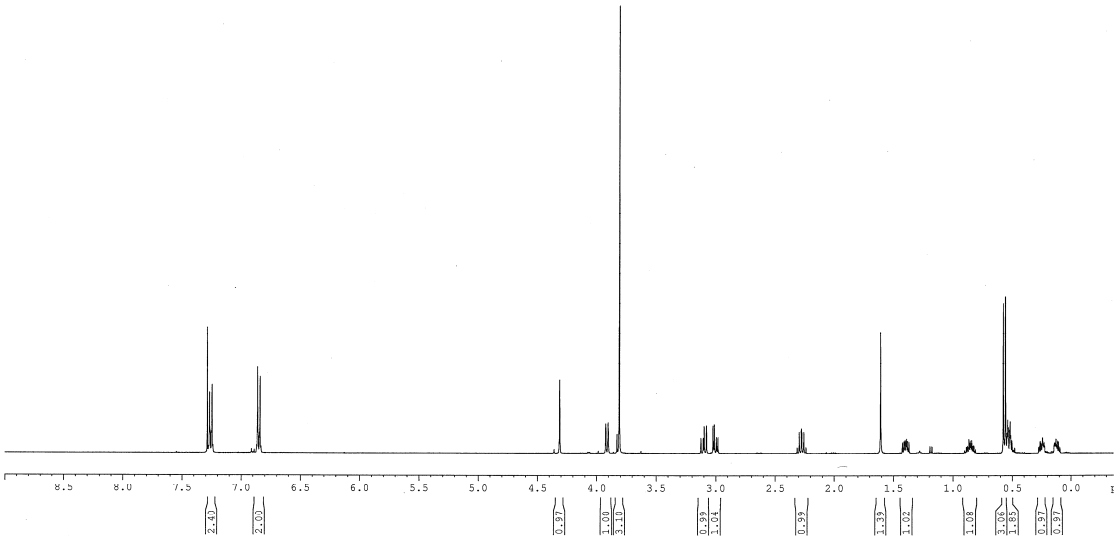
S-4 (DY-3-69)

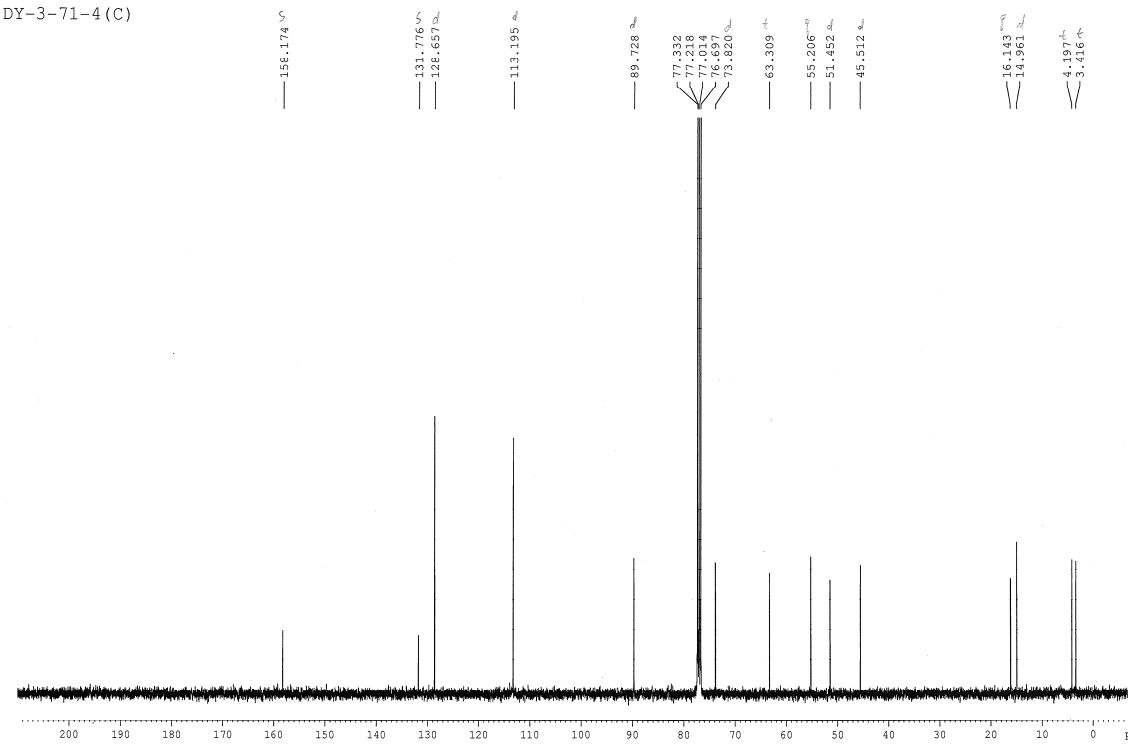

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.98
1.48
1.95
1.06
1.06
1.01
4.08
1.06
1.04
3.10
1.03
2.03
1.00
1.00


DY-3-70-4(C)
160.910
134.446
130.456
129.968
127.524
123.567
113.817
77.338
77.020
76.702
71.623
55.337
44.699
18.091
13.513
3.452
2.804
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

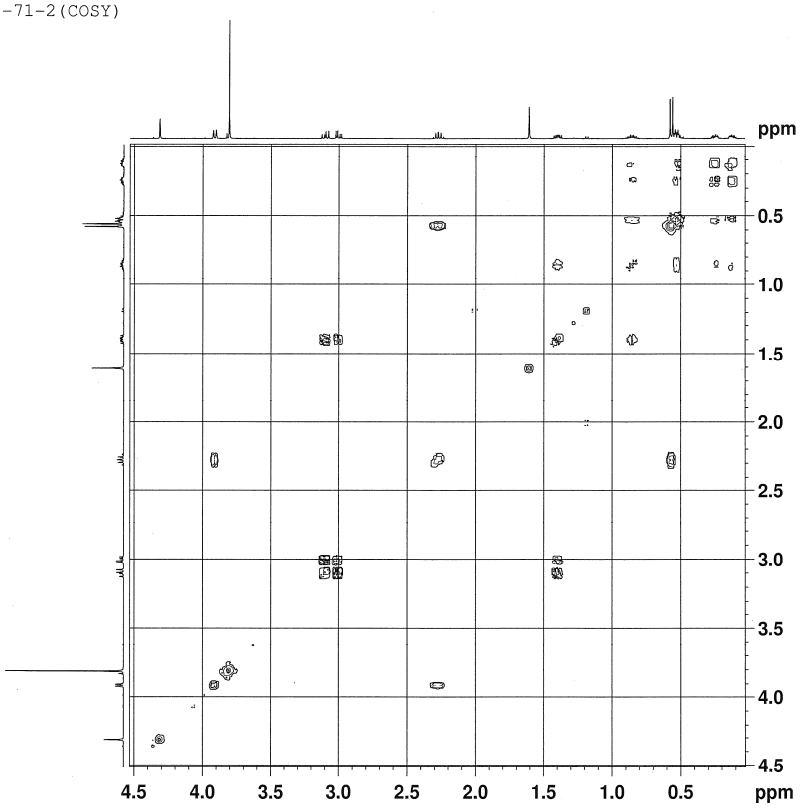

OMe
N
O

39 (DY-3-71)

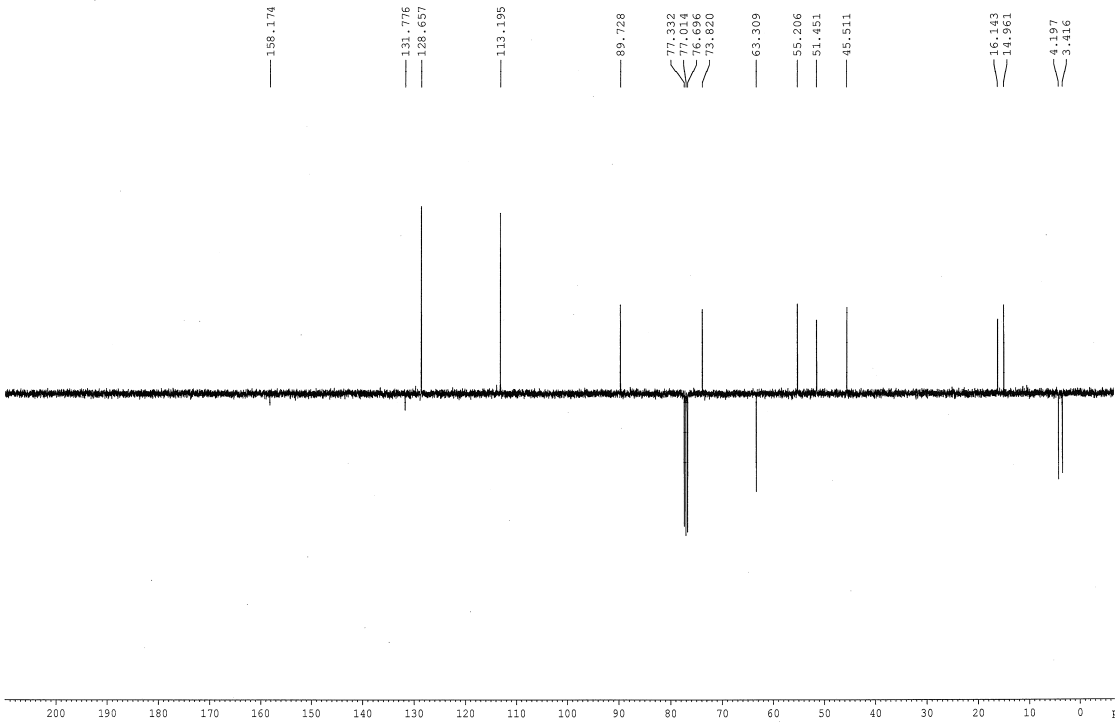

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.40
2.00
0.97
1.00
3.10
0.99
1.04
0.99
3.39
1.02
1.68
3.06
1.85
0.97
0.97

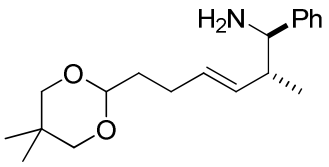

DY-3-71-4(C)
158.174
131.776
128.657
113.195
89.728
77.332
77.218
77.014
76.697
73.820
63.309
55.206
51.452
45.512
16.143
14.961
4.197
3.416
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

DY-3-71-2(COSY)

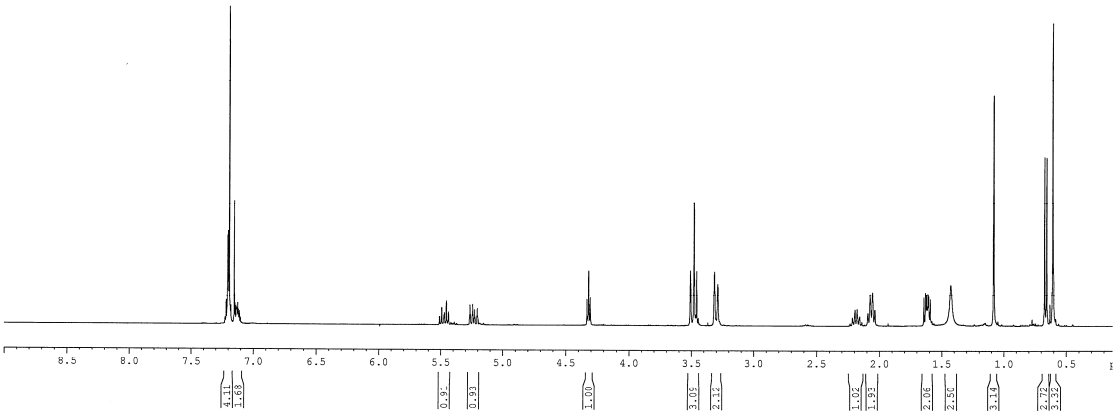


DY-3-71-3(APT

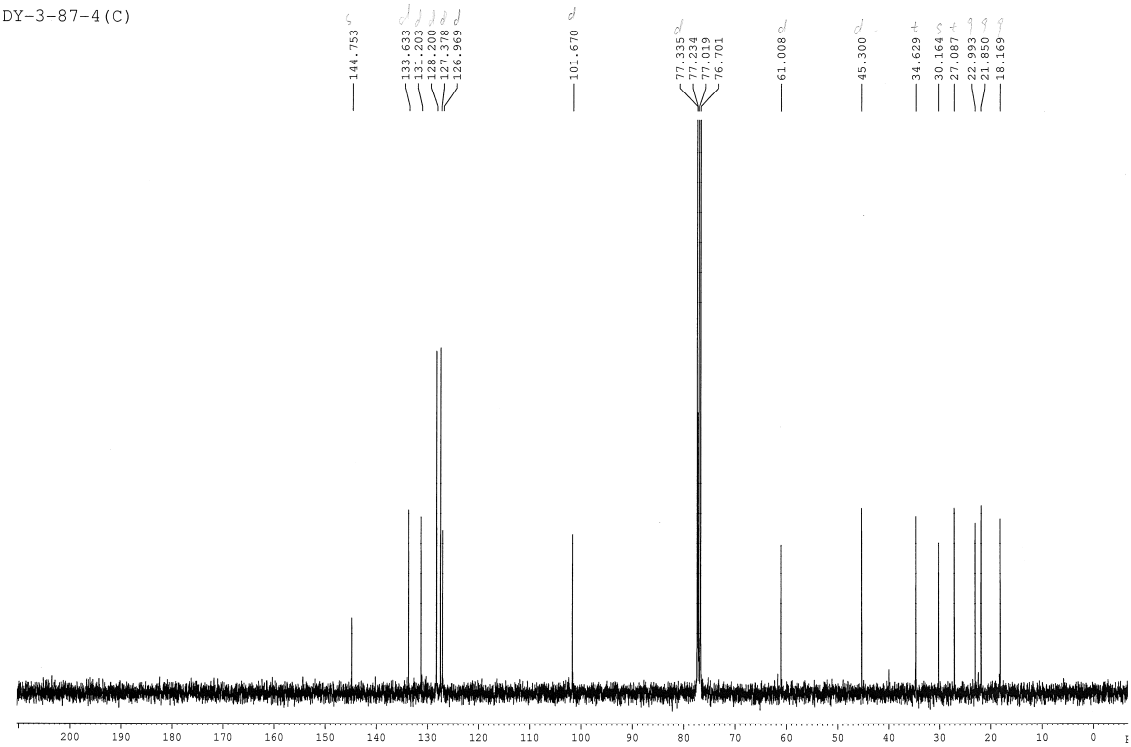


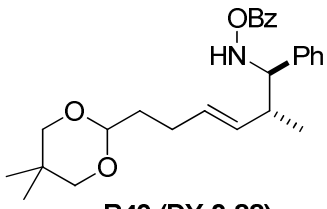


S-5 (DY-3-87)

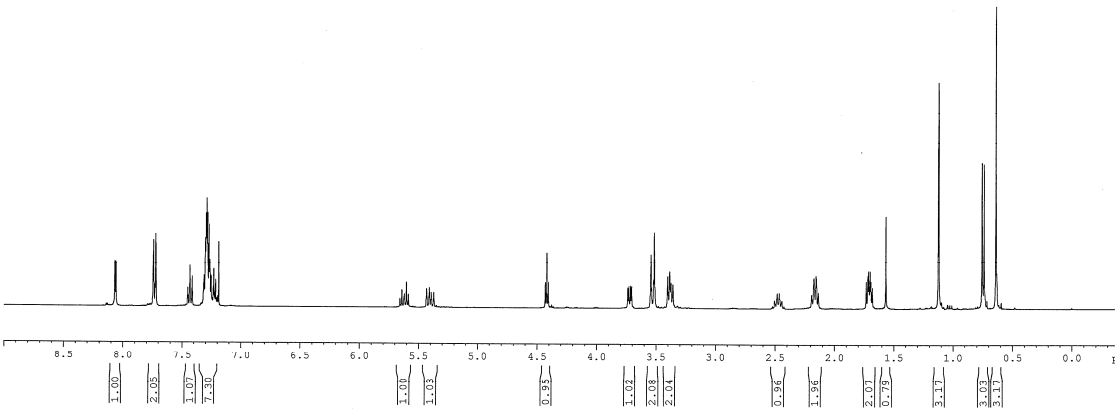


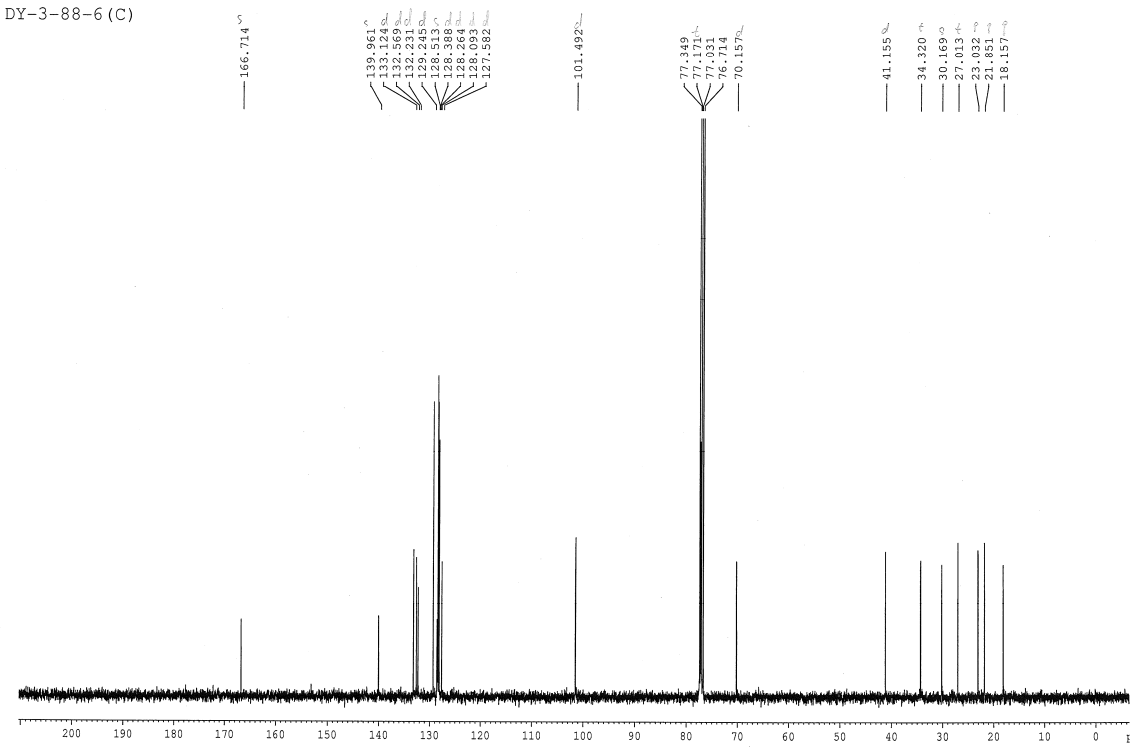
DY-3-87-4(C)

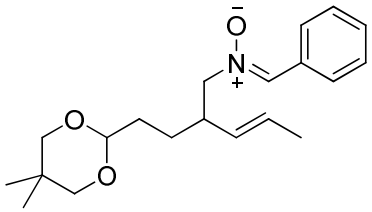



OBz
HN
Ph
O
O

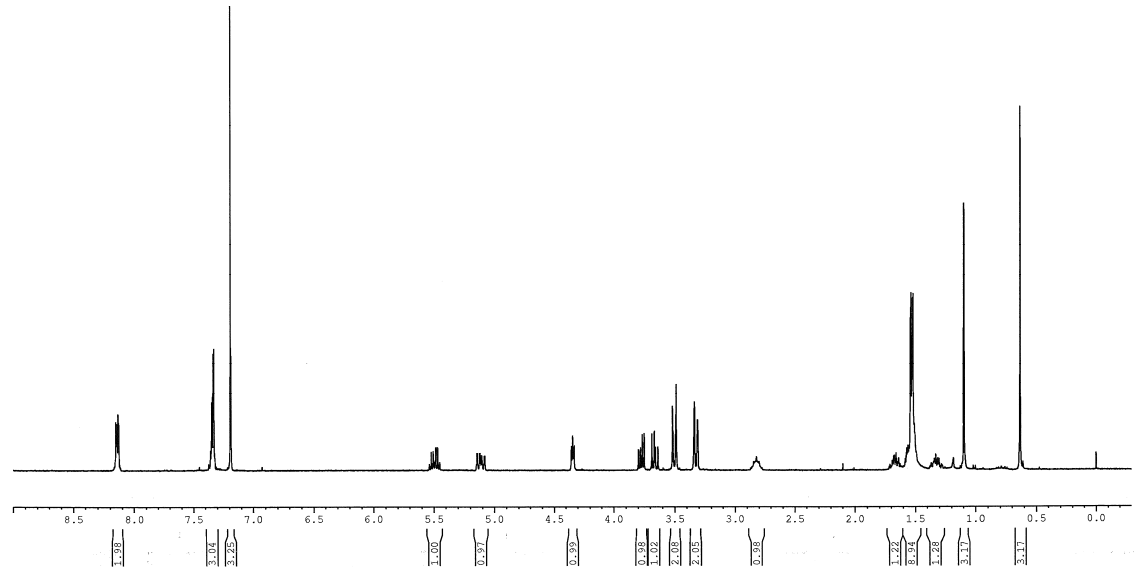
B40 (DY-3-88)

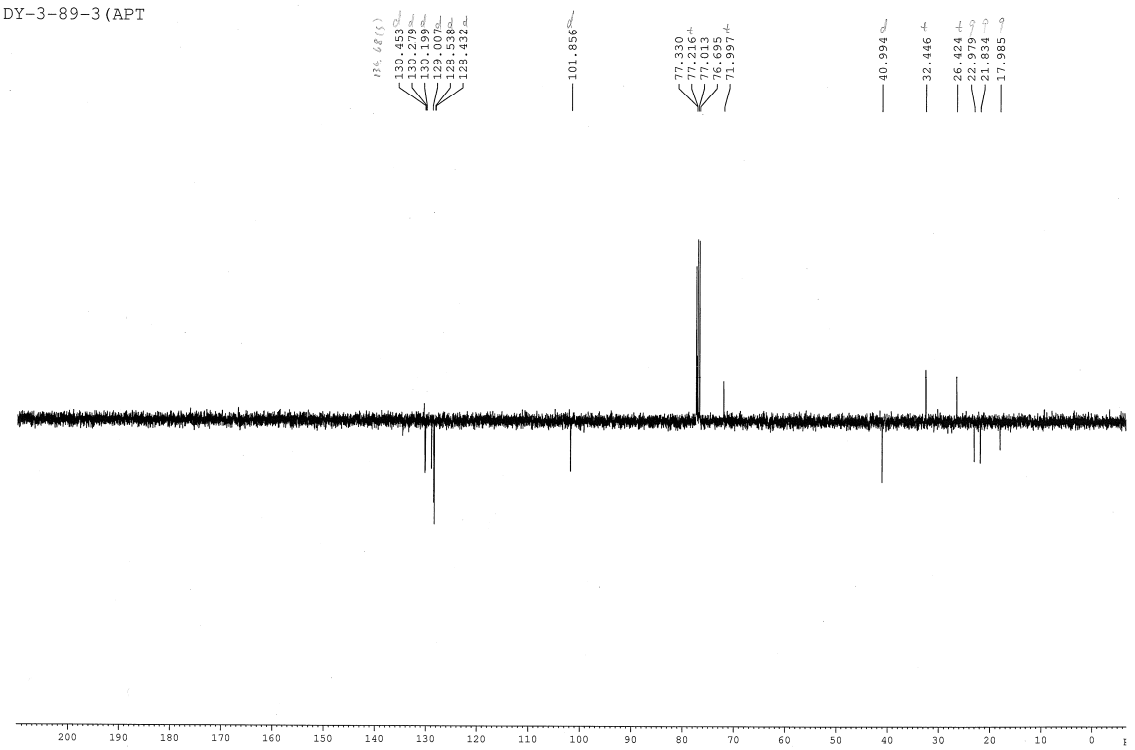

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.00
2.05
1.07
7.30
1.01
1.03
0.95
1.02
2.08
2.04
0.96
1.96
2.07
0.79
3.17
3.03
3.17

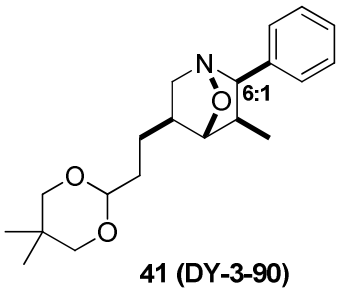

DY-3-88-6(C)
166.714
139.961
133.124
132.569
132.231
129.245
128.513
128.388
128.264
128.093
127.582
101.492
77.349
77.171
76.993
76.714
70.157
41.155
34.320
30.169
27.013
23.032
21.851
18.157
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



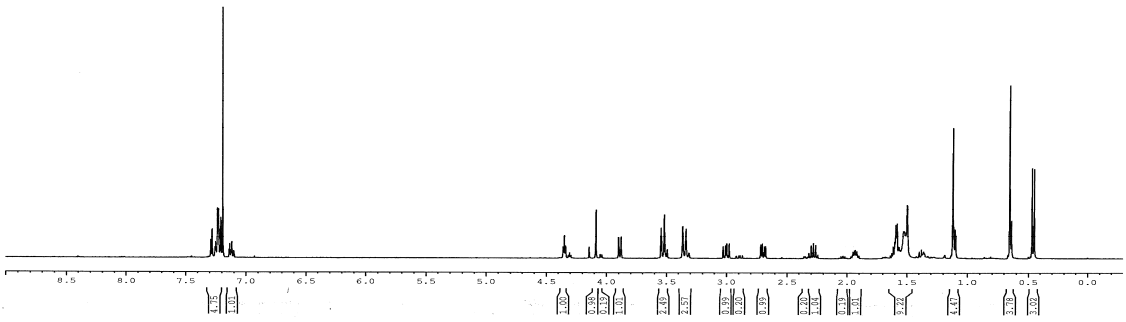
S-6 (DY-3-89)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.98
3.04
3.25
1.00
0.97
0.99
0.98
1.02
2.08
2.05
0.98
1.22
8.94
1.28
3.17
3.17

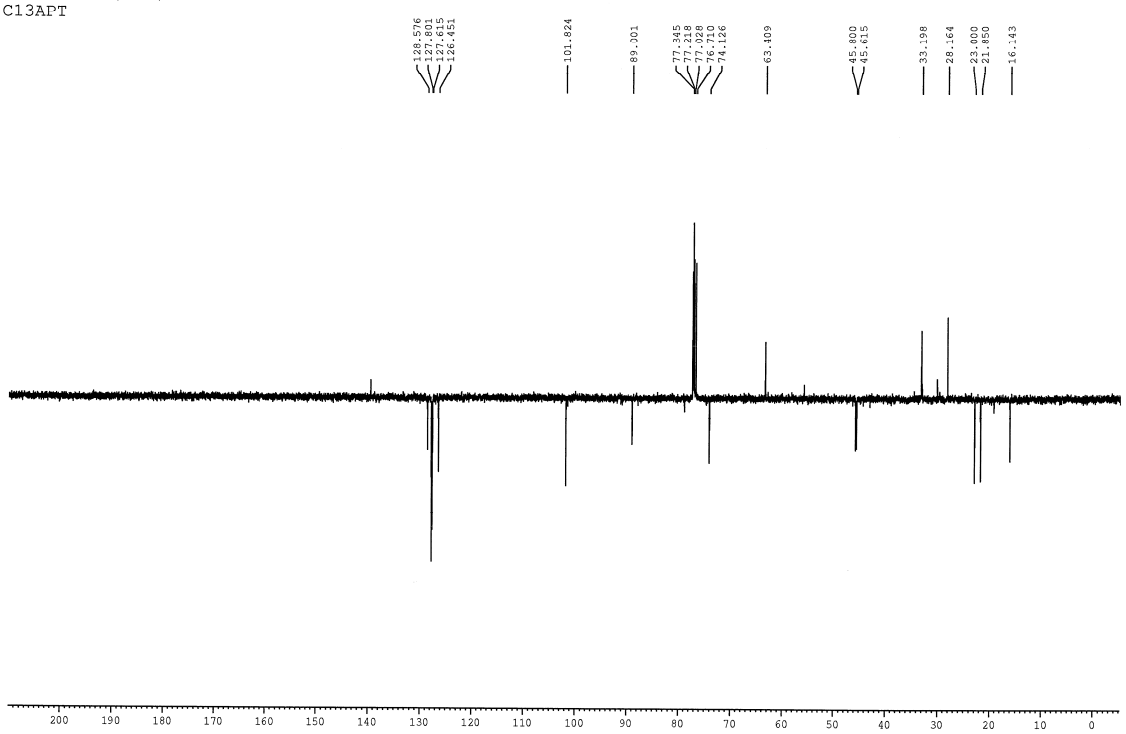

DY-3-89-3(APT
130.453
133.279
133.199
129.007
128.538
128.432
101.858
77.330
77.216
77.013
76.695
71.997
40.994
32.446
26.424
22.979
21.834
17.985
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

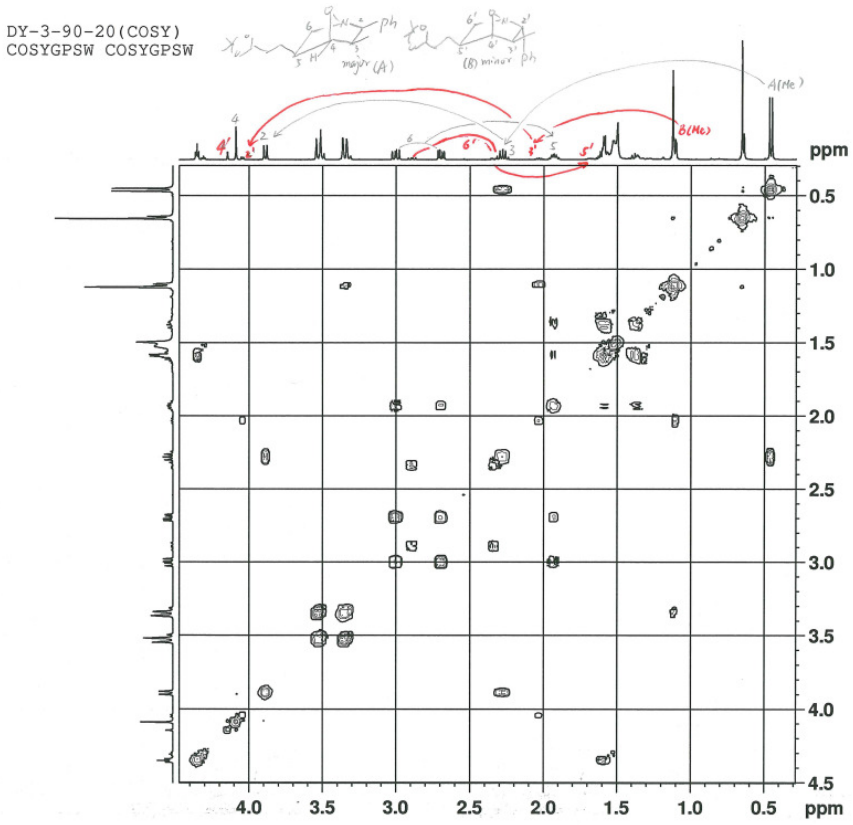


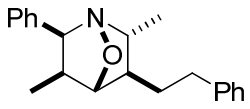
41 (DY-3-90)



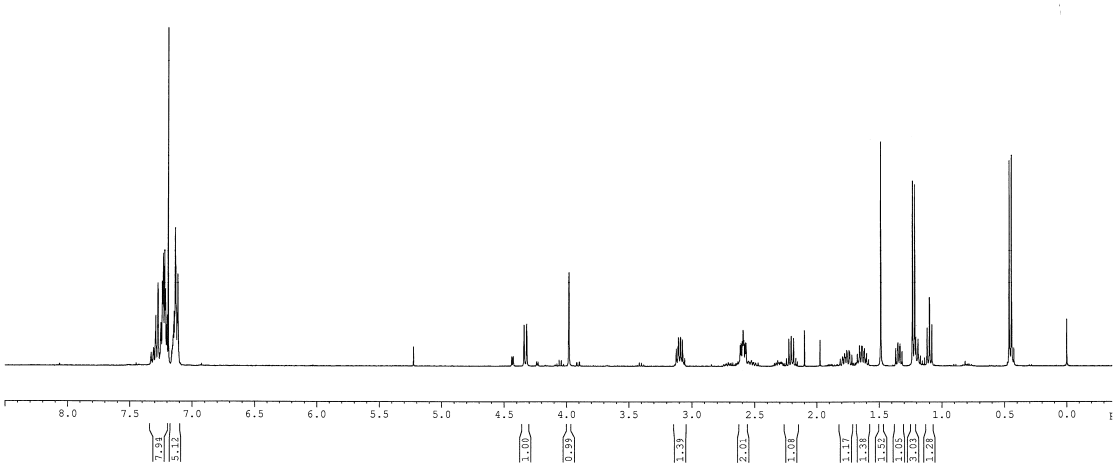
DY-3-90-20(APT)
C13APT



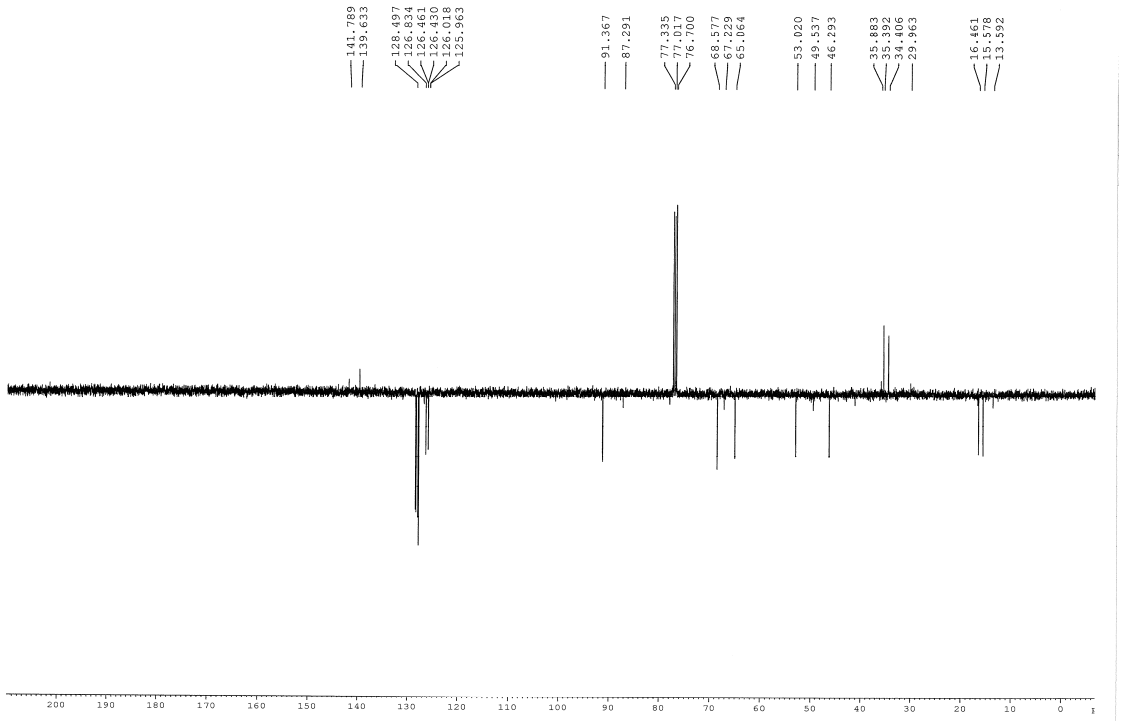

DY-3-90-20(COSY)
COSYGPSW COSYGPSW
major (A)
(B) minor
A(Me)
B(Me)
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

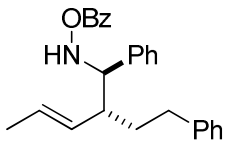


42 (DY-2-186)

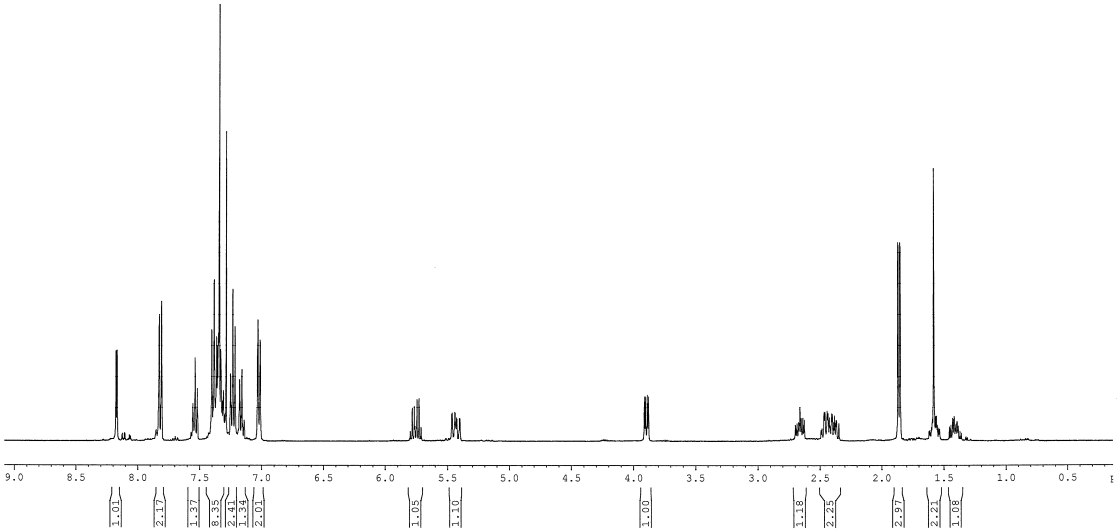


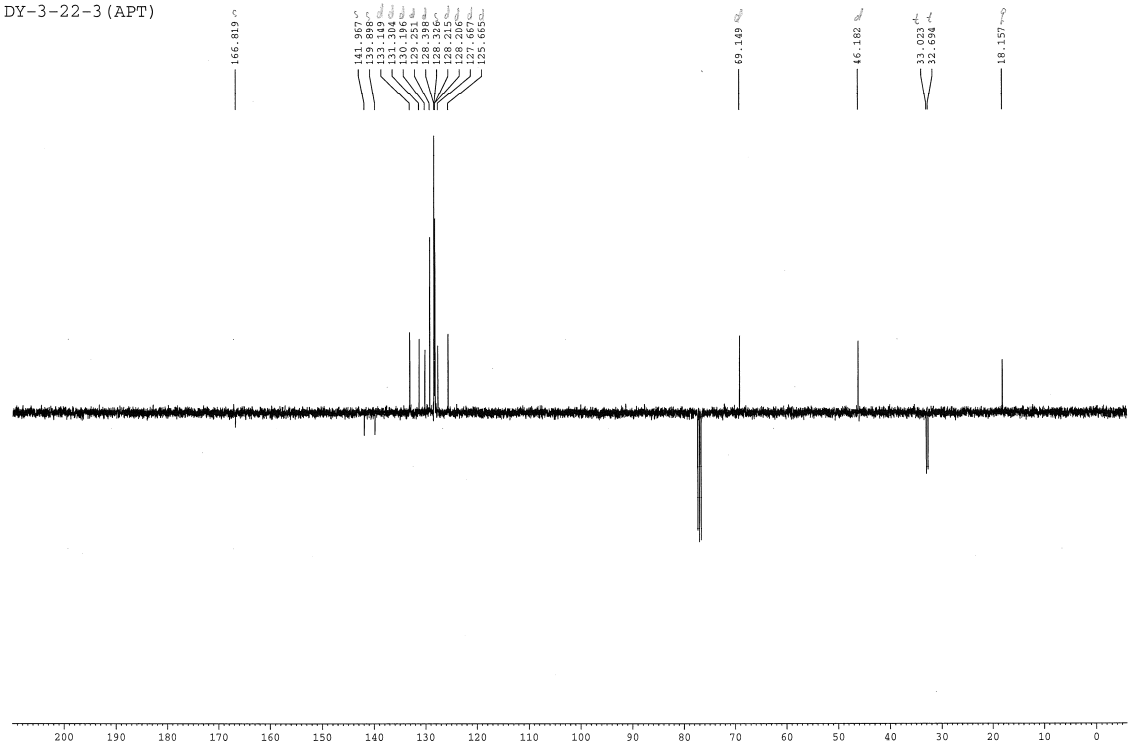
DY-2-186B-21(

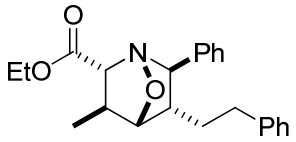



OBz
HN
Ph
Ph

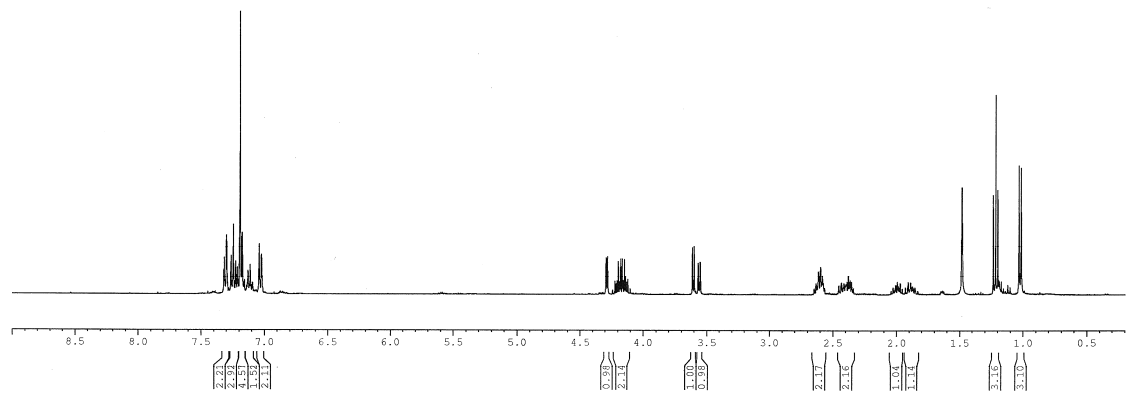
B43 (DY-3-22)

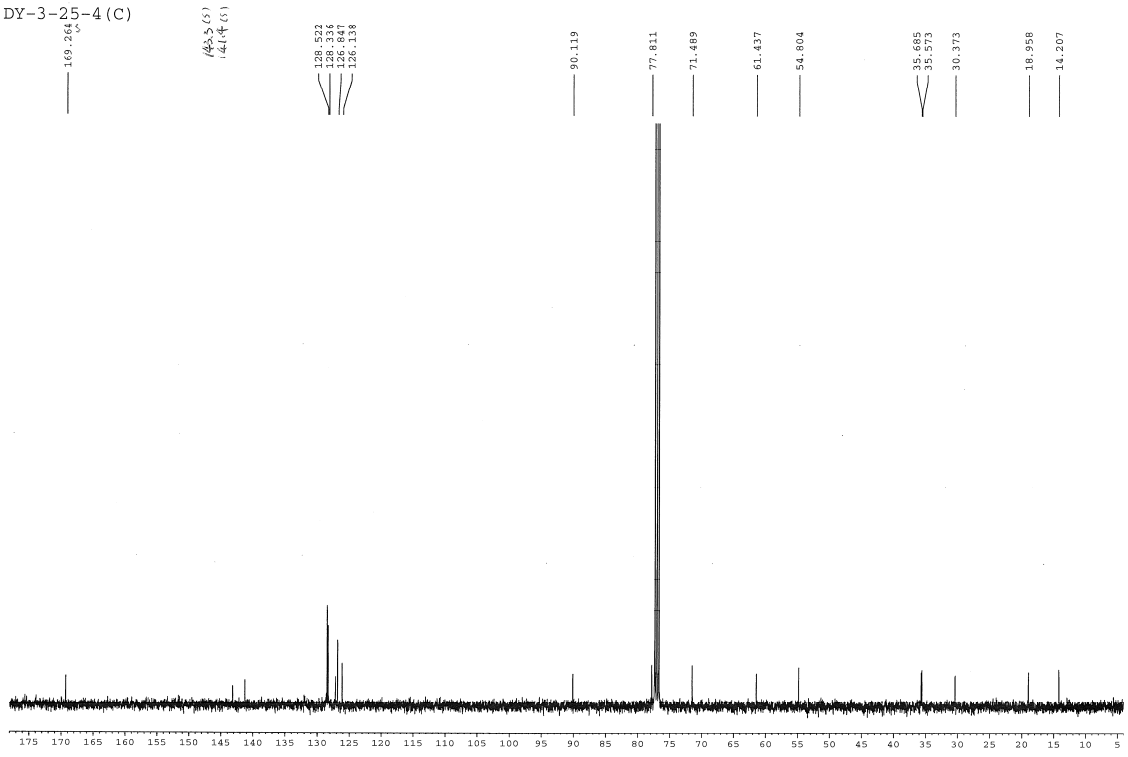

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.01
2.17
1.37
8.35
2.41
1.34
2.01
1.05
1.10
1.00
1.18
2.25
2.97
2.21
1.08

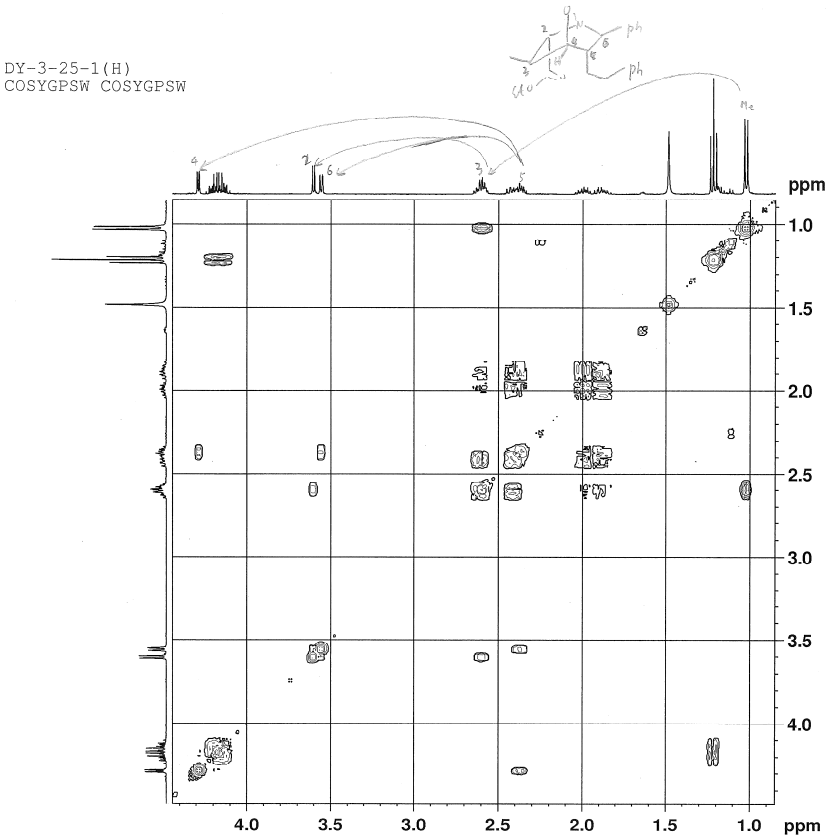

DY-3-22-3 (APT)
166.819
141.967
139.898
133.149
131.304
130.196
129.251
128.398
128.326
128.215
128.209
127.057
125.665
69.149
46.182
33.023
32.694
18.157
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

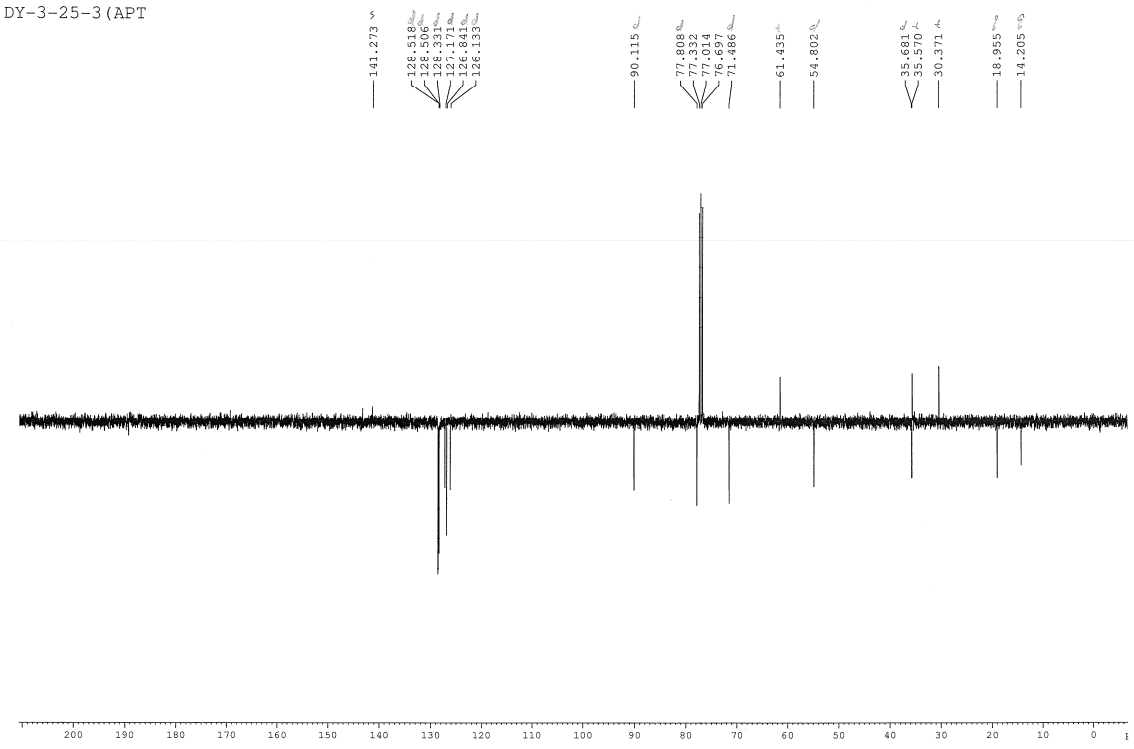

O
EtO
N
Ph
O
Ph

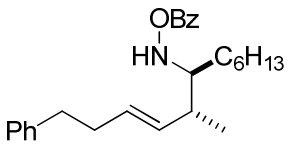
44 (DY-3-25)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
2.24
2.41
4.51
1.58
2.11
0.98
2.14
1.00
0.98
2.17
2.16
1.04
1.14
3.16
3.10

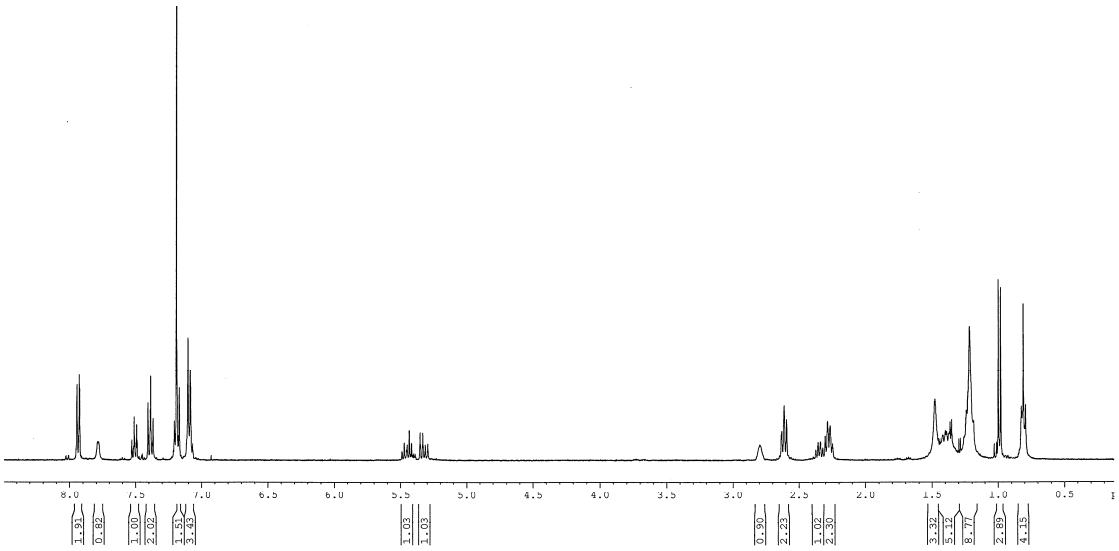

DY-3-25-4(C)
169.264
128.522
128.338
126.847
126.138
90.119
77.811
71.489
61.437
54.804
35.685
35.573
30.373
18.958
14.207
175
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5

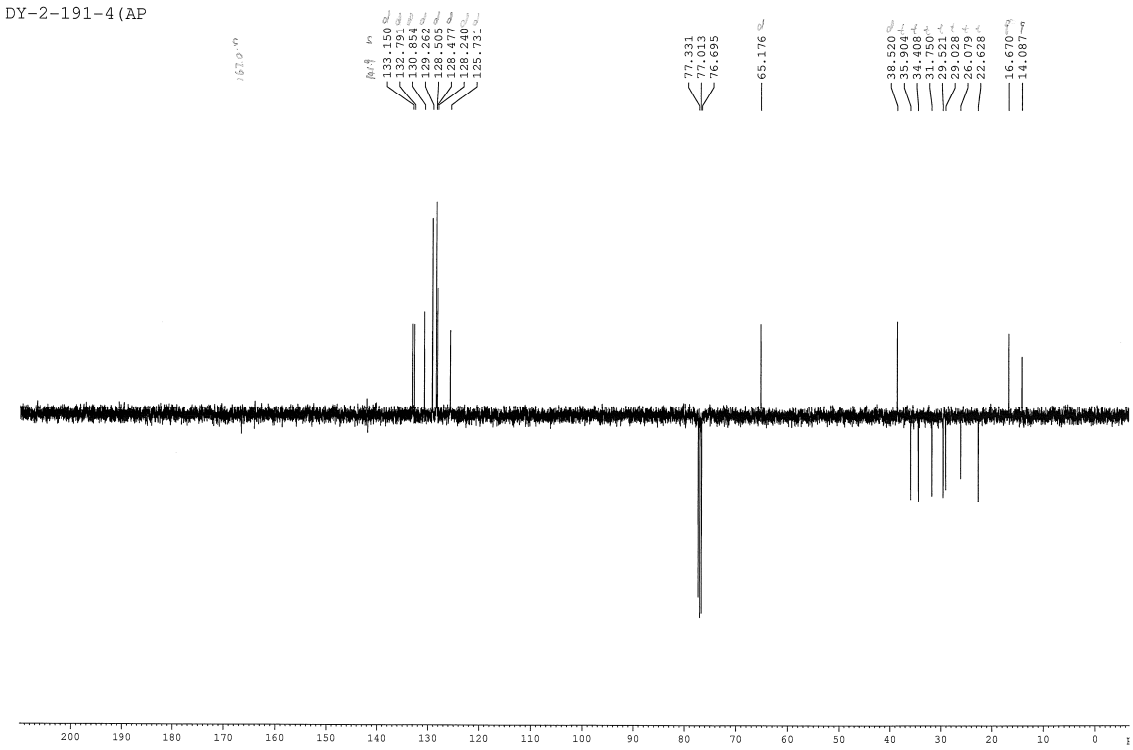

DY-3-25-1(H)
COSYGPSW COSYGPSW
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

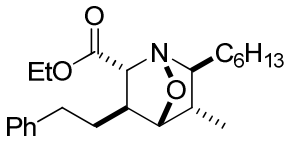

DY-3-25-3(APT
141.273
128.518
128.506
128.331
127.171
126.841
126.133
90.115
77.808
77.332
77.014
76.697
71.486
61.435
54.802
35.681
35.570
30.371
18.955
14.205
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


OBz
HN
C6H13
Ph

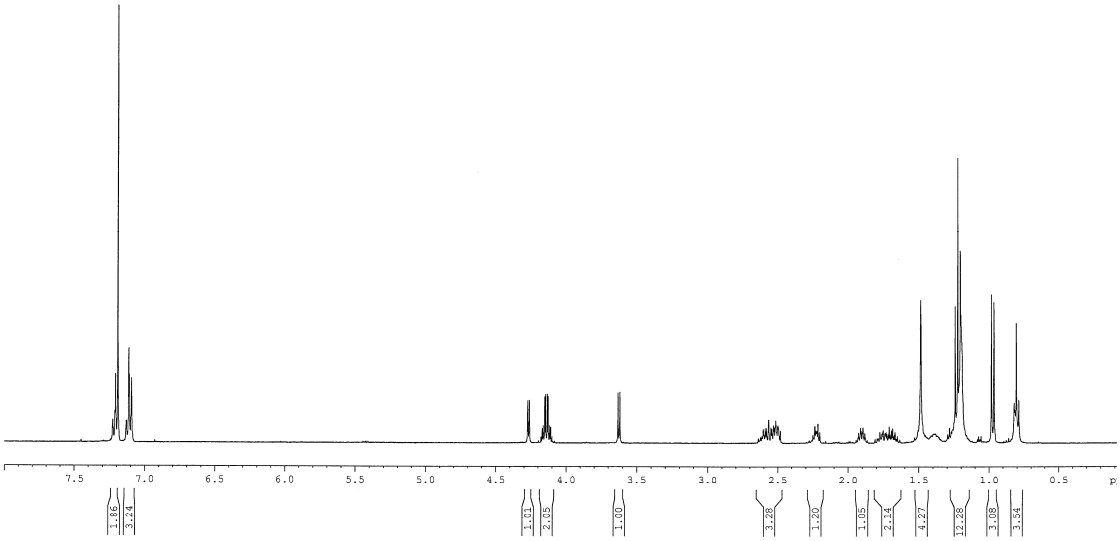
B45 (DY-3-3)

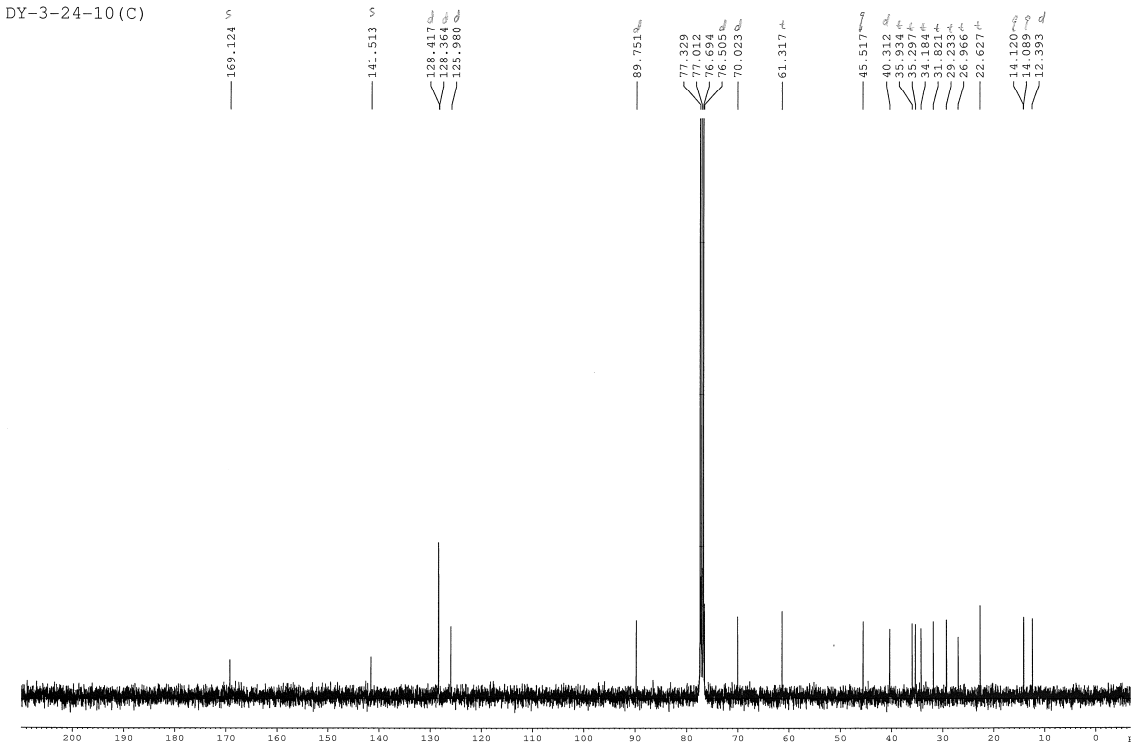

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.91
0.82
1.00
2.02
1.51
3.43
1.03
1.03
0.90
2.23
1.02
2.30
3.32
5.12
8.77
2.89
4.15


DY-2-191-4(AP
133.150
132.791
130.854
129.262
128.505
128.477
128.240
125.731
77.331
77.013
76.695
65.176
38.520
35.904
34.408
31.750
29.521
29.028
26.079
22.628
16.670
14.087
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

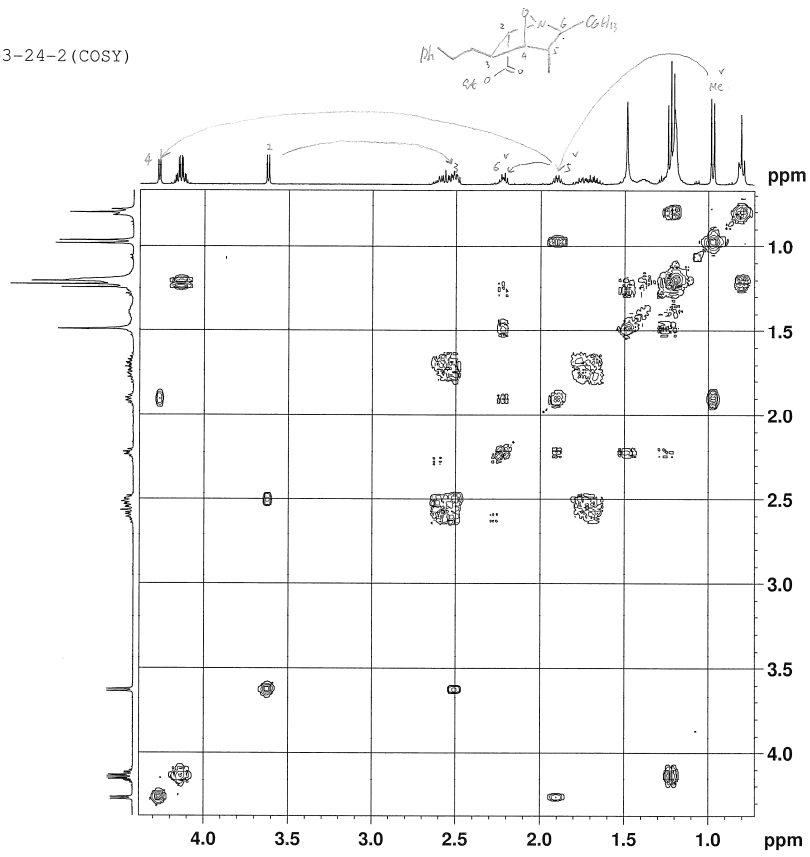

O
EtO
N
O
C6H13
Ph

46 (DY-3-24)

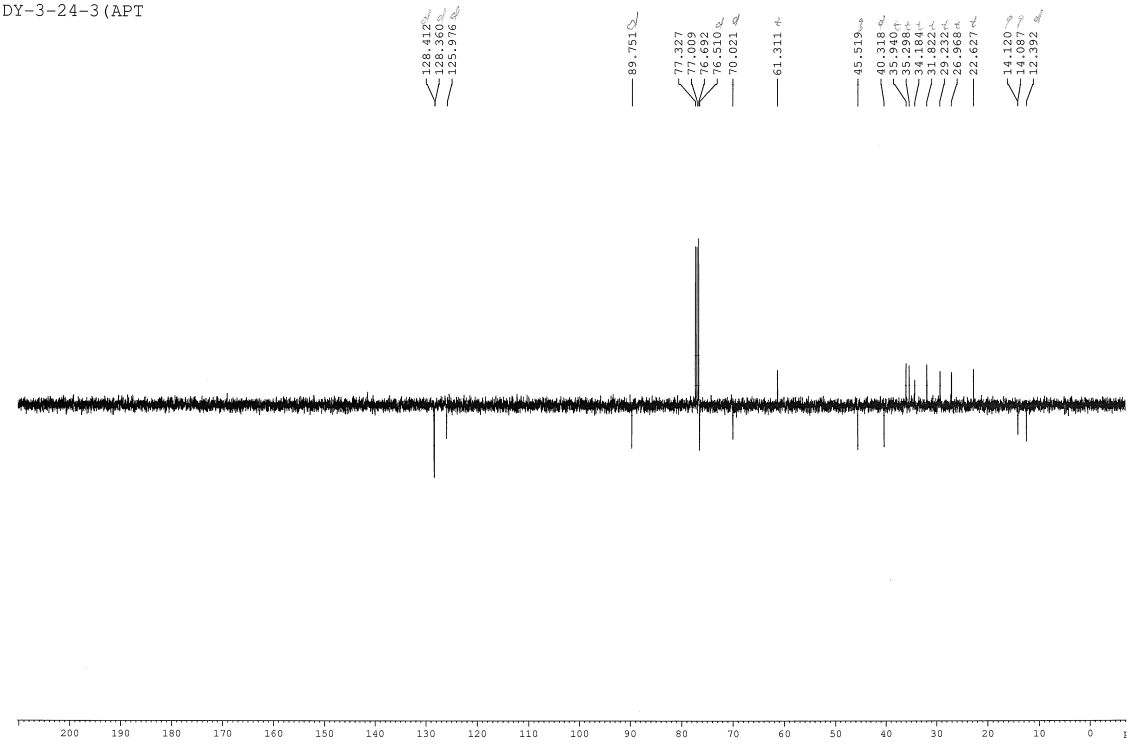

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.16
3.24
1.01
2.05
1.00
3.28
1.20
1.05
2.14
4.27
12.28
3.08
3.54

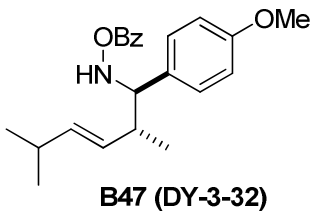

DY-3-24-10(C)
169.124
14..513
128.417
128.364
125.980
89.751
77.329
77.012
76.694
76.505
70.023
61.317
45.517
40.312
35.934
35.297
34.184
31.821
29.233
26.966
22.627
14.120
14.089
12.393
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

DY-3-24-2(COSY)

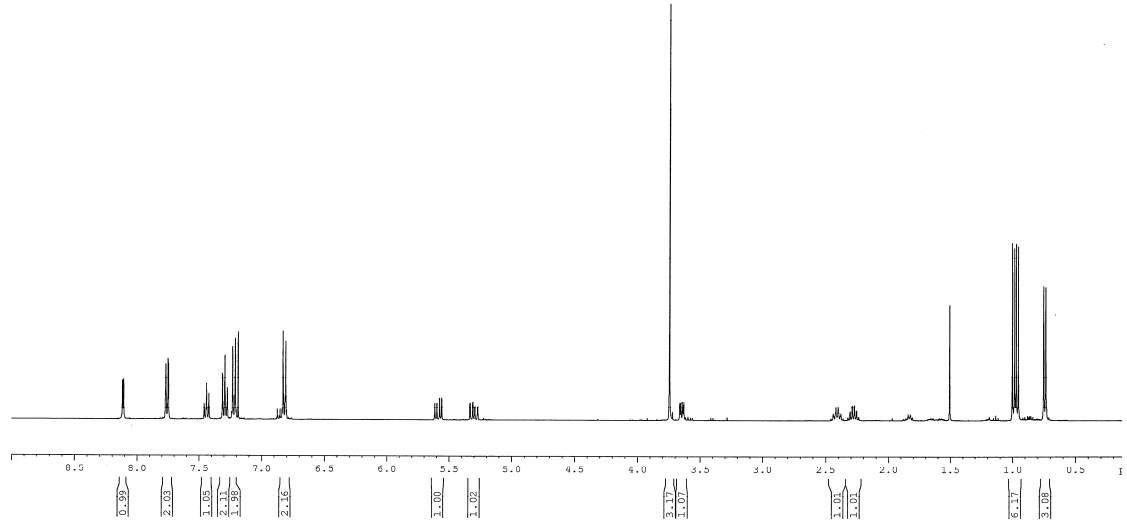


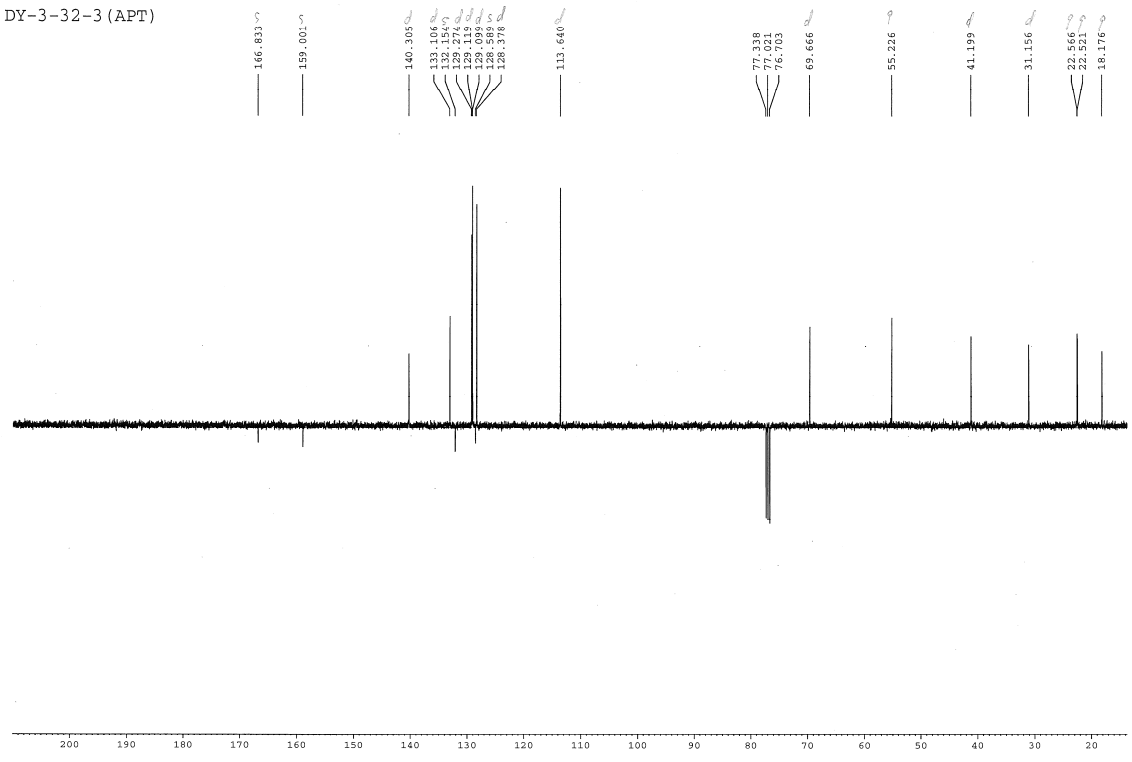
DY-3-24-3(APT

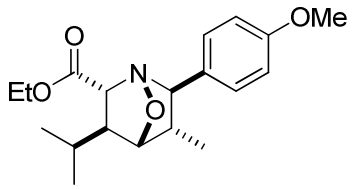



OBz
HN
OMe

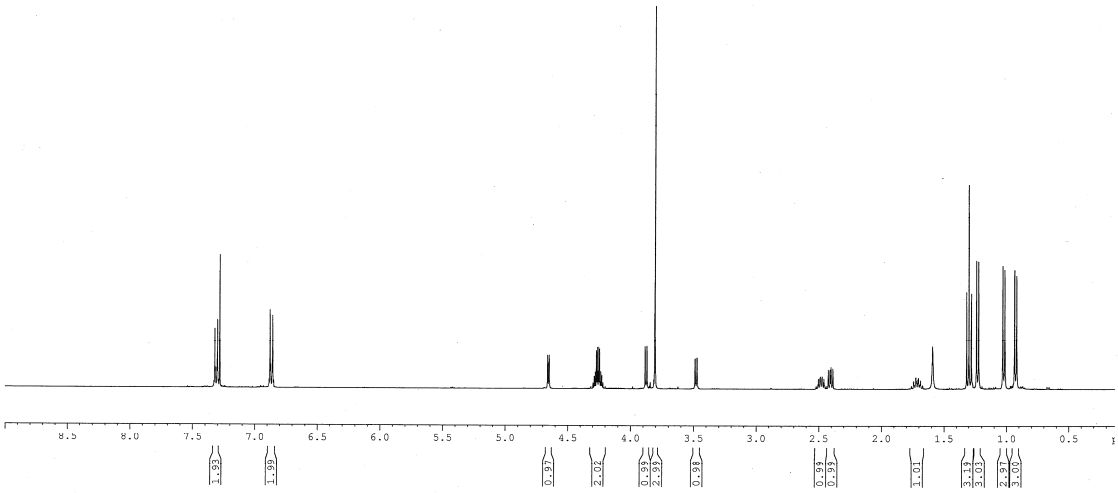
B47 (DY-3-32)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.99
2.03
1.05
2.11
1.98
2.16
1.00
1.02
3.17
1.07
1.05
1.01
6.17
3.08

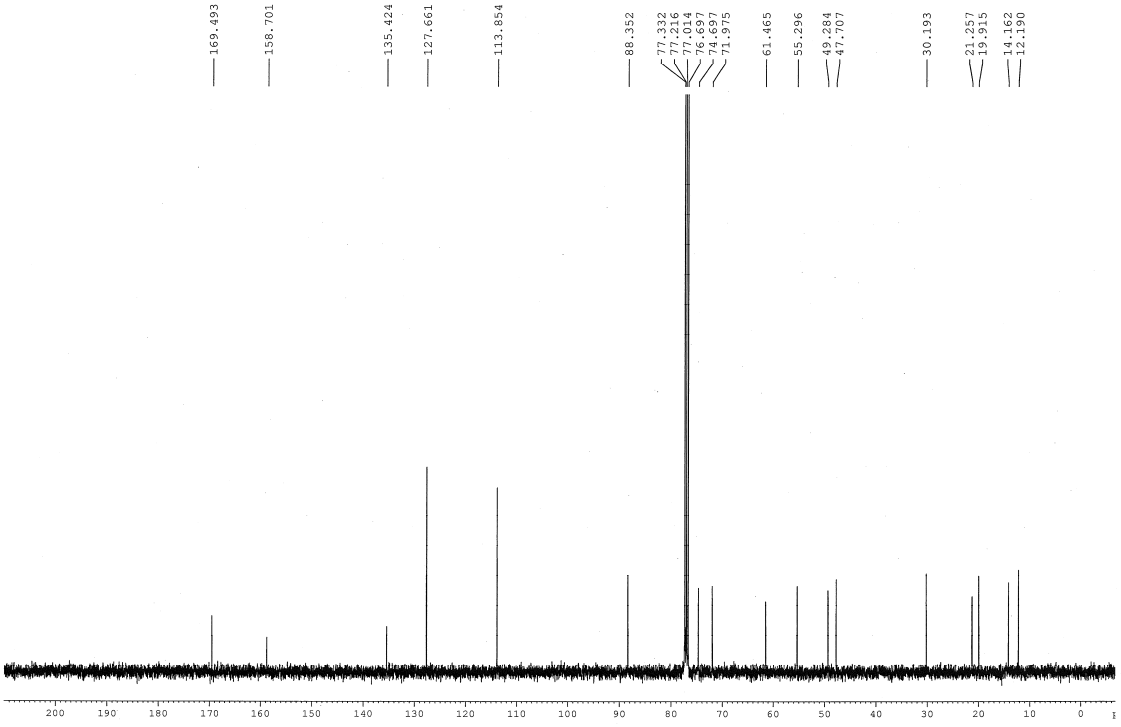

DY-3-32-3(APT)
166.833
159.001
140.305
133.106
132.154
130.274
129.114
129.099
128.589
128.378
113.640
77.338
77.021
76.703
69.666
55.226
41.199
31.156
22.566
22.521
18.176
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20



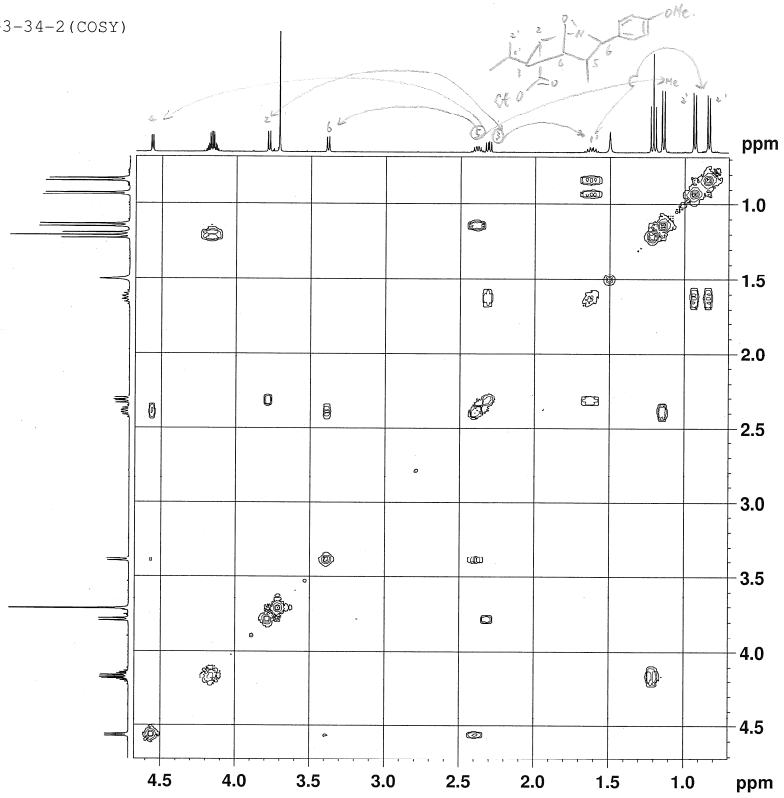
48 (DY-3-34)



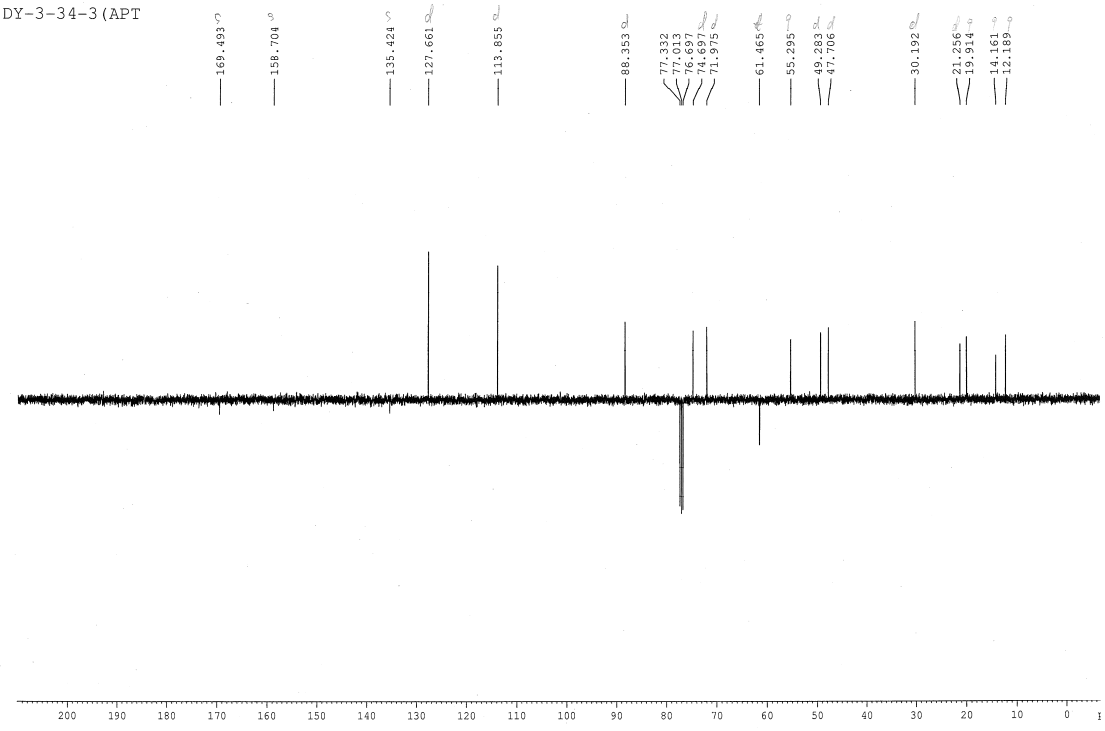
DY-3-34-4(C)

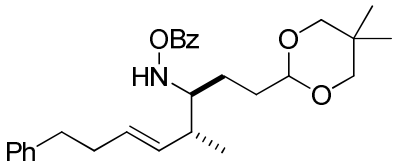


DY-3-34-2(COSY)



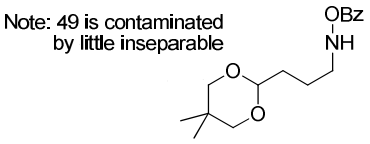
DY-3-34-3(APT

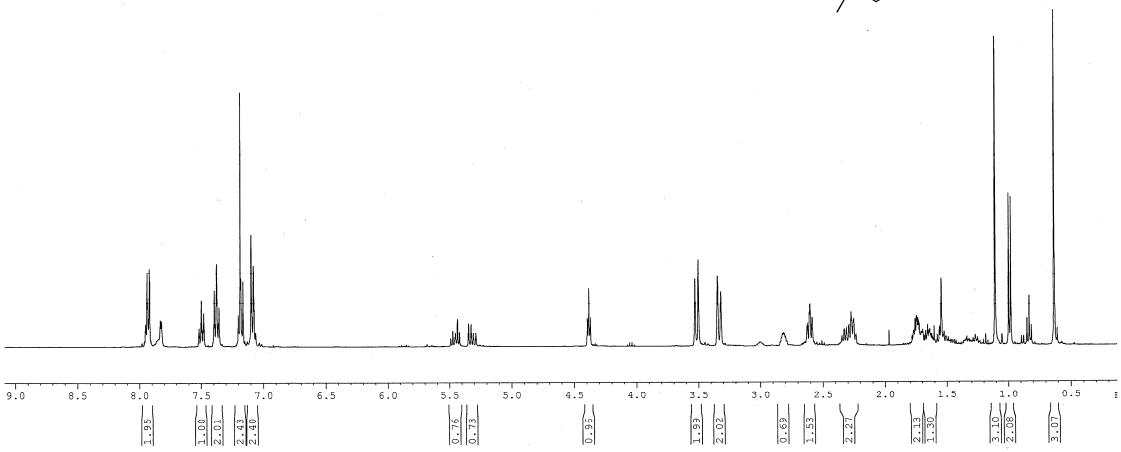


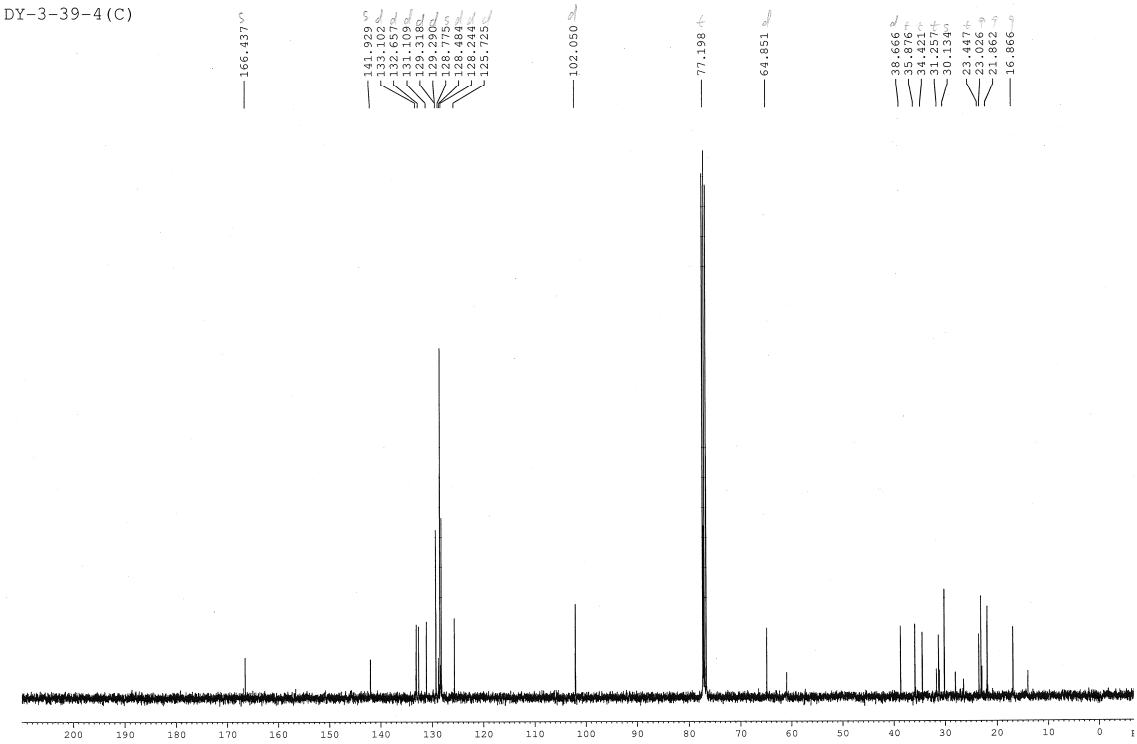


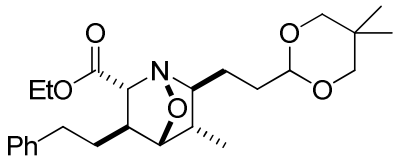
B49 (DY-3-39)

Note: 49 is contaminated by little inseparable

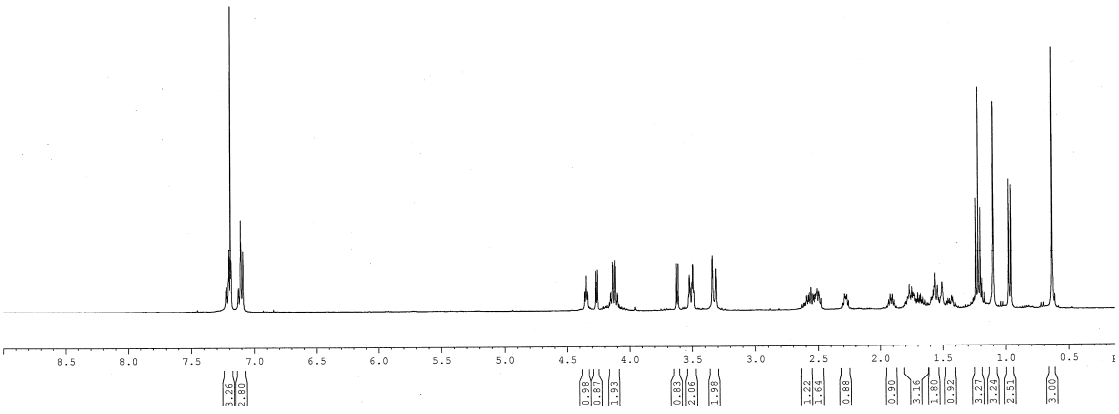


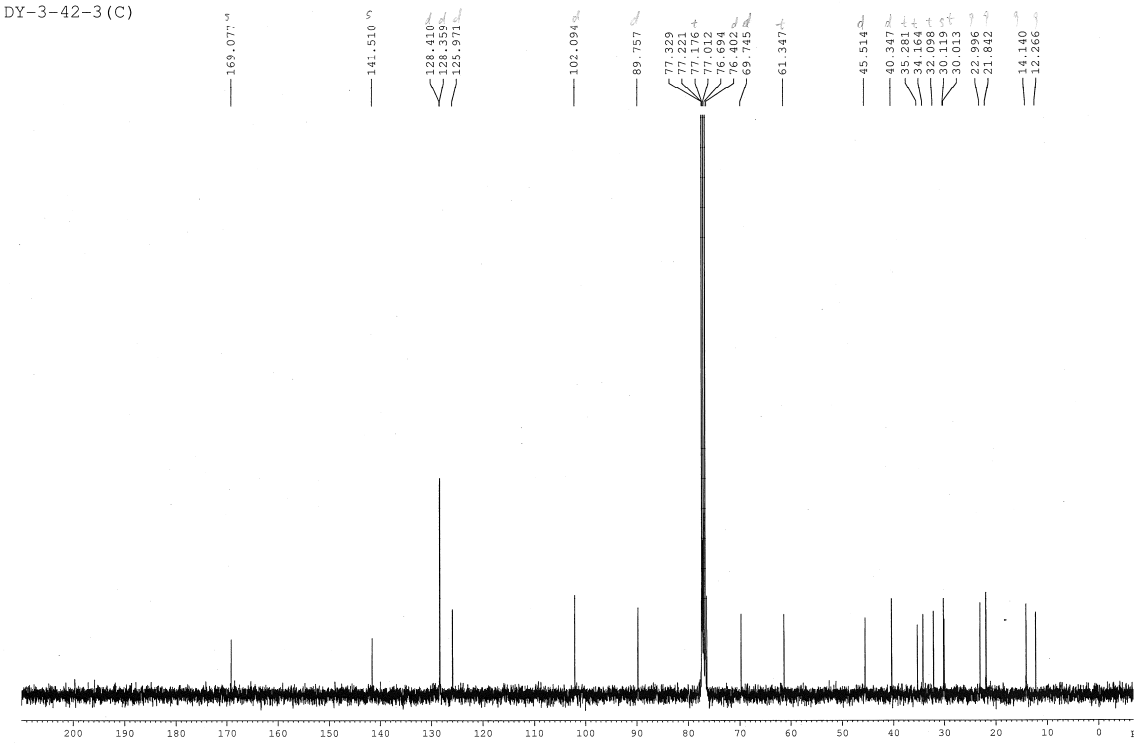


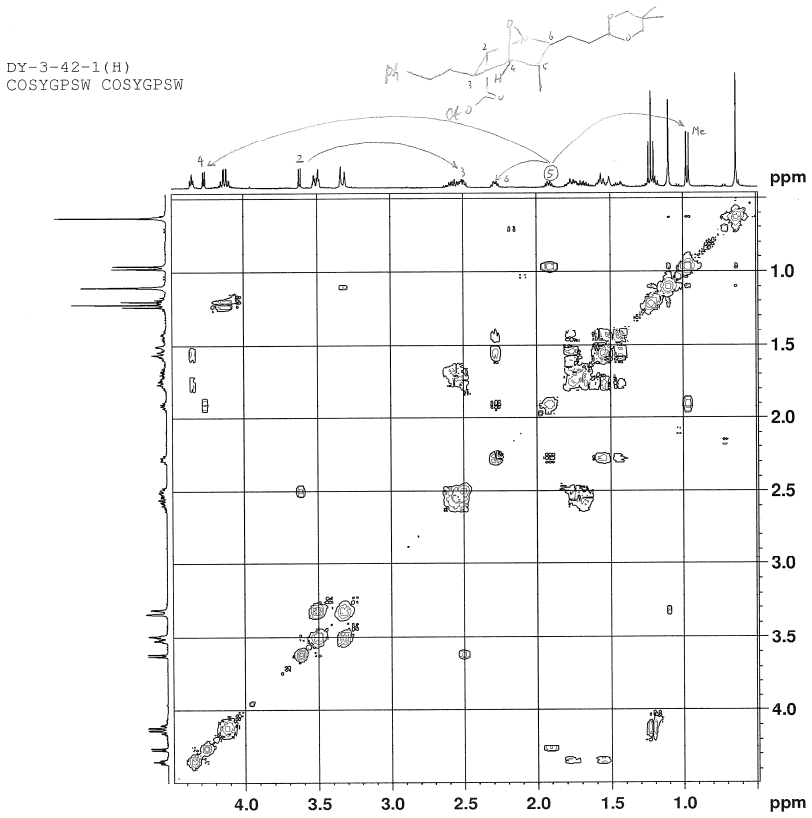


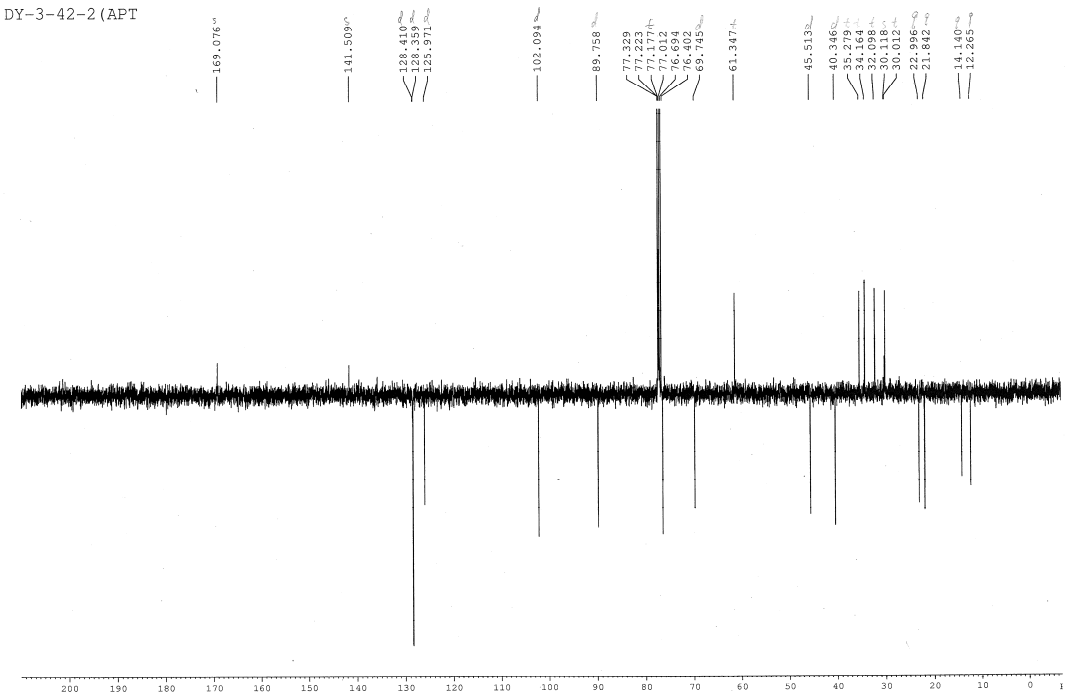

O
EtO
N
O
O
O
Ph

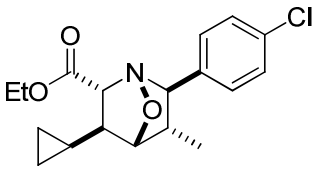
50 (DY-3-42)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
3.26
2.80
0.98
0.87
1.93
0.83
2.06
1.98
1.22
1.64
0.88
0.90
3.16
1.80
0.92
3.27
3.24
2.51
3.00

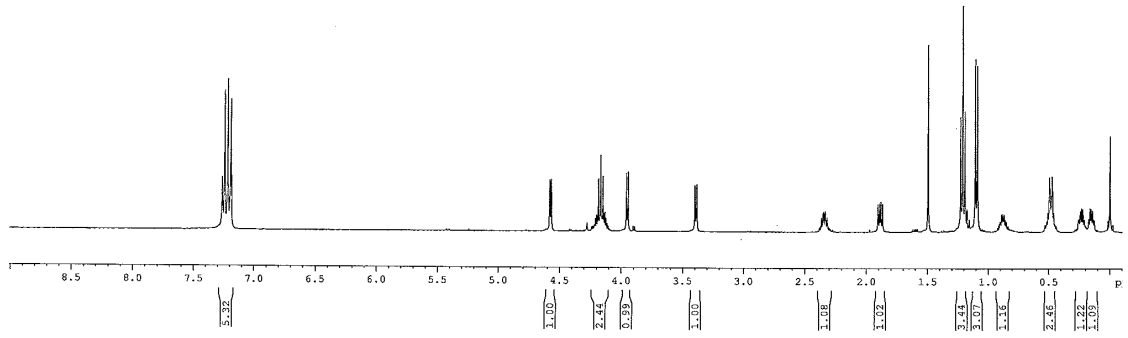

DY-3-42-3(C)
169.077
141.510
128.410
128.359
125.971
102.094
89.757
77.329
77.221
77.176
77.012
76.694
76.402
69.745
61.347
45.514
40.347
35.281
34.164
32.098
30.119
30.013
22.996
21.842
14.140
12.266
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

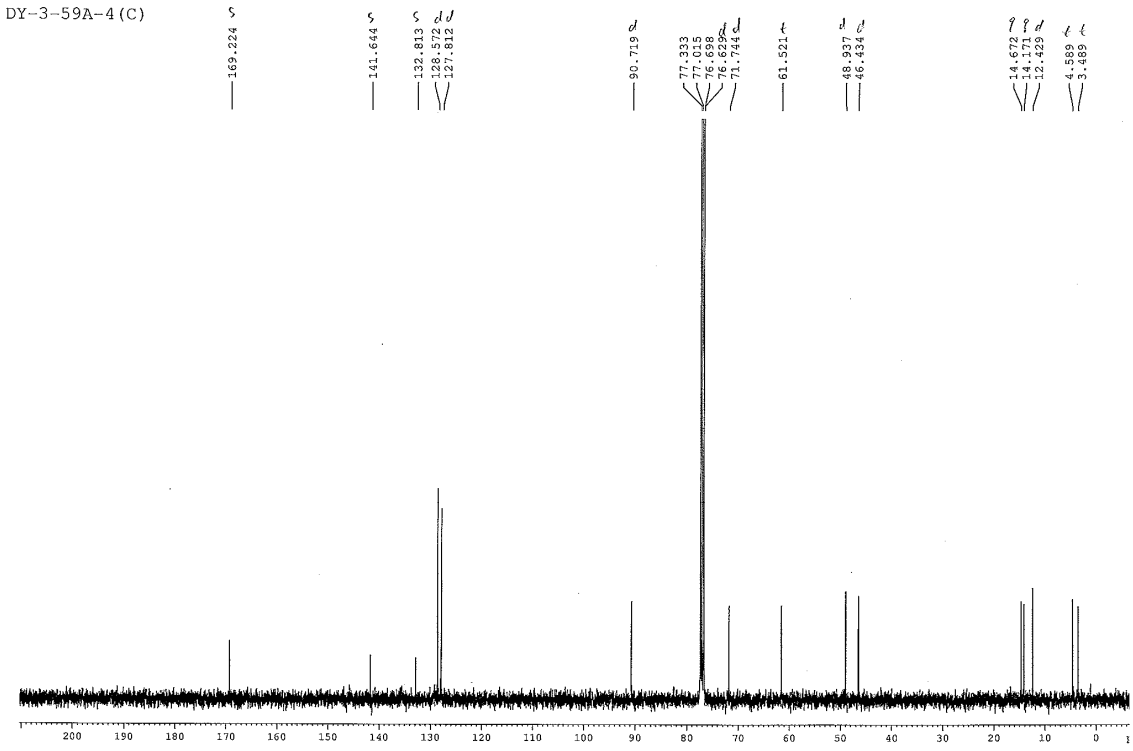

DY-3-42-1(H)
COSYGPSW COSYGPSW
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

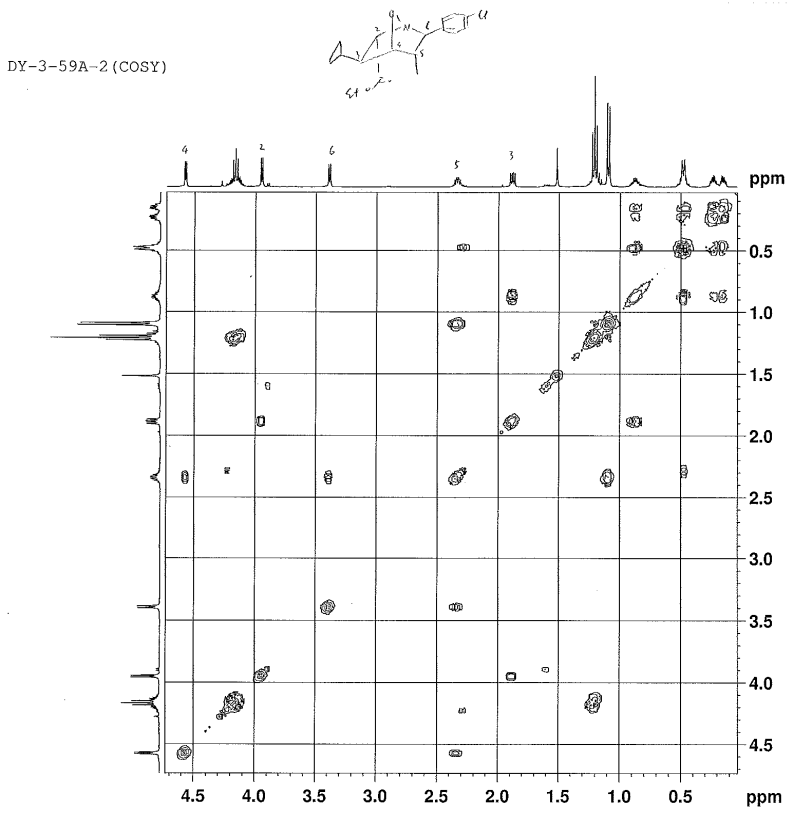

DY-3-42-2(APT
169.076
141.509
128.410
128.359
125.971
102.094
89.758
77.329
77.223
77.117
77.012
76.694
76.402
69.745
61.347
45.513
40.346
35.279
34.564
32.098
30.118
30.012
22.996
21.842
14.140
12.265
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

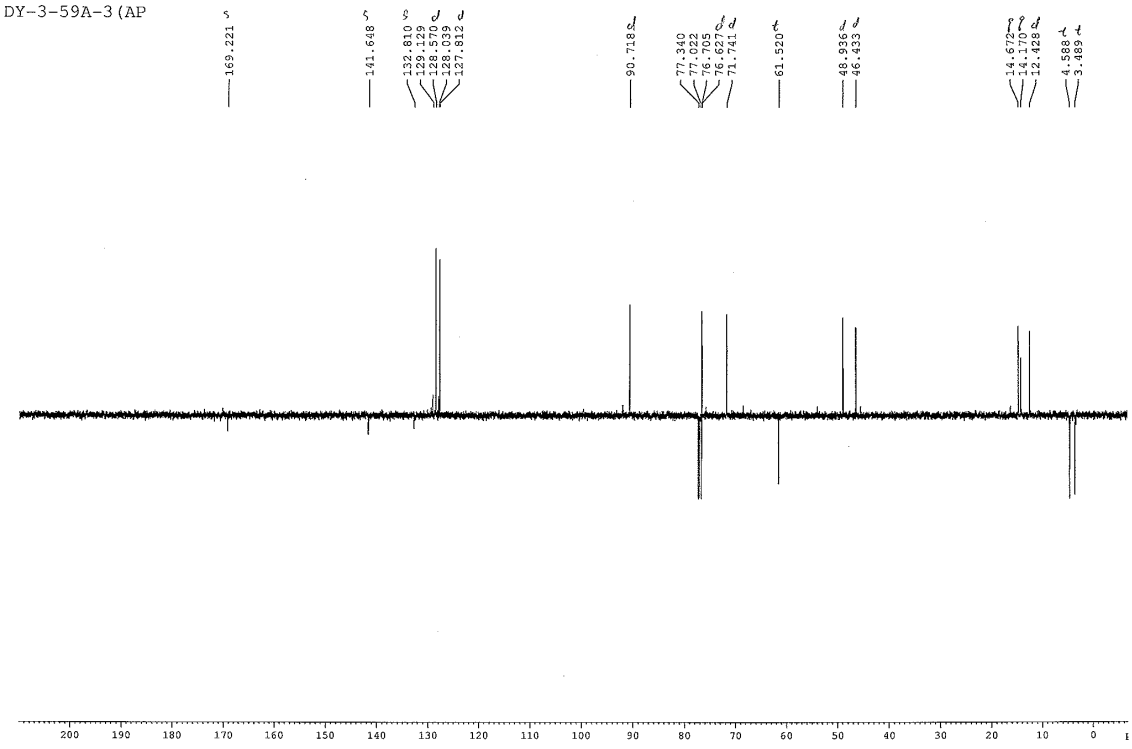

O
EtO
N
O
Cl

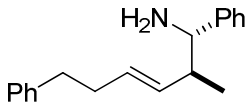
51 (DY-3-59)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
5.32
1.00
2.44
0.99
1.00
1.08
1.02
3.44
3.07
1.16
2.46
1.22
1.09

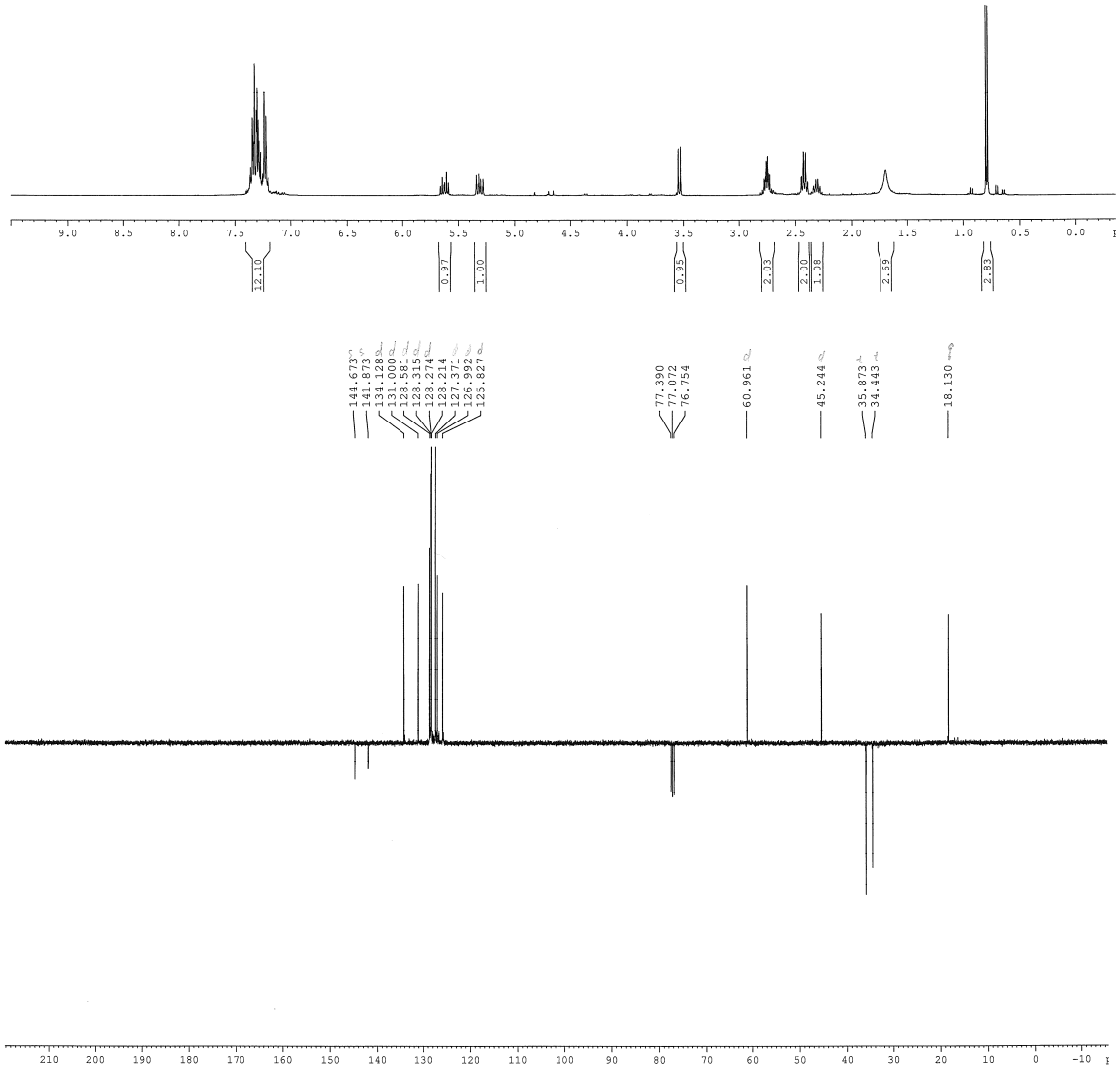

DY-3-59A-4(C)
169.224
141.644
132.813
128.572
127.812
90.719
77.333
77.015
76.698
76.629
71.744
61.521
48.937
46.434
14.672
14.171
12.429
4.589
3.489
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

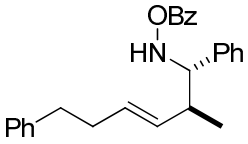

DY-3-59A-2(COSY)
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5


DY-3-59A-3(AP
169.221
141.648
132.810
129.129
128.570
128.039
127.812
90.718
77.340
77.022
76.705
76.627
71.741
61.520
48.936
46.433
14.672
14.170
12.428
4.588
3.489

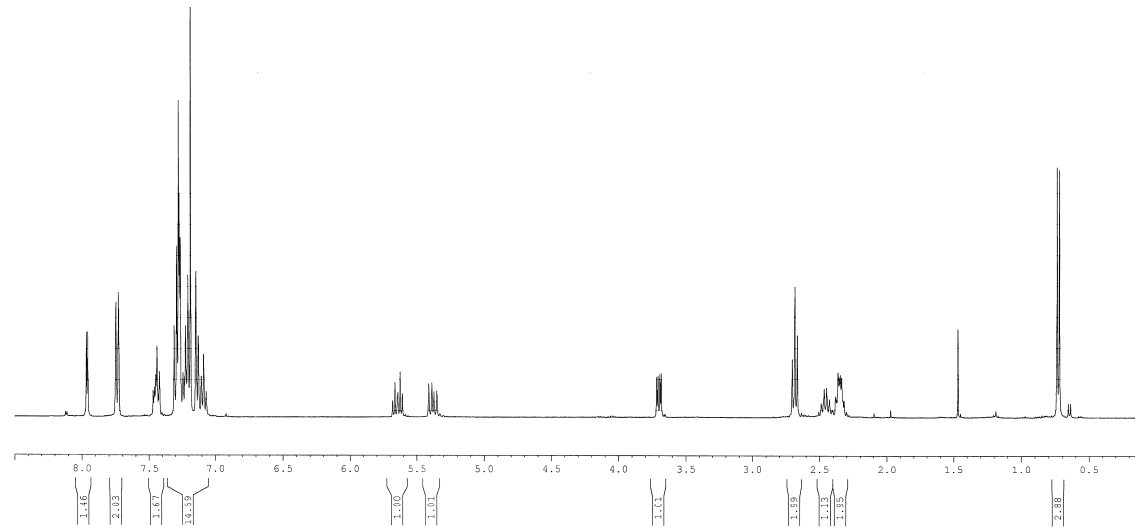

H2N
Ph
Ph

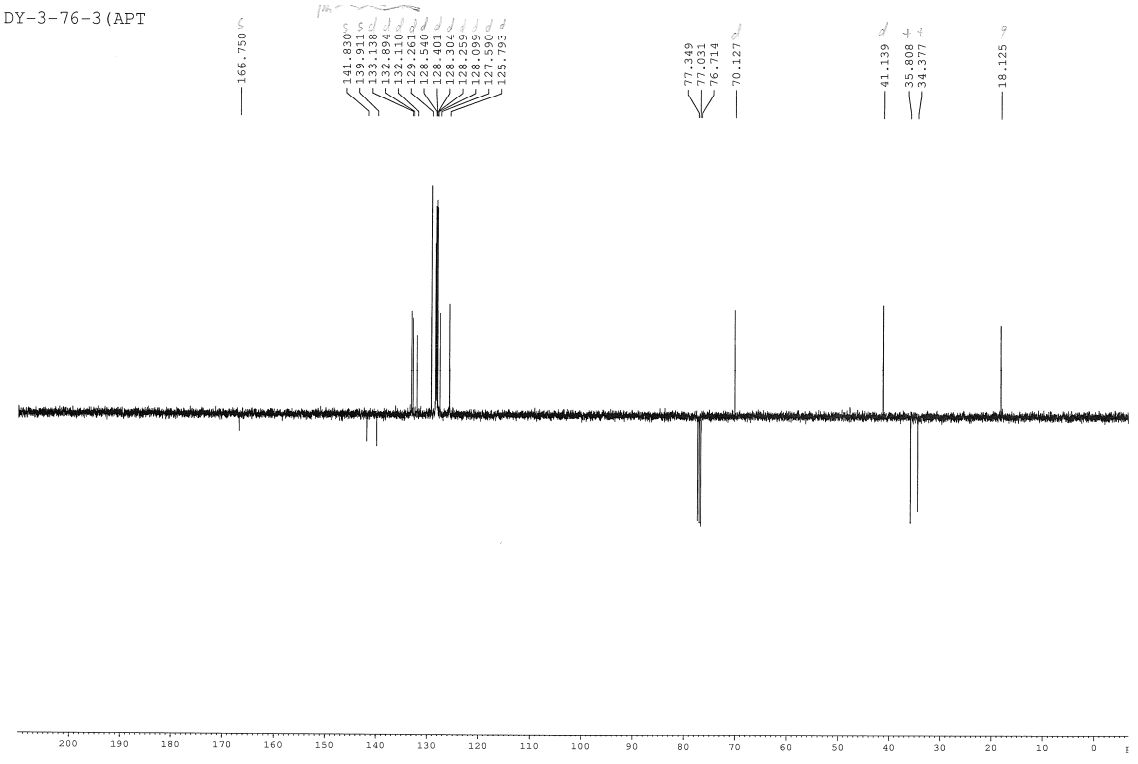
52 (DY-3-75)

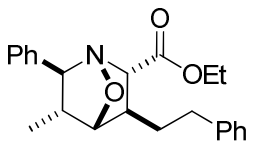

12.10
0.37
1.00
0.95
2.33
2.10
1.98
2.59
2.83
141.673
141.873
134.128
131.000
123.58
123.315
123.274
123.214
127.37
126.992
125.827
77.390
77.072
76.754
60.961
45.244
35.873
34.443
18.130


OBz
HN
Ph
Ph

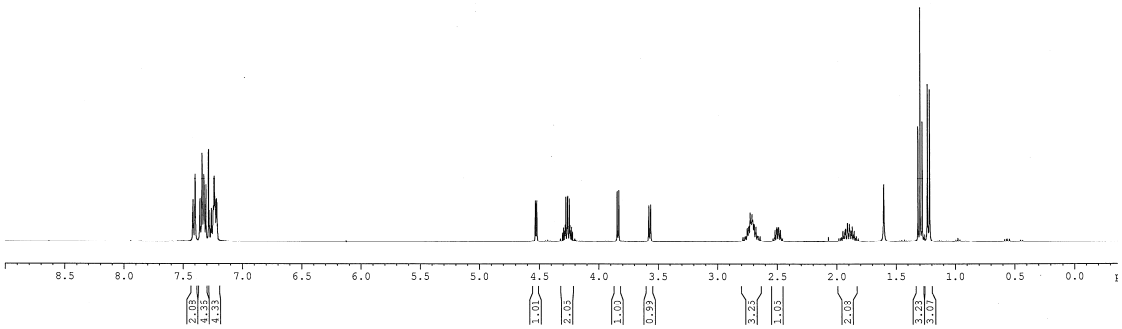
53 (DY-3-76)


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.46
2.03
3.67
14.59
1.40
1.01
1.14
1.59
1.13
1.15
2.88

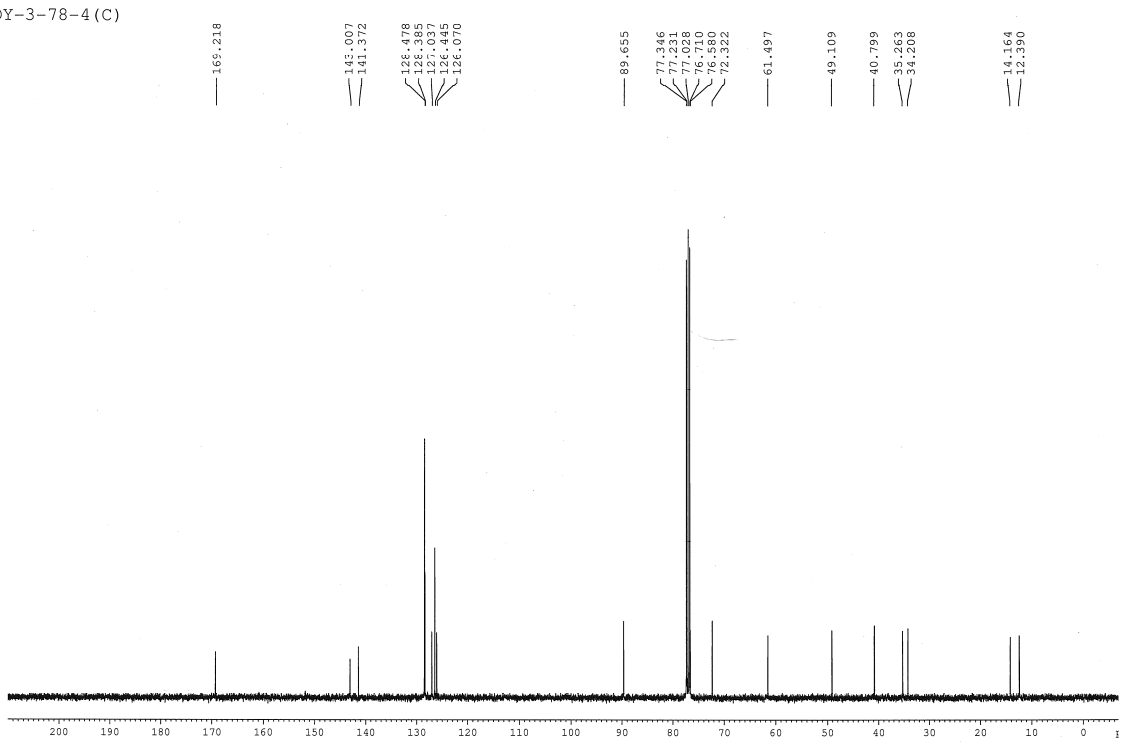

DY-3-76-3(APT
166.750
141.830
139.911
133.138
132.894
132.110
129.261
128.540
128.401
128.302
128.259
128.095
127.790
127.702
125.792
77.349
77.031
76.714
70.127
41.139
35.808
34.377
18.125
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

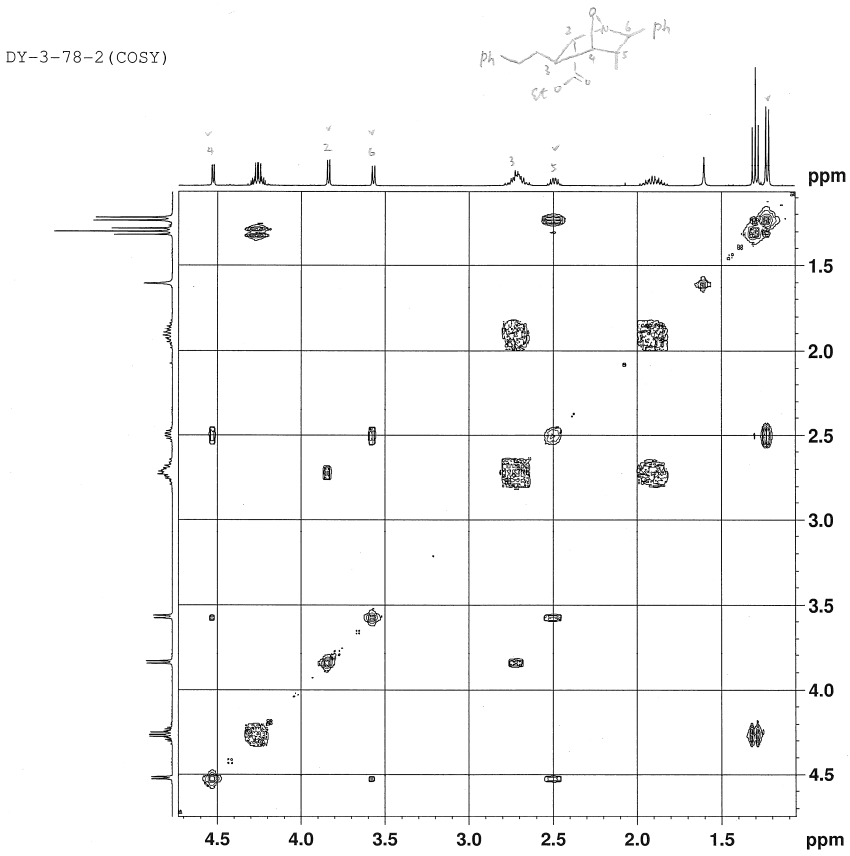


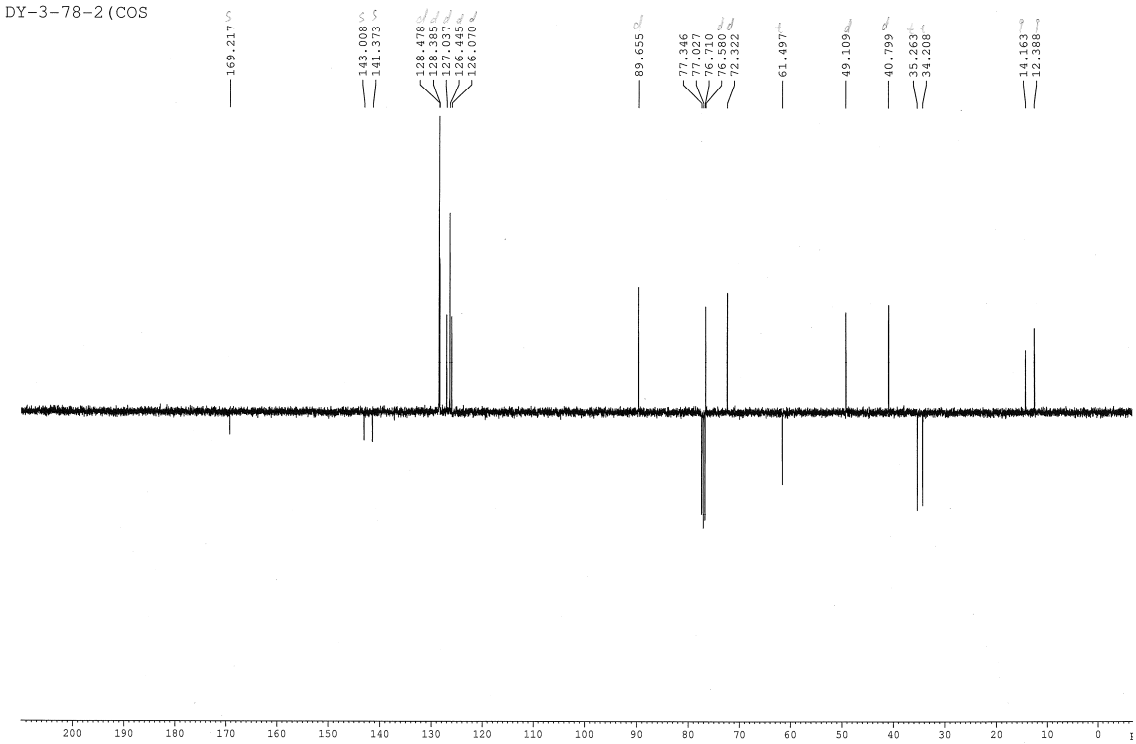
54 (DY-3-78)

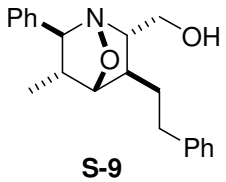


DY-3-78-4(C)

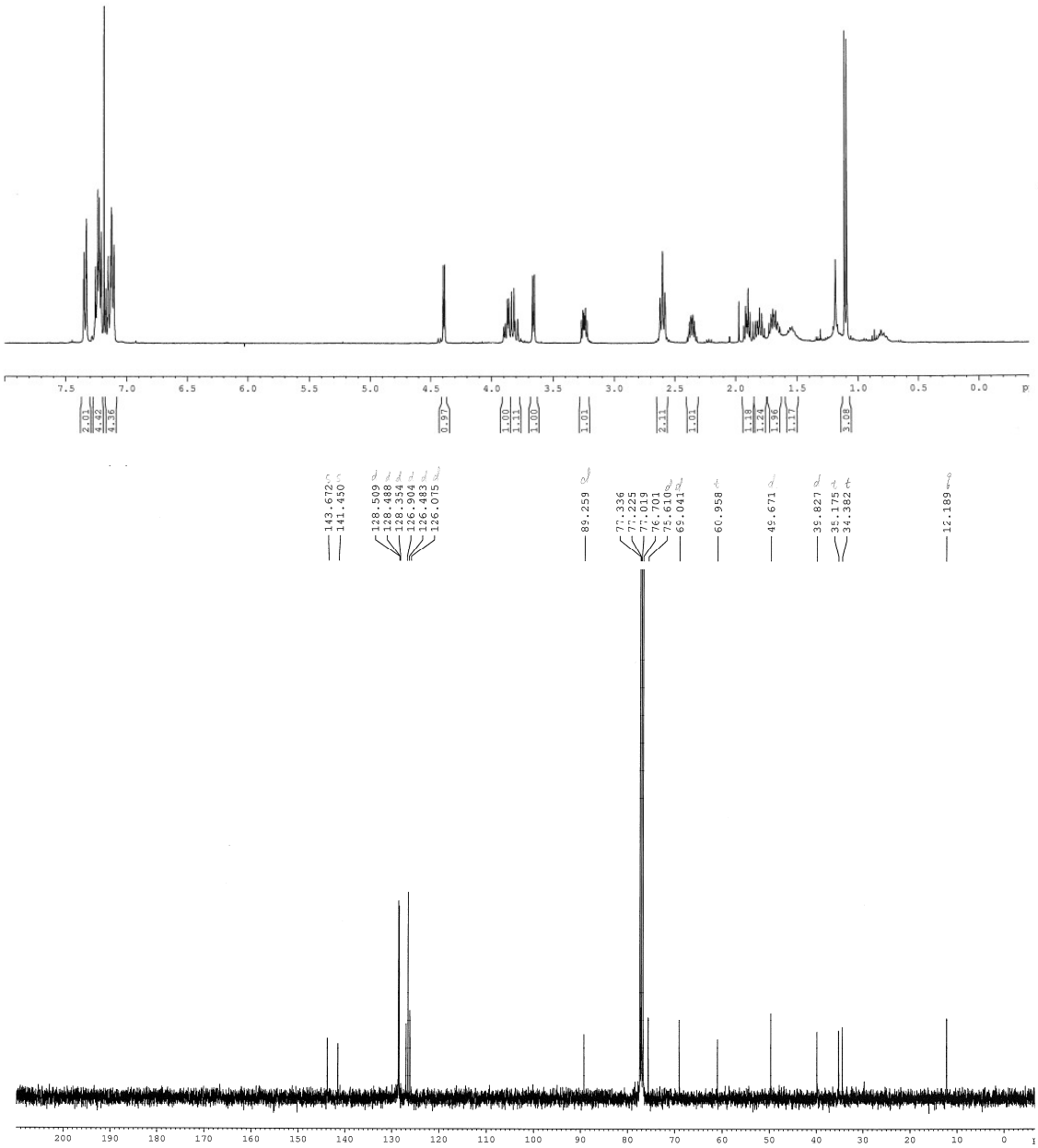


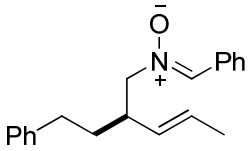

DY-3-78-2(COSY)
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.5
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm


DY-3-78-2(COS
169.217
143.008
141.373
128.478
128.385
127.037
126.445
126.070
89.655
77.346
77.027
76.710
76.580
72.322
61.497
49.109
40.799
35.263
34.208
14.163
12.388
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

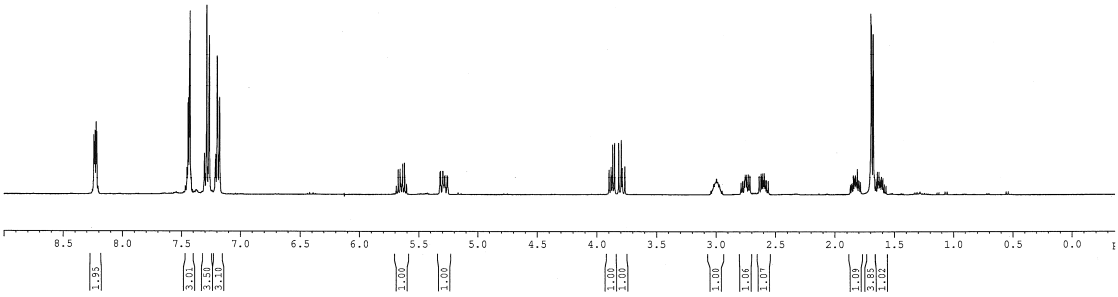

Ph
N
O
OH
Ph

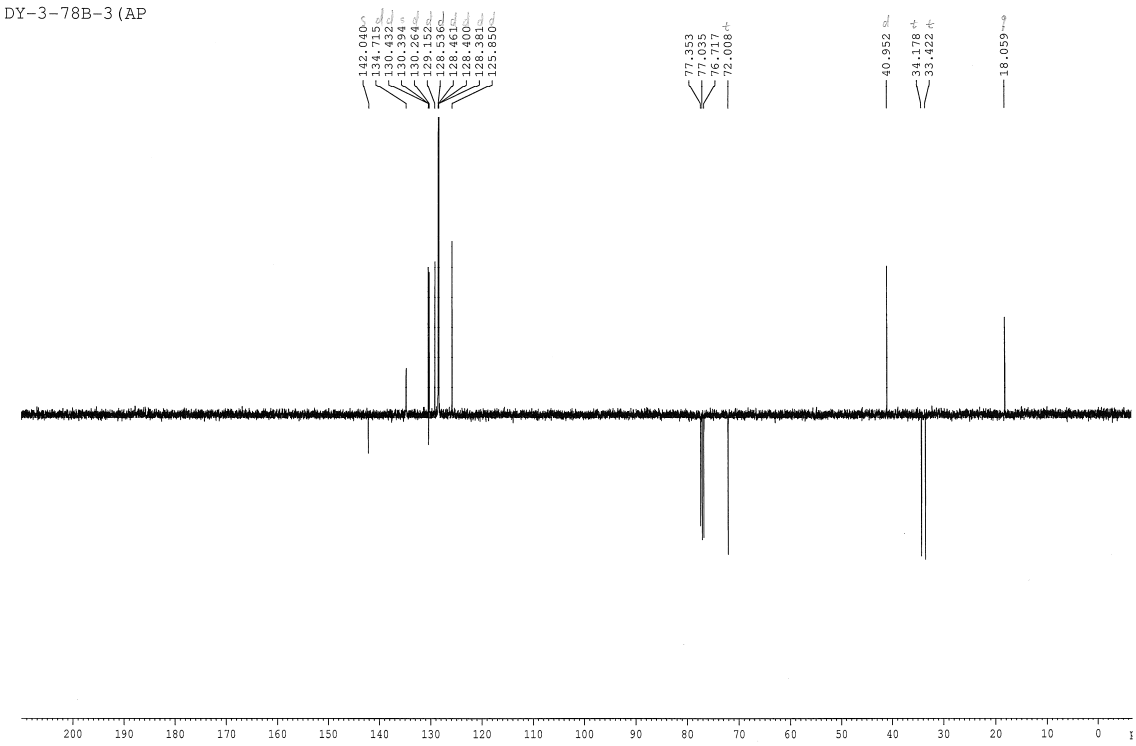
S-9

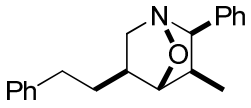

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.01
4.42
4.36
0.97
1.00
1.11
1.00
1.01
2.11
1.01
1.18
1.24
1.96
1.17
3.08
143.672
141.450
128.509
128.488
128.354
126.904
126.483
126.075
89.259
77.336
77.225
77.019
76.701
75.610
65.041
60.958
45.671
35.827
35.175
34.382
12.189
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


O
N
Ph
Ph

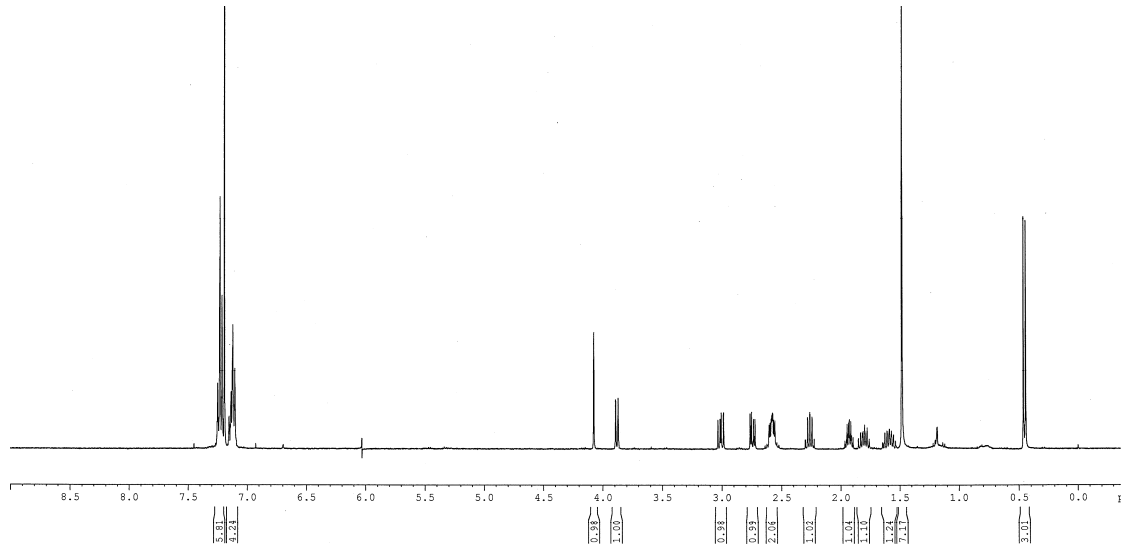
S-8 (DY-3-79A)

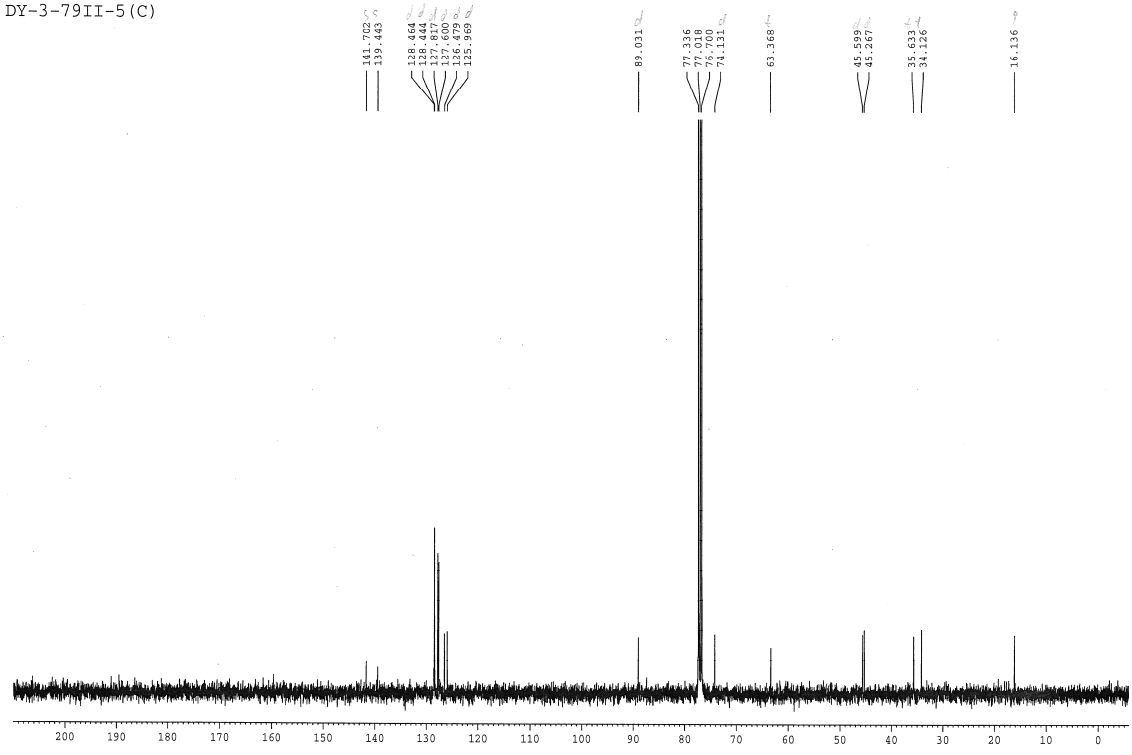

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.95
3.01
3.56
3.10
1.00
1.00
1.00
1.00
1.00
1.06
1.07
1.09
3.83
1.02


DY-3-78B-3(AP
142.040
134.715
130.432
130.394
130.264
129.152
128.536
128.461
128.400
128.381
125.850
77.353
77.035
76.717
72.008
40.952
34.178
33.422
18.059
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

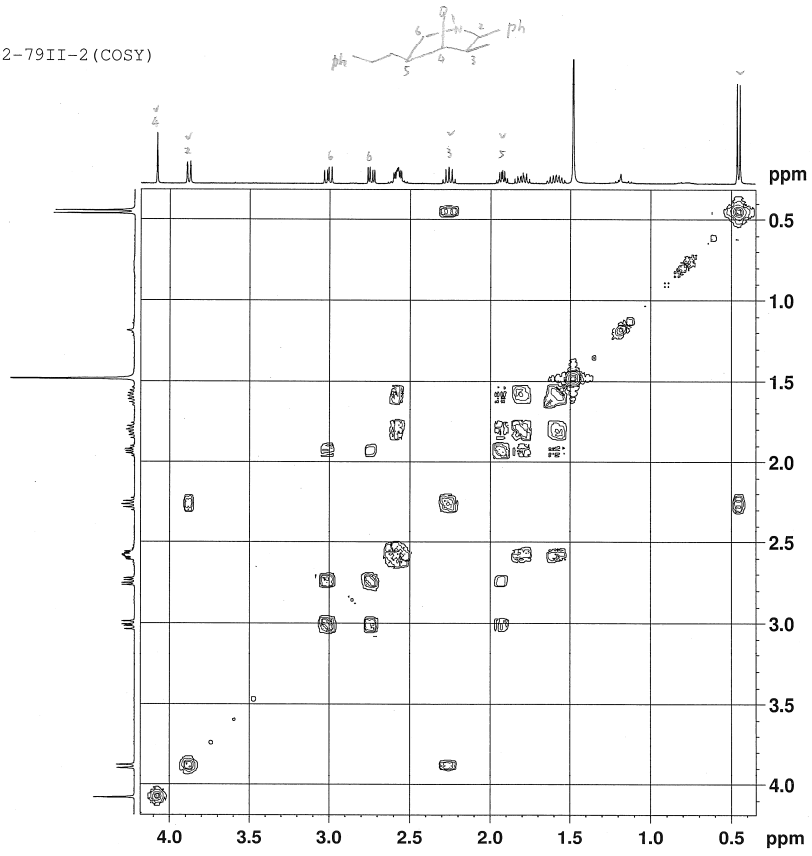

N
Ph
O
Ph

55 (DY-3-79B)

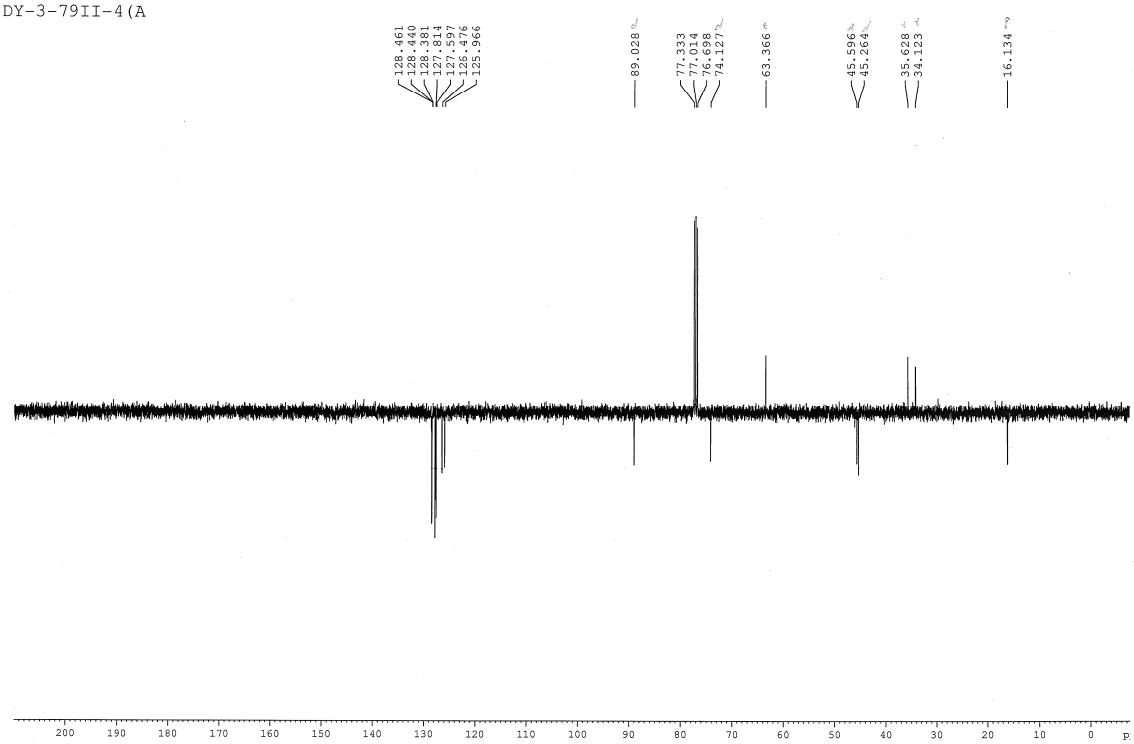

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.01
4.24
0.98
1.00
0.88
0.93
2.06
1.02
1.04
1.10
1.24
2.13
3.01

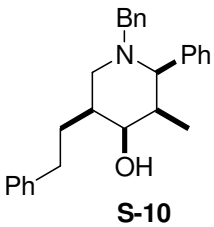

DY-3-79II-5(C)
141.702
139.443
128.464
128.444
127.817
127.600
126.489
125.969
89.031
77.336
77.018
76.700
74.131
63.368
45.599
45.267
35.633
34.426
16.136
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

DY-2-79II-2(COSY)

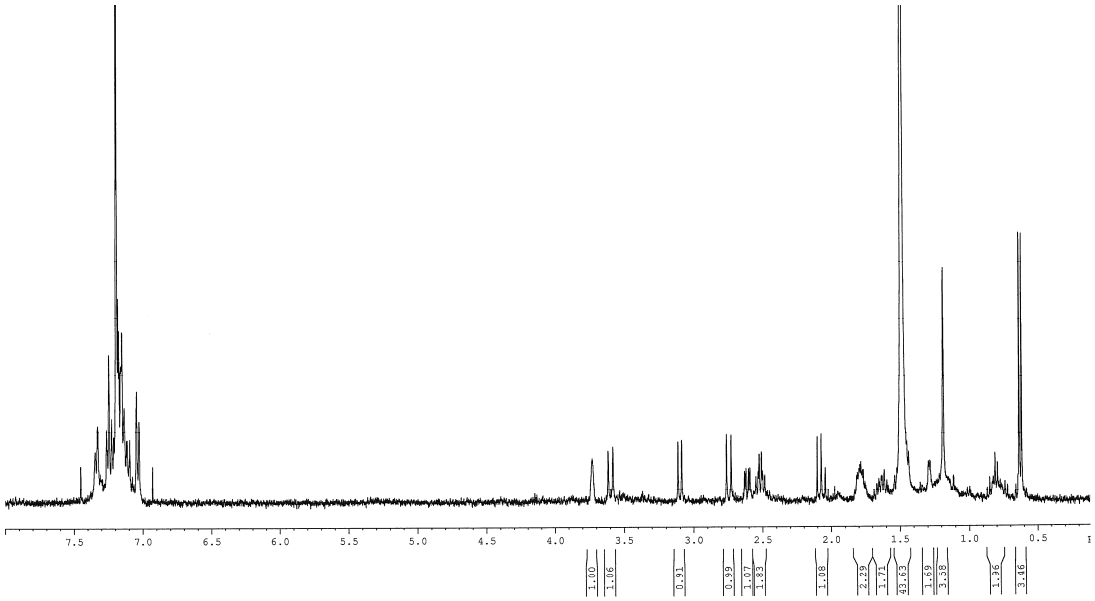


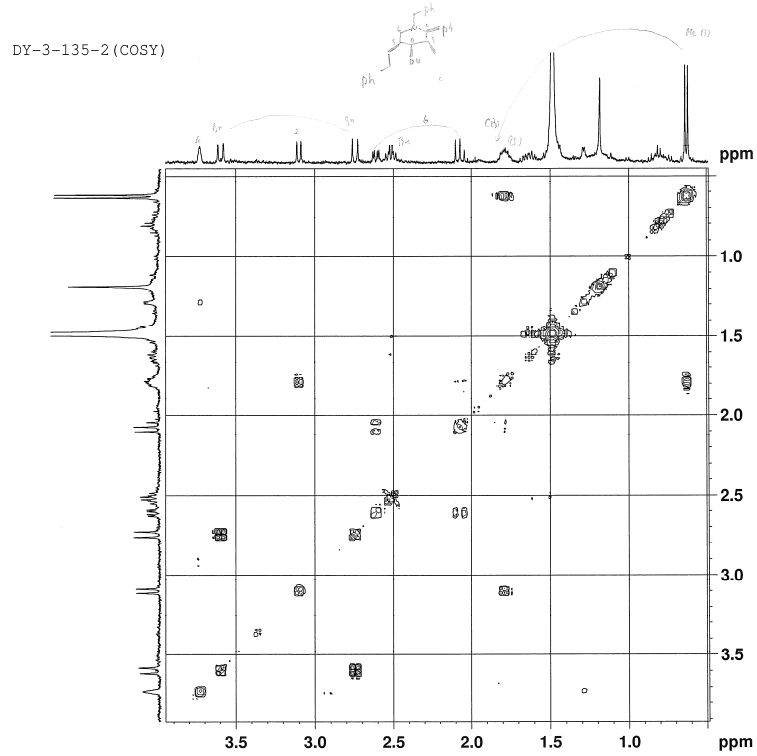
DY-3-79II-4(A

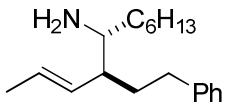



Bn
N
Ph
OH
Ph

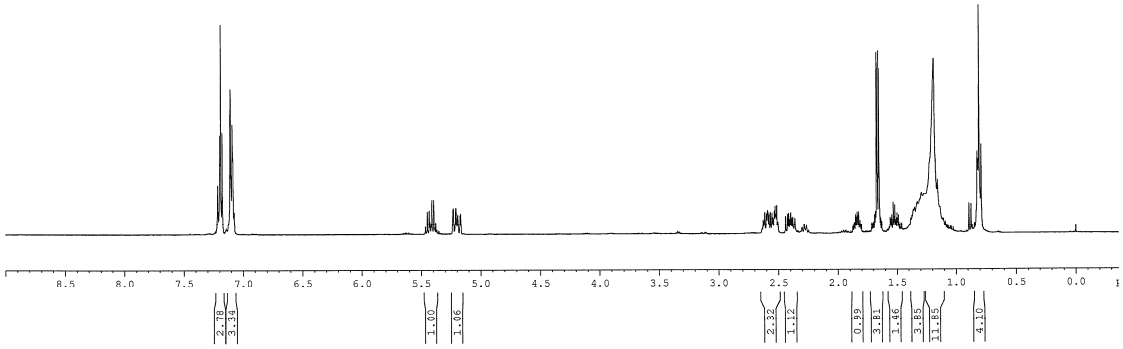
S-10

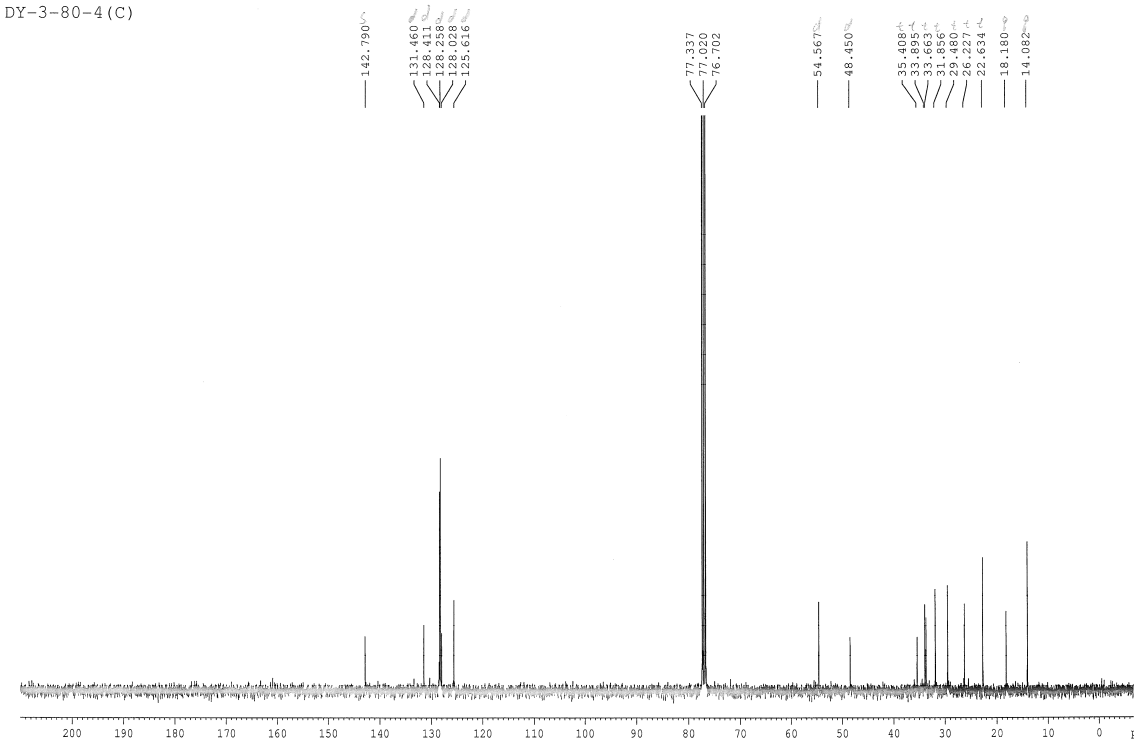

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
1.16
0.91
0.99
1.07
1.83
1.08
2.29
1.71
43.63
1.69
3.38
1.36
3.46

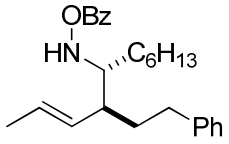

DY-3-135-2(COSY)
ppm
1.0
1.5
2.0
2.5
3.0
3.5
3.5
3.0
2.5
2.0
1.5
1.0
ppm


H2N
C6H13
Ph

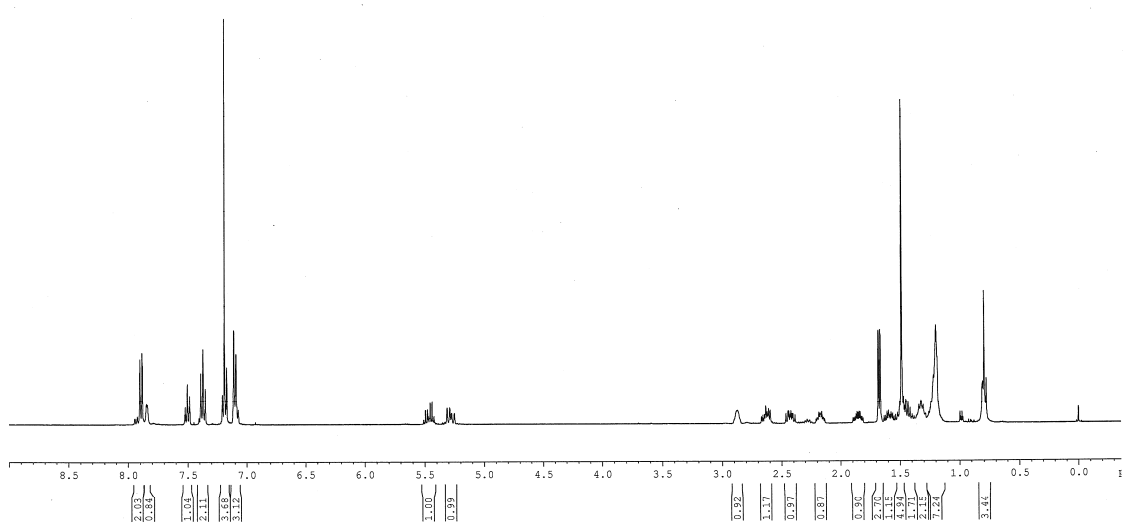
56 (DY-3-80)


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.78
3.34
1.40
1.06
2.32
1.12
0.99
3.81
1.46
3.85
11.85
4.10

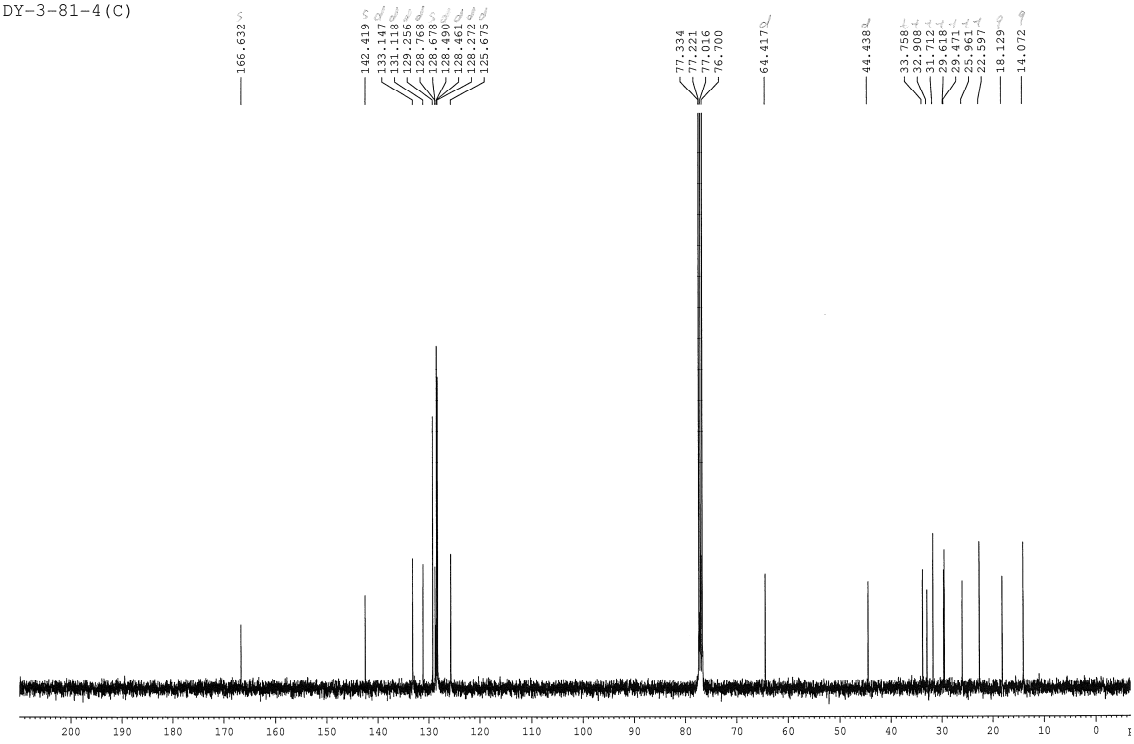

DY-3-80-4(C)
142.790
131.460
128.411
128.258
126.028
125.616
77.337
77.020
76.702
54.567
48.450
35.408
33.863
33.663
31.856
29.480
26.227
22.634
18.180
14.082
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

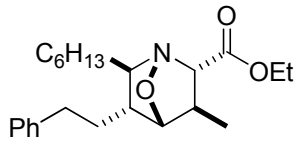


57 (DY-3-81)

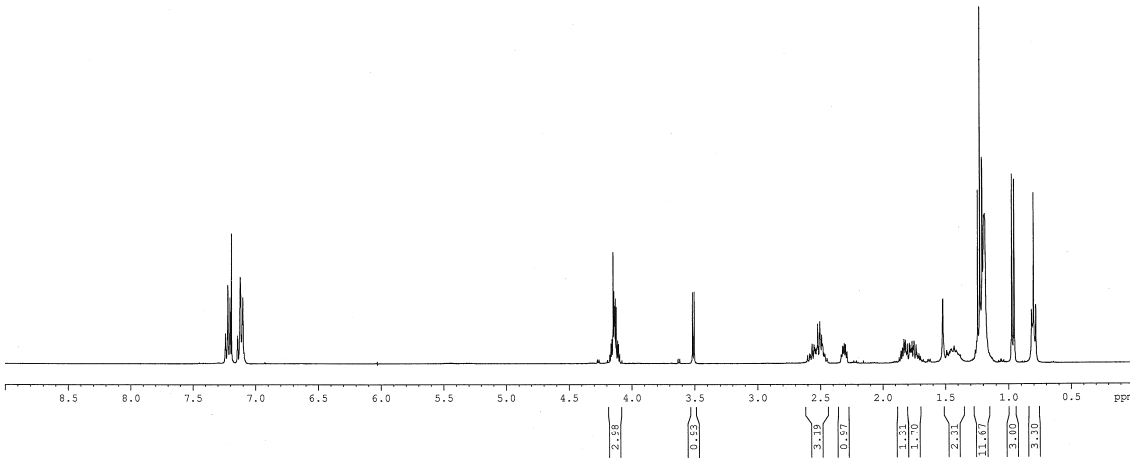


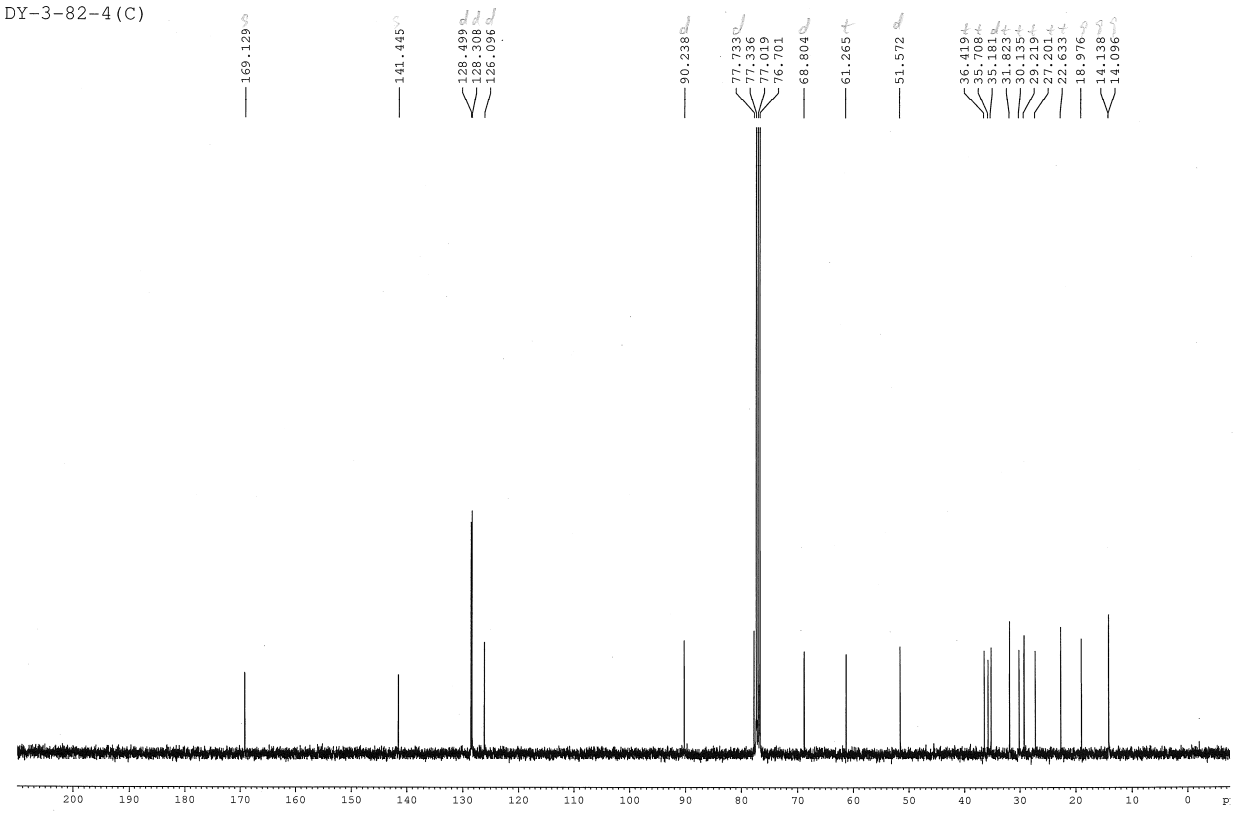
DY-3-81-4(C)



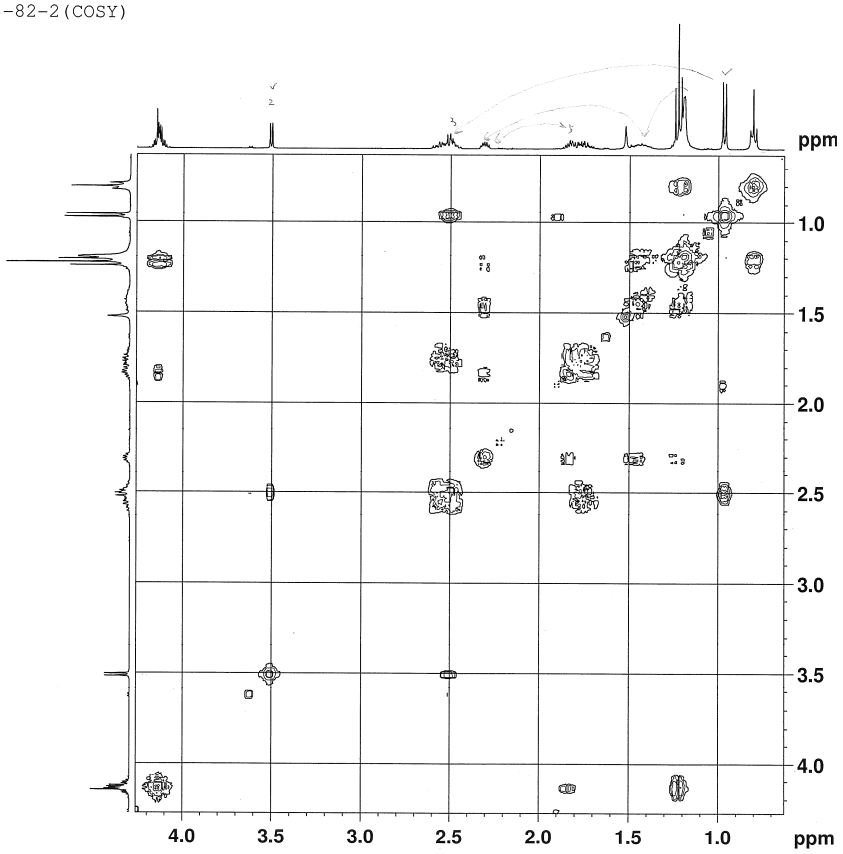

C6H13
N
O
O
OEt
Ph

58 (DY-3-82)

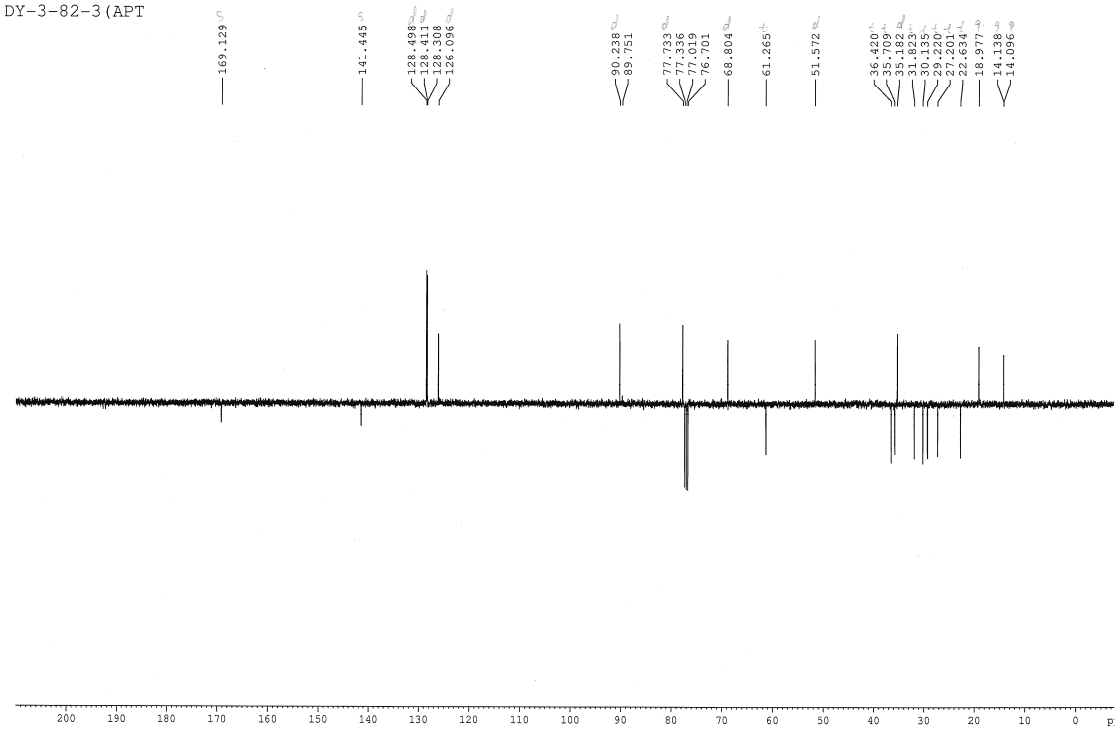

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.98
0.93
3.19
0.97
1.31
1.70
2.31
11.67
3.00
3.20

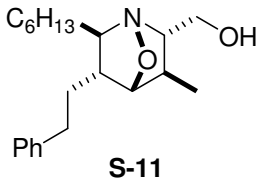

DY-3-82-4(C)
169.129
141.445
128.499
128.308
126.096
90.238
77.733
77.336
77.019
76.701
68.804
61.265
51.572
36.419
35.708
35.181
31.823
30.135
29.219
27.201
22.633
18.976
14.138
14.096
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

DY-3-82-2(COSY)

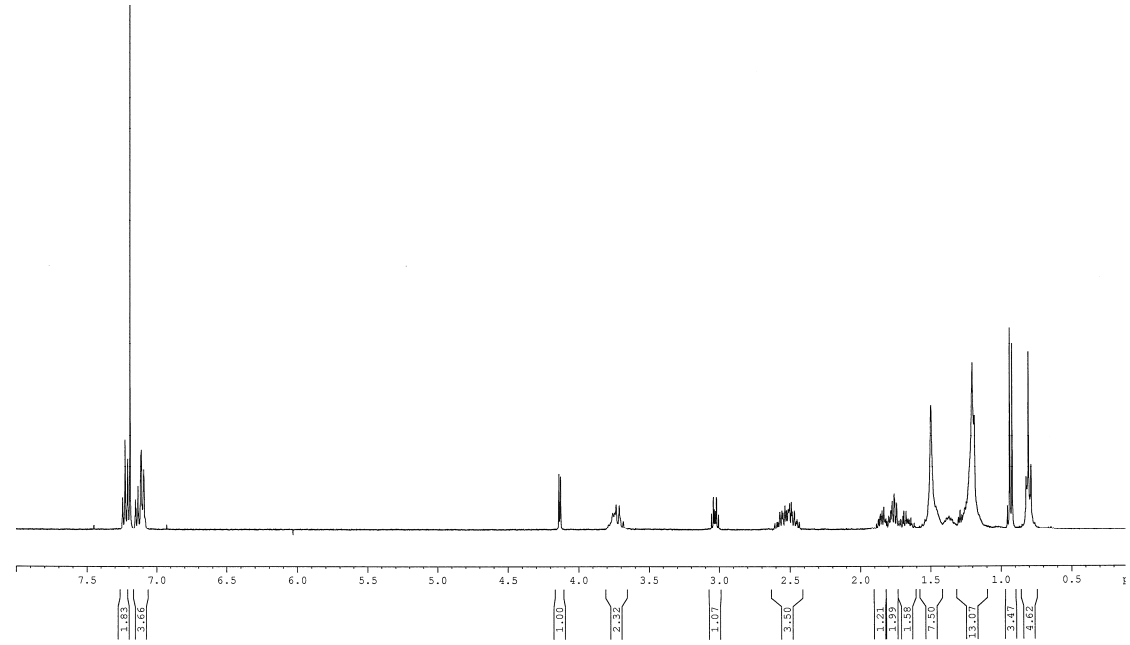


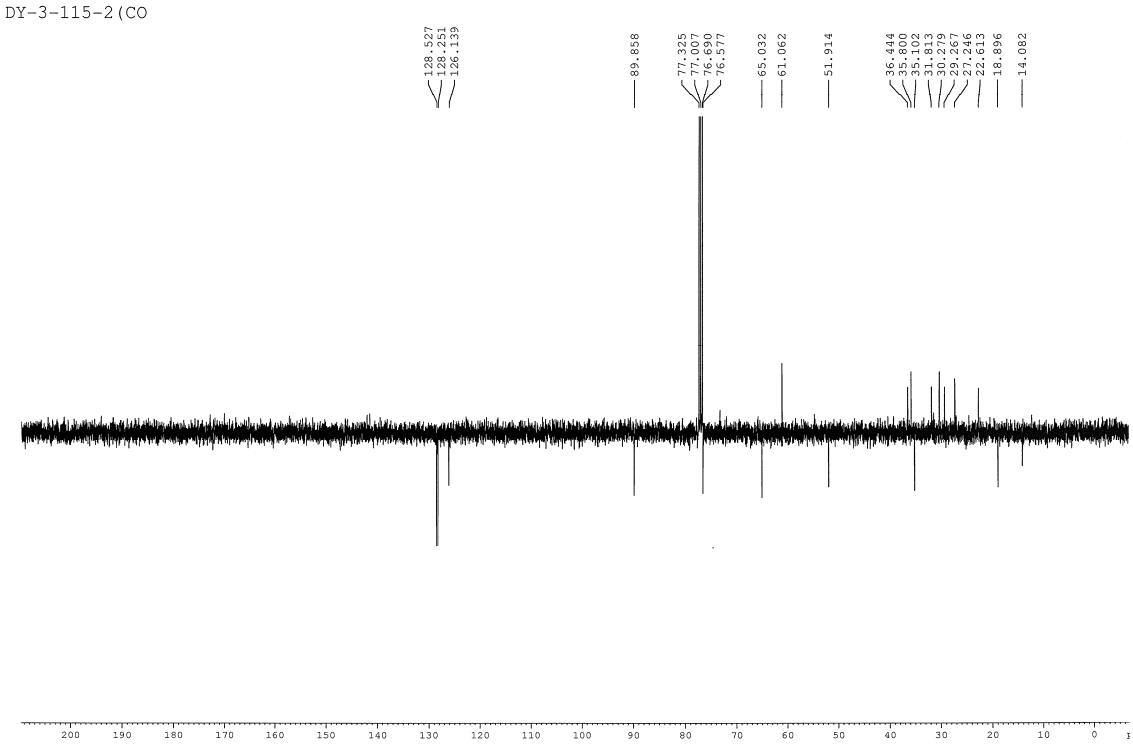
DY-3-82-3(APT




C6H13
N
OH
O
Ph

S-11


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.83
3.66
1.00
2.32
1.07
3.50
1.21
1.99
1.58
7.50
13.07
3.47
4.62


DY-3-115-2(CO
128.527
128.251
126.139
89.858
77.325
77.007
76.690
76.577
65.032
61.062
51.914
36.444
35.800
35.102
31.813
30.279
29.267
27.246
22.613
18.896
14.082
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0