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Supporting Information

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Highly Enantioselective and Diastereoselective Cycloaddition of Cyclopropanes with Nitrones and Its Application in the Kinetic Resolution of 2-Substituted Cyclopropane-1,1-dicarboxylates

Yan-Biao Kang, Xiu-Li Sun, and Yong Tang*

The State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai, 200032, China.. E-mail: tangy@mail.sioc.ac.cn

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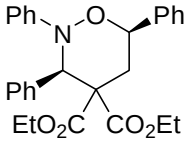
General information.

All reactions were carried out under dry nitrogen atmosphere. Dimethoxyl ethane (DME) was distilled over calcium hydride prior to use. Activated molecular sieves powder 4Å (MS 4 Å) was dried at 250 °C in vacuum before use. All of the nitrones[1] and 2-substituted cyclopropane-1,1-dicarboxylates[2] were synthesized according to the literature. All glassware was oven-dried, assembled hot, and cooled under a stream of dry nitrogen before use.

^{1}H NMR was recorded on a Varian Mercury-300 (300 MHz). Chemical shifts are reported in parts per million (ppm) down field from TMS, using residual $CDCl_3$ (7.26 ppm) as an internal standard. ^{13}C NMR was recorded on a Varian Mercury-300 (75 MHz) spectrometers using proton decoupling. Chemical shifts are reported in parts per million (ppm) down field from TMS, using the middle resonance of $CDCl_3$ (77 ppm) as an internal standard.

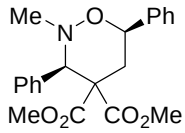
Typical procedure for the enantioselective [3 + 3] cycloadditions.

A mixture of $Ni(ClO_4)_2{\cdot}6H_2O$ (0.040 mmol) and trisoxazoline (0.044 mmol) in dimethoxyethane (1 mL) was stirred at 50 ^{o}C for 2 hours under nitrogen. The mixture was cooled to room temperature and then was transferred to cyclopropane diester (0.44 mmol) *via* a syringe. To the resulting solution was added activated molecular sieves 4Å (100 mg). The mixture was stirred at -30 ^{o}C for 30 minutes and then nitrone (0.20 mmol) was added. After the reaction was complete (monitored by TLC), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with CH_2Cl_2 (50 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography.



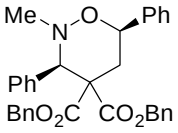
(cis)-diethyl 2-phenyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.61-7.55 (m, 4H), 7.49-7.39 (m, 3H), 7.20-7.09 (m, 7H), 6.83-6.80 (m, 1H), 5.79 (s, 1H), 5.04 (dd, *J* = 3.3, 14.4 Hz, 1H), 4.39 (dd, *J* = 7.2, 14.4 Hz, 2H), 3.91 (m, 2H), 2.88-2.81 (m, 2 H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): 169.56, 167.88, 148.57, 139.56, 134.95, 130.56, 128.60, 128.48, 128.23, 127.98, 127.85, 126.38, 121.48, 115.71, 78.81, 65.74, 62.32, 61.79, 59.29, 31.81, 14.15, 13.68; **IR** (thin film, cm^{-1}) 2978, 1737, 1586, 1492, 1446, 1255, 1231, 747, 692; **Anal.** Calcd for $C_{28}H_{29}NO_5$: C, 73.18%; H, 6.36%; N, 3.05%; Found: C, 72.92%, H, 6.42%, N, 3.13%; **LRMS-EI** (m/e): 459 (M^+, 4.5), 198(100.0). The ees listed in table 1 were determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 90/10 as eluent, 254 nm.



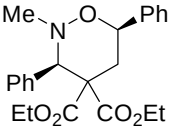
(cis)-dimethyl 2-methyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 3 days, 82% yield for *cis*-isomer, dr = 13/1, 90% ee. 43% conversion of cyclopropane (by ^{1}H NMR). Analytical data [3,4]: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62-7.31 (m, 10H), 4.89 (dd, *J* = 2.8 Hz, 11.6 Hz, 1H), 4.85 (s, 1H), 3.89 (s, 3H), 3.39 (s, 3H), 2.78-2.60 (s, 2H), 2.54 (s, 3H); $[\alpha]_D^{25}$ = +160.8 ° (c 1.0, $CHCl_3$, 90% ee.). 90% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 90/10 as eluent, 254 nm, t_{R1} = 6.10 min (minor), t_{R2} = 9.94 min (major). The absolute configuration for the cycloadducts has not been established and positive polar rotation was given, which was accorded with that of literature (+154.7 °, same conditions).[3]



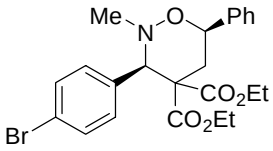
(cis)-dibenzyl 2-methyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-40°C, 4 days, 62% yield for *cis*-isomer, dr = 10/1, 97% ee. 41% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 6.6 Hz, 2H), 7.43-7.22 (m, 16H), 7.04-7.01 (m, 2H), 5.30 (s, 2H), 4.90 (dd, *J* = 3.4 Hz, 11.2 Hz, 1H), 4.86 (s, 1H), 4.77-4.65 (m, 2H), 2.79-2.63 (m, 2H), 2.52 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.51, 167.69, 135.44, 134.75, 131.02, 128.55, 128.44, 128.35, 128.25, 128.20, 128.16, 128.05, 126.31, 77.98, 67.73 (2C), 67.26, 59.41, 43.31, 31.23. **IR** (thin film, cm^{-1}) 3032, 2957, 2885, 1741, 1496, 1454, 1257, 1098, 749, 698; **Anal.** Calcd. For $C_{33}H_{31}NO_5$: C, 75.99; H, 5.99; N, 2.69. Found: C, 75.66; H, 6.14; N, 2.66. **LRMS-ESI**: 522 ($M + H^+$, 100). $[\alpha]_D^{25}$ = +127.6 ° (c 1.0, $CHCl_3$, 97% ee.), 97% ee was determined by HPLC analysis using a Chiralpak OD-H column with hexane/*i*-PrOH 90/10 as eluent, 1 mL/min, 254 nm, t_{R1} = 5.79 min (major), t_{R2} = 6.81 min (minor).



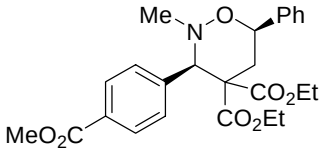
(cis)-diethyl 2-methyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 88% yield for *cis*-isomer, dr = 11/1, 95% ee. 48% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62-7.30 (m, 10H), 4.89 (dd, *J* = 3.3 Hz, 11.7 Hz, 1H), 4.84 (s, 1H), 4.40-4.33 (m, 2H), 3.92-3.72 (m, 2H), 2.78-2.60 (m, 2H), 2.53 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.71, 167.97, 140.14, 134.59, 131.02, 128.47, 128.09, 127.96, 127.88, 126.25, 77.88, 67.73, 61.99, 61.49, 59.02, 43.26, 31.07, 14.02, 13.55. **IR** (thin film, cm^{-1}) 3029, 2984, 2885, 1738, 1494, 1453, 1366, 1253, 1099, 753, 700; **Anal.** Calcd. For $C_{23}H_{27}NO_5$: C, 69.50; H, 6.85; N, 3.52. Found: C, 69.48; H, 7.09; N, 3.46. **LRMS-ESI**: 398 ($M + H^+$, 100). $[\alpha]_D^{25}$ = +160.3 ° (c 1.0, $CHCl_3$, 95% ee.), 95% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 90/10 as eluent, 1 mL/min, 254 nm, t_{R1} = 6.48 min (minor), t_{R2} = 7.94 min (major).



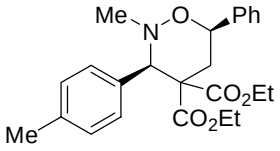
(cis)-diethyl 3-(4-bromophenyl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 85% yield for *cis*-isomer, dr = 12/1, 97% ee. 45% conversion of cyclopropane (by ^{1}H NMR). Analytical data: ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.53-7.34 (m, 9H), 4.90 (t, *J* = 7.4 Hz, 1H), 4.82 (s, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.97-3.76 (m, 2H), 2.66-2.64 (m, 2H), 2.51 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 169.48, 167.86, 139.93, 133.73, 132.66, 131.12, 128.57, 128.09, 126.22, 122.48, 77.87, 67.11, 62.17, 61.70, 58.93, 43.26, 30.93, 14.05, 13.68. **IR** (thin film, cm^{-1}) 2983, 2960, 2884, 1738, 1486, 1253, 1183, 1011, 968, 755, 698; **LRMS-ESI**: 476 ($M + H^+$, 100). **HRMS-ESI** calcd. for $C_{23}H_{27}BrNO_5^+$ is 476.1067: observed: 476.1076; $[\alpha]_D^{25}$ = +156.7 ° (c 1.0, $CHCl_3$, 97% ee.), 97% ee was determined by HPLC analysis using a Chiralcel OD-H column with hexane/*i*-PrOH 50/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 5.49 min (major), t_{R2} = 6.87 min (minor).



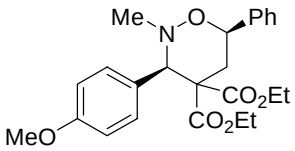
(cis)-diethyl 3-(4-(methoxycarbonyl)phenyl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 97% yield, dr = 11/1, 97% ee. 46% conversion of cyclopropane (by ^{1}H NMR). Analytical data: ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.48-7.32 (m, 5H), 4.95-4.90 (m, 1H), 4.91 (s, 1H), 4.41-4.34 (m, 2H), 3.93-3.73 (m, 2H), 3.90 (s, 3H), 2.74-2.63 (m, 2H), 2.52 (s, 3H), 1.33 (t, *J* = 6.9 Hz, 3H), 0.99 (t, *J* = 6.9 Hz, 3H); ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 169.42, 167.76, 166.72, 140.06, 131.06, 129.82, 129.08, 128.56, 128.08, 126.21, 109.68, 77.92, 67.48, 62.18, 61.67, 58.93, 52.06, 43.27, 31.08, 14.03, 13.63. **IR** (thin film, cm^{-1}) 2984, 2956, 2885, 1725, 1436, 1279, 1186, 1105, 699; **LRMS-ESI**: 456 ($M + H^+$, 100). **HRMS-ESI** calcd. for $C_{25}H_{30}BrNO_7^+$ is 456.2017: observed: 456.2024; $[\alpha]_D^{25}$ = +144.1 ° (c 1.0, $CHCl_3$, 97% ee.), 97% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 90/10 as eluent, 1 mL/min, 254 nm, t_{R1} = 8.53 min (minor), t_{R2} = 11.44 min (major).



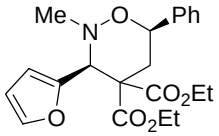
(cis)-diethyl 2-methyl-6-phenyl-3-*p*-tolyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 80% yield for *cis*-isomer, dr = 12/1, 96% ee. 41% conversion of cyclopropane (by ^{1}H NMR). Analytical data: ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.51-7.33 (m, 7H), 7.12 (d, *J* = 7.8 Hz, 2H), 4.90 (dd, *J* = 3.0 Hz, 12.0 Hz, 1H), 4.81 (s, 1H), 4.36 (q, *J* = 6.9 Hz, 1H), 3.95-3.73 (m, 2H), 2.77-2.53 (m, 2H), 2.52 (s, 3H), 2.32 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 169.81, 168.06, 140.14, 137.73, 131.41, 130.91, 128.63, 128.49, 127.96, 126.31, 77.92, 67.47, 61.96, 61.47, 59.09, 43.25, 31.08, 21.03, 14.04, 13.62. **IR** (thin film, cm^{-1}) 2982, 2885, 1739, 1254, 1181, 1098, 698; **LRMS-ESI**: 412 ($M + H^+$, 100). **HRMS-ESI** calcd. for $C_{24}H_{30}BrNO_5^+$ is 412.2118: observed: 412.2123; $[\alpha]_D^{25}$ = +157.7 ° (c 1.0, $CHCl_3$, 96% ee.), 96% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 90/10 as eluent, 1 mL/min, 254 nm, t_{R1} = 6.60 min (minor), t_{R2} = 9.67 min (major).



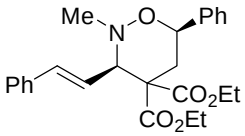
(cis)-diethyl 3-(4-methoxyphenyl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 92% yield for *cis*-isomer, dr = 13/1, 90% ee. 47% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55-7.31 (m, 7H), 6.85 (d, *J* = 9.0 Hz, 2H), 4.90 (dd, *J* = 3.0 Hz, 11.6 Hz, 1H), 4.80 (s, 1H), 4.37 (q, *J* = 7.2 Hz, 1H), 3.96-3.80 (m, 2H), 3.79 (s, 3H), 2.84-2.59 (m, 2H), 2.51 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.84, 168.09, 159.30, 140.24, 132.24, 128.51, 127.98, 126.29, 113.24, 77.90, 67.08, 61.99, 61.49, 59.14, 55.06, 43.22, 31.04, 14.05, 13.70. **IR** (thin film, cm^{-1}) 2983, 2885, 1738, 1511, 1252, 1180, 699; **LRMS-ESI**: 428 (M + H$^+$, 100). **HRMS-ESI** calcd. for $C_{24}H_{30}BrNO_5^+$ is 428.2068: observed: 428.2078; $[\alpha]_D^{25}$ = +150.9 ° (c 1.0, $CHCl_3$, 90% ee.), 90% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 19/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 12.66 min (minor), t_{R2} = 16.15 min (major).



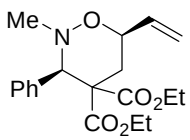
(cis)-diethyl 3-(furan-2-yl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 99% yield, dr = 13/1, 93% ee. 45% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45-7.25 (m, 6H), 6.49 (d, *J* = 3.3 Hz, 1H), 6.38 (t, *J* = 1.5 Hz, 1H), 4.98 (s, 1H), 4.93 (dd, *J* = 2.8 Hz, 11.2 Hz, 1H), 4.40-4.30 (m, 2H), 4.09-3.92 (m, 2H), 2.70-2.53 (m, 2H), 2.51 (s, 3H), 1.33 (t, *J* = 7.0 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.94, 167.78, 148.5, 142.14, 140.10, 128.42, 127.99, 126.42, 111.51, 110.15, 78.11, 62.11, 62.08, 61.64, 58.04, 42.97, 32.16, 14.00, 13.70. **IR** (thin film, cm^{-1}) 2982, 2884, 1738, 1257, 1187, 1099, 1016, 754, 700; **LRMS-ESI**: 388 (M + H$^+$, 100). **Anal.** Calcd. For $C_{21}H_{25}NO_6$: C, 65.10; H, 6.50; N, 3.61. Found: C, 64.85; H, 6.64; N, 3.44. $[\alpha]_D^{25}$ = +130.6 ° (c 1.0, $CHCl_3$, 93% ee.), 93% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 50/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 12.80 min (minor), t_{R2} = 15.74 min (major).



(cis,*E*)-diethyl 2-methyl-6-phenyl-3-styryl-[1,2]oxazinane-4,4-dicarboxylate

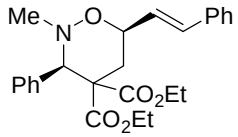
-30°C, 3 days, 76% yield for *cis*-isomer, dr = 4/1, 92% ee. 47% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45-7.24 (m, 10H), 6.69-6.50 (m, 2H), 4.89 (dd, *J* = 2.4 Hz, 12.0 Hz, 1H), 4.38-4.30 (m, 3H), 4.12-4.04 (m, 2H), 2.64 (s, 3H), 2.64-2.59 (m, 1H), 2.40 (dd, *J* = 12.0 Hz, 14.4 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.24, 168.19, 140.02, 137.44, 136.19, 128.54, 128.43, 128.04, 127.99, 126.54, 126.38, 120.96, 78.19, 67.15, 61.86, 61.72, 59.01, 43.15, 31.86, 14.04. **IR** (thin film, cm^{-1}) 2981, 2883, 1737, 1450, 697; **LRMS-ESI**: 424 (M + H$^+$, 100). **HRMS-ESI** calcd. for $C_{25}H_{30}NO_5^+$ is 424.2118: observed: 424.2127; $[\alpha]_D^{25}$ = +239.3 ° (c 1.0, $CHCl_3$, 92% ee.), 92% ee was determined by HPLC analysis using a Chiralcel OD-H column with hexane/*i*-PrOH 30/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 4.86 min (major), t_{R2} = 5.53 min (minor).



(cis)-diethyl 2-methyl-3-phenyl-6-vinyl-[1,2]oxazinane-4,4-dicarboxylate

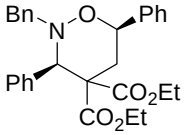
-40°C, 3 days, 88% yield for *cis*-isomer, dr = 6/1, 80% ee. 46% conversion of cyclopropane (by ^{1}H NMR). Analytical data [4]:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.51 (m, 2H), 7.30-7.27 (m, 3H), 6.04-5.93 (m, 1H), 5.39 (d, *J* = 17.1 Hz, 1H), 5.27 (d, *J* = 10.5 Hz, 1H), 4.74 (s, 1H), 4.40-4.29 (m, 3H), 3.91-3.71 (m, 2H), 2.46-2.43 (m, 5H), 1.31 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); $[\alpha]_D^{25}$ = +155.2 (c 1.0, $CHCl_3$, 80% ee.), 80% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 50/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 6.89 min (major), t_{R2} = 9.59 min (minor).



(cis,*E*)-diethyl 2-methyl-3-phenyl-6-styryl-[1,2]oxazinane-4,4-dicarboxylate

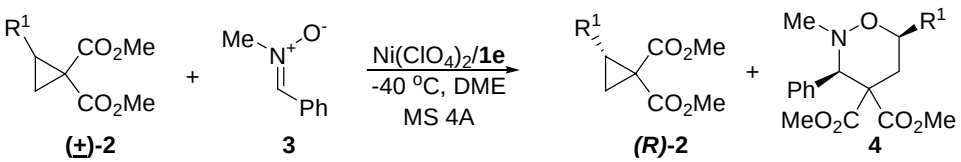
-40°C, 5 hrs, 84% yield, dr = 5/1, 80% ee. 41% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56-7.26 (m, 10H), 6.72 (d, *J* = 15.9 Hz, 1H), 6.34 (dd, *J* = 5.8 Hz, 15.8 Hz, 1H), 4.78 (s, 1H), 4.57-4.55 (m, 1H), 4.35 (q, *J* = 6.9 Hz, 2H), 3.93-3.72 (m, 2H), 2.62-2.50 (m, 2H), 2.50 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.77, 168.11, 136.49, 134.72, 132.16, 131.15, 128.54, 128.17, 127.92, 127.89, 127.74, 126.60, 76.29, 68.02, 62.07, 61.56, 58.73, 43.34, 30.12, 14.08, 13.64. **IR** (thin film, cm^{-1}) 2981, 2885, 1738, 1252, 701; **LRMS-ESI**: 424 ($M + H^+$, 100). **HRMS-ESI** calcd. for $C_{25}H_{30}NO_5^+$ is 424.2118: observed: 424.2118; $[\alpha]_D^{25}$ = +121.9 ° (c 1.0, $CHCl_3$, 80% ee.), 80% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 19/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 7.61 min (major), t_{R2} = 8.40 min (minor).



(cis)-diethyl 2-benzyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 5 days, 74% yield for *cis*-isomer, dr = 11/1, 93% ee. 48% conversion of cyclopropane (by ^{1}H NMR). Analytical data: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.60-7.24 (m, 15H), 4.96 (t, *J* = 7.2 Hz, 1H), 4.90 (s, 1H), 4.42-4.25 (m, 2H), 3.92 (d, *J* = 13.8 Hz, 1H), 3.90-3.70 (m, 2H), 3.64 (d, *J* = 13.8 Hz, 1H), 2.74 (s, 1H), 2.71 (s, 1H), 1.30 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.53, 168.09, 140.21, 136.92, 134.89, 131.28, 128.79, 128.35, 128.10, 127.92, 127.88, 127.74, 126.97, 126.09, 77.70, 65.70, 61.92, 61.44, 59.38, 59.28, 31.26, 14.05, 13.54. **IR** (thin film, cm^{-1}) 3062, 3030, 2981, 2937, 1739, 1453, 1253, 1199, 755, 699; **LRMS-ESI**: 474 ($M + H^+$, 100). **HRMS-ESI** calcd. for $C_{29}H_{32}NO_5^+$ is 474.2275: observed: 474.2266; $[\alpha]_D^{25}$ = +113.3 ° (c 1.0, $CHCl_3$, 93% ee.), 93% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 30/1 as eluent, 1 mL/min, 254 nm, t_{R1} = 8.27 min (minor), t_{R2} = 11.19 min (major). When this reaction scale was enlarged by 2 times, the results are similar as above: cyclopropane/nitrone = 0.88 mmol/0.40 mmol, -30°C, 7 days, 83% yield for *cis*-isomer, dr = 10/1, 94% ee, 49% conversion of cyclopropane (by ^{1}H NMR).

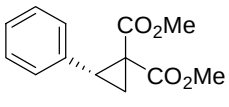
General procedure for kinetic resolution of cyclopropane-1,1-diester.



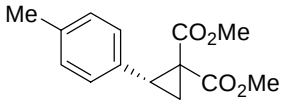
(±)-2 **3** ***(R)*-2** **4**

A mixture of $Ni(ClO_4)_2 \cdot 6H_2O$ (0.040 mmol) and trisoxazoline **1e** (0.044 mmol) in dimethoxyl ethane (1 mL) was stirred at 50 °C for 2 hours under nitrogen. The mixture was cooled to room temperature and then was transferred to cyclopropane diester (0.44 mmol) *via* a syringe. To the resulting solution was added activated molecular sieves 4Å (100 mg). The mixture

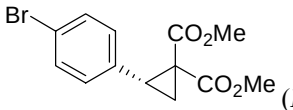
was stirred at -30°C for 30 minutes and then nitrone (0.23 mmol) was added. After the conversion of (±) **2** was higher than 50% (monitored by ^{1}H NMR), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with CH_2Cl_2 (50 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography. The absolute configuration for recovered cyclopropanes was assigned *R* by comparing its polar rotation with that reported in the reference.[5]



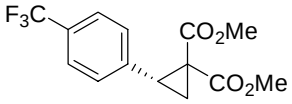
(*R*)-dimethyl 2-phenylcyclopropane-1,1-dicarboxylate.[5] Cyclopropane/nitrone = 0.40 mmol/0.40 mmol, at -40 °C, 30 hours, 55 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 43%. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.30-7.17 (m, 5H), 3.78 (s, 3H), 3.35 (s, 3H), 3.23 (t, *J* = 8.7 Hz, 1H), 2.20 (dd, *J* = 5.1 Hz, 8.1 Hz, 1H), 1.74 (dd, *J* = 5.1 Hz, 9.3 Hz, 1H). $[\alpha]_D^{25}$ = +131.9 (*c* 1.0, PhH), 91% ee determined by HPLC analysis using a Chiralcel OD-H with hexane/*i*-PrOH = 50/1 v/v, 1.0 mL/min, 254 nm, t_{R1}= 7.70 min (minor), t_{R2}= 8.14 min (major).



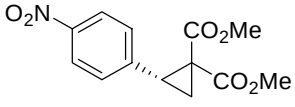
(*R*)-dimethyl 2-*p*-tolylcyclopropane-1,1-dicarboxylate.[5] Cyclopropane/nitrone = 0.4 mmol/0.25 mmol, at -40 °C, 48 hours, 50 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 49%. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.07 (s, 4H), 3.78 (s, 3H), 3.38 (s, 3H), 3.19 (t, *J* = 8.6 Hz, 1H), 2.30 (s, 3H), 2.17 (dd, *J* = 5.1 Hz, 8.1 Hz, 1H), 1.72 (dd, *J* = 5.1 Hz, 9.3 Hz, 1H). $[\alpha]_D^{25}$ = +119.3 ° (*c* 1.0, PhH), 96% ee determined by HPLC analysis using a Chiralcel OD-H with hexane/*i*-PrOH = 500/3 v/v, 0.6 mL/min, 254 nm, t_{R1} = 18.63 min (minor), t_{R2} = 19.86 min (major).



(*R*)-dimethyl 2-(4-bromophenyl)cyclopropane-1,1-dicarboxylate.[5] Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at -30 °C, 67 hours, 51 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 49%. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 3.79 (s, 3H), 3.41 (s, 3H), 3.16 (t, *J* = 8.7 Hz, 1H), 2.15 (dd, *J* = 5.1 Hz, 8.0 Hz, 1H), 1.74 (dd, *J* = 5.1 Hz, 9.3 Hz, 1H). $[\alpha]_D^{25}$ = +90.1 ° (*c* 1.0, PhH), 95% ee determined by HPLC analysis using a Chiralcel AD-H with hexane/*i*-PrOH = 50/1 v/v, 0.8 mL/min, 254 nm, t_{R1} = 12.02 min (minor), t_{R2} = 13.46 min (major).

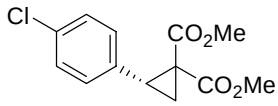


(*R*)-dimethyl 2-(4-(trifluoromethyl)phenyl)cyclopropane-1,1-dicarboxylate.[5] Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at 0 °C, 168 hours, 50 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 49%. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 3.81 (s, 3H), 3.39 (s, 3H), 3.26 (t, *J* = 8.7 Hz, 1H), 2.21 (dd, *J* = 5.4 Hz, 8.2 Hz, 1H), 1.79 (dd, *J* = 5.4 Hz, 9.6 Hz, 1H). $[\alpha]_D^{25}$ = +44.5 ° (*c* 1.0, PhH), 96% ee determined by HPLC analysis using a Chiralcel AD-H with hexane/*i*-PrOH = 50/1 v/v, 0.8 mL/min, 238 nm, t_{R1} = 7.91 min (minor), t_{R2} = 9.32 min (major).

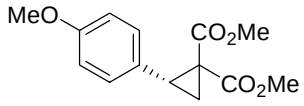


(*R*)-dimethyl 2-(4-nitrophenyl)cyclopropane-1,1-dicarboxylate.[6] Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at 0 °C, 96 hours, 53 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 45%. **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.14 (d, *J* = 9.0 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 3.81 (s, 3H), 3.41 (s, 3H), 3.28 (t, *J* = 8.7 Hz, 1H), 2.22 (dd, *J* = 5.4 Hz, 7.7 Hz, 1H), 1.83 (dd, *J* = 5.4 Hz, 9.3 Hz, 1H). $[\alpha]_D^{25}$ = +100.5 ° (*c* 1.0, PhH), 97% ee determined by HPLC analysis

using a Chiralcel AD-H with hexane/*i*-PrOH = 90/10 v/v, 0.7 mL/min, 254 nm, t_{R1} = 11.82 min (minor), t_{R2} = 14.63 min (major).

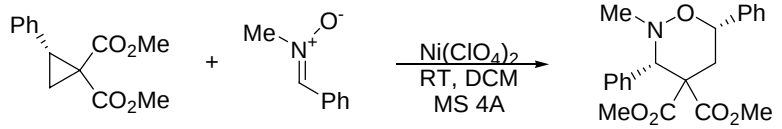


(R)-dimethyl 2-(4-chlorophenyl)cyclopropane-1,1-dicarboxylate.[5] Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, -30 °C, 72 hours, 50 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 49%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.24 (d, *J* = 6.9 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 3.41 (s, 3H), 3.19 (t, *J* = 8.4 Hz, 1H), 2.16 (dd, *J* = 5.1 Hz, 8.0 Hz, 1H), 1.75 (dd, *J* = 5.1 Hz, 9.6 Hz, 1H). $[\alpha]_D^{25}$ = +95.8 ° (*c* 1.0, PhH), 94% ee estimated on the basis of HPLC analysis using a chiral column: Diacel Chiralcel AD-H with hexane/*i*-PrOH = 50/1 v/v, 0.8 mL/min, 254 nm, t_{R1} = 10.79 min (minor), t_{R2} = 12.31 min (major).



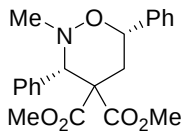
(R)-dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate.[7] Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at -30°C, 48 hours, 57 % conversion of cyclopropane by ^{1}H NMR. Recovered yield: 40%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.10 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.38 (s, 3H), 3.17 (t, *J* = 8.6 Hz, 1H), 2.14 (dd, *J* = 5.1 Hz, 8.0 Hz, 1H), 1.71 (dd, *J* = 5.1 Hz, 9.3 Hz, 1H). $[\alpha]_D^{25}$ = +56.4 ° (*c* 1.0, PhH), 92% ee estimated on the basis of HPLC analysis using a chiral column: Diacel Chiralpak AD-H with hexane/*i*-PrOH = 20/1 v/v, 1.0 mL/min, 254 nm, t_{R1} = 9.26 min (minor), t_{R2} = 10.24 min (major).

Procedure for cycloaddition of nitrone with (R)-dimethyl 2-phenyl cyclopropane-1,1-dicarboxylate.



(R) 91% ee **(-)-3a**: 90% ee

A mixture of (*R*)-dimethyl 2-phenylcyclopropane-1,1-dicarboxylate (91% ee, 0.1 mmol), nitrone (0.12 mmol), MS 4Å (100 mg) and $Ni(ClO_4)_2 \cdot 6H_2O$ (0.01 mmol, absence of ligand) in dry CH_2Cl_2 (1 mL) was stirred at room temperature for 48 hours under nitrogen. After the reaction was complete (monitored by TLC), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with CH_2Cl_2 (50 mL). The filtrate was concentrated under reduced pressure and the residue (used for the determination of the diastereomer ratio by ^{1}H NMR) was purified by flash chromatography. The *ee* was determined by HPLC analysis using a Chiralpak AD-H column with hexane/*i*-PrOH 20/1 as eluent, 254 nm, t_{R1} = 13.19 min (major), t_{R2} = 24.19 min (minor).



(3S, 6S)-dimethyl 2-methyl-3,6-diphenylmorpholine-4,4-dicarboxylate. Room temperature, 48 hours, dr > 99/1, 83% yield, 90% ee, $[\alpha]_D^{25}$ = -152.9 ° ($CHCl_3$, c 1.0, 90% ee).

References

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[5] P. Müller, A. Ghanem, *Org. Lett*. **2004**, *6*, 4347-4350.

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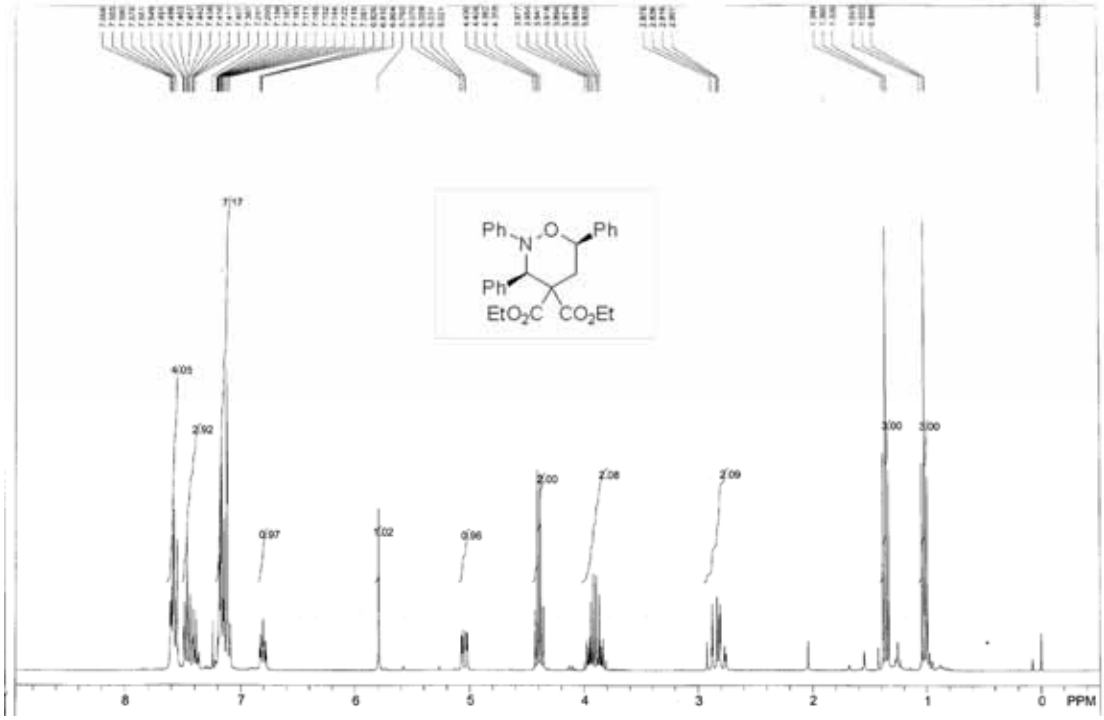
NMR spectra.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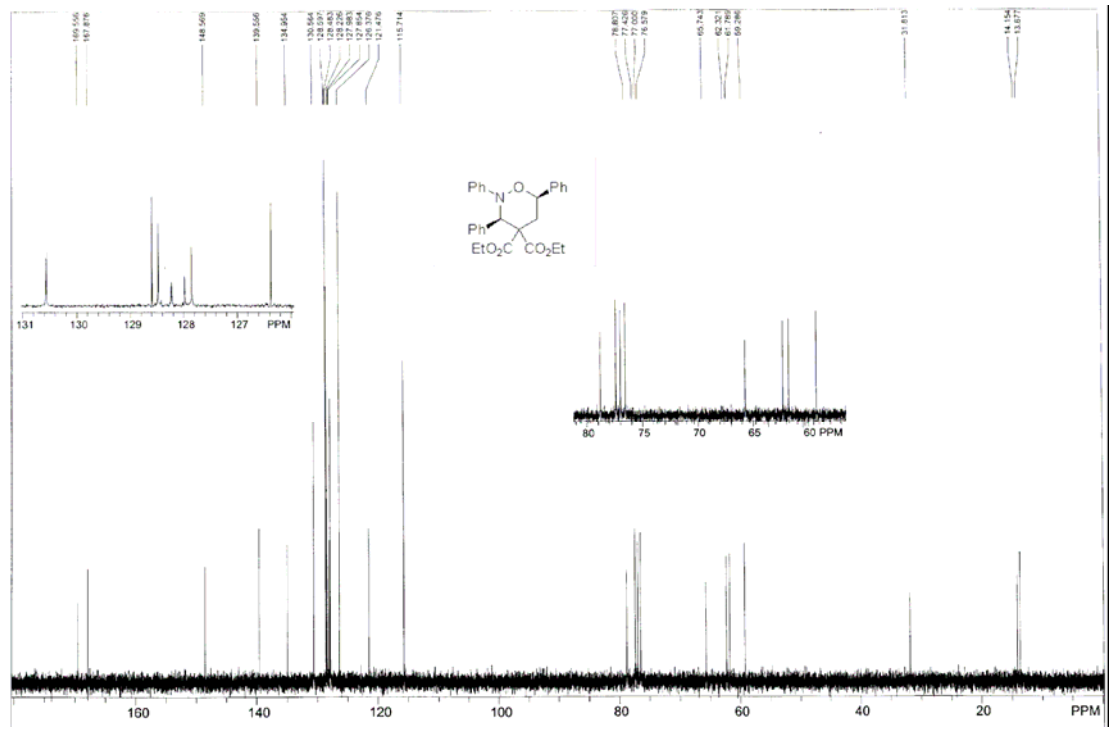
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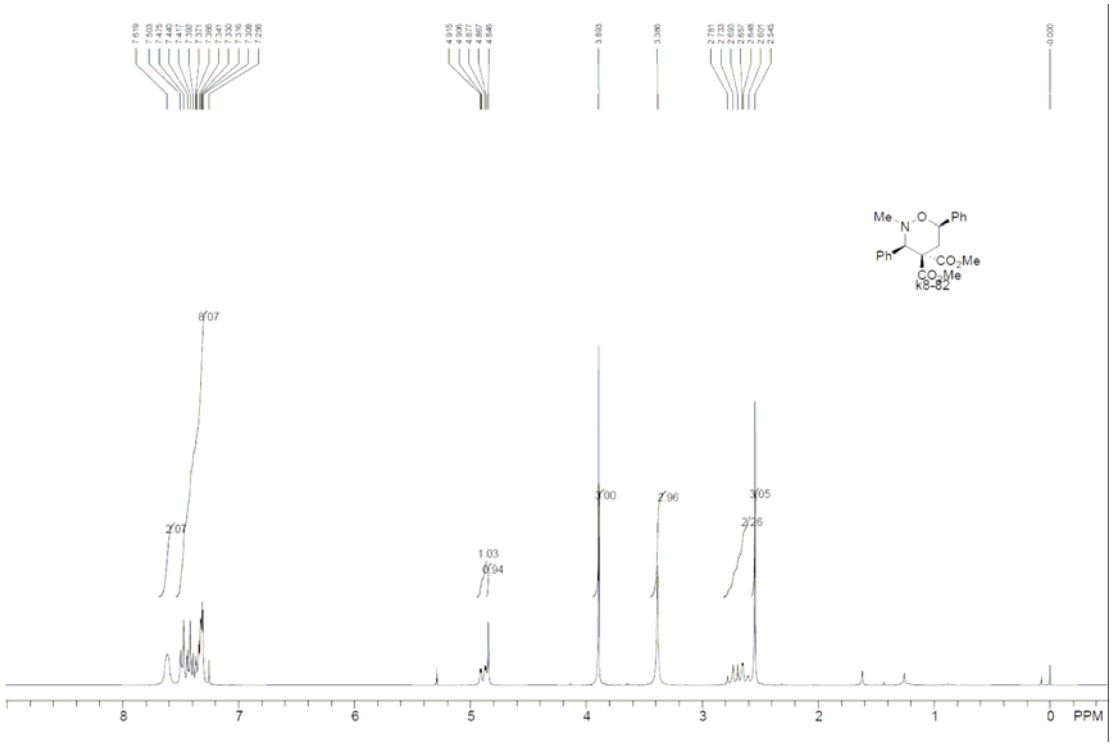
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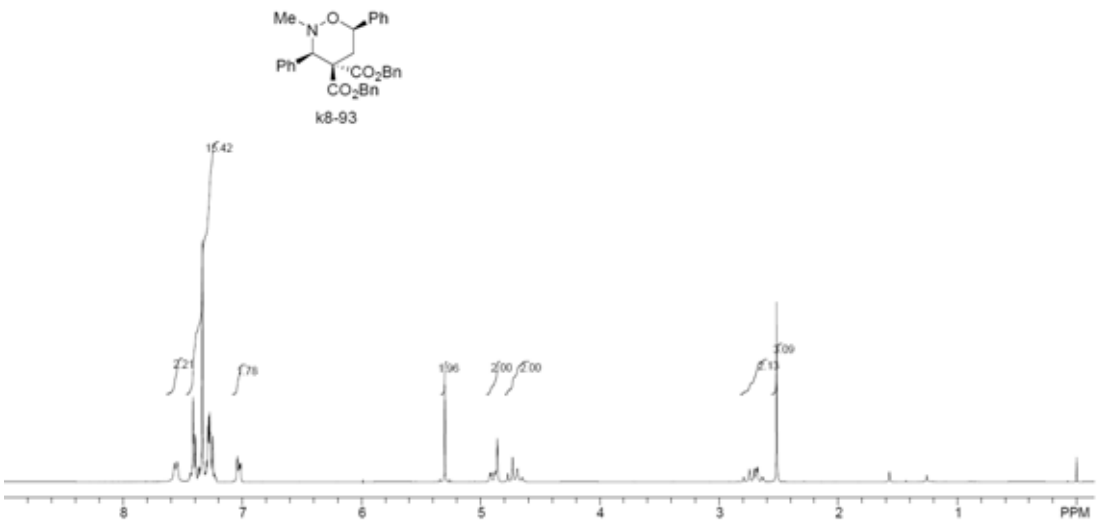
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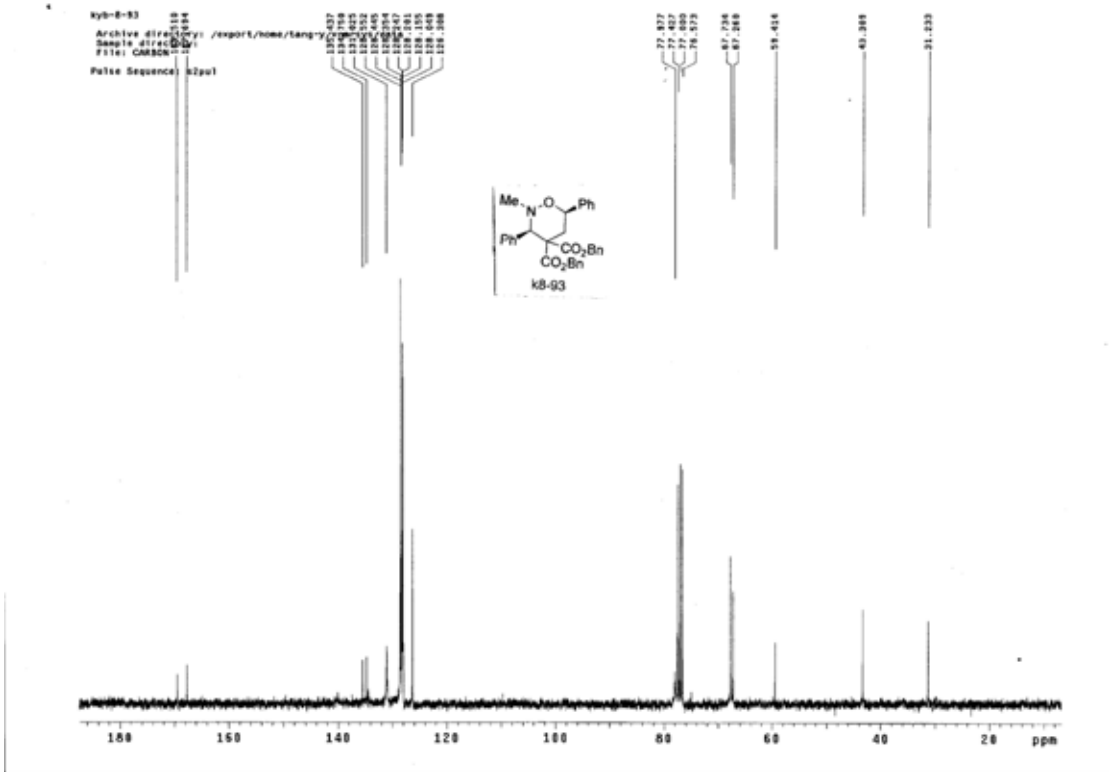
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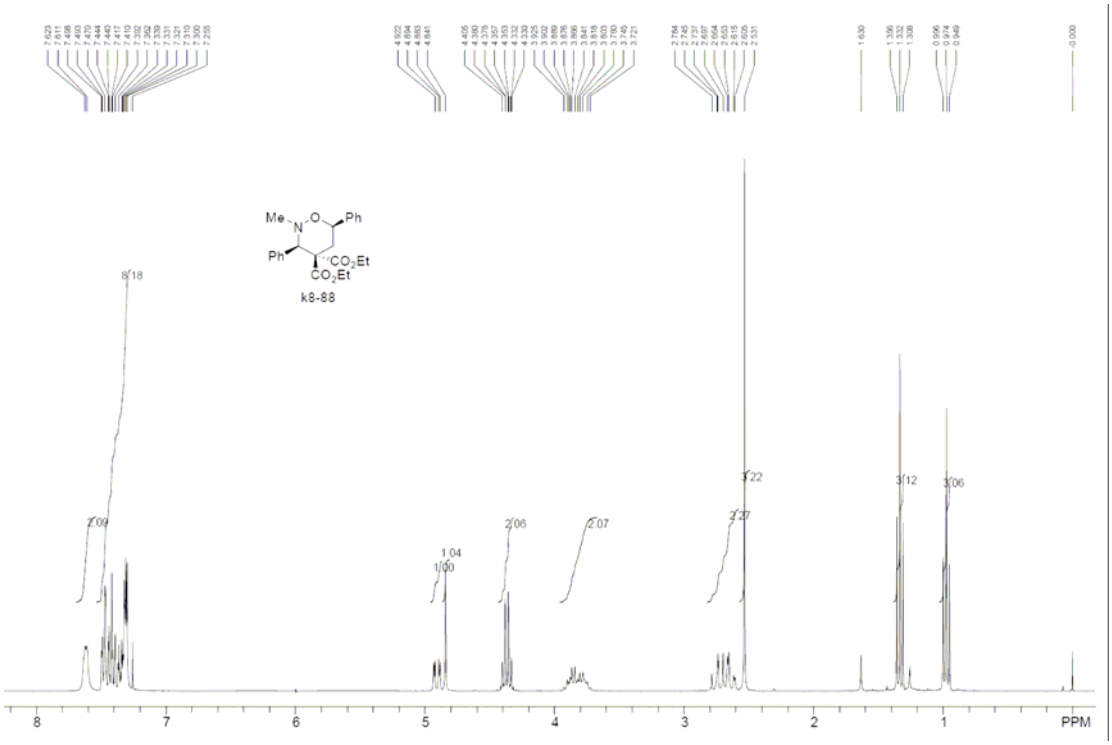
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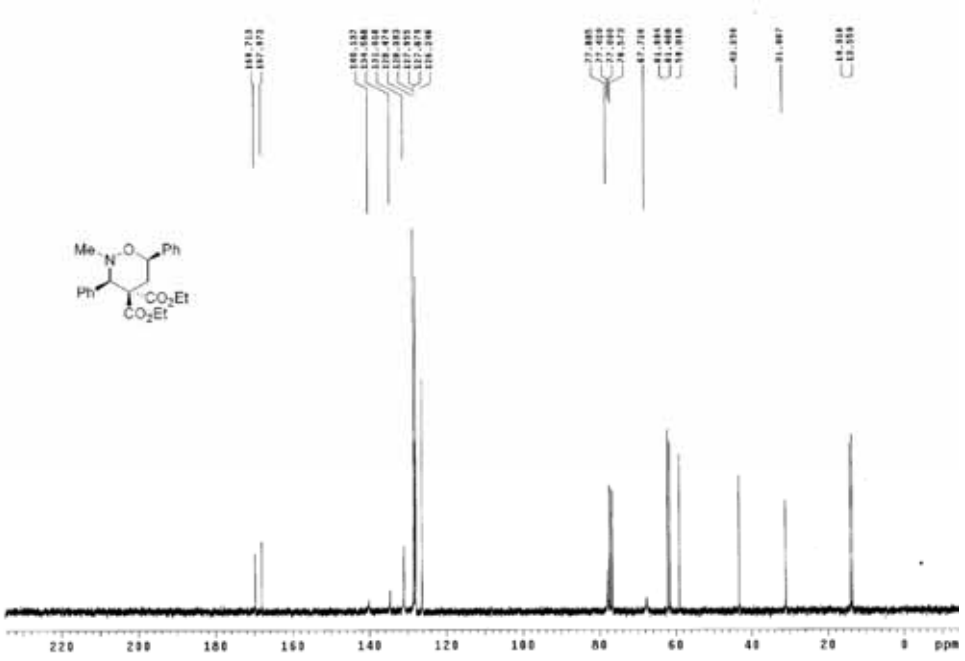
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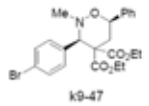
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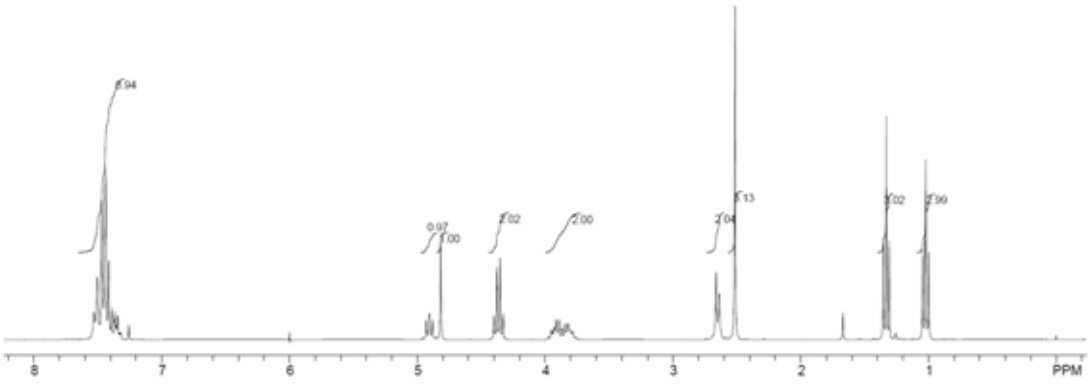
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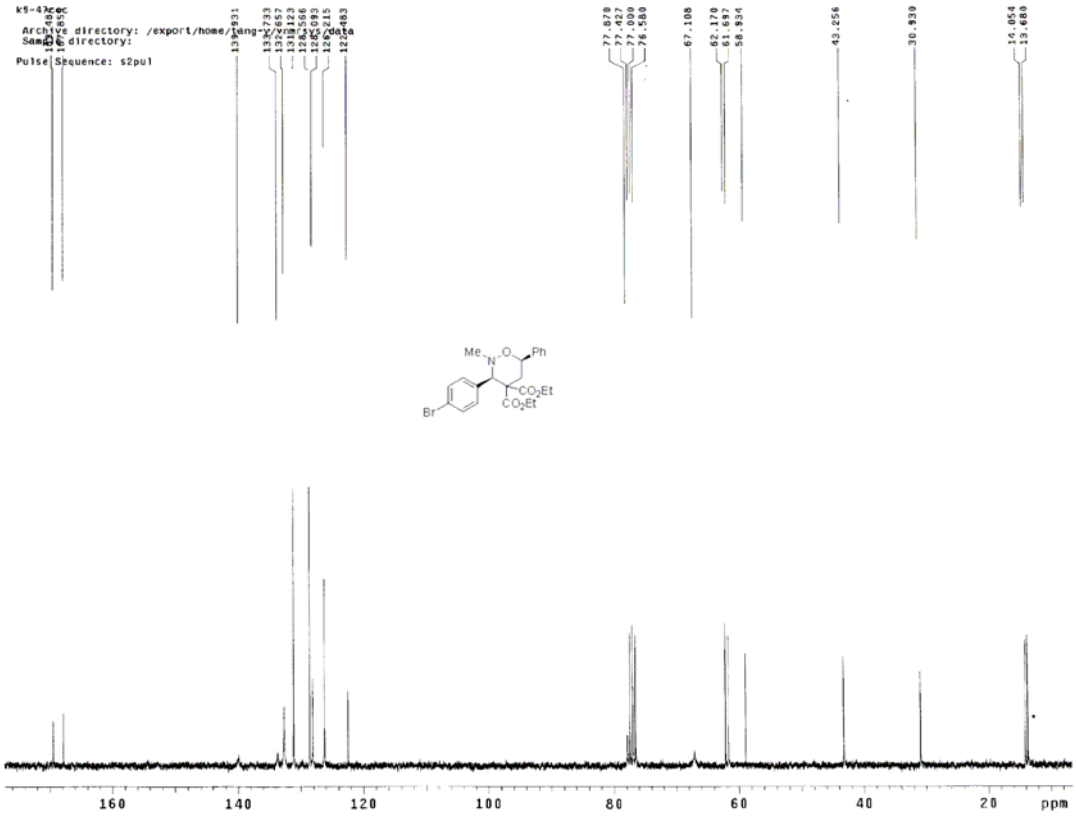
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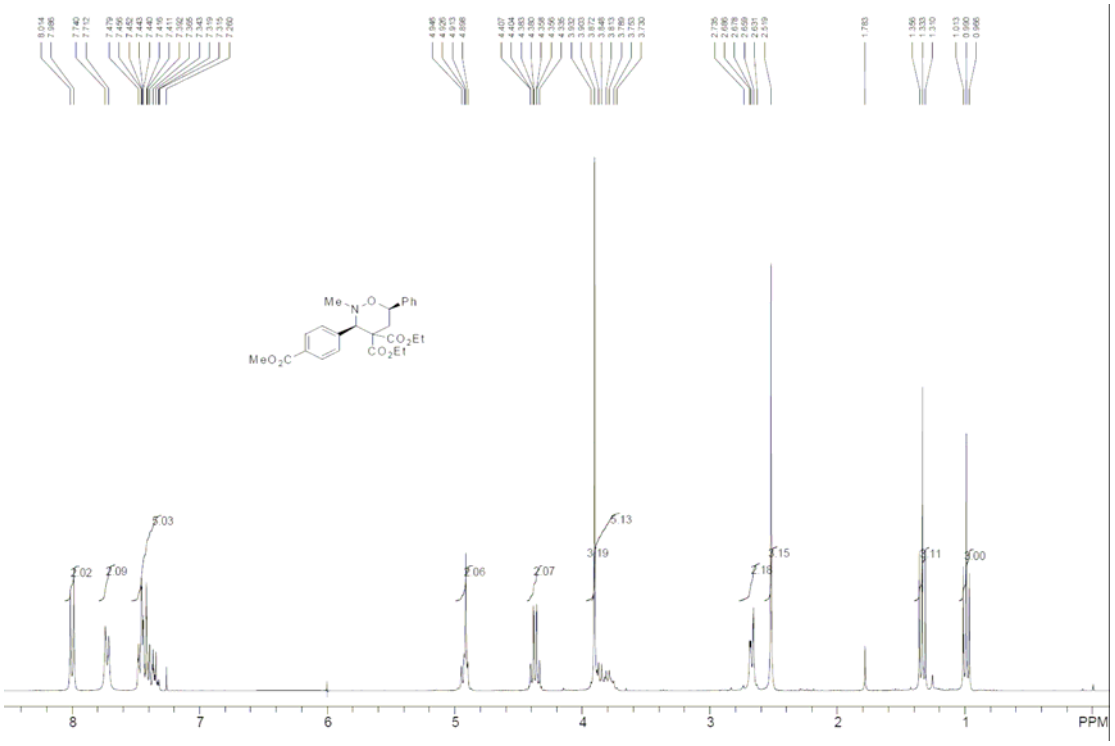
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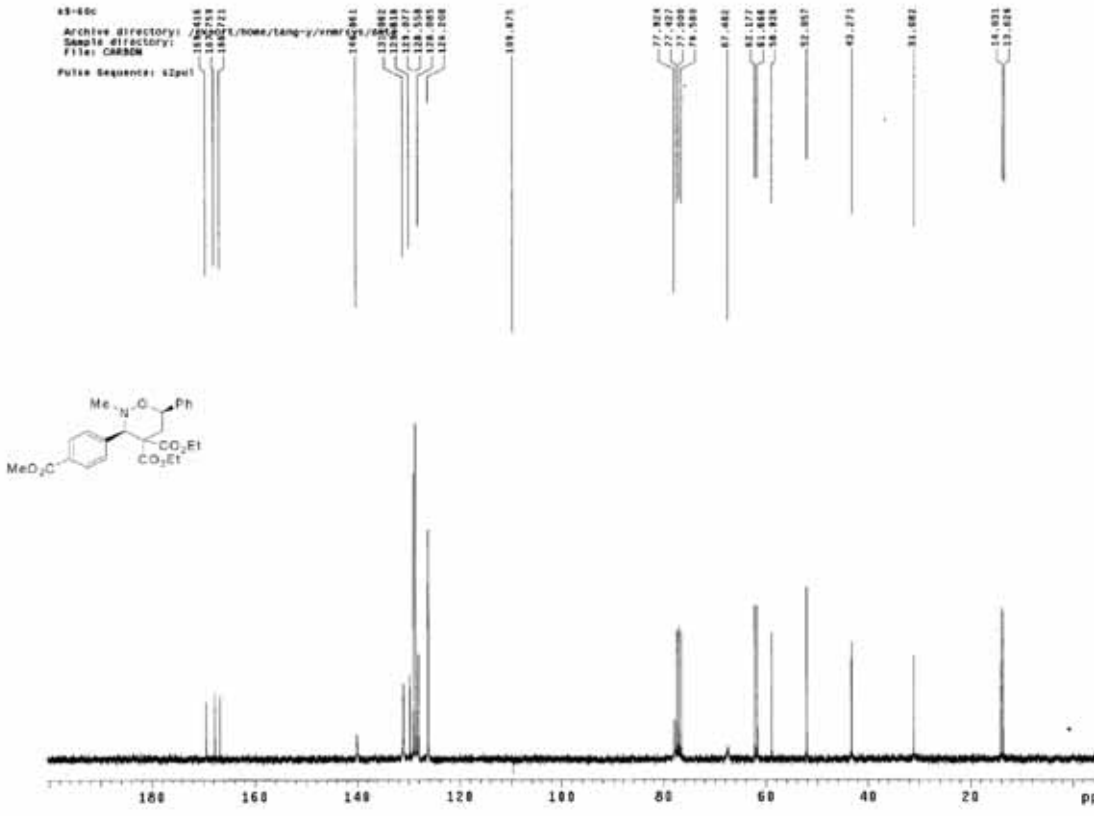
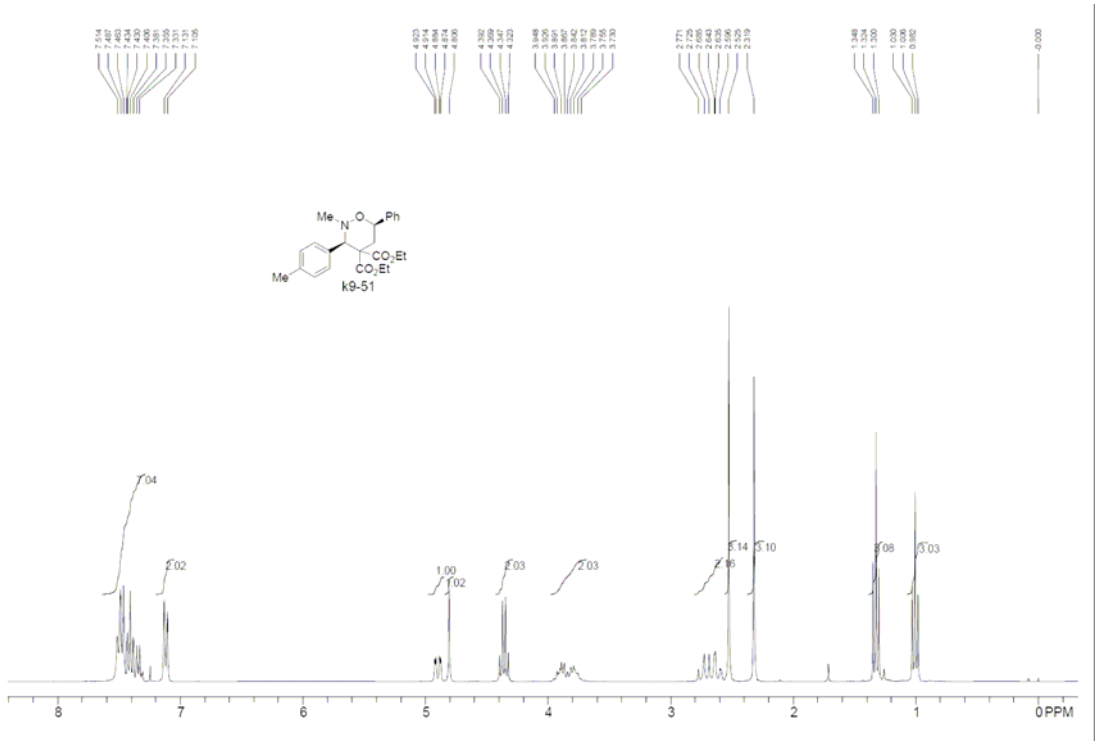
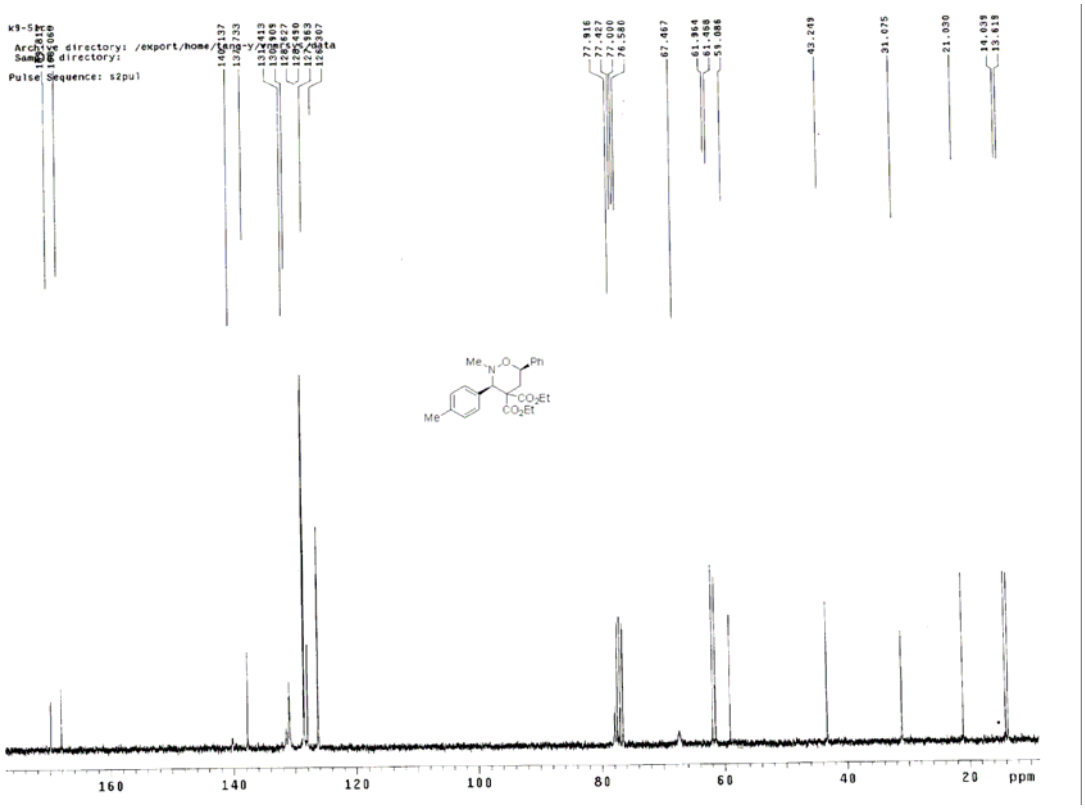
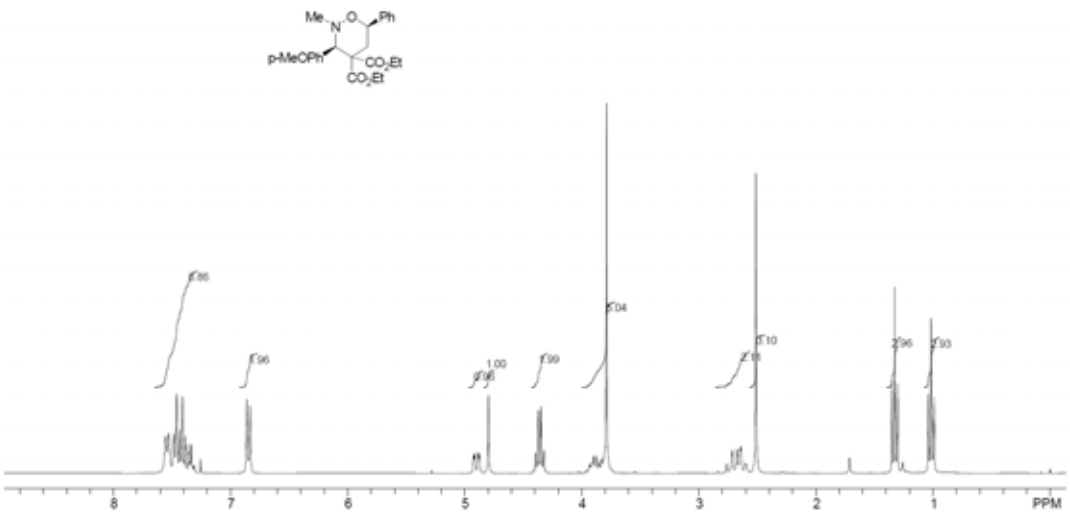
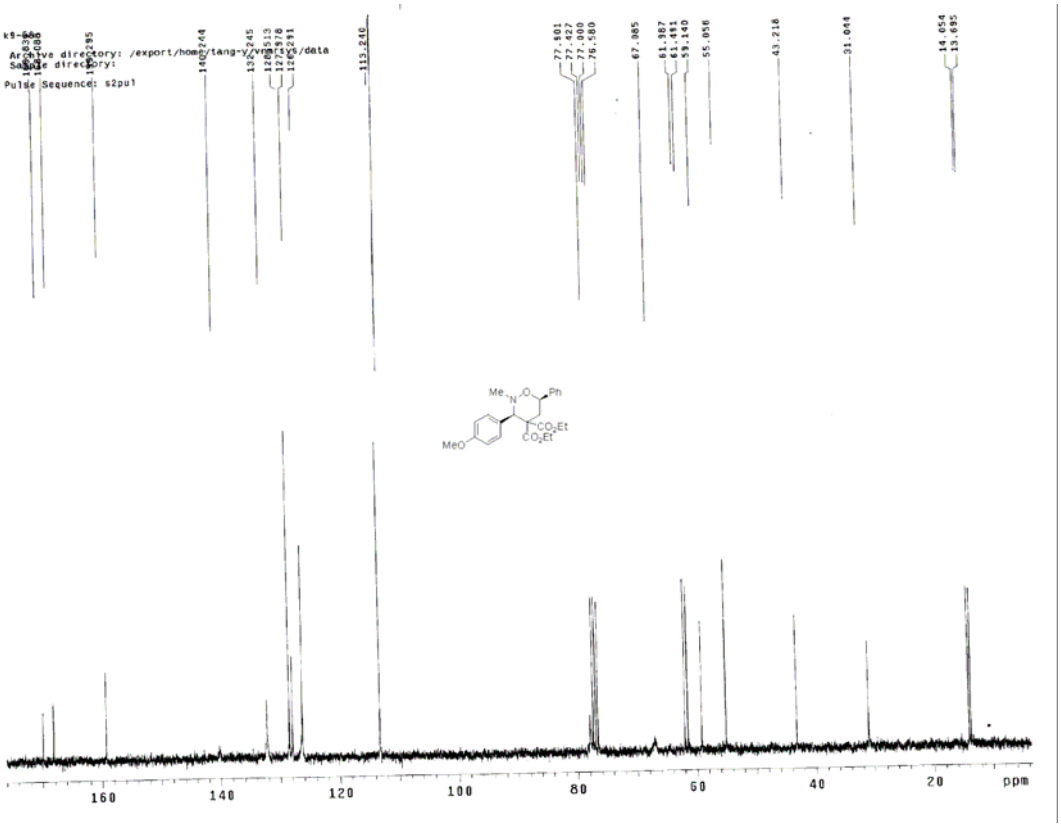
1
PPM

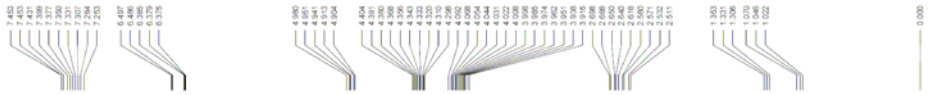

Me
N
O
Ph
CO2Et
CO2Et
MeO2C
180
160
140
120
100
80
60
40
20

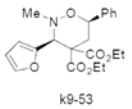

Me
N
O
Ph
CO2Et
CO2Et
Me
k9-51
1.04
2.02
1.00
1.02
2.03
2.03
1.14
1.10
3.08
3.03
8
7
6
5
4
3
2
1
0PPM


Me
N
O
Ph
CO2Et
CO2Et
Me
160
140
120
100
80
60
40
20
ppm

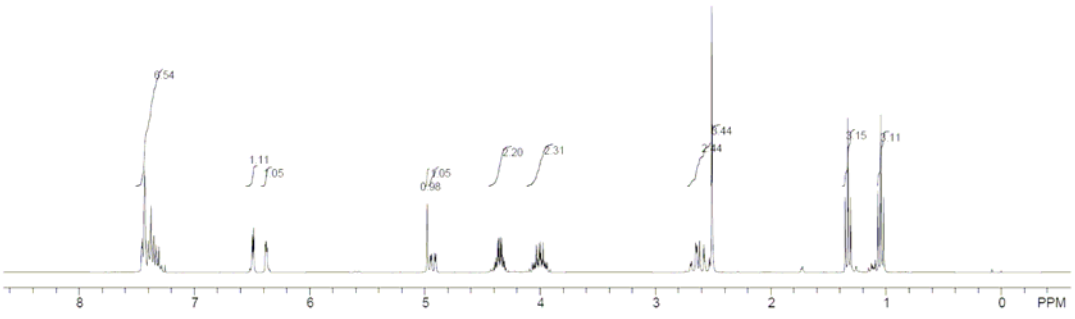

Me
N
O
Ph
p-MeOPh
CO2Et
CO2Et
1.00
8
7
6
5
4
3
2
1
PPM

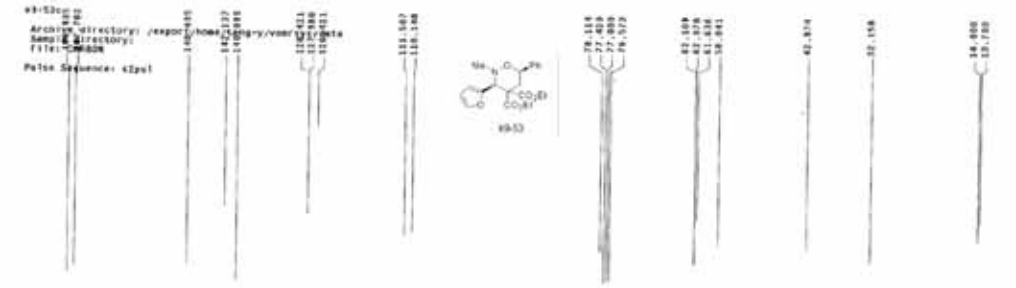

Archive directory: /export/home/tang-y/vnmrsys/data
Pulse Sequence: s2pul
Me
N
O
Ph
CO2Et
CO2Et
MeO
160
140
120
100
80
60
40
20
ppm

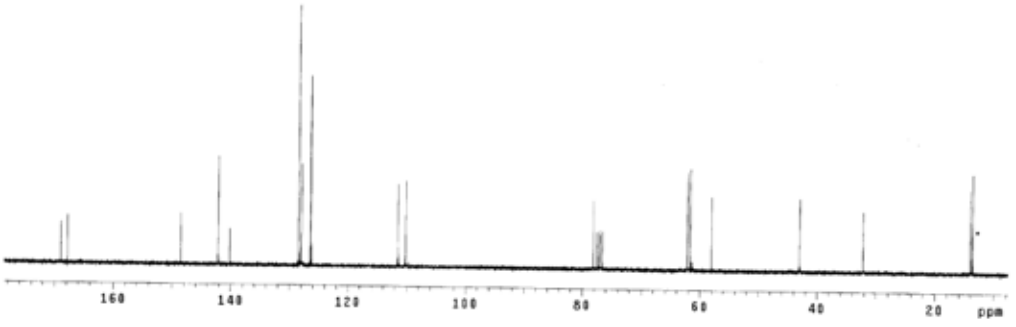


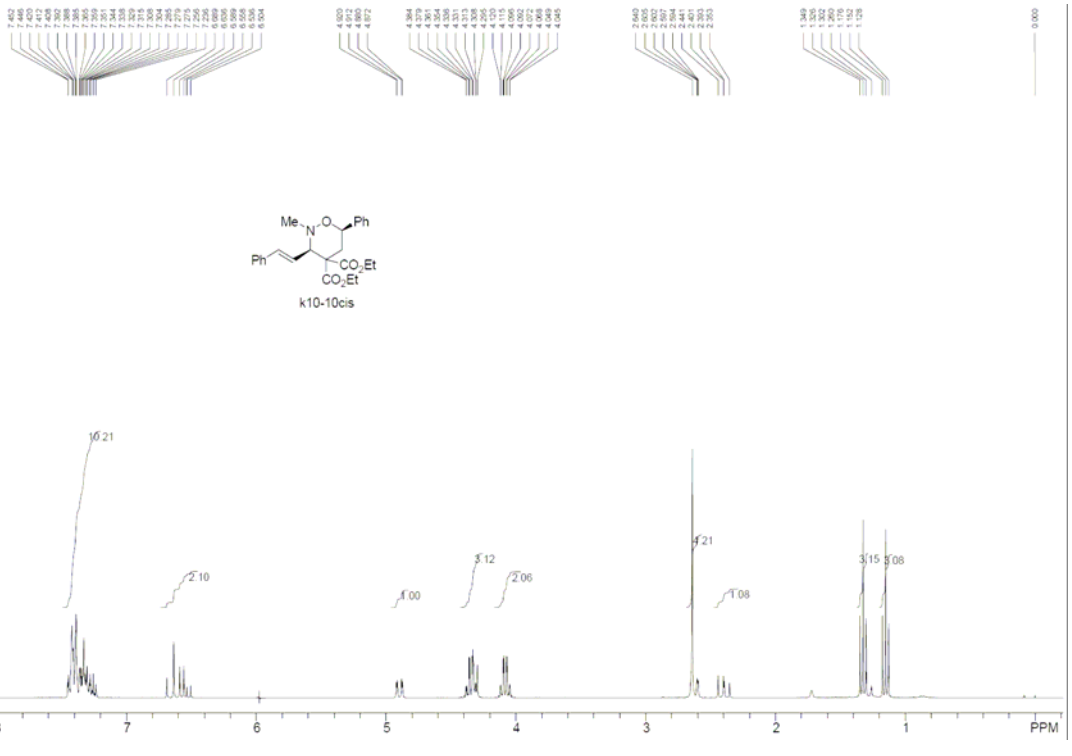

Me
N
O
Ph
CO2Et
CO2Et

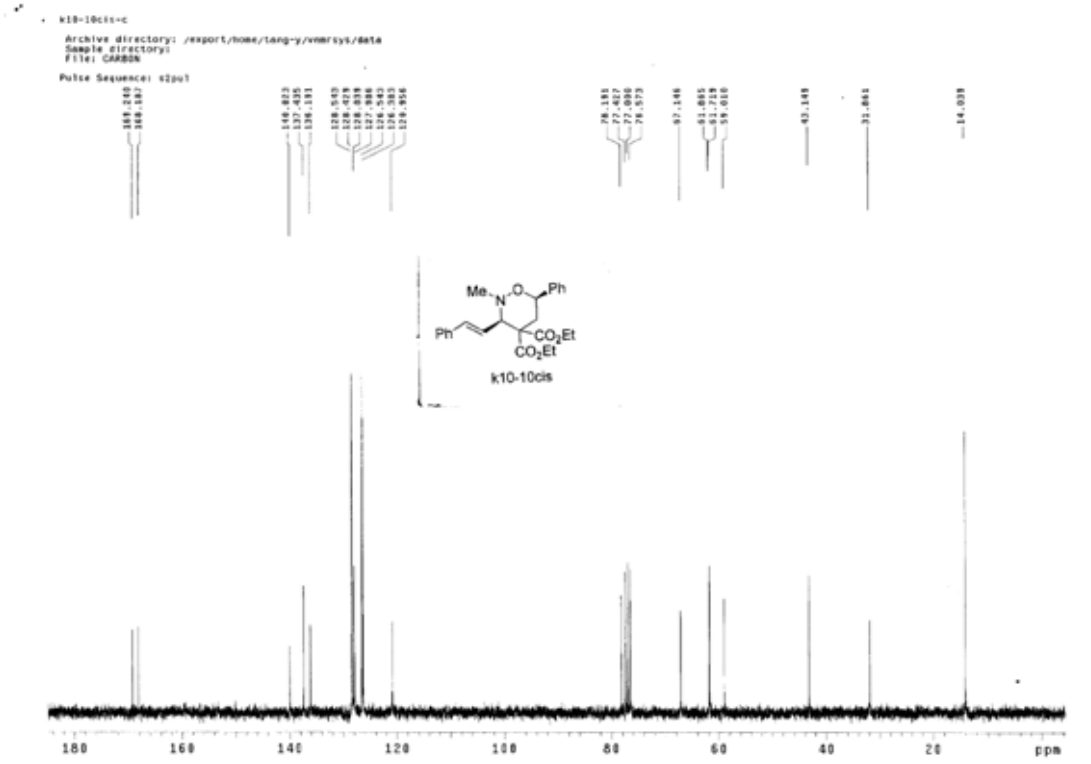
k9-53

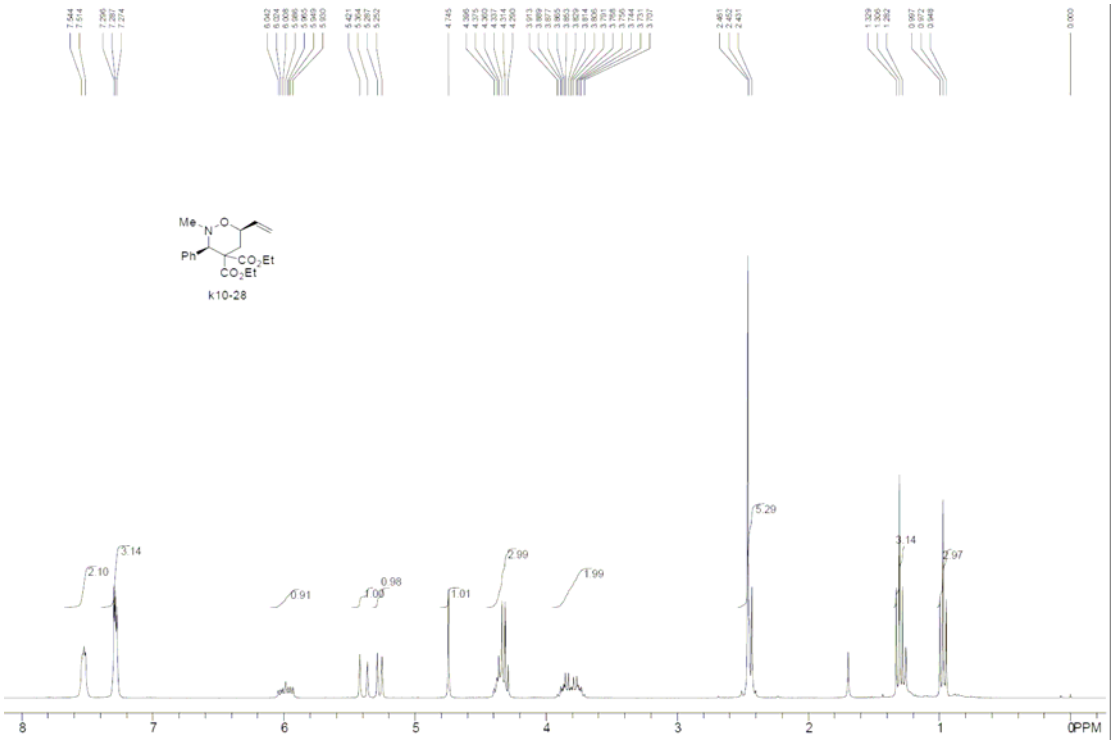

8
7
6
5
4
3
2
1
0
PPM

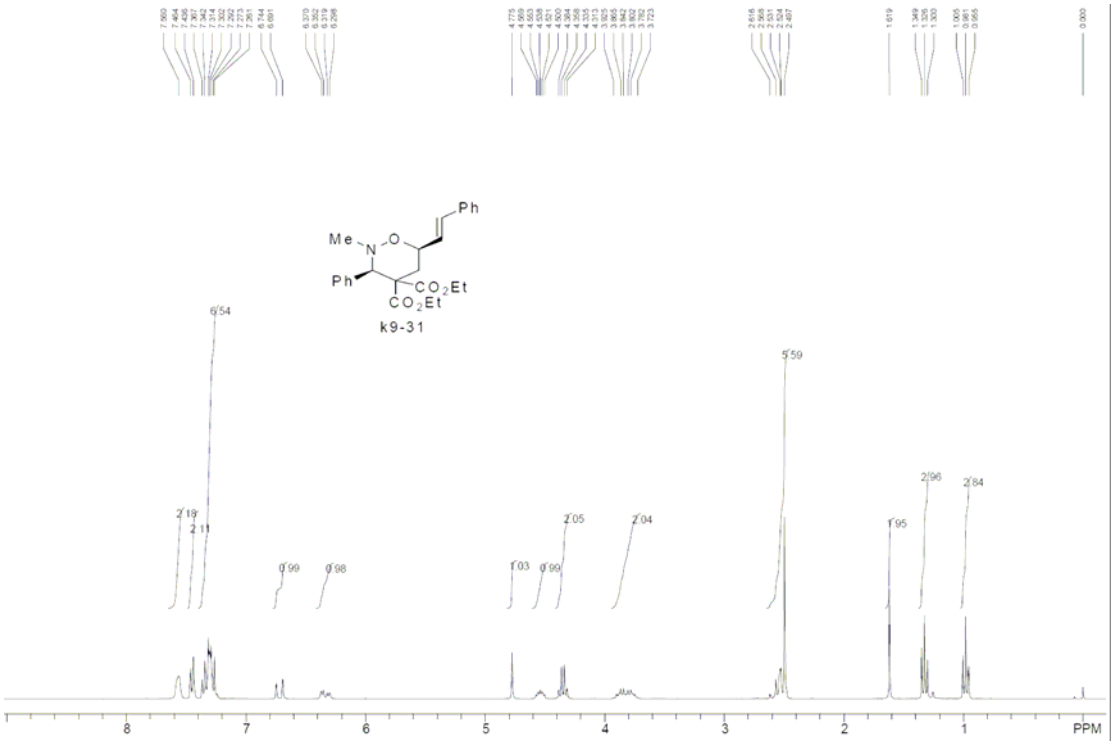


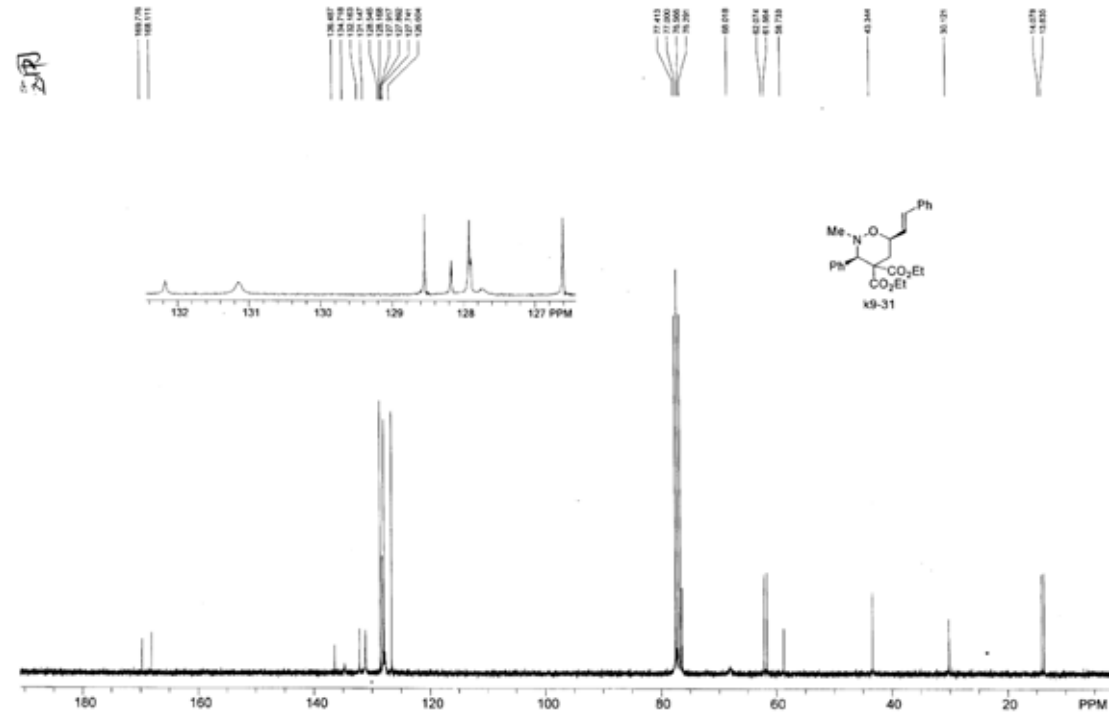


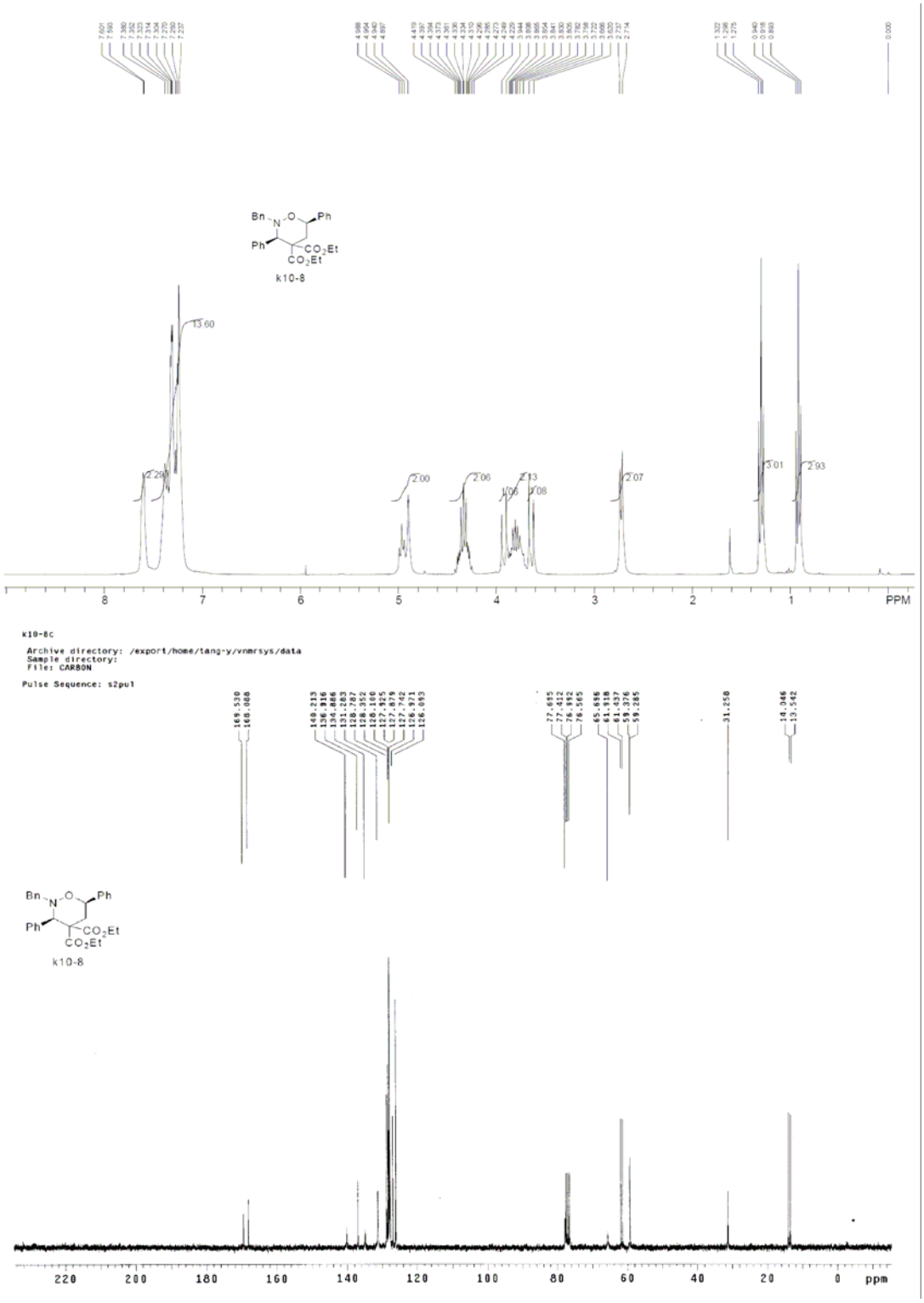

Me
N
O
Ph
Ph
CO2Et
CO2Et
k10-10cis
10.21
2.10
1.00
3.12
2.06
4.21
1.08
3.15
3.08
PPM

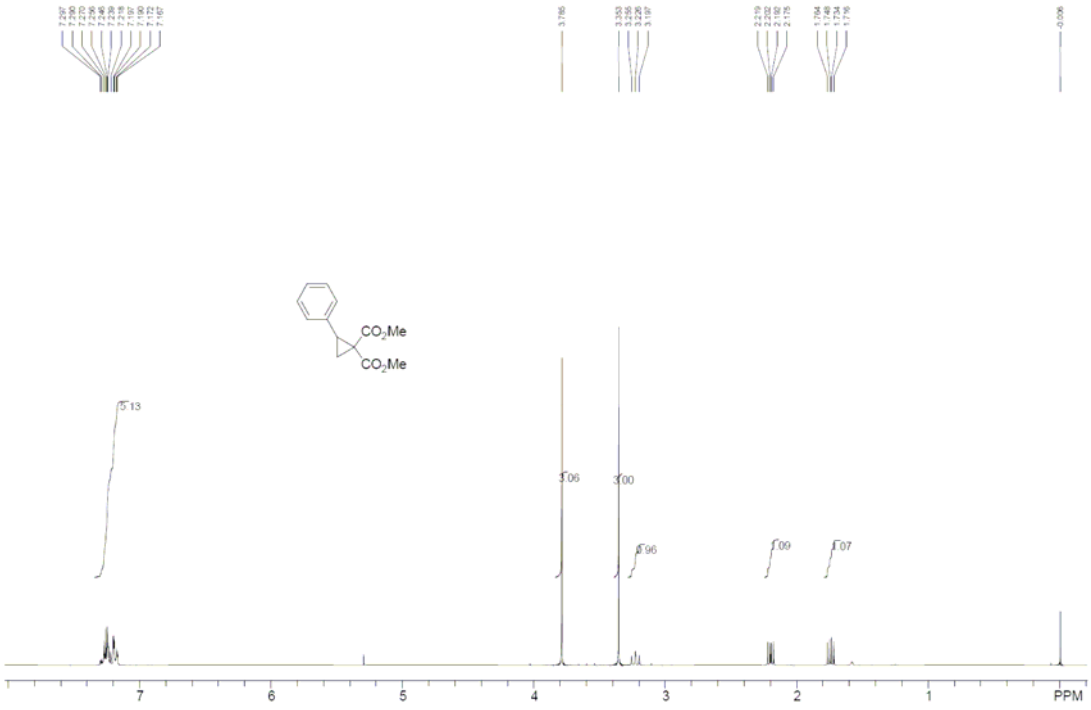

k10-10cis-c
Archive directory: /export/home/tang-y/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
k10-10cis
ppm

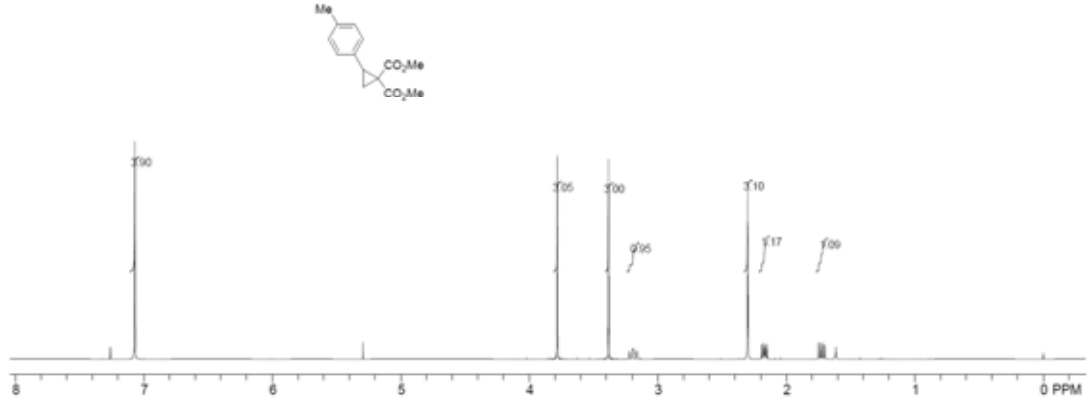

k10-28
2.10
3.14
0.91
1.00
0.98
1.01
2.99
1.99
5.29
3.14
2.97
PPM

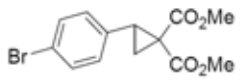

Ph
Me
N
O
Ph
CO2Et
CO2Et
k9-31
6.54
5.59
2.19
2.11
0.99
0.98
1.03
0.99
2.05
2.04
1.95
2.96
2.84
8
7
6
5
4
3
2
1
PPM

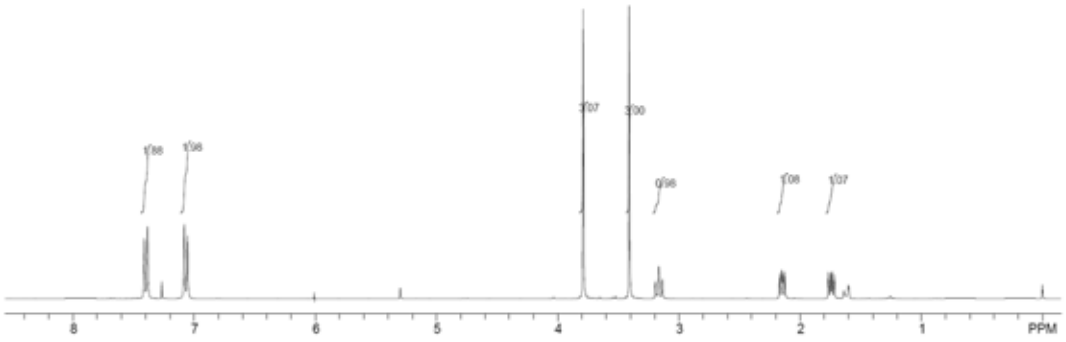

Ph
Me
N
O
Ph
CO2Et
CO2Et
k9-31
132
131
130
129
128
127 PPM
180
160
140
120
100
80
60
40
20
PPM

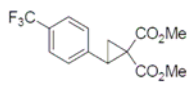

k10-8
13.60
2.29
2.00
2.06
2.13
1.06
1.08
2.07
3.01
2.93
PPM
k10-8c
Archive directory: /export/home/tang-y/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
k10-8
ppm


CO2Me
CO2Me
5.13
3.06
3.00
0.96
1.09
1.07
7
6
5
4
3
2
1
PPM

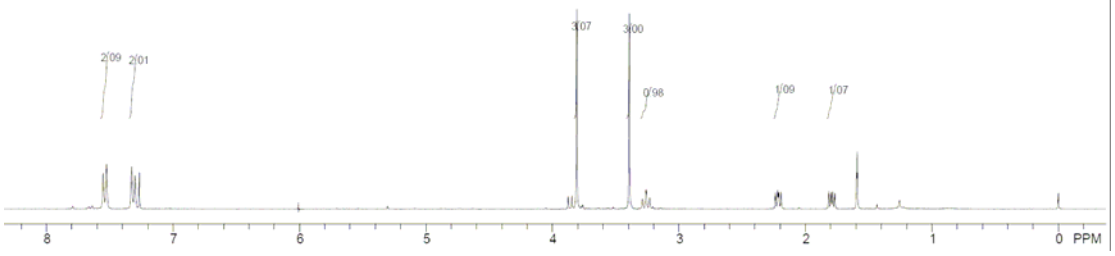

Me
CO2Me
CO2Me
3.00
1.05
1.00
0.95
3.10
1.17
1.09
8
7
6
5
4
3
2
1
0 PPM

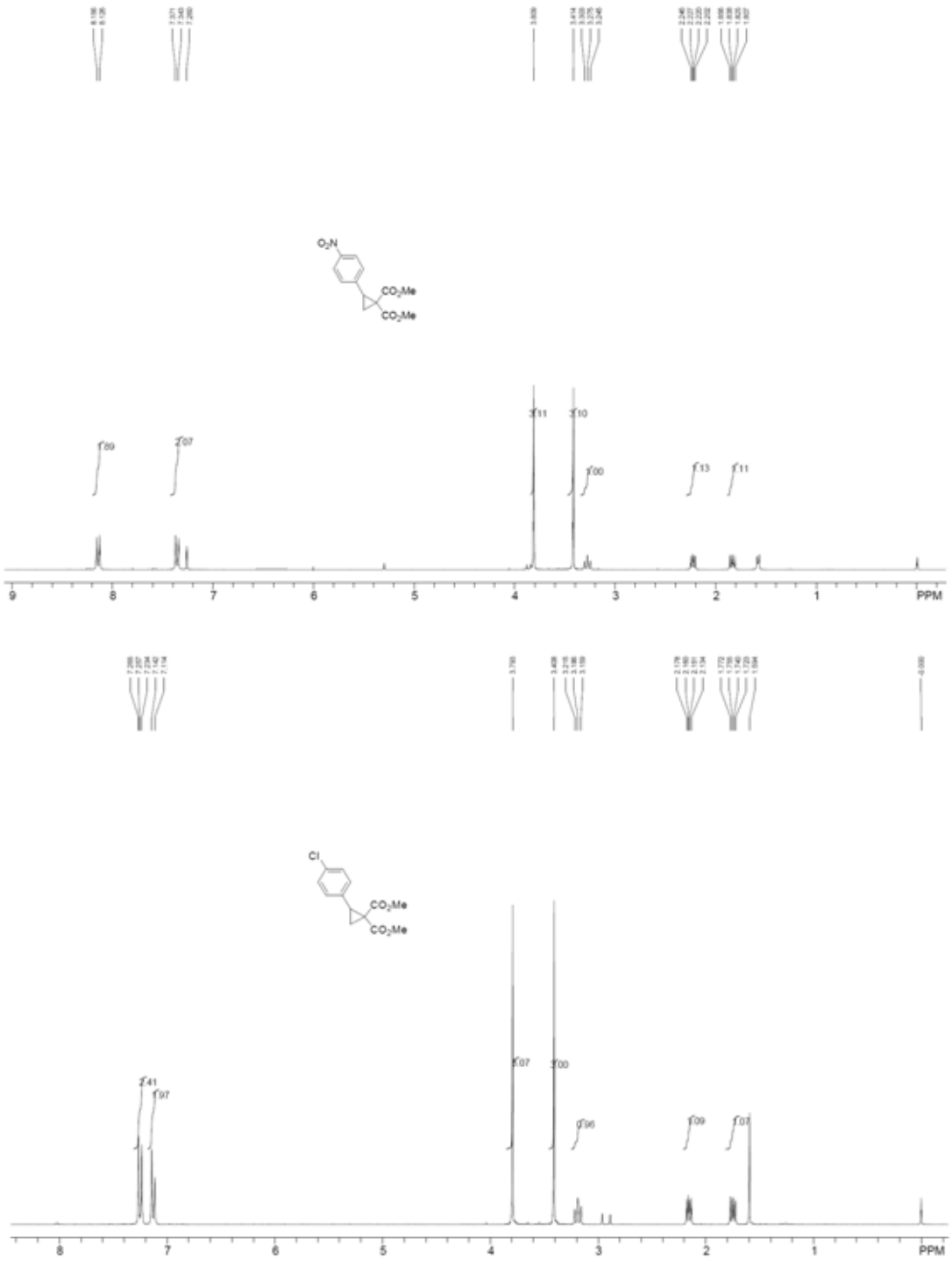

Br
CO2Me
CO2Me

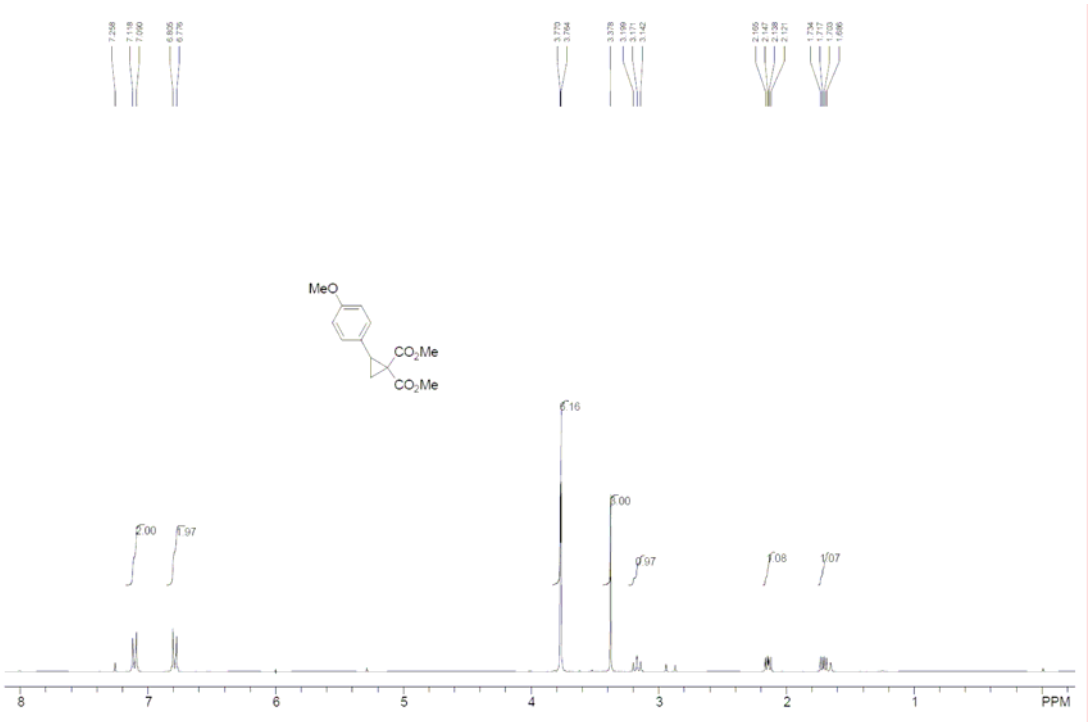

1.88
1.98
3.07
3.00
0.98
1.08
1.07
8
7
6
5
4
3
2
1
PPM


F3C
CO2Me
CO2Me

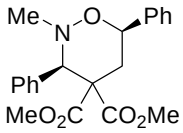
k9-95

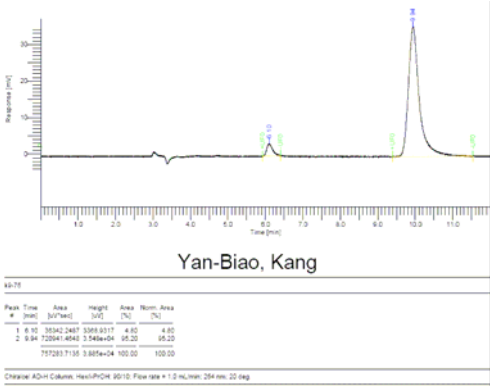

3.07
3.00
2.09
2.01
0.98
1.09
1.07
8
7
6
5
4
3
2
1
0 PPM

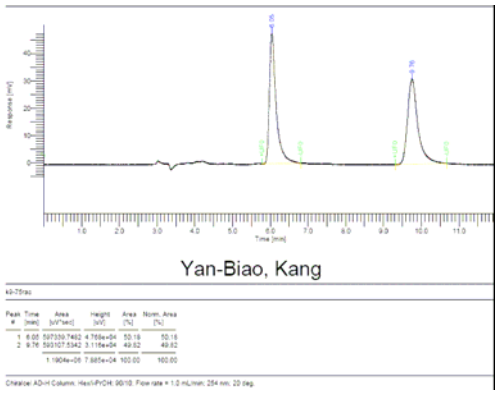

O2N
CO2Me
CO2Me
PPM
Cl
CO2Me
CO2Me
PPM

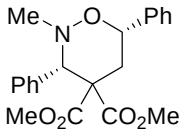

MeO
CO2Me
CO2Me
6.16
2.00
1.97
3.00
0.97
1.08
1.07
8
7
6
5
4
3
2
1
PPM

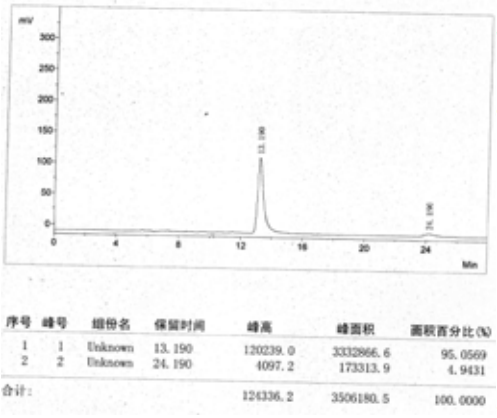
HPLC analytical spectra.



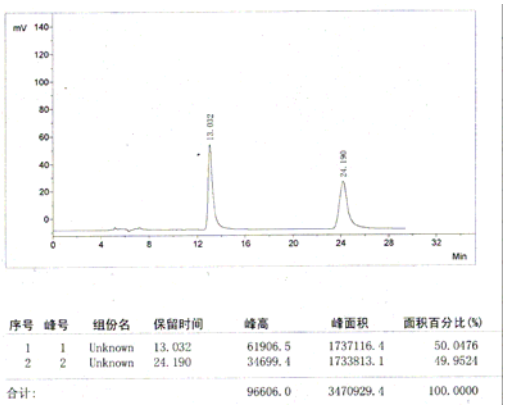




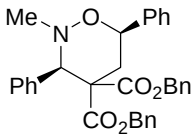


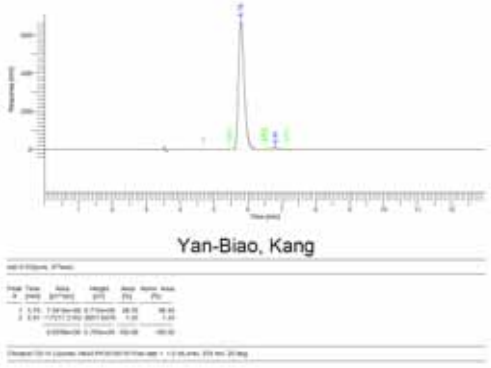


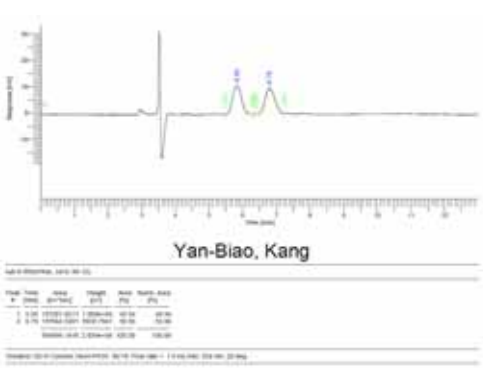
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	13.190	120239.0	3332866.6	95.0569
2	2	Unknown	24.190	4097.2	173313.9	4.9431
合计:				124336.2	3506180.5	100.0000

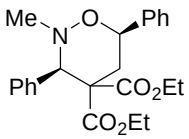


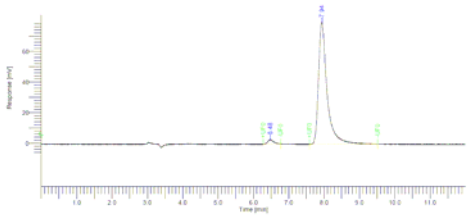
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	13.032	61906.5	1737116.4	50.0476
2	2	Unknown	24.190	34699.4	1733813.1	49.9524
合计:				96606.0	3470929.4	100.0000











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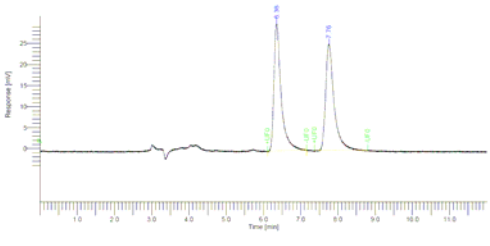

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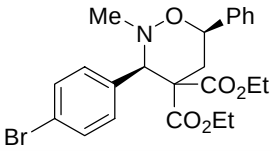

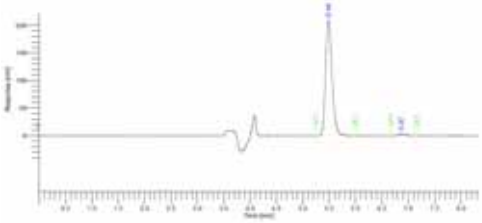

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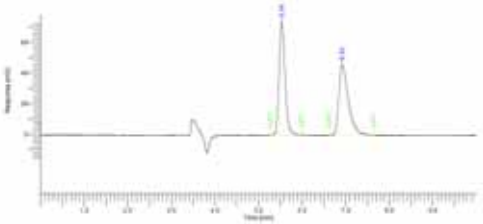

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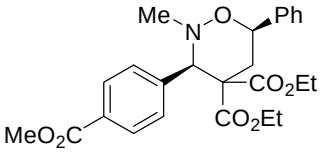

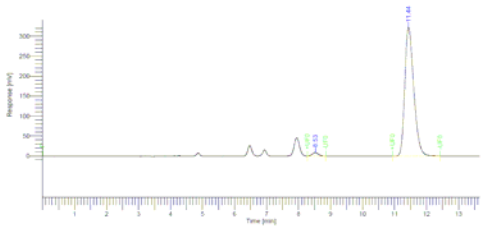

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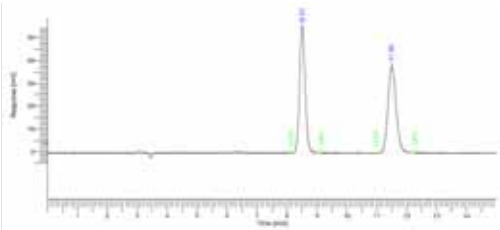

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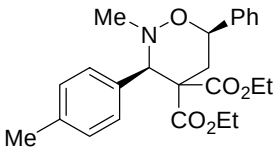

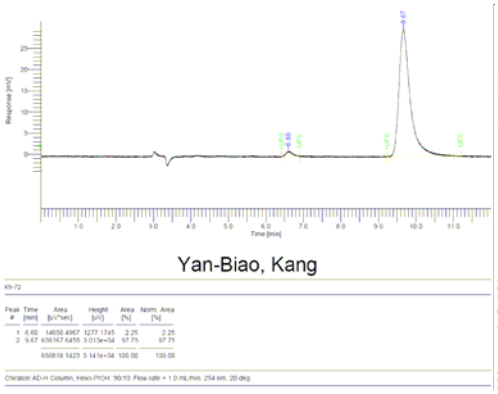
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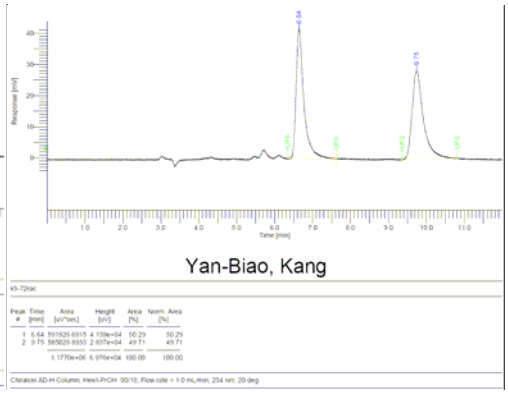
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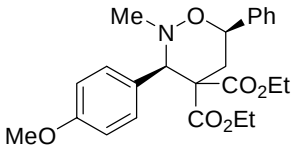
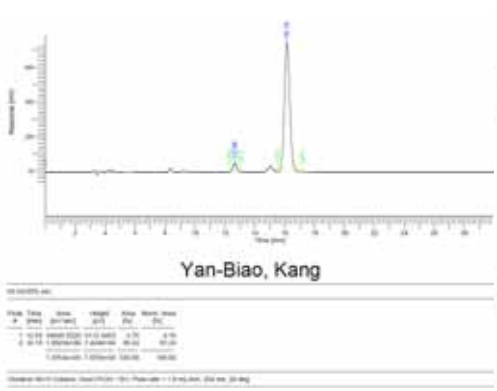

Me
N
O
Ph
CO2Et
CO2Et
MeO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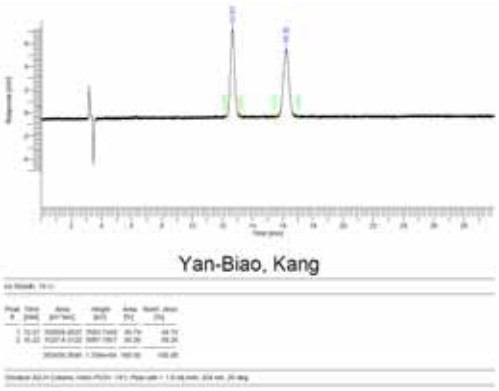
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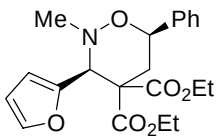
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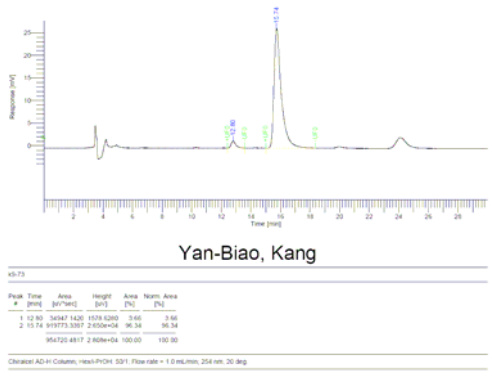
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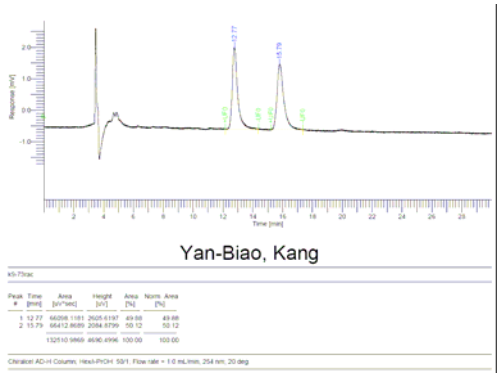
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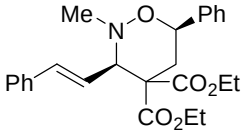
Me
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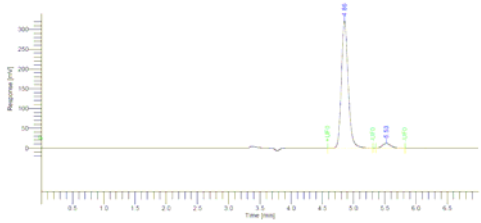

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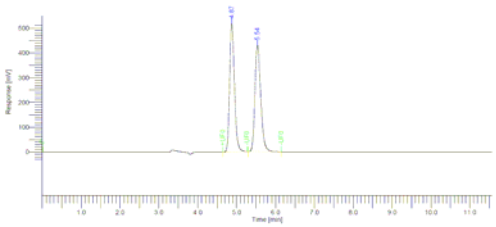

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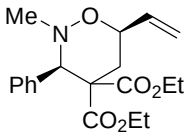

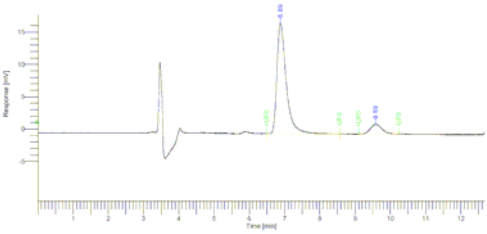

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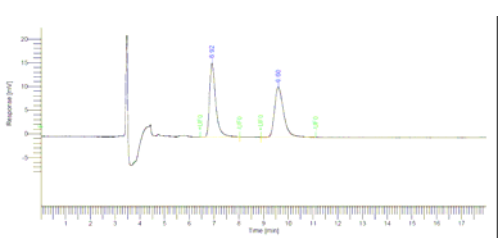

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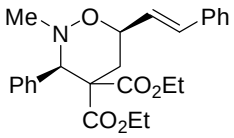

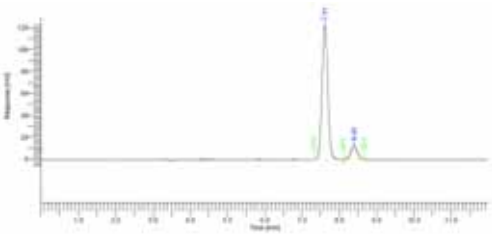

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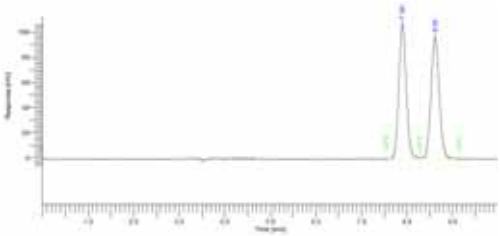

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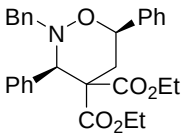

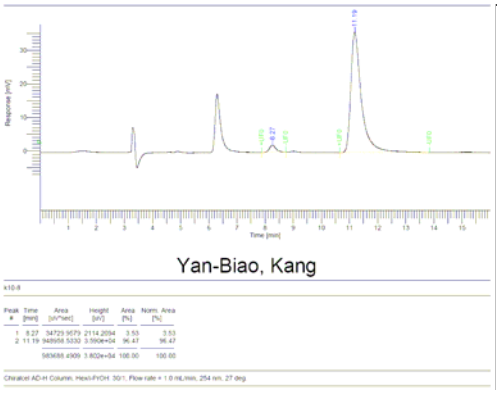
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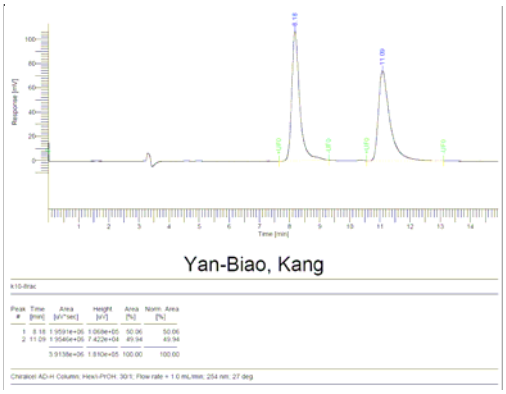
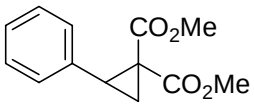

Yan-Biao, Kang


CO2Me
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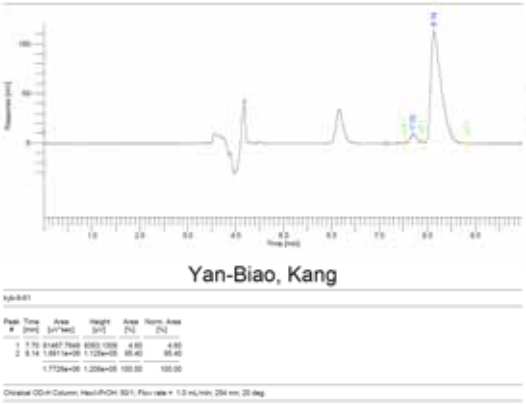
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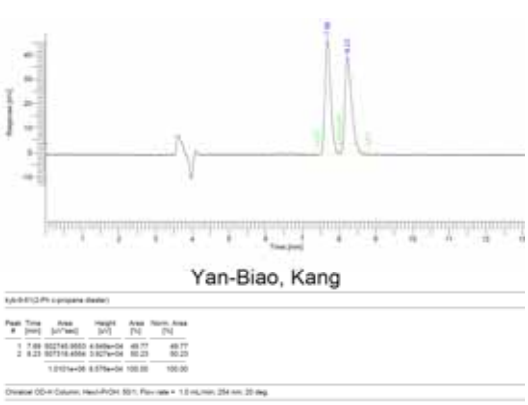
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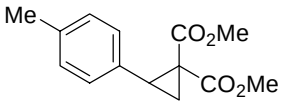
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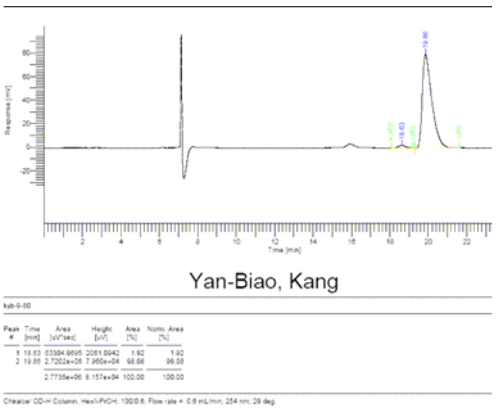
CO2Me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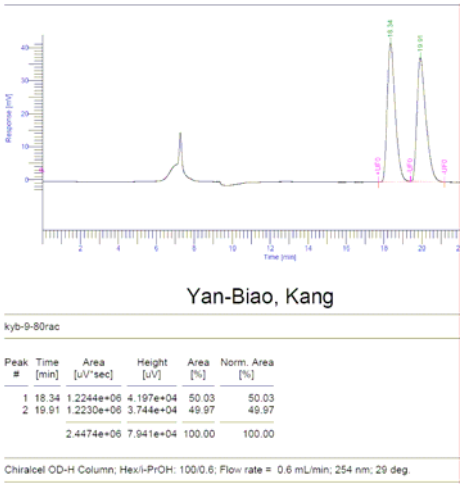
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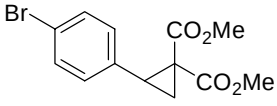
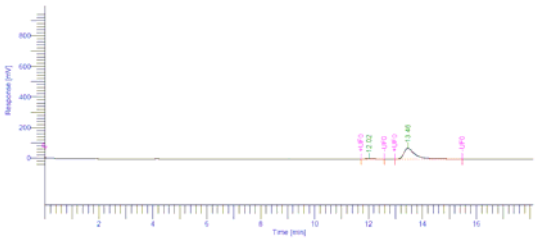
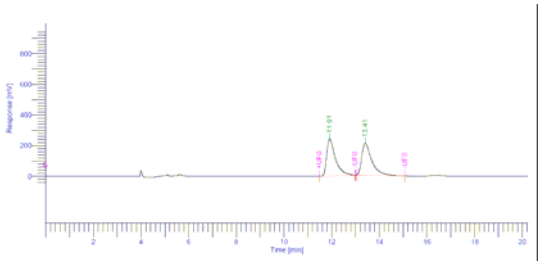
kyb-9-80rac
Peak # Time [min] Area [uV*sec] Height [uV] Area [%] Norm. Area [%]
1 18.34 1.2244e+06 4.197e+04 50.03 50.03
2 19.91 1.2230e+06 3.744e+04 49.97 49.97
2.4474e+06 7.941e+04 100.00 100.00
Chiralcel OD-H Column; Hex/i-PrOH: 100/0.6; Flow rate = 0.6 mL/min; 254 nm; 29 deg.


Br
CO2Me
CO2Me



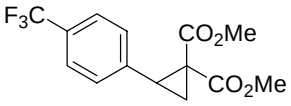
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	12.02	52688.7728	2468.9031	2.49	2.49
2	13.46	2.0603e+06	7.120e+04	97.51	97.51
		2.1129e+06	7.367e+04	100.00	100.00

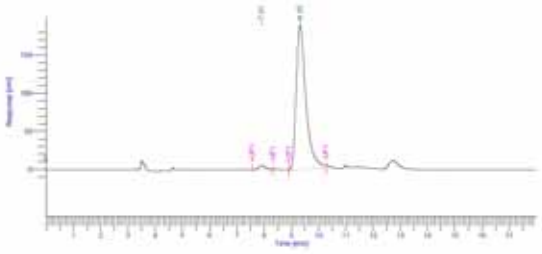
kyb-11-30cp: Chiralcel AD-H Column; Hex/i-PrOH:50/1; Flow rate = 0.8 mL/min; 254 nm; 25 deg.



Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	11.91	6.1334e+06	2.409e+05	49.95	49.95
2	13.41	6.1468e+06	2.096e+05	50.05	50.05
		1.2280e+07	4.505e+05	100.00	100.00

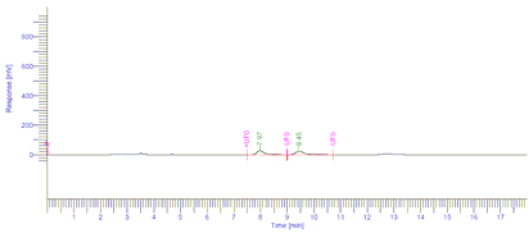
kyb-11-30cp: Chiralcel AD-H Column; Hex/i-PrOH:50/1; Flow rate = 0.8 mL/min; 254 nm; 25 deg.





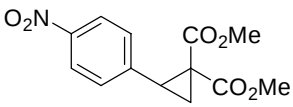
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	7.91	87894.0226	4968.2338	1.82	1.82
2	8.32	4.7307e+06	1.896e+05	98.18	98.18
		4.8186e+06	1.946e+05	100.00	100.00

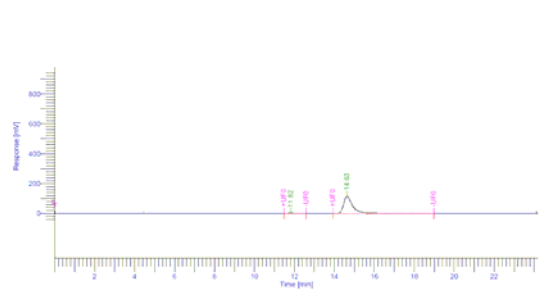
kyb-11-57cp: Chiralcel AD-H Column; Hex/i-PrOH:50/1; Flow rate = 0.8 mL/min; 254 nm; 25 deg.



Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	7.97	558364.1501	2.769e+04	50.42	50.42
2	9.45	549164.8655	2.299e+04	49.58	49.58
		1.1075e+06	5.068e+04	100.00	100.00

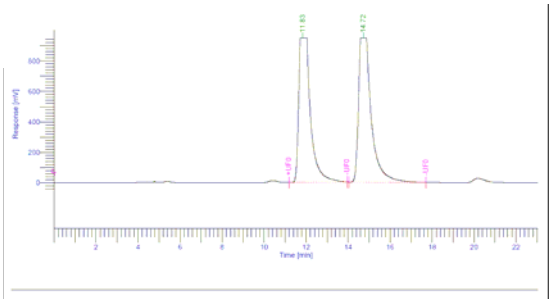
kyb-11-57cp-rac: Chiralcel AD-H Column; Hex/i-PrOH:50/1; Flow rate = 0.8 mL/min; 238 nm; 25 deg.





Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	11.82	49868.4987	2369.9022	1.31	1.31
2	14.63	3.7483e+06	1.162e+05	98.69	98.69
		3.7961e+06	1.185e+05	100.00	100.00

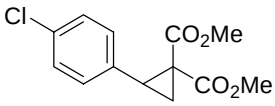
kyb-11-56cp: Chiralcel AD-H Column; Hex/i-PrOH:90/10; Flow rate = 0.7 mL/min; 254 nm; 25 deg.

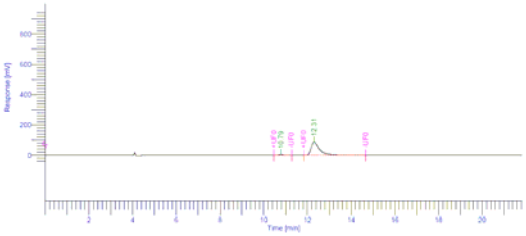


Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	11.83	4.3186e+07	1.488e+06	49.99	49.99
2	14.72	4.3207e+07	1.226e+06	50.01	50.01
		8.6393e+07	2.714e+06	100.00	100.00

Warning -- Signal level out-of-range in peak

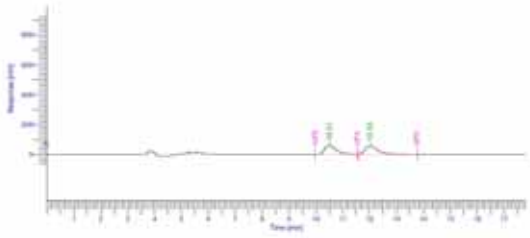
kyb-11-56cp-rac: Chiralcel AD-H Column; Hex/i-PrOH:90/10; Flow rate = 0.7 mL/min; 254 nm; 25 deg.





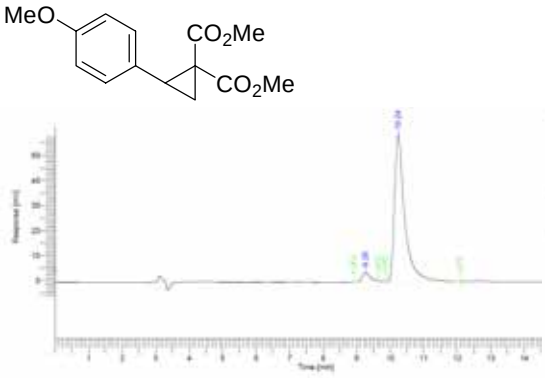
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	10.79	75681.1503	3900.5453	3.09	3.09
2	12.31	2.3735e+06	8.646e+04	96.91	96.91
		2.4492e+06	9.036e+04	100.00	100.00

kyb-11-29cp: Chiralcel AD-H Column; Hex/i-PrOH:50/1; Flow rate = 0.8 mL/min; 254 nm; 25 deg.



Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]
1	10.51	1.7520e+06	5.974e+04	49.79	49.79
2	12.03	1.7664e+06	5.447e+04	50.21	50.21
		3.5184e+06	1.142e+05	100.00	100.00

kyb-11-29cp-rac: Chiralcel AD-H Column; Hex/i-PrOH:50/1; Flow rate = 0.8 mL/min; 254 nm; 25 deg.



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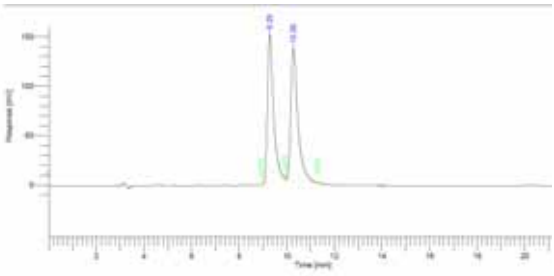

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