Highly Diastereo- and Enantioselective Homoenolate Additions to Nitrones Catalyzed by *N*-Heterocyclic Carbenes

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Supporting Information

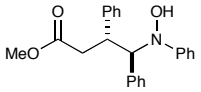
General Information

All reactions were carried out under a nitrogen atmosphere in flame-dried glassware with magnetic stirring. CH_2Cl_2 was purified by passage through a bed of activated alumina.[1] Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.[2] Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and ceric ammonium nitrate stain or potassium permangenate stain followed by heating. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Varian Inova 500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C-NMR spectra were recorded on a Varian Inova 500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). Mass spectra data were obtained on a Varian 1200 Quadrupole Mass Spectrometer and Micromass Quadro II Spectrometer.

All nitrones were prepared according to Fu.[3]

General Procedure for the Synthesis of Methyl Esters

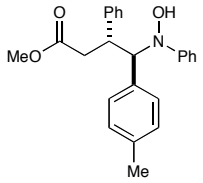
To an oven-dried 2-dram vial containing a magnetic stirring bar was added azolium salt **D** (19 mg, 0.04 mmol) and the corresponding nitrone (0.4 mmol) in a glove box. The heterogeneous mixture was diluted with CH_2Cl_2 (2 mL, 0.1 M). The flask was then cooled to 0 °C. To the flask was added the corresponding aldehyde (0.2 mmol) and Et_3N (6.1 μL, 0.04 mmol). The screw cap/septum was wrapped in parafilm and the vial was cooled to –25 °C. Upon consumption of the aldehyde (48 hr unless otherwise stated), the reaction was warmed to 0 °C and 0.2 mmol of NaOMe (1.0 M in MeOH) was added via syringe. After 1 min the reaction was diluted with diethyl ether and filtered through a pad of silica gel. The reaction mixture was concentrated and purified by flash column chromatography on silica gel with 10% diethyl ether in hexanes as an eluent to afford the corresponding methyl ester.



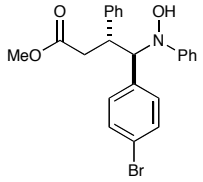
(3*R*, 4*R*)-methyl-4-(hydroxy(phenyl)amino)-3,4-diphenylbutanoate (5): Prepared according to general procedure using *trans*-cinnamaldehyde (25 μL, 0.2 mmol) and (*Z*)-*N*-benzylideneaniline oxide (80 mg, 0.4 mmol) to afford 51 mg (70%) of **5** as a yellow solid. Analytical data for **5**: IR (film) 3531, 3061, 3024, 2955, 2941, 1737, 1488, 1267 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.
2. Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals;* 3rd Ed., Pergamon Press, Oxford. 1988.
3. Lo, M. M. C.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 4572-4573.

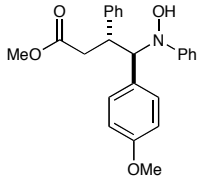
(d, *J* = 7.3 Hz, 2H), 7.37-7.34 (m, 2H), 7.28-7.21 (m, 6H), 7.08 (t, *J* = 7.8 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.80 (d, *J* = 7.3, 1H), 4.75 (s, 1H), 4.70 (d, *J* = 10.8 Hz, 1H), 4.21-4.17 (m, 1H), 3.46 (s, 3H), 2.50 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 151.7, 142.5, 136.1, 129.8, 128.9, 128.7, 128.6, 128.2 (x2), 127.2, 122.1, 117.6, 75.3, 51.8, 44.6, 39.2; LRMS (ES): Mass calcd for $C_{23}H_{23}NO_3$ $[M+H]^+$, 362. Found $[M+H]^+$, 362; Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 22.2, Rt_2 = 25.8).



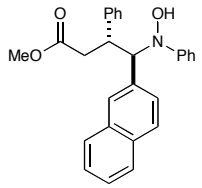
(3*R*, 4*R*)-methyl-4-(hydroxy(phenyl)amino)-3-phenyl-4-p-tolylbutanoate (6): Prepared according to general procedure using *trans*-cinnamaldehyde (25 μL, 0.2 mmol) and (*Z*)-*N*-(4-methylbenzylidene)aniline oxide (85 mg, 0.4 mmol) to afford 53 mg (71%) of **6** as a yellow solid. Analytical data for **6**: IR (film) 3539, 3053, 2984, 2955, 1733, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 2H), 7.35 (m, 2H), 7.24 (m, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.8 Hz, 2H), 7.02 (d, *J* = 7.3 Hz, 2H), 6.83 (d, *J* = 7.8 Hz, 2H), 6.79 (m, 1H), 4.69 (m, 2H), 4.16 (m, 1H), 3.45 (s, 3H), 2.49 (m, 2H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 151.7, 142.6, 137.6, 132.9, 129.6, 128.9, 128.5, 128.3, 128.1, 127.1, 121.9, 117.4, 47.8, 51.7, 44.6, 39.2, 21.3; LRMS (ES): Mass calcd for $C_{24}H_{25}NO_3$ $[M+H]^+$, 376. Found $[M+H]^+$, 376; Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 19.1, Rt_2 = 31.7).



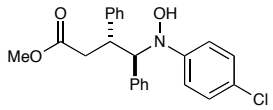
(3*R*, 4*R*)-methyl-4-(4-bromophenyl)-4-(hydroxy(phenyl)amino)-3-phenylbutanoate (7): Prepared according to general procedure using *trans*-cinnamaldehyde (25 μL, 0.2 mmol) and (*Z*)-*N*-(4-bromobenzylidene)aniline oxide (111 mg, 0.4 mmol) to afford 62 mg (68%) of **7** as a yellow solid. Analytical data for **7**: IR (film) 3531, 3049, 2988, 2951, 2310, 1729, 1492, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.33 (m, 6H), 7.27 (m, 1H), 7.15 (d, *J* = 8.3 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 2H), 6.83-6.82 (m, 3H), 4.80 (s, 1H), 4.67 (d, *J* = 10.8 Hz, 1H), 4.15-4.10 (m, 1H), 3.47 (s, 3H), 2.49-2.47 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 151.5, 142.2, 135.2, 131.5, 131.4, 129.4, 129.0, 128.7, 128.1, 127.3, 122.2, 117.7, 74.8, 51.9, 44.6, 39.1; LRMS (ES): Mass calcd for $C_{23}H_{22}BrNO_3$ $[M]^+$, 439. Found $[M]^+$, 439; Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 17.1, Rt_2 = 27.1).



(3*R*, 4*R*)-methyl-4-(hydroxy(phenyl)amino)-4-(4-methoxyphenyl)-3-phenylbutanoate (8): Prepared according to general procedure using *trans*-cinnamaldehyde (25 μL, 0.2 mmol) and (*Z*)-*N*-(4-methoxybenzylidene)aniline oxide (91 mg, 0.4 mmol) to afford 49 mg (62%) of **8** as a yellow solid. Analytical data for **8**: IR (film) 3435, 3062, 2953, 2838, 1734, 1598, 1357 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.3 Hz, 2H), 7.35 (m, 2H), 7.25 (m, H), 7.19 (d, *J* = 8.8 Hz, 2H), 7.09 (t, *J* = 7.8 Hz, 2H), 6.84-6.80 (m, 3H), 6.75 (d, *J* = 7.8 Hz, 2H), 4.71 (s, 1H), 4.66 (d, *J* = 10.4 Hz, 1H), 4.15 (m, 1H), 3.75 (s, 3H), 3.46 (s, 3H), 2.51 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 159.3, 151.9, 142.7, 130.9, 128.9, 128.6, 128.4, 128.2, 127.1, 122.0, 117.6, 113.6, 74.7, 55.4, 51.8, 44.8, 39.3; LRMS (ES): Mass calcd for $C_{24}H_{25}NO_4$ $[M-1]^+$, 390. Found $[M-1]^+$, 390; Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 27.7, Rt_2 = 40.6).

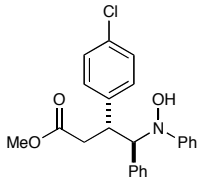


(3*R*, 4*R*)-methyl-4-(hydroxy(phenyl)amino)-4-(naphthalene-2-yl)-3-phenylbutanoate (9): Prepared according to general procedure using *trans*-cinnamaldehyde (25 μL, 0.2 mmol) and (*Z*)-*N*-(naphthalene-2-ylmethylene)aniline oxide (99 mg, 0.4 mmol) to afford 57 mg (69%) of **9** as a yellow solid. Analytical data for **9**: IR (film) 3408, 3059, 3030, 2952, 2927, 1734, 1597, 1265 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78-7.69 (m, 4H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.47-7.42 (m, 4H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.28-7.26 (m, 1H), 7.05 (t, *J* = 7.8 Hz, 2H), 6.87 (d, *J* = 7.8 Hz, 2H), 6.76 (t, *J* = 6.8 Hz, 1H), 4.90 (d, *J* = 10.7 Hz, 1H), 4.84 (s, 1H), 4.32-4.27 (m, 1H), 3.41 (s, 3H), 2.53-2.51 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 151.7, 142.6, 134.0, 133.3, 129.0 (x2), 128.7 (x2), 128.3 (x2), 127.8 (x2), 127.2 (x2), 126.2, 122.1 (x2), 117.6, 75.3, 51.8, 44.8, 39.3; LRMS (ES): Mass calcd for $C_{27}H_{25}NO_3$ $[M+1]^+$, 412. Found $[M+1]^+$, 412; Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 27.2, Rt_2 = 35.3).

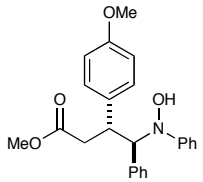


(3*R*, 4*R*)-methyl 4-((4-chlorophenyl)(hydroxy)amino)-3,4-diphenylbutanoate (10): Prepared according to general procedure using *trans*-cinnamaldehyde (25 μL, 0.2 mmol) and (*Z*)-*N*-benzylidene-4-chloroaniline oxide (93 mg, 0.4 mmol) to afford 64 mg (80%) of **10** as a pale yellow solid. Analytical data for **10**: IR (film) 3409, 3037, 2951, 1733, 1488 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42-7.35 (m, 4H), 7.29-7.25 (m, 6H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 4.83 (s, 1H), 4.65 (d, *J* = 10.7 Hz, 1H), 4.18 (m, 1H), 3.47 (s, 3H), 2.50 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 150.3, 142.3, 135.8, 129.7, 129.0, 128.5, 128.3 (x2), 128.1, 127.8, 127.2, 118.9, 75.4, 51.8, 44.6, 39.2; LRMS (ES): Mass calcd for $C_{23}H_{22}ClNO_3$

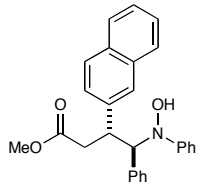
$[M+H]^+$, 396. Found $[M+H]^+$, 396; Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 20.8, Rt_2 = 27.8).



(3*R*, 4*R*)-methyl 3-(4-chlorophenyl)-4-(hydroxy(phenyl)amino)-4-phenylbutanoate (11): Prepared according to general procedure using *(E)*-3-(4-chlorophenyl)prop-2-enal (33 mg, 0.2 mmol) and (*Z*)-*N*-benzylideneaniline oxide (80 mg, 0.4 mmol) to afford 62 mg (78%) of **11** as a yellow solid. Analytical data for **11**: IR (film) 3417, 3061, 3030, 2952, 1734, 1595, 1490 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (m, 4H), 7.26 (m, 6H), 7.10 (t, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 4.70 (s, 1H), 4.66 (d, *J* = 10.8 Hz, 1H), 4.20 (td, *J* = 10.3, 4.9 Hz, 1H), 3.50 (s, 3H), 2.50 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 151.5, 141.0, 135.6 132.8, 129.7, 129.6, 129.1 (x2), 128.7, 128.3, 122.4, 117.7, 75.4, 51.9, 43.9, 38.9; LRMS (ES): Mass calcd for $C_{23}H_{22}ClNO_3$ $[M+H]^+$, 396. Found $[M+H]^+$, 396; Enantiomeric ratio was measured by HPLC (Chiralcel OD-H, 95:4:1 Hexanes:IPA:EtOH, 1 mL/min, Rt_1 = 10.8, Rt_2 = 12.9).

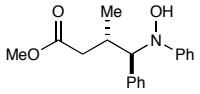


(3*R*, 4*R*)-methyl 4-(hydroxy(phenyl)amino)-3-(4-methoxyphenyl)-4-phenylbutanoate (12): Prepared according to general procedure using *(E)*-3-(4-methoxyphenyl)prop-2-enal (32 mg, 0.2 mmol) and (*Z*)-*N*-benzylideneaniline oxide (80 mg, 0.4 mmol) to afford 56 mg (72%) of **12** as a yellow solid. Analytical data for **12**: IR (film) 3422, 3113, 2953, 2837, 1732, 1512, 1250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2H), 7.28-7.25 (m, 2H), 7.21 (d, *J* = 5.4 Hz, 3H), 7.08 (t, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 4.76 (s, 1H), 4.76 (d, *J* = 10.7 Hz, 1H), 4.13 (td, *J* = 9.8, 5.4 Hz, 1H), 3.80 (s, 3H), 3.47 (s, 3H), 2.48-2.45 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 158.6, 151.6, 136.2, 134.3, 129.7, 129.0, 128.5, 128.2 (x2), 122.0, 117.5, 114.3, 75.2, 55.4, 51.8, 43.8, 39.3; LRMS (ES): Mass calcd for $C_{24}H_{25}NO_4$ $[M]^+$, 391. Found $[M]^+$, 391; Enantiomeric ratio was measured by HPLC (Chiralcel OD-H, 95:4:1 Hexanes:IPA:EtOH, 1 mL/min, Rt_1 = 12.8, Rt_2 = 16.6).

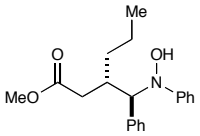


(3*R*, 4*R*)-methyl 4-(hydroxy(phenyl)amino)-3-(naphthalen-2-yl)-4-phenylbutanoate (13): Prepared according to general procedure using *(E)*-3-(naphthalene-2-yl)prop-2-enal (36 mg, 0.2 mmol) and (*Z*)-*N*-benzylideneaniline oxide (80 mg, 0.4 mmol) to afford 60 mg (73%) of **13** as a yellow solid. Analytical data for **13**: IR (film) 3415, 3057, 2952, 1732, 1597, 1265 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.90–7.83 (m, 4H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.48 (m, 2H), 7.34 (m,

2H), 7.26-7.23 (m, 3H), 7.08 (t, *J* = 7.5 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 4.84 (d, *J* = 10.8 Hz, 1H), 4.79 (s, 1H), 4.39 (m, 1H), 3.44 (s, 3H), 2.62-2.57 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 151.6, 140.1, 136.0, 133.9, 132.9, 130.2, 129.8, 128.7, 128.6, 128.3, 128.2, 127.9, 127.3, 126.3, 125.9, 122.1, 117.6, 75.2, 51.8, 44.9, 39.1; LRMS (ES): Mass calcd for $C_{27}H_{25}NO_3$ $[M+1]^+$, 412.2. Found $[M+1]^+$, 412.0; Enantiomeric ratio was measured by HPLC (Chiralcel OD-H, 95:4:1 Hexanes:IPA:EtOH, 0.25 mL/min, Rt_1 = 49.6, Rt_2 = 54.3).

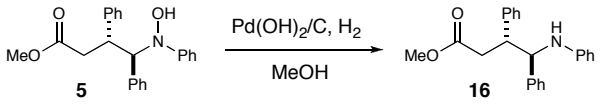


(3*S*, 4*R*)-methyl 4-(hydroxy(phenyl)amino)-3-methyl-4-phenylbutanoate (14): Prepared with DBU (6.6 μL, 0.04 mmol) instead of Et_3N using *trans*-crotonaldehyde (17 μL, 0.2 mmol) and (*Z*)-*N*-benzylideneaniline oxide (80 mg, 0.4 mmol) to afford 43 mg (72%) of **14** as a yellow solid. Analytical data for **14**: IR (film) 3442, 3062, 2952, 1735, 1437, 1174 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.15 (m, 7H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.89 (t, *J* = 7.4 Hz, 1H), 4.99 (s, 1H), 4.21 (d, *J* = 9.8 Hz, 1H), 3.64 (s, 3H), 3.03 (m, 1H), 2.31 (dd, *J* = 15.7, 4.4 Hz, 1H), 2.01 (dd, *J* = 15.6, 8.8 Hz, 1H), 1.25 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 152.1, 136.2, 129.8, 128.7, 128.1, 127.9, 122.4, 118.2, 76.1, 51.9, 38.8, 32.1, 18.4; LRMS (ES): Mass calcd for $C_{18}H_{21}NO_3$ $[M+H]^+$, 298. Found $[M+H]^+$, 298. Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 14.0, Rt_2 = 17.7).

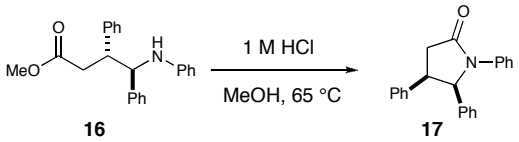


(S)-methyl 3-((R)-(hydroxy(phenyl)amino)(phenyl)methylhexanoate (15): Prepared with DBU (6.6 μL, 0.04 mmol) instead of Et_3N using *trans*-2-hexen-1-al (23 μL, 0.2 mmol) and (*Z*)-*N*-benzylideneaniline oxide (80 mg, 0.4 mmol) to afford 41 mg (64%) of **15** as a yellow solid. Analytical data for **15**: IR (film) 3441, 3061, 3029, 2957, 2870, 1717, 1595, 1168 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.14 (m 7H), 6.99 (d, *J* = 7.8 Hz, 2H), 6.90 (t, *J* = 7.3 Hz, 1H), 5.20 (s, 1H), 4.42 (d, *J* = 8.8 Hz, 1H), 3.64 (s, 3H), 2.96 (bs, 1H), 2.33 (dd, *J* = 15.7, 5.4 Hz, 1H), 2.14 (dd, *J* = 15.6, 6.8 Hz, 1H), 1.73 (m, 1H), 1.51-1.44 (m, 3H), 0.96 (t, *J* = 6.3 Hz, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 151.8, 136.3, 129.9, 128.7, 128.0, 127.8, 122.9, 119.0, 74.1, 51.9, 36.6, 35.6, 34.1, 20.0, 14.9; LRMS (ES): Mass calcd for $C_{20}H_{25}NO_3$ $[M–H]^+$, 326. Found $[M–H]^+$, 326. Enantiomeric ratio was measured by HPLC (Chiralcel AD-H, 5% IPA/Hexanes, 1 mL/min, Rt_1 = 16.6, Rt_2 = 20.6).

Procedure for Synthesis of γ-Lactam



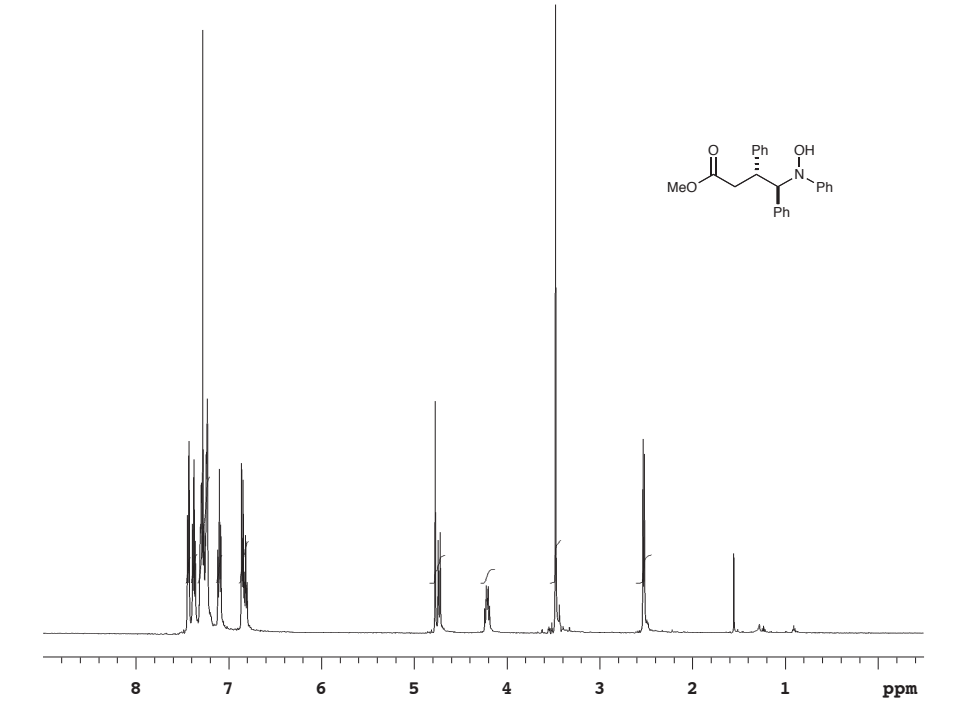
To a flame dried 10 mL round bottom flask equipped with magnetic stirring bar was added **5** (35 mg, 0.1 mmol). The solid was diluted with MeOH (1 mL, 0.1 M). The flask was purged with nitrogen gas. $Pd(OH)_2/C$ (5 mol %) was then added and the flask was purged with nitrogen for a second time. The flask was purged with hydrogen using a balloon and the reaction was then stirred under the hydrogen atmosphere for 30 min. The reaction mixture was then filtered through Celite with CH_2Cl_2 as an eluent and concentrated to afford 29 mg (82%) of **16** as a pale yellow solid. Spectroscopic data for **16** matched previously reported.[4] Compound **16** was judged by NMR spectroscopy to be >95% pure and thus used without further purification in the lactam forming reaction.

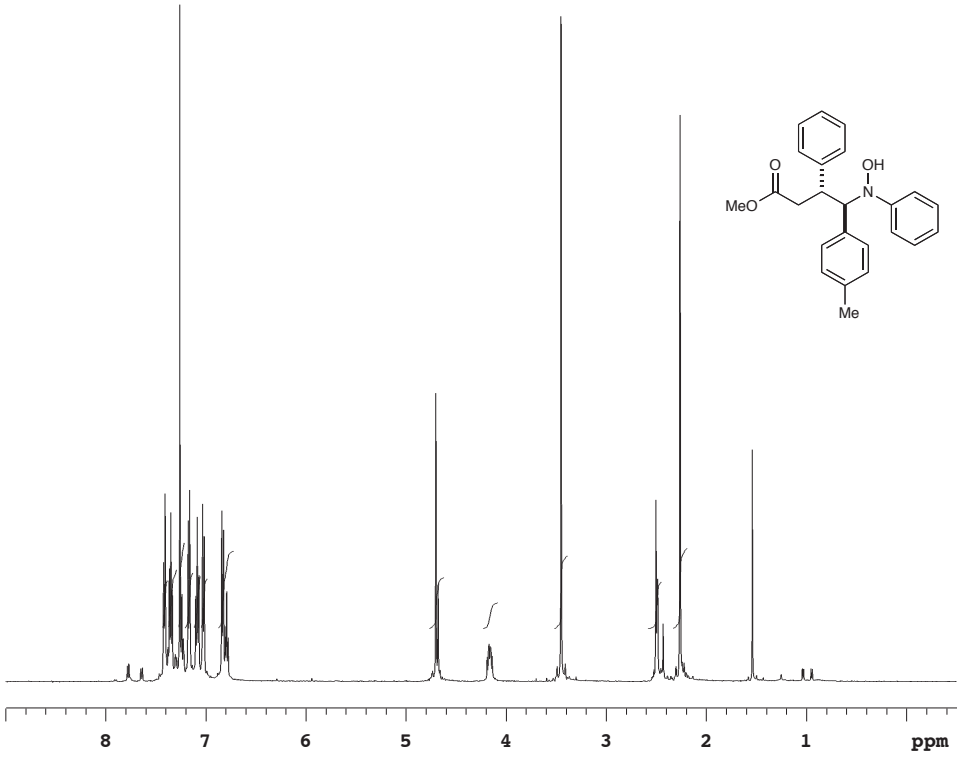


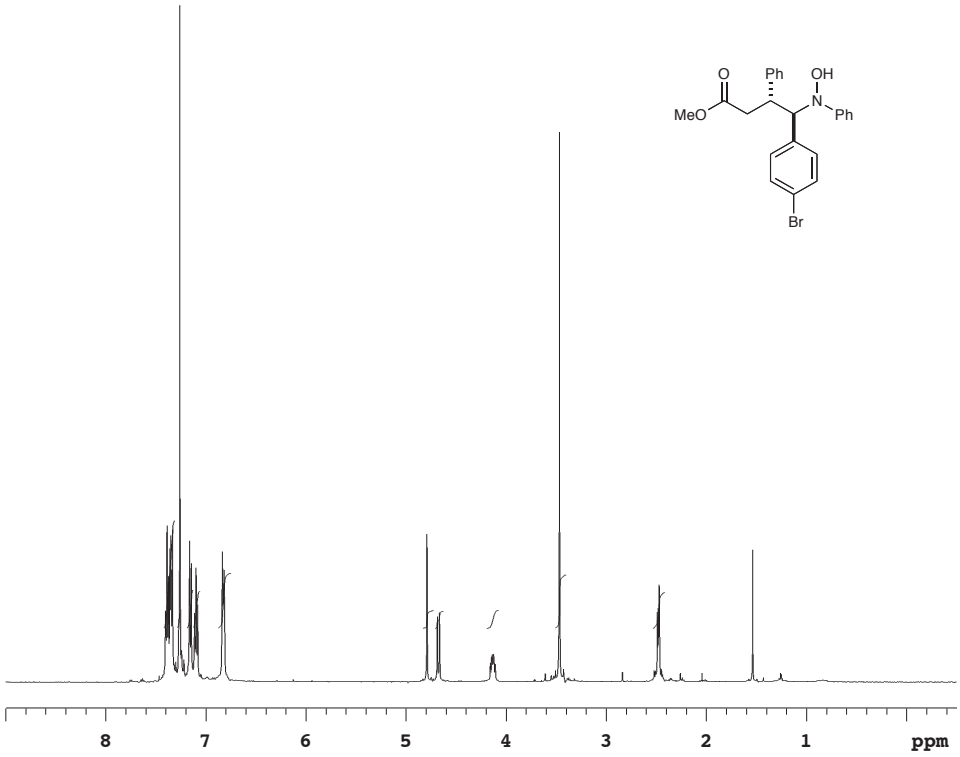
To a 10 mL round bottom flask equipped with magnetic stirring bar was added **16** (35 mg, 0.1 mmol). The solid was diluted with MeOH (1 mL, 0.1 M) and 1 M HCl (1 mL). The reaction was heated to 65 °C for 24 hours. The reaction was cooled to 23 °C and was diluted with diethyl ether and poured into a separatory funnel. The organic layer was washed with water and separated. The aqueous layer was extracted 2x with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated to afford 28 mg (88%) of lactam **17** which was judge to be pure by NMR spectroscopy. All spectroscopic data (1H and 13C NMR spectroscopy, mass spectrometry) for this lactam (**17**) matched previously reported.[5]

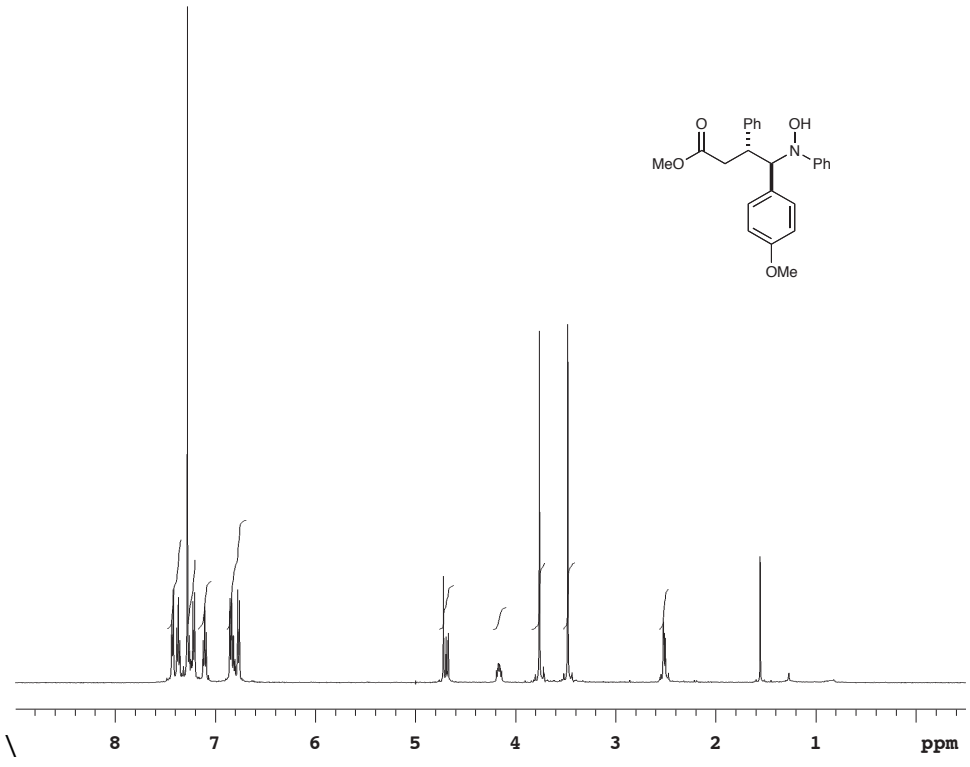
4. Alonso, E.; Ramon, D. J.; Yus, M. *Tetrahedron* **1997**, *53*, 2641-2652.
5. Katritzky, A. R.; Feng, D. M.; Lang, H. Y. *J. Org. Chem.* **1997**, *62*, 706-714.

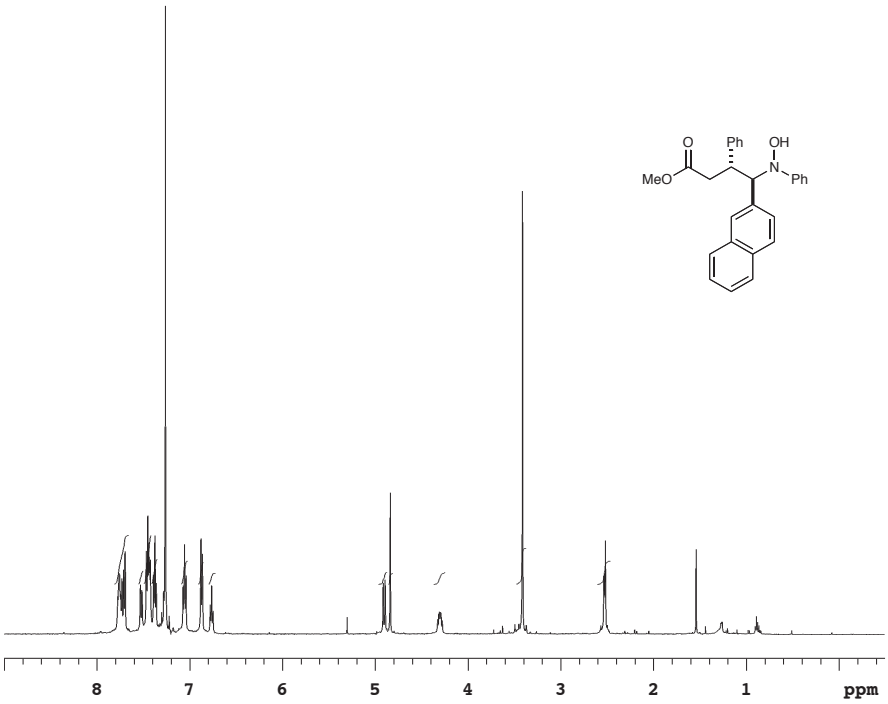
Selected NMR Spectra

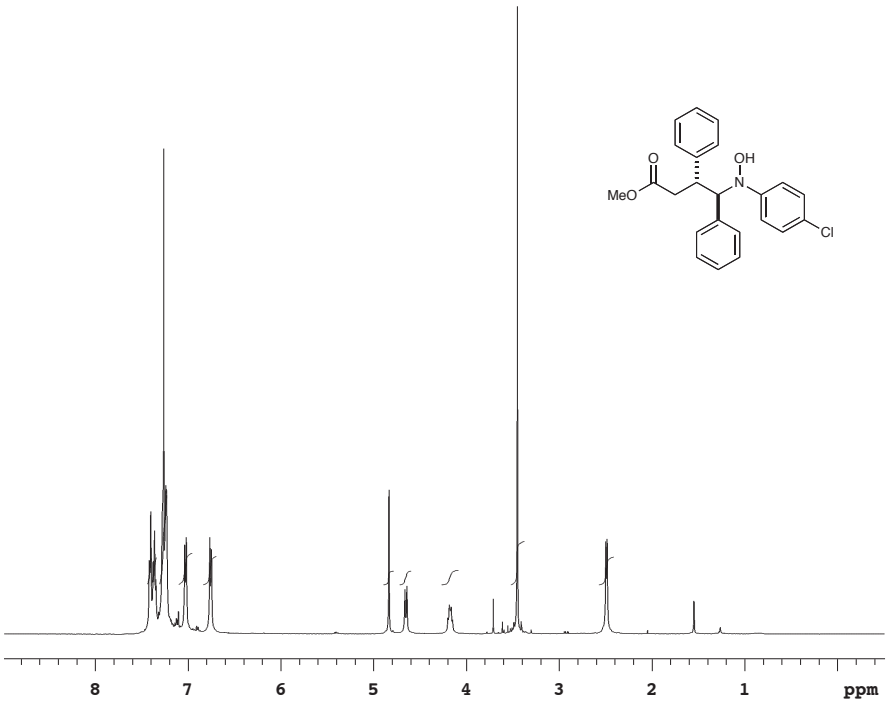





O
Ph
OH
MeO
N
Ph
Br
8
7
6
5
4
3
2
1
ppm


O
Ph
OH
MeO
N
Ph
OMe
8
7
6
5
4
3
2
1
ppm


O
Ph
OH
MeO
N
Ph
8
7
6
5
4
3
2
1
ppm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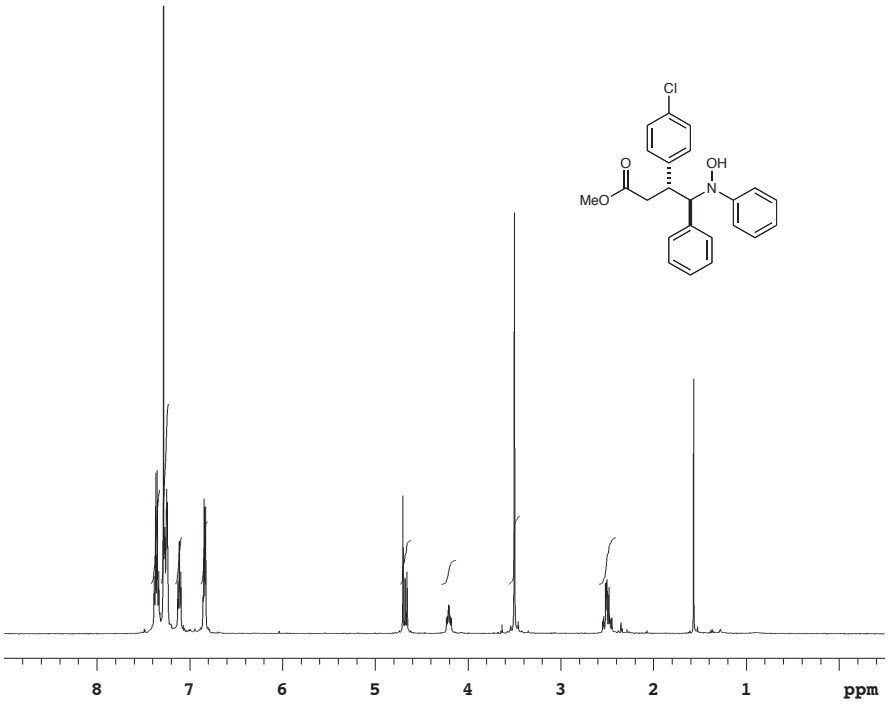
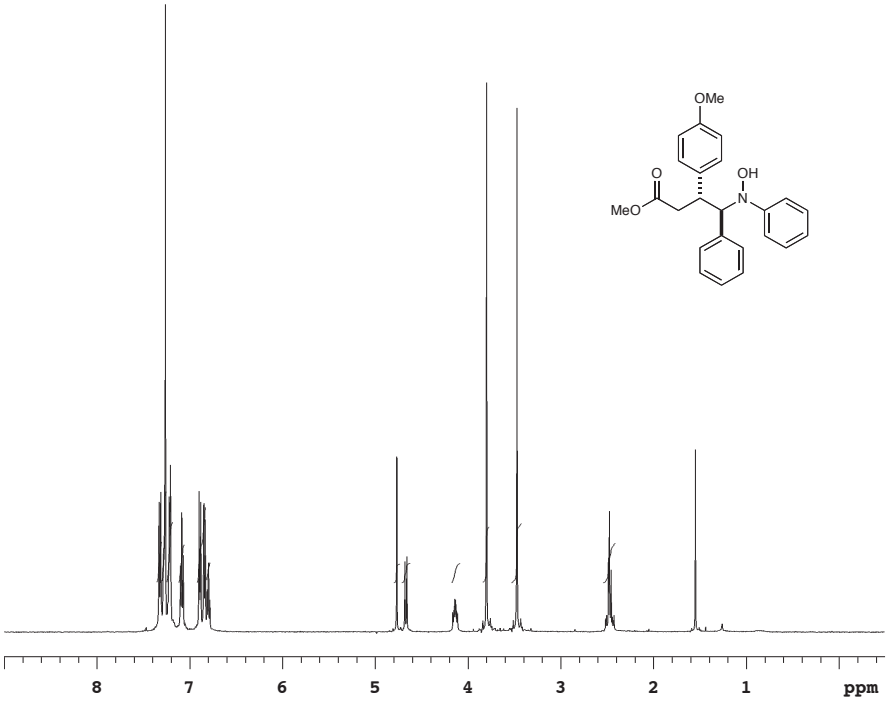
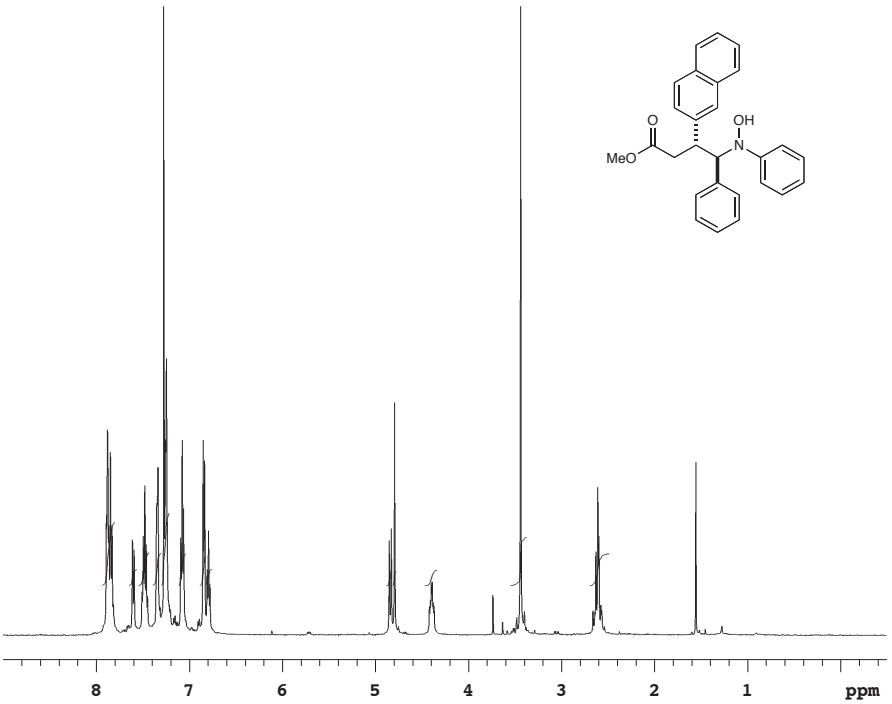
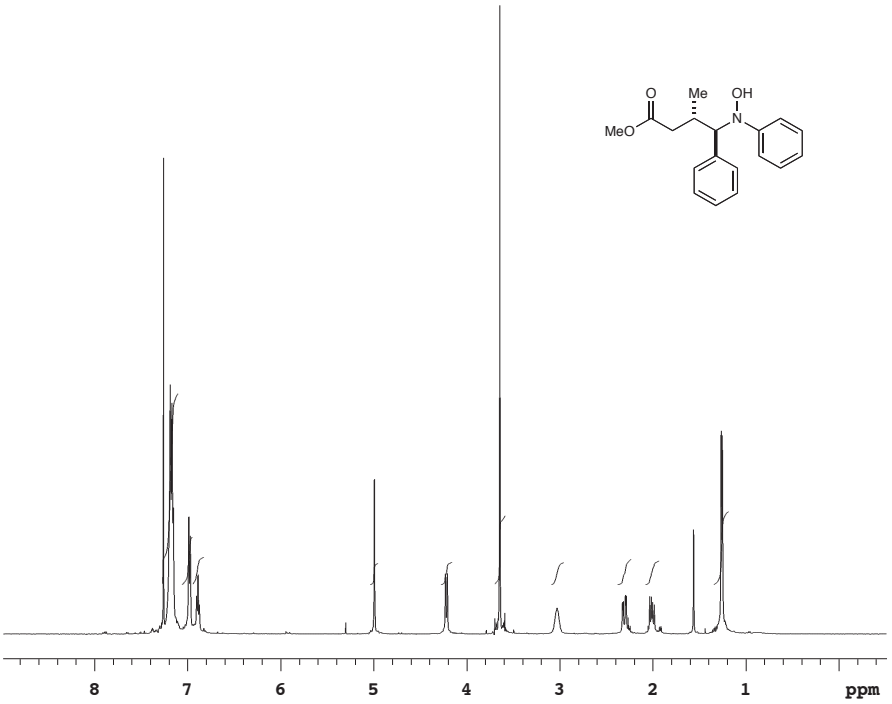
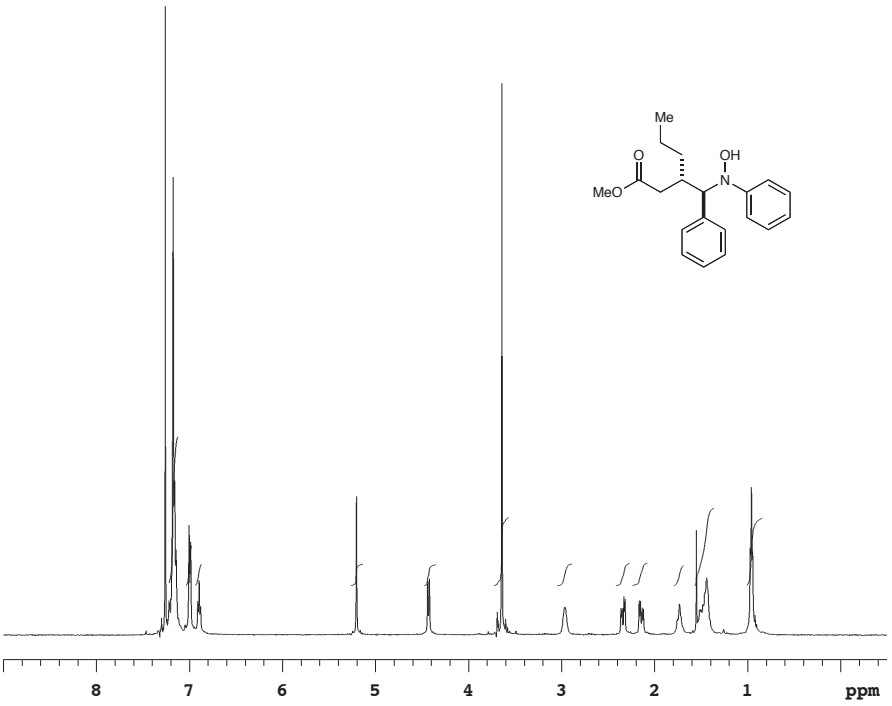
OH
MeO
N
Cl
8
7
6
5
4
3
2
1
ppm


Cl
O
MeO
OH
N
8
7
6
5
4
3
2
1
ppm


OMe
O
MeO
OH
N
8
7
6
5
4
3
2
1
ppm

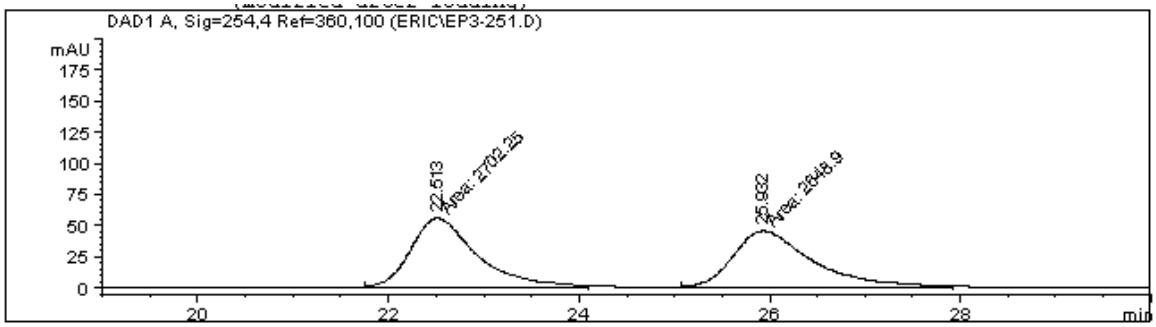

O
MeO
OH
N
8
7
6
5
4
3
2
1
ppm


O
Me
OH
MeO
N
8
7
6
5
4
3
2
1
ppm


Me
O
OH
MeO
N
8
7
6
5
4
3
2
1
ppm

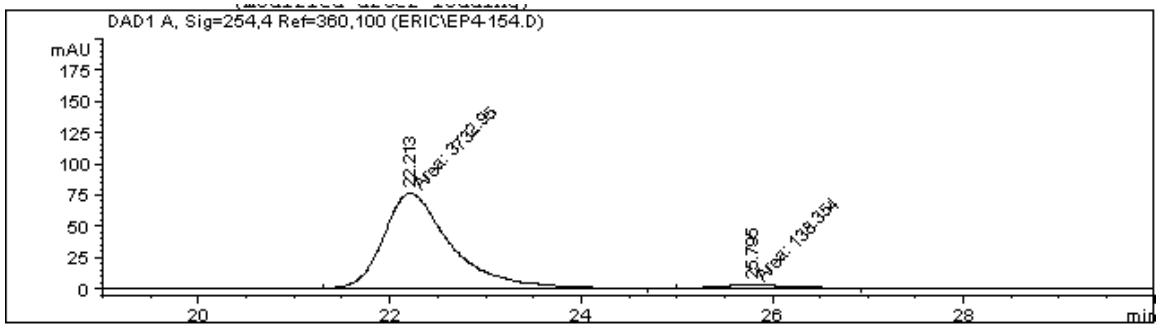
HPLC Traces of Racemic and Enantioenriched Compounds

Racemic 5



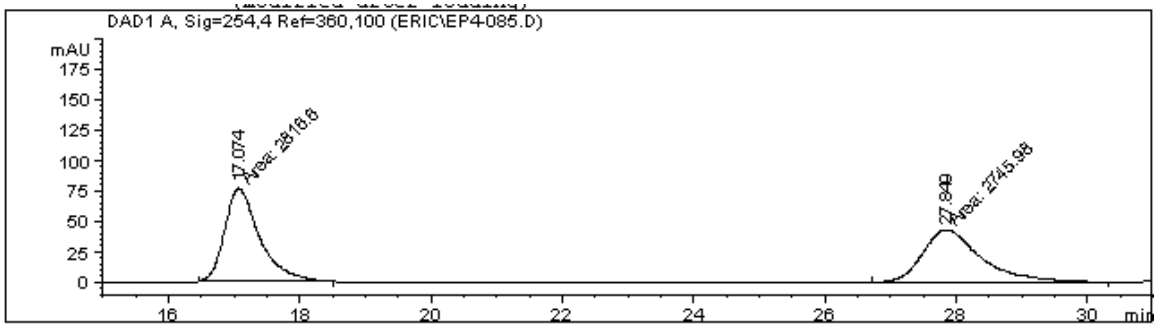

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.513 MM    0.8119 2702.24854   55.47131  50.4985
   2  25.932 MM    0.9774 2648.89551   45.16974  49.5015
```

Enantioenriched 5



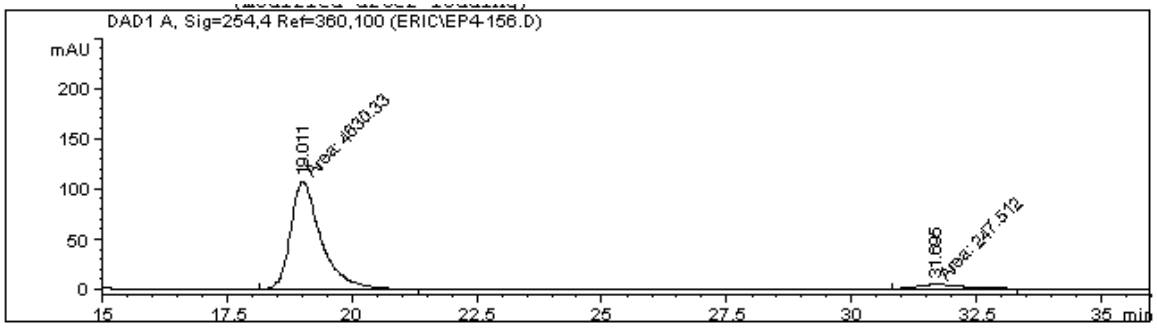

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.213 MM    0.8158 3732.95435   76.26228  96.4262
   2  25.795 MM    0.9413  138.35440    2.44983   3.5738
```

Racemic 6



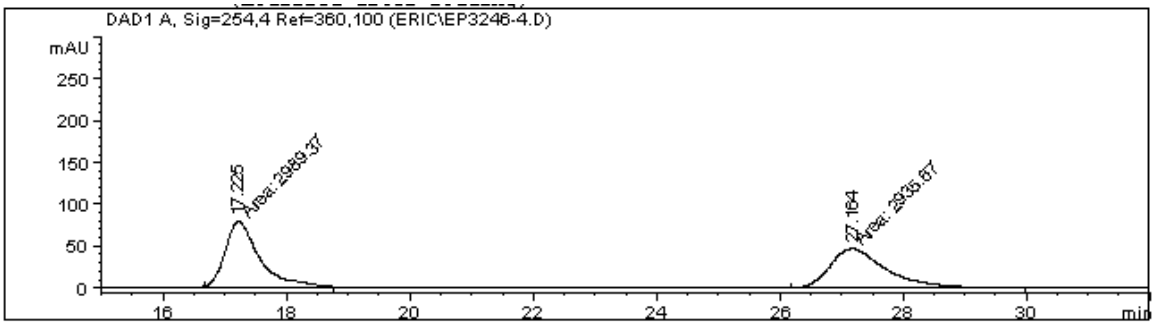

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.074 MM    0.6148 2816.60083   76.35253  50.6348
   2  27.849 MM    1.0579 2745.97705   43.26215  49.3652
```

Enantioenriched 6




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  19.011 MM    0.7165 4630.33301  107.70879  94.9258
   2  31.695 MM    1.0948  247.51207    3.76792   5.0742
```

Racemic 7

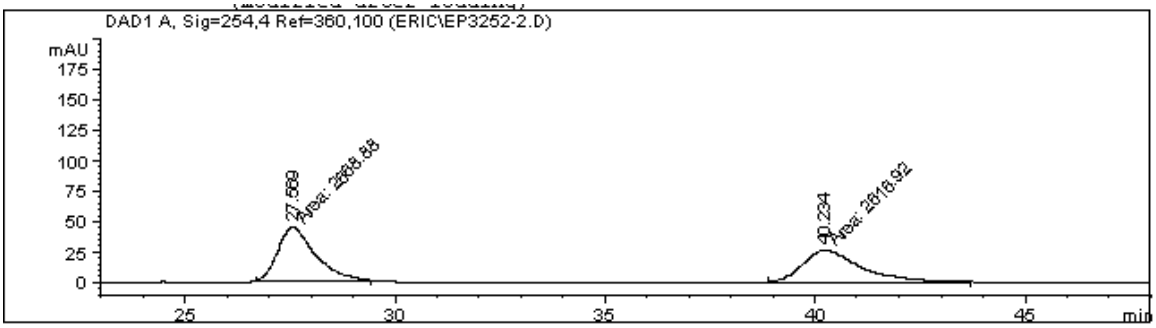



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.225 MM    0.6451 2989.36865   77.23407  50.4532
   2  27.164 MM    1.0591 2935.66797   46.19893  49.5468
```

Enantioenriched 7

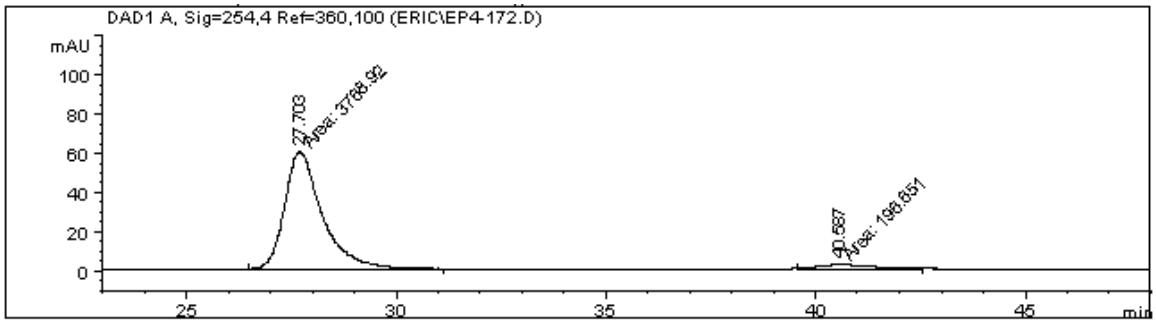

```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.117 MM    0.6429 5399.71631  139.98798  91.7762
   2  27.094 MM    0.8929  483.85028    9.03124   8.2238
```

Racemic 8



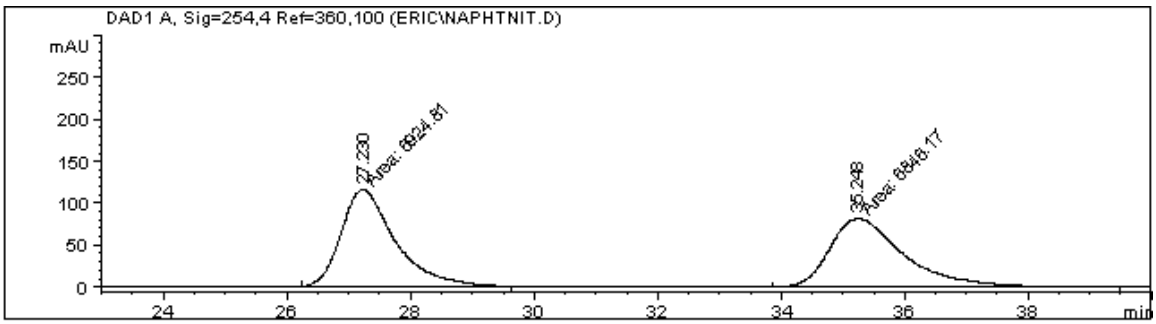

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  27.569 MM    1.0193 2668.88208   43.63824  50.4915
   2  40.234 MM    1.6582 2616.91870   26.30255  49.5085
```

Enantioenriched 8



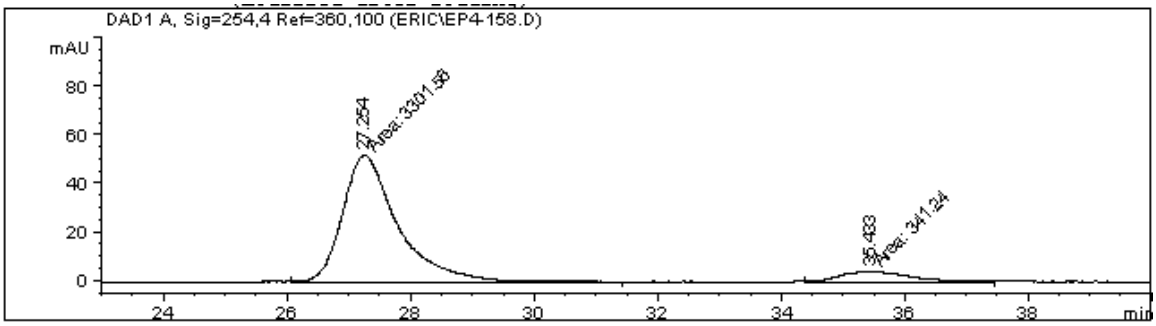

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  27.703 MM    1.0520 3768.91772   59.71017  95.0410
   2  40.587 MM    1.5997  196.65140    2.04883   4.9590
```

Racemic 9



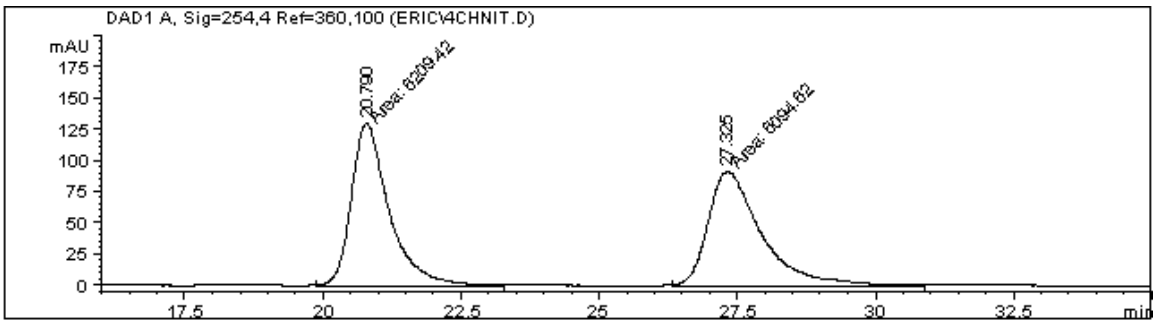

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  27.230 MM    1.0065 6924.81152  114.66558  50.2855
   2  35.248 MM    1.3962 6846.16553   81.72227  49.7145
```

Enantioenriched 9



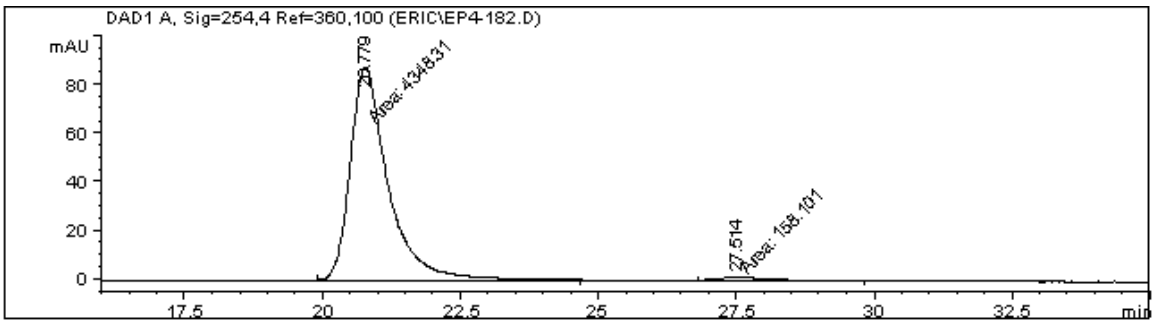

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  27.254 MM    1.0575 3301.56079   52.03489  90.6325
   2  35.433 MM    1.2843  341.24017    4.42826   9.3675
```

Racemic 10



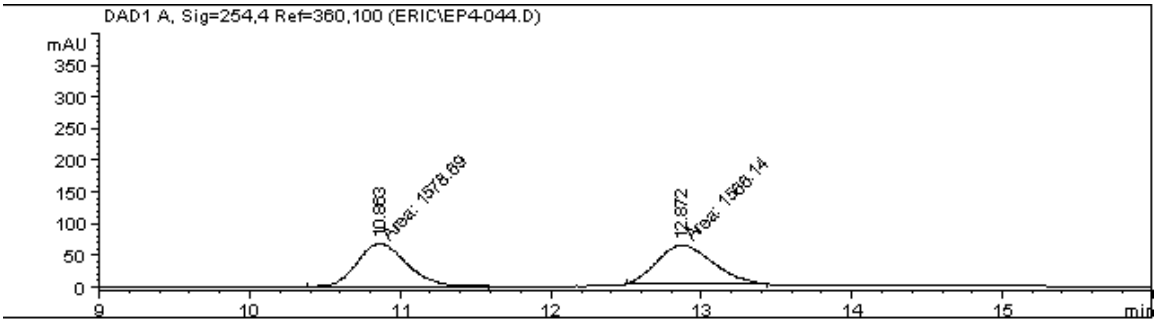

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  20.790 MM    0.7944 6209.42236  130.27071  50.4665
   2  27.325 MM    1.1132 6094.61914   91.25045  49.5335
```

Enantioenriched 10



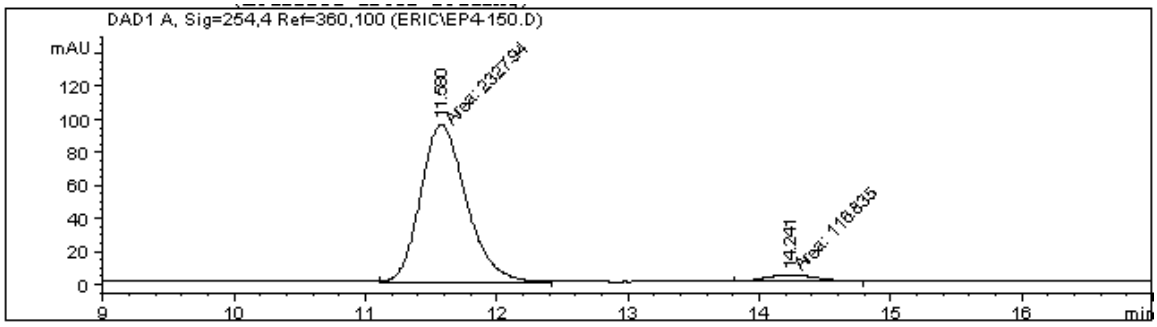

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  20.779 MM    0.8245 4348.31152   87.89635  96.4916
   2  27.514 MM    1.3539  158.10110    1.94631   3.5084
```

Racemic 11



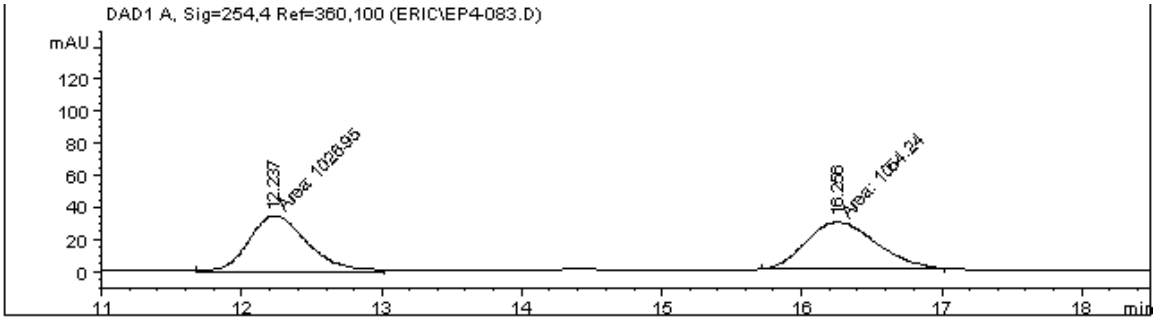

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.863 MM    0.3875 1578.69165   67.89874  50.1996
   2  12.872 MM    0.4313 1566.14038   60.52247  49.8004
```

Enantioenriched 11



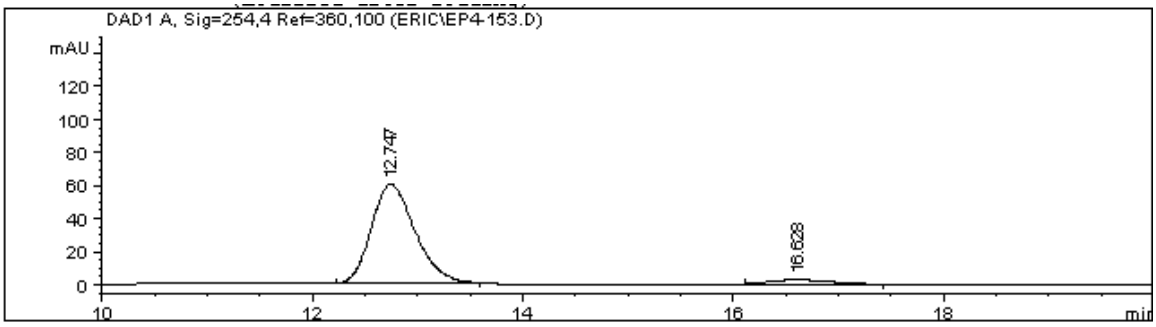

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.580 MM    0.4067 2327.94165   95.41018  95.2210
   2  14.241 MM    0.4849  116.83501    4.01568   4.7790
```

Racemic 12



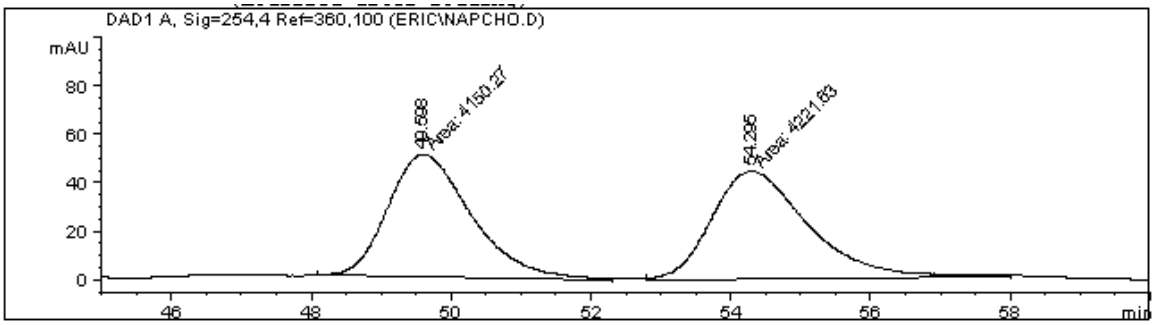

```
================================================================================
                           Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.237 MM    0.4858 1026.95142   35.23169  49.3443
   2  16.256 MM    0.5921 1054.24219   29.67536  50.6557
```

Enantioenriched 12



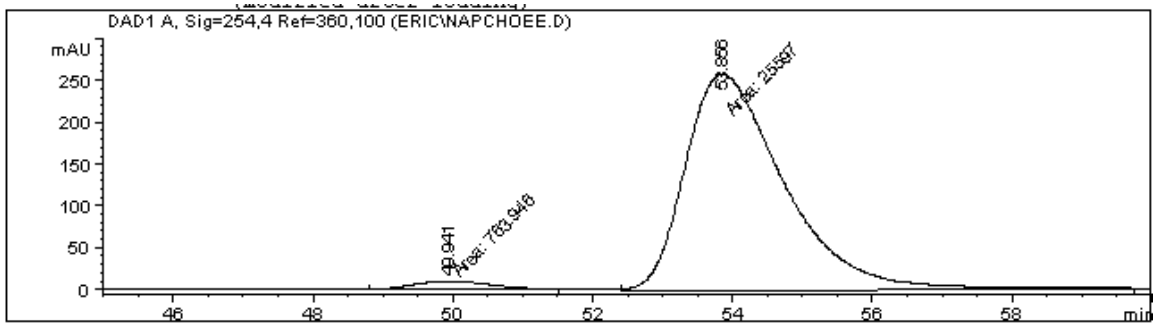

```
================================================================================
                           Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.747 BB    0.4459 1750.41040   60.07641  94.5692
   2  16.628 BB    0.4242  100.52006    2.84517   5.4308

Totals :                  1850.93046   62.92158
```

Racemic 13



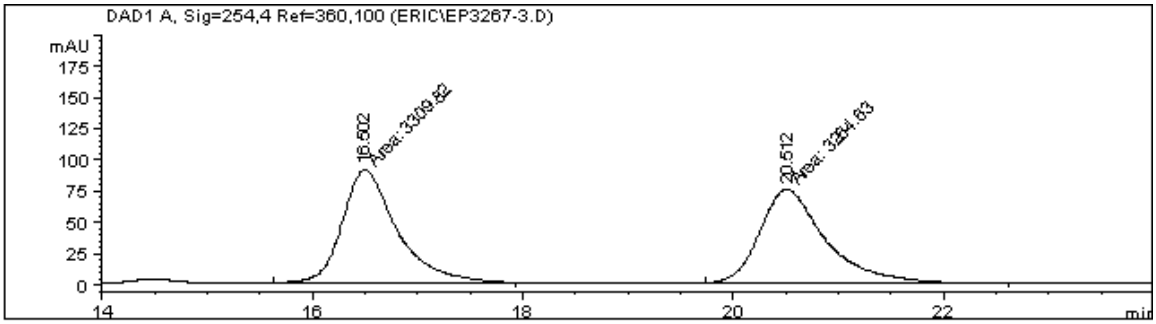

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  49.598 MM    1.3774 4150.26758   50.22043  49.5738
   2  54.295 MM    1.5997 4221.63428   43.98330  50.4262
```

Enantioenriched 13



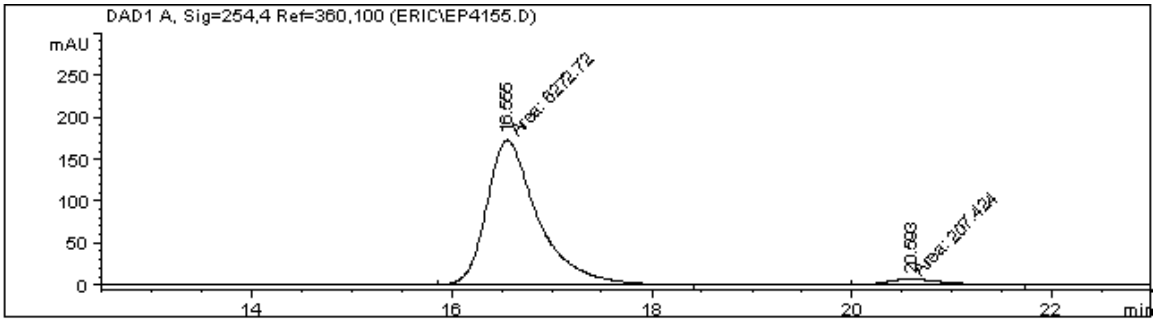

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  49.941 MM    1.3314  763.94629    9.56300   2.8980
   2  53.856 MM    1.6532 2.55970e4   258.05209  97.1020
```

Racemic 14



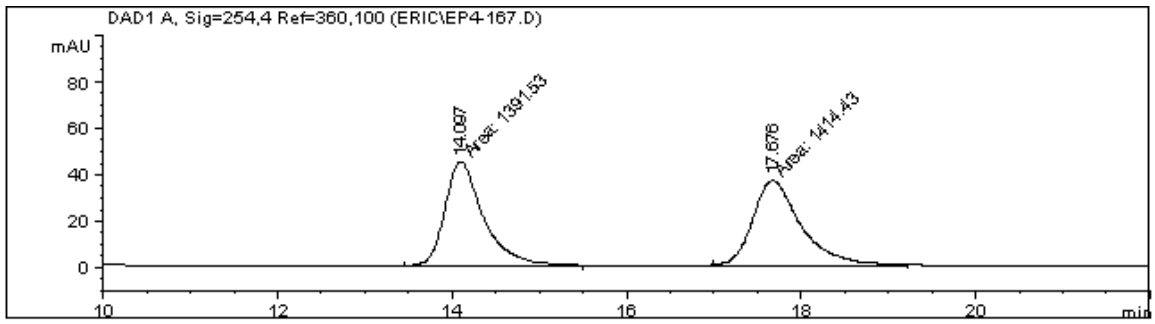

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.502 MM    0.6111 3309.81909   90.26875  50.3437
   2  20.512 MM    0.7298 3264.63086   74.55844  49.6563
```

Enantioenriched 14



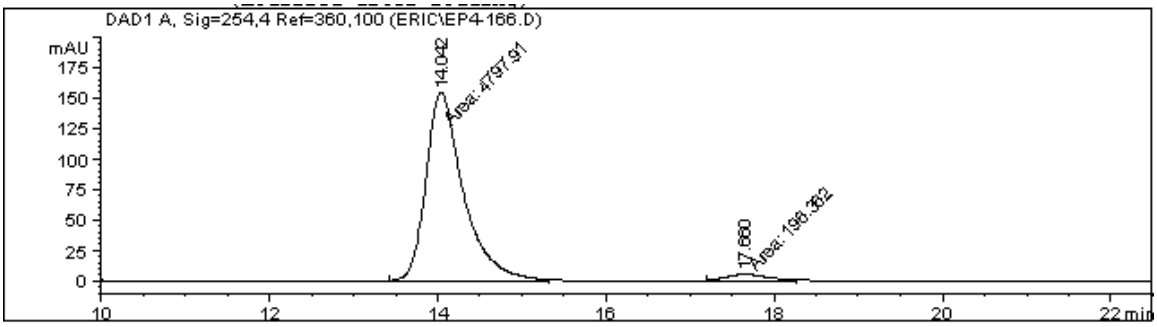

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.555 MM    0.6048 6272.71875  172.84526  96.7991
   2  20.593 MM    0.5948  207.42419    5.81236   3.2009
```

Racemic 15




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.097 MM    0.5147 1391.53296   45.05816  49.5921
   2  17.676 MM    0.6437 1414.42664   36.62404  50.4079
```

Enantioenriched 15




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.042 MM    0.5194 4797.91113  153.95663  96.0683
   2  17.660 MM    0.6248  196.36220    5.23771   3.9317
```

X-Ray Crystallography of 7

X-ray diffraction was performed at –120 °C and raw frame data were processed using SAINT. Molecular structure was solved using direct methods and refined by F2 by full-matrix least-squares techniques. The GOF = 0.975 for 261 variables refined to R1 = 0.0283 for 6844 reflections with I>2α(I). There was no absorption correction of Flack parameters. Further information is contained in the CIF file.