Asymmetric Brønsted Acid Catalyzed Carbonyl Activation – Organocatalytic Domino Electrocyclization-Halogenation Reaction

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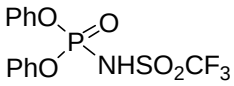
Supporting information

General: Unless otherwise noted, all commercially available compounds were used as provided without further purification. 2,4,4,6-Tetrabromo-2,5-cyclohexadiene-1-one (TBCHD) was recrystallized from hexane/CH_2Cl_2 mixture prior to use. Solvents for chromatography were technical grade and distilled prior to use. The chloroform used in reactions was reagent grade and distilled from CaH_2. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel Merck 60 (particle size 0.063-0.2 mm). Solvent mixtures are understood as volume/volume.
^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker AM 250 spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); coupling constants (*J*) are in Hertz (Hz). Mass spectra (MS-EI, 70 eV) were conducted on GC-MS Shimadzu QP2010 (column: Equity®-5, length × I.D. 30 m × 0.25 mm, d_f 0.25 µm, lot # 28089-U, Supelco). IR spectra were recorded on a Jasco FT/IR-420 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Optical rotations were measured on a Perkin Elmer 241 polarimeter. The enantiomeric excesses were determined by HPLC analysis using a chiral stationary phase column (column, Daicel Co. CHIRALCEL OD-H or CHIRALPAK AD-H; eluent: hexane/2-propanol). The chiral HPLC methods were calibrated with the corresponding racemic mixtures. Chemical yields refer to pure isolated substances. The yields and enantiomeric excesses are given in table.

Preparation of the substrates: The preparation of substrate **1a** was reported.[1] Preparation of the other substrates followed the same strategy and general procedures described in the same paper.[1]

Preparation of catalysts: The chiral *N*-triflyl phosphoramide **3a-3j** were prepared according to the procedure of Yamamoto, et al.[2]

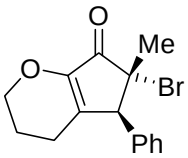
General procedure for Nazarov-halogenation reaction. The substrate (50 mg) and brominating agent (2 equiv.) were suspended in chloroform (0.1 M) in a screw-capped test-tube and allowed to stir at 0 °C for 10 min. The catalyst (5 mol%) was added to the reaction mixture. The reaction was stirred at 0 °C for 2 h and then allowed to warm to 5 or 10 °C for 60 h (see table). The reaction mixture was purified by column chromatography on silica gel (ethyl acetate/hexane) which was neutralized with triethylamine prior to use to afford the product. The racemic compounds were prepared by using achiral catalyst **A** (10 mol%) at 0 °C to room temperature for overnight.



achiral catalyst **A**

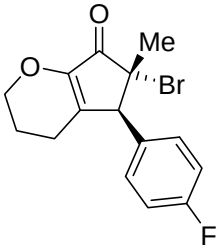
Physical data:

(5*S*,6*R*)-6-bromo-6-methyl-5-phenyl-3,4,5,6-tetrahydrocyclopenta-[*b*]pyran-7(2*H*)-one 5a



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.32-7.21 (m, 3H), 7.03 (d, J = 7.1 Hz, 2H), 4.45 (s, 1H), 4.28-4.09 (m, 2H), 2.14 (t, J = 6.7 Hz, 2H), 2.02-1.84 (m, 2H), 1.21 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 195.17, 149.00, 141.93, 136.81, 129.01, 128.20, 67.32, 60.92, 59.69, 24.84, 22.47, 21.50; IR ($CHCl_3$): $\tilde{\nu}$ = 3023, 2928, 2884, 1719, 1646, 1595, 1493, 1455, 1435, 1403, 1375, 1305, 1184, 1109, 1049, 988, 754, 703, 667 cm^{-1}; EI-MS: m/z (relative intensity) = 308 (46) $[C_{15}H_{15}{}^{81}BrO_2]^{+\bullet}$, 306 (50) $[C_{15}H_{15}{}^{79}BrO_2]^{+\bullet}$, 227 (100) $[M\text{-}Br]^+$, 199 (22), 171 (20), 143 (35), 142 (29), 141 (45), 129 (45), 128 (76), 127 (20), 115 (85), 105 (56), 91 (33), 77 (28), 66 (15), 65 (16); $[\alpha]_D^{RT}$ = +71.1 (c = 1.0 in $CHCl_3$); HPLC conditions: OD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 1 mL min^{-1}, major enantiomer: t_R = 16.04 min; minor enantiomer: t_R = 13.03 min.

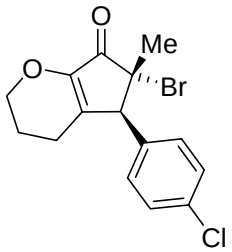
(5*S*,6*R*)-6-bromo-5-(4-fluorophenyl)-6-methyl-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(2*H*)-one 5b



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.10-6.93 (m, 4H), 4.44 (s, 1H), 4.28-4.09 (m, 2H), 2.13 (t, J = 6.0 Hz, 2H), 2.04-1.84 (m, 2H), 1.20 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 194.95, 162.50 (d, $J_{C\text{-}F}$ = 247.8 Hz), 149.07, 141.49, 132.53 (d, $J_{C\text{-}F}$ = 3.3 Hz), 116.21, 115.87, 67.33, 60.17, 59.39, 24.89, 22.39, 21.45; IR (neat): $\tilde{\nu}$ = 2926, 1723, 1648, 1601, 1508, 1435, 1375, 1303, 1271, 1229, 1159, 1109, 1048, 988, 842, 758 cm^{-1}; EI-MS: m/z (relative intensity) = 326 (42) $[C_{15}H_{14}{}^{81}BrFO_2]^{+\bullet}$, 324 (58) $[C_{15}H_{14}{}^{79}BrFO_2]^{+\bullet}$, 245 (100) [M-

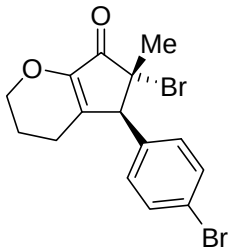
Br]$^+$, 217 (24), 189 (27), 161 (42), 160 (30), 159 (41), 147 (45), 146 (80), 133 (96), 123 (76), 109 (43); $[\alpha]_D^{RT}$ = +59.3 (*c* = 1.0 in $CHCl_3$); HPLC conditions: OD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 28.94 min; minor enantiomer: t_R = 25.13 min.

(5*S*,6*R*)-6-bromo-5-(4-chlorophenyl)-6-methyl-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(2*H*)-one 5c



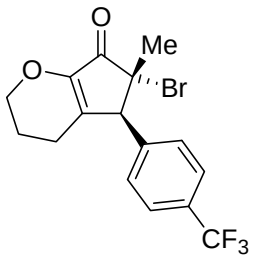
^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.28 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 4.43 (s, 1H), 4.28-4.08 (m, 2H), 2.12 (t, *J* = 6.3 Hz, 2H), 2.03-1.85 (m, 2H), 1.21 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 194.84, 149.15, 141.28, 135.28, 134.17, 129.27, 67.35, 60.27, 59.14, 24.93, 22.38, 21.43; IR (neat): $\tilde{\nu}$ = 2926, 1726, 1649, 1594, 1489, 1434, 1409, 1374, 1302, 1270, 1184, 1110, 1091, 1048, 1014, 988, 841, 813, 757 cm^{-1}; EI-MS: m/z (relative intensity) = 344 (15) $[C_{15}H_{14}{}^{81}Br^{37}ClO_2]^{+\bullet}$, 342 (50) $[C_{15}H_{14}{}^{81}Br^{35}ClO_2]^{+\bullet}$ and $[C_{15}H_{14}{}^{79}Br^{37}ClO_2]^{+\bullet}$, 340 (30) $[C_{15}H_{14}{}^{79}Br^{35}ClO_2]^{+\bullet}$, 263 (34), 262 (24), 261 (94) [M-Br]$^+$, 233 (19), 205 (17), 177 (17), 163 (15), 142 (40), 141 (75), 139 (60), 128 (35), 127 (32), 125 (19), 114 (25), 115 (100), 111 (22), 77 (24); $[\alpha]_D^{RT}$ = +100.1 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 22.54 min; minor enantiomer: t_R = 26.29 min.

(5*S*,6*R*)-6-bromo-5-(4-bromophenyl)-6-methyl-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(2*H*)-one 5d



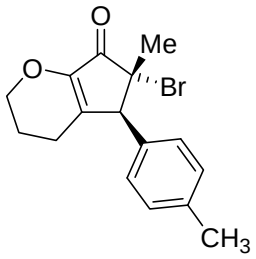
^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.43 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 4.41 (s, 1H), 4.27-4.08 (m, 2H), 2.12 (t, *J* = 6.2 Hz, 2H), 2.05-1.83 (m, 2H), 1.20 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 194.80, 149.13, 141.35, 135.77, 132.21, 122.24, 67.36, 60.29, 59.10, 24.97, 22.38, 21.41; IR ($CHCl_3$): $\tilde{\nu}$ = 2925, 1720, 1648, 1592, 1486, 1435, 1405, 1271, 1184, 1109, 1048, 1010, 987, 837, 755 cm^{-1}; EI-MS: m/z (relative intensity) = 388 (24) $[C_{15}H_{14}{}^{81}Br_2O_2]^{+\bullet}$, 386 (45) $[C_{15}H_{14}{}^{81}Br^{79}BrO_2]^{+\bullet}$, 384 (22) $[C_{15}H_{14}{}^{79}Br_2O_2]^{+\bullet}$, 307 (57) [M-Br]$^+$, 305 (62) [M-Br]$^+$, 277 (13), 249 (8), 198 (21), 185 (17), 183 (22), 170 (28), 155 (23), 142 (44), 141 (70), 128 (43), 127 (20), 115 (100), 111 (17), 102 (14), 89 (13), 77 (21); $[\alpha]_D^{RT}$ = +94.7 (*c* = 1.0 in $CHCl_3$); HPLC conditions: OD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 33.92 min; minor enantiomer: t_R = 29.25 min.

(5*S*,6*R*)-6-bromo-6-methyl-5-(4-(trifluoromethyl)phenyl)-3,4,5,6-tetrahydrocyclopenta [*b*]pyran-7(*2H*)-one 5e



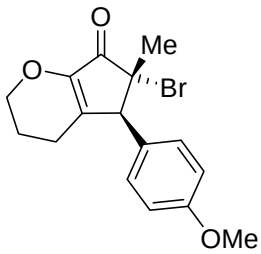
^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 4.52 (s, 1H), 4.32-4.09 (m, 2H), 2.20-2.07 (m, 2H), 2.04-1.86 (m, 2H), 1.20 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 194.64, 149.34, 140.87, 131.34, 130.82, 130.30, 126.02 (*C*F_3, q, *J* = 3.7 Hz), 121.74, 67.38, 60.60, 58.75, 24.99, 22.39, 21.40; IR (neat): $\tilde{\nu}$ = 2925, 1724, 1649, 1434, 1325, 1271, 1166, 1112, 1067, 1048, 1018, 988, 851 cm^{-1}; EI-MS: m/z (relative intensity) = 376 (54) $[C_{16}H_{14}{}^{81}BrF_3O_2]^{+\bullet}$, 374 (56) $[C_{16}H_{14}{}^{79}BrF_3O_2]^{+\bullet}$, 296 (23), 295 (100) $[M\text{-}Br]^+$, 294 (18), 267 (23), 239 (23), 211 (23), 197 (26), 191 (22), 173 (39), 159 (17), 142 (29), 141 (57), 128 (29), 115 (61), 94 (15), 79 (21), 69 (27); $[\alpha]_D^{RT}$ = +59.8 (*c* = 1.0 in $CHCl_3$); HPLC conditions: OD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 30.38min; minor enantiomer: t_R = 22.01 min.

(5*S*,6*R*)-6-bromo-6-methyl-5-p-tolyl-3,4,5,6-tetrahydrocyclopenta-[*b*]pyran-7(*2H*)-one 5f



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.10 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 2H), 4.41 (s, 1H), 4.28-4.06 (m, 2H), 2.27 (s, 3H), 2.13 (t, *J* = 6.3 Hz, 2H), 2.00-1.82 (m, 2H), 1.20 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 195.31, 148.87, 142.22, 137.99, 133.72, 129.69, 67.31, 60.57, 59.89, 24.83, 22.46, 21.51, 21.17; IR (neat): $\tilde{\nu}$ = 2924, 1720, 1648, 1512, 1442, 1402, 1373, 1304, 1272, 1177, 1109, 1048, 987, 831, 814 cm^{-1}; EI-MS: m/z (relative intensity) = 322 (33) $[C_{16}H_{17}{}^{81}BrO_2]^{+\bullet}$, 320 (32) $[C_{16}H_{17}{}^{79}BrO_2]^{+\bullet}$, 241 (100) $[M\text{-}Br]^+$, 213 (23), 185 (22), 157 (21), 156 (20), 142 (37), 141 (56), 129 (33), 128 (47), 119 (49), 115 (58), 111 (18), 91 (34), 77 (21), 65 (22); $[\alpha]_D^{RT}$ = +41.5 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 17.89 min; minor enantiomer: t_R = 22.47 min.

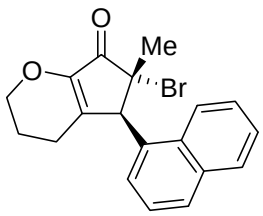
(5*S*,6*R*)-6-bromo-5-(4-methoxyphenyl)-6-methyl-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(*2H*)-one 5g



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 6.95 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 4.39 (s, 1H), 4.27-4.07 (m, 2H), 3.74 (s, 3H), 2.13 (t, *J* = 6.7 Hz, 2H), 2.05-1.83 (m, 2H), 1.21 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 195.32, 159.45, 148.84, 142.16, 128.74, 114.37, 67.30, 60.20, 60.03, 55.35, 24.83, 22.45, 21.52; IR (neat): $\tilde{\nu}$ =

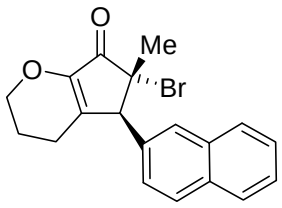
2929, 1714, 1645, 1609, 1549, 1512, 1455, 1402, 1379, 1302, 1248, 1177, 1110, 1048, 988, 839, 736 cm^{-1}; EI-MS: m/z (relative intensity) = 338 (31) $[C_{16}H_{17}{}^{81}BrO_3]^{+\bullet}$, 336 (28) $[C_{16}H_{17}{}^{79}BrO_3]^{+\bullet}$, 258 (22), 257 (100) $[M\text{-}Br]^+$, 256 (31), 229 (29), 201 (16), 172 (14), 158 (17), 141 (14), 135 (44), 129 (26), 128 (32), 115 (40), 111 (31), 103 (20), 91 (17), 77 (27); $[\alpha]_D^{RT}$ = +50.3 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 26.90 min; minor enantiomer: t_R = 33.65 min.

(5*S*,6*R*)-6-bromo-6-methyl-5-(naphthalen-1-yl)-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(2*H*)-one 5h



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 8.32 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.64-7.55 (m, 1H), 7.54-7.46 (m, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 7.1, 1.1 Hz, 1H), 5.26 (s, 1H), 4.37-4.14 (m, 2H), 2.36-1.93 (m, 4H), 1.12 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 195.52, 149.49, 141.91, 134.14, 133.28, 129.10, 128.71, 127.17, 126.30, 125.33, 125.28, 123.97, 67.40, 59.41, 55.75, 23.50, 22.84, 21.59; IR ($CHCl_3$): $\tilde{\nu}$ = 2925, 1719, 1649, 1441, 1402, 1182, 1109, 1050, 986, 803, 785, 755 cm^{-1}; EI-MS: m/z (relative intensity) = 358 (58) $[C_{19}H_{17}{}^{81}BrO_2]^{+\bullet}$, 356 (64) $[C_{19}H_{17}{}^{79}BrO_2]^{+\bullet}$, 278 (34), 277 (93) $[M\text{-}Br]^+$, 276 (25), 249 (51), 233 (17), 231 (18), 221 (39), 205 (20), 195 (31), 191 (41), 179 (34), 178 (54), 165 (100), 155 (25), 152 (40), 127 (42); $[\alpha]_D^{RT}$ = –32.0 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 21.68 min; minor enantiomer: t_R = 23.91 min.

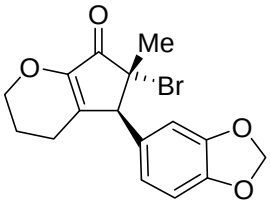
(5*S*,6*R*)-6-bromo-6-methyl-5-(naphthalen-2-yl)-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(2*H*)-one 5i



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.81-7.71 (m, 3H), 7.54 (s, 1H), 7.39 (m, 2H), 7.09 (d, *J* = 8.7 Hz, 1H), 4.61 (s, 1H), 4.31-4.10 (m, 2H), 2.15 (t, *J* = 6.5 Hz, 2H), 2.02-1.87 (m, 2H), 1.24 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 195.22, 149.10, 141.98, 134.30, 133.44, 133.05, 128.85, 127.86, 127.80, 126.72, 126.50, 67.39, 61.09, 59.68, 24.84, 22.54, 21.52; IR ($CHCl_3$): $\tilde{\nu}$ = 2925, 1720, 1647, 1435, 1420, 1375, 1270, 1185, 1109, 1048, 755 cm^{-1}. EI-MS: m/z (relative intensity) = 358 (52) $[C_{19}H_{17}{}^{81}BrO_2]^{+\bullet}$, 356 (59) $[C_{19}H_{17}{}^{79}BrO_2]^{+\bullet}$, 278 (44), 277 (100) $[M\text{-}Br]^+$, 276 (46), 250(22), 249 (63), 235 (16), 221 (56), 192 (28), 191 (37), 179 (34), 178 (66), 165 (72), 155 (28), 152 (34), 141 (19), 127

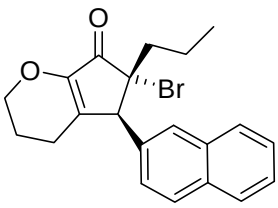
(34), 115 (17); $[\alpha]_D^{RT}$ = +111.1 (*c* = 1.0 in $CHCl_3$); HPLC conditions: OD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 33.86 min; minor enantiomer: t_R = 38.68 min.

(5*S*,6*R*)-5-(1,3-benzodioxol-5-yl)-6-bromo-6-methyl-3,4,5,6-tetra-hydrocyclopenta [*b*]pyran-7(*2H*)-one 5j



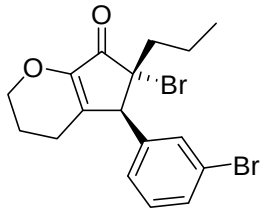
^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 6.73 (d, *J* = 8.1 Hz, 1H), 6.60-6.41 (m, 2H), 5.91 (s, 2H), 4.36 (s, 1H), 4.28-4.02 (m, 2H), 2.15 (t, *J* = 6.3 Hz, 2H), 2.02-1.87 (m, 2H), 1.25 (s, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 195.12, 148.96, 148.28, 147.54, 141.79, 130.52, 108.68, 101.38, 67.31, 60.60, 59.80, 24.64, 22.43, 21.49; IR ($CHCl_3$): $\tilde{\nu}$ = 2925, 1719, 1647, 1595, 1502, 1487, 1436, 1234, 1189, 1109, 1039, 929, 756 cm^{-1}; EI-MS: m/z (relative intensity) = 352 (72) $[C_{16}H_{15}{}^{81}BrO_4]^{+\bullet}$, 350 (69) $[C_{16}H_{15}{}^{79}BrO_4]^{+\bullet}$, 272 (25), 271 (76) $[M\text{-}Br]^+$, 270 (43), 243 (100), 228 (16), 215 (48), 186 (28), 157 (22), 149 (56), 129 (48), 128 (74), 127 (27), 115 (53), 111 (28), 103 (35), 102 (42), 77 (35); $[\alpha]_D^{RT}$ = +54.0 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 38.57 min; minor enantiomer: t_R = 59.78 min.

(5*S*,6*R*)-6-bromo-5-(naphthalen-2-yl)-6-propyl-3,4,5,6-tetrahydro-cyclopenta[*b*]pyran-7(*2H*)-one 5k



^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.83 (m, 3H), 7.57 (s, 1H), 7.50-7.39 (m, 2H), 7.11 (d, *J* = 8.6 Hz, 1H), 4.54 (s, 1H), 4.30-4.05 (m, 2H), 2.24-1.62 (m, 5H), 1.52-1.38 (m, 1H), 1.28-1.92 (m, 2H), 0.40 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 194.97, 148.74, 142.25, 134.39, 133.30, 132.97, 128.57, 127.86, 127.80, 126.65, 126.48, 67.33, 66.40, 61.11, 37.12, 22.38, 21.55, 18.83, 13.99; IR (neat): $\tilde{\nu}$ = 2960, 2928, 2871, 1715, 1650, 1595, 1455, 1433, 1271, 1231, 1112, 1066, 859, 820, 754 cm^{-1}; EI-MS: m/z (relative intensity) = 386 (13) $[C_{21}H_{21}{}^{81}BrO_2]^{+\bullet}$, 384 (21) $[C_{21}H_{21}{}^{79}BrO_2]^{+\bullet}$, 306 (32), 305 (100) $[M\text{-}Br]^+$, 277 (19), 275 (15), 264 (26), 263 (29), 247 (8), 235 (13), 207 (13), 191 (26), 179 (20), 178 (39), 165 (45), 155 (38), 152 (24), 141 (17), 128 (22), 127 (21), 115 (12), 111 (17); $[\alpha]_D^{RT}$ = +84.0 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 21.13 min; minor enantiomer: t_R = 23.88 min.

(5*S*,6*R*)-6-bromo-5-(3-bromophenyl)-6-propyl-3,4,5,6-tetrahydrocyclopenta[*b*]pyran-7(*2H*)-one 5l

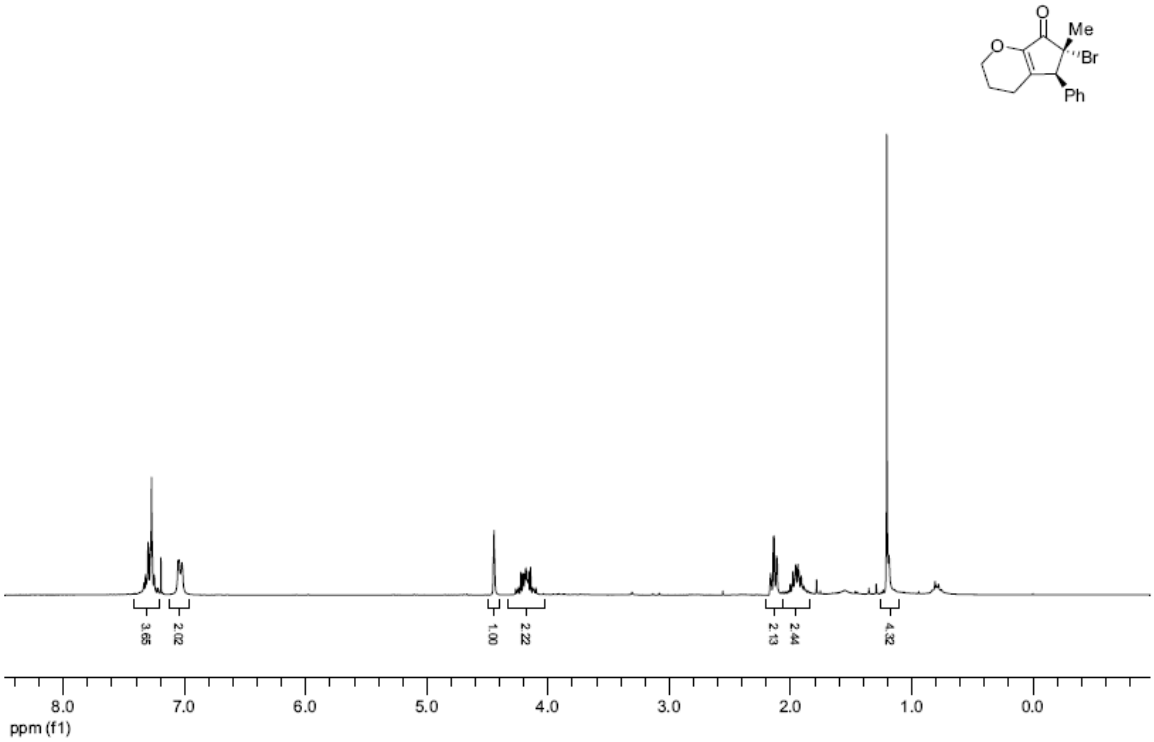


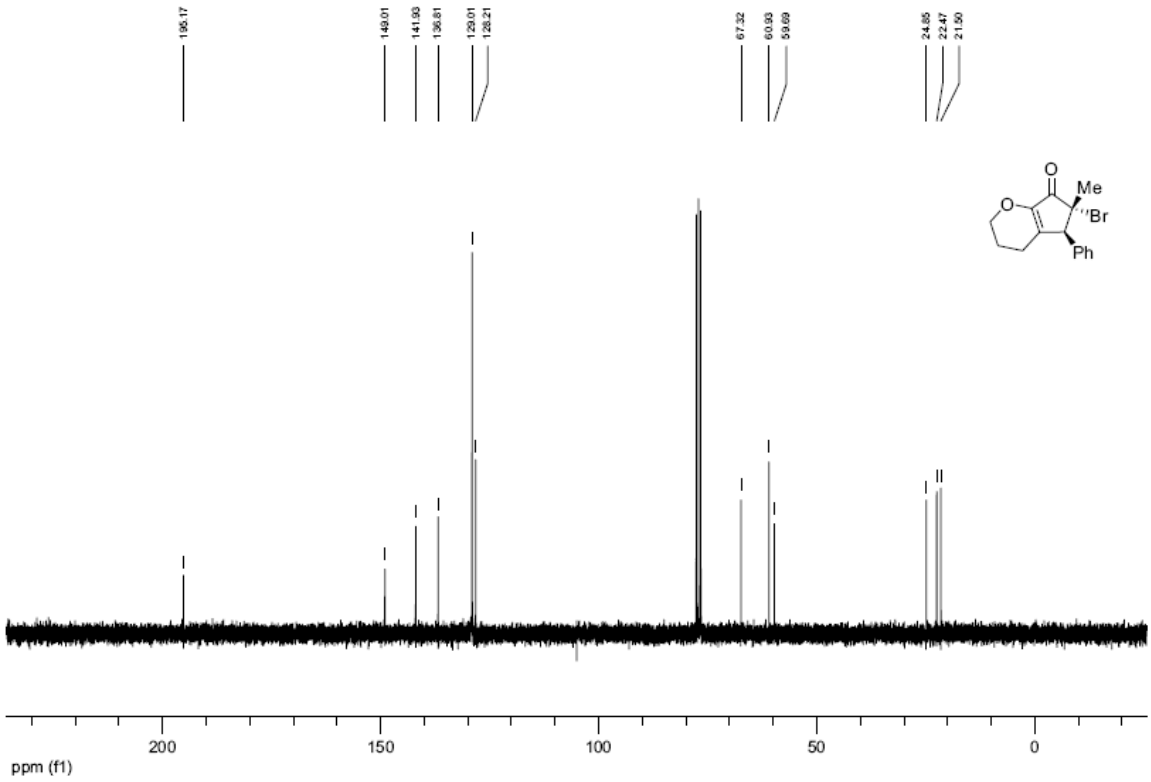
^{1}H-NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ 7.72-7.61 (m, 1H), 7.19 (s, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 4.34 (s, 1H), 4.29-4.04 (m, 2H), 2.20-1.79 (m, 4H), 1.77-1.59 (m, 1H), 1.54-1.37 (m, 1H), 1.15-0.95 (m, 2H), 0.53 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ 193.41, 147.87, 140.22, 138.22, 130.29, 129.26, 121.89, 66.24, 64.54, 59.50, 36.03, 21.20, 20.38, 17.73, 12.90; IR (neat): $\tilde{\nu}$ = 2960, 2928, 1722, 1650, 1590, 1566, 1474, 1432, 1402, 1292, 1269, 1171, 1113, 1071, 912, 793, 738, 698, 680 cm^{-1}; EI-MS: m/z (relative intensity) = 416 (2) $[C_{17}H_{18}{}^{81}Br_2O_2]^{+\bullet}$, 414 (2) $[C_{17}H_{18}{}^{81}Br^{79}BrO_2]^{+\bullet}$, 374 (5), 372 (8), 335 (20) $[M\text{-}Br]^+$, 333 (20) $[M\text{-}Br]^+$, 307 (5), 305 (6), 303 (6), 293 (6), 291 (7), 193 (11), 169 (21), 165 (21), 153 (19), 141 (63), 128 (58), 115 (100), 102 (13), 91 (30), 77 (46); $[\alpha]_D^{RT}$ = +96.0 (*c* = 1.0 in $CHCl_3$); HPLC conditions: AD-H column, *n*-hexane/2-propanol = 95/5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 15.74 min; minor enantiomer: t_R = 21.83 min.

References:

[1] G. Liang, S. N. Gradl, D. Trauner, *Org. Lett*. **2003**, *5*, 4931.

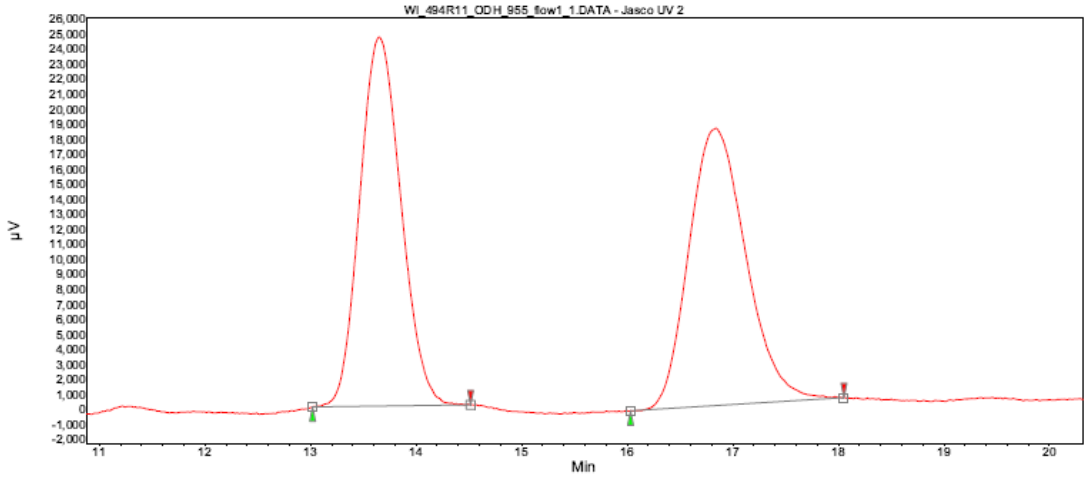
[2] D. Nakashima, H. Yamamoto, *J. Am, Chem. Soc*. **2006**, *128*, 9626.


O
Me
Br
Ph
3.65
2.02
1.00
2.22
2.13
2.44
4.32
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


195.17
149.01
141.93
136.81
129.01
128.21
67.32
60.93
59.69
24.85
22.47
21.50
O
Me
Br
Ph
200
150
100
50
0
ppm (f1)

Chromatogram : WI_494R11_ODH_955_flow1_1

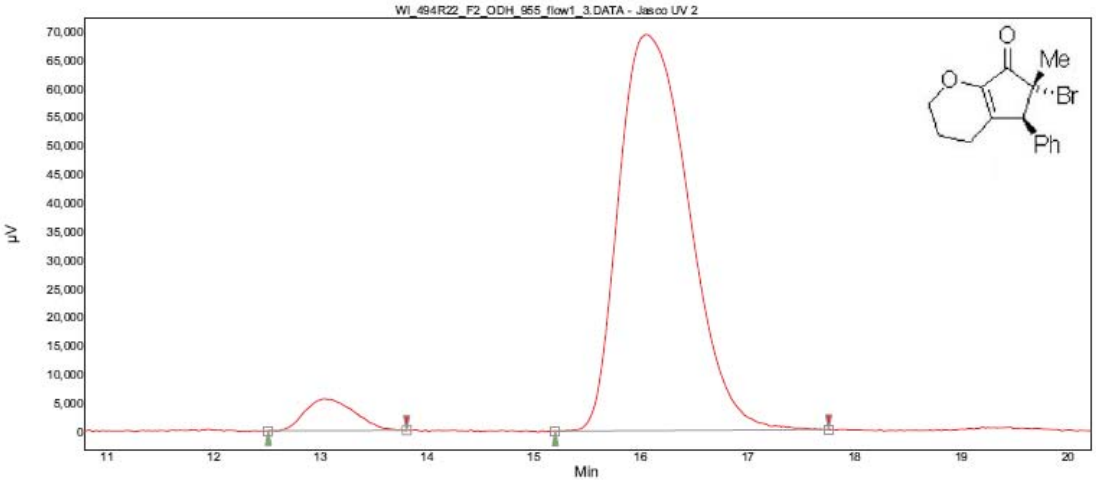
Method: HPLC1_ODH_955_flow1_acq_45
Data file: WI_494R11_ODH_955_flow1_1.DATA
Date: 4/20/2007 1:25:52 PM



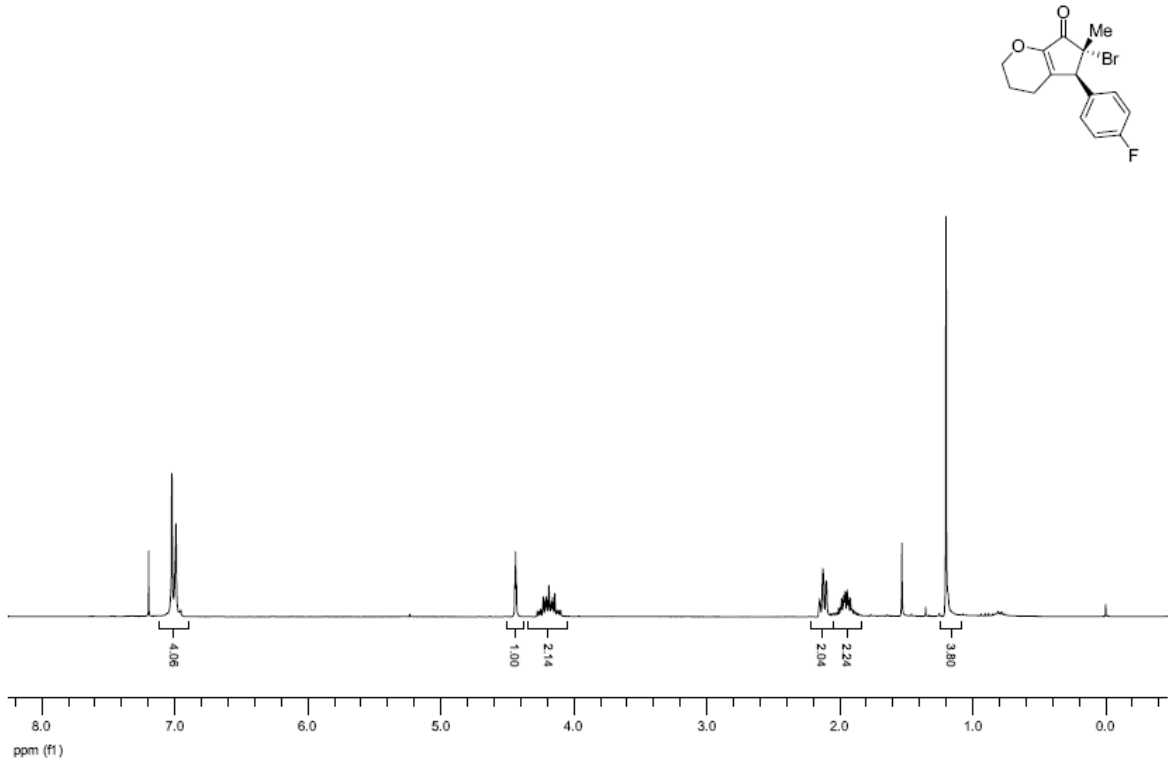
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	13.020	13.650	14.516	49.075
2	16.032	16.842	18.053	50.925
Total				100.000

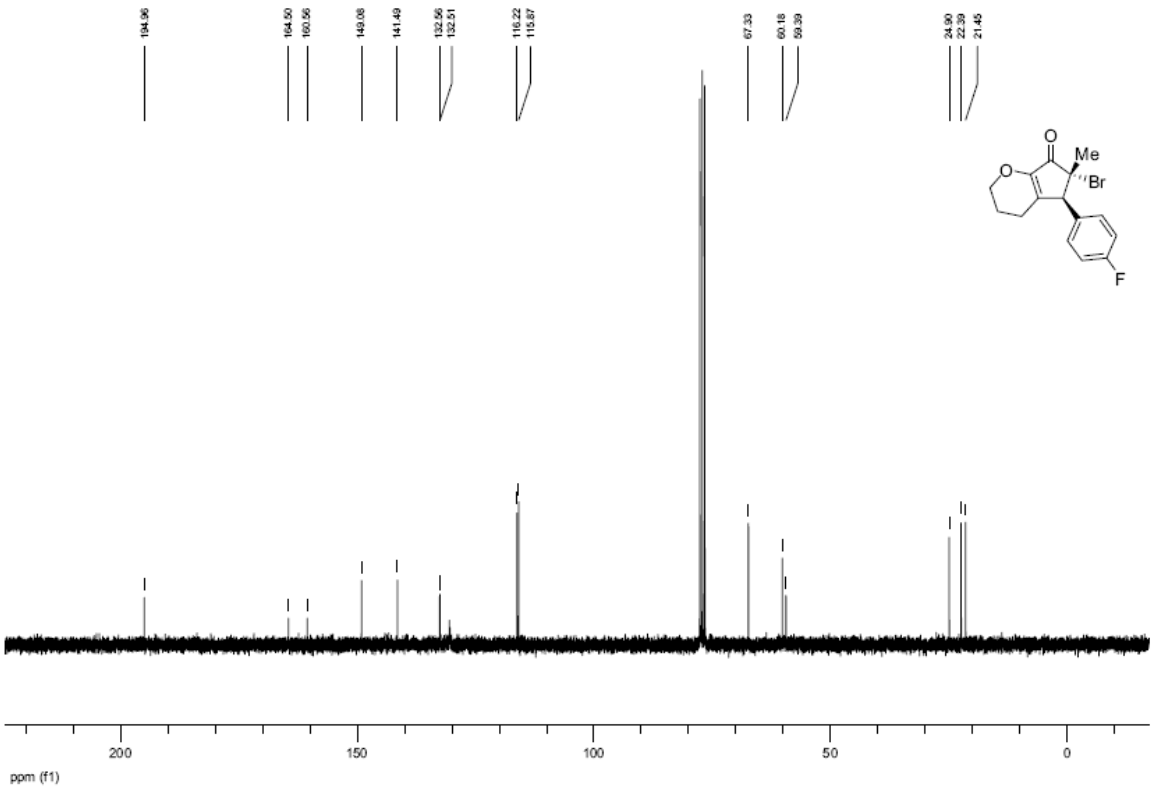
Chromatogram : WI_494R22_F2_ODH_955_flow1_3

Method: HPLC1_ODH_955_flow1_acq_30
Data file: WI_494R22_F2_ODH_955_flow1_3.DATA
Date: 8/21/2007 5:31:09 PM



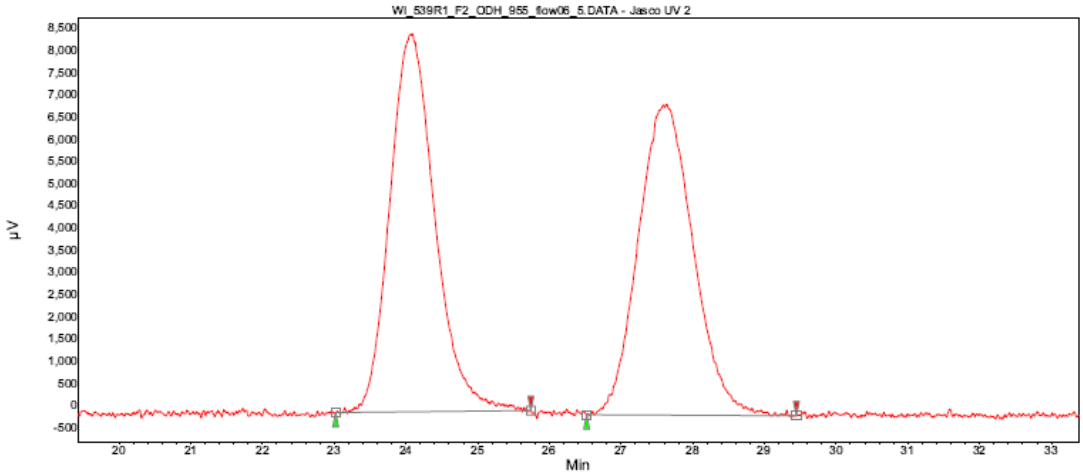
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
2	12.508	13.033	13.802	5.355
1	15.194	16.042	17.754	94.645
Total				100.000


O
Me
Br
O
F
4.06
1.00
2.14
2.04
2.24
3.80
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


194.96
164.50
160.56
149.08
141.49
132.56
132.51
116.22
115.87
67.33
60.18
59.59
24.96
24.22
21.14
O
Me
Br
O
F
200
150
100
50
0
ppm (f1)

Chromatogram : WI_539R1_F2_ODH_955_flow06_5

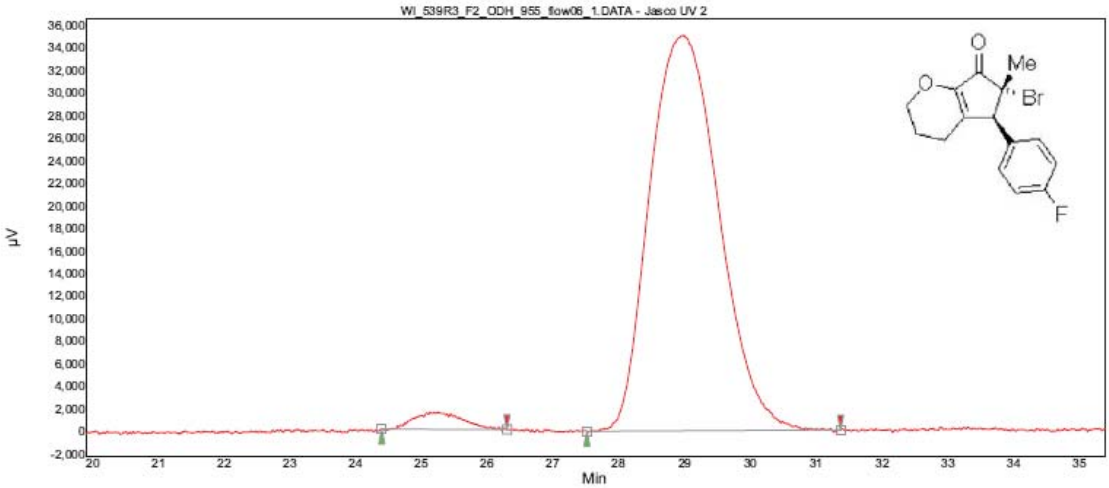
Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_539R1_F2_ODH_955_flow06_5.DATA
Date: 7/21/2007 2:38:35 AM



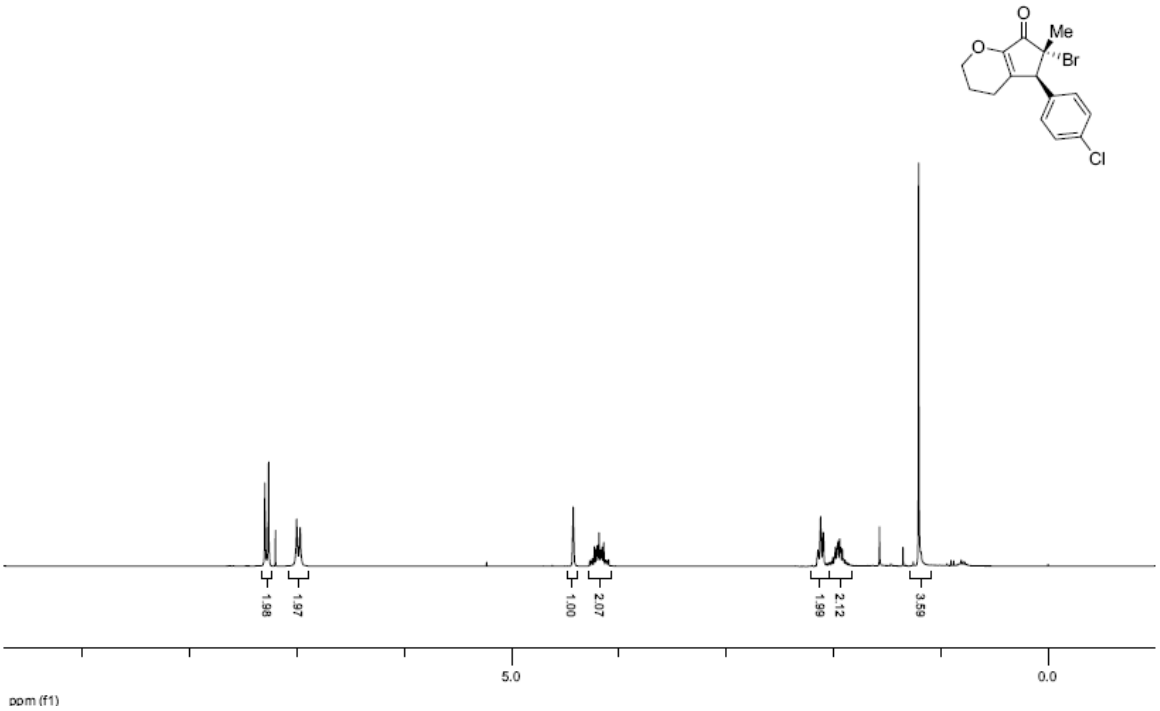
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	23.019	24.058	25.742	49.904
2	26.520	27.633	29.445	50.096
Total				100.000

Chromatogram : WI_539R3_F2_ODH_955_flow06_1

Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_539R3_F2_ODH_955_flow06_1.DATA
Date: 8/16/2007 2:35:28 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	24.390	25.133	26.294	2.928
2	27.509	28.942	31.363	97.072
Total				100.000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Me
Br
O
Cl
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1.99
2.12
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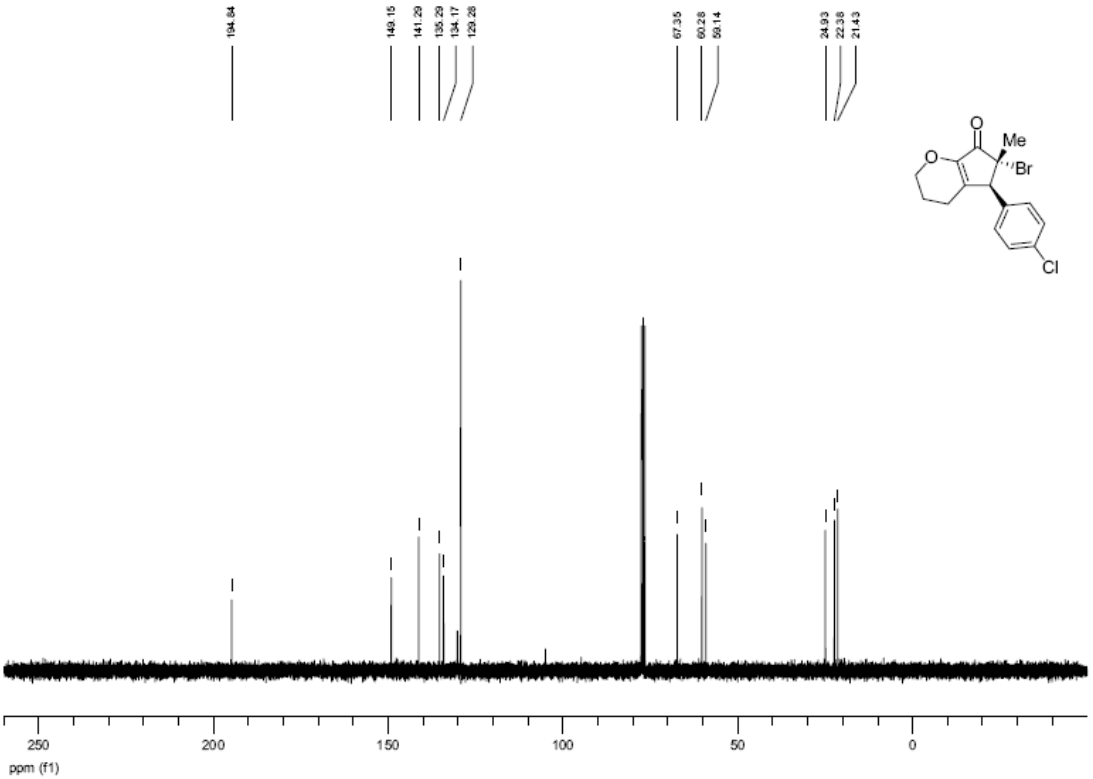
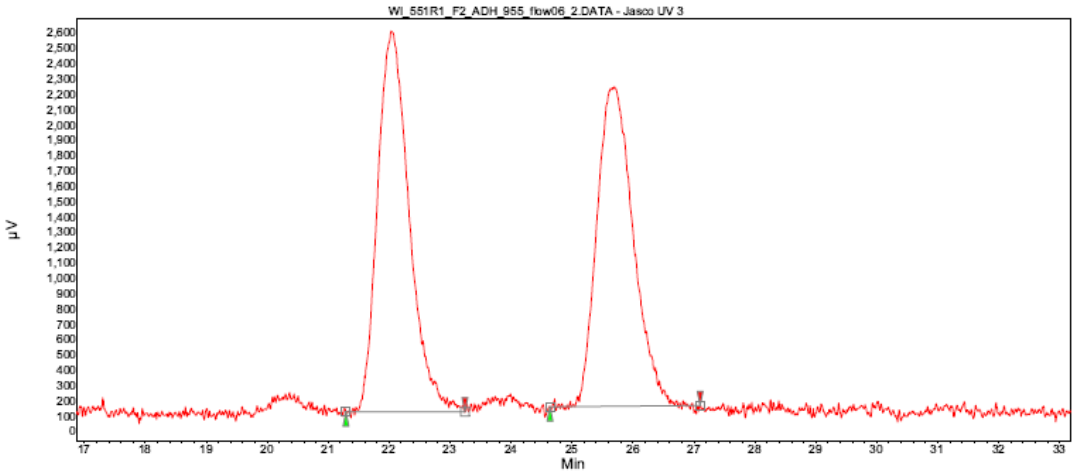
5.0
0.0
ppm (f1)


194.84
149.15
141.29
135.29
134.17
129.28
67.35
60.28
59.14
24.93
22.38
21.43
O
Me
Br
O
Cl
250
200
150
100
50
0
ppm (f1)

Chromatogram : WI_551R1_F2_ADH_955_flow06_2

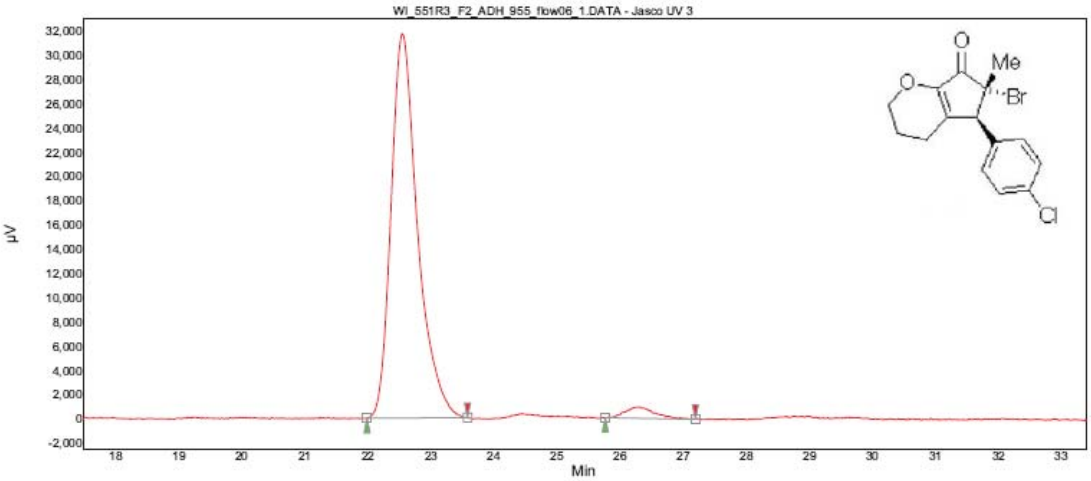
Method: HPLC1_ADH_955_flow06_acq_45
Data file: WI_551R1_F2_ADH_955_flow06_2.DATA
Date: 7/21/2007 1:43:55 PM



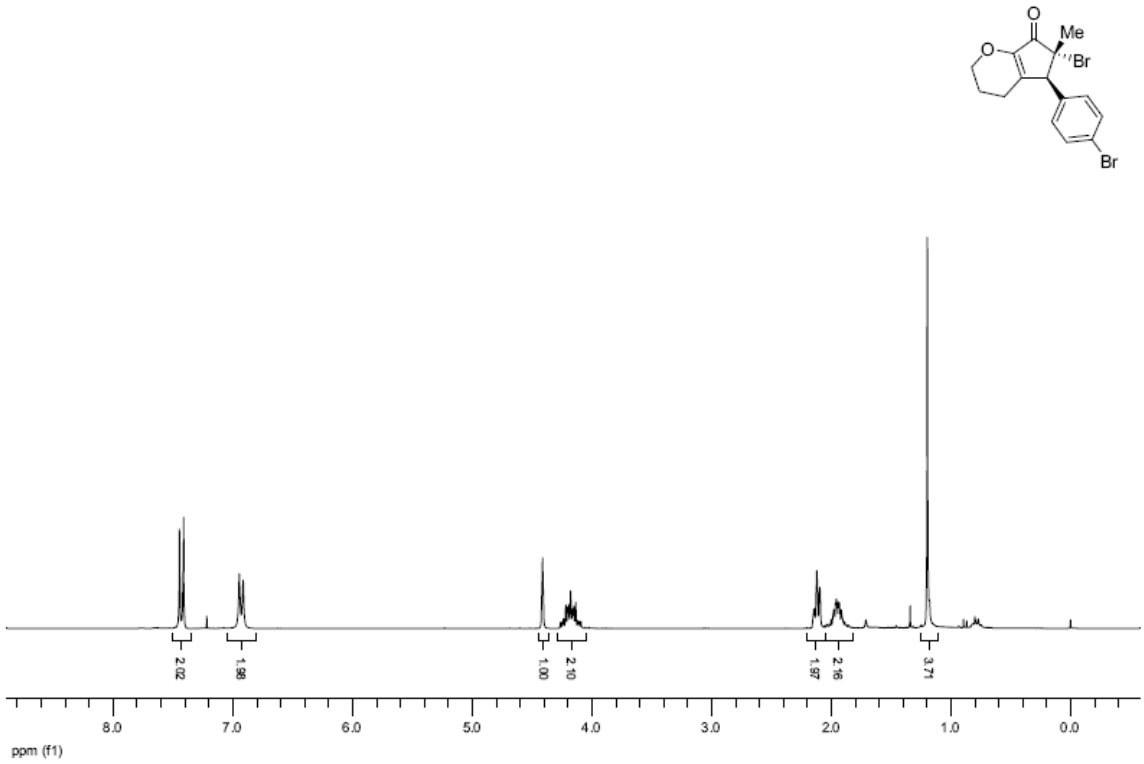
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	21.291	22.050	23.244	50.984
2	24.638	25.650	27.102	49.016
Total				100.000

Chromatogram : WI_551R3_F2_ADH_955_flow06_1

Method: HPLC1_ADH_955_flow06_acq_45
Data file: WI_551R3_F2_ADH_955_flow06_1.DATA
Date: 8/17/2007 11:47:17 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	21.980	22.542	23.573	96.858
2	25.757	26.292	27.186	3.142
Total				100.000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Me
Br
O
Br
2.02
1.98
1.00
2.10
1.97
2.96
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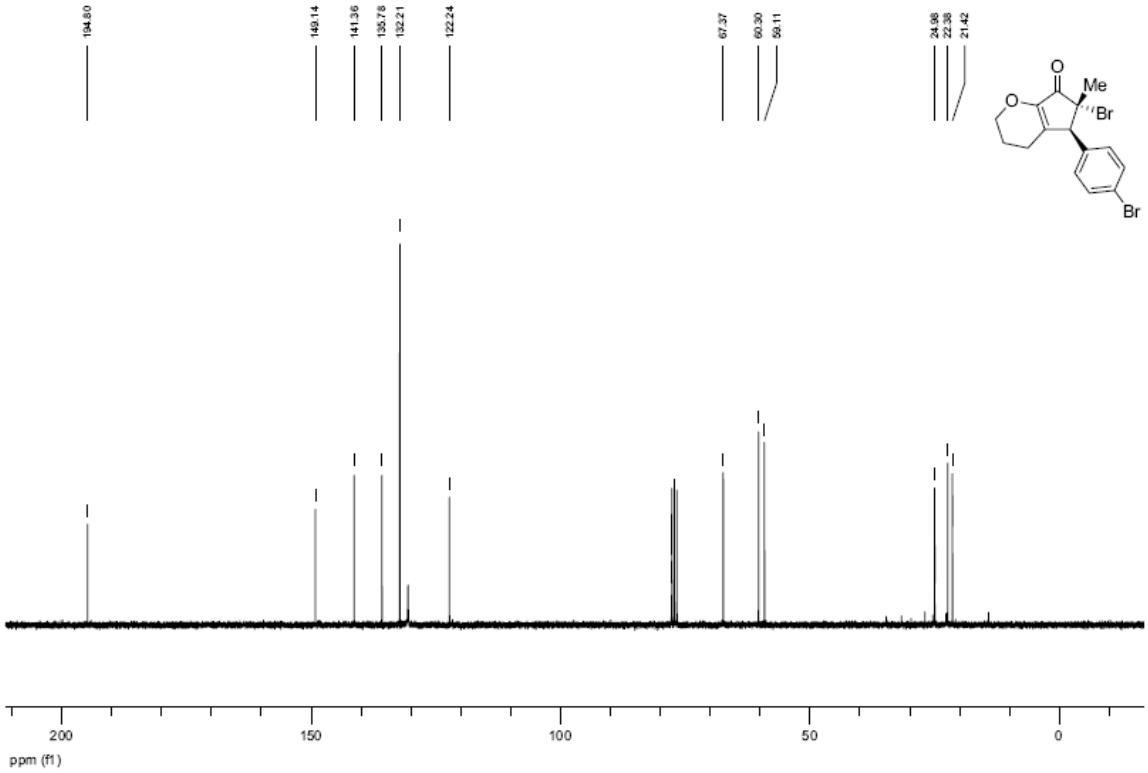
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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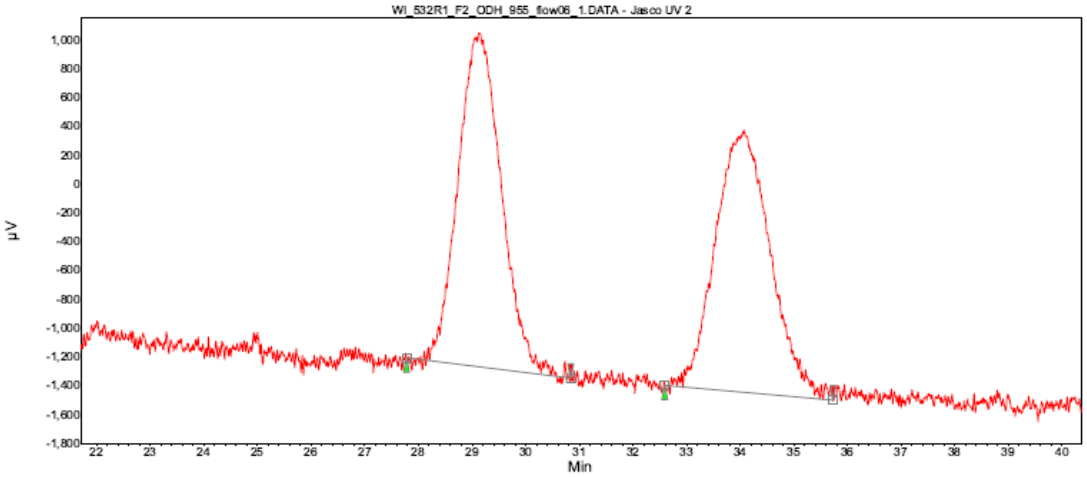
141.36
135.78
132.21
122.24
67.37
60.30
59.11
24.98
22.38
21.42
O
Me
Br
O
Br
200
150
100
50
0
ppm (f1)

Chromatogram : WI_532R1_F2_ODH_955_flow06_1

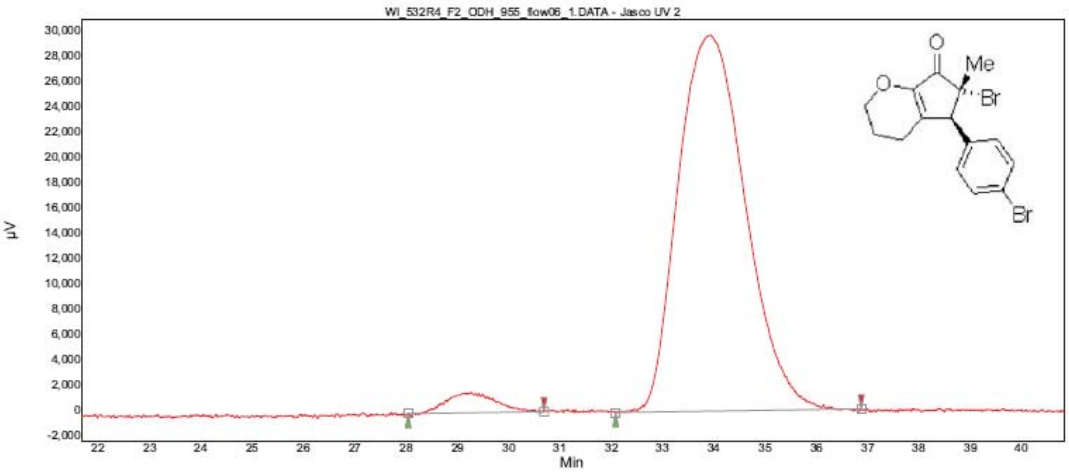
Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_532R1_F2_ODH_955_flow06_1.DATA
Date: 7/23/2007 5:59:49 PM



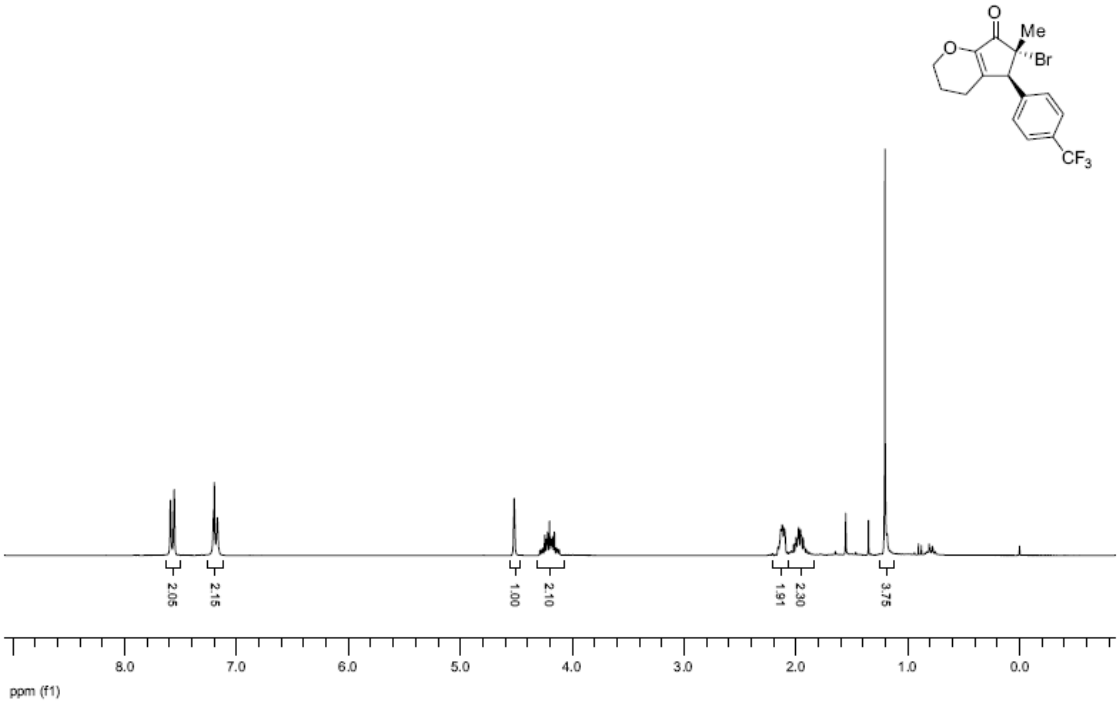
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	27.776	29.133	30.838	49.955
2	32.590	34.067	35.729	50.045
Total				100.000

Chromatogram : WI_532R4_F2_ODH_955_flow06_1

Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_532R4_F2_ODH_955_flow06_1.DATA
Date: 8/16/2007 1:00:03 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	28.032	29.258	30.682	3.706
2	32.076	33.917	36.865	96.294
Total				100.000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Me
Br
O
CF3
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1.00
2.10
1.91
2.30
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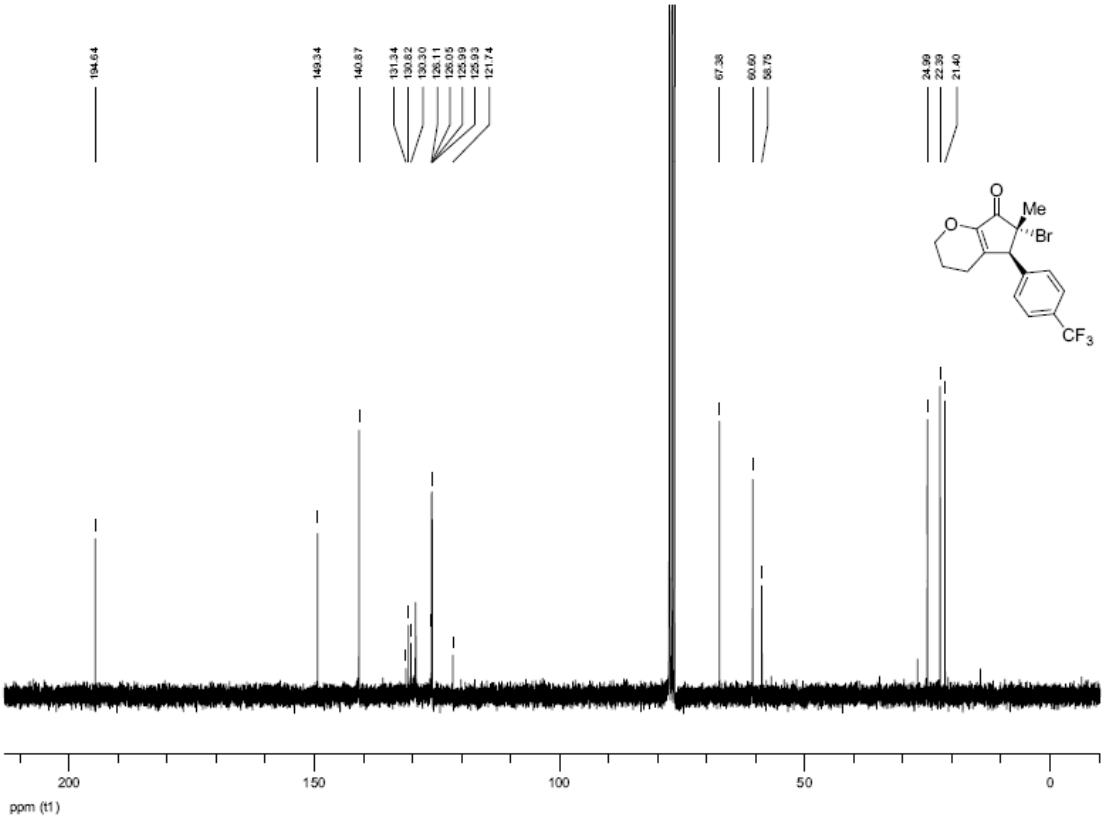
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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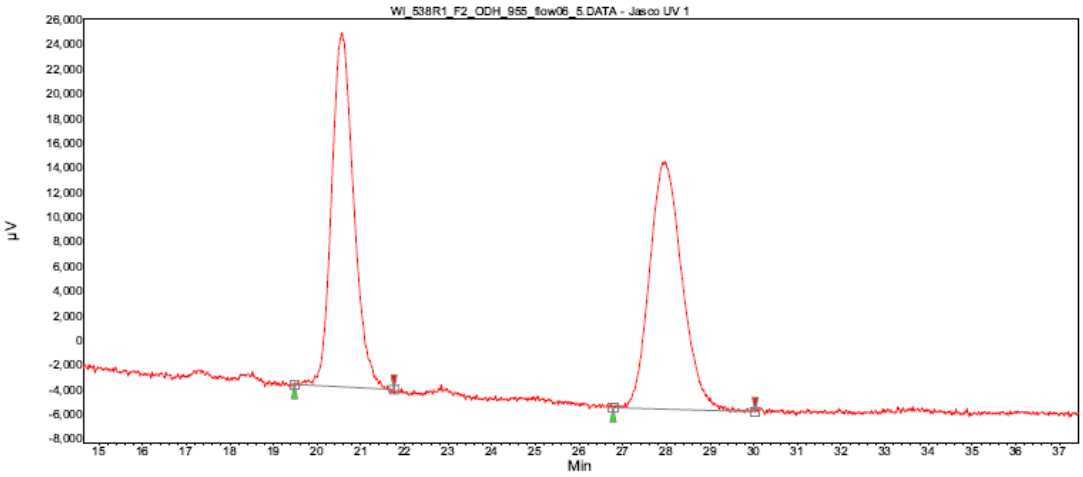
131.34
130.82
130.30
126.11
126.05
125.99
125.93
121.74
67.38
60.60
58.75
24.99
22.39
21.40
O
Me
Br
O
CF3
200
150
100
50
0
ppm (f1)

Chromatogram : WI_538R1_F2_ODH_955_flow06_5

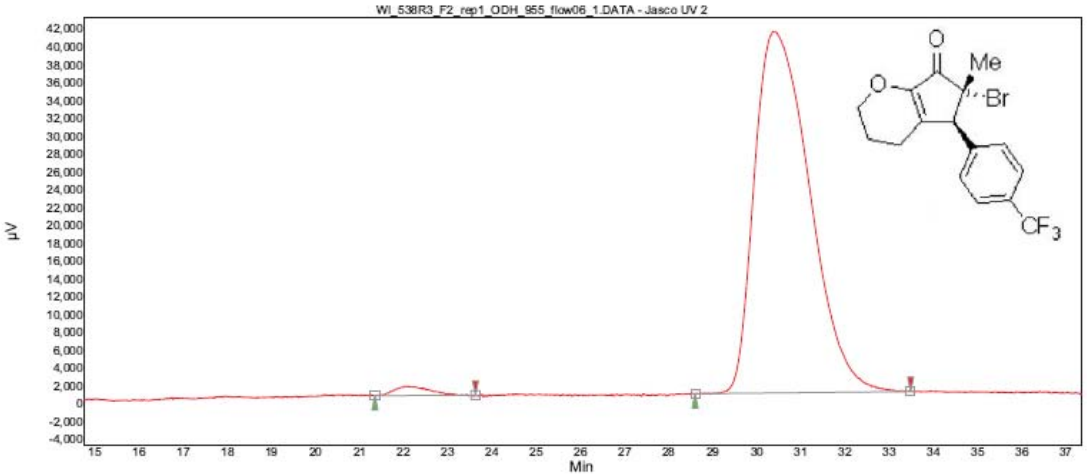
Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_538R1_F2_ODH_955_flow06_5.DATA
Date: 7/21/2007 1:50:49 AM



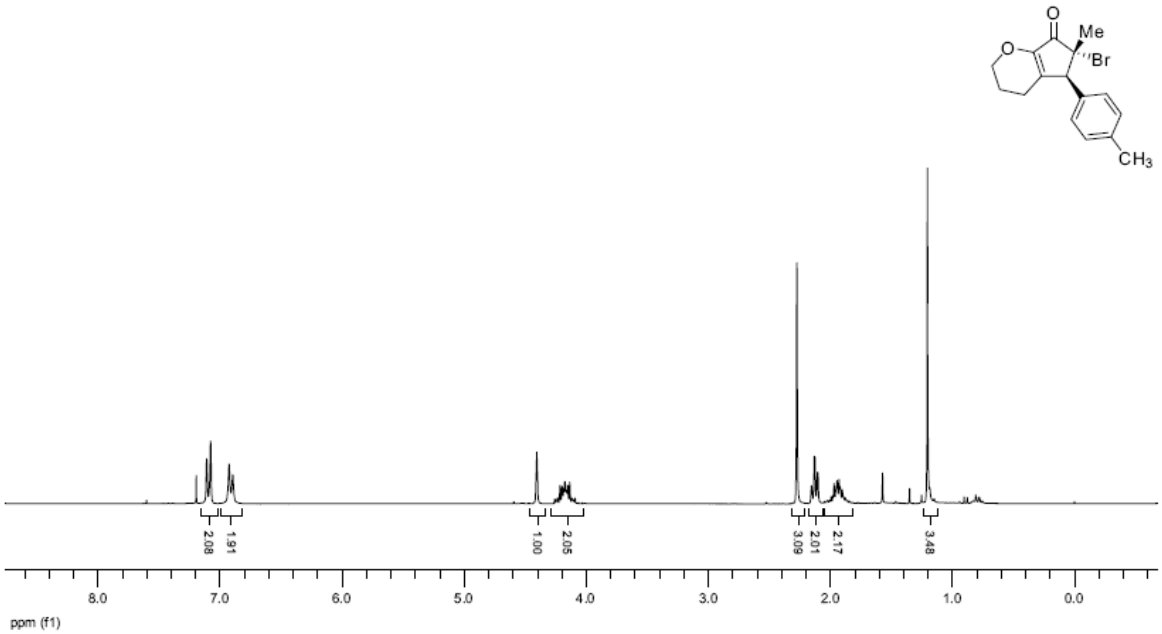
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	19.478	20.567	21.756	49.171
2	26.777	27.925	30.031	50.829
Total				100.000

Chromatogram : WI_538R3_F2_rep1_ODH_955_flow06_1

Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_538R3_F2_rep1_ODH_955_flow06_1.DATA
Date: 9/7/2007 4:08:01 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	21.338	22.008	23.616	1.592
2	28.590	30.375	33.471	98.408
Total				100.000


O
Me
Br
O
CH3
2.08
1.91
1.00
2.05
3.09
2.01
2.17
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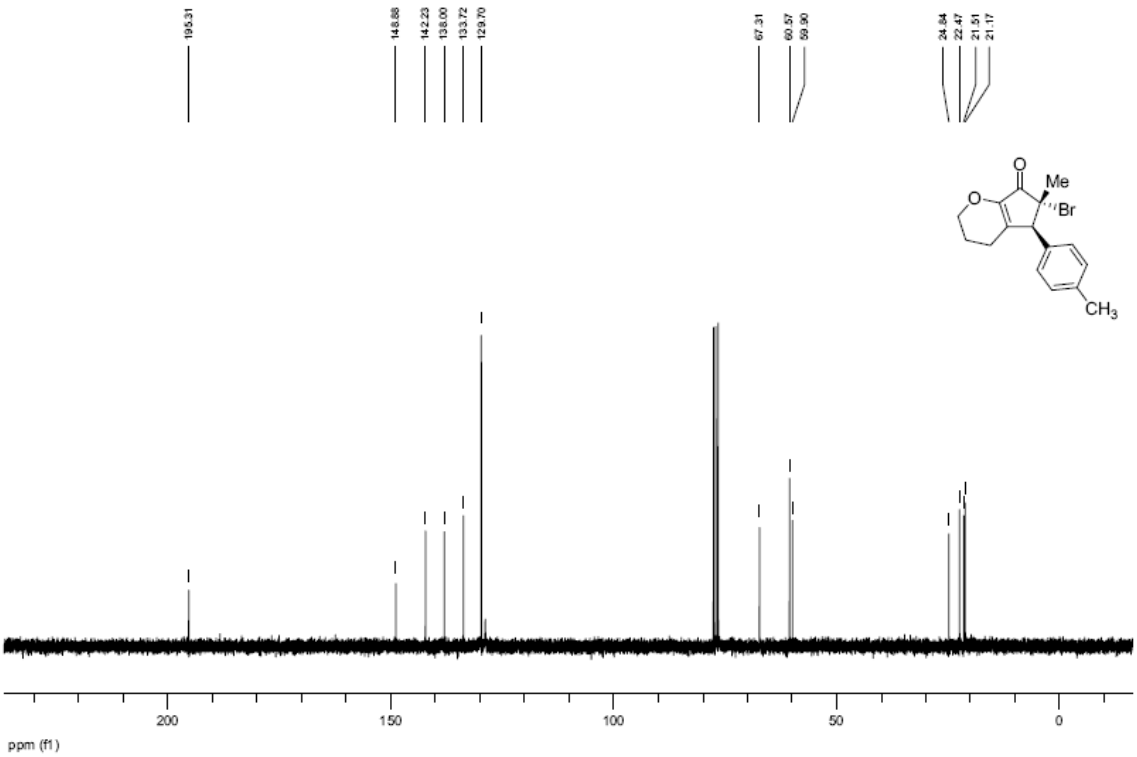
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


195.31
148.88
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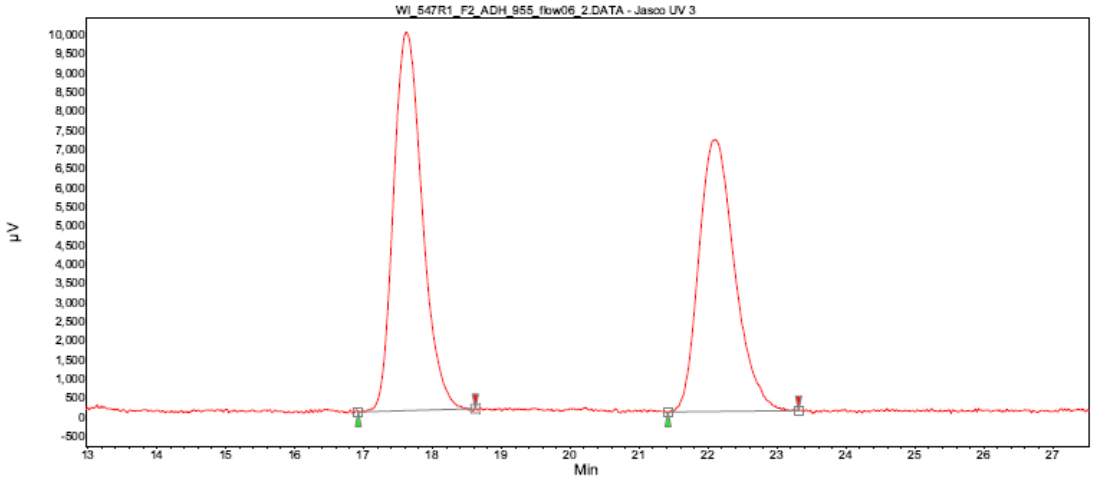
138.00
133.72
129.70
67.31
60.57
59.90
24.84
22.47
21.51
21.17
O
Me
Br
O
CH3
200
150
100
50
0
ppm (f1)

Chromatogram : WI_547R1_F2_ADH_955_flow06_2

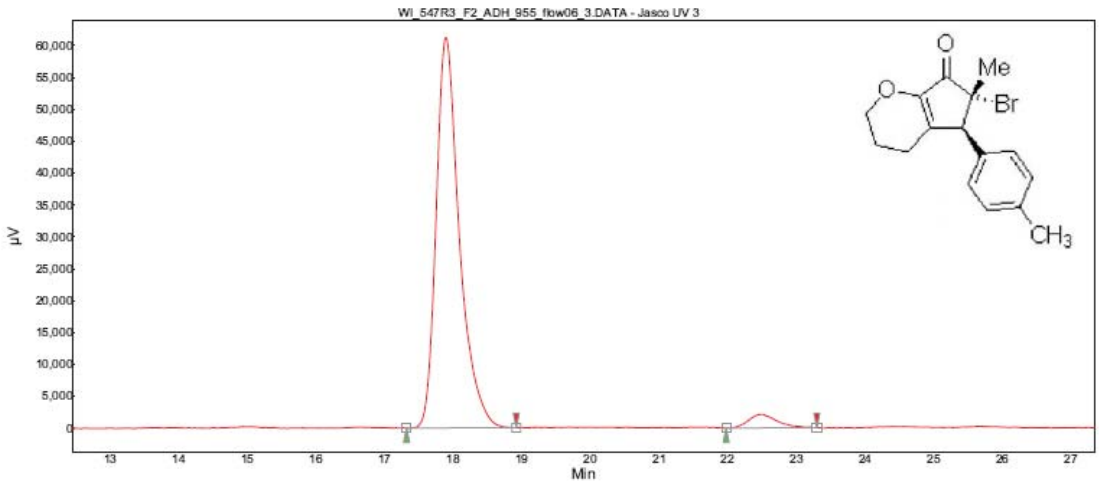
Method: HPLC1_ADH_955_flow06_acq_45
Data file: WI_547R1_F2_ADH_955_flow06_2.DATA
Date: 7/21/2007 10:50:46 AM



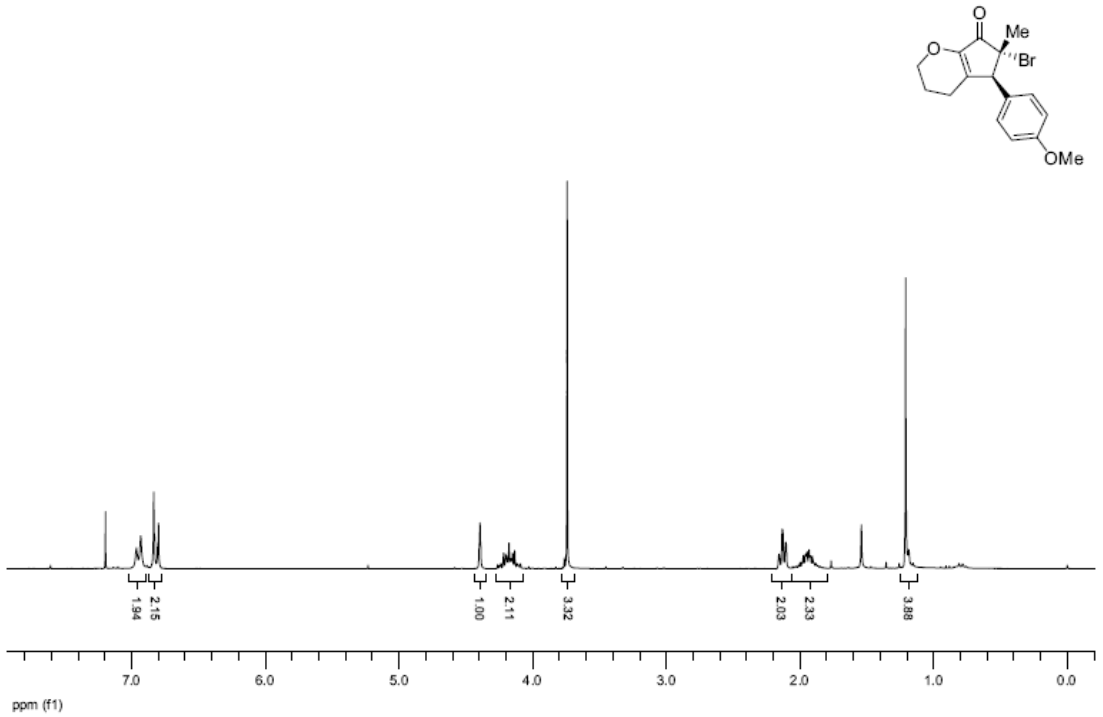
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	16.923	17.617	18.622	52.773
2	21.418	22.108	23.312	47.227
Total				100.000

Chromatogram : WI_547R3_F2_ADH_955_flow06_3

Method: HPLC1_ADH_955_flow06_acq_30
Data file: WI_547R3_F2_ADH_955_flow06_3.DATA
Date: 8/21/2007 7:09:10 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	17.315	17.892	18.913	95.889
2	21.971	22.467	23.293	4.111
Total				100.000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Br
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3.32
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2.33
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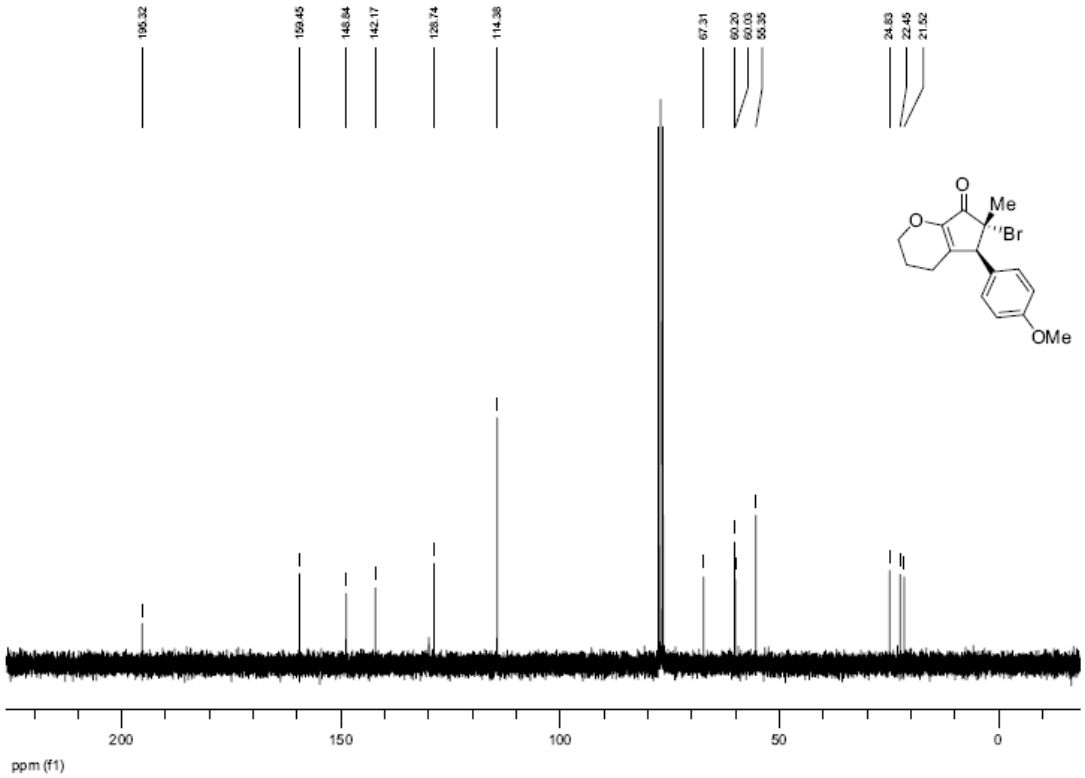
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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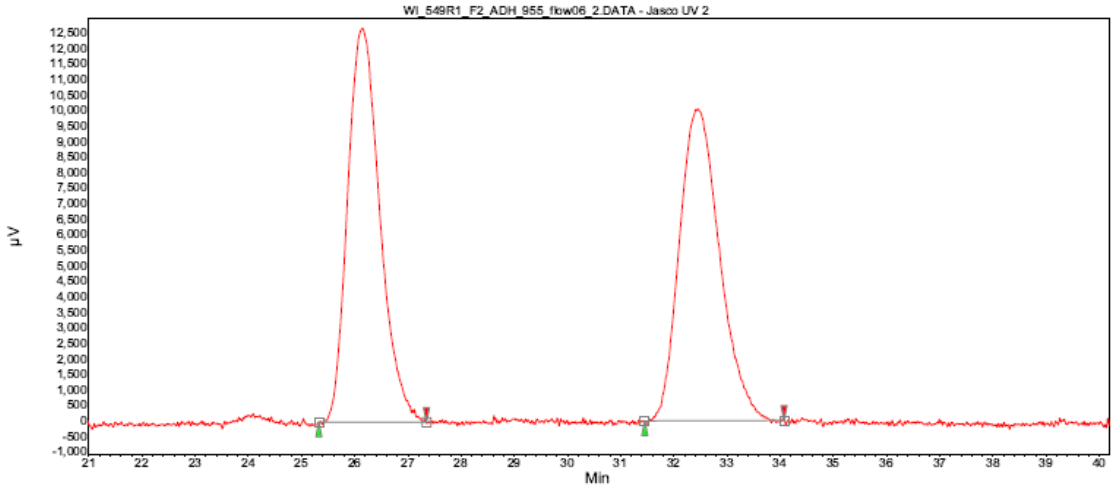
142.17
128.74
114.38
67.31
60.20
60.03
55.35
24.83
22.45
21.52
O
Me
Br
O
OMe
200
150
100
50
0
ppm (f1)

Chromatogram : WI_549R1_F2_ADH_955_flow06_2

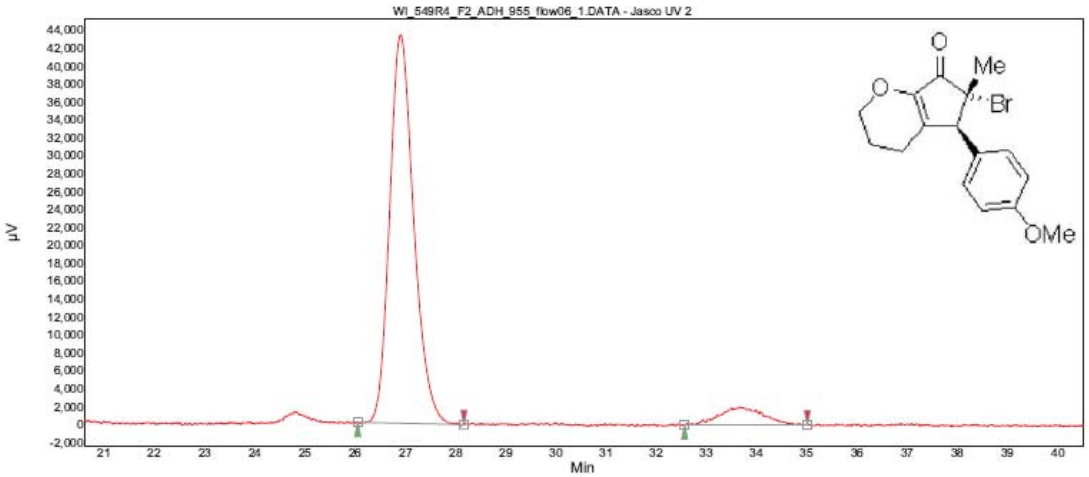
Method: HPLC1_ADH_955_flow06_acq_60
Data file: WI_549R1_F2_ADH_955_flow06_2.DATA
Date: 7/21/2007 12:41:12 PM



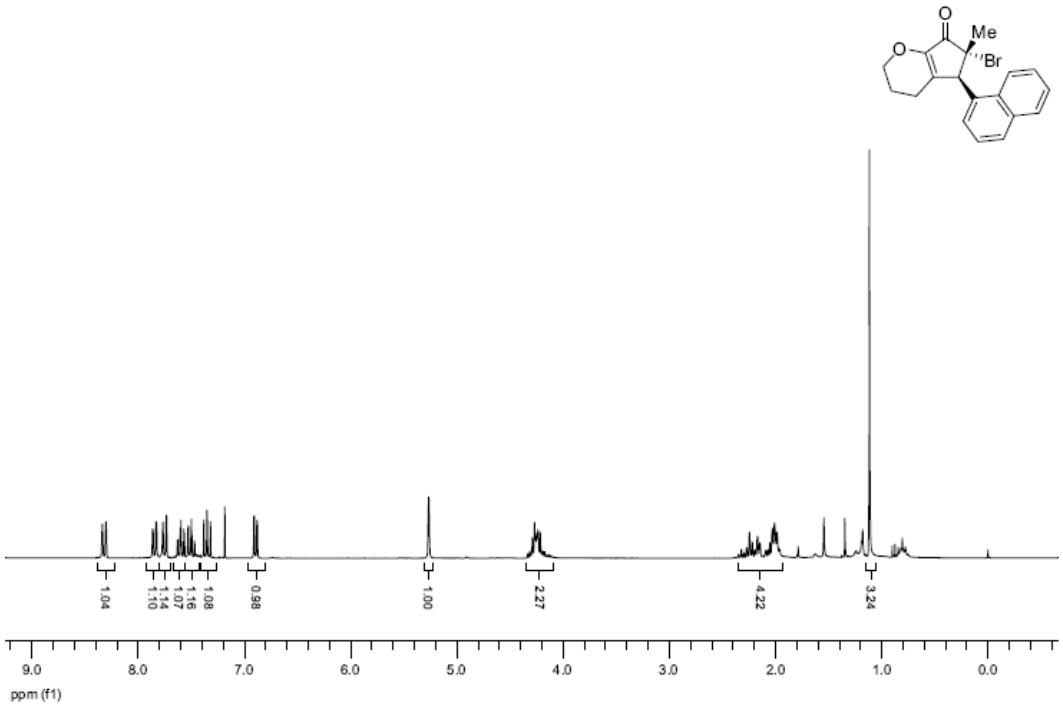
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	25.324	26.133	27.347	50.328
2	31.452	32.425	34.070	49.672
Total				100.000

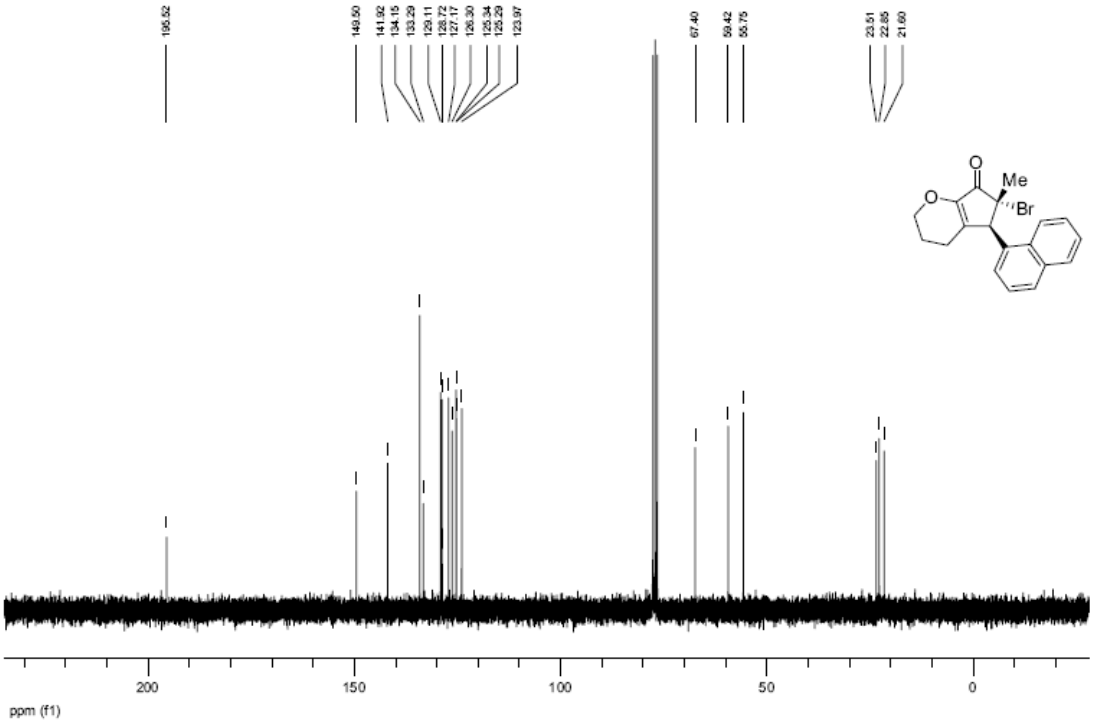
Chromatogram : WI_549R4_F2_ADH_955_flow06_1

Method: HPLC1_ADH_955_flow06_acq_45
Data file: WI_549R4_F2_ADH_955_flow06_1.DATA
Date: 9/2/2007 8:03:52 PM



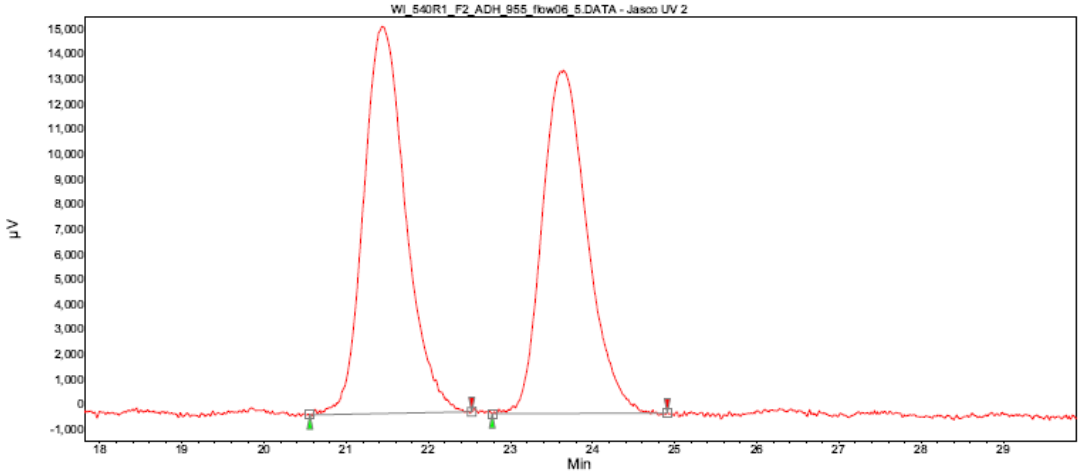
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	26.041	26.900	28.158	92.367
2	32.557	33.650	35.003	7.633
Total				100.000


O
Me
Br
O
1.04
1.14
1.10
1.07
1.16
1.08
0.98
1.00
2.27
4.22
3.24
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


196.52
149.50
141.92
134.15
133.29
129.11
128.72
127.17
126.30
125.34
125.29
123.97
67.40
59.42
55.75
23.51
22.85
21.60
O
Me
Br
O
200
150
100
50
0
ppm (f1)

Chromatogram : WI_540R1_F2_ADH_955_flow06_5

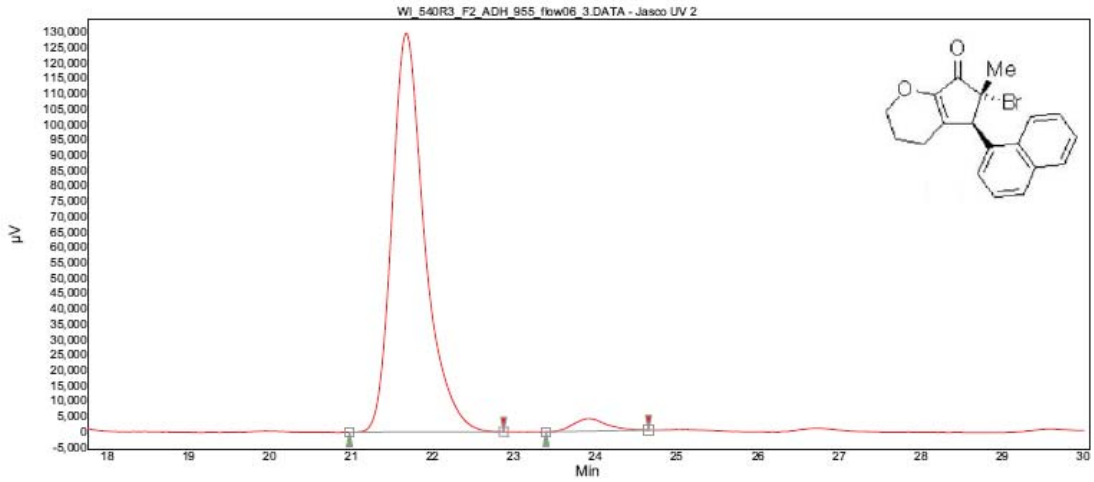
Method: HPLC1_ADH_955_flow06_acq_45
Data file: WI_540R1_F2_ADH_955_flow06_5.DATA
Date: 7/21/2007 8:27:37 AM



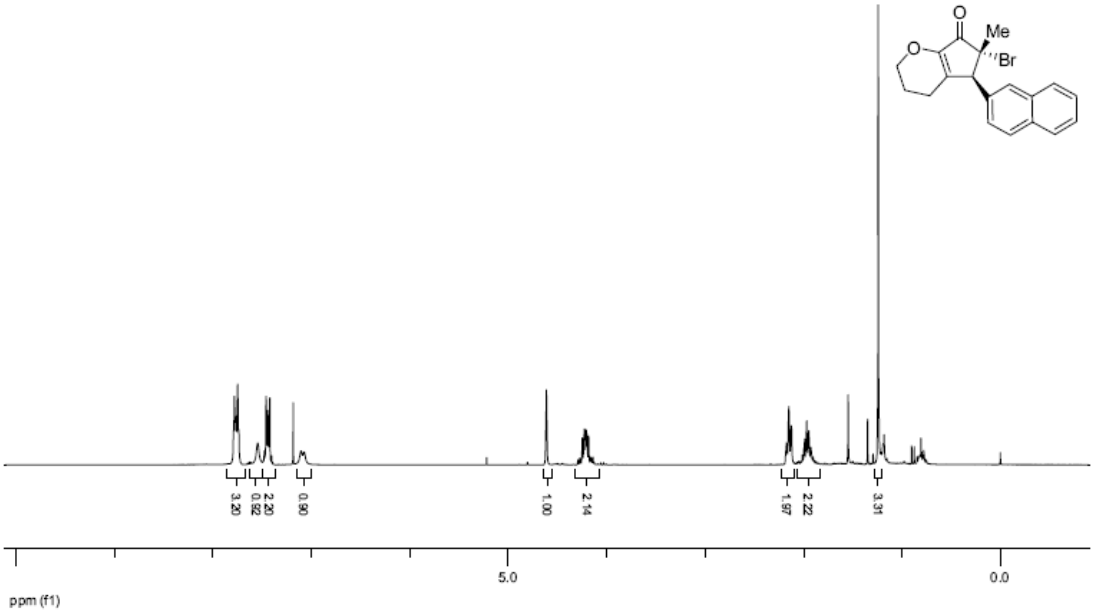
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	20.557	21.433	22.527	51.307
2	22.776	23.617	24.908	48.693
Total				100.000

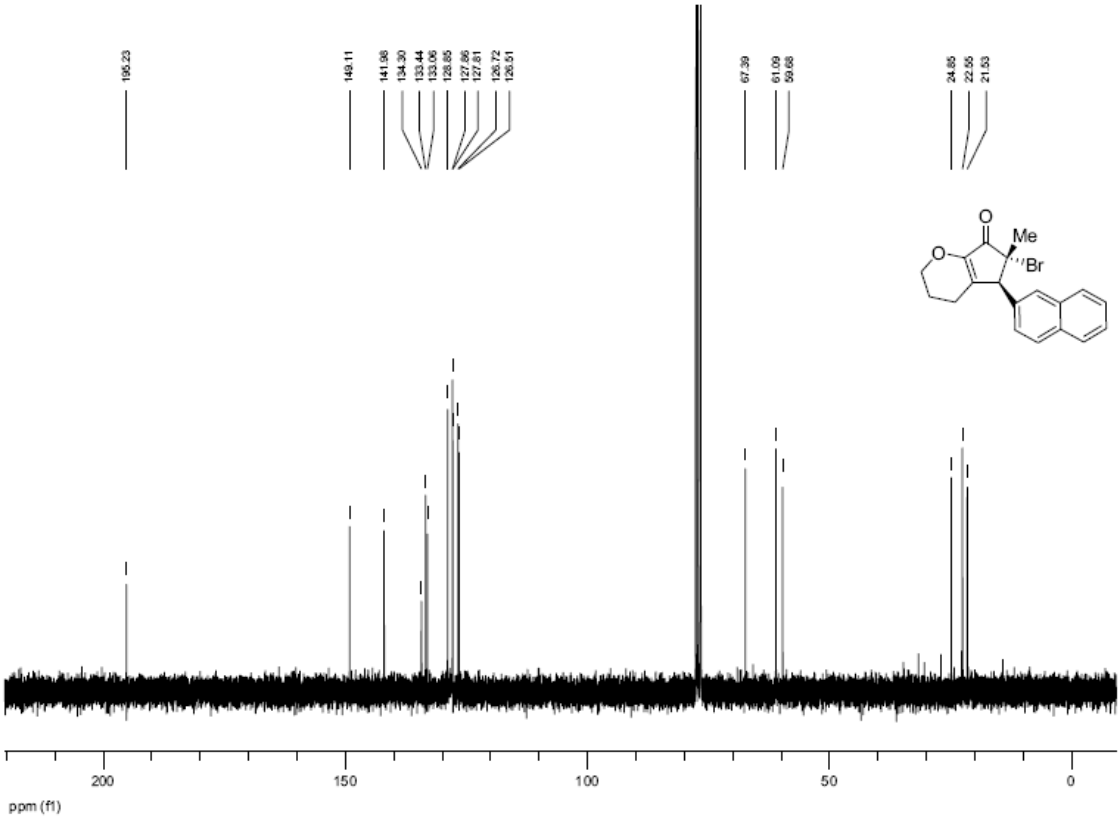
Chromatogram : WI_540R3_F2_ADH_955_flow06_3

Method: HPLC1_ADH_955_flow06_acq_30
Data file: WI_540R3_F2_ADH_955_flow06_3.DATA
Date: 8/21/2007 6:36:27 PM



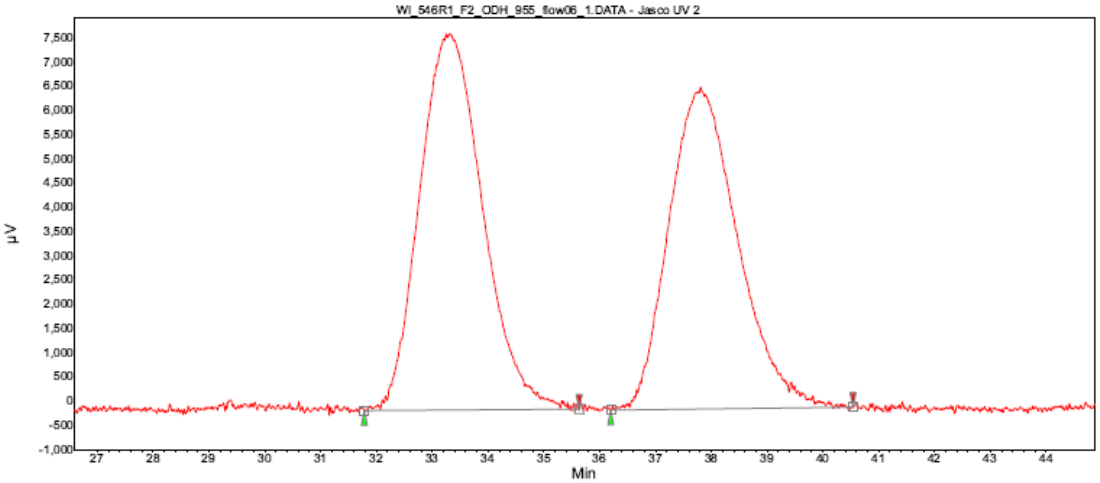
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	20.975	21.675	22.870	96.836
2	23.391	23.908	24.650	3.164
Total				100.000


O
Me
Br
O
3.20
0.92
2.20
0.90
1.00
2.14
1.97
2.22
3.31
5.0
0.0
ppm (f1)


195.23
149.11
141.98
134.30
133.44
133.06
128.85
127.86
127.81
126.72
126.51
67.39
61.09
59.68
24.85
22.55
21.53
O
Me
Br
O
200
150
100
50
0
ppm (f1)

Chromatogram : WI_546R1_F2_ODH_955_flow06_1

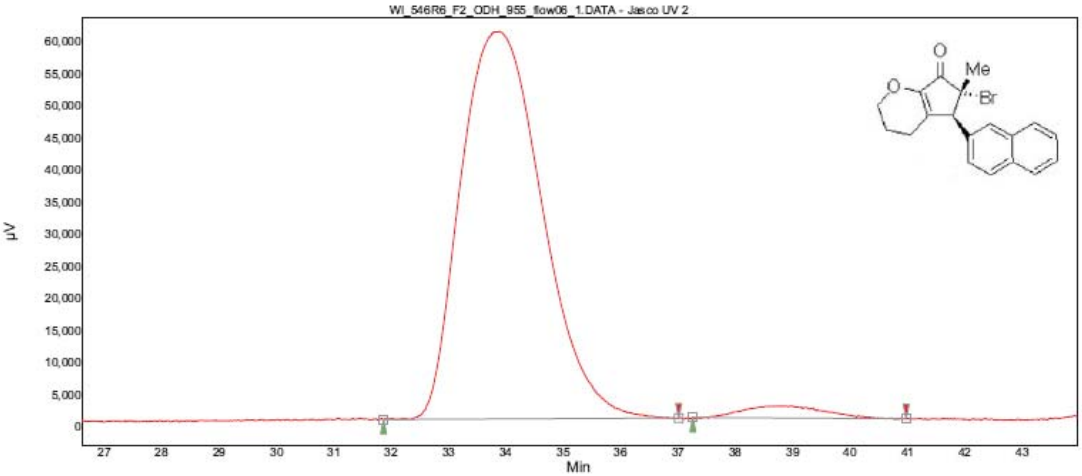
Method: HPLC1_ODH_955_flow06_acq_45
Data file: WI_546R1_F2_ODH_955_flow06_1.DATA
Date: 7/21/2007 3:26:18 AM



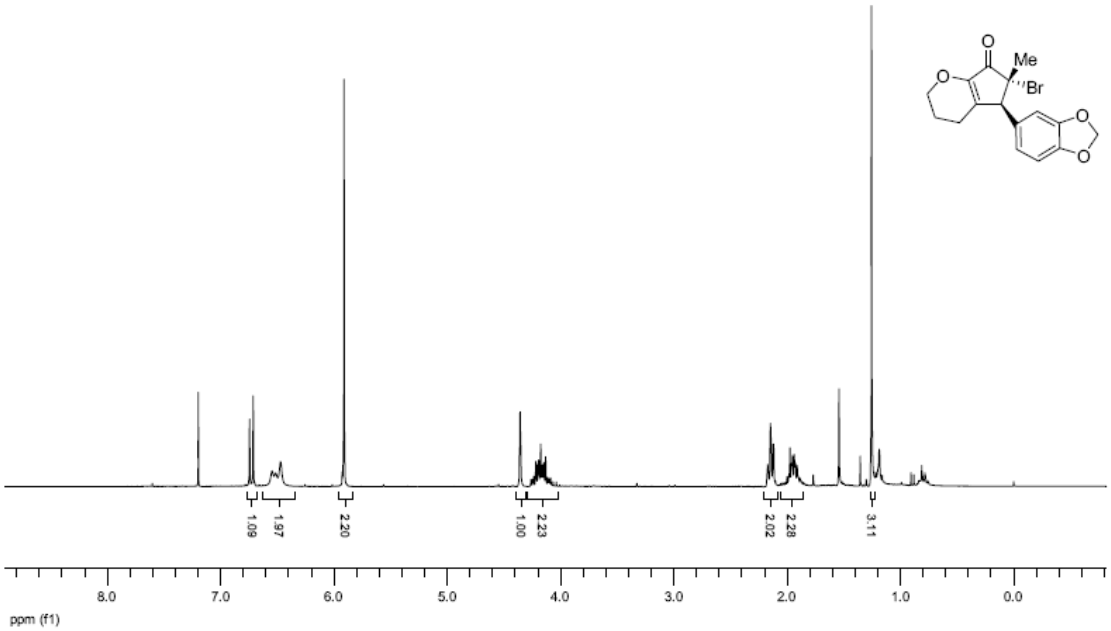
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	31.781	33.325	35.631	51.774
2	36.198	37.808	40.538	48.226
Total				100.000

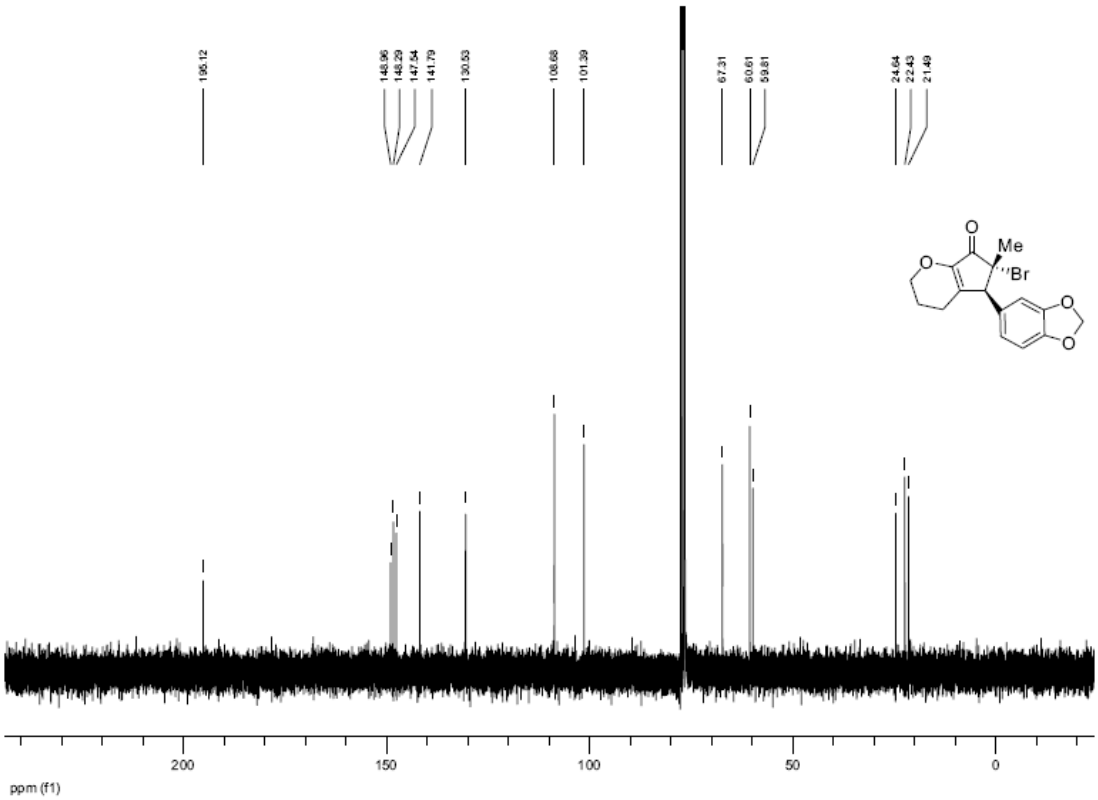
Chromatogram : WI_546R6_F2_ODH_955_flow06_1

Method: HPLC1_ODH_955_flow06_acq_60
Data file: WI_546R6_F2_ODH_955_flow06_1.DATA
Date: 8/16/2007 8:07:29 PM



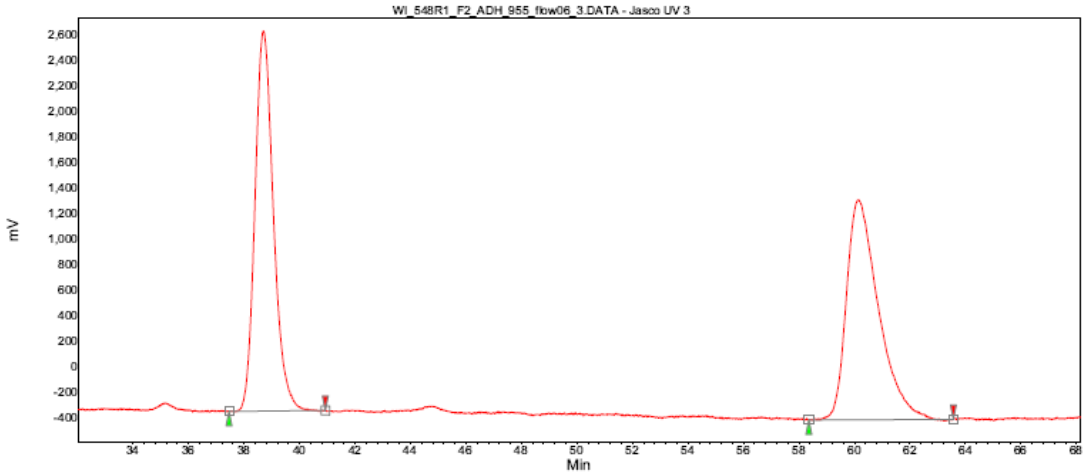
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	31.860	33.875	37.004	96.997
2	37.252	38.875	40.971	3.003
Total				100.000


Me
Br
1.09
1.97
2.20
1.00
2.23
2.02
2.28
3.11
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


195.12
148.96
148.29
147.54
141.79
130.53
108.68
101.39
67.31
60.61
59.81
24.64
22.43
21.49
Me
Br
200
150
100
50
0
ppm (f1)

Chromatogram : WI_548R1_F2_ADH_955_flow06_3

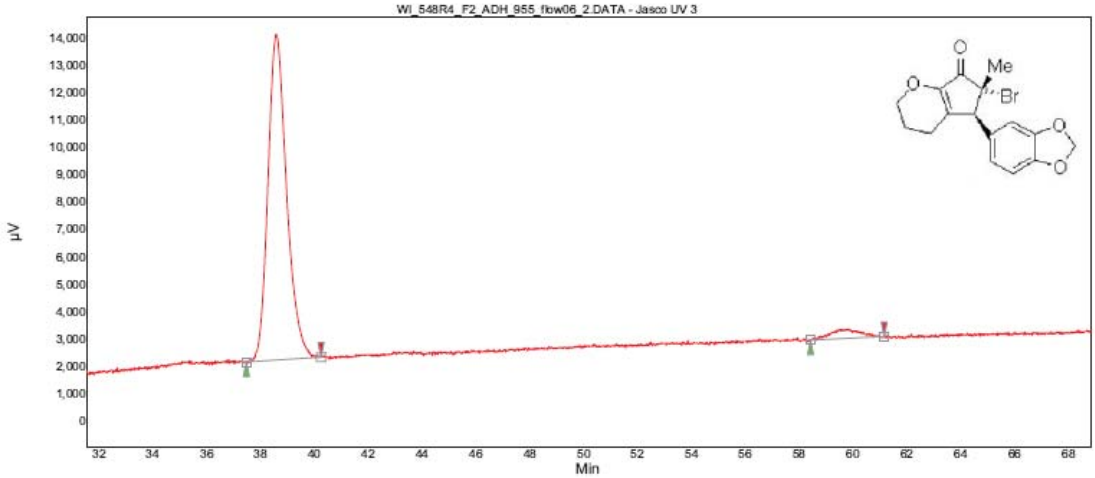
Method: HPLC2_ADH_955_flow06_acq70
Data file: WI_548R1_F2_ADH_955_flow06_3.DATA
Date: 7/24/2007 9:41:43 PM



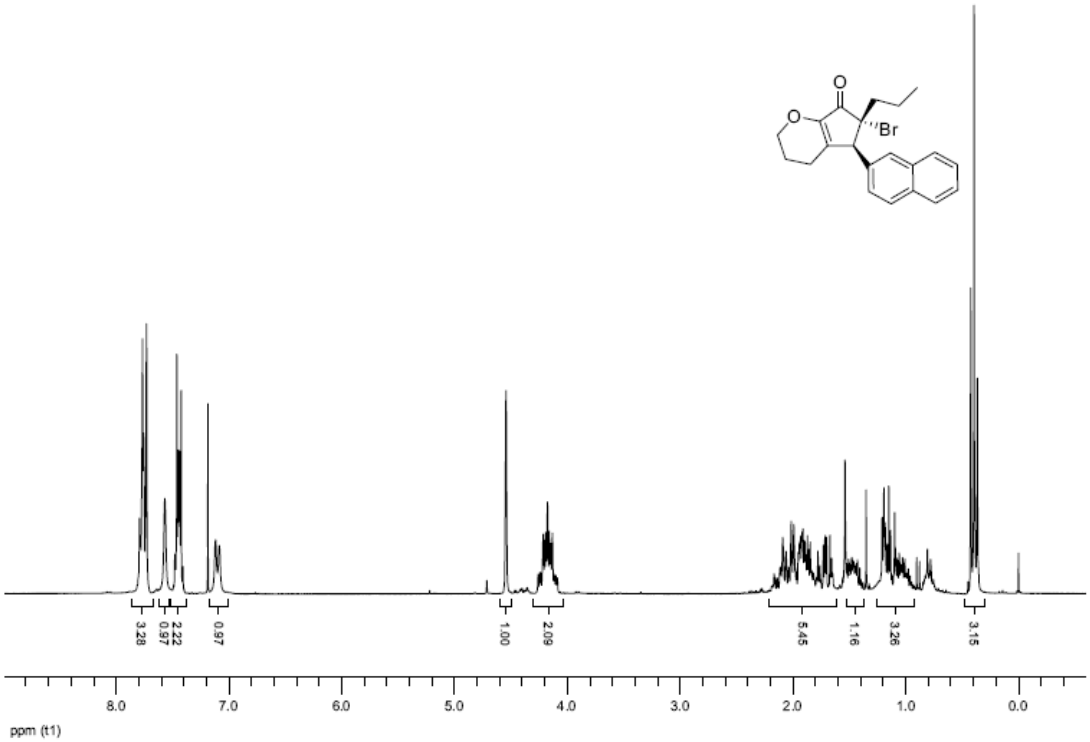
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	37.459	38.692	40.930	49.946
2	58.357	60.133	63.564	50.054
Total				100.000

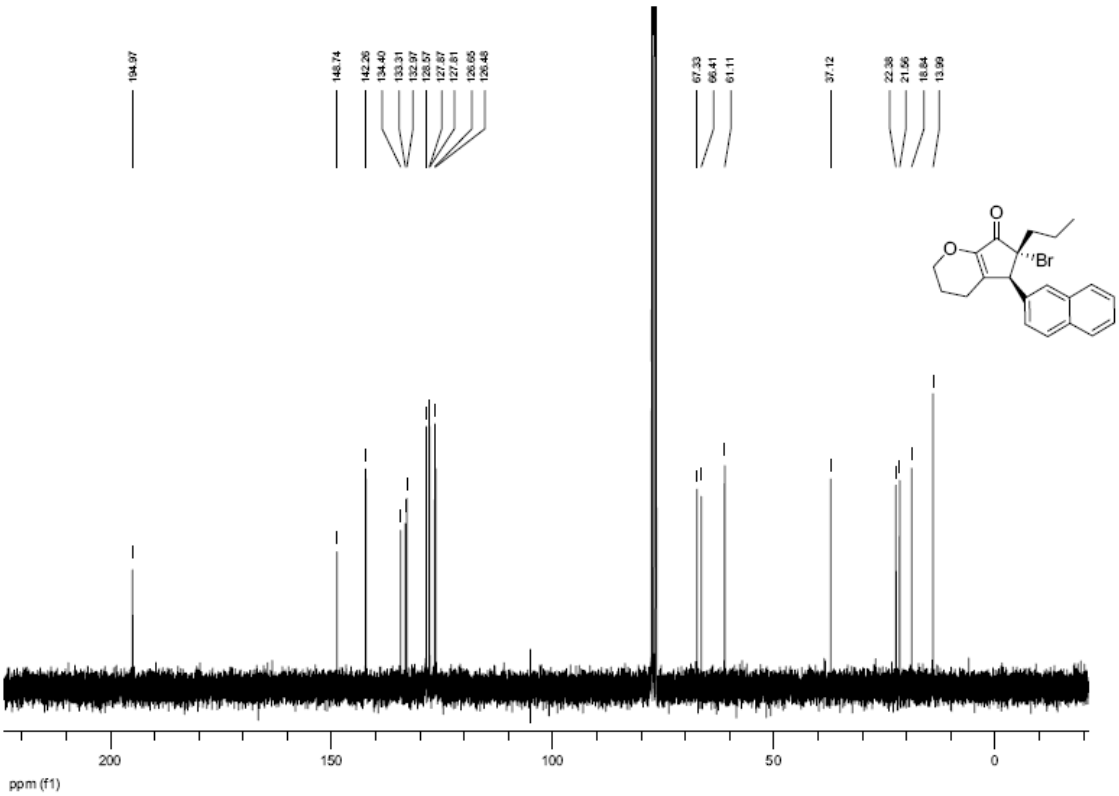
Chromatogram : WI_548R4_F2_ADH_955_flow06_2

Method: HPLC1_ADH_955_flow06_acq_75
Data file: WI_548R4_F2_ADH_955_flow06_2.DATA
Date: 9/3/2007 10:11:09 AM



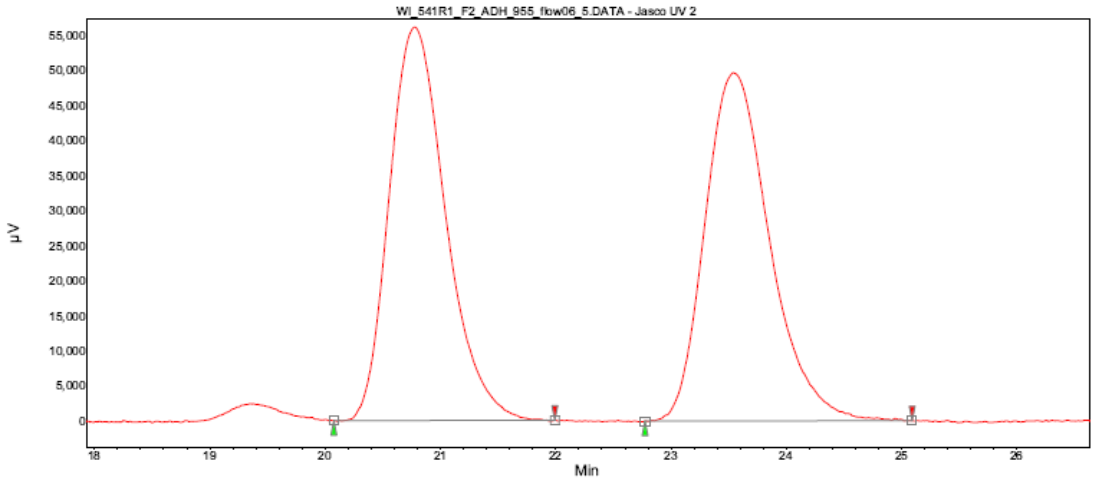
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	37.463	38.575	40.235	95.760
2	58.407	59.475	61.140	4.240
Total				100.000


O
O
Br
3.28
0.97
2.22
0.97
1.00
2.09
5.45
1.16
3.26
3.15
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


194.97
148.74
142.26
134.40
133.31
132.97
128.57
127.87
127.51
126.65
126.48
67.33
66.41
61.11
37.12
22.38
21.56
18.84
13.99
O
O
Br
200
150
100
50
0
ppm (f1)

Chromatogram : WI_541R1_F2_ADH_955_flow06_5

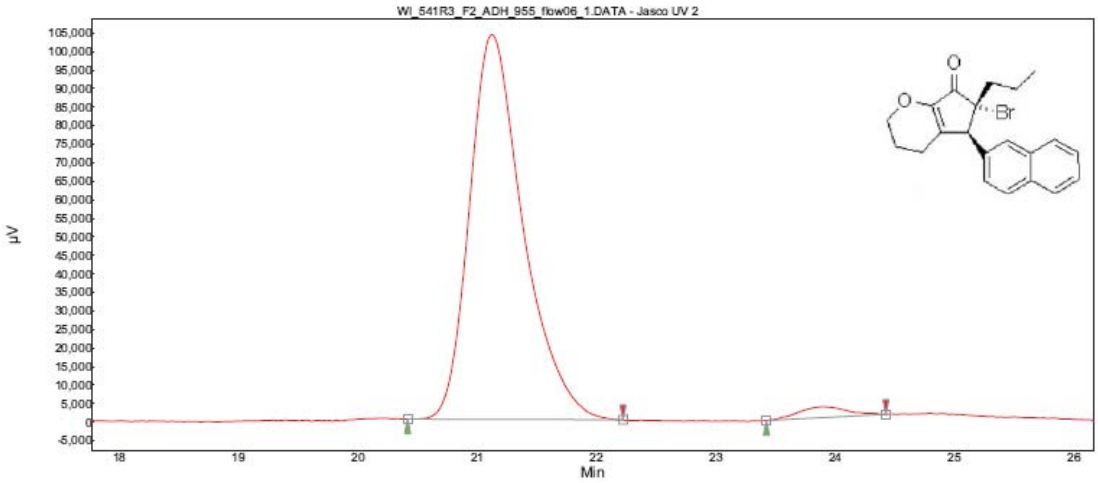
Method: HPLC1_ADH_955_flow06_acq_45
Data file: WI_541R1_F2_ADH_955_flow06_5.DATA
Date: 7/21/2007 9:15:20 AM



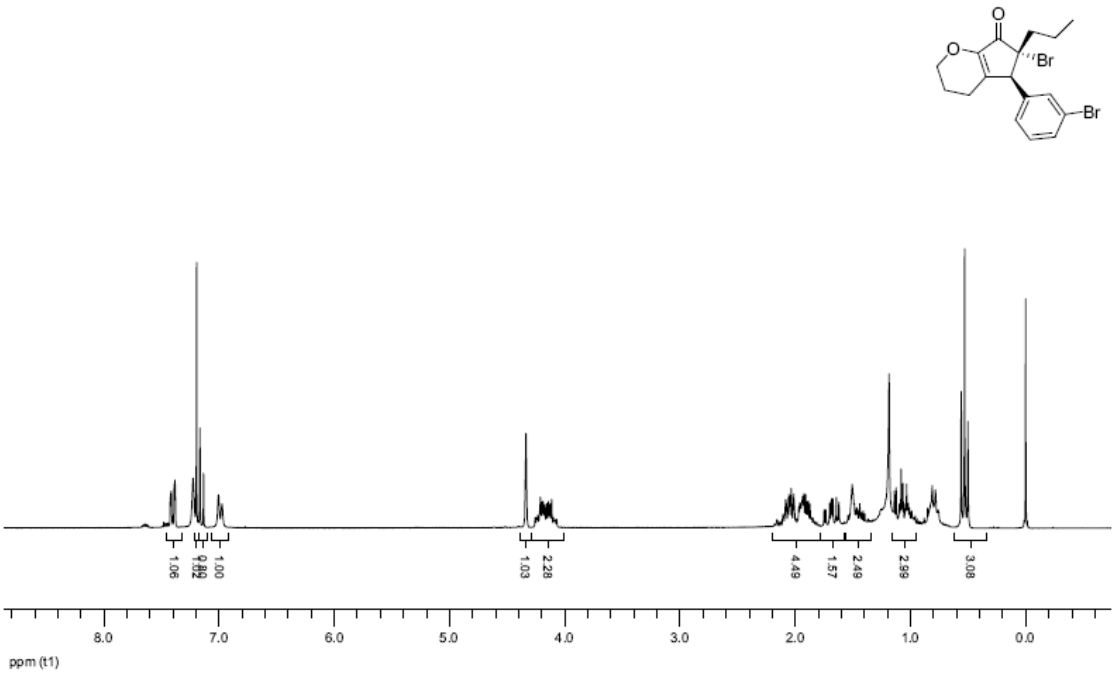
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	20.075	20.775	21.992	49.580
2	22.774	23.542	25.091	50.420
Total				100.000

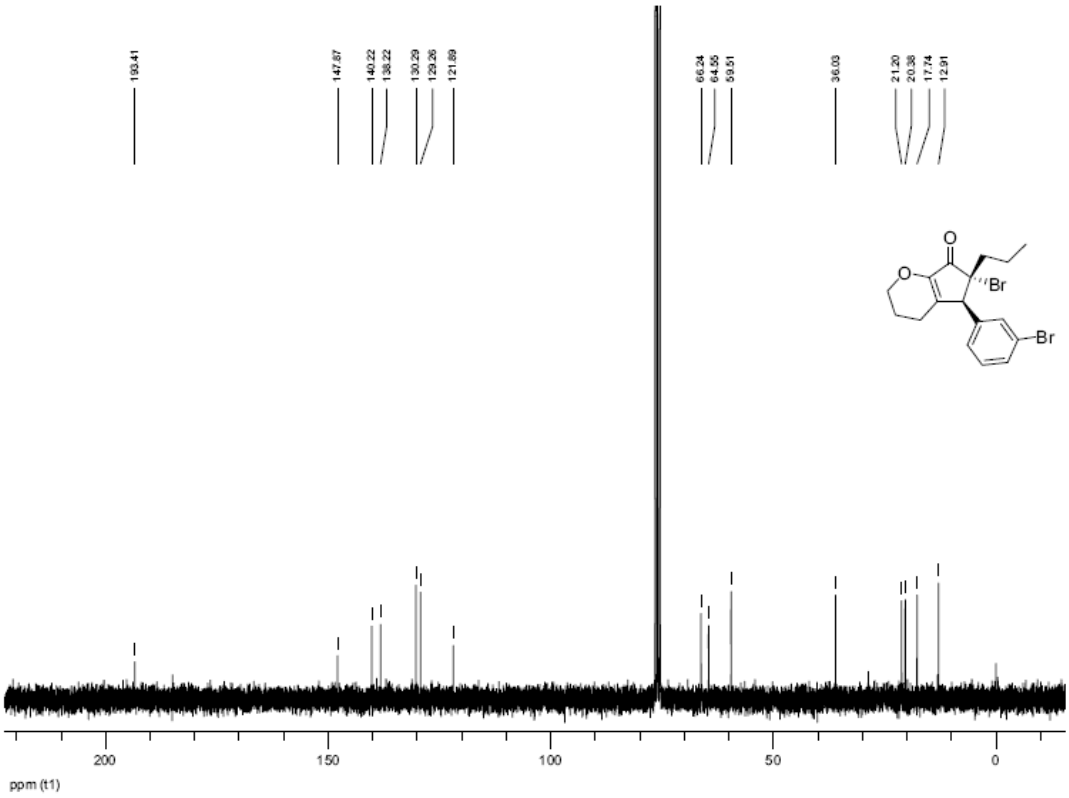
Chromatogram : WI_541R3_F2_ADH_955_flow06_1

Method: HPLC1_ADH_955_flow06_acq_30
Data file: WI_541R3_F2_ADH_955_flow06_1.DATA
Date: 8/17/2007 2:13:40 AM



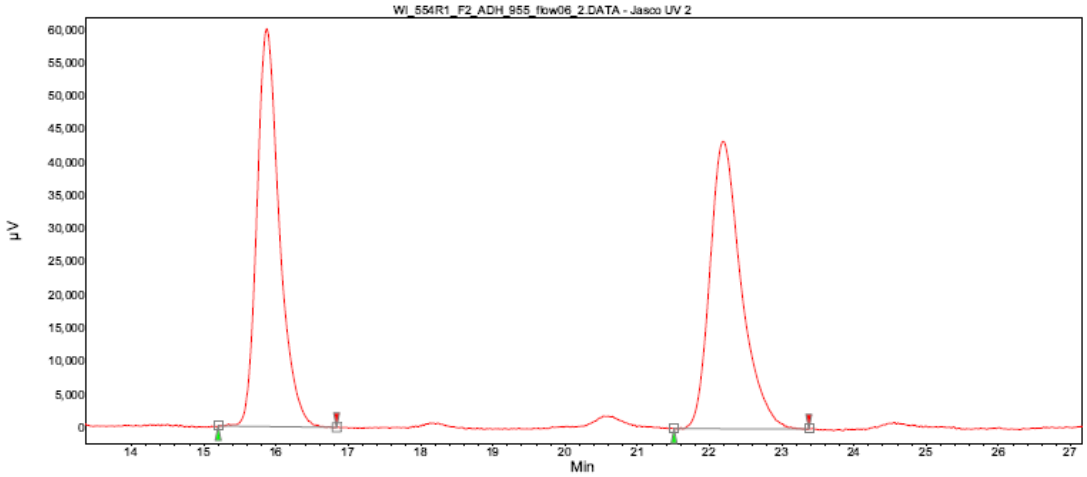
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	20.413	21.125	22.220	97.510
2	23.421	23.875	24.423	2.490
Total				100.000


O
O
Br
Br
1.06
1.00
1.03
2.28
4.49
1.57
2.49
2.99
3.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


193.41
147.67
140.22
138.22
130.29
129.26
121.89
66.24
64.55
59.51
36.03
21.20
20.38
17.74
12.91
O
O
Br
Br
200
150
100
50
0
ppm (t1)

Chromatogram : WI_554R1_F2_ADH_955_flow06_2

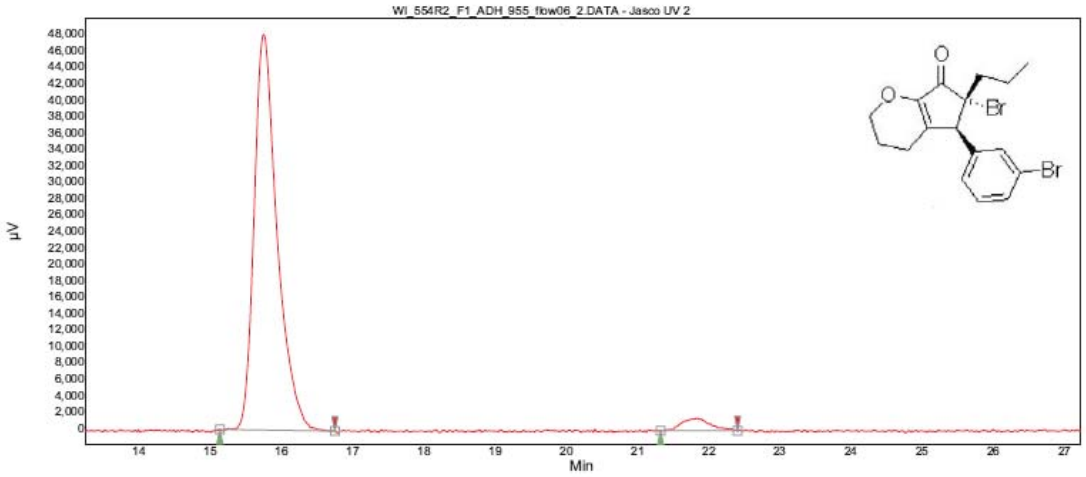
Method: HPLC1_ADH_955_flow06_acq_60
Data file: WI_554R1_F2_ADH_955_flow06_2.DATA
Date: 9/4/2007 10:24:55 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	15.199	15.867	16.837	49.865
2	21.509	22.192	23.375	50.135
Total				100.000

Chromatogram : WI_554R2_F1_ADH_955_flow06_2

Method: HPLC1_ADH_955_flow06_acq_30
Data file: WI_554R2_F1_ADH_955_flow06_2.DATA
Date: 9/10/2007 1:13:15 PM



Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	15.125	15.742	16.742	96.234
2	21.319	21.825	22.402	3.766
Total				100.000