

# **Highly enantioselective cascade synthesis of spiropyrazolones**

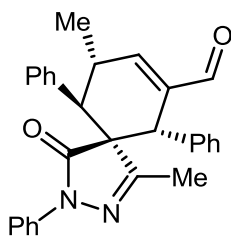
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Ramon Rios<sup>a,c\*</sup>**

## **Supporting Information**

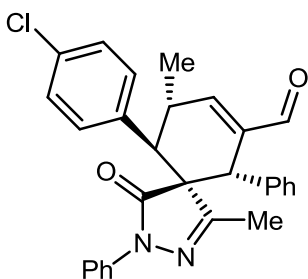
**NMR spectra and HPLC traces**

## General methods.

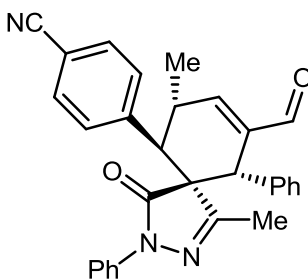
Chemicals and solvents were either purchased *puriss p.A.* from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (25 g),  $\text{Ce}(\text{SO}_4)_2 \cdot \text{H}_2\text{O}$  (10 g), conc.  $\text{H}_2\text{SO}_4$  (60 mL), and  $\text{H}_2\text{O}$  (940 mL) followed by heating or by treatment with a solution of *p*-anisaldehyde (23 mL), conc.  $\text{H}_2\text{SO}_4$  (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating. Flash chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm),  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on Varian AS 400. Chemical shifts are given in ppm relative to tetramethylsilane (TMS) and the coupling constants *J* are given in Hz. The spectra were recorded in  $\text{CDCl}_3$  as solvent at room temperature. TMS served as internal standard ( $\delta = 0$  ppm) for  $^1\text{H}$  NMR,  $\text{CDCl}_3$  was used as internal standard ( $\delta = 77.0$  ppm) for  $^{13}\text{C}$  NMR. High-resolution mass spectra were recorded on a Bruker MicroTOF spectrometer.



**7a:** White powder.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 0.95 (s, 3H), 1.21-1.19 (d,  $J = 7.2$  Hz, 3H), 3.09-3.07 (d,  $J = 10.0$  Hz, 1H), 3.53-3.48 (m, 1H), 4.17 (s, 1H), 7.40-7.08 (m, 14H), 7.77-7.75 (d,  $J = 8$  Hz, 2H), 9.51 (s, 1H). **IR** ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 580, 638, 676, 694, 756, 798, 828, 874, 893, 921, 1017, 1122, 1163, 1282, 1374, 1446, 1485, 1494, 1512, 1599, 1690, 2925, 3020.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 15.9, 18.6, 34.8, 45.4, 47.2, 60.5, 119.5, 125.5, 127.8, 128.1, 128.4, 128.8, 129.0, 129.5, 131.9, 137.4, 137.9, 138.3, 138.4, 156.1, 161.6, 174.3, 192.5. **HRMS (ESI):** calcd. for  $[\text{M}+\text{Na}]^+$  ( $\text{C}_{29}\text{H}_{26}\text{N}_2\text{NaO}_2$ ) requires 457.1886, found 457.1904. **HPLC** (Chiralpak IA, *n*-hexane: *i*-PrOH = 95:5,  $\lambda = 254$  nm, 1.0 mL/min):  $t_{\text{R}} = 21.5, 32.8$  min.

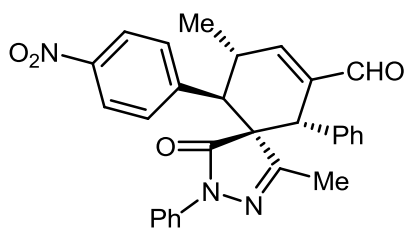


**7b:** White powder.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 0.95 (s, 3H), 1.20-1.18 (d,  $J = 7.2$  Hz, 3H), 3.08-3.06 (d,  $J = 10.4$  Hz, 1H), 3.48-3.43 (m, 1H), 4.17 (s, 1H), 7.41-7.03 (m, 13H), 7.77-7.75 (d,  $J = 7.6$  Hz, 2H), 9.50 (s, 1H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 15.9, 18.5, 34.7, 45.4, 46.6, 60.4, 119.4, 120.7, 125.6, 127.7, 128.5, 128.8, 129.1, 129.2, 129.6, 131.9, 134.0, 137.1, 137.4, 137.8, 138.2, 155.6, 161.4, 174.1, 192.4. **IR** ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 625, 688, 698, 758, 796, 818, 867, 891, 921, 1010, 1120, 1161, 1276, 1345, 1444, 1478, 1487, 1517, 1584, 1686, 2925, 3010. **HRMS (ESI):** calcd. for  $[\text{M}+\text{Na}]^+$  ( $\text{C}_{29}\text{H}_{25}\text{ClN}_2\text{NaO}_2$ ) requires 491.1497, found 491.1492. **HPLC** (Chiralpak IA, *n*-hexane: *i*-PrOH = 90:10,  $\lambda = 254$  nm, 1.0 mL/min):  $t_{\text{R}} = 10.1, 13.2$  min.

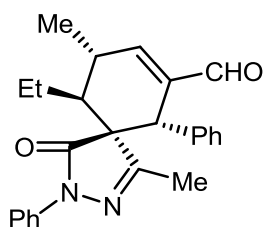


**7c:** White powder.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 0.94 (s, 3H), 1.20-1.19 (d,  $J = 7.2$  Hz, 3H), 3.15-3.18 (d,  $J = 10.4$  Hz, 1H), 3.52-3.47 (m, 1H), 4.20 (s, 1H), 7.66-7.14 (m, 13H), 7.76-7.74 (d,  $J = 8.0$  Hz, 2H), 9.51 (s, 1H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 15.9, 18.6, 34.5, 45.3, 47.4, 60.3, 112.4, 119.4, 120.9, 125.8, 126.0, 127.6, 128.7, 129.4, 129.7, 130.3, 131.9, 132.7, 132.8, 133.7, 137.4, 137.9, 138.5, 144.2, 146.7, 148.3, 154.9, 160.9, 173.8, 192.3. **IR** ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 555, 579, 628, 670, 691, 756, 793, 818, 872, 893, 921, 1017, 1091, 1128, 1160, 1292, 1391, 1452, 1485, 1494, 1513, 1597, 1691, 2228, 2922. **Mp:** 104-108°C. **HRMS (ESI):**

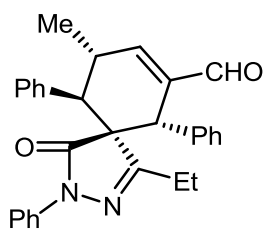
calcd. for  $[M+H]^+$  ( $C_{30}H_{26}N_3O_2$ ) requires 460.2020, found 460.2034. **HPLC** (Chiralpak IC, *n*-hexane: *i*-PrOH = 90:10,  $\lambda$  = 220 nm, 1.0 mL/min):  $t_R$  = 11.7, 16.7 min.



**7d:** Yellow oil.  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 0.95 (s, 3H), 1.20 (d,  $J$ =7.2 Hz, 3H), 3.23 (d,  $J$ =10.4 Hz, 1H), 3.46-3.57 (m, 1H), 4.21 (s, 1H), 7.10-7.50 (m, 6H), 7.70-7.77 (m, 4H), 8.03-8.07 (m, 2H), 8.07-8.11 (m, 1H), 8.18-8.23 (m, 2H), 9.50 (s, 1H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 15.6, 18.3, 34.3, 45.0, 46.9, 60.1, 119.1, 120.6, 123.8, 124.0, 125.8, 127.4, 128.4, 128.4, 128.7, 128.9, 129.0, 129.5, 129.7, 130.1, 131.7, 146.0, 147.6, 154.5, 160.7, 170.1, 173.5, 192.0. **IR** ( $\nu_{max}$ ,  $cm^{-1}$ ): 694, 756, 798, 896, 931, 1132, 1282, 1358, 1372, 1438, 1476, 1492, 1512, 1532, 1602, 1680, 2954. **HRMS (ESI):** calcd. for  $[M+H]^+$  ( $C_{29}H_{26}N_3O_4$ ) requires 480.1918, found 480.1919. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH = 90:10,  $\lambda$ =254 nm, 1.0 mL/min):  $t_R$  = 14.0, 19.4 min.  $[\alpha]_D^{25}$  = -9.5 ( $c$ =1.0,  $CHCl_3$ , ee > 99%, (*R*-Cat.).

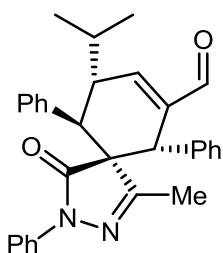


**7e:** Yellow oil.  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 0.85 (t,  $J$ =7.6 Hz, 3H), 1.12 (s, 3H), 1.46 (d,  $J$ =7.3 Hz, 3H), 1.97-2.21 (m, 3H), 3.10-3.21 (m, 1H), 4.00 (s, 1H), 7.00-7.05 (m, 2H), 7.15-7.20 (m, 1H), 7.26-7.42 (m, 6H), 7.85-7.90 (m, 2H), 9.43 (s, 1H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 11.4, 15.5, 19.3, 23.0, 32.4, 39.1, 44.9, 59.9, 118.8, 125.0, 127.6, 128.0, 128.8, 131.7, 131.7, 136.8, 138.3, 156.5, 162.4, 192.2. **IR** ( $\nu_{max}$ ,  $cm^{-1}$ ): 576, 638, 676, 828, 874, 899, 921, 1017, 1126, 1161, 1282, 1372, 1441, 1483, 1494, 1512, 1599, 1691, 2925. **HRMS (ESI):** calcd. for  $[M+H]^+$  ( $C_{25}H_{27}N_2O_2$ ) requires 387.2067, found 387.2067. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH = 90:10,  $\lambda$ =254 nm, 1.0 mL/min):  $t_R$  = 6.7, 7.6 min.  $[\alpha]_D^{25}$  = -111.1 ( $c$ =0.6,  $CHCl_3$ , ee > 99%, (*S*-Cat.).

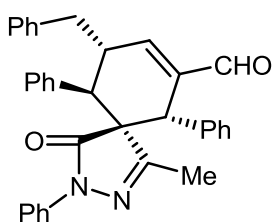


**7f:** Yellow oil.  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 9.48 (s, 1H), 8.10-7.00 (m, 16 H), 4.14 (s, 1H), 3.51-3.43 (m, 1H), 3.09 (d,  $J$ =10.4 Hz, 1H), 1.18 (d,  $J$ =7.3 Hz, 3H), 0.95 (q,  $J$ =7.1 Hz, 2H), 0.57 (t,  $J$ =7.1 Hz, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 13.6,

18.3, 22.4, 34.8, 45.3, 47.1, 60.5, 119.3, 120.7, 125.1, 125.4, 126.8, 127.6, 127.8, 128.1, 128.4, 128.8, 128.9, 129.1, 130.1, 131.6, 133.4, 138.3, 142.2, 152.3, 156.0. 165.3, 170.3, 174.3, 192.4. **IR** ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 580, 801, 838, 877, 893, 921, 1021, 1128, 1161, 1282, 1374, 1446, 1485, 1494, 1502, 1589, 1689, 2925, 3021. **HRMS (ESI)**: calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_2$ ) requires 449.2224, found 449.2217. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH = 90:10,  $\lambda=254$  nm, 1.0 mL/min):  $t_{\text{R}} = 6.5, 9.0$  min.  $[\alpha]_{\text{D}}^{25} = 4.3$  ( $c=1.5$ ,  $\text{CHCl}_3$ , ee > 99%, (*S*)-Cat.).

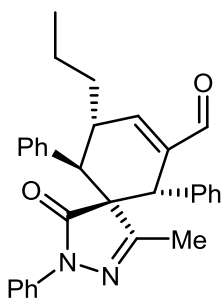


**7i**: White powder.  **$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm)**: 0.95 (s, 3H), 1.09-1.07 (d,  $J = 6.8$  Hz, 3H), 1.17-1.15 (d,  $J = 7.2$  Hz, 3H), 1.75-1.66 (m, 1H), 3.39-3.36 (d,  $J = 10.8$  Hz, 1H) 3.51-3.47 (m, 1H), 4.15 (s, 1H), 7.40-7.09 (m, 14H), 7.76-7.74 (d,  $J = 7.6$  Hz, 2H), 9.54 (s, 1H).  **$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm)**: 15.9, 17.3, 21.7, 31.1, 42.8, 44.7, 45.3, 60.7, 119.5, 120.6, 125.4, 125.6, 127.4, 127.5, 128.1, 128.3, 128.6, 128.7, 128.8, 129.0, 129.3, 131.9, 137.9, 138.4, 138.8, 139.7, 151.9, 161.7, 174.5, 192.4. **IR** ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 576, 648, 690, 696, 752, 867, 921, 1013, 1112, 1156, 1281, 1379, 1456, 1484, 1513, 1594, 1692, 2929, 3034. **HRMS (ESI)**: calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{31}\text{H}_{31}\text{N}_2\text{O}_2$ ) requires 463.2380, found 463.2384. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH= 91:9,  $\lambda= 254$  nm, 1.0 mL/min):  $t_{\text{R}}= 5.8, 8.9$  min.

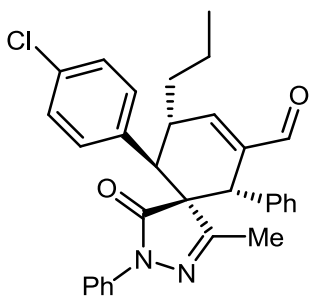


**7j**: Yellow oil.  **$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm)** = 0.95 (s, 3H), 2.56 (dd,  $J_1=8.2$  Hz,  $J_2=13.7$  Hz, 1H), 3.06 (dd,  $J_1=4.0$  Hz,  $J_2=13.7$  Hz, 1H), 3.27 (d,  $J=10.6$  Hz, 1H), 3.80-3.88 (m, 1H), 4.08 (s, 1H), 6.90-7.50 (m, 15H), 7.58-7.63 (m, 1H), 7.69-7.64 (m, 2H), 8.09-8.14 (m, 3H), 9.45 (s, 1H).  **$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm)** = 15.2, 37.3, 40.9, 43.6, 44.8, 60.6, 119.3, 120.4, 125.2, 126.9, 127.6, 128.0, 128.1, 128.3, 128.4, 128.6, 128.6, 128.7, 128.8, 128.9, 129.0, 129.4, 129.5, 129.7, 130.2, 131.6, 133.6, 137.7, 137.8, 138.1, 153.3, 161.3, 171.3, 173.9, 192.1. **IR** ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 580, 638, 676, 883, 1027, 1156, 1279, 1324, 1443, 1492, 1500, 1605, 1694, 2929, 3034. **HRMS (ESI)**: calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{35}\text{H}_{31}\text{N}_2\text{O}_2$ ) requires 511.2380, found 511.2378. **HPLC** (Chiralpak IB, *n*-hexane:

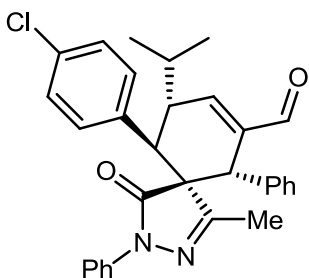
*i*-PrOH = 90:10,  $\lambda$ =220 nm, 1.0 mL/min):  $t_R$  = 7.6, 22.0 min.  $[\alpha]_D^{25}$  = 18.0 ( $c$ =1.0, CHCl<sub>3</sub>, ee = 98%, (*S*)-Cat.).



**7k:** White powder. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm): 0.88-0.94 (m, 7H), 0.95 (s, 3H), 3.23-3.20 (d,  $J$  = 10.8 Hz, 1H), 3.48-3.42 (m, 1H), 4.15 (s, 1H), 7.45-7.078 (m, 14H), 7.75-7.73 (d,  $J$  = 7.6 Hz, 2H), 9.52 (s, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm): 14.4, 15.9, 19.7, 22.9, 39.0, 45.0, 45.3, 60.6, 119.5, 120.5, 125.4, 125.8, 127.8, 128.1, 128.3, 128.4, 128.7, 128.8, 129.0, 129.2, 129.5, 131.9, 137.9, 138.0, 138.4, 138.6, 154.5, 161.7, 174.3, 192.5. IR ( $\nu_{max}$ , cm<sup>-1</sup>): 578, 641, 667, 889, 1034, 1162, 1280, 1327, 1448, 1498, 1502, 1608, 1692, 2930, 3031. HRMS (ESI): calcd. for [M+H]<sup>+</sup> (C<sub>31</sub>H<sub>31</sub>N<sub>2</sub>O<sub>2</sub>) requires 463.2380, found 463.2382. HPLC (Chiralpak IC, *n*-hexane: *i*-PrOH = 90:10,  $\lambda$  = 254 nm, 1.0 mL/min):  $t_R$  = 13.8, 18.7 min.

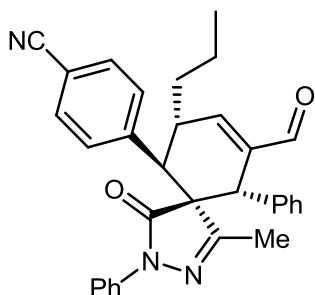


**7m:** White scum. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm): 0.93-0.86 (m, 7H), 0.95 (s, 3H), 3.22-3.19 (d,  $J$  = 10.4 Hz, 1H), 3.43-3.37 (m, 1H), 4.15 (s, 1H), 7.52-7.00 (m, 13H), 7.76-7.74 (d,  $J$  = 7.6 Hz, 2H), 9.51 (s, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm): 13.5, 14.4, 19.7, 29.9, 39.0, 44.4, 45.2, 60.5, 119.4, 121.3, 125.3, 126.3, 127.7, 128.2, 128.6, 128.8, 129.0, 129.1, 129.6, 131.1, 131.5, 135.1, 137.0, 137.7, 138.4, 139.5, 145.4, 150.9, 161.4, 174.1, 192.5. IR ( $\nu_{max}$ , cm<sup>-1</sup>): 578, 625, 682, 698, 758, 796, 818, 867, 891, 1120, 1161, 1276, 1345, 1444, 1478, 1485, 1517, 1584, 1686, 2926, 3023. HRMS (ESI): calcd. for [M+H]<sup>+</sup> (C<sub>31</sub>H<sub>30</sub>ClN<sub>2</sub>O<sub>2</sub>) requires 497.1990, found 497.1990. HPLC (Chiralpak IA, *n*-hexane: *i*-PrOH = 90:10,  $\lambda$  = 254 nm, 1.0 mL/min):  $t_R$  = 7.6, 8.7 min.

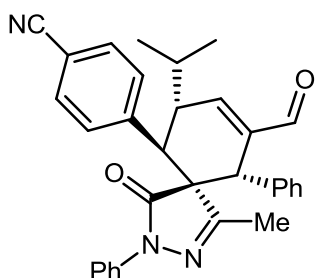


**7n:** White scum. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm): 0.95 (s, 3H), 1.08-1.07 (d,  $J$  = 6.8 Hz, 3H), 1.17-1.15 (d,  $J$  = 7.2 Hz, 3H), 1.67-1.62 (m, 1H), 3.38-3.35 (d,  $J$  = 11.2 Hz, 1H), 3.46-3.42 (m, 1H), 4.15 (s, 1H), 7.41-7.14 (m, 13H), 7.77-7.75 (d,  $J$  = 7.6 Hz, 2H), 9.53 (s, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm): 15.9, 17.3, 21.7, 27.4, 42.3, 44.7, 45.3, 60.6, 119.4, 120.5, 125.6, 127.5, 128.4, 128.8, 129.1,

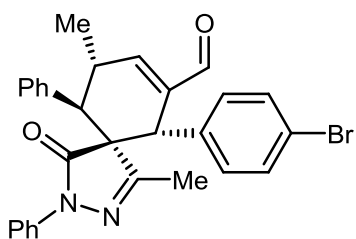
129.6, 131.9, 134.0, 137.0, 137.8, 138.7, 139.6, 151.4, 161.4, 174.2, 192.3. **Mp:** 94-96°C (decomp.). **IR** ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 576, 622, 672, 698, 758, 796, 818, 867, 891, 1113, 1169, 1278, 1355, 1478, 1485, 1517, 1582, 1685, 2925, 3033. **HRMS (ESI):** calcd. for  $[\text{M}+\text{Na}]^+$  ( $\text{C}_{31}\text{H}_{29}\text{ClN}_2\text{NaO}_2$ ) requires 519.1810, found 519.1806. **HPLC** (Chiralpak IA, *n*-hexane: *i*-PrOH= 90:10,  $\lambda$ = 254 nm, 1.0 mL/min):  $t_{\text{R}}$ = 7.0, 7.7 min.



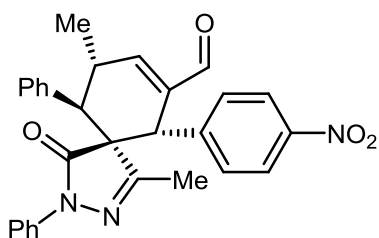
**7o:** White powder.  **$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm):** 0.93-0.86 (m, 7H), 0.95 (s, 3H), 3.31-3.28 (d,  $J$ = 10.4 Hz, 1H), 3.48-3.41 (m, 1H), 4.18 (s, 1H), 7.52-7.12 (m, 13H), 7.74-7.72 (d,  $J$ = 8.0 Hz, 2H), 9.52 (s, 1H).  **$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm):** 14.3, 15.8, 19.7, 31.7, 38.7, 39.8, 45.5, 60.4, 112.4, 119.4, 125.5, 125.8, 127.8, 128.1, 128.3, 128.6, 128.9, 129.0, 129.1, 130.3, 132.8, 133.1, 138.5, 138.7, 139.5, 144.2, 150.5, 153.2, 160.9, 161.7, 174.2, 192.3. **Mp:** 74-77°C (decomp.). **IR** ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 693, 756, 793, 818, 893, 921, 1088, 1118, 1161, 1291, 1391, 1452, 1485, 1494, 1514, 1598, 1699, 2223, 2922, 3030. **HRMS (ESI):** calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{32}\text{H}_{30}\text{N}_3\text{O}_2$ ) requires 488.2333, found 488.2335. **HPLC** (Chiralpak IC, *n*-hexane: *i*-PrOH= 90:10,  $\lambda$ = 254 nm, 1.0 mL/min):  $t_{\text{R}}$ = 17.7, 19.2 min.



**7p:** White scum.  **$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm):** 0.94 (s, 3H), 1.10-1.08 (d,  $J$ = 7.2 Hz, 3H), 1.18-1.16 (d,  $J$ = 6.8 Hz, 3H), 1.72-1.66 (m, 1H), 3.49-3.47 (m, 2H), 4.18 (s, 1H), 7.50-7.14 (m, 13H), 7.74-7.72 (d,  $J$ = 7.6 Hz, 2H), 9.54 (s, 1H).  **$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm):** 17.3, 21.6, 27.6, 31.1, 43.0, 44.4, 45.1, 60.4, 112.3, 118.3, 119.5, 120.3, 125.8, 128.7, 128.9, 129.4, 129.7, 130.9, 131.3, 131.9, 132.1, 133.8, 136.9, 137.6, 138.4, 139.6, 143.5, 144.3, 150.6, 161.0, 173.9, 192.2. **IR** ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 580, 629, 690, 756, , 893, 921, 1017, 1091, 1128, 1160, 1292, 1391, 1452, 1485, 1491, 1517, 1589, 1699, 2221, 2912, 3045. **HRMS (ESI):** calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{32}\text{H}_{30}\text{N}_3\text{O}_2$ ) requires 488.2333, found 488.2328. **HPLC** (Chiralpak IC, *n*-hexane: *i*-PrOH= 90:10,  $\lambda$ = 210 nm, 1.0 mL/min):  $t_{\text{R}}$ = 18.7, 20.5 min.

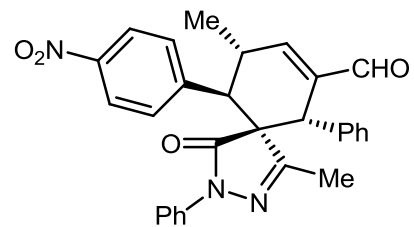


**7q:** White powder.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  (ppm): 1.03 (s, 3H), 1.20-1.18 (d,  $J=7.5$  Hz, 3H), 3.02-2.98 (d,  $J=10.2$  Hz, 1H), 3.53-3.47 (m, 1H), 4.12 (s, 1H), 7.55-7.01 (m, 13H), 7.75-7.73 (d,  $J=8.4$  Hz, 2H), 9.50 (s, 1H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 16.2, 18.6, 34.8, 44.8, 47.2, 60.3, 119.5, 122.5, 125.6, 128.2, 128.3, 129.0, 129.1, 129.4, 132.0, 132.6, 133.5, 137.1, 137.6, 137.8, 138.0, 156.5, 161.1, 174.1, 192.4. **IR** ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 578, 632, 678, 786, 812, 847, 893, 1113, 1169, 1278, 1346, 1468, 1489, 1522, 1591, 1695, 2935, 3043 **HRMS** (ESI): calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{29}\text{H}_{26}\text{BrN}_2\text{O}_2$ ) requires 513.1172, found 513.1172. **HPLC** (Chiralpak IA, *n*-hexane: *i*-PrOH= 90:10,  $\lambda=254$  nm, 1.0 mL/min):  $t_{\text{R}}=15.9, 20.4$  min.



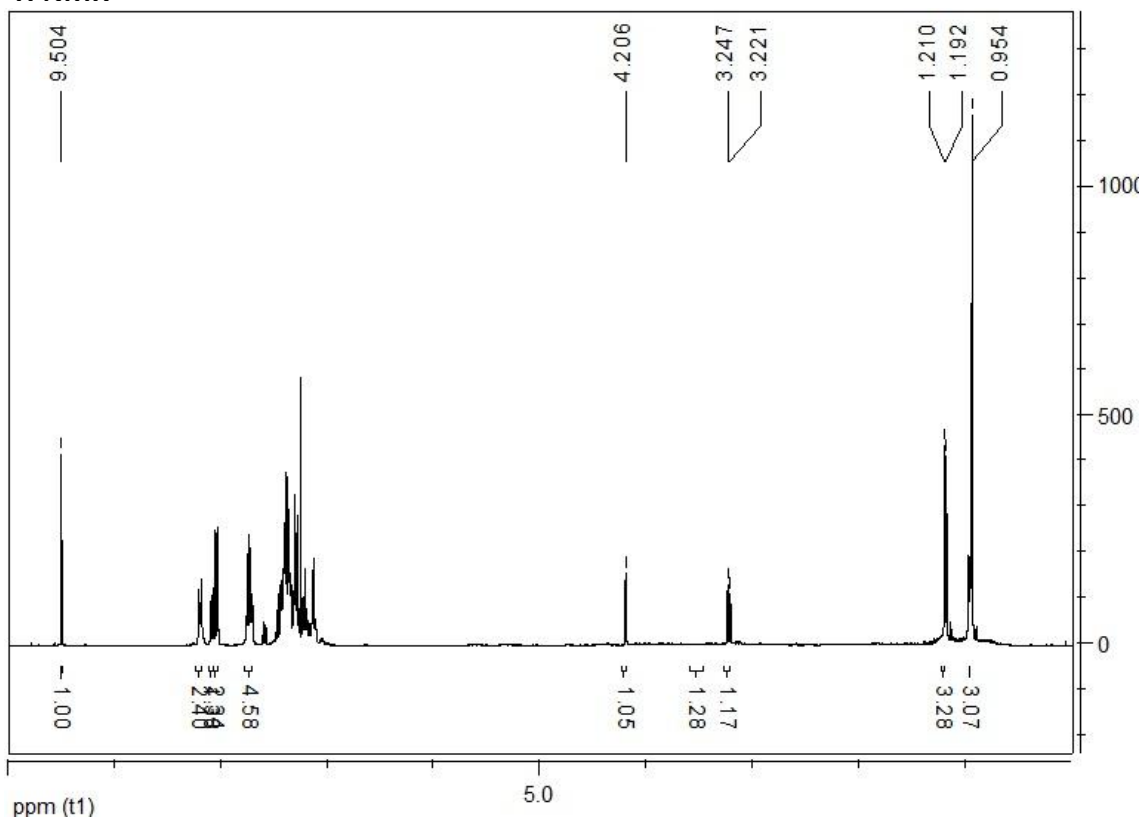
**7r:** White powder.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  (ppm): 0.99 (s, 3H), 1.23-1.21 (d,  $J=7.6$  Hz, 3H), 3.00-2.98 (d,  $J=10.4$  Hz, 1H), 3.58-3.52 (m, 1H), 4.25 (s, 1H), 7.75-7.07 (m, 13H), 7.75-7.73 (d,  $J=7.6$  Hz, 2H), 9.51 (s, 1H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 16.2, 18.6, 34.7, 44.9, 47.4, 60.1, 119.5, 120.1, 123.8, 124.0, 124.5, 125.8, 128.1, 128.5, 128.7, 129.1, 129.2, 130.4, 132.9, 133.9, 136.6, 137.6, 146.1, 147.8, 157.2, 160.2, 170.9, 173.7, 192.2. **Mp:** 86-88°C (decomp.). **IR** ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 576, 695, 756, 798, 895, 931, 1132, 1282, 1358, 1372, 1438, 1476, 1492, 1512, 1533, 1601, 1682, 2954, 3022. **HRMS** (ESI): calcd. for  $[\text{M}+\text{H}]^+$  ( $\text{C}_{29}\text{H}_{26}\text{N}_3\text{O}_4$ ) requires 480.1918, found 480.1916. **HPLC** (Chiralpak IA, *n*-hexane: *i*-PrOH= 90:10,  $\lambda=254$  nm, 1.0 mL/min):  $t_{\text{R}}=8.3, 11.1$  min.



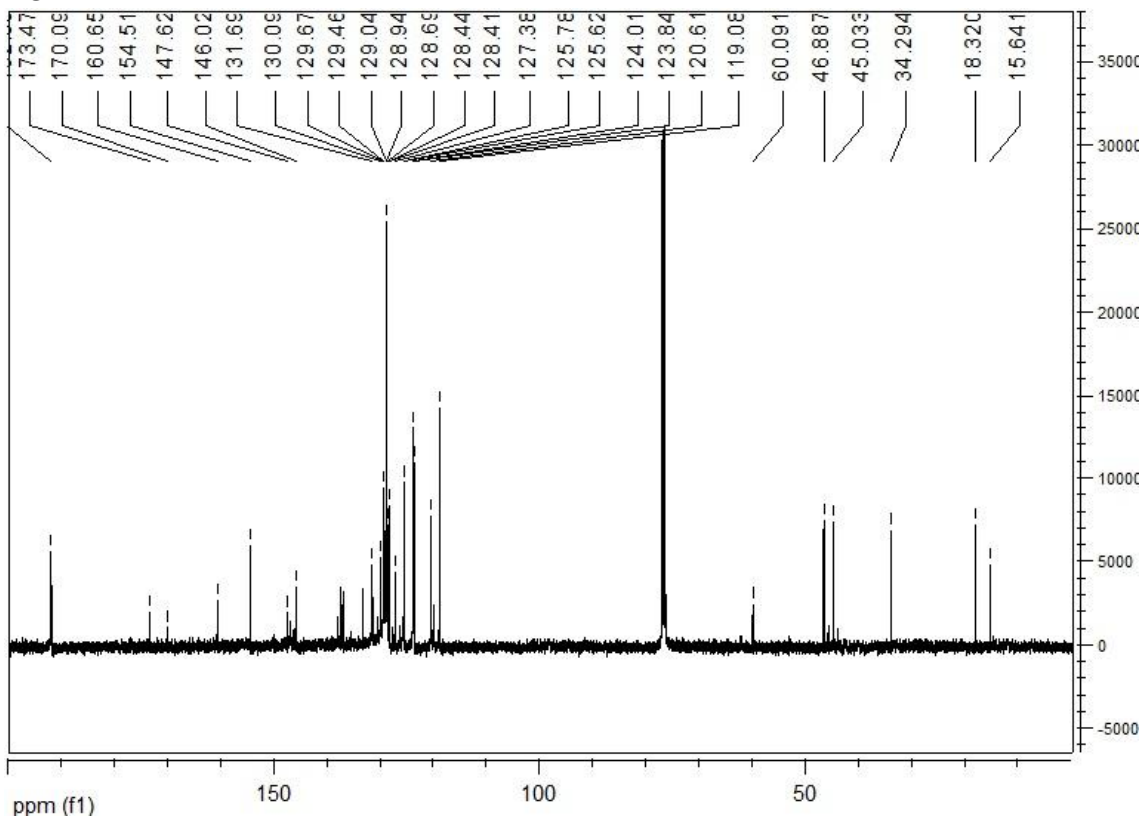


7d

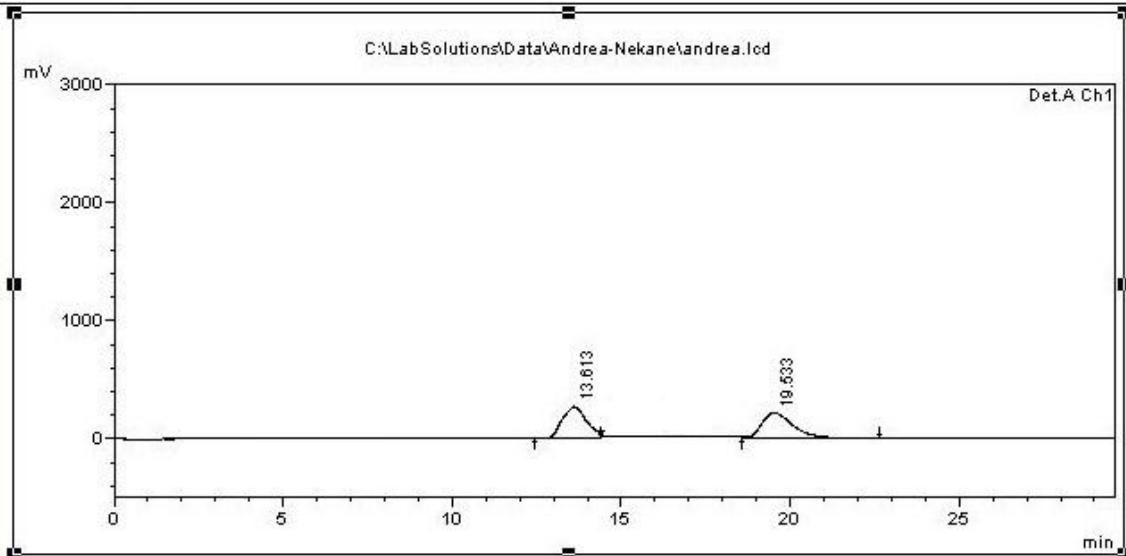
<sup>1</sup>H NMR



<sup>13</sup>C NMR



HPLC; Rac.:

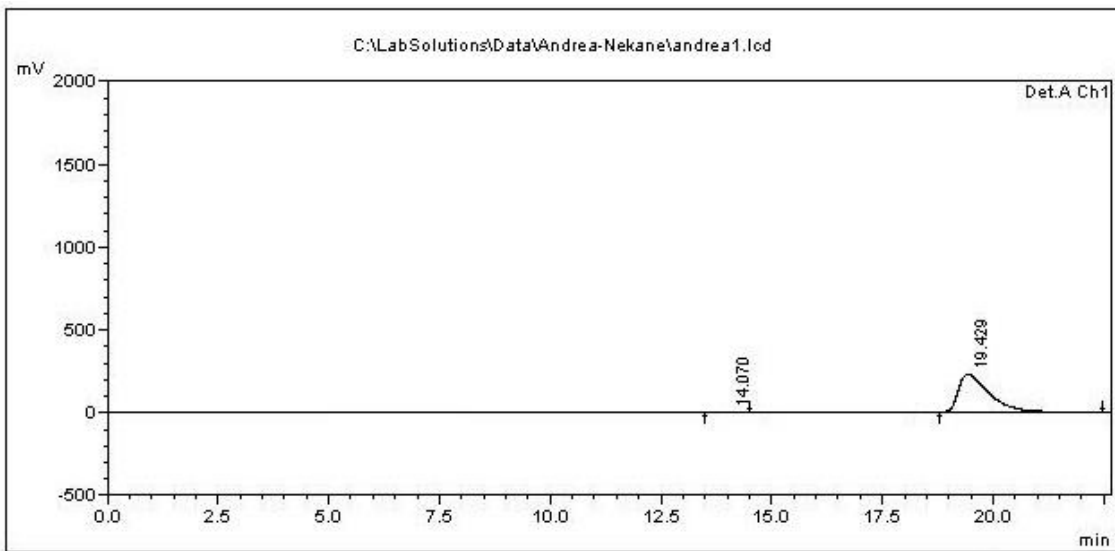


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	13.613	13317897	48.356
2	19.533	14223551	51.644
Total		27541448	100.000

(R)-Cat.

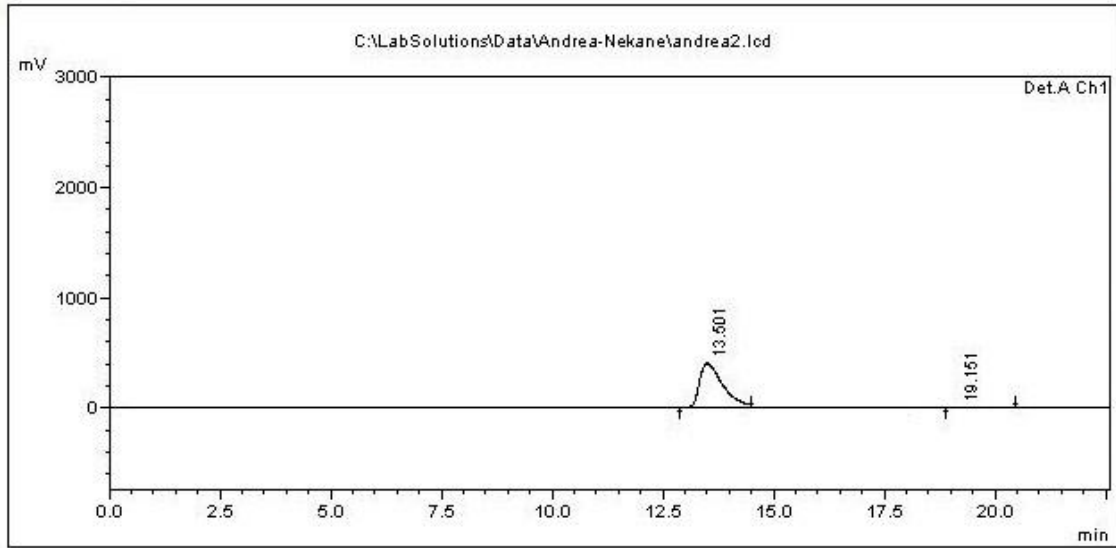


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	14.070	115916	1.005
2	19.429	11420143	98.995
Total		11536059	100.000

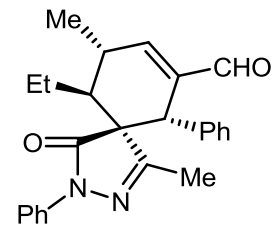
(S)-Cat.



PeakTable

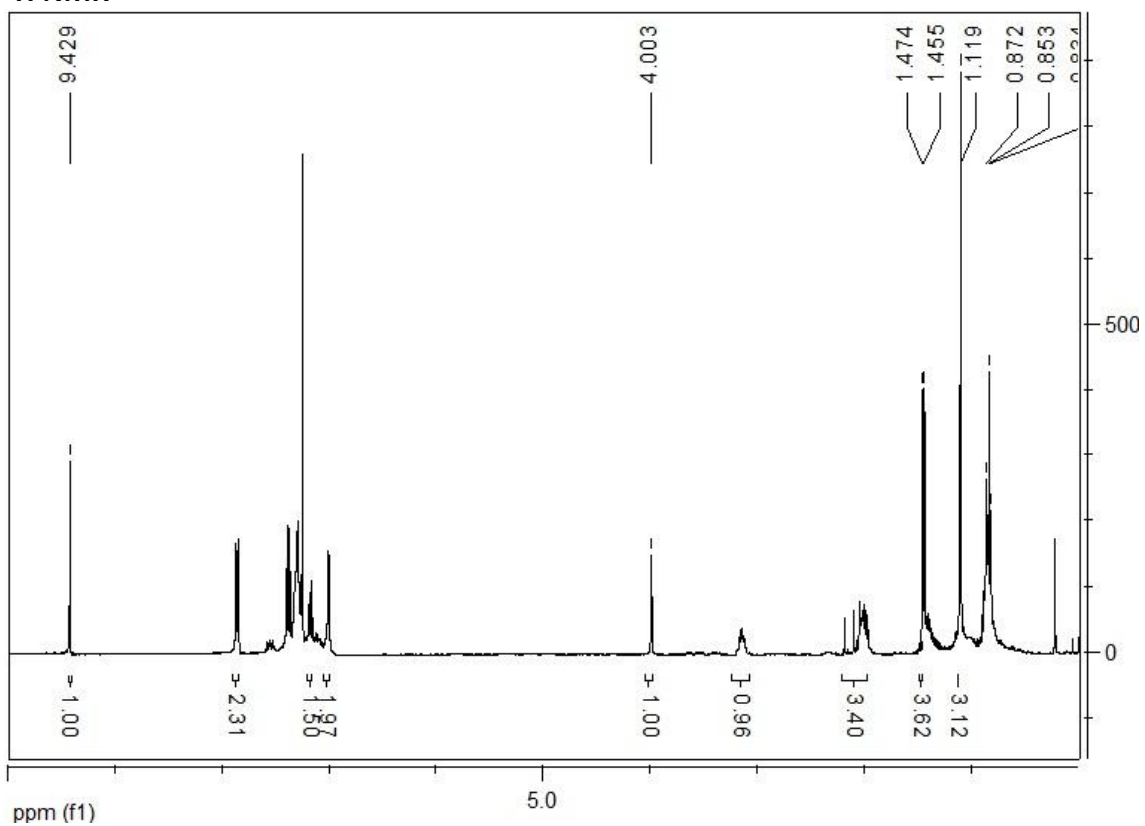
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	13.501	14996319	99.631
2	19.151	55474	0.369
Total		15051793	100.000

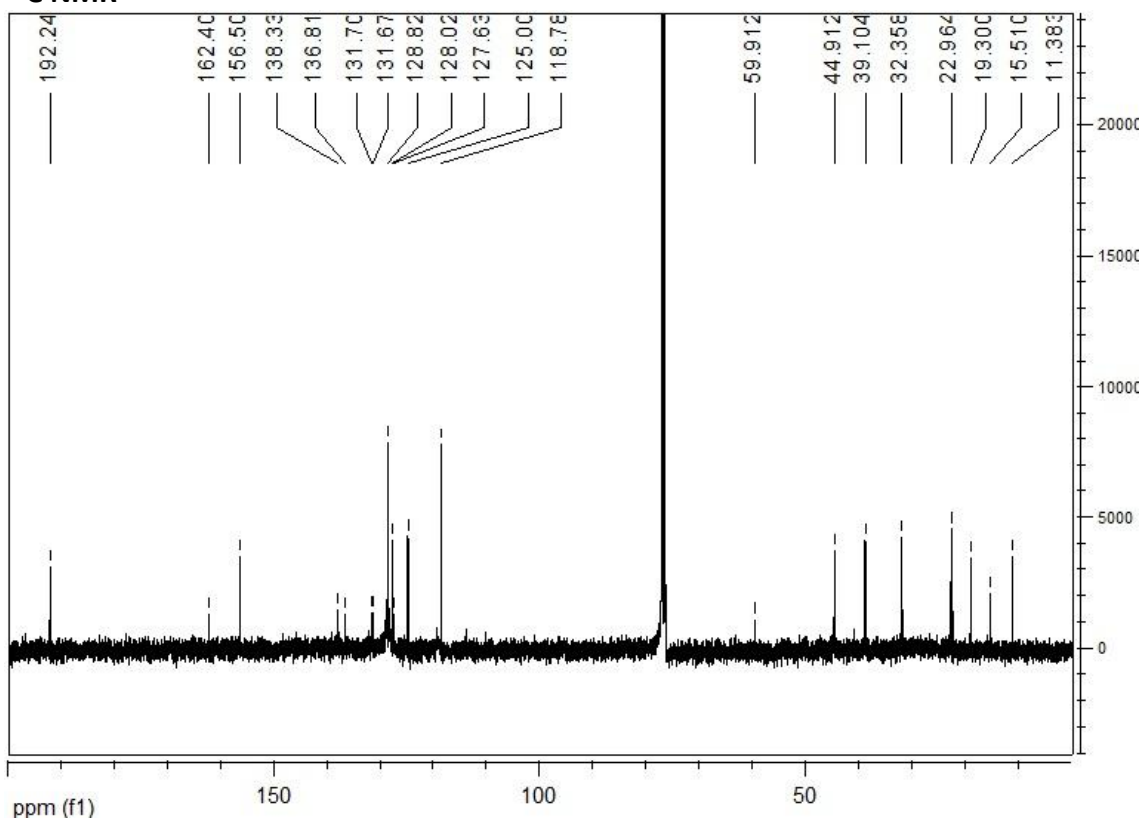


7e

<sup>1</sup>H NMR

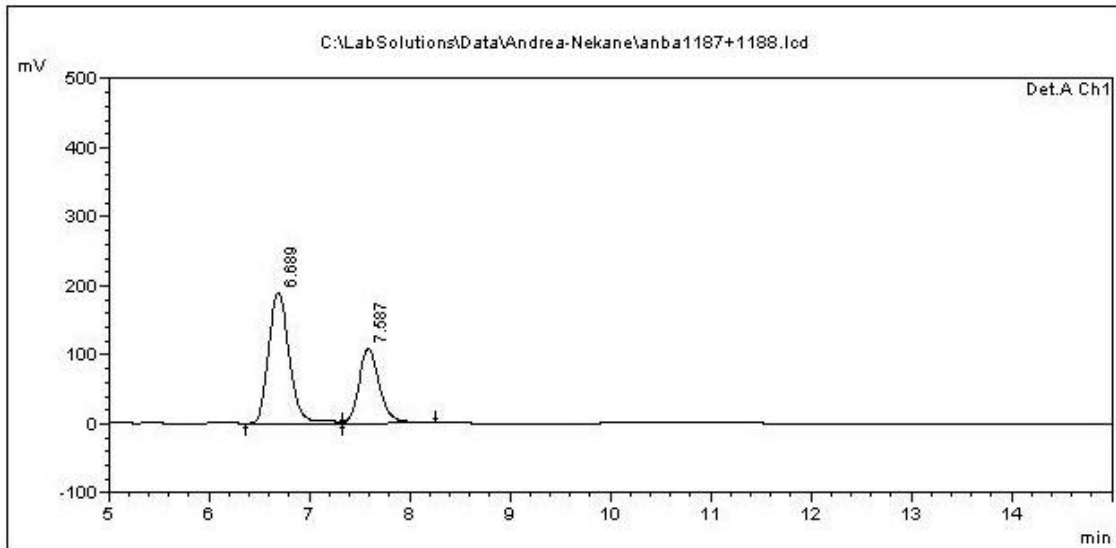


<sup>13</sup>C NMR



# HPLC

Rac.:

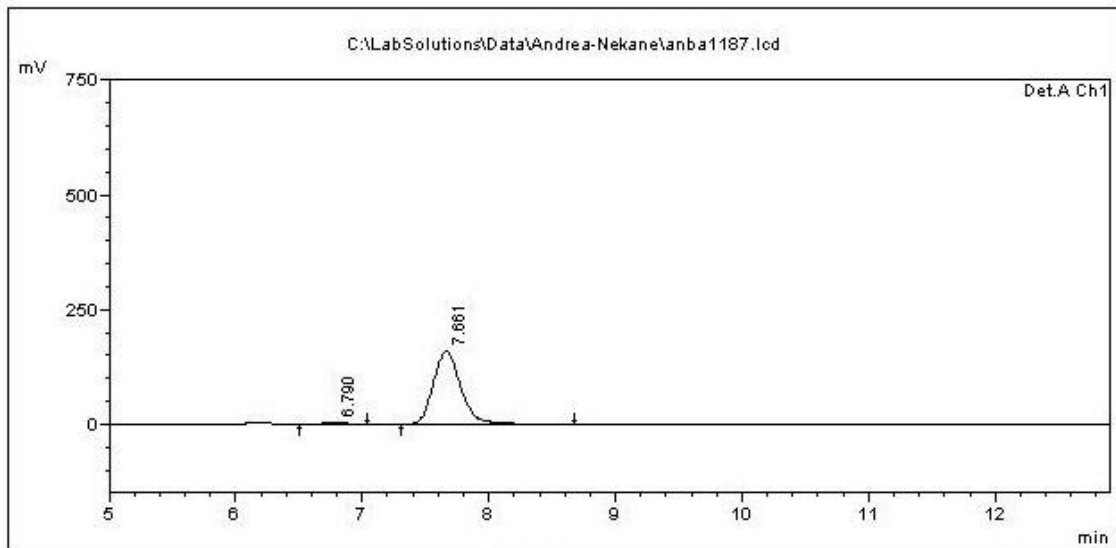


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	6.689	2726525	64.211
2	7.587	1519684	35.789
Total		4246209	100.000

(R)-Cat.

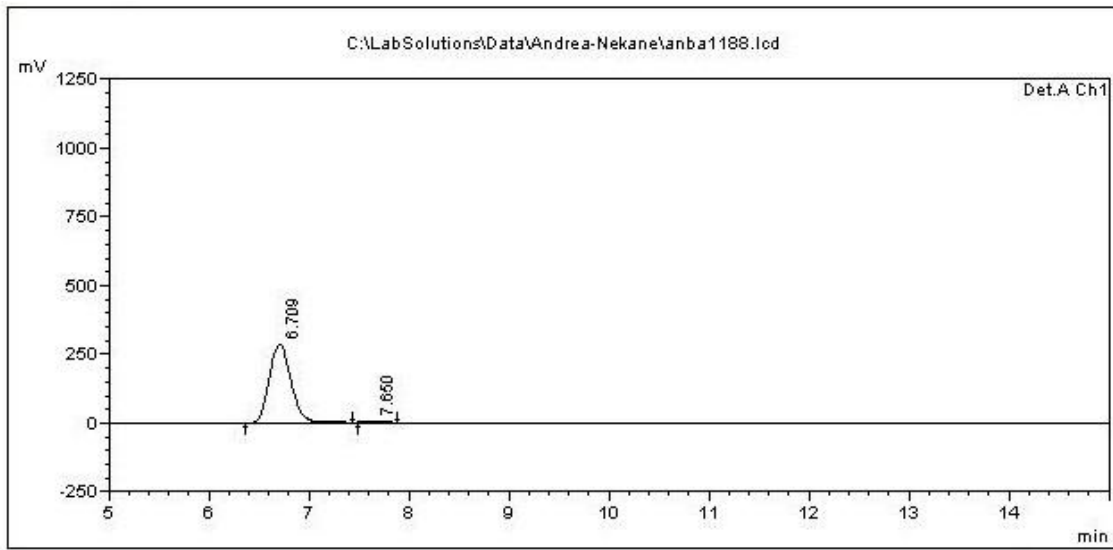


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	6.790	31363	1.300
2	7.661	2381480	98.700
Total		2412843	100.000

(S)-Cat.



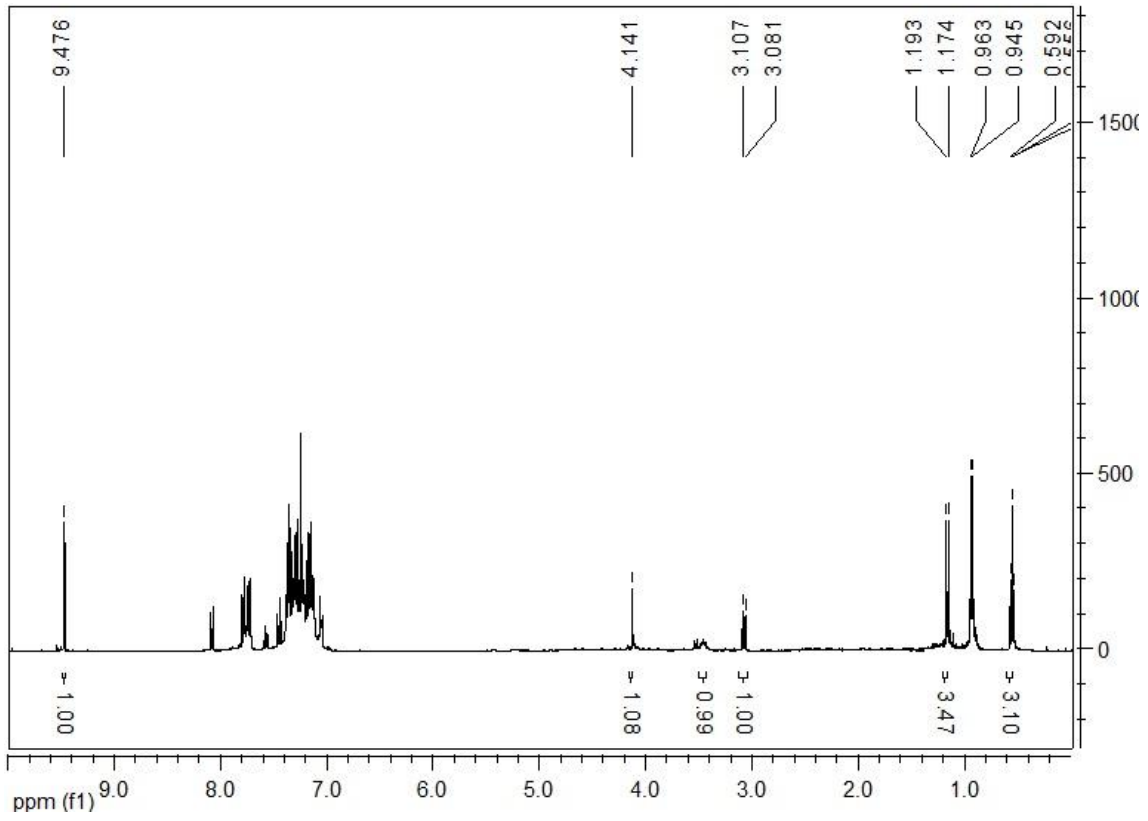
PeakTable

Detector A Ch1 254nm

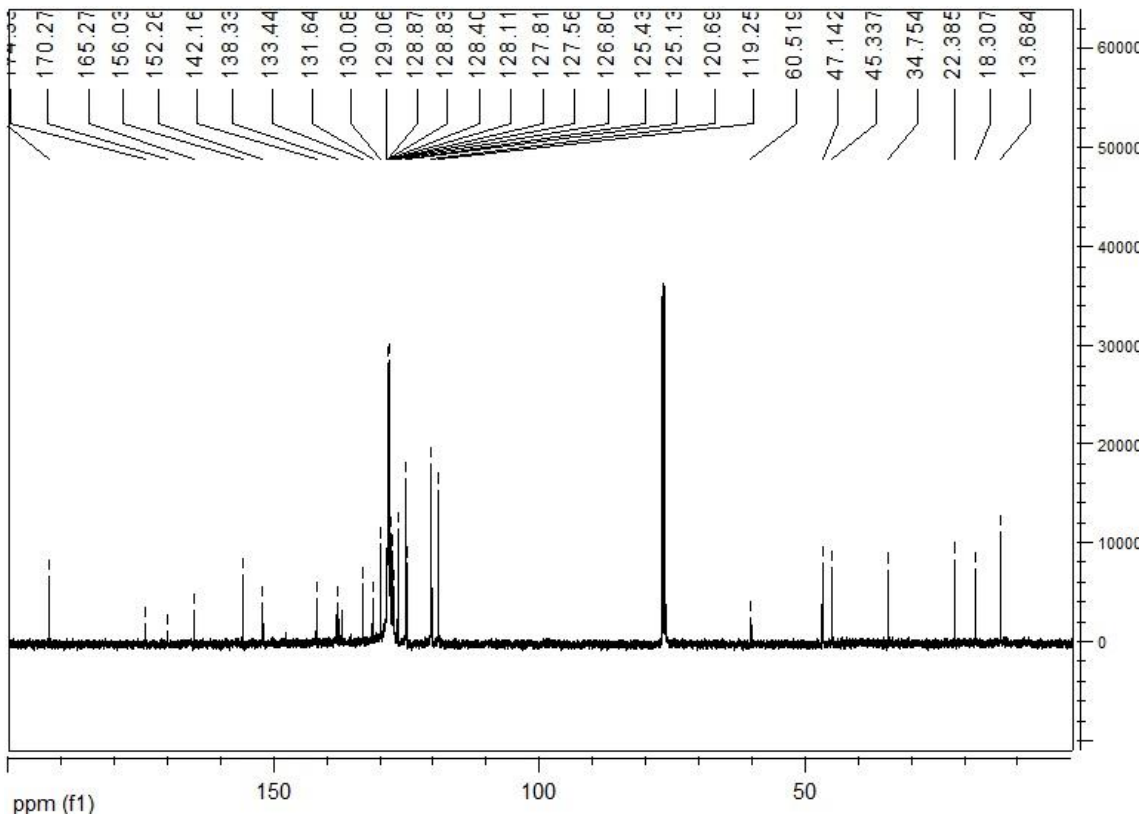
Peak#	Ret. Time	Area	Area %
1	6.709	4356112	98.329
2	7.650	74038	1.671
Total		4430150	100.000

7f

<sup>1</sup>H NMR

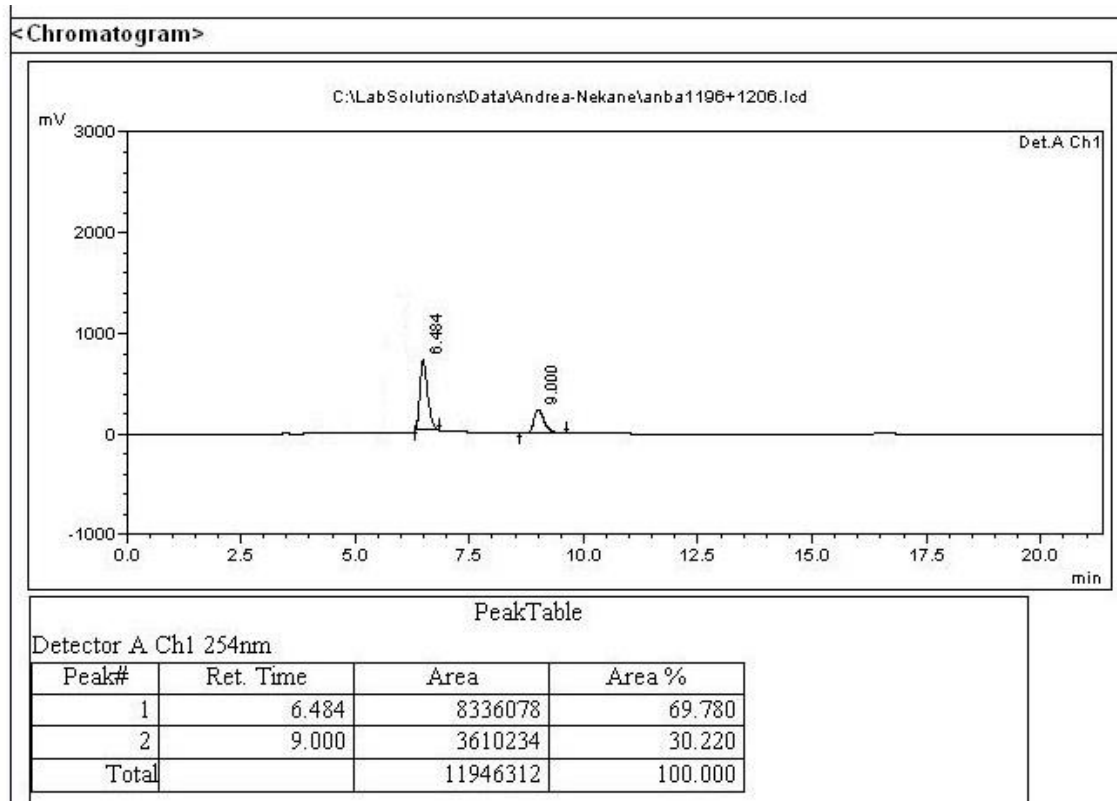


<sup>13</sup>C NMR

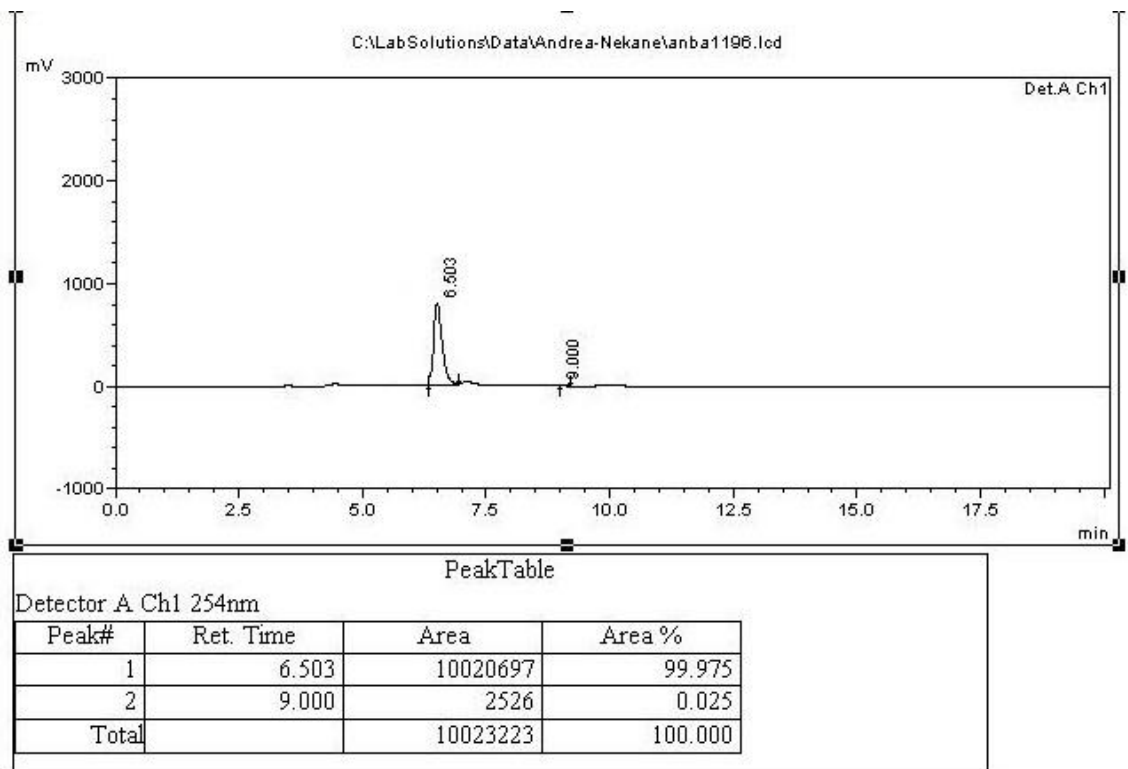


# HPLC

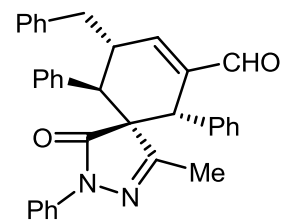
Rac.:



(S)-Cat.

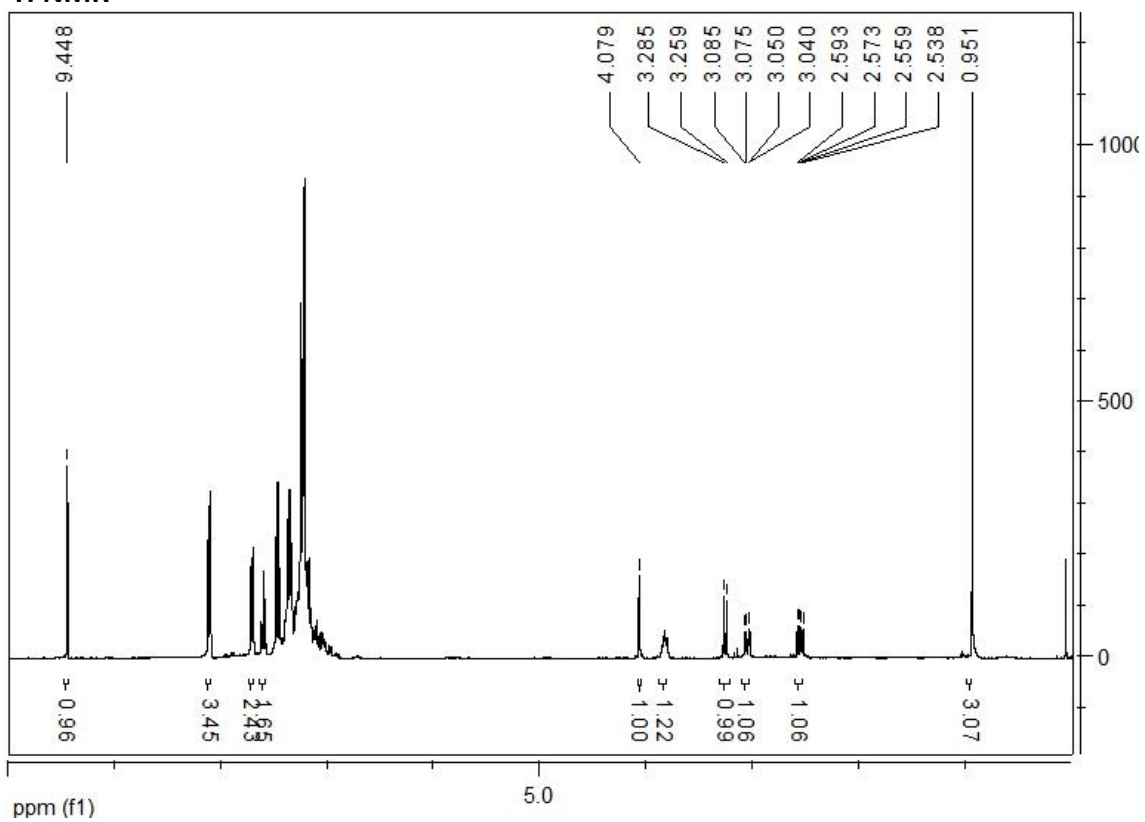




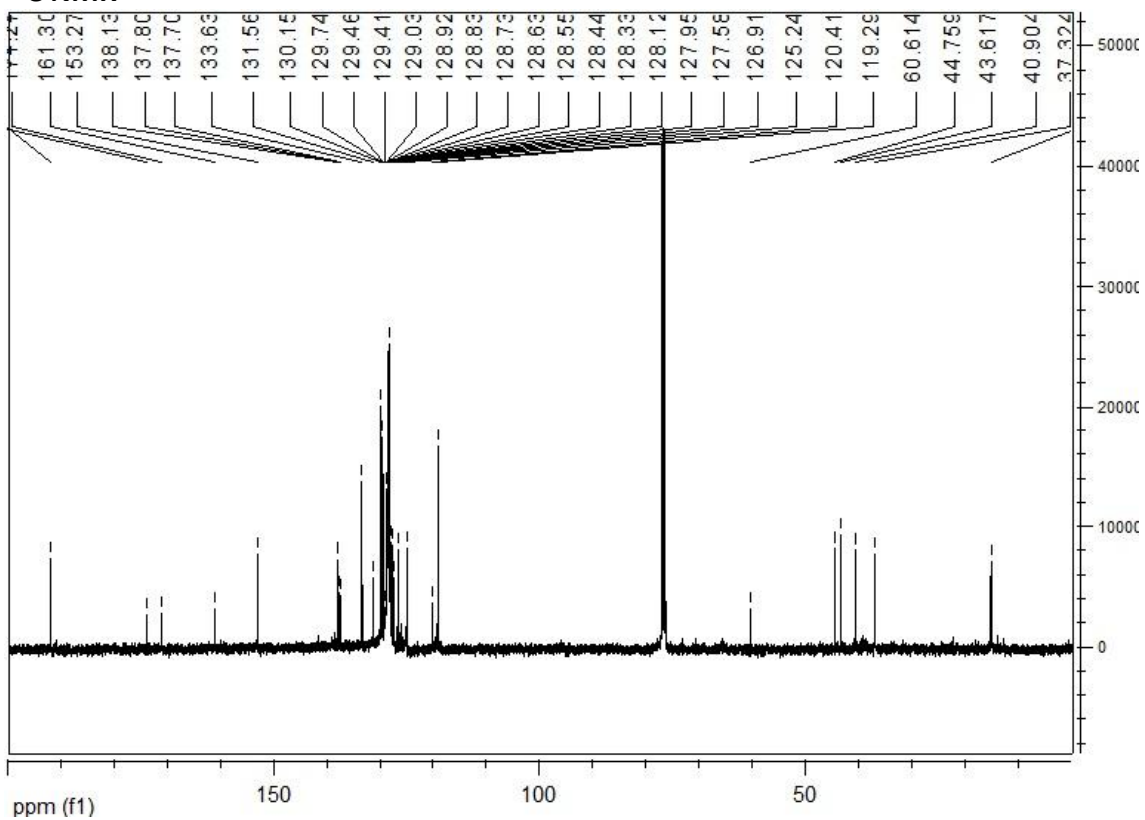


7j

<sup>1</sup>H NMR

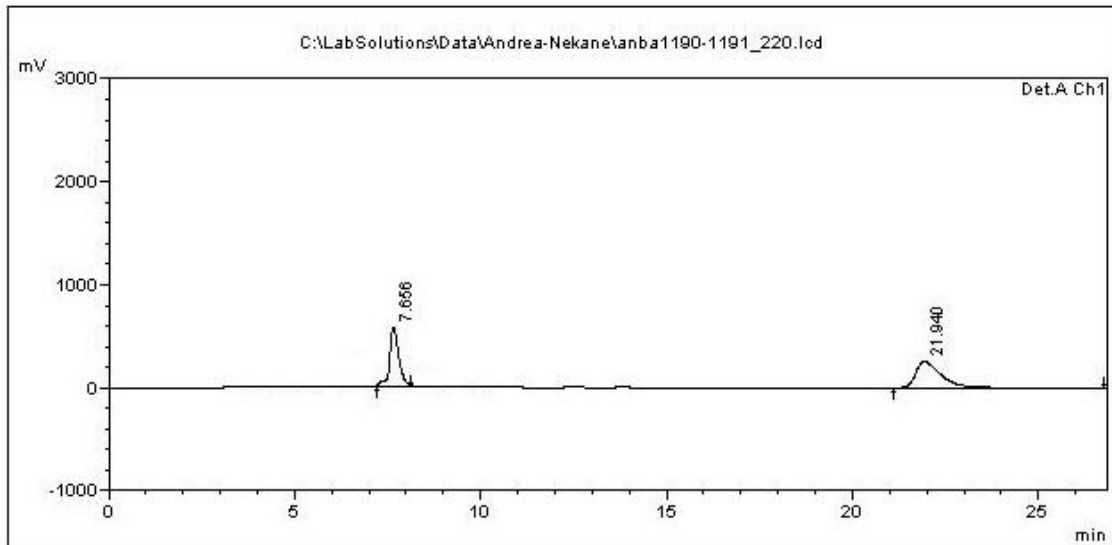


<sup>13</sup>C NMR



# HPLC

Rac.:

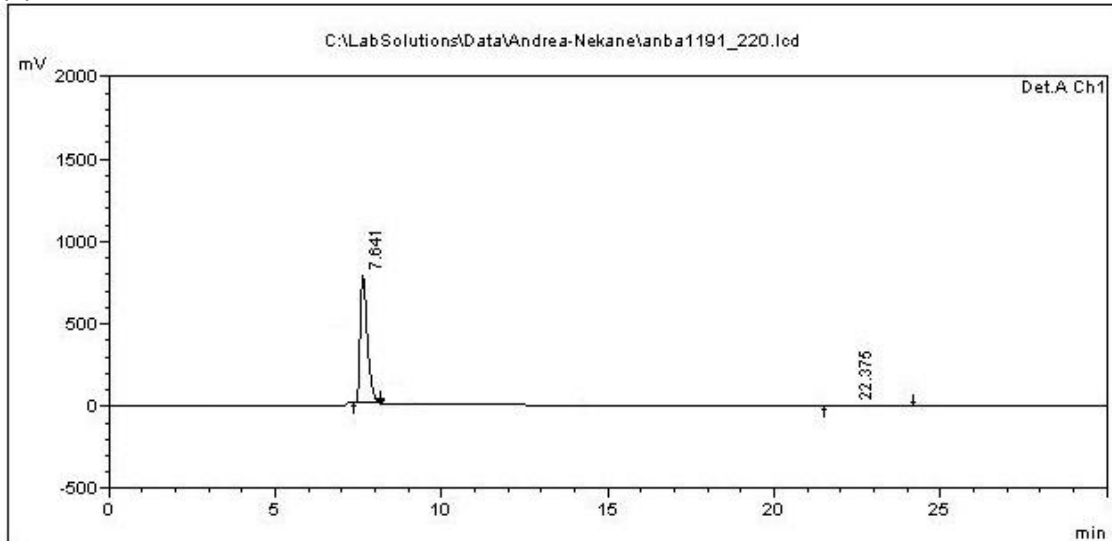


PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Area %
1	7.656	10103927	46.078
2	21.940	11824099	53.922
Total		21928026	100.000

(S)-Cat.

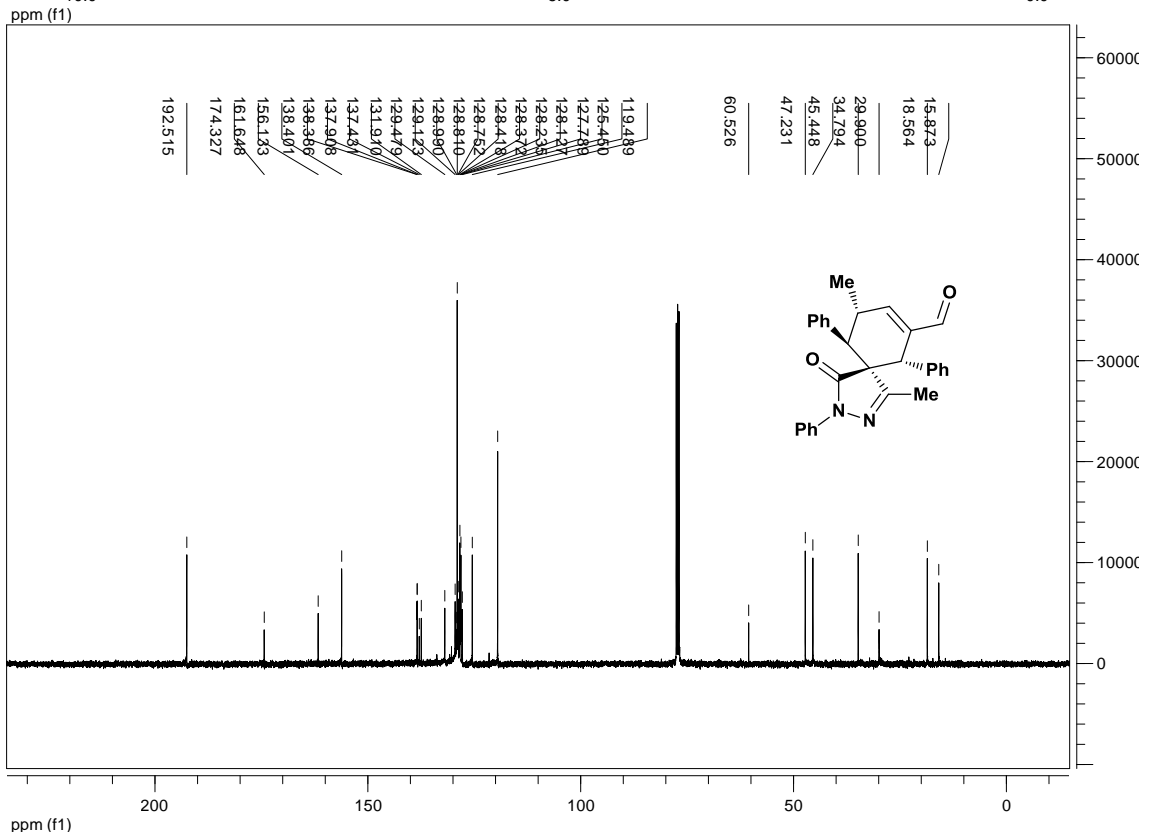
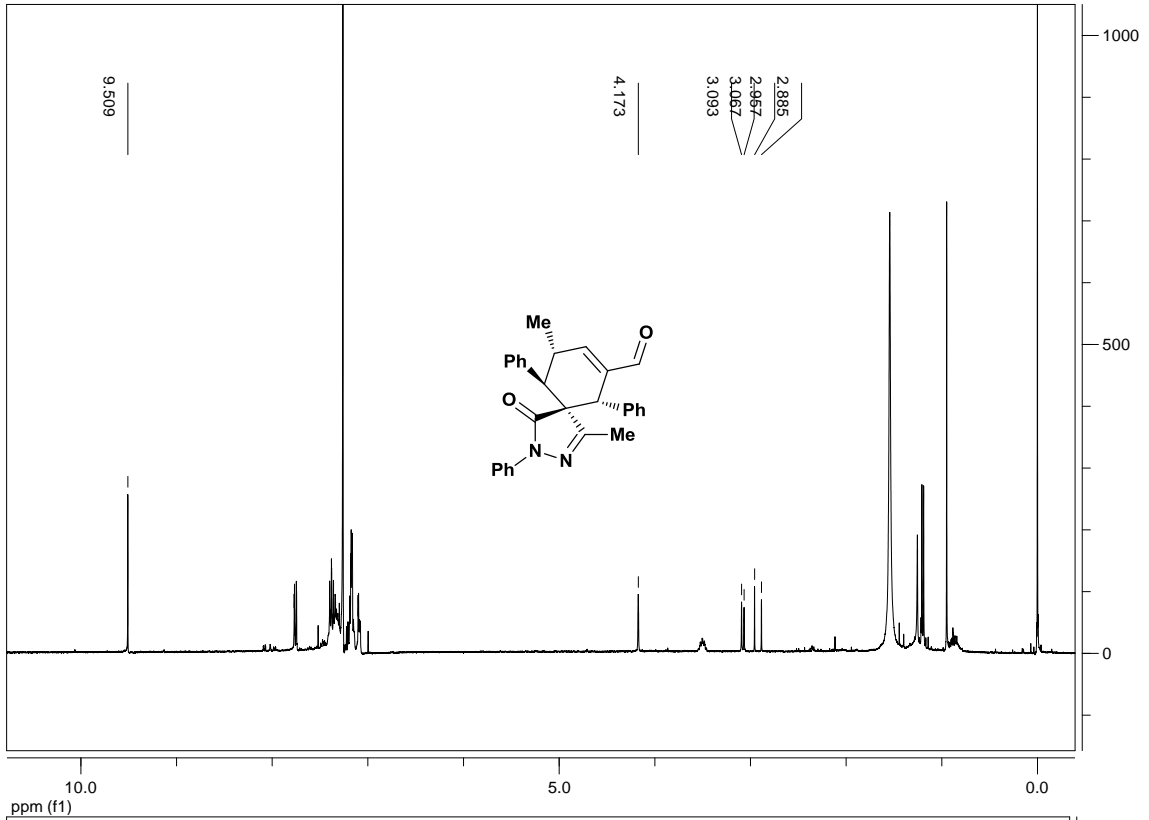


PeakTable

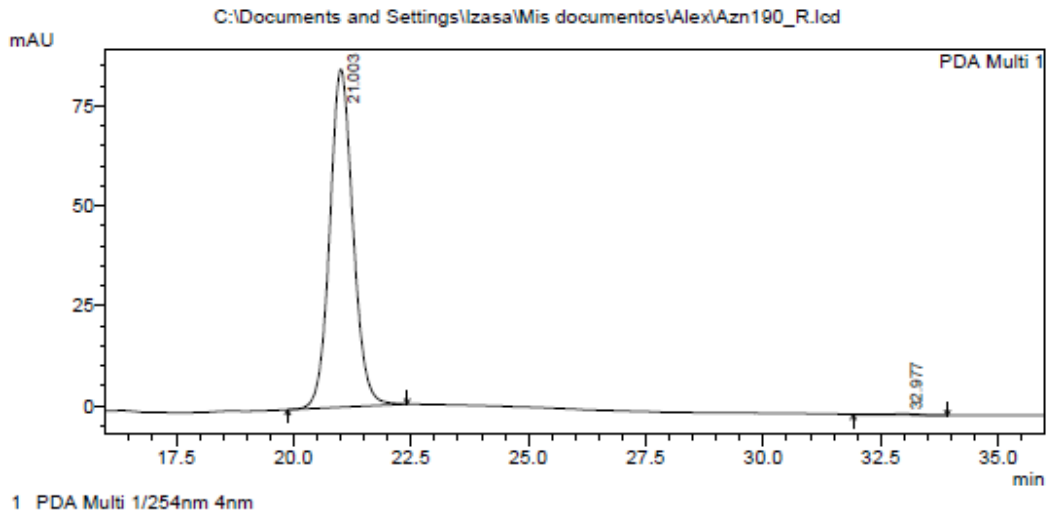
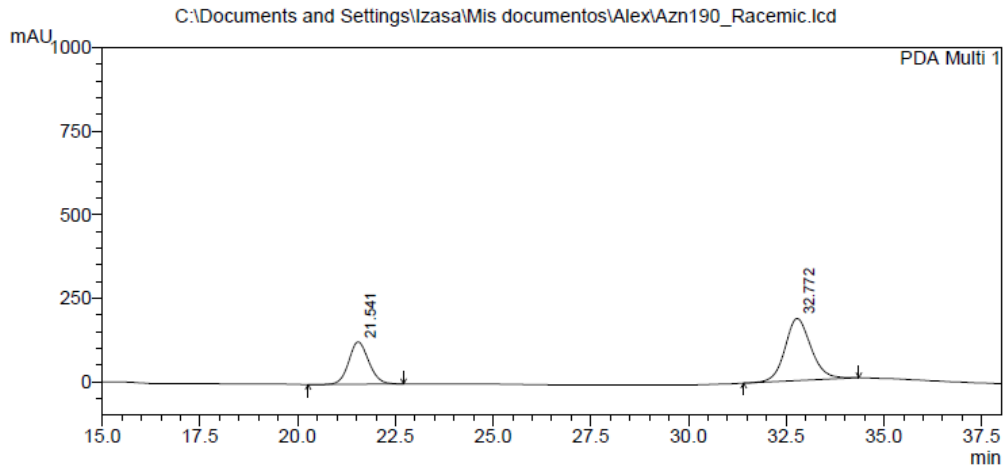
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Area %
1	7.641	11642891	98.838
2	22.375	136917	1.162
Total		11779808	100.000

7a



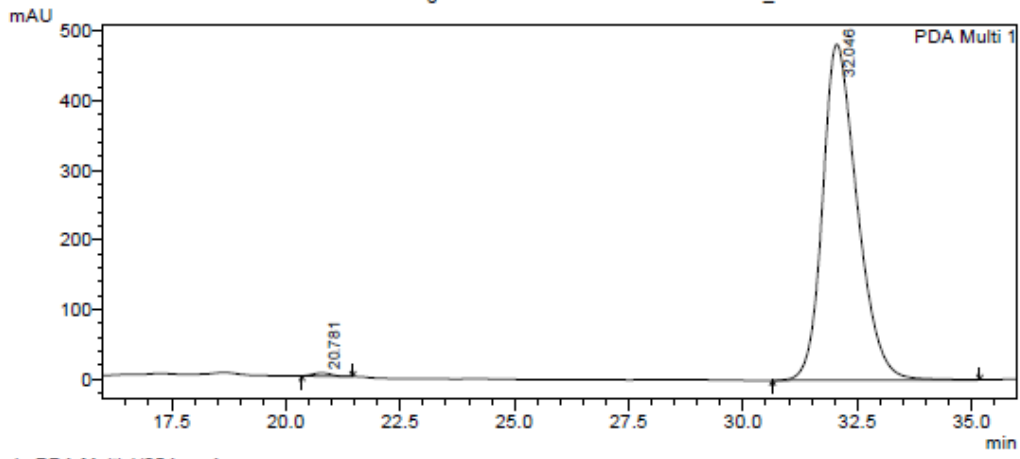
<Chromatogram>



PDA Ch1 254nm 4nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.003	2910351	84445	99.663	99.708
2	32.977	9848	247	0.337	0.292
Total		2920199	84692	100.000	100.000

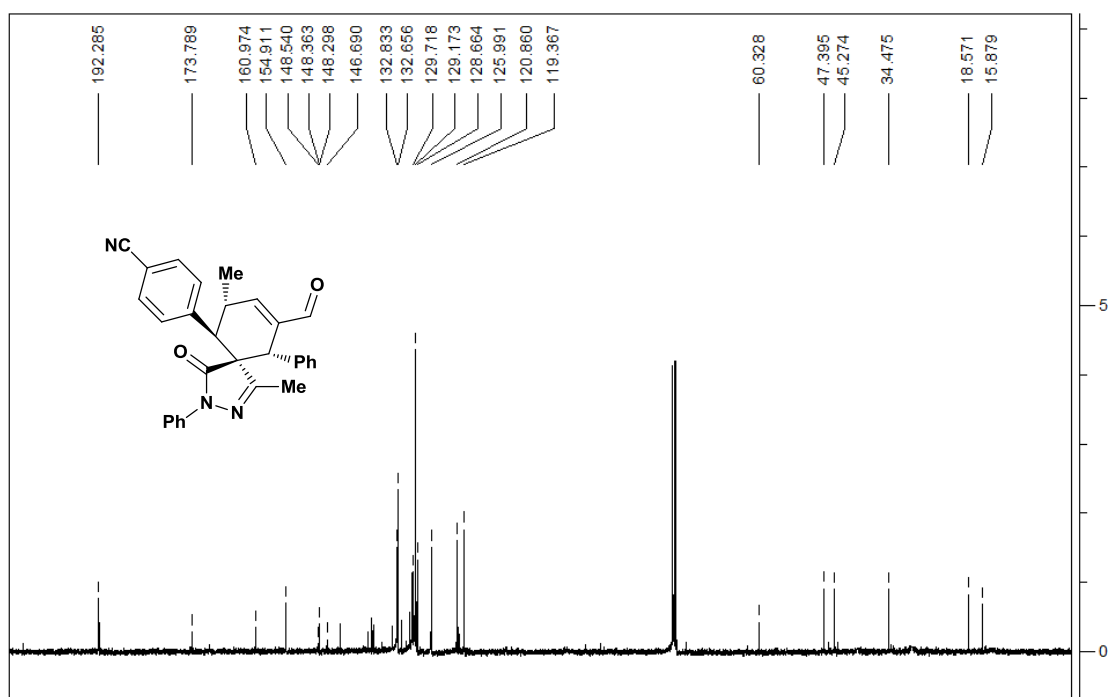
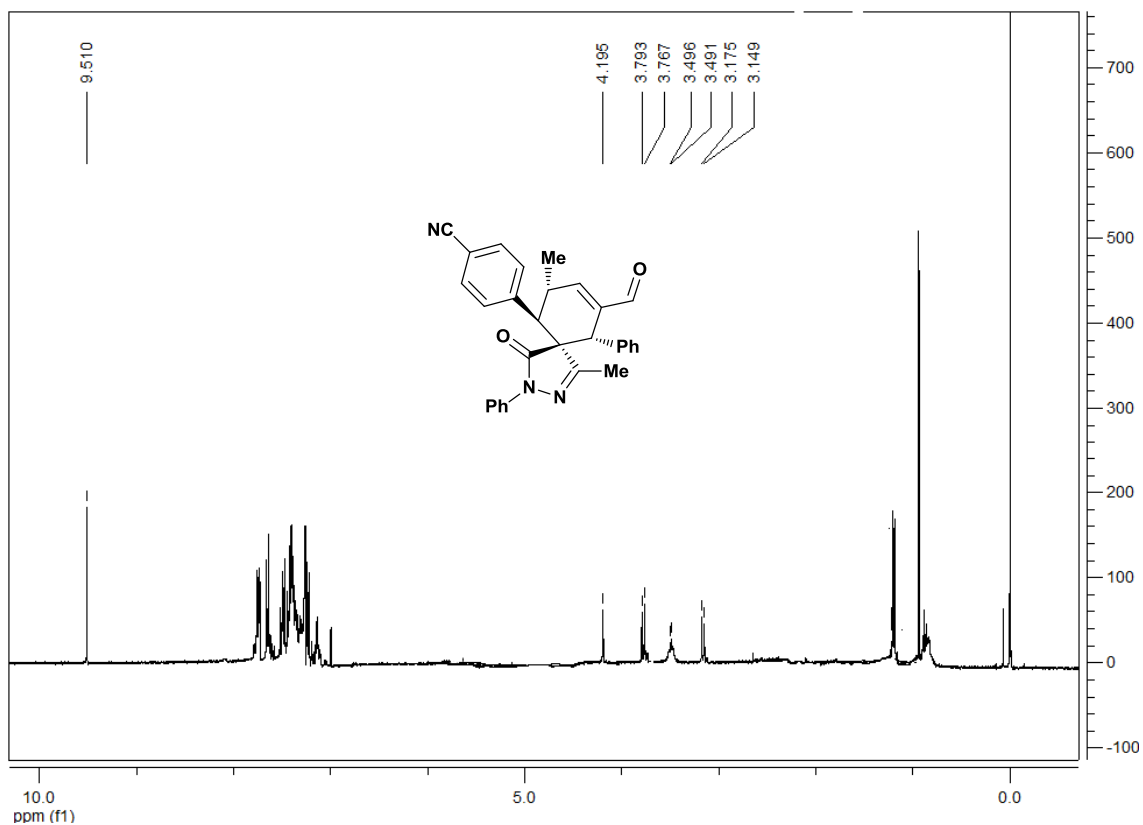


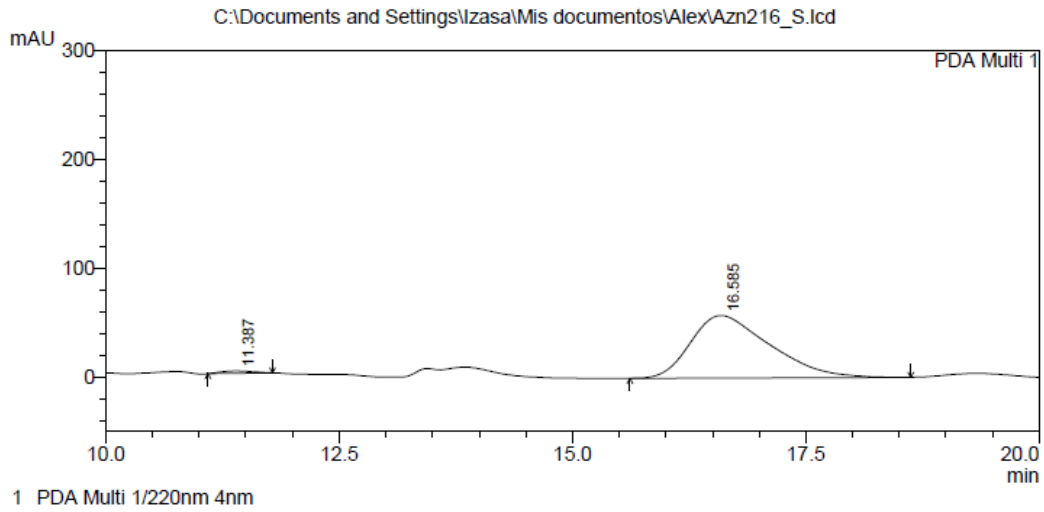
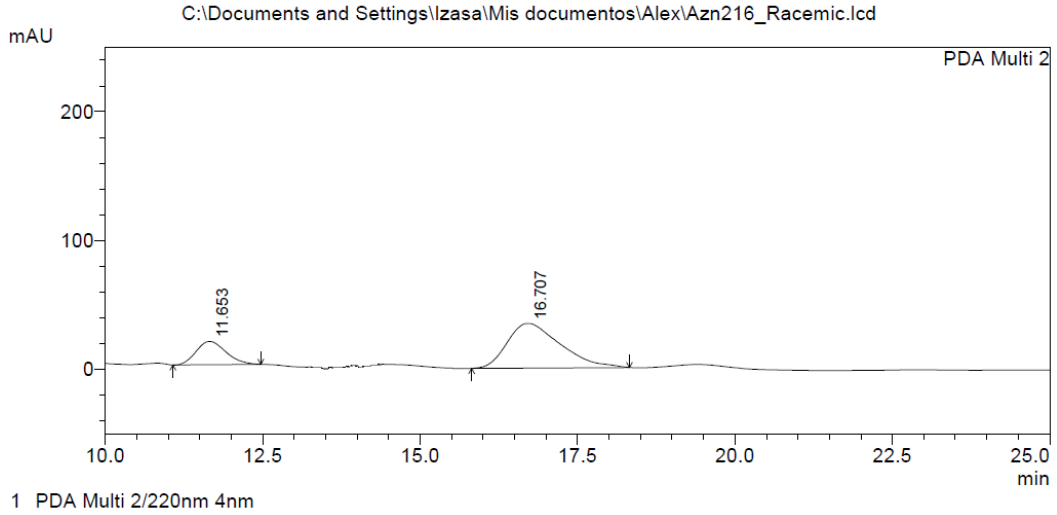
1 PDA Multi 1/254nm 4nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.781	121086	4544	0.473	0.932
2	32.046	25485544	482960	99.527	99.068
Total		25606630	487504	100.000	100.000

7c

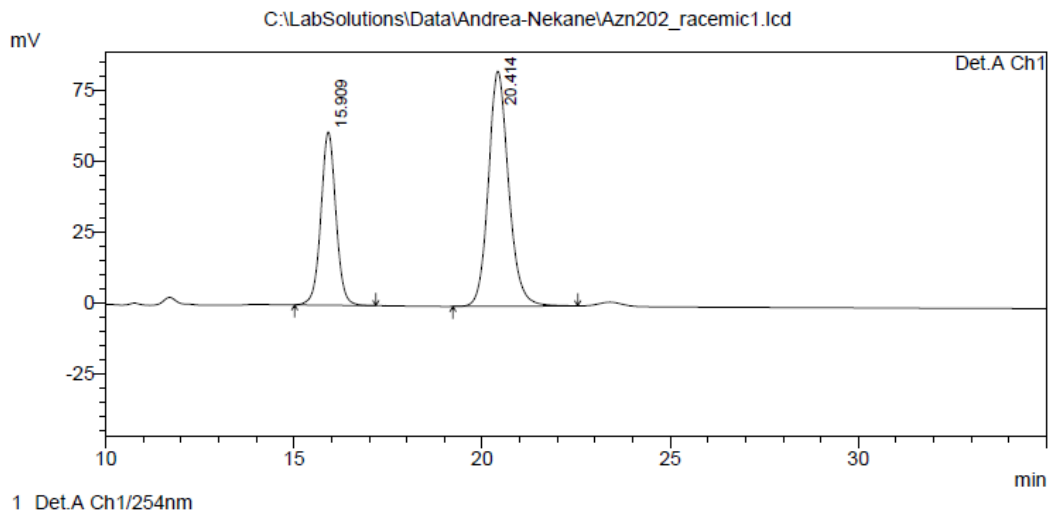
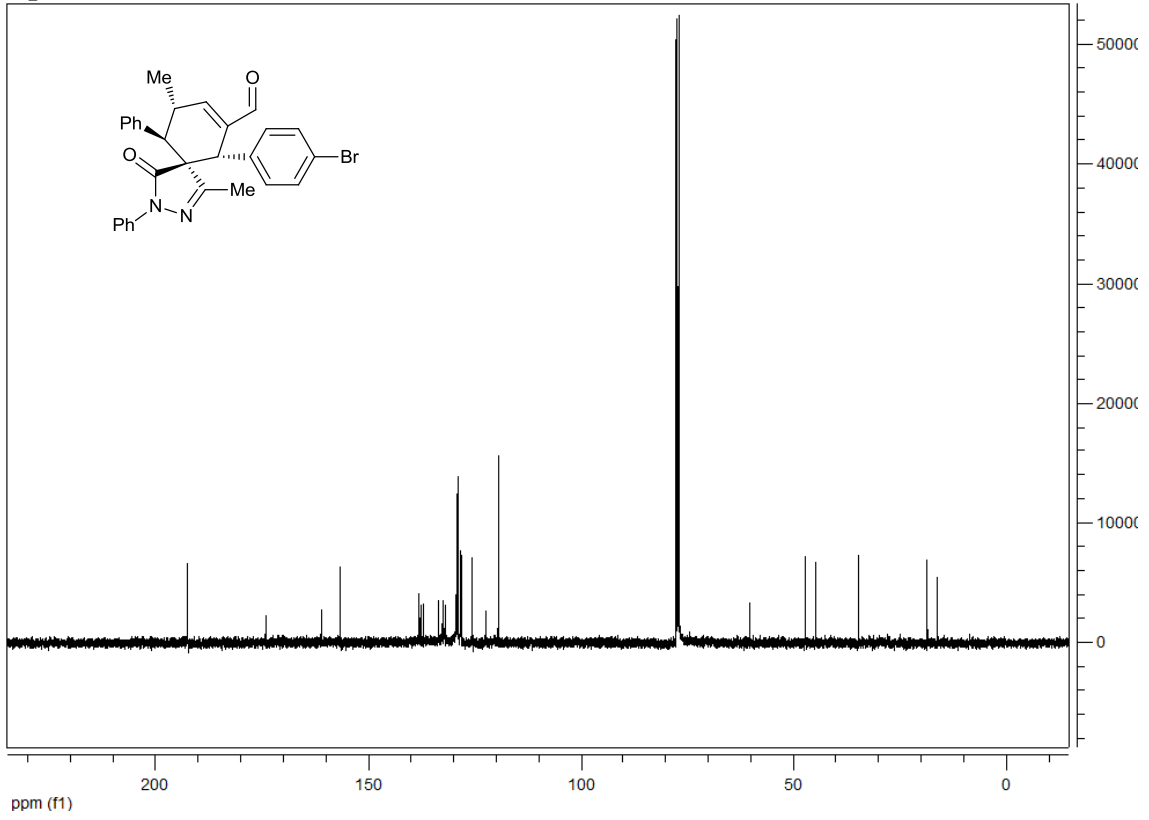




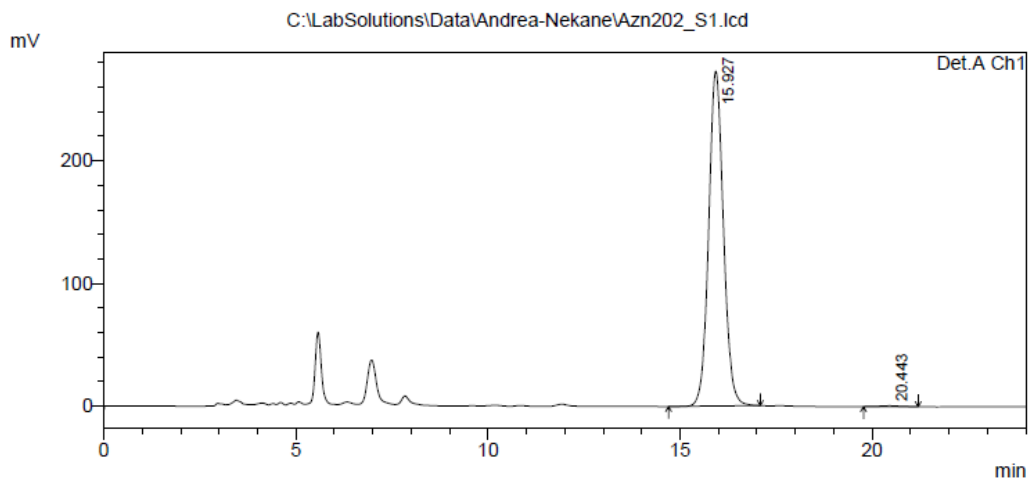
PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.387	48436	2027	1.417	3.416
2	16.585	3368736	57313	98.583	96.584
Total		3417172	59340	100.000	100.000

7q

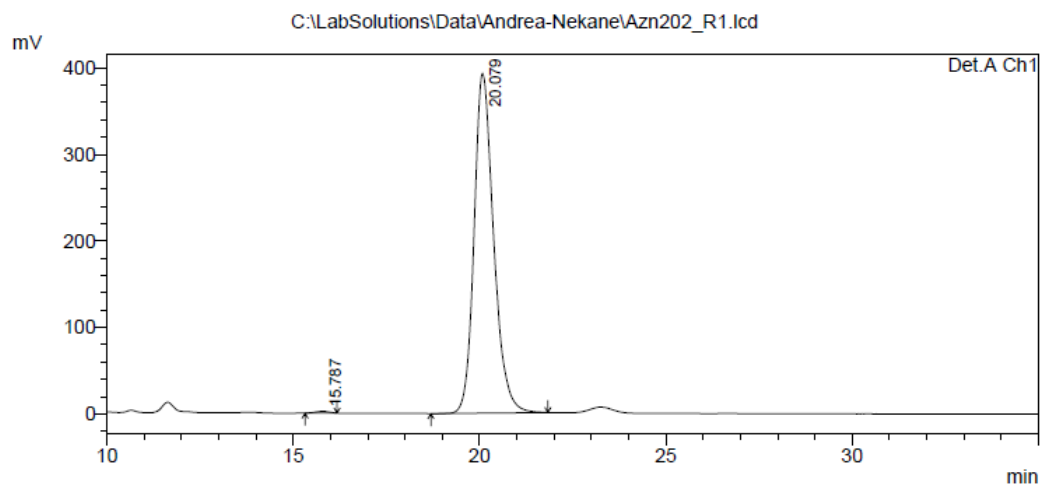






PeakTable

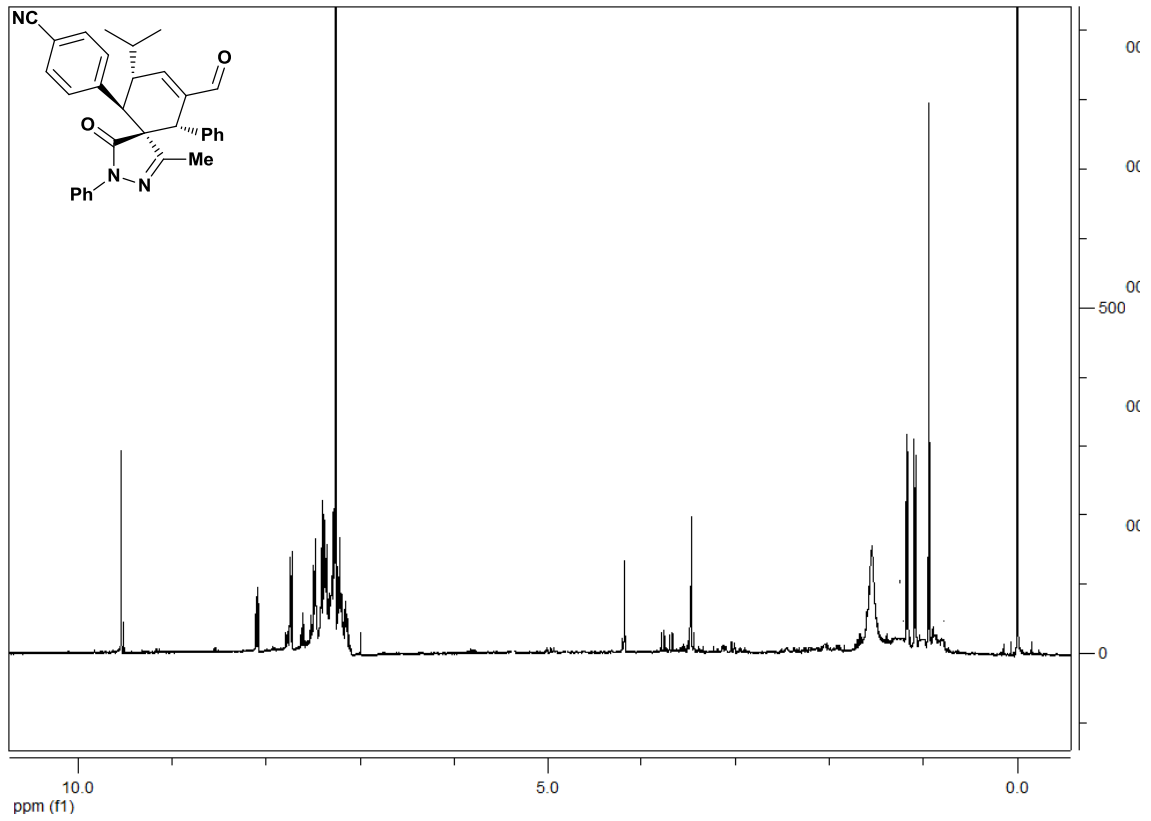
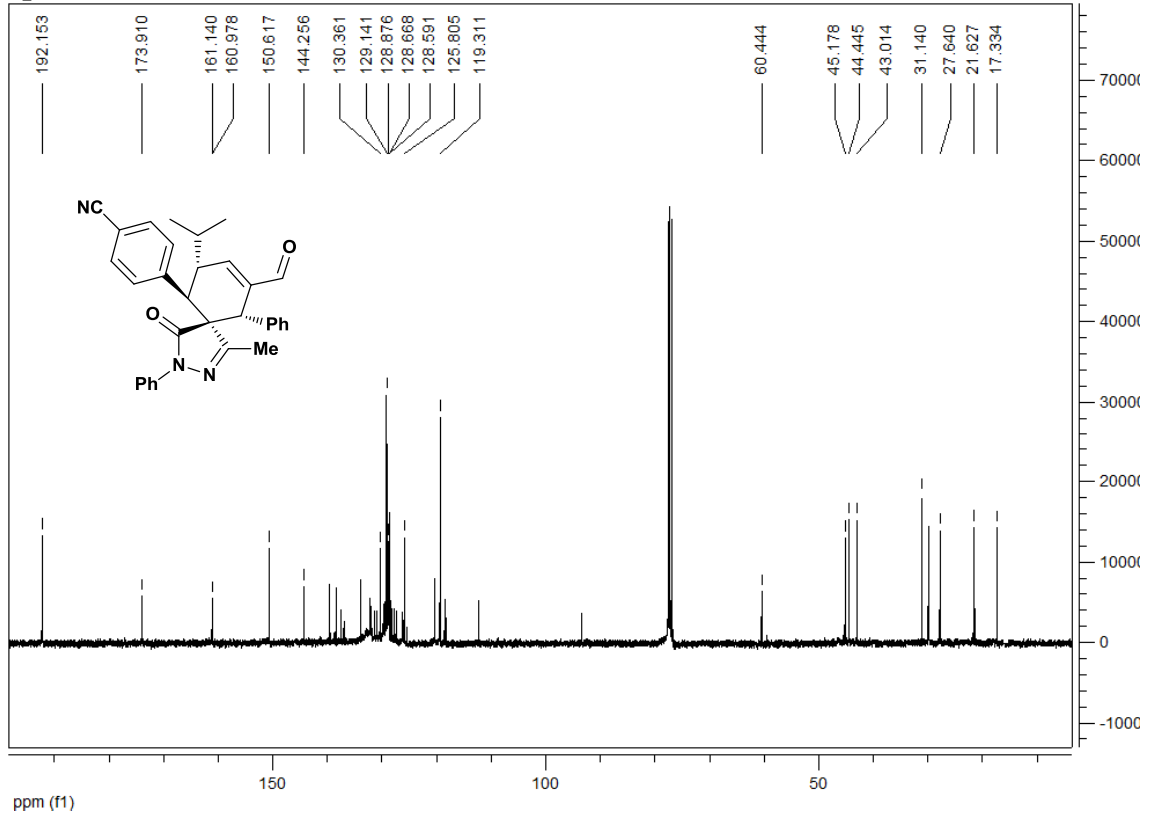
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.927	7312212	273272	99.648	99.729
2	20.443	25866	741	0.352	0.271
Total		7338078	274014	100.000	100.000

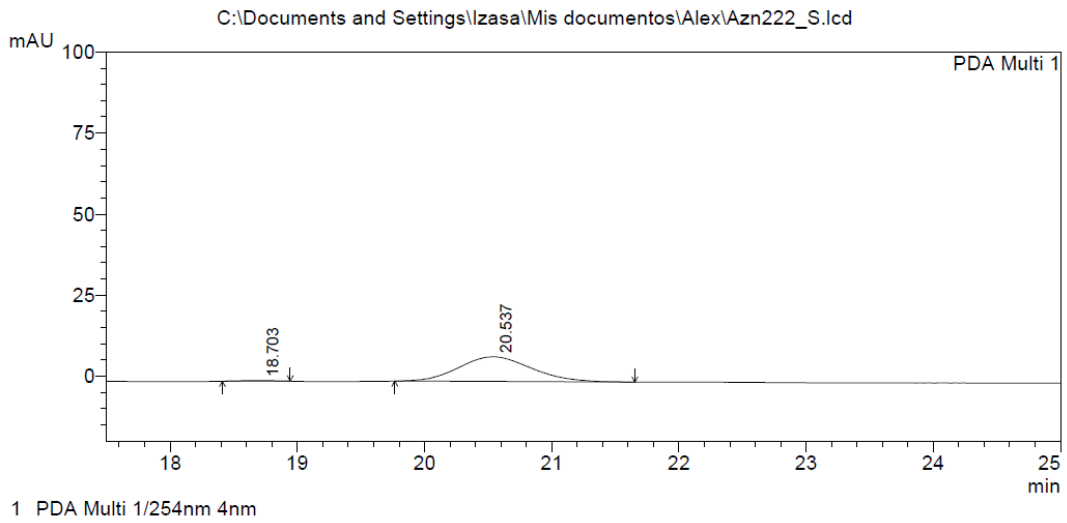
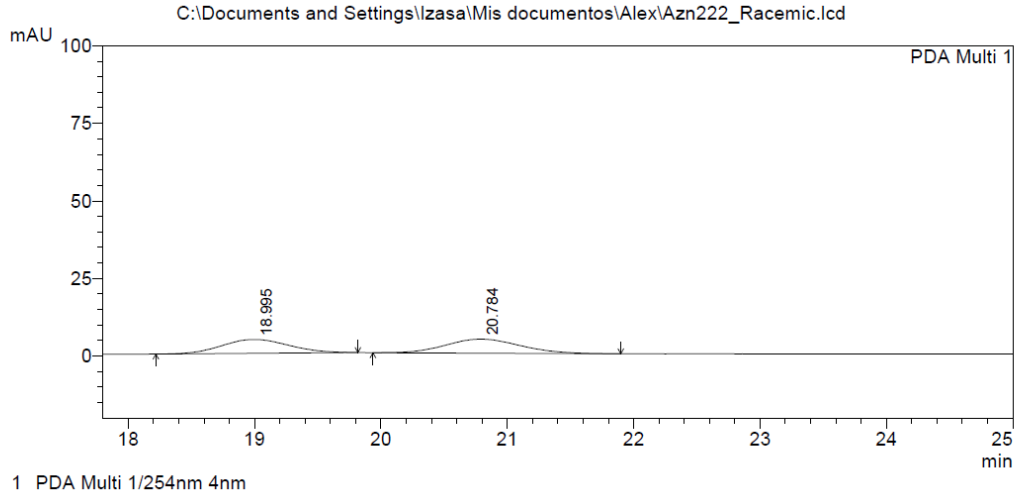


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.787	52614	2124	0.366	0.537
2	20.079	14339397	393122	99.634	99.463
Total		14392011	395246	100.000	100.000

7p



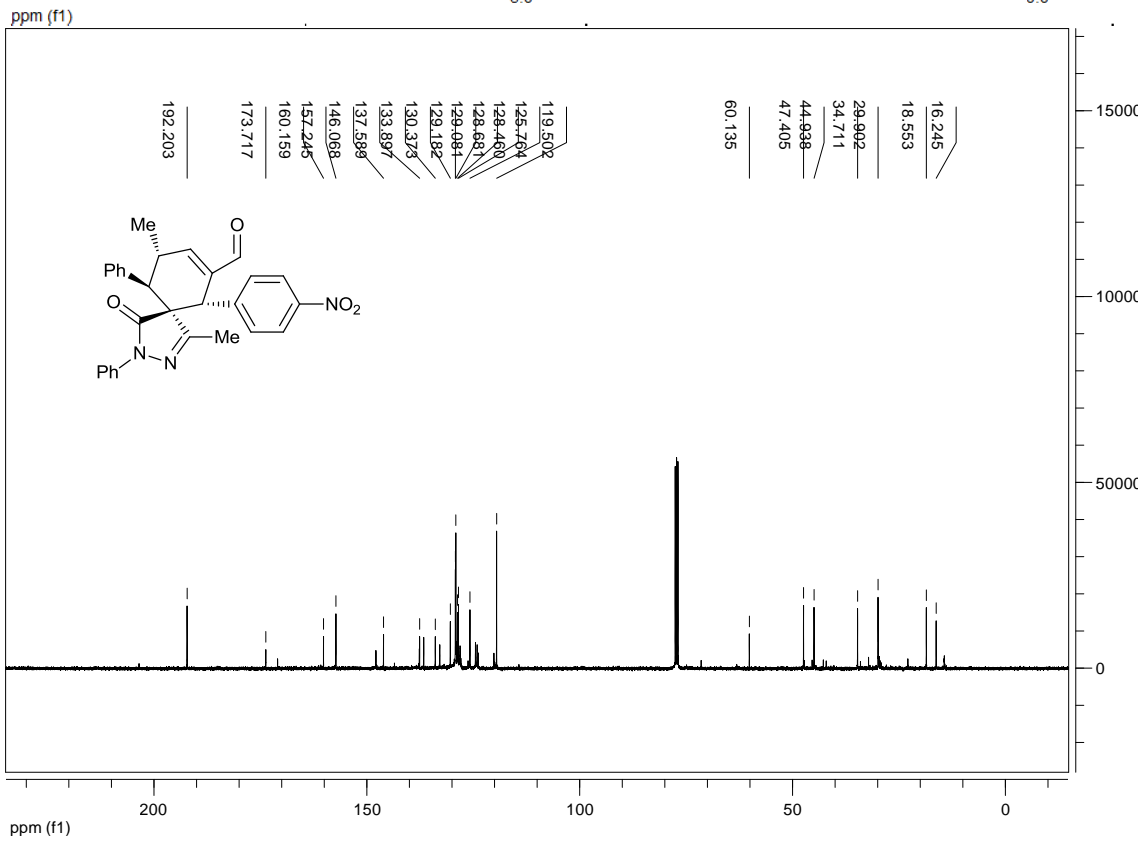
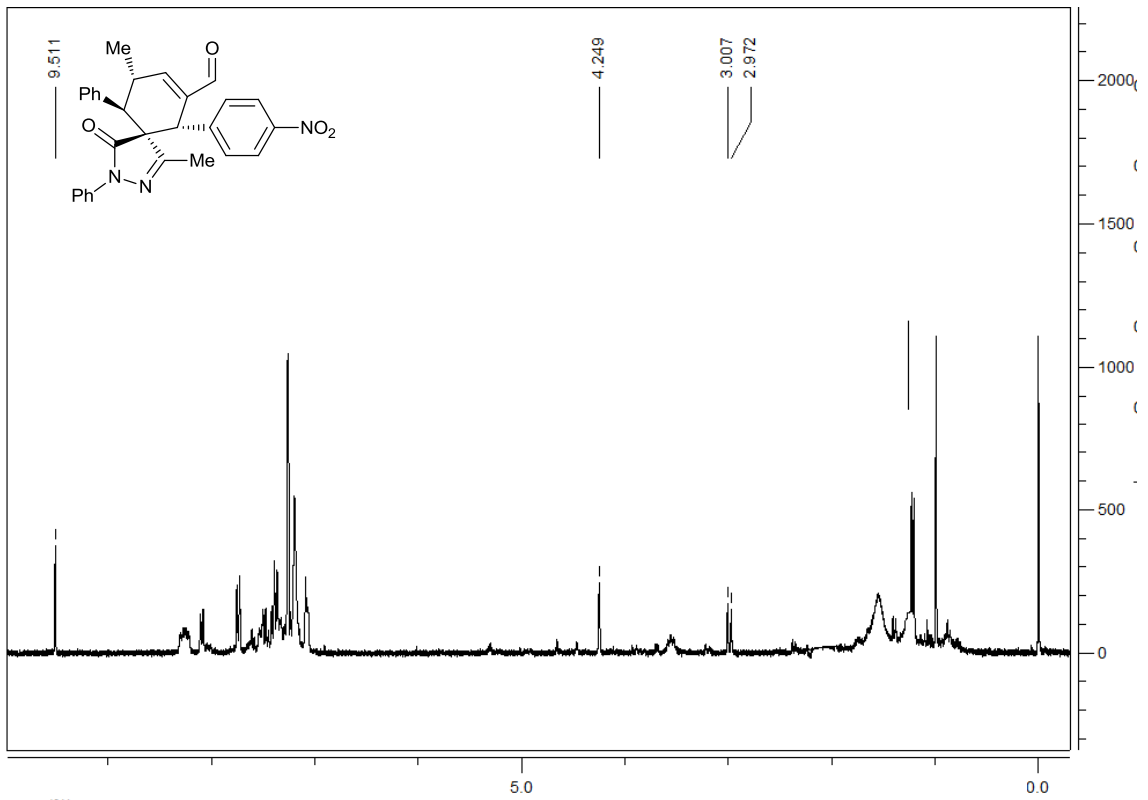


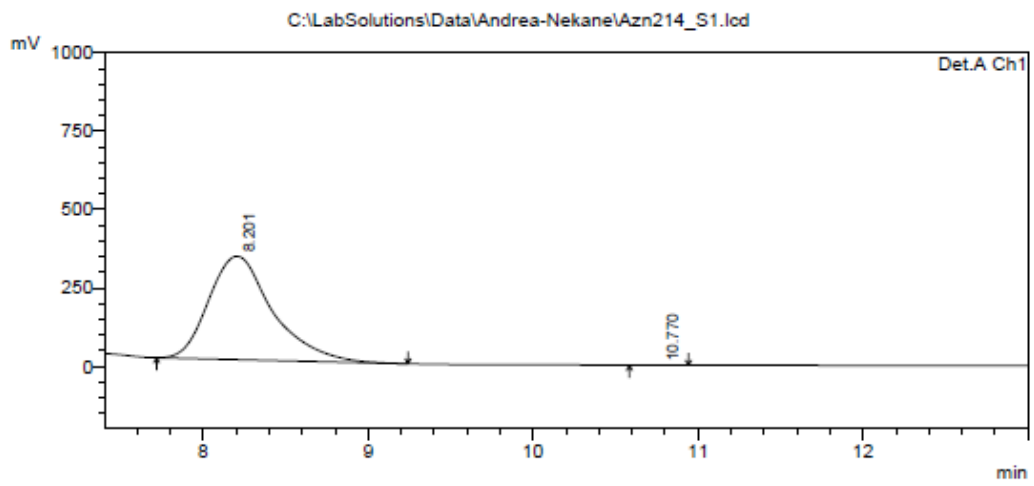
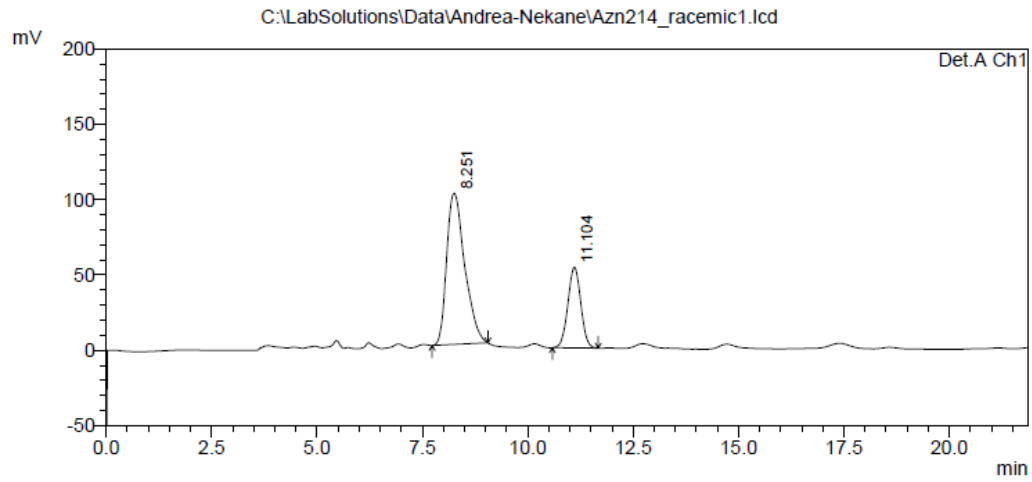
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.703	2894	146	0.951	1.883
2	20.537	301375	7595	99.049	98.117
Total		304268	7741	100.000	100.000

7r

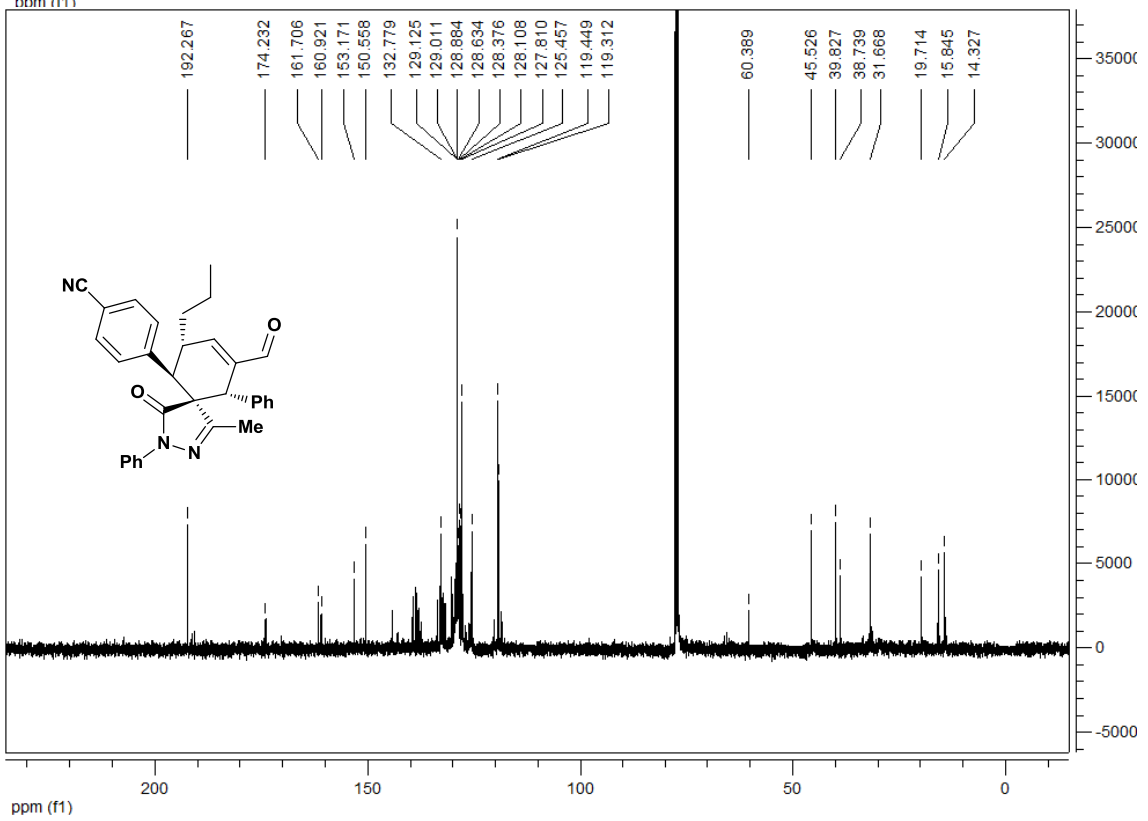
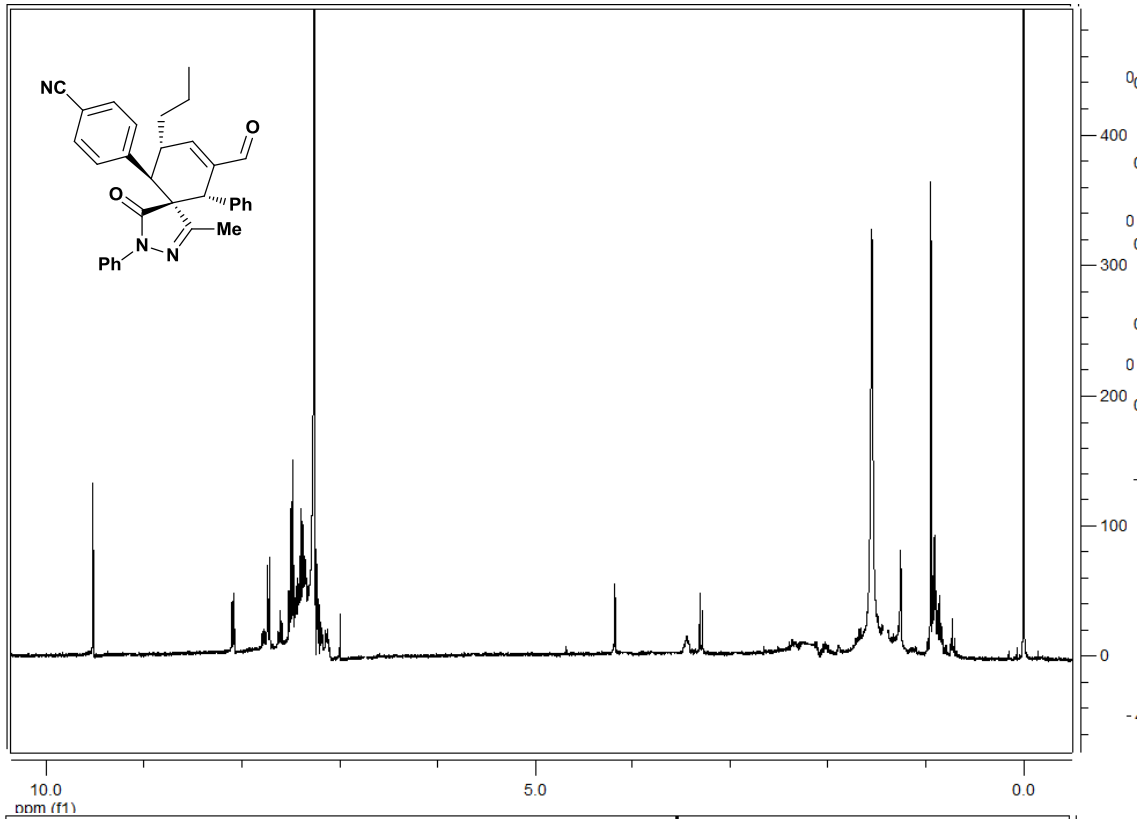


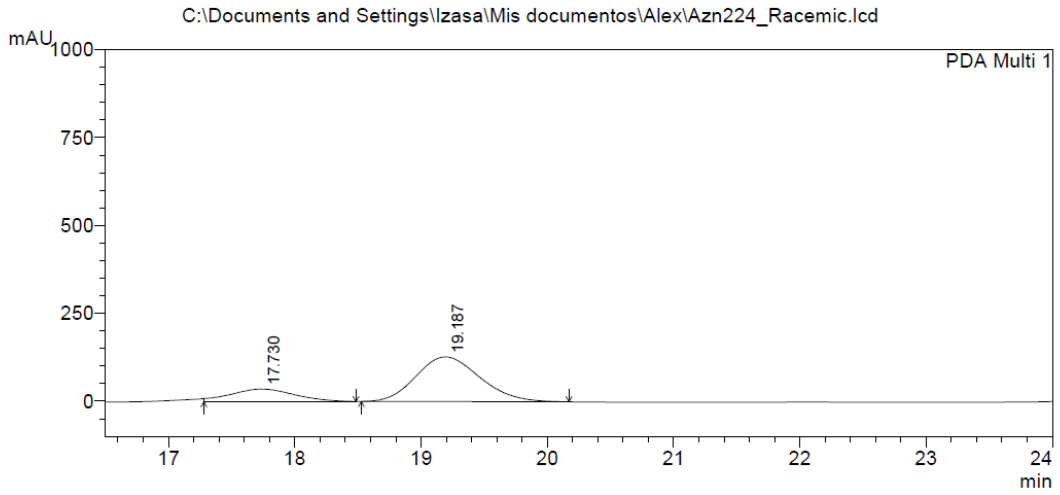


PeakTable

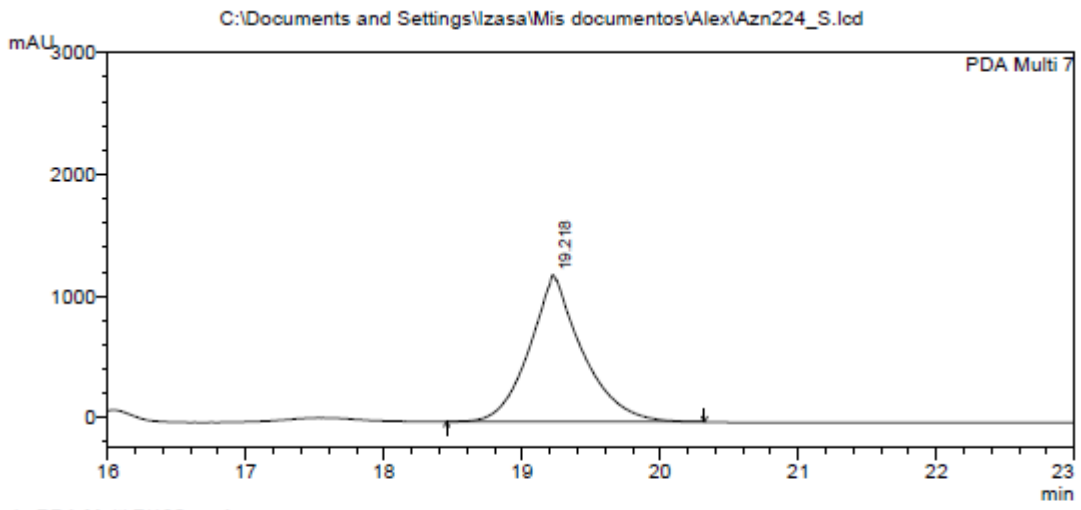
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.201	8866080	330203	99.937	99.858
2	10.770	5600	471	0.063	0.142
Total		8871681	330674	100.000	100.000

7o





1 PDA Multi 1/254nm 4nm

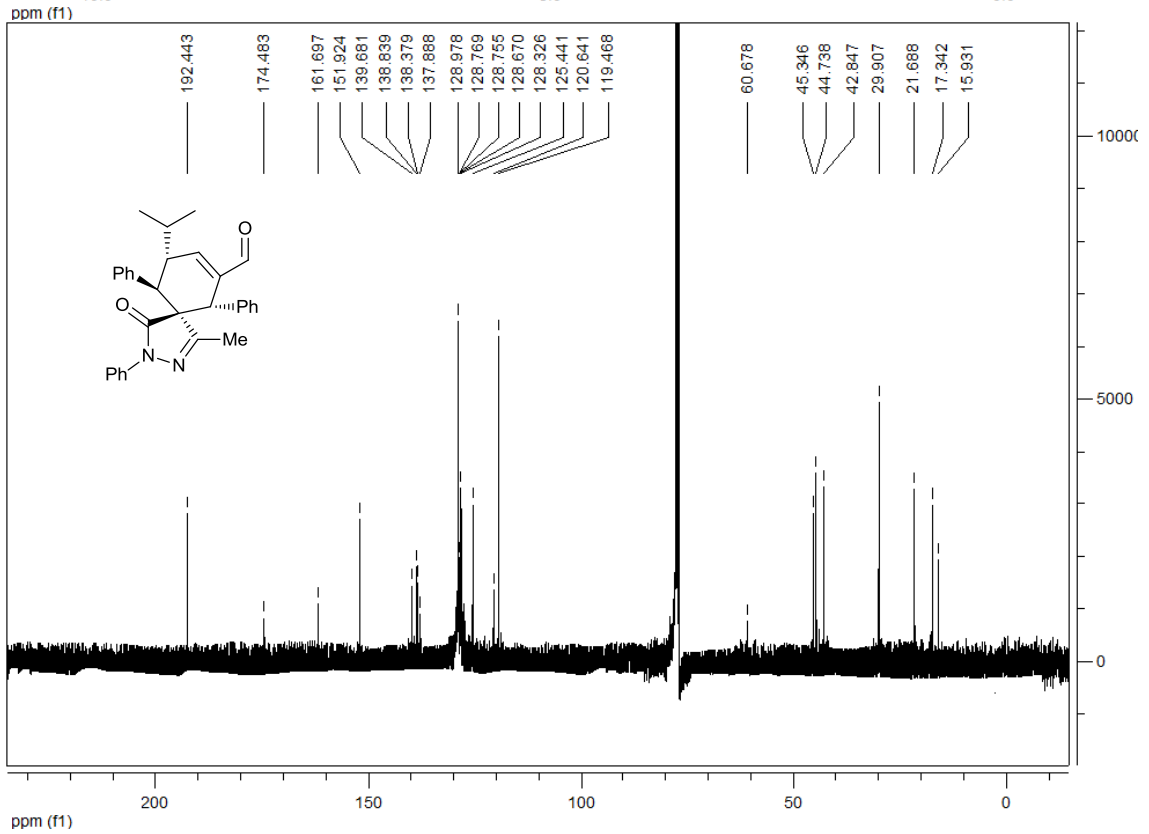
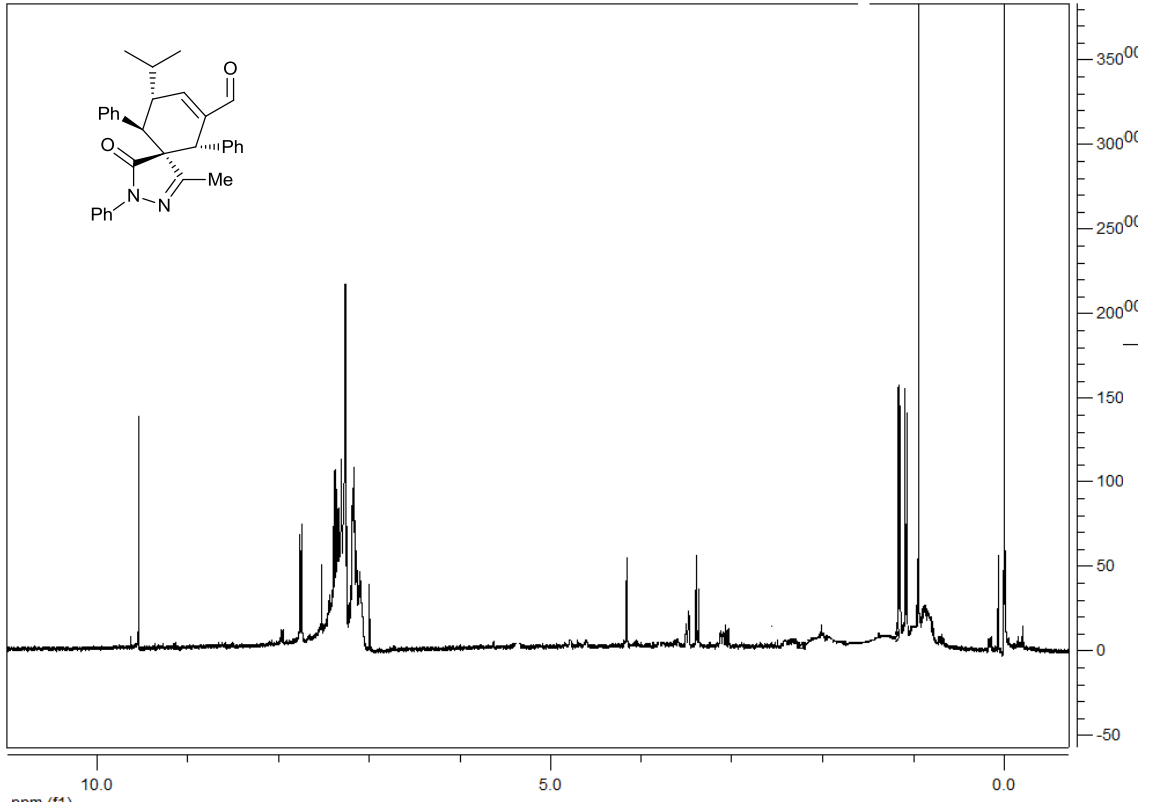


1 PDA Multi 7/190nm 4nm

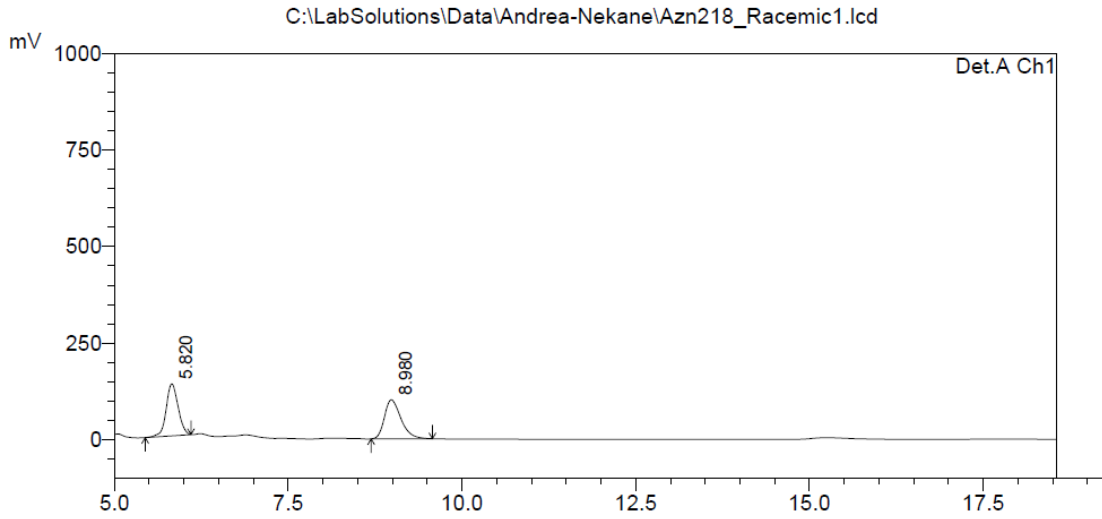
PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.218	31991587	1210050	100.000	100.000
Total		31991587	1210050	100.000	100.000

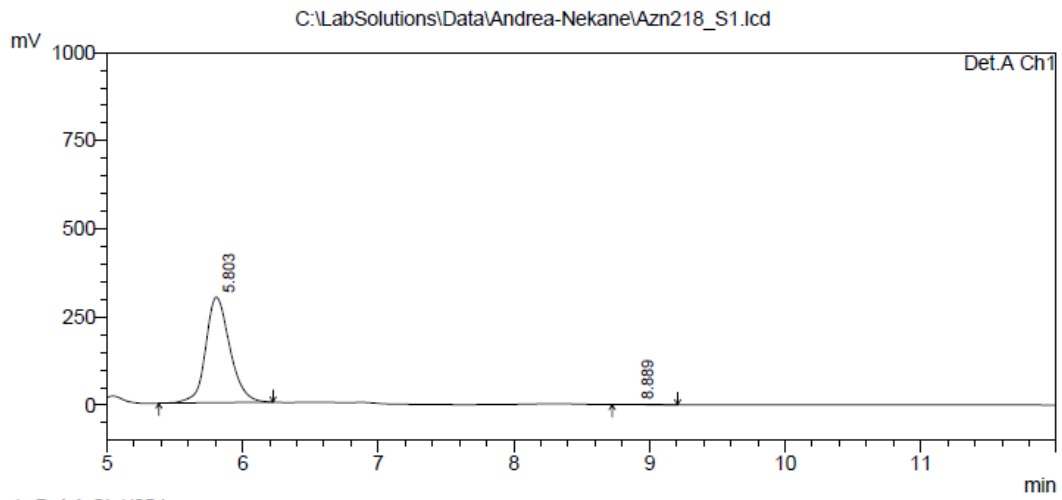
7i







1 Det.A Ch1/254nm



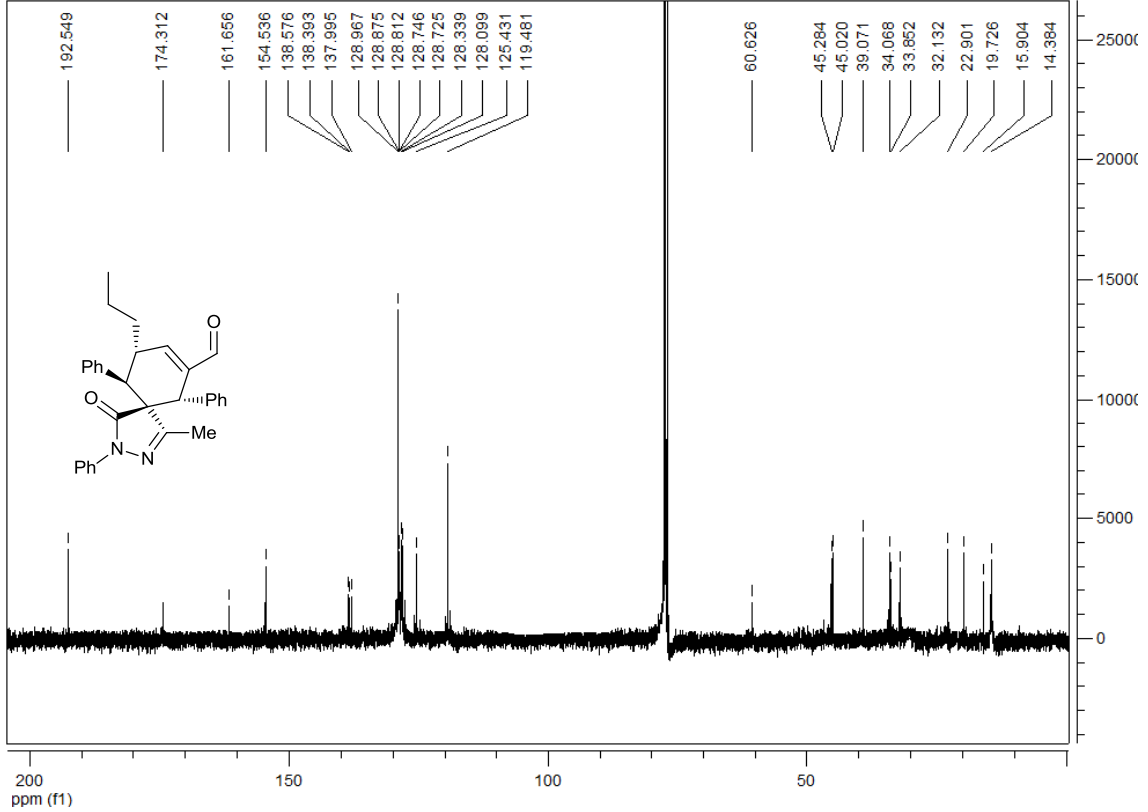
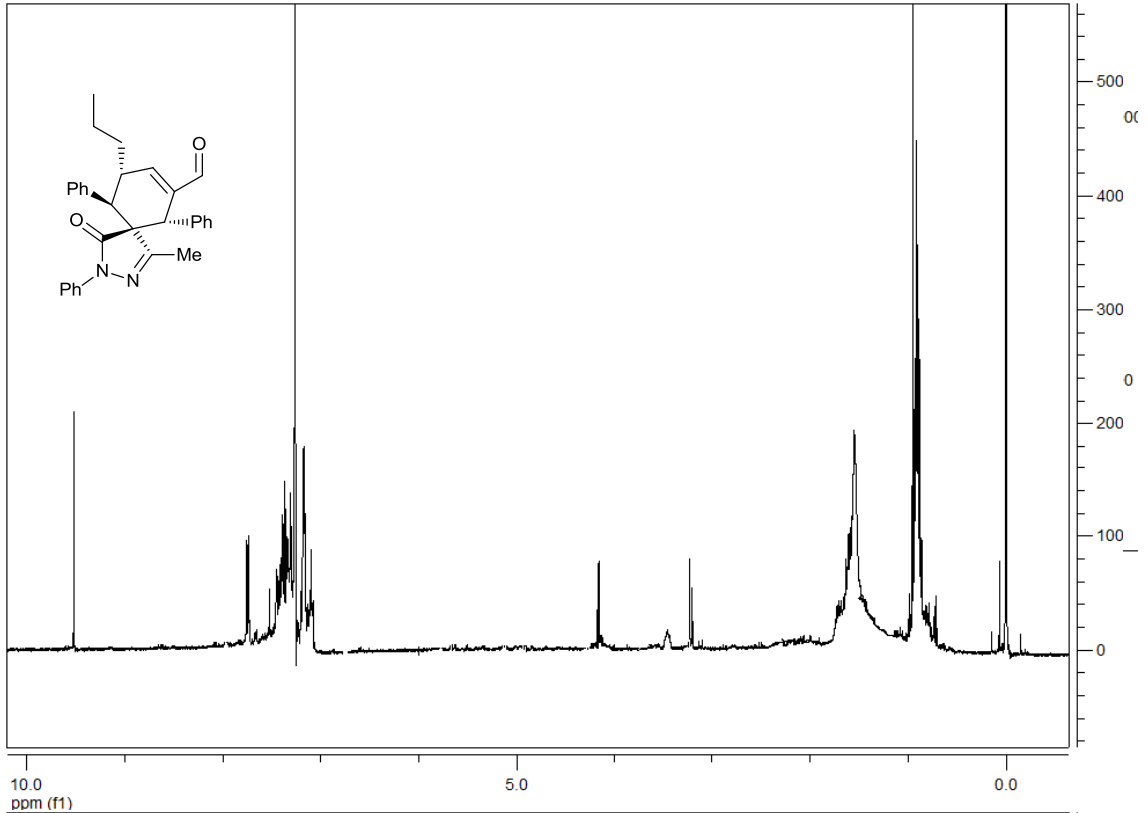
1 Det.A Ch1/254nm

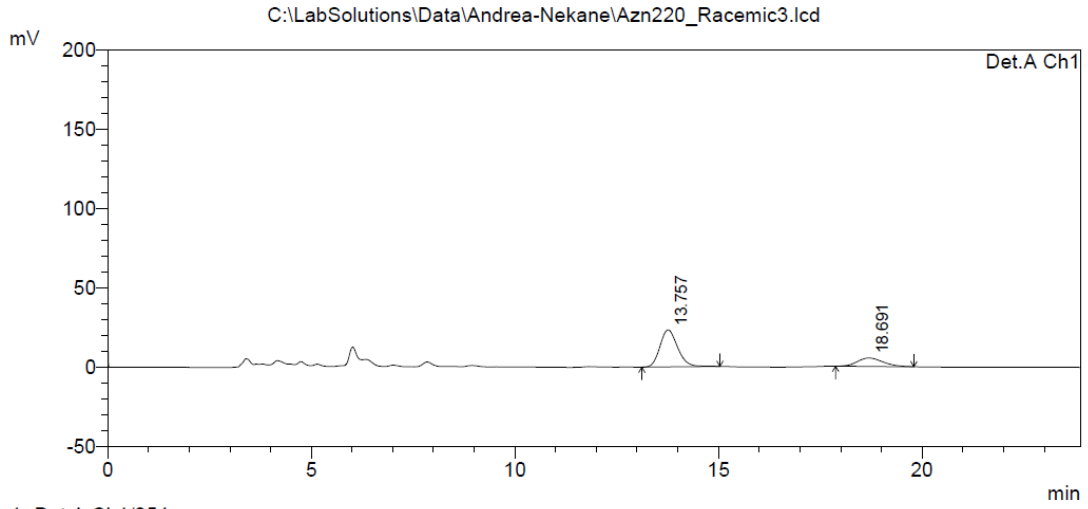
PeakTable

Detector A Ch1 254nm

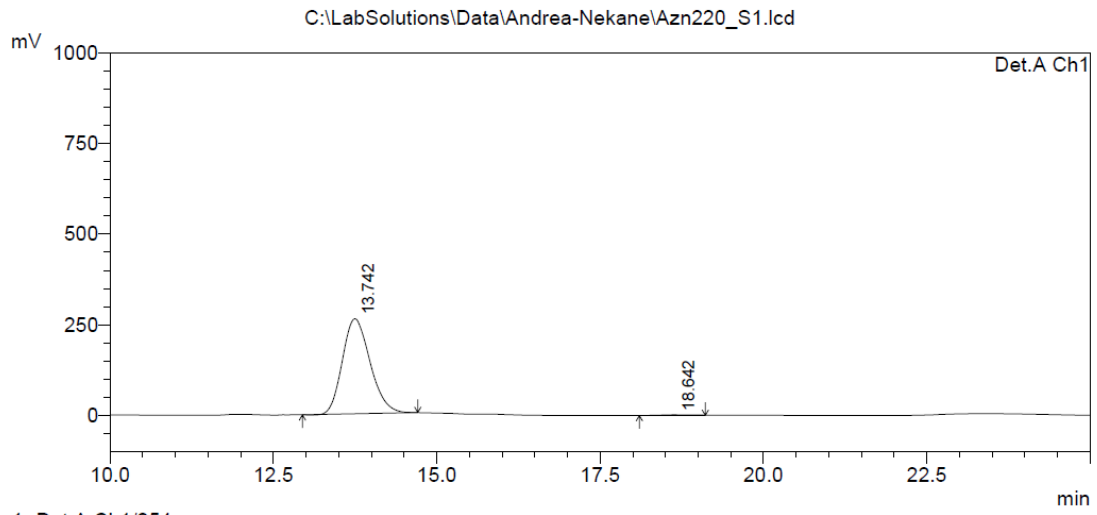
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.803	3715192	299658	99.668	99.703
2	8.889	12373	891	0.332	0.297
Total		3727565	300549	100.000	100.000

7k





1 Det.A Ch1/254nm



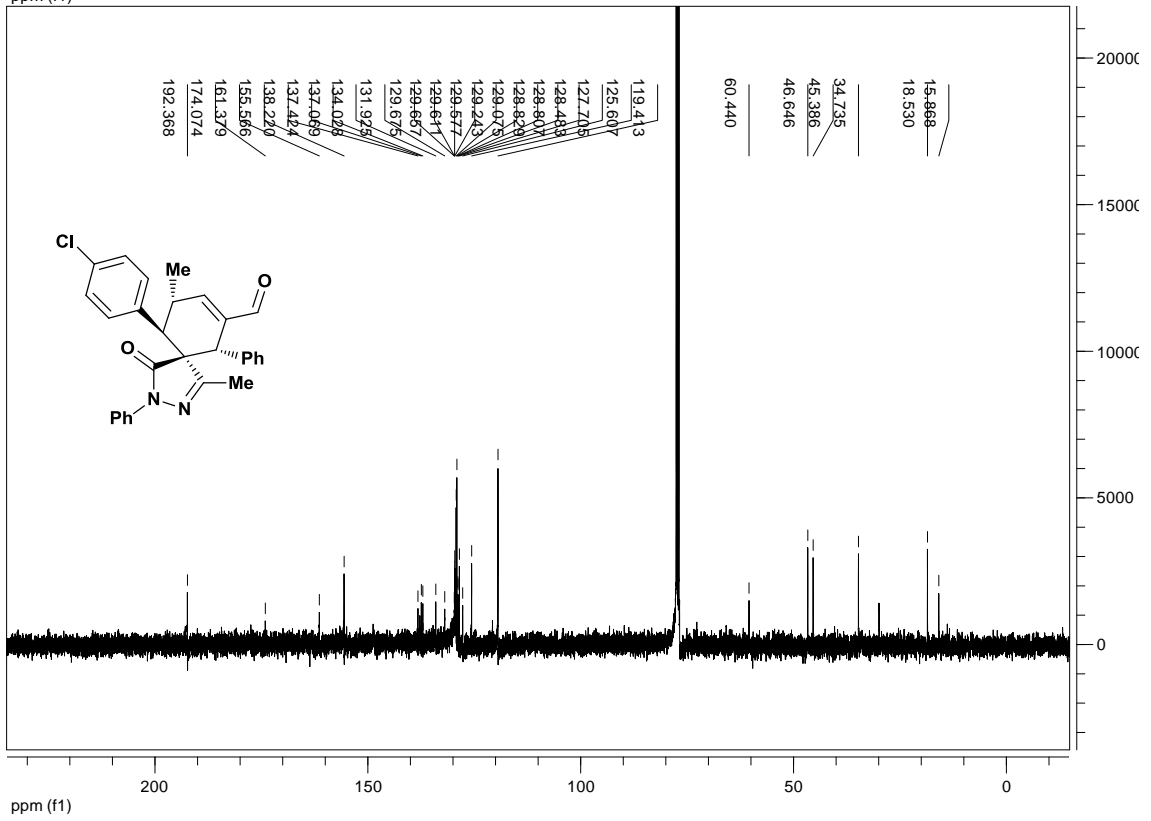
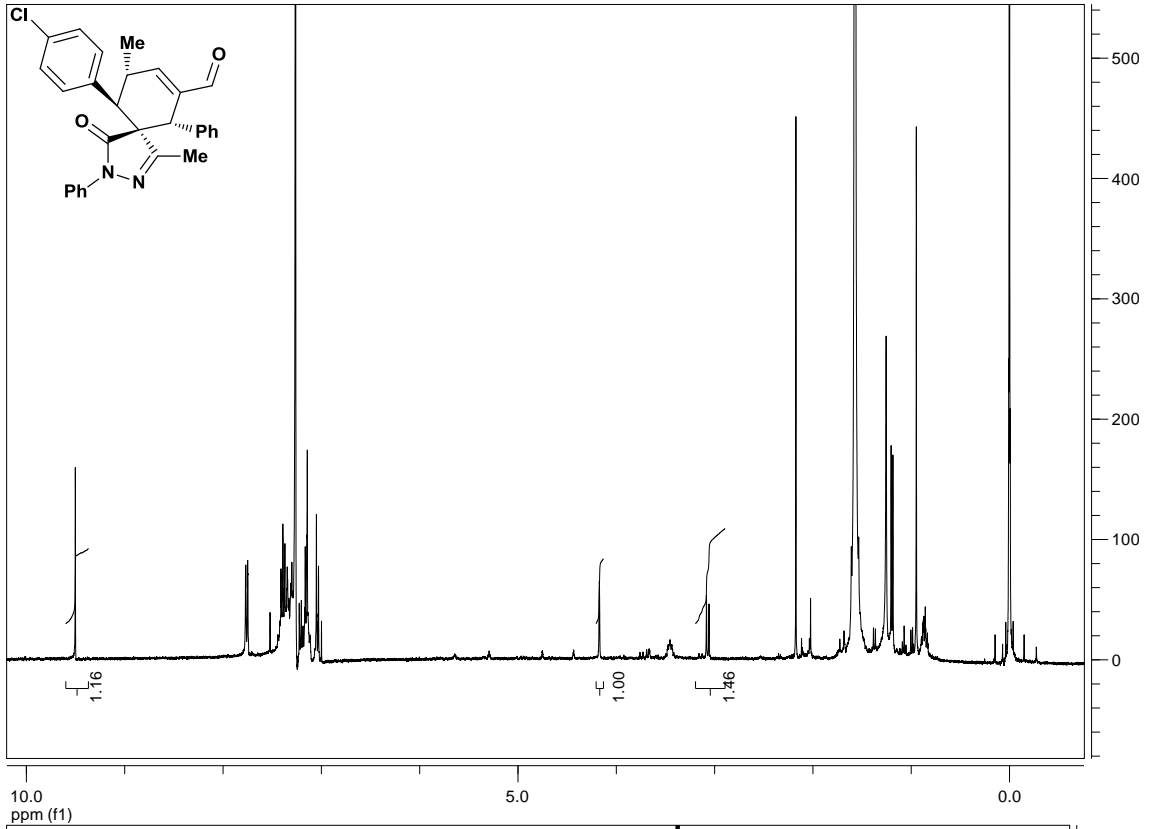
1 Det.A Ch1/254nm

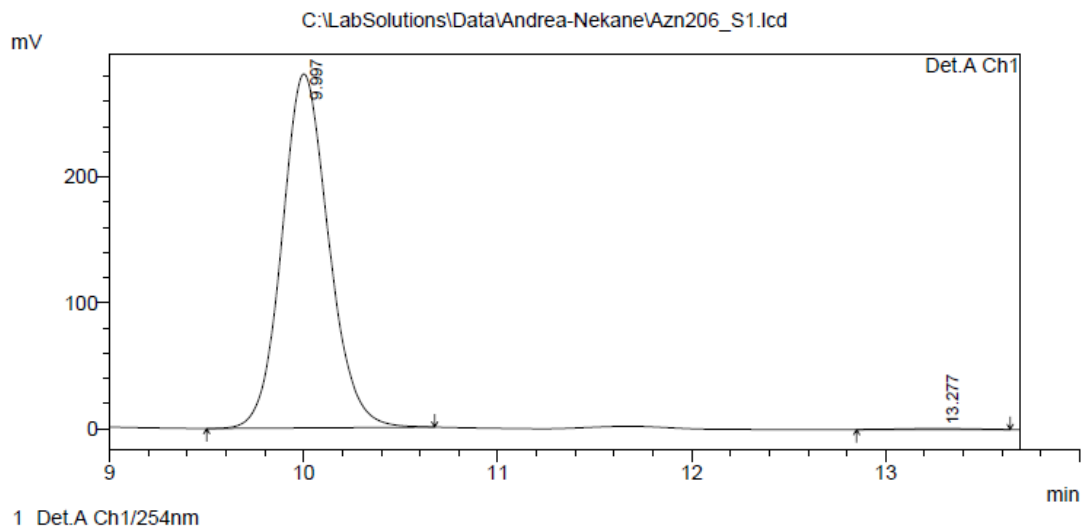
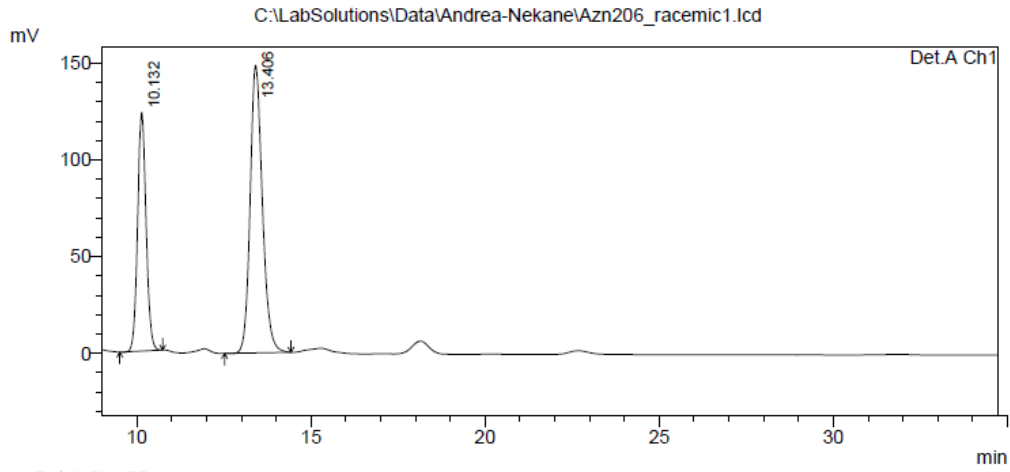
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.742	7724380	261717	99.198	99.333
2	18.642	62480	1758	0.802	0.667
Total		7786859	263475	100.000	100.000

7b

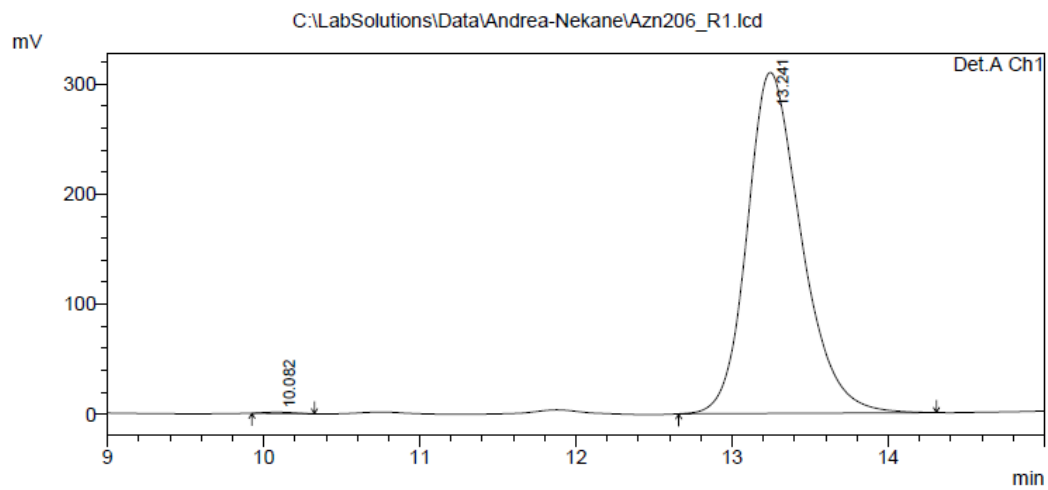




Detector A Ch1 254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.997	4709726	281217	99.622	99.729
2	13.277	17849	765	0.378	0.271
Total		4727575	281982	100.000	100.000

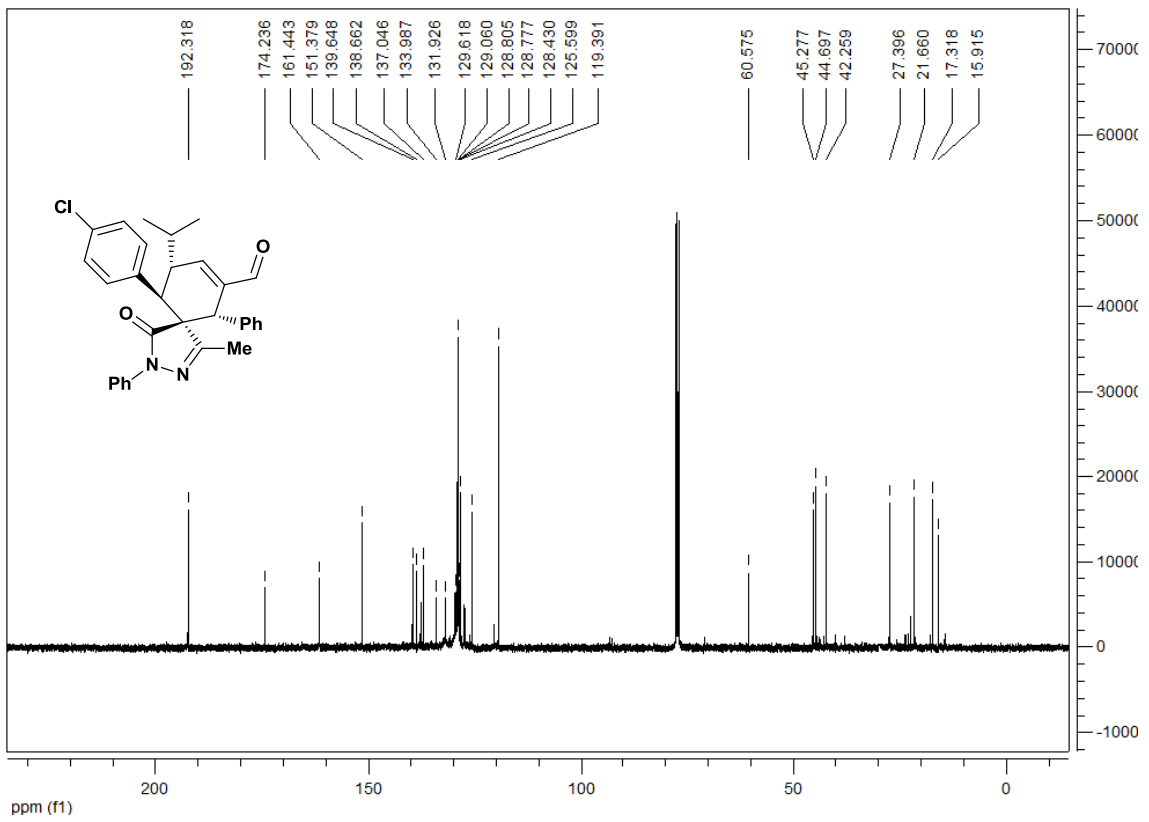
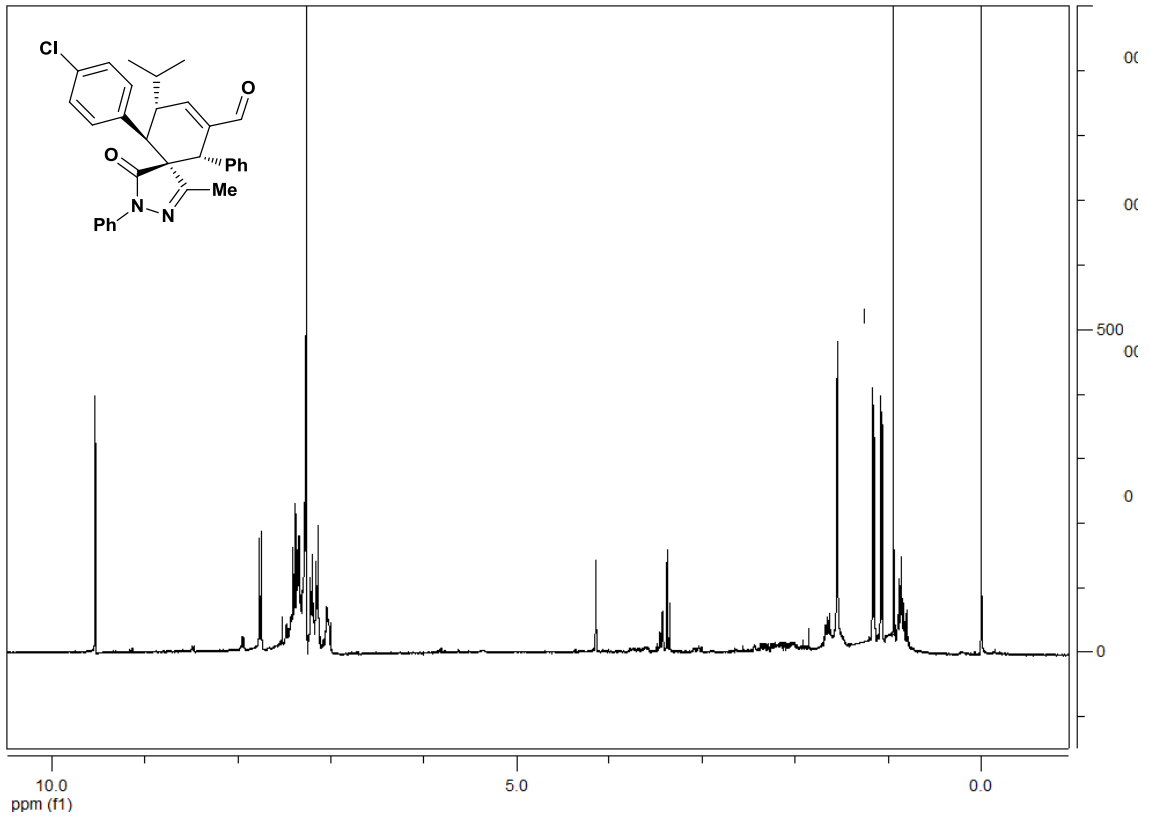


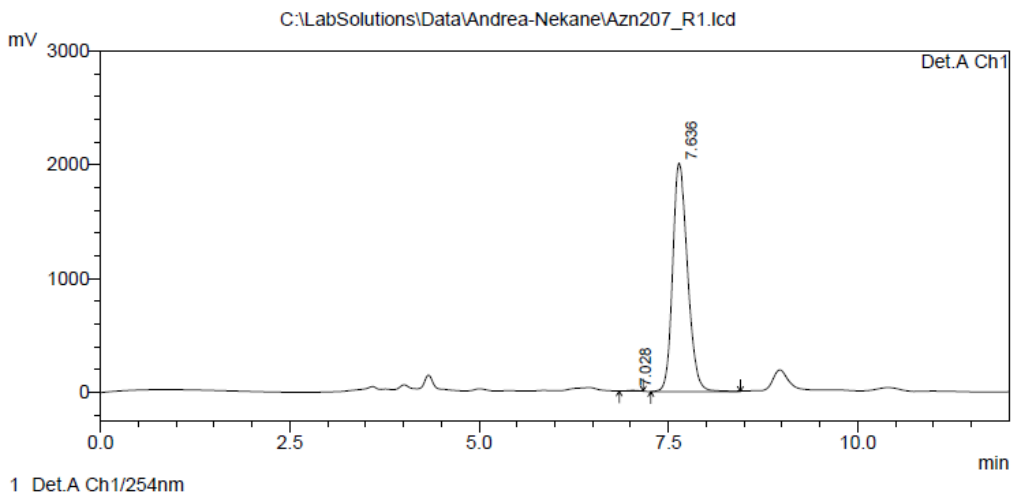
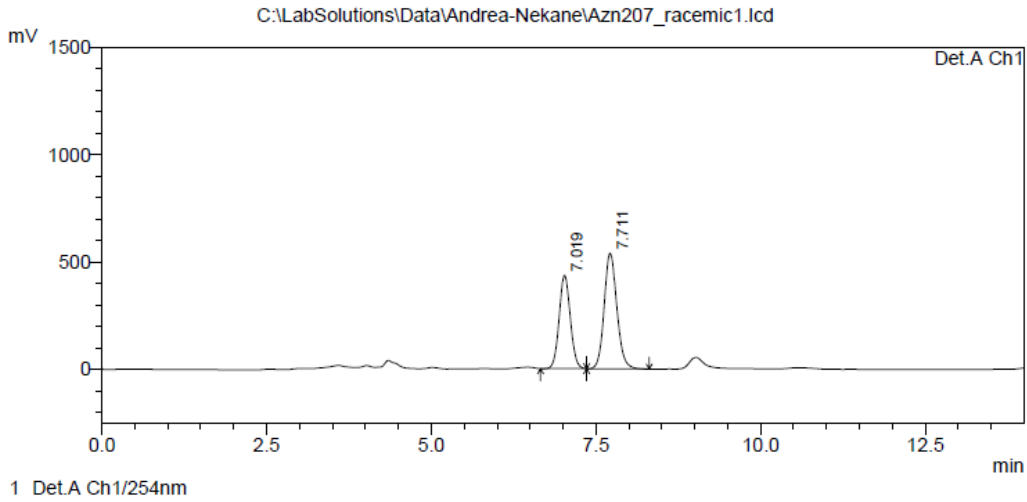
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.082	14680	1152	0.196	0.371
2	13.241	7462295	309140	99.804	99.629
Total		7476975	310291	100.000	100.000

7n

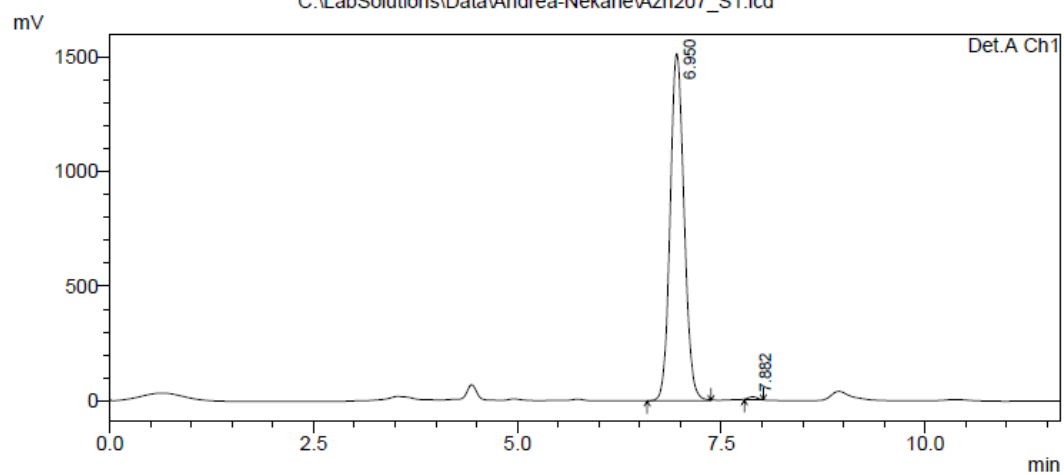




PeakTable

Detector A Ch1 254nm						
Peak#	Ret. Time	Area	Height	Area %	Height %	
1	7.028	51087	5175	0.186	0.257	
2	7.636	27414170	2008261	99.814	99.743	
Total		27465257	2013436	100.000	100.000	





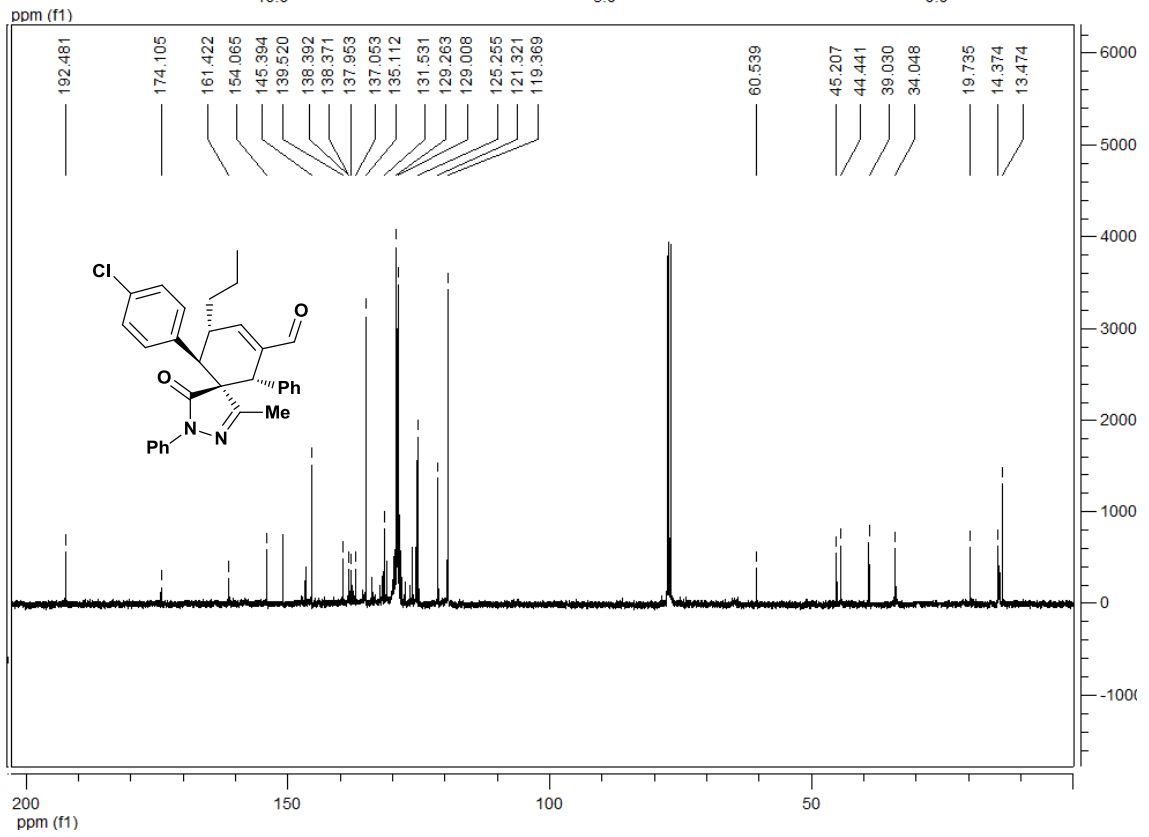
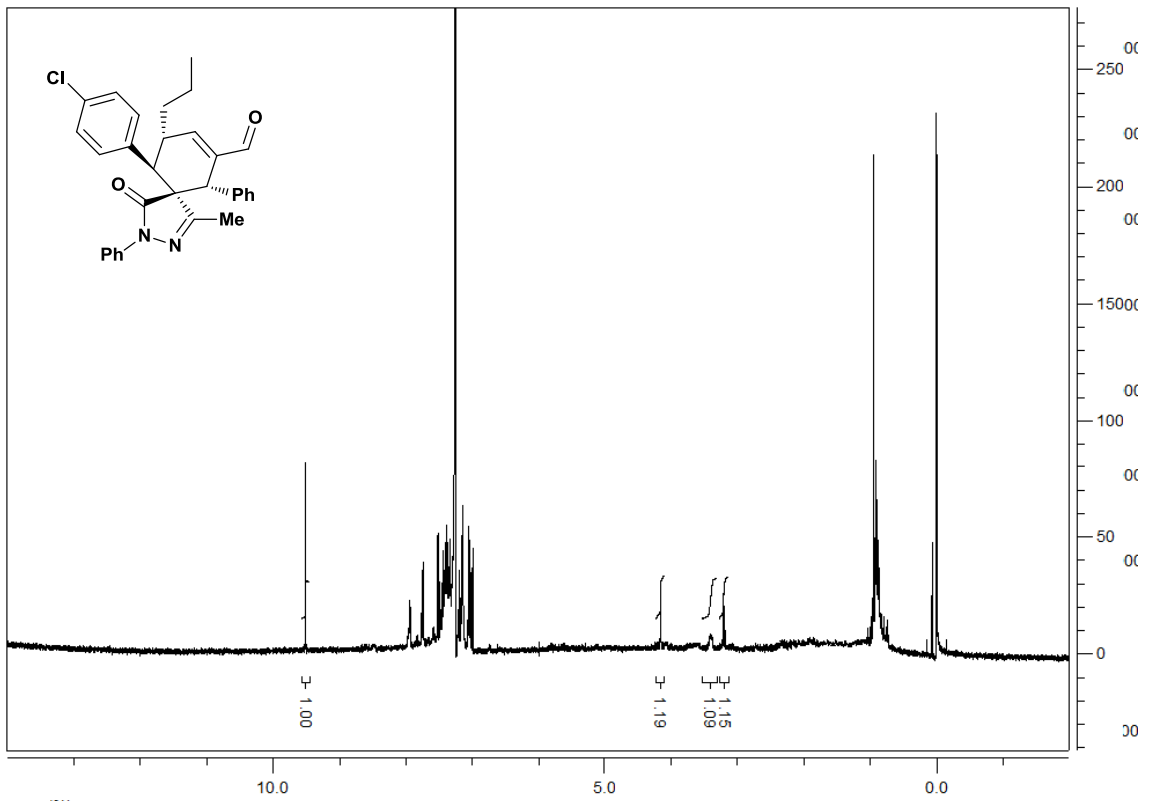
1 Det.A Ch1/254nm

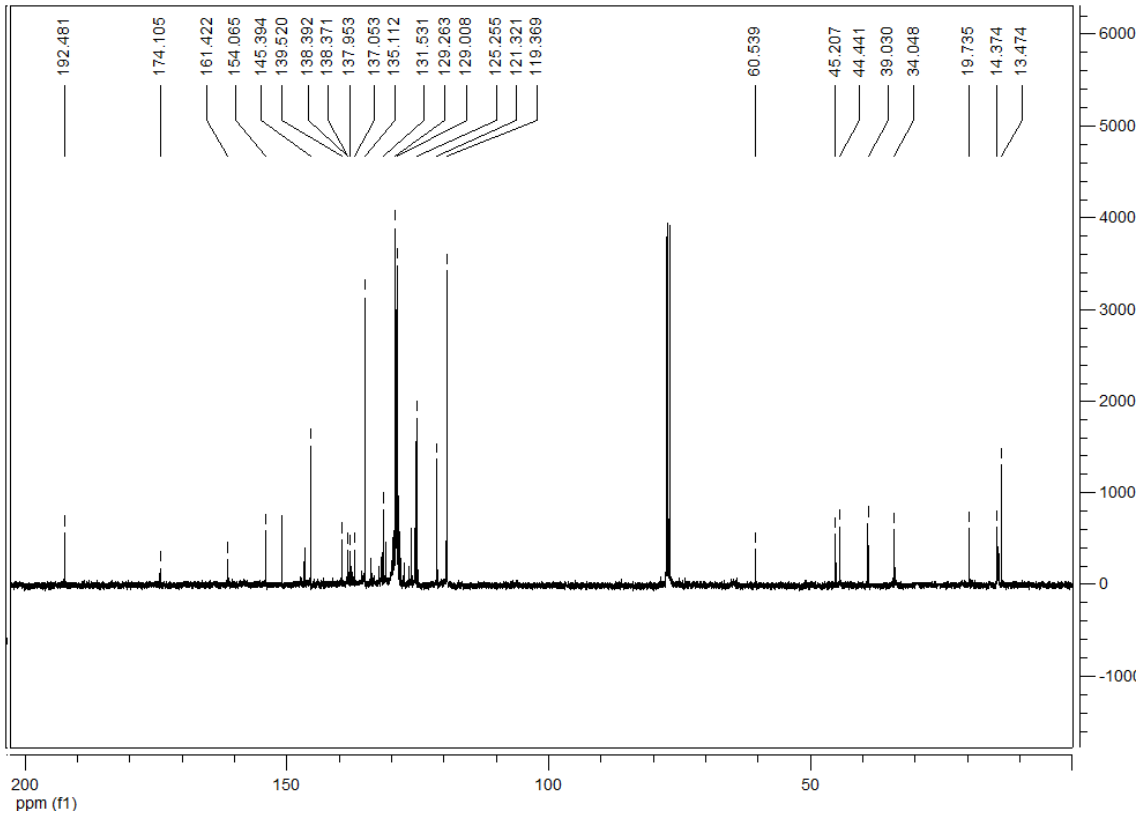
PeakTable

Detector A Ch1 254nm

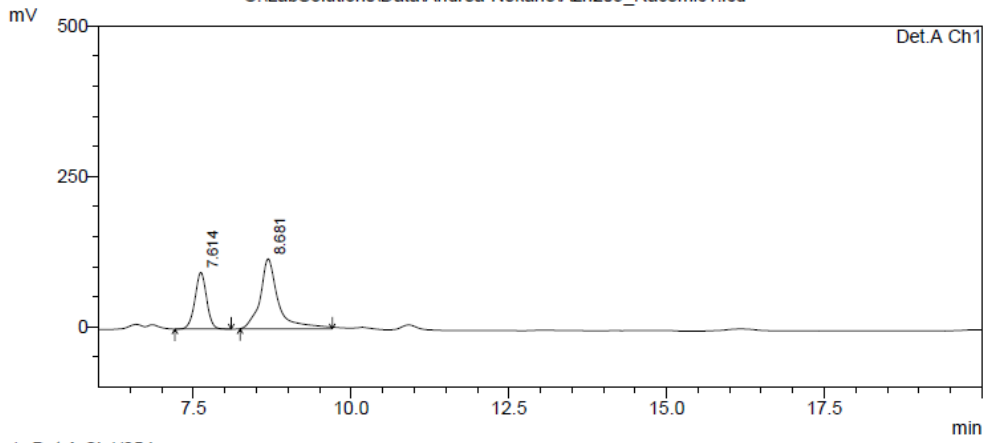
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.950	18017985	1513427	99.404	99.125
2	7.882	107946	13354	0.596	0.875
Total		18125931	1526781	100.000	100.000

7m

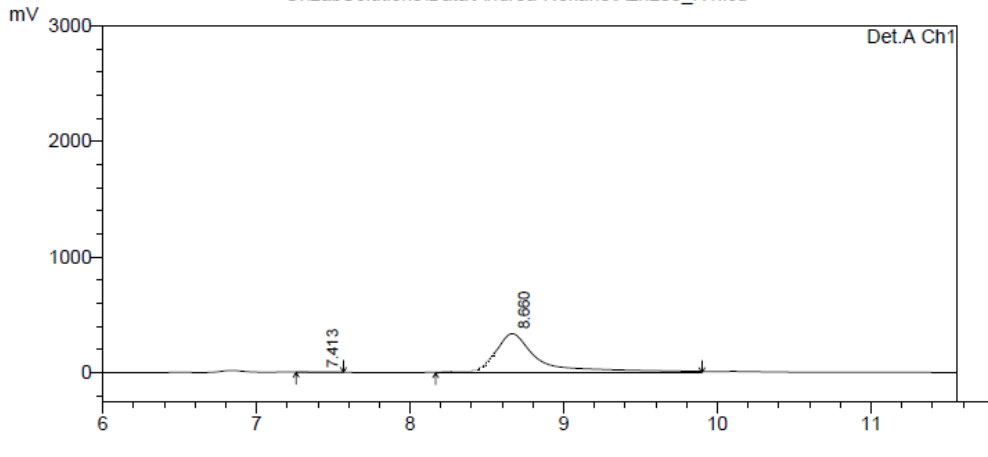




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1 Det.A Ch1/254nm



1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm						
Peak#	Ret. Time	Area	Height	Area %	Height %	
1	7.413	2992	381	0.040	0.113	
2	8.660	7514055	337588	99.960	99.887	
Total		7517048	337969	100.000	100.000	