Supporting Information

Organocatalytic synthesis of spiro compounds via a cascade Michael-Michael-Aldol reaction.

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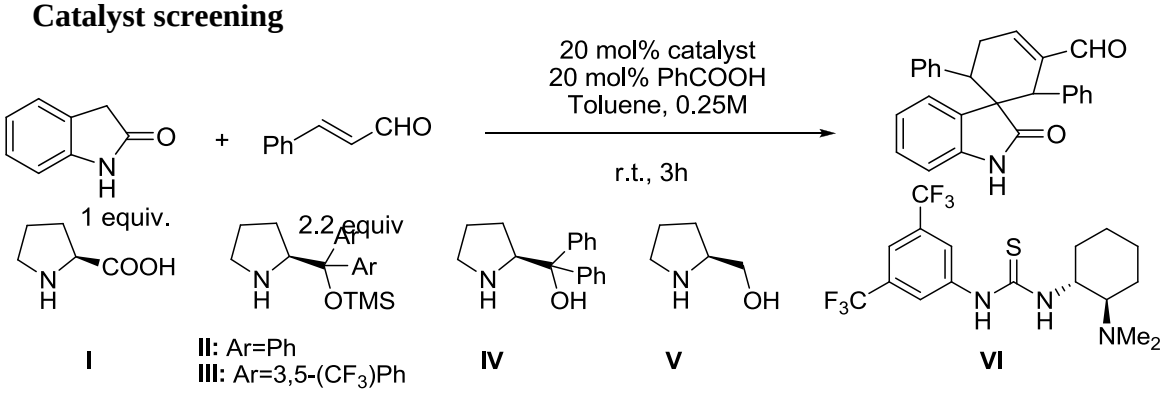
General methods.

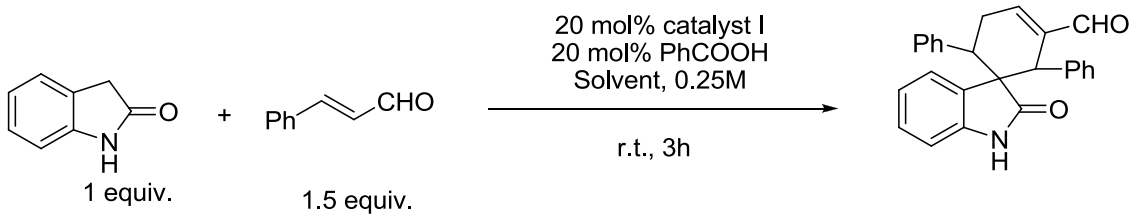
Chemicals and solvents were either purchased *puriss p.A.* from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), conc. H_2SO_4 (60 mL), and H_2O (940 mL) followed by heating or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_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}H NMR, ^{19}F NMR and ^{13}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 $CDCl_3$ as solvent at room temperature. TMS served as internal standard (δ = 0 ppm) for ^{1}H NMR, $CDCl_3$ was used as internal standard (δ = 77.0 ppm) for ^{13}C NMR and TFA was used as external standard for ^{19}F NMR. High-resolution mass spectra were recorded on a Bruker MicrOTOF spectrometer.

Catalyst screening



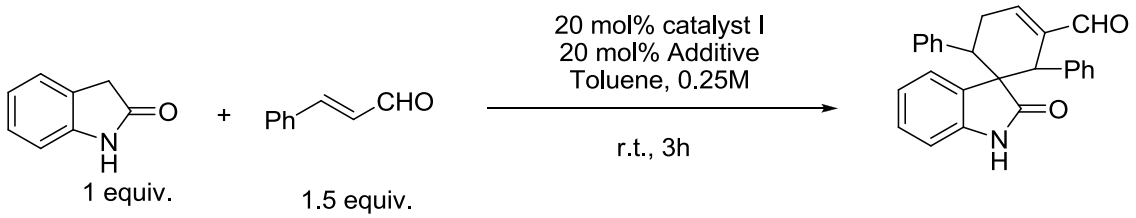
Entry	Catalyst	Conversion (3h)	d.r.	e.e
1	I	--	--	--
2	II	100%	>25:1	>99%
3	III	--	--	--
4	IV	--	--	--
5	V	15%	n.d.	n.d.
6	VI	--	--	--

Solvent screening



Entry	Solvent	Conversion	d.r.	e.e
1	MeCN	100%	10:1	>99%
2	$CHCl_3$	50%	18:1	>99%
3	Toluene	100%	>25:1	>99%
4	MeOH	Traces	n.d.	n.d.
5	AcOEt	54%	22:1	>99%
6	DMSO	Traces	n.d.	n.d.

Additive screening



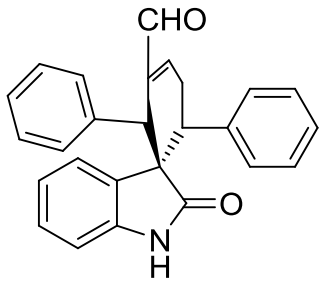
1 equiv. 1.5 equiv.

Entry	Acid	Conversion	d.r.	e.e.
1	--	traces	n.d.	n.d.
2	PhCOOH	100%	>25:1	>99%
2	2-F-PhCOOH	100%	>25:1	>99%
3	3-F-PhCOOH	100%	>25:1	>99%
4	4-F-PhCOOH	100%	>25:1	>99%

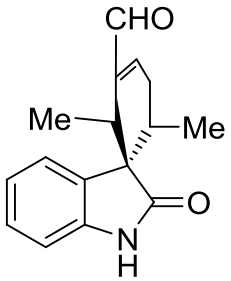
General Procedure for the synthesis of spiro compounds via a cascade reaction:

In a small flask, oxindole (or heterocycle) (0.25 mmol, 1equiv.) and α,β-unsaturated aldehyde (0.75 mmol, 1.5 equiv.) were stirred in toluene at room temperature in the presence of catalyst **I** (0.05 mmol, 0.2 equiv.) and benzoic acid (0.05 mmol, 0.2 equiv.). The reaction was stirred overnight, monitored by ^{1}H-NMR. Then, the crude mixture was purified by column chromatography to affors the spiro compound in yields and stereoselectivities cited in the text.

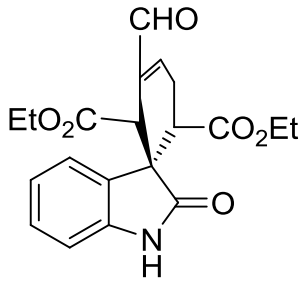
For racemic compounds, sometimes we run independently reaction using in each one the enantiopure catalyst. The "racemic" mixture was obtained after mixing both isolated products. This method was used when the use of racemic catalysts gave complexe mixtures of diastereomers.



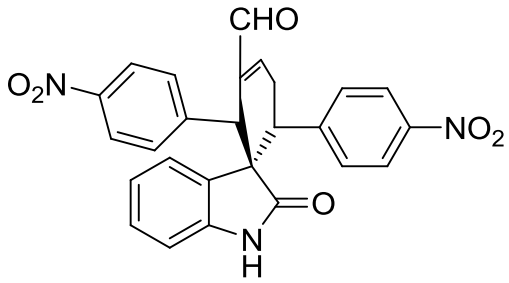
3a: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.54 (s,1H), 7.39-7.36 (m, 2H), 7.26 (s, 4H), 6.98 (s, 5H), 6.88 (dt, J_1=7.7Hz, J_2=1.2Hz, 1H), 6.51 (m, 1H), 6.45 (dt, J_1=7.7Hz, J_2=1.2Hz, 1H), 5.42 (m, 1H), 4.74 (bs, 1H), 3.98 (s, 1H), 3.61 (dd, J_1=11.4Hz, J_2=4.8Hz, 1H), 3.52 (m, 1H), 2.94 (dt, J_1=19.2Hz, J_2=4.7Hz, 1H).**^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 192.5, 179.4, 151.1, 139.7, 139.6, 139.4, 138.8, 128.5, 127.9, 127.6, 127.5, 126.8, 120.7, 108.6, 53.9, 45.3, 41.9, 31.5.**HRMS [M+H]$^{+}$:** Calculated for $[C_{26}H_{22}NO_2]^{+}$: 380.1645; found: 380.1641. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1})**:** t_R= 16.1, 21.9 min.
IR (ν_{max}, cm^{-1}): 529, 561, 594, 667, 700, 739, 755, 775, 1080, 1112, 1156, 1181, 1232, 1264, 1354, 1408, 1452, 1472, 1484, 1493, 1599, 1619, 1650, 1688, 3028, 3059, 3265. $[\alpha]_D^{25}$ = -78.9 (c=0.95, $CHCl_3$).



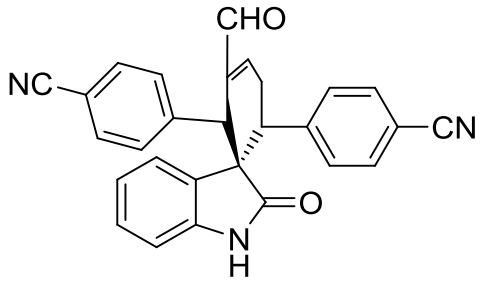
3b: Colorless oil. ^{1}H-NMR (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.43 (s, 1H), 7.76 (bs, 1H), 7.22 (td, J_1=7.7Hz, J_2=1.0Hz, 1H), 7.15 (d, J= 7.5Hz, 1H), 7.02 (td, J_1=7.5Hz, J_2=1.0Hz, 1H), 6.94 (t, J=3.7Hz, 1H), 6.87 (d, J=7.7Hz, 1H), 2.82 (q, J=7.1Hz, 1H), 2.69-2.62 (m, 2H), 2.52-2.42 (m, 1H), 1.18 (d, J=7.1Hz, 3H), 0.73 (d, J=6.7Hz, 3H).
^{13}C-NMR (75 MHz. $CDCl_3$): δ(ppm)= 193.4, 179.9, 150.8, 142.8, 140.7, 130.0, 127.9, 125.7, 121.6, 109.5, 53.5, 32.4, 32.2, 29.0, 17.6, 16.4. HRMS $[M+H]^{+}$: Calculated for $[C_{17}H_{20}NO_2]^{+}$: 270.1489; found: 270.1492. HPLC (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1}): t_R= 10.64, 11.67 min. **IR (ν_{max}, cm^{-1}):** 639, 708, 757, 806, 976, 1023, 1072, 1102, 1165, 1190, 1234, 1261, 1379, 1471, 1485, 1618, 1687, 2926, 3255. $[\alpha]_D^{25}$ = +60.7 (c=0.15, $CHCl_3$).



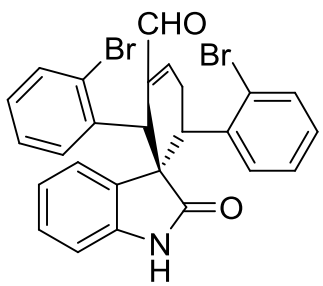
3c: Colorless oil. ^{1}H-NMR (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.51 (s, 1H), 7.69 (s, 1H), 7.22 (m, 2H), 6.96 (m, 1H), 6.86 (d, J_1=7.9Hz, 1H), 3.85 (m, 4H), 3.61 (s, 1H), 3.26 (qt, J_1=11.1Hz, J_2=2.2Hz, 1H), 2.91 (dt, J_1=19.9Hz, J_2=5.6Hz, 1H), 1.04 (t, J=7.1Hz, 3H), 0.93 (t, J=7.1Hz, 3H). ^{13}C-NMR (75 MHz. $CDCl_3$): δ(ppm)= 192.1, 177.7, 171.8, 170.7, 151.1, 140.8, 136.1, 129.1, 123.7, 121.9, 109.7, 61.2, 60.8, 44.7, 43.3, 30.9, 27.0, 13.7, 13.6.HRMS $[M+H]^+$: Calculated for $[C_{20}H_{22}NO_6]^+$: 372.1443; found: 372.1442. HPLC (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1}): t_R= 22.1, 34.9 min. **IR (ν_{max}, cm^{-1}):** 565, 585, 659, 754, 858, 1022, 1097, 1159, 1179, 1235, 1262, 1315, 1344, 1368, 1473, 1619, 1686, 1719, 2853, 2923, 3295. $[\alpha]_D^{25}$ = -63.3 (c=0.4, $CHCl_3$).



3d: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.55 (s, 1H), 7.90-7.83 (m, 5H), 7.48-7.43 (m, 2H), 7.16 (d,J=8.5Hz,3H), 7.01-6.93 (m, 2H), 6.61 (d, J=7.8Hz, 1H), 6.52 (t, J=7.8Hz, 1H), 5.47 (d, J=7.8Hz, 1H), 4.12 (s, 1H), 3.67-3.61 (m, 1H), 3.61-3.50 (m, 1H), 3.02 (dt, J_1=19.5Hz, J_2=4.7Hz, 1H).**^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 193.0, 179.3, 151.9, 147.6, 147.1, 140.6, 131.2, 130.8, 130.5, 130.4, 129.9, 129.6, 127.2, 124.5, 124.4, 124.3, 124.3, 124.2, 124.1, 123.8, 122.5, 110.7, 66.4, 46.1, 43.1, 31.9.**HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{26}H_{18}N_3O_6]^+$: 468.1201; found: 468.1206. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 75:25, 254 nm^{-1})**:** t_R= 25.4, 30.8 min. **IR (ν_{max}, cm^{-1}):** 560, 598, 655, 698, 733, 853, 901, 973, 1014, 1108, 1156, 1179, 1264, 1341, 1407, 1471, 1514, 1596, 1618, 1682, 2851, 2922, 3058. $[\alpha]_D^{25}$ **=** -87.0 (c=0.5, $CHCl_3$).

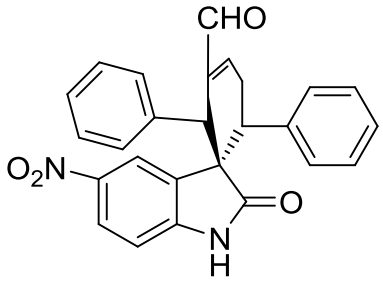


3e: ^{1}H-NMR (400 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.54 (s, 1H), 7.50-6.90 (m, xxH), 6.58 (d, J=7.9Hz, 1H), 6.52 (t, J=7.4 Hz, 1H), 5.41 (d, J=7.4 Hz, 1H), 4.05 (s, 1H), 3.58-3.45 (m, 2H), 3.04-2.92 (m, 1H). **^{13}C-NMR** (100 MHz. $CDCl_3$): δ(ppm)= 192.3, 178.8, 151.3, 144.8, 144.3, 139.9, 139.0, 132.1, 132.0, 129.5, 128.9, 127.7, 126.2, 121.5, 118.6, 11.8, 11.3, 109.8, 53.5, 45.4, 42.3, 31.1. **HRMS (ESI) $[M-H]^-$:** Calculated for $[C_{28}H_{18}N_3O_2]^-$: 428.1405; found: 428.1403. HPLC: Chiralcel IB, hexane-IPA 80:20, 1 mL/min, tr_1: 26 min tr_2: 28 min.

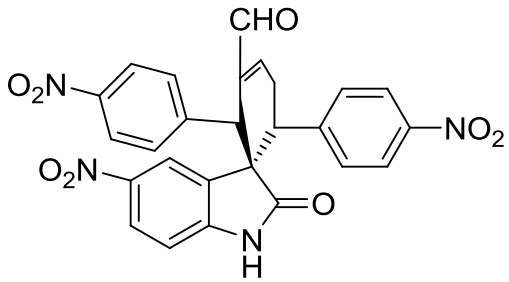


3f: ^{1}H-NMR (400 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.54 (s, 1H), 7.50-6.90 (m, xxH), 6.57 (d, J=7.7Hz, 1H), 6.44 (t, J=7.4 Hz, 1H), 5.68 (d, J=7.1 Hz, 1H), 4.69 (s, 1H), 4.44 (dd, J=11.7, 5.6 Hz, 1H), 3.45-3.25 (m, 1H), 2.95-2.85 (m, 1H). **^{13}C-NMR** (100 MHz. $CDCl_3$): δ(ppm)= 192.3, 180.0, 151.3, 140.4, 140.2, 139.9, 138.1, 132.9, 132.8, 129.9, 129.5, 129.1, 128.6,

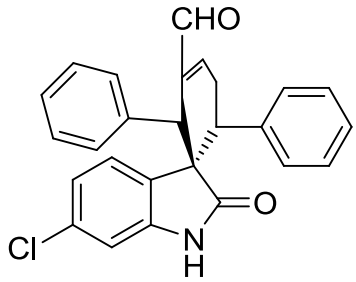
128.2, 128.0, 127.5, 127.1, 125.5, 125.4, 121.5, 108.9, 53.3, 43.9, 39.9, 31.5. **HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{26}H_{20}Br_2NO_2]^+$: 535.9855; found: 535.9848. HPLC: Chiralcel IB, hexane-IPA 90:10, 1 mL/min, tr_1: 17. min tr_2: 37 min.



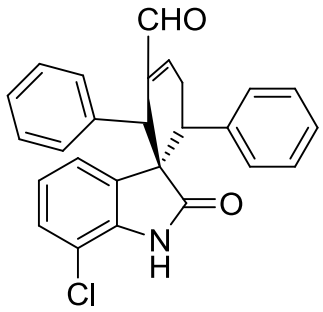
3g: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.74 (s,1H), 8.71 (s, 1H), 8.06 (dd, J_1= 8.6Hz, J_2=2.3Hz, 1H), 7.60-7.42 (m, 6H), 7.24-7.10 (m, 5H), 6.81 (d, J=8.6Hz, 1H), 6.4 (d, J=2.3Hz, 1H), 4.21 (s, 1H), 3.89-3.79 (m ,1H), 3.76-3.64 (m, 1H), 3.19 (dt, J_1=20Hz, J_2=5.5Hz, 1H), **^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 192.3**,** 179.8, 150.8, 145.5, 141.8, 138.9, 138.4, 137.6, 133.4, 132.8, 130.1, 130.1, 128.4, 128.3, 128.2, 127.3, 124.7, 122.6, 108.6, 54.3, 45.1, 41.8, 31.1. **HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{26}H_{19}N_2O_4]^+$: 423.1350; found: 423.1350. **HPLC** (Chiralpak IA©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1})**:** t_R= 36.6, 53.1 min. **IR (ν_{max}, cm^{-1}):** 701, 736, 758, 1080, 1108, 1158, 1176, 1224, 1335, 1453, 1481, 1521, 1600, 1624, 1652, 1684, 1716, 2851, 2921. $[\alpha]_D^{25}$ **=** -21.6 (c=0.25, $CHCl_3$).



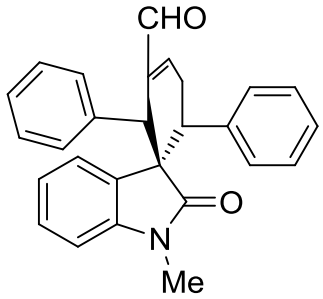
3h: Colorless oil. **^{1}H-NMR** (300 MHz. $(CD_3)_2CO$, TMS_{int}): δ(ppm)= 9.62 (s, 1H), 8.08-7.92 (m, 2H), 7.97-7.86 (m, 4H), 7.68-7.61 (m, 1H), 7.45-7.39 (m, 3H), 6.85 (d, J=8.6Hz, 1H), 6.38 (d, J=2.2Hz, 1H), 4.28 (s, 1H), 4.13-4.07 (m, 1H), 3.58-3.45 (m, 1H), 3.19 (td, J_1=20.2Hz, J_2=5.5Hz, 1H).**^{13}C-NMR** (75 MHz. $(CD_3)_2CO$): δ(ppm)= 193.9, 153.5, 149.3, 149.0, 148.8, 148.4, 143.4, 140.3, 136.1, 131.7, 131.0, 129.6, 127.0, 125.3, 125.0, 124.9, 124.5, 124.4, 123.7, 111.2, 55.2, 46.3, 43.2, 32.2. **HRMS (ESI) $[M+H]^-$:** Calculated for $[C_{26}H_{17}N_4O_8]^-$:513.1052; found: 513.1043. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 70:30, 254 nm^{-1})**:** t_R= 33.9, 51.1 min. **IR (ν_{max}, cm^{-1}):** 553, 607, 644, 696, 735, 755, 846, 914, 1013, 1079, 1107, 1177, 1221, 1260, 1337, 1402, 1450, 1481, 1514, 1597, 1625, 1681, 1720, 2924. $[\alpha]_D^{25}$ **=** -121.5 (c=0.2, $CHCl_3$, 88% ee).



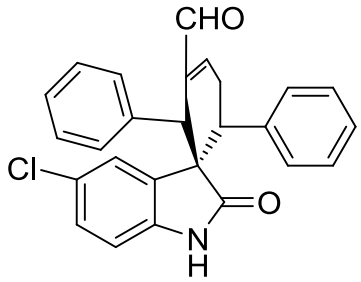
3i: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.52 (s, 1H), 8.32 (s, 1H), 7.42-7.38 (m, 2H), 7.31-7.25 (m, 2H), 7.04-6.89 (m, 7H), 6.55 (d, J=2Hz, 1H), 6.43 (dd, J_1=7.9Hz, J_2=2.0Hz, 1H), 5.31 (d, J=8.0Hz, 1H), 3.98 (s, 1H), 3.62-3.54 (m, 1H), 3.54-3.41 (m, 1H), 2.94 (dt, J_1=19.2Hz, J_2=4.4Hz, 1H).**^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 193.7, 181.2, 152.3, 142.2, 140.7, 140.5, 139.7, 134.5, 130.2, 129.6, 129.4, 128.9, 128.8, 128.4, 121.9, 110.8, 55.212, 46.5, 43.1, 32.7. **HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{26}H_{21}ClNO_2]^-$: 414.1255; found: 414.1260. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1})**:** t_R= 16.9, 26.1 min. **IR (ν_{max}, cm^{-1}):** 535, 554, 586, 603, 629, 668, 698, 717, 737, 759, 854, 916, 1072, 1124, 1158, 1178, 1213, 1247, 1263, 1337, 1373, 1397, 1451, 1485, 1615, 1647, 1673, 1715, 2851, 2921, 3351. $[\alpha]_D^{25}$ **=** -106.3 (c=0.52, $CHCl_3$).



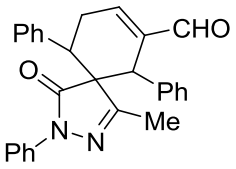
3j: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.53 (s, 1H), 8.12-8.06 (m, 1H), 7.50-7.42 (m 1H), 7.39-7.34 (m, 2H), 7.31-7.24 (m, 1H), 7.03-6.93 (m, 7H), 6.88 (d, J=8.1Hz, 1H), 6.41 (t, J=7.8 Hz, 1H), 5.32 (d, J=7.8Hz, 1H), 4.02 (s, 1H), 3.63-3.57 (m, 1H), 3.57-3.43 (m, 1H), 2.95 (dt, J_1=19.3Hz, J_2=4.6Hz, 1H).**^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 192.3, 178.7, 150.8, 139.3, 139.1, 138.4, 133.4, 130.4, 130.1, 128.4, 128.2, 128.1, 127.9, 127.9, 127.6, 127.5, 127.1, 125.0, 121.5, 113.9, 55.3, 41.9, 45.2, 31.3. **HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{26}H_{19}ClNO]^-$: 396.1150; found: 396.1147. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1})**:** t_R= 11.1, 21.2 min. **IR (ν_{max}, cm^{-1}):** 570, 595, 628, 661, 698, 733, 758, 782, 877, 915, 1024, 1080, 1138, 1157, 1172, 1221, 1264, 1318, 1339, 1372, 1409, 1474, 1584, 1617, 1651, 1683, 1702, 2341, 2359, 3029. $[\alpha]_D^{25}$ = -79.3 (c=1.3, $CHCl_3$).



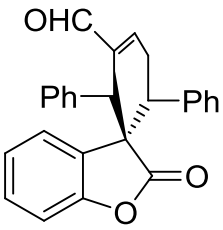
3k: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.54 (s, 1H), 7.42-7.35 (m, 3H), 7.31-7.25 (m, 2H), 6.99-6.92 (m, 5H), 6.89-6.83 (m, 2H), 6.51-6.42 (m, 2H), 5.42 (d, J=7.5Hz, 1H), 3.93 (s, 1H), 3.64-3.57 (m, 1H), 3.57-3.44 (m, 1H), 3.06 (s, 3H), 2.93 (td, J_1=19.1Hz, J_2=4.5Hz, 1H).**^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 192.5, 177.4, 151.0, 142.8, 139.8, 139.3, 139.1, 133.5, 128.3, 127.7, 127.6, 127.5, 127.4, 126.7, 126.3, 120.7, 107.1, 53.6, 44.9, 42.2, 31.3, 25.8.**HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{27}H_{24}NO_2]^+$:394.1802; found: 394.1806. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1})**:** t_R= 10.4 i 24.1 min. **IR (ν_{max}, cm^{-1}):**528, 574, 604, 624, 675, 699, 735, 753, 806, 915, 931, 976, 1000, 1091, 1130, 1156, 1301, 1350, 1375, 1409, 1452, 1609, 1652, 1682, 2920, 3028, 3056. $[\alpha]_D^{25}$ = -63.8 (c=1.2, $CHCl_3$).



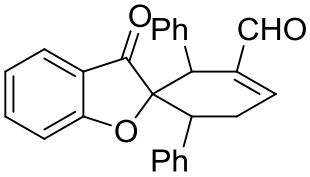
3l: Colorless oil. **^{1}H-NMR** (300 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.54 (s, 1H), 7.96 (s, 1H), 7.48-7.49 (m, 5H), 7.05-6.93 (m, 6H), 6.87 (dd, J_1=8.4Hz, J_2=2.2Hz, 1H), 6.64 (bs, 1H), 6.45 (d, J=8.4Hz, 1H), 5.28 (d, J=2.2Hz, 1H), 3.99 (s, 1H), 3.59-3.41 (m, 2H), 3.03-2.87 (m, 1H). **^{13}C-NMR** (75 MHz. $CDCl_3$): δ(ppm)= 192.4, 179.5, 150.9, 139.3, 139.1, 138.3, 133.4, 130.9, 128.3, 128.1, 127.9, 127.4, 127.1, 126.1, 109.7, 54.5, 45.1, 41.7, 31.3. **HRMS (ESI) $[M+H]^+$:** Calculated for $[C_{26}H_{21}ClNO_2]^-$: 414.1255; found: 414.1259. **HPLC** (Chiralpak IB©, 1mLmin^{-1}, Hexane:IPA 90:10, 254 nm^{-1})**:** t_R= 15.1, 26.9 min. **IR (ν_{max}, cm^{-1}):** 528, 555, 574, 622, 646, 700, 734, 760, 775, 916, 929, 1001, 1030, 1079, 1121, 1156, 1177, 1216, 1233, 1264, 1336, 1372, 1408, 1452, 1620, 1650, 1685, 2851, 2922, 3028, 3255. $[\alpha]_D^{25}$ = -87.8 (c=0.45, $CHCl_3$).



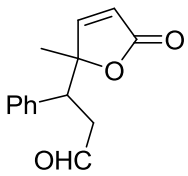
4a: White solid. **^{1}H NMR (400 MHz, $CDCl_3$): δ =** 9.51 (s, 1H), 7.80-7.66 (m, 2H), 7.42-7.30 (m, 8H), 7.23-7.09 (m, 6H), 4.20 (s, 1H), 3.57 (dd, J_1=5.6 Hz, J_2=11.5 Hz, 1H), 3.45-3.35 (m, 1H), 2.96-2.87 (m, 1H), 0.95 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 191.1, 150.3, 139.3, 138.5, 131.7, 131.6, 129.3, 128.9, 128.8, 128.5, 128.2, 127.9, 127.6, 127.6, 125.3, 45.3, 39.6, 31.5, 15.6. **HRMS (ESI):** calcd. for $[M+H]^+$ ($C_{28}H_{25}N_2O_2$) requires 421.1911, found 421.1912. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH = 95:5, λ=254 nm, 1.0 mL/min): t_R = 13.3, 27.0 min. **IR (ν_{max}, cm^{-1}):** 703, 758, 1123, 1159, 1288, 1365, 1391, 1454, 1498, 1595, 1651, 1687. $[\alpha]_D^{25}$ **=** +69.8 (c=0.7, $CHCl_3$, e.r. 99.9:0.1, (*R*)-Cat.).



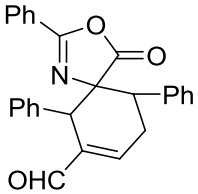
5a: Colorless oil. **^{1}H-NMR** (400 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.55 (s, 1H), 7.50-6.90 (m, 10H), 6.75 (d, J=7.7Hz, 1H), 6.58 (t, J=7.7 Hz, 1H), 5.43 (d, J=7.7 Hz, 1H), 4.09 (s, 1H), 3.63 (dd, J=10.2, 6.4 Hz, 1H), 3.44 (dd, J=20.2, 10.2 Hz, 1H), 3.01 (m, 1H). **^{13}C-NMR** (100 MHz. $CDCl_3$): δ(ppm)= 193.2, 178.1, 153.5, 151.7, 140.4, 139.8, 138.7, 129.7, 129.5, 129.3, 129.2, 129.1, 128.5, 127.8, 123.6, 111.0, 54.5, 47.0, 43.5, 32.4. **HPLC (ESI)**: Chiralcel IB, hexane-IPA 90:10, 1 mL/min, t_R: 10.0, 20.0 min. HRMS (ESI): calcd. for $[M+H]^+$ ($C_{26}H_{21}O_3$) requires 381.1485, found 381.1487. $[\alpha]_D^{25}$ **=** +56.2 (c=0.38, $CHCl_3$, e.r. 96.5:3.5, (*R*)-Cat.).



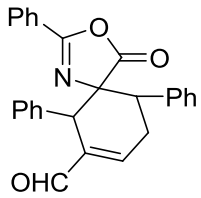
6a: Colorless oil. **^{1}H-NMR** (400 MHz. $CDCl_3$, TMS_{int}): δ(ppm)= 9.56 (s, 1H), 7.50-6.90 (m, 10H), 6.90 (t, J=6.9 Hz, 1H), 6.72 (d, J=8.0Hz, 1H), 4.16 (s, 1H), 3.65-3.45 (m, 2H), 3.05-2.95 (m, 1H). **^{13}C-NMR** (100 MHz. $CDCl_3$): δ(ppm)= 203.0, 192.9, 171.9, 152.0, 140.2, 138.9, 138.4, 137.8, 131.0, 130.0, 129.2, 128.9, 128.6, 128.5, 125.2, 122.7, 114.2, 113.8, 44.7, 43.0, 32.0. **HPLC**: Chiralcel IB, hexane-IPA 90:10, 1 mL/min, t_R: 10.1, 21.1 min. **HRMS (ESI):** calcd. for $[M+H]^+$ ($C_{26}H_{21}O_3$) requires 381.1485, found 381.1493. **IR (ν_{max}, cm^{-1}):** 647, 713, 754, 816, 1009, 1072, 1461, 1475, 1486, 1608, 1683, 1705, 2340, 2359, 2921. $[\alpha]_D^{25}$ **=** +56.9 (c=0.75, $CHCl_3$, e.r. 99.5:0.5, (*R*)-Cat.).



7a: Colorless oil. Mixture of diastereomers, d.r.=1.2:1. **^{1}H NMR (300 MHz, $CDCl_3$): δ =** 9.63 (t, J=1.4 Hz, 1H), 9.58 (t, J=1.2 Hz, 1H), 7.35-7.27 (m, 10H), 7.18-7.14 (m, 2H), 6.06 (d, J=5.6 Hz, 1H), 5.91 (d, J=5.7 Hz, 1H), 3.73 (dd, J_1=5.7 Hz, J_2=8.5 Hz, 1H), 3.55 (dd, J_1=5.7 Hz, J_2=7.9 Hz, 1H), 2.94-2.83 (m, 4H), 1.45 (s, 3H), 1.30 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 199.7, 199.6, 172.2, 171.8, 160.7, 158.6, 138.2, 138.0, 129.3, 128.9, 128.7, 128.6, 127.9, 127.8, 121.4, 89.9, 89.7, 47.5, 45.8, 44.6, 44.0, 23.6, 22.1. **HRMS (ESI):** calcd. for $[M+H]^+$ ($C_{14}H_{15}O_3$) requires 231.1016, found 231.1018.



8a (major diastereomer): Colorless oil. **^{1}H NMR (300 MHz, $CDCl_3$): δ =** 9.55 (s, 1H), 7.94-7.89 (m, 2H), 7.61-7.30 (m, 9H), 7.22-7.09 (m, 5H), 4.00 (s, 1H), 3.64 (dd, J_1=5.9 Hz, J_2=11.2 Hz, 1H), 3.26-3.13 (m, 1H), 3.04-2.93 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 191.9, 175.0, 161.1, 149.3, 139.8, 137.3, 135.6, 132.8, 130.7, 130.2, 130.0, 129.1, 129.0, 128.7, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 74.6, 47.9, 41.4, 31.4. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH = 90:10, λ=254 nm, 1.0 mL/min): t_R = 9.5, 17.1 min. **HRMS (ESI):** calcd. for $[M+H]^+$ ($C_{27}H_{22}NO_3$) requires 408.1594, found 408.1594. **IR (ν_{max}, cm^{-1}):** 700, 732, 761, 781, 864, 882, 914, 944, 968, 1095, 1154, 1179, 1291, 1321, 1451, 1493, 1601, 1650, 1686, 1816, 2924. $[\alpha]_D^{25}$ **=** -43.6 (c=1.0, $CHCl_3$, e.r. 99.7:0.3, (*S*)-Cat.).

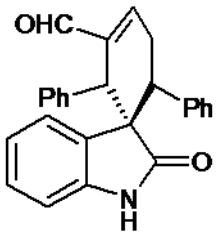


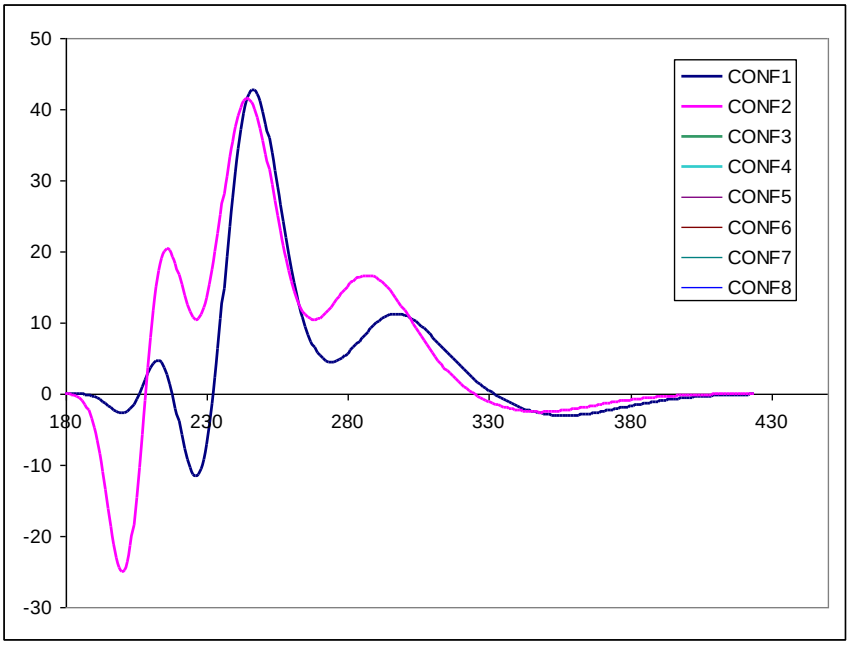
8a (minor diastereomer): Colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$): δ =** 9.58 (s, 1H), 8.14-8.11 (m, 2H), 7.66-7.59 (m, 2H), 7.51-7.29 (m, 7H), 7.17-7.05 (m, 5H), 4.20 (s, 1H), 3.65 (dd, J_1=6.1 Hz, J_2=11.0 Hz, 1H), 3.43-3.33 (m, 1H), 3.08-2.99 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 191.7, 178.0, 171.8, 159.1, 150.6, 138.9, 137.4, 136.8, 133.8, 132.5, 130.2, 128.5, 128.4, 128.3, 128.0, 127.7, 127.7, 127.6, 73.0, 45.8, 41.9, 30.2. **HPLC** (Chiralpak IB, *n*-hexane: *i*-PrOH = 90:10, λ=254 nm, 1.0 mL/min): t_R = 9.8, 20.0 min. **HRMS (ESI):** calcd. for $[M+H]^+$ ($C_{27}H_{22}NO_3$) requires 408.1594, found 408.1595. **IR (ν_{max}, cm^{-1}):** 663, 700, 762, 777, 883, 934, 987, 1113, 1154, 1174, 1287, 1319, 1414, 1451, 1494, 1582, 1602, 1653, 1804, 2923. $[\alpha]_D^{25}$ **=** -117.1 (c=0.9, $CHCl_3$, e.r. >99.9:0.1, (*S*)-Cat.).

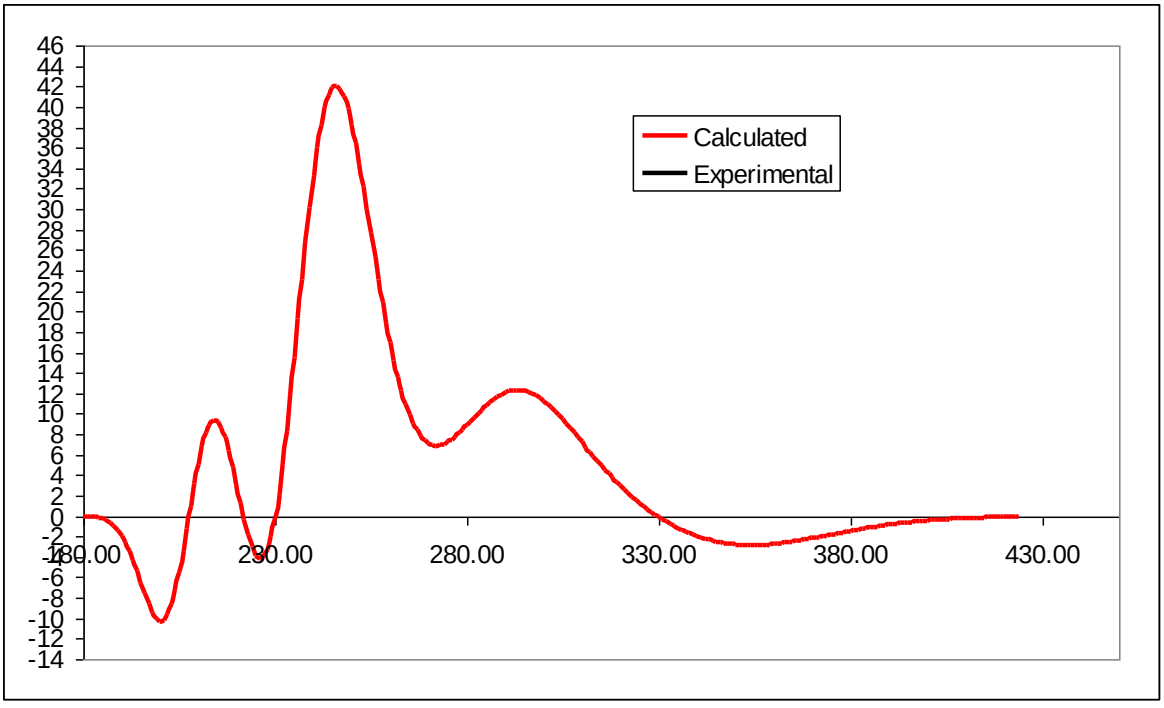
Figure 1

DC of compound **3a**

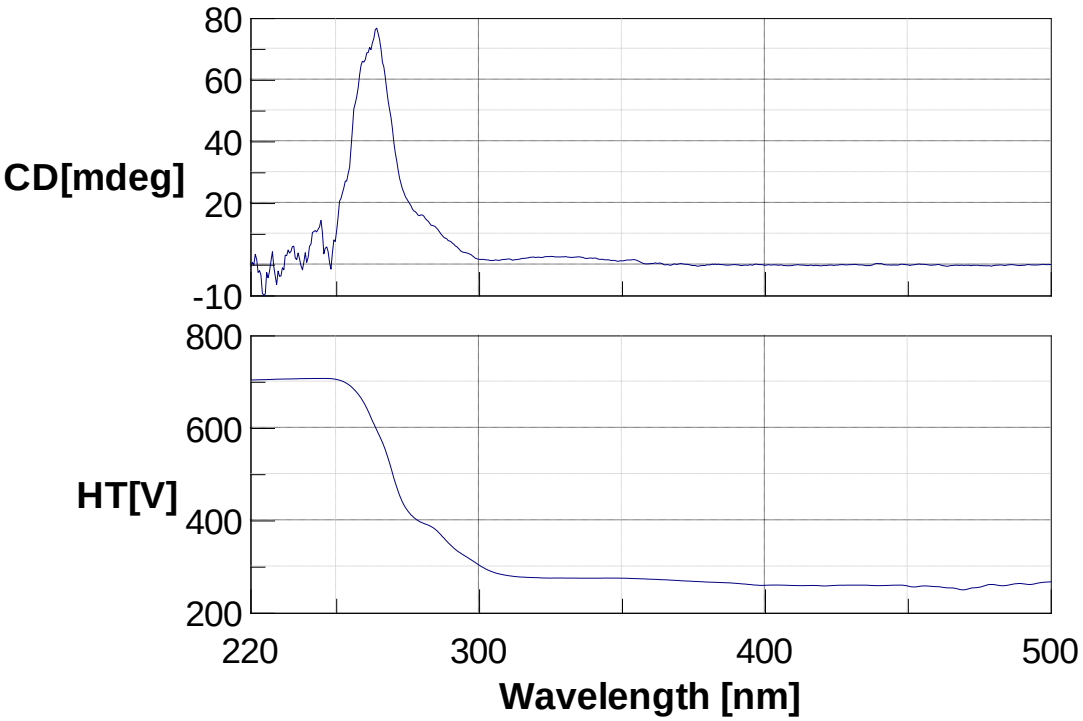
calculated





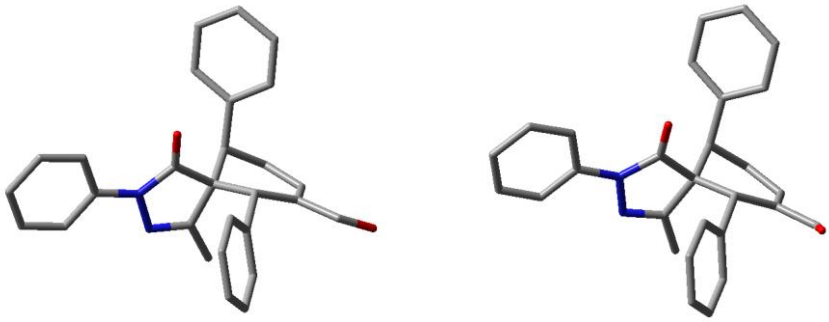


Experimental DC for the product **3a** obtained with (*R*)-catalyst



Absolute configuration of compound 4a (pyrazole)

In the present case, theoretical calculation of ECD spectra and the assignment of the absolute configuration was carried out by means of the TD-DFT method, since this technique has been successfully employed several times to predict ECD spectra and to assign the AC of organic molecules[i] Starting from the relative configuration obtained by NMR analysis, a conformational search has been carried out using Monte Carlo searching together with the MMFF94 molecular mechanics force field (as implemented in Titan 1.0.5). All conformations within a 5 kcal/mol window were then optimized using DFT at the B3LYP/6-31G(d) level[ii], and the harmonic vibrational frequencies of each conformation were calculated at the same level to confirm their stability (no imaginary frequencies observed), and to evaluate the free energy of each conformation by ZPE correction. After DFT minimization, the MMFF structures clustered in two conformations (**a** and **b**), that are different because of the different disposition of the CHO group (see Figure S1 and Table S1). This means that the molecule is quite rigid, and this feature greatly enhance the reliability of the method, being the correct determination of the energy of each conformation its main weakness.



Conf **a** Conf. **b**

Figure S1: 3D view of the two most stable conformations of compound **4a** (energies in kcal/mol)

Table S1: Calculated relative energies (E) and free energies (G) of the conformations of **4a** (in kcal/mol, B3LYP/6-31G(d) level). Populations percentages (P) are calculated assuming Boltzmann statistics at T=25°C.

Molecule	Conf	E	G	Pop (ΔG)
4a	**a**	0.00	0.00	66
	b	0.37	0.40	34

Calculation of the Electronic Circular Dichroism spectra of both the conformations were carried out using the TD-DFT - BH&HLYP/6-311+G(d,p)//B3LYP/6-31G(d) level[iii], and assuming 5*S*, 6*S*, 10*R* absolute configuration[iv]. Rotational strength were calculated in both length and velocity representation. The resulting values are very similar, therefore the errors due to basis set incompleteness are very small.[v] Electronic excitation energies and rotational strengths have been calculated for the two conformations, and the ECD spectra were obtained by applying a 0.4 eV Gaussian shaped line width[vi]. In order to cover the 170-400 nm range, 70 transition were calculated for each conformation (Figure S2).

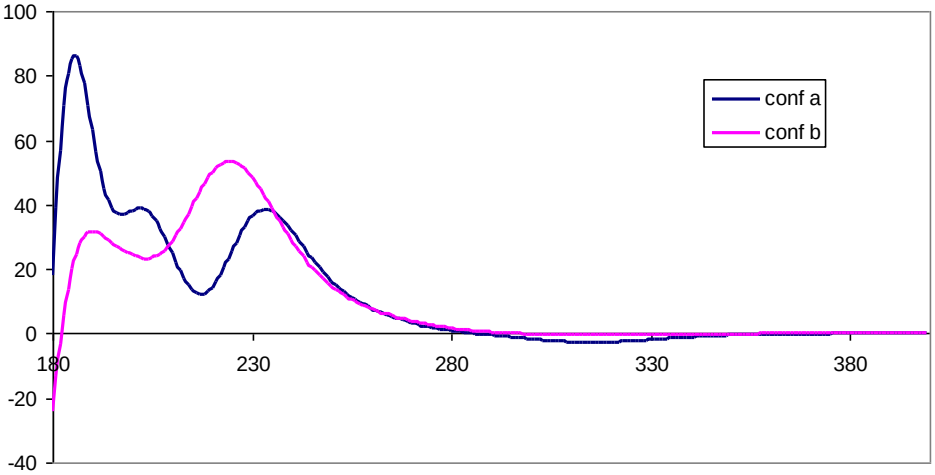


Figure S2. Calculated ECD spectra for the two conformations of **compound 4a**. vertical scale is in Δε, horizontal scale is in nm.

The trend of the two spectra are similar and in both spectra the cotton effects below 250 nm are positive, indicating that the resulting weighted ECD spectrum is not strongly influenced by the relative population of the conformations. The final simulated ECD spectra was obtained taking into account the 66:34 population ratios determined starting from the calculated free energies at the B3LYP/6-31G(d) level, and assuming Boltzmann statistics (Figure S2) The simulated spectrum is in good agreement with the experimental one, and the 5*S*, 6*S*, 10*R* configuration can be reliably assigned to compound **4a**.

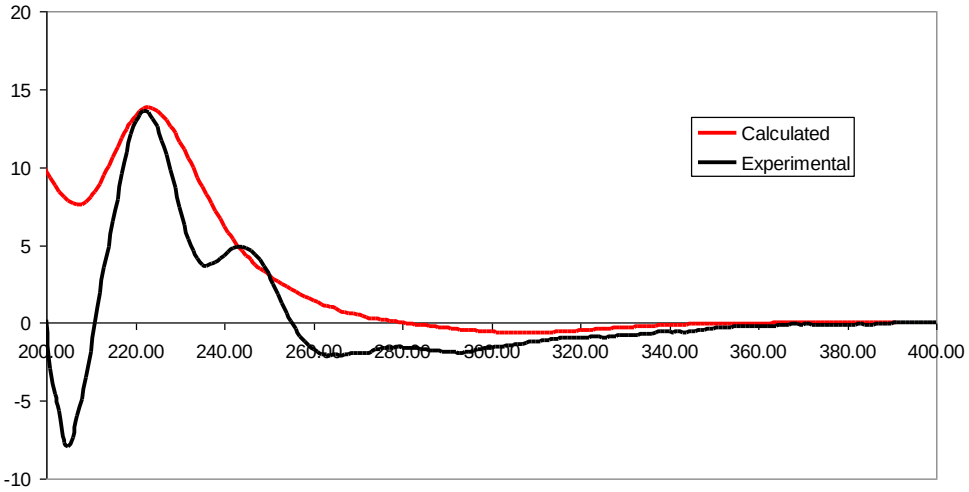
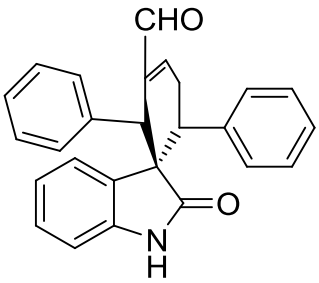
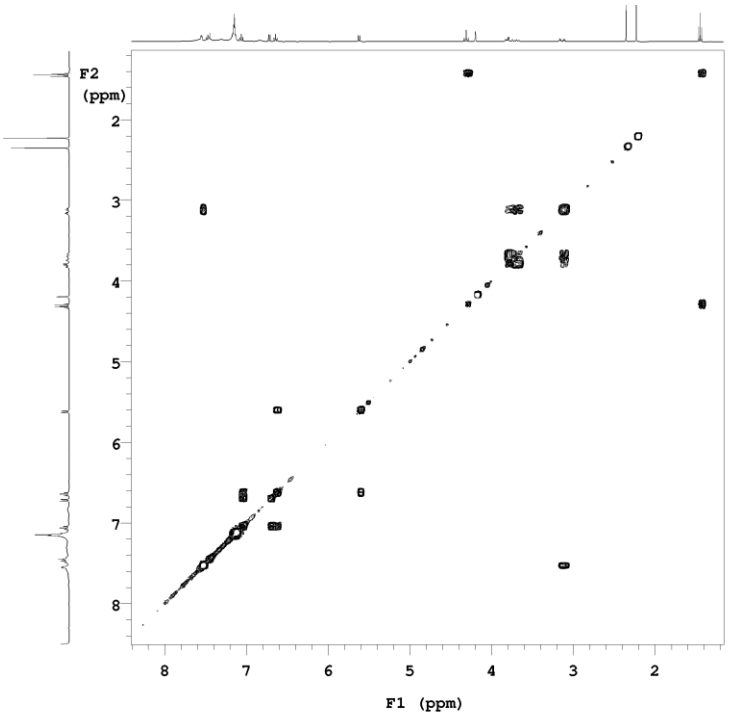
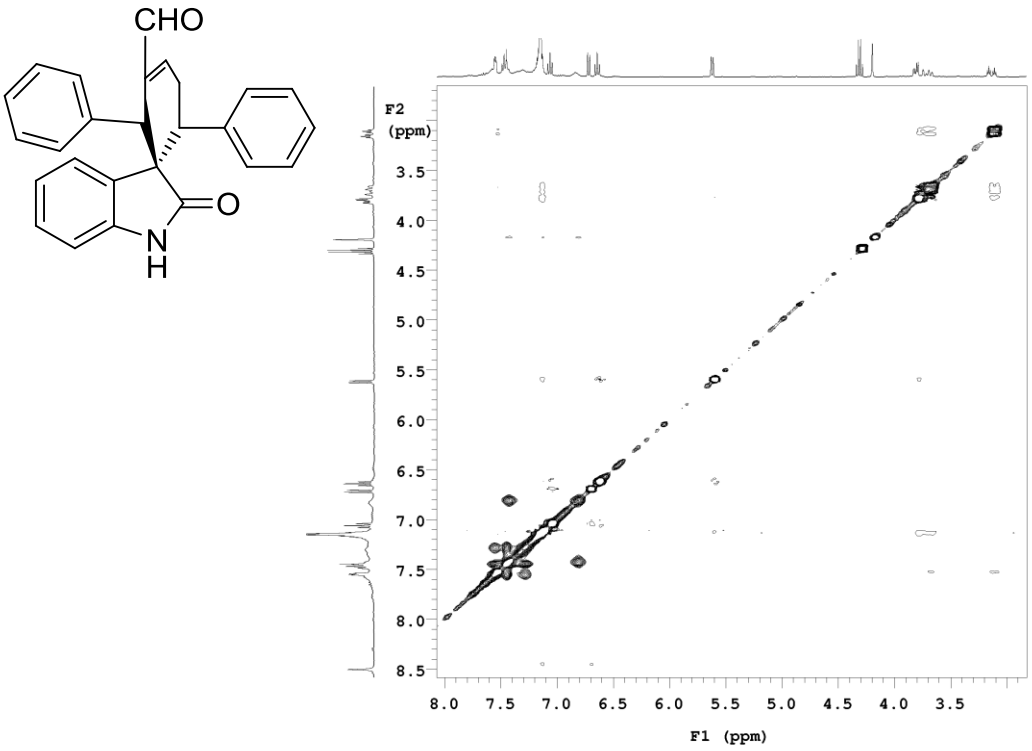


Figure S2: Experimental ECD spectrum (in black) and simulated spectrum (in red) assuming 5*S*, 6*S*, 10*R* absolute configuration. The vertical scale is in mdeg, and the simulated spectrum has been scaled accordingly. The simulated spectrum has been blue-shifted by 8 nm in order to match the experimental trace.

Compound **3a** (gCOSY, NOESY, TOCSY)



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4.5
5.0
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6.0
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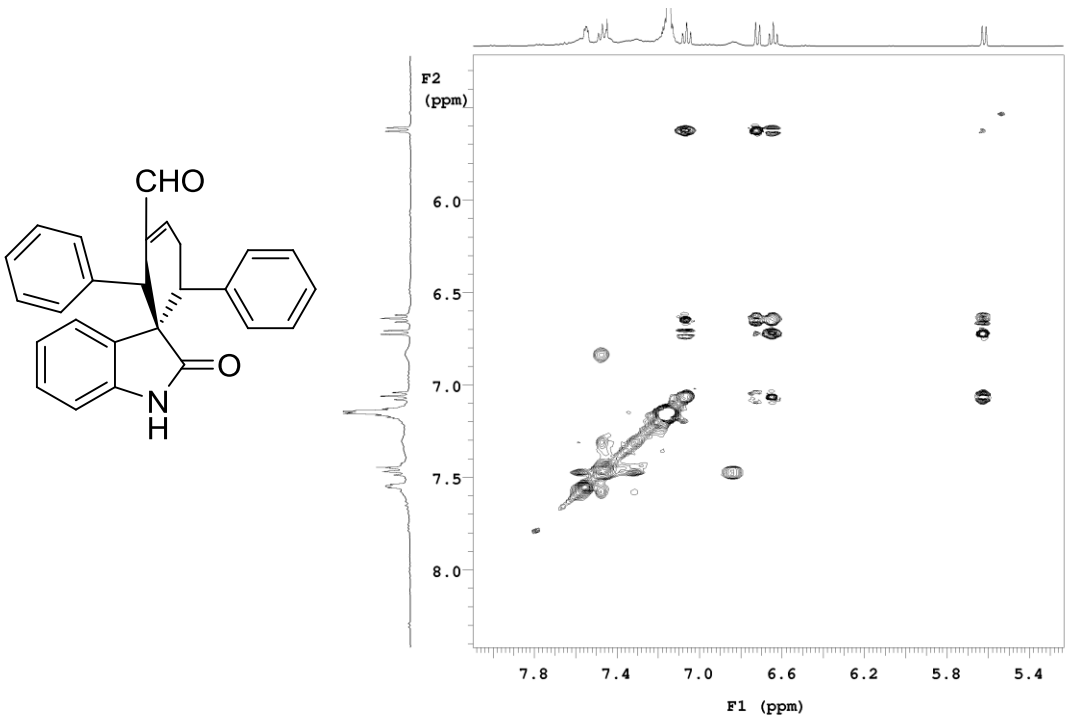
7.0
7.5
8.0
8.5
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5
F1 (ppm)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F2
(ppm)
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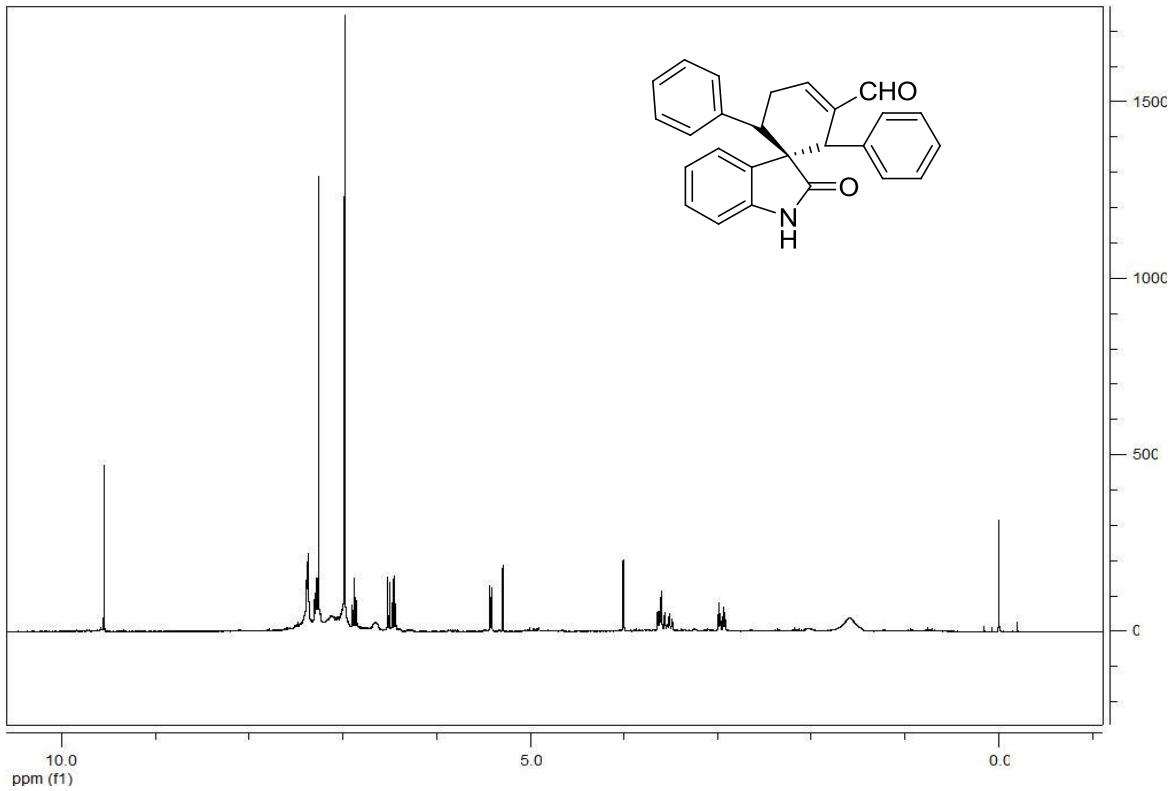
F1 (ppm)

3a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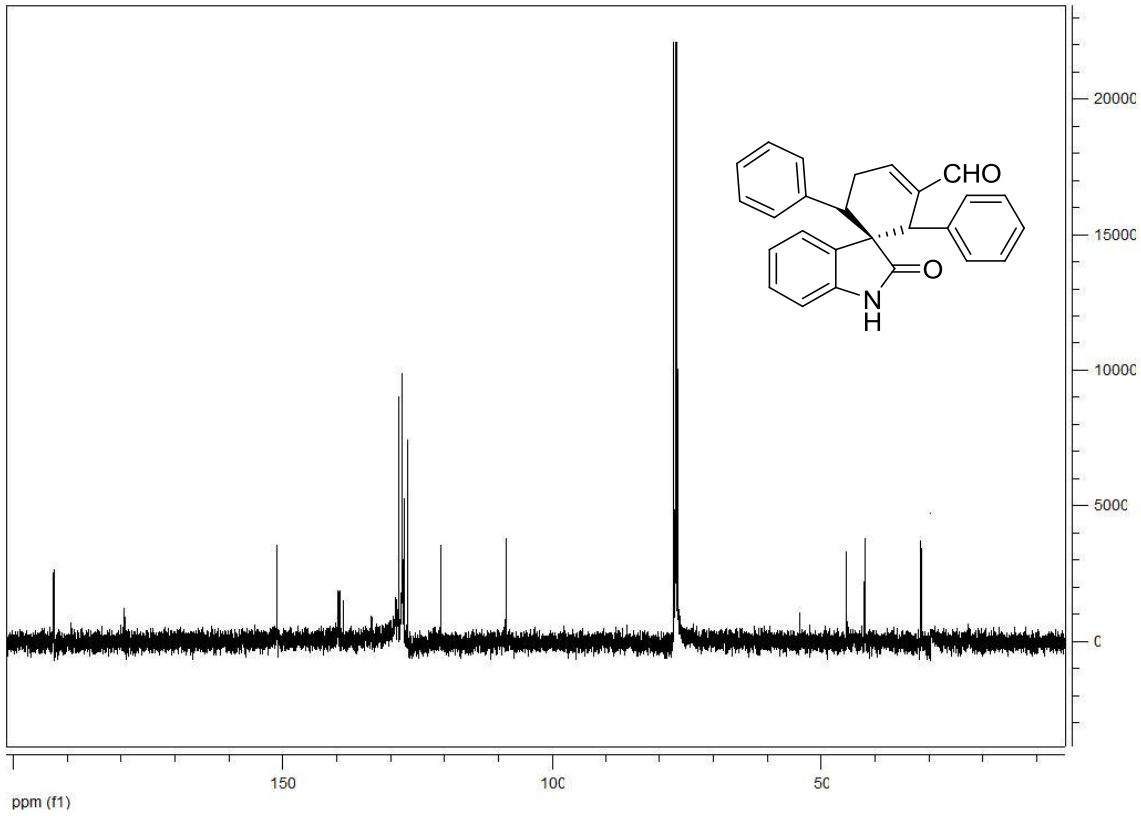
ppm (f1)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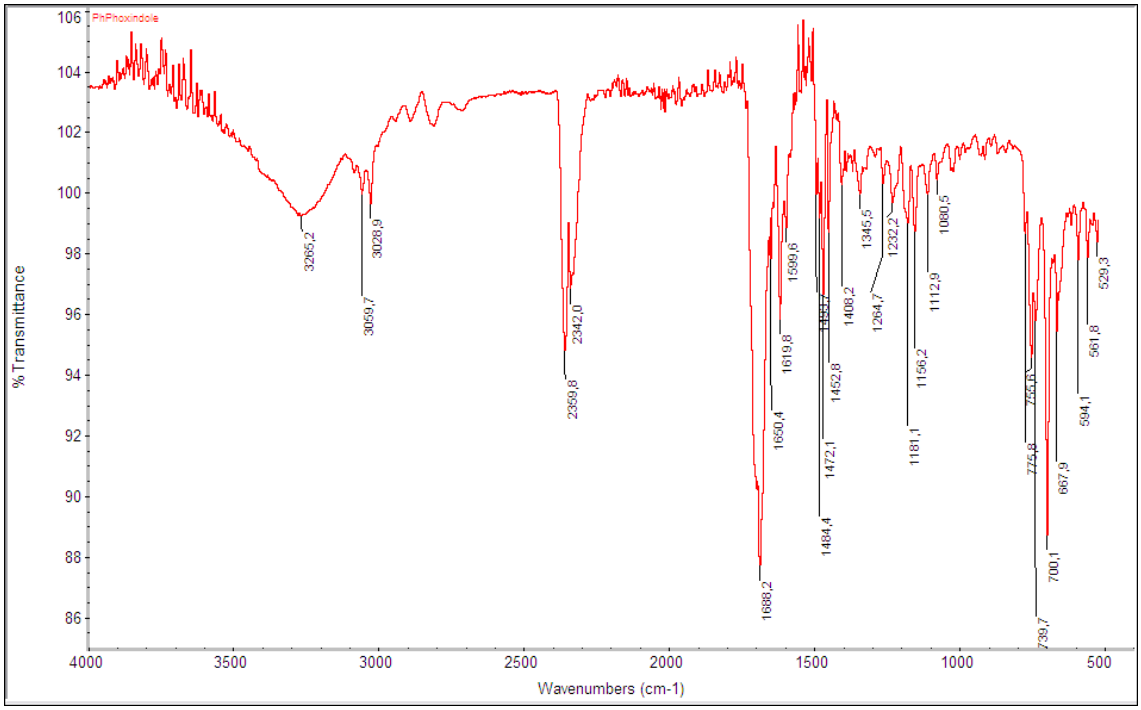
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Wavenumbers (cm-1)
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102
100
98
96
94
92
90
88
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3500
3000
2500
2000
1500
1000
500
3265,2
3059,7
3028,9
2359,8
2342,0
1688,2
1650,4
1619,8
1599,6
1484,4
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1408,2
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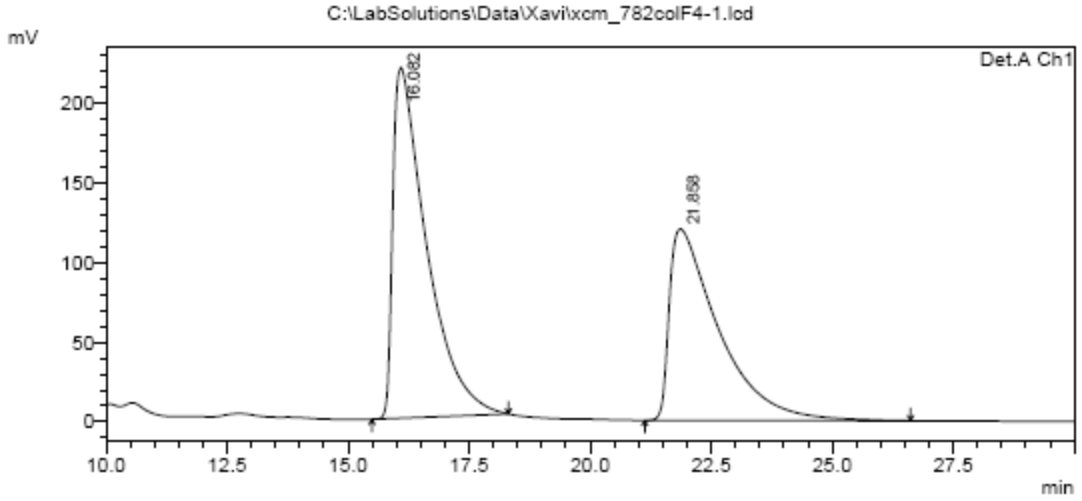

1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

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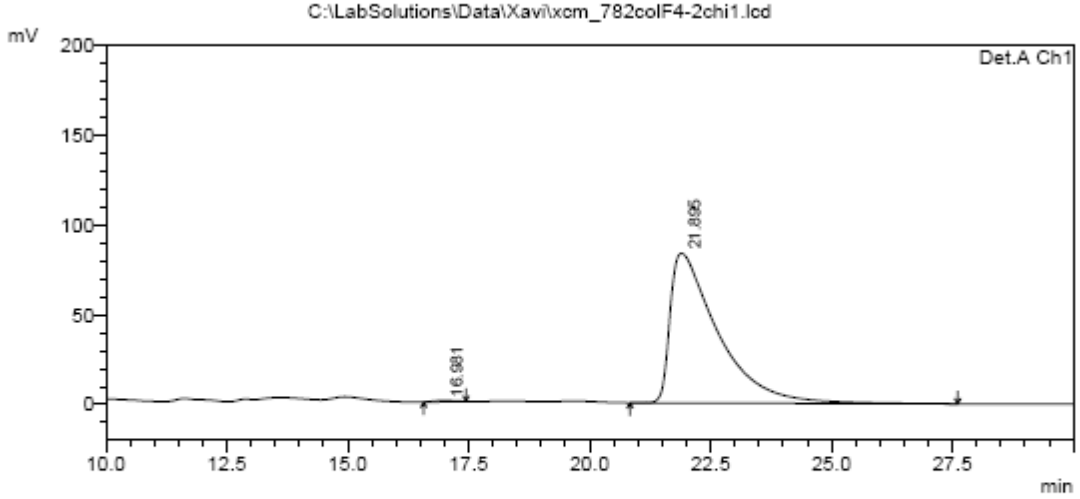


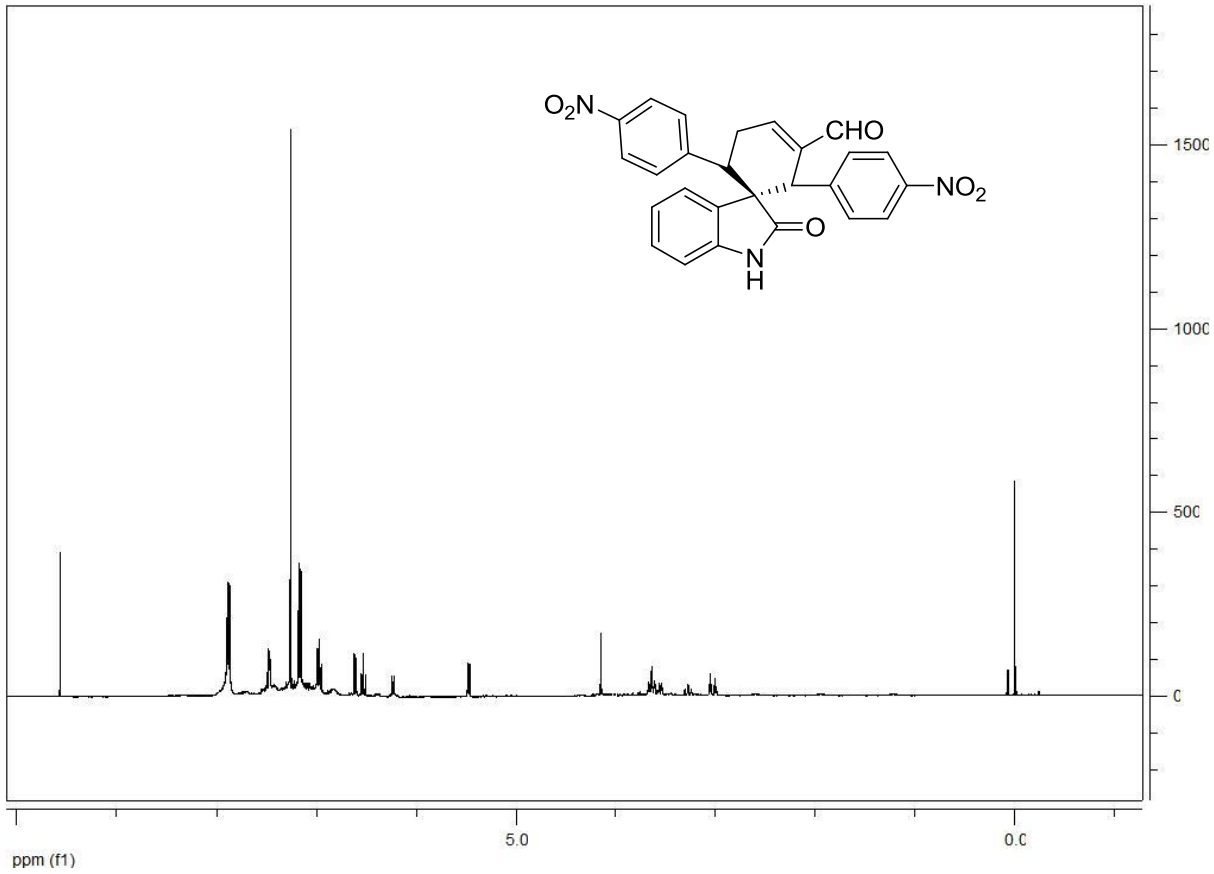
1 Det.A Ch1/254nm

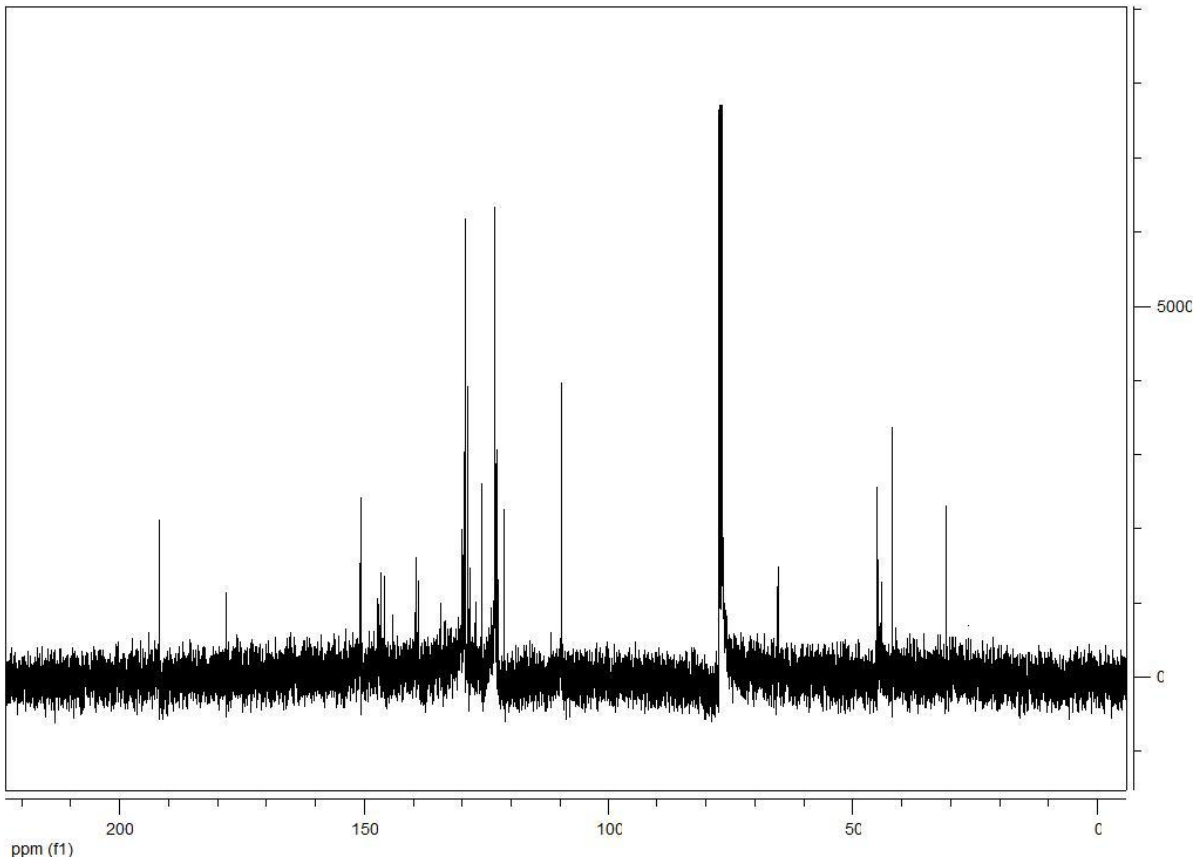
PeakTable

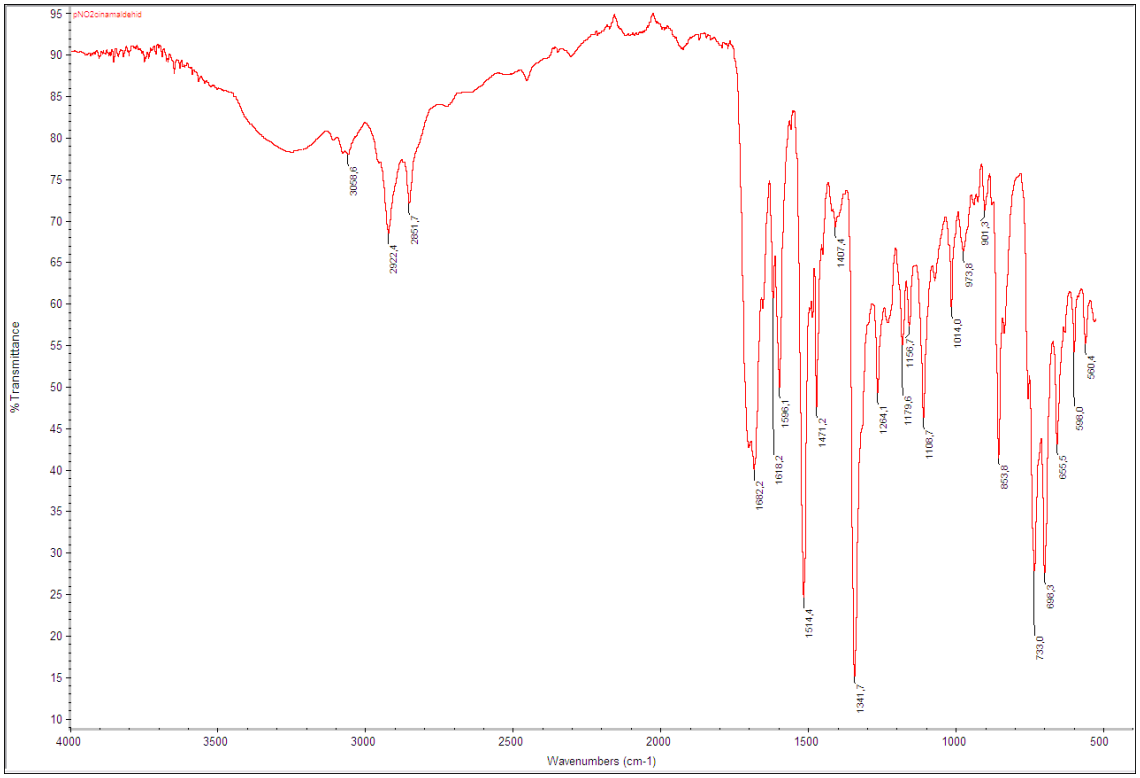
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.981	20362	700	0.355	0.831
2	21.895	5720342	83483	99.645	99.169
Total		5740703	84183	100.000	100.000

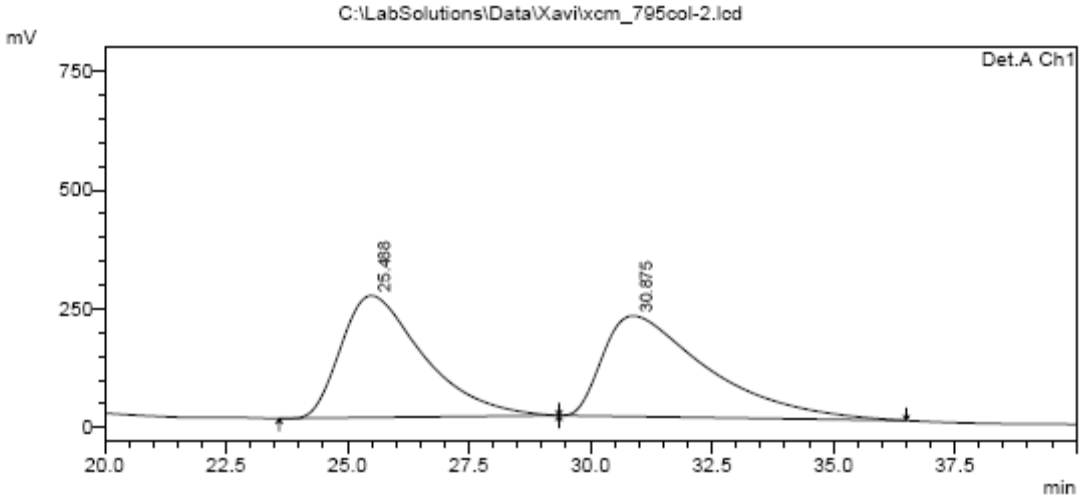
3d


O2N
CHO
NO2
O
N
H
1500
1000
500
0
5.0
0.0
ppm (f1)


5000
0
200
150
100
50
0
ppm (f1)


pNO2cinamaldehid
% Transmittance
Wavenumbers (cm-1)
3058,6
2922,4
2851,7
1682,2
1618,2
1596,1
1514,4
1471,2
1407,4
1341,7
1264,1
1179,6
1156,7
1108,7
1014,0
973,8
901,3
853,8
733,0
698,3
655,6
598,0
560,4

<Chromatogram>



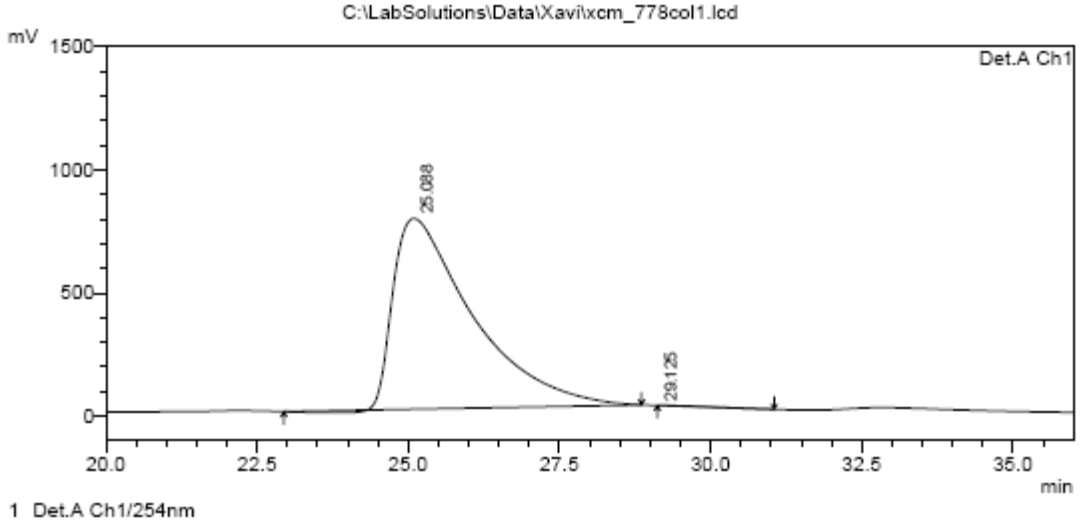
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.488	30305892	256715	48.918	54.768
2	30.875	31646482	212020	51.082	45.232
Total		61952374	468735	100.000	100.000

<Chromatogram>



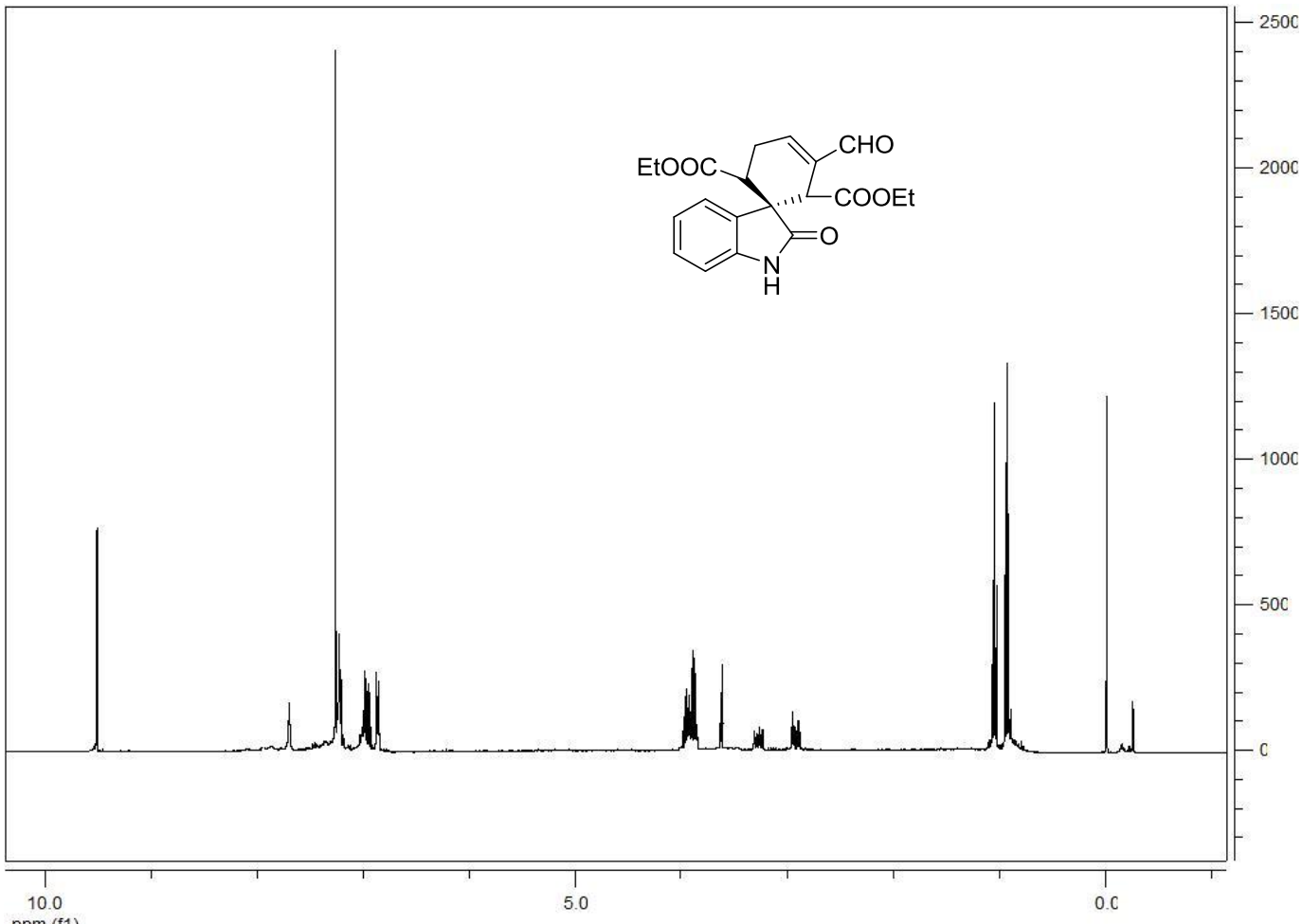
1 Det.A Ch1/254nm

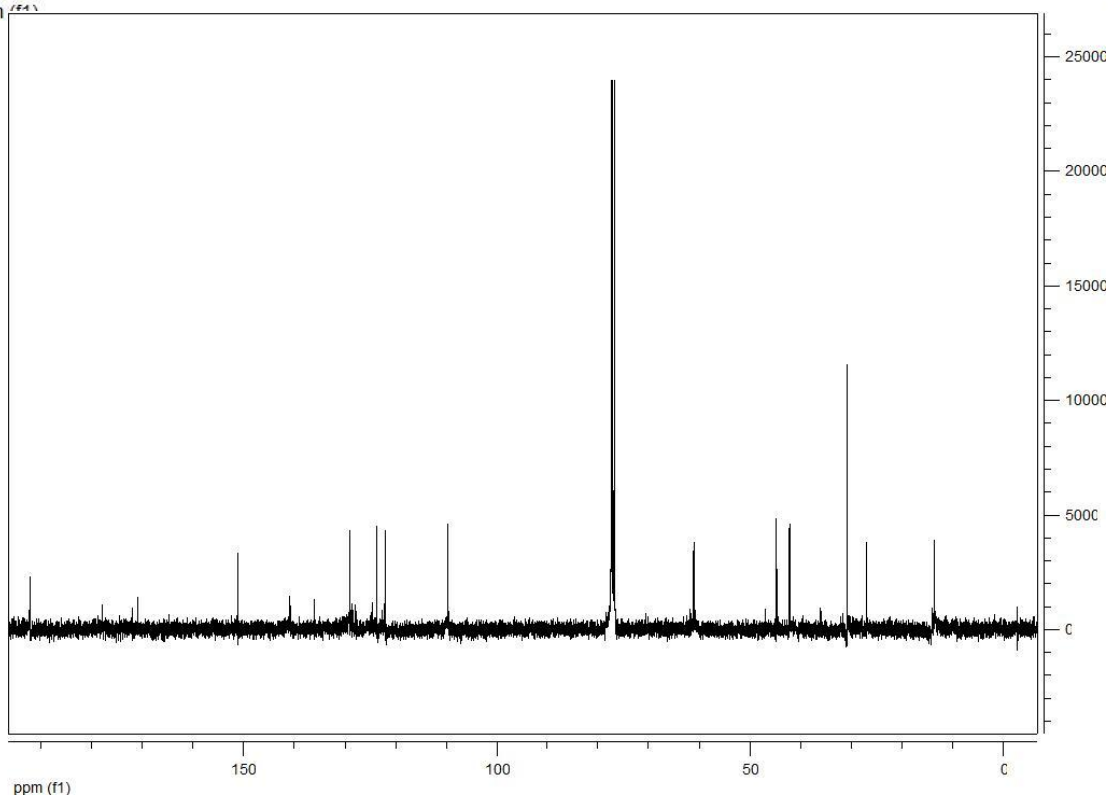
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.088	70357387	774205	99.913	99.997
2	29.125	61548	26	0.087	0.003
Total		70418935	774231	100.000	100.000

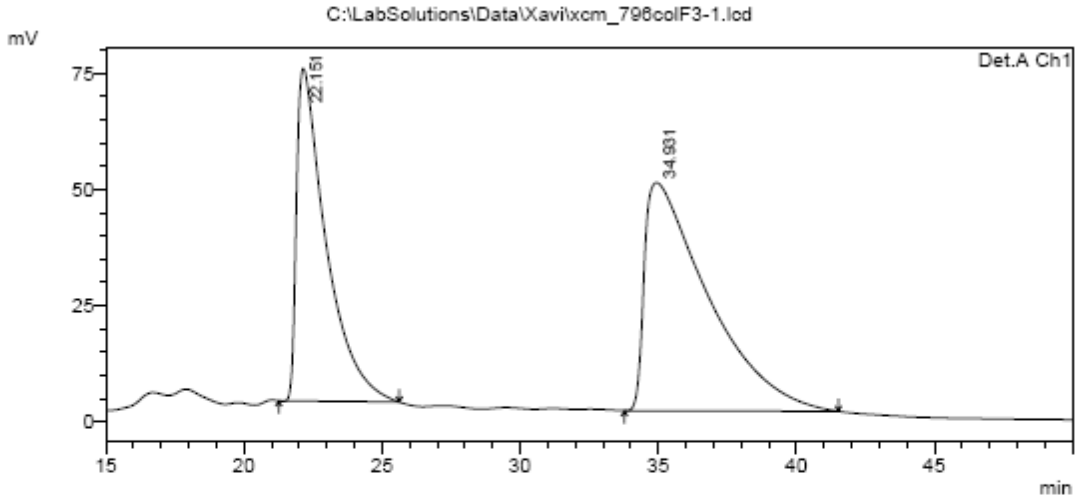
3c


EtOOC
CHO
COOEt
O
N
H
2500
2000
1500
1000
500
0
10.0
5.0
0.0
ppm


25000
20000
15000
10000
5000
0
150
100
50
0
ppm (f1)


Tue Jul 27 15:32:26 2010 (GMT+02:00)
% Transmittance
Wavenumbers (cm-1)
3294,5
2923,6
2853,0
1719,4
1688,0
1619,0
1473,0
1368,6
1315,2
1344,2
1295,3
1262,0
1179,3
1159,2
1097,3
1022,7
859,9
754,6
659,8
585,3
566,9

<Chromatogram>



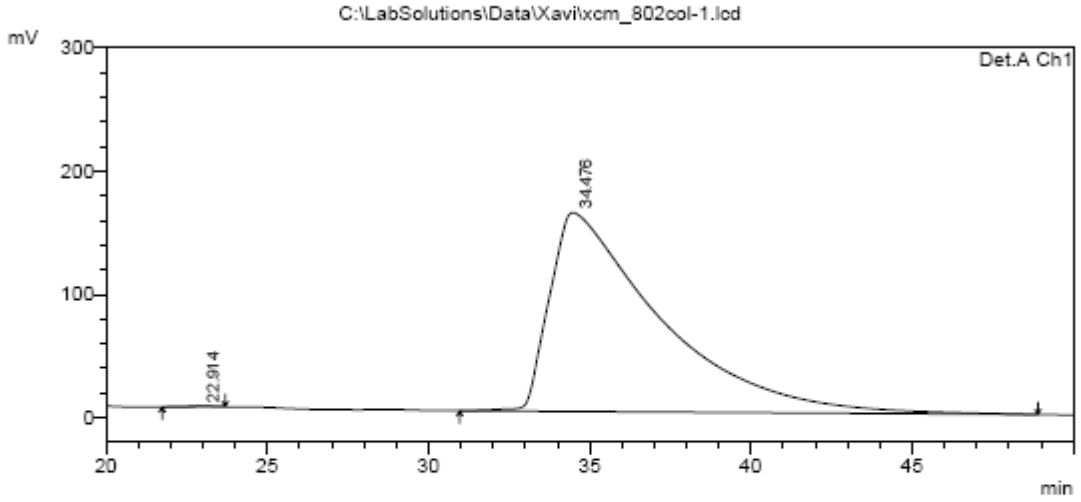
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.151	5323208	71555	40.365	59.328
2	34.931	7864429	49055	59.635	40.672
Total		13187638	120610	100.000	100.000

<Chromatogram>



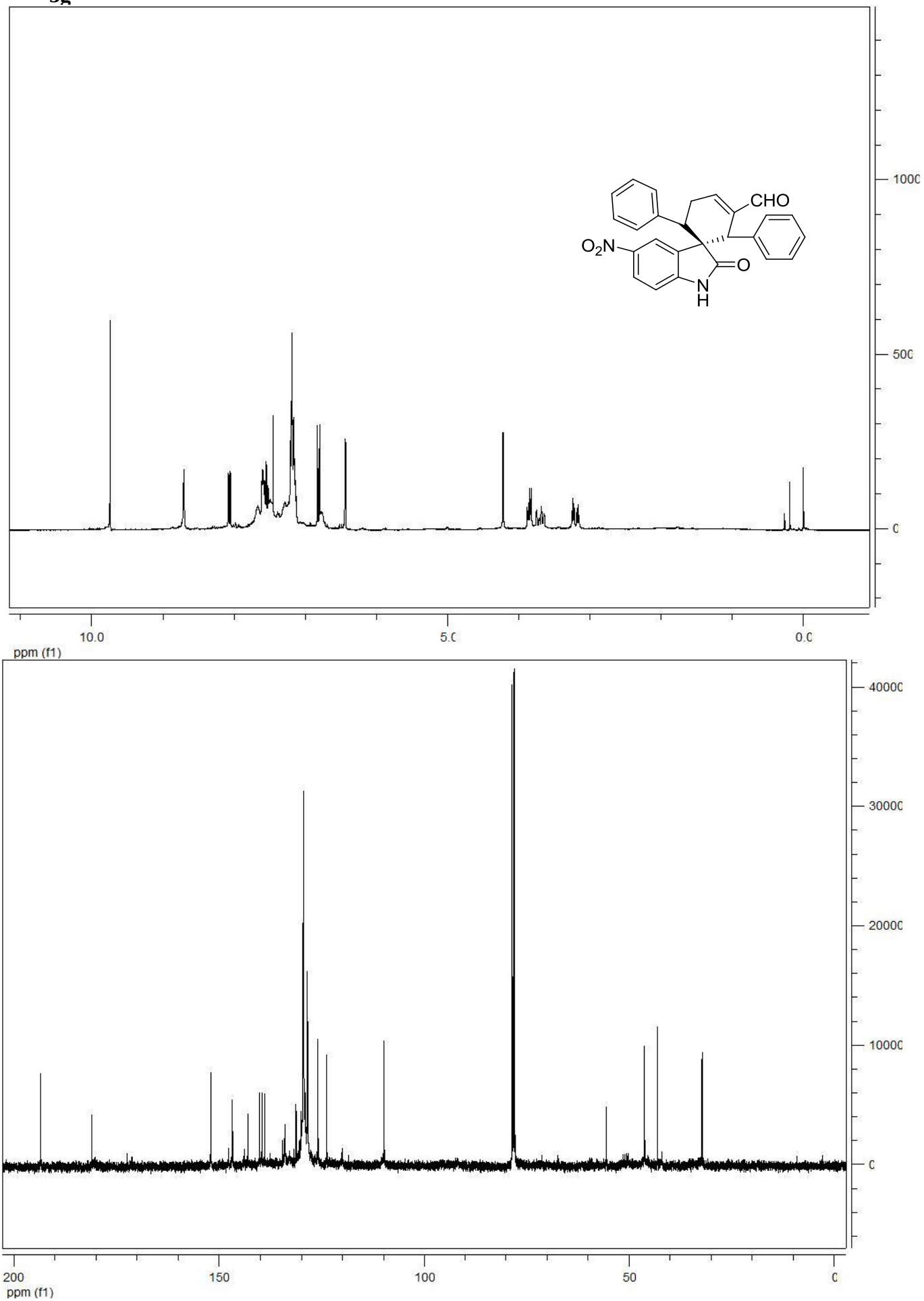
1 Det.A Ch1/254nm

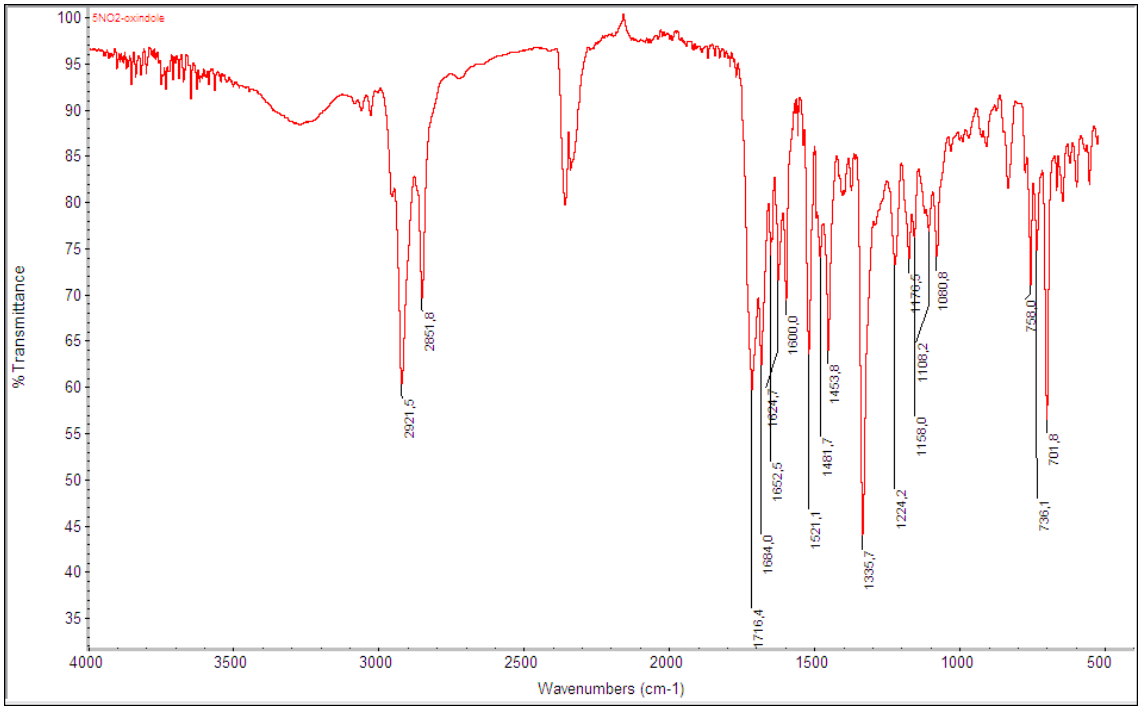
PeakTable

Detector A Ch1 254nm

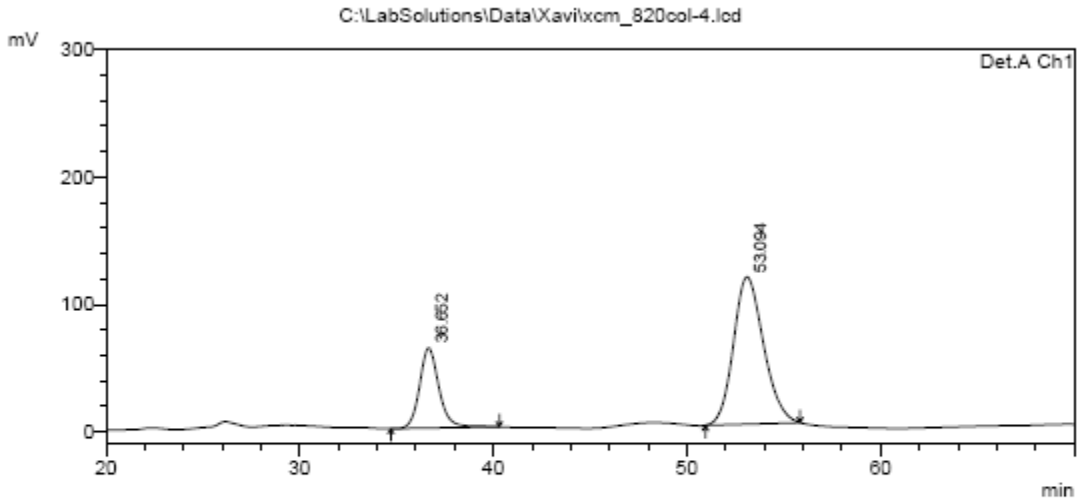
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.914	39881	579	0.104	0.358
2	34.476	38286891	161163	99.896	99.642
Total		38326772	161742	100.000	100.000

3g


CHO
O2N
O
N
H
1000
500
0
10.0
5.0
0.0
ppm (f1)
40000
30000
20000
10000
0
200
150
100
50
0
ppm (f1)


5NO2-oxindole
% Transmittance
Wavenumbers (cm-1)
100
95
90
85
80
75
70
65
60
55
50
45
40
35
4000
3500
3000
2500
2000
1500
1000
500
2921,5
2851,8
1716,4
1684,0
1652,5
1624,7
1600,0
1521,1
1481,7
1453,8
1395,7
1224,2
1176,5
1158,0
1108,2
1080,8
758,0
736,1
701,8

<Chromatogram>



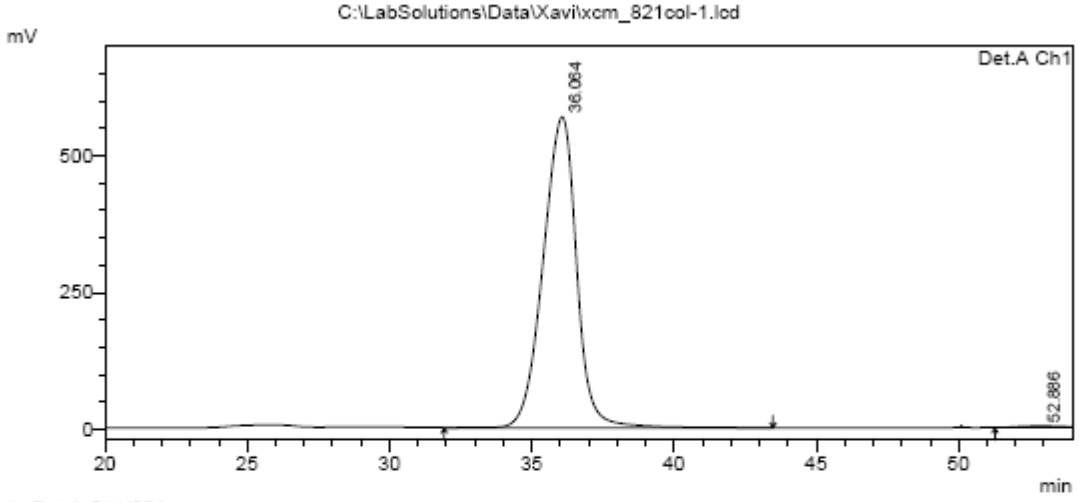
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.652	4397679	62889	25.976	35.212
2	53.094	12531786	115714	74.024	64.788
Total		16929465	178602	100.000	100.000

<Chromatogram>



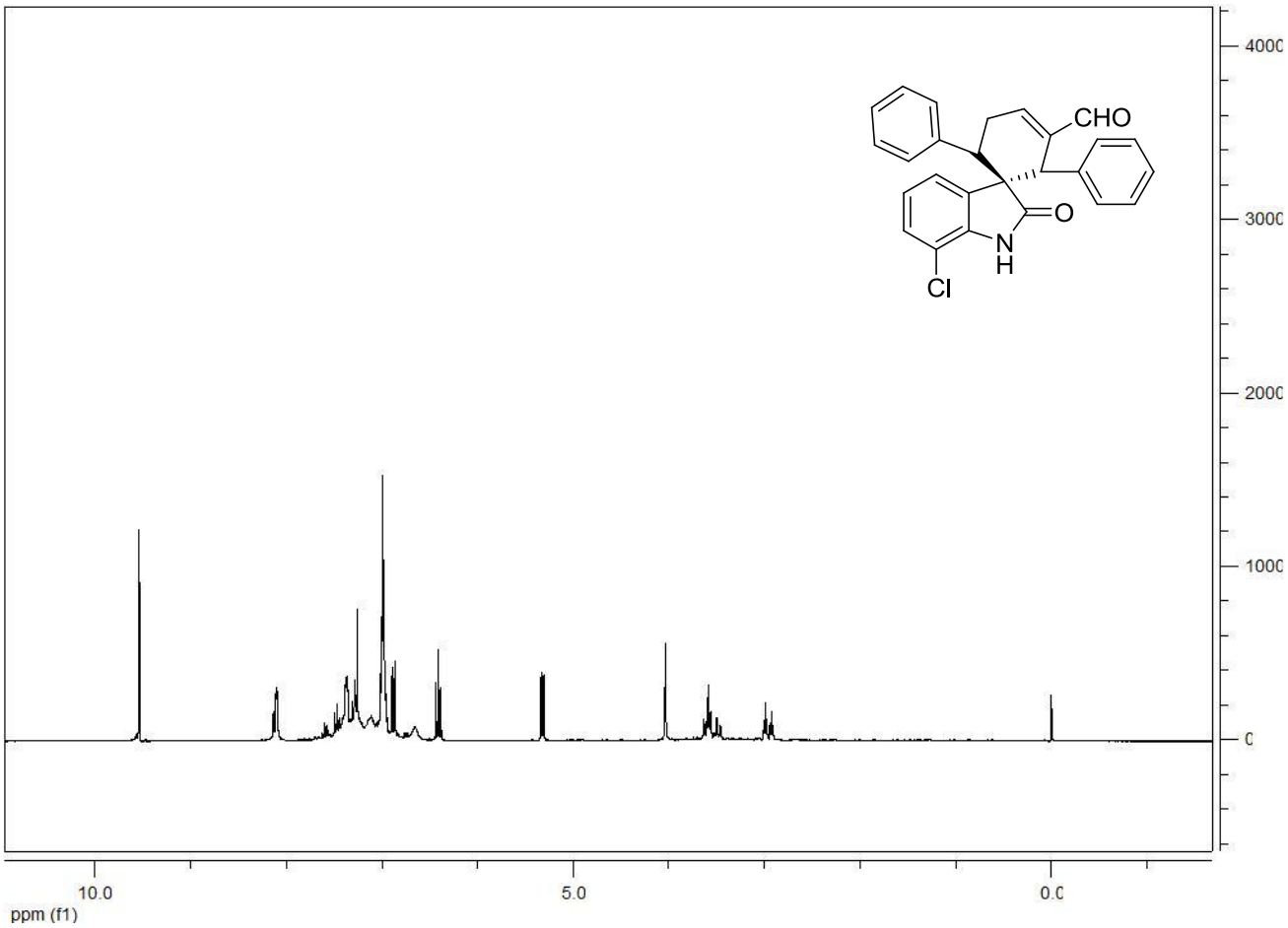
1 Det.A Ch1/254nm

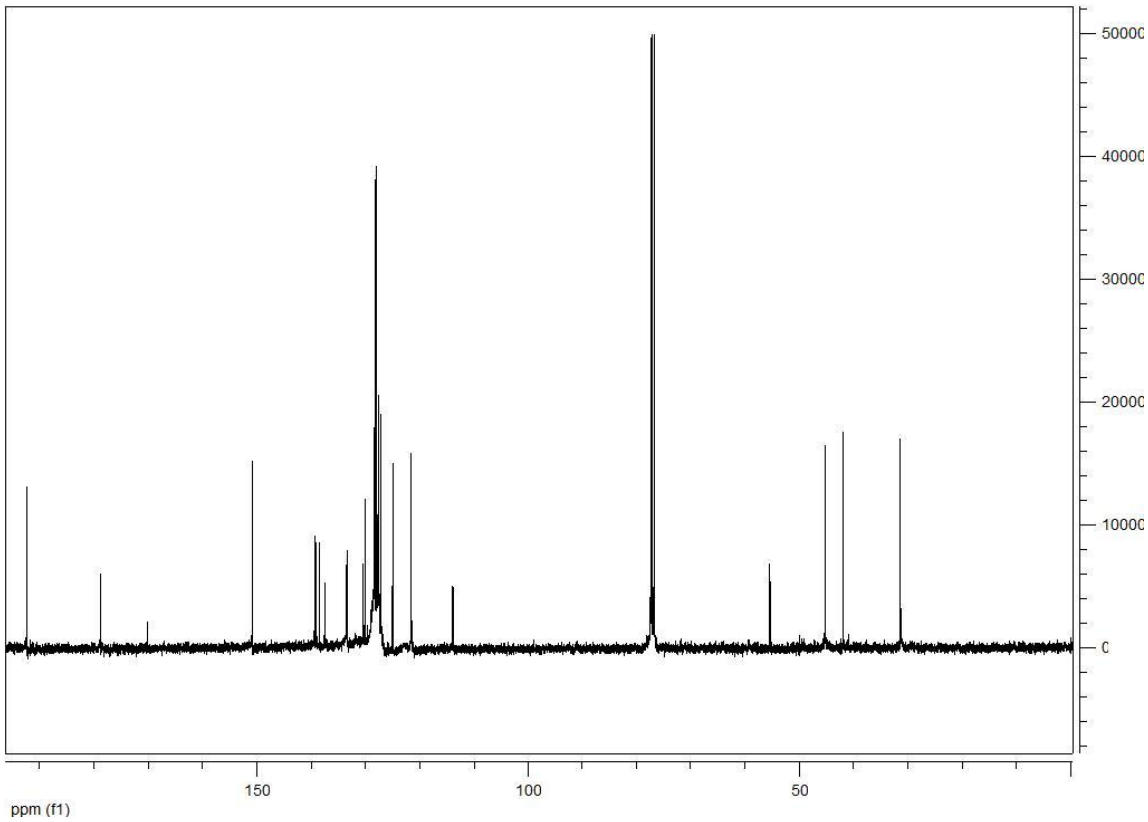
PeakTable

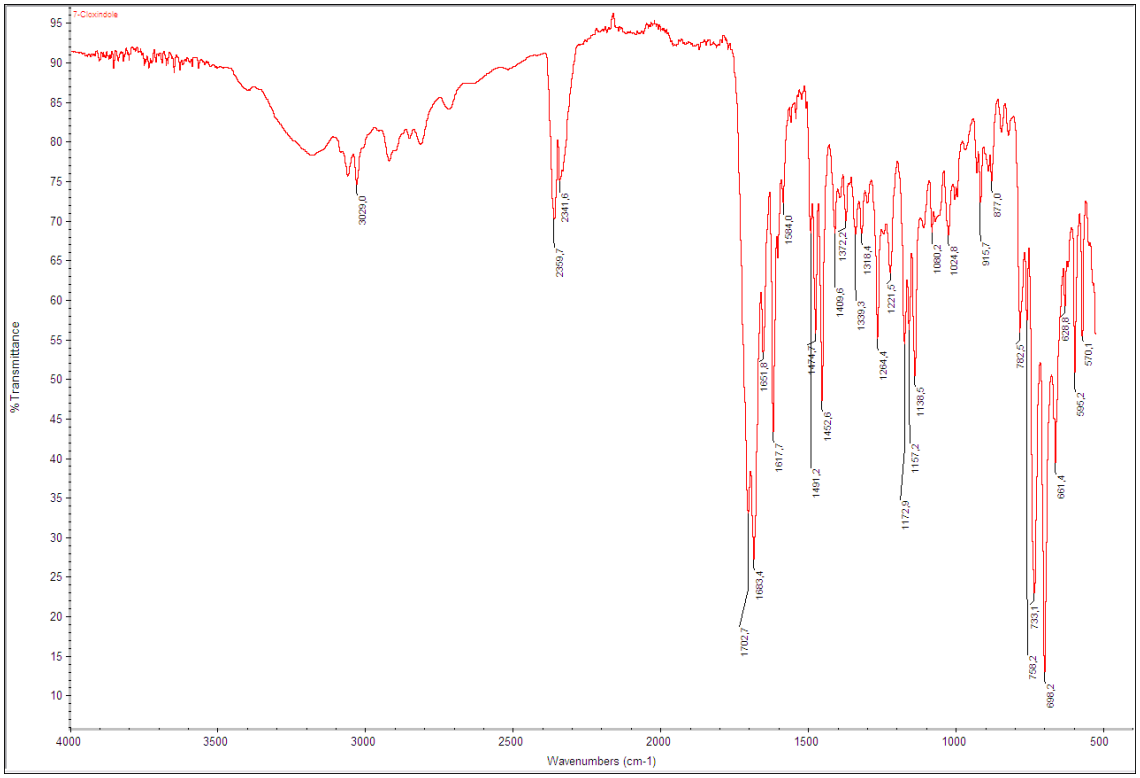
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.064	46588129	568622	99.354	99.503
2	52.886	302858	2842	0.646	0.497
Total		46890987	571464	100.000	100.000

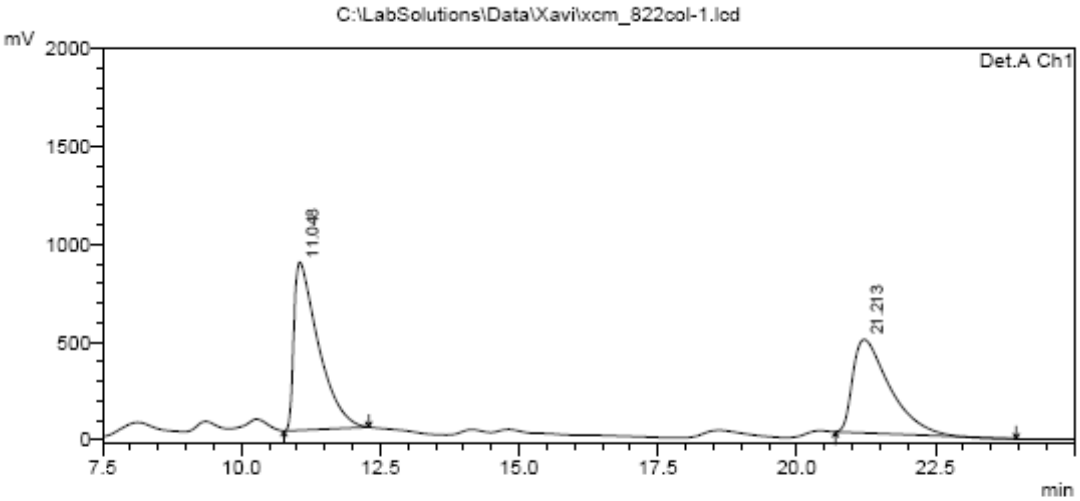
3j


CHO
O
N
H
Cl
4000
3000
2000
1000
0
10.0
5.0
0.0
ppm (f1)


50000
40000
30000
20000
10000
0
150
100
50
ppm (f1)


T-Cloximdole
% Transmittance
Wavenumbers (cm-1)
4000
3500
3000
2500
2000
1500
1000
500
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
3029,0
2359,1
2341,6
1702,7
1683,4
1651,8
1617,7
1584,0
1491,2
1474,3
1452,6
1409,6
1372,2
1339,3
1318,4
1264,4
1221,5
1172,9
1157,2
1138,6
1080,2
1024,8
915,7
877,0
782,5
758,2
733,1
698,2
661,4
628,0
595,2
570,1

<Chromatogram>



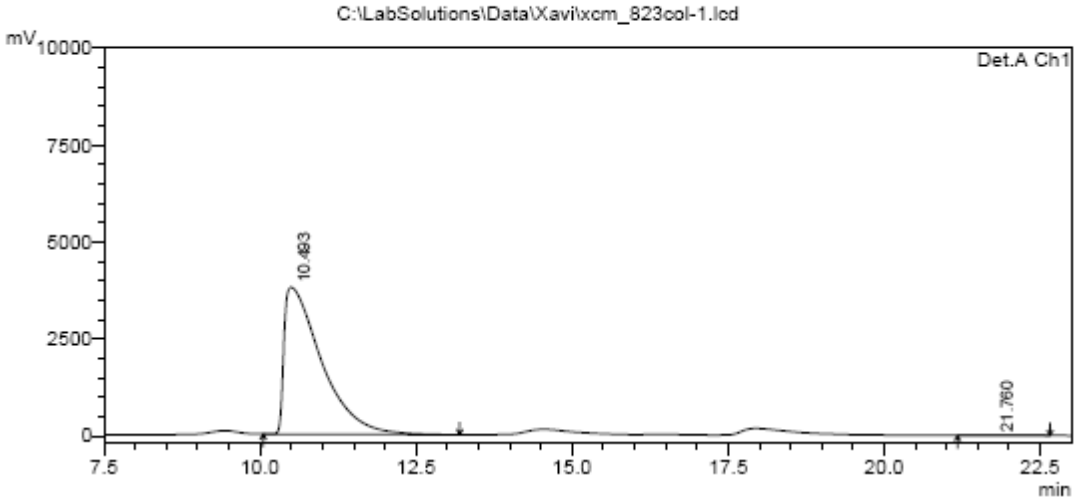
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.048	26371704	858797	54.357	64.249
2	21.213	22143851	477878	45.643	35.751
Total		48515555	1336675	100.000	100.000

<Chromatogram>



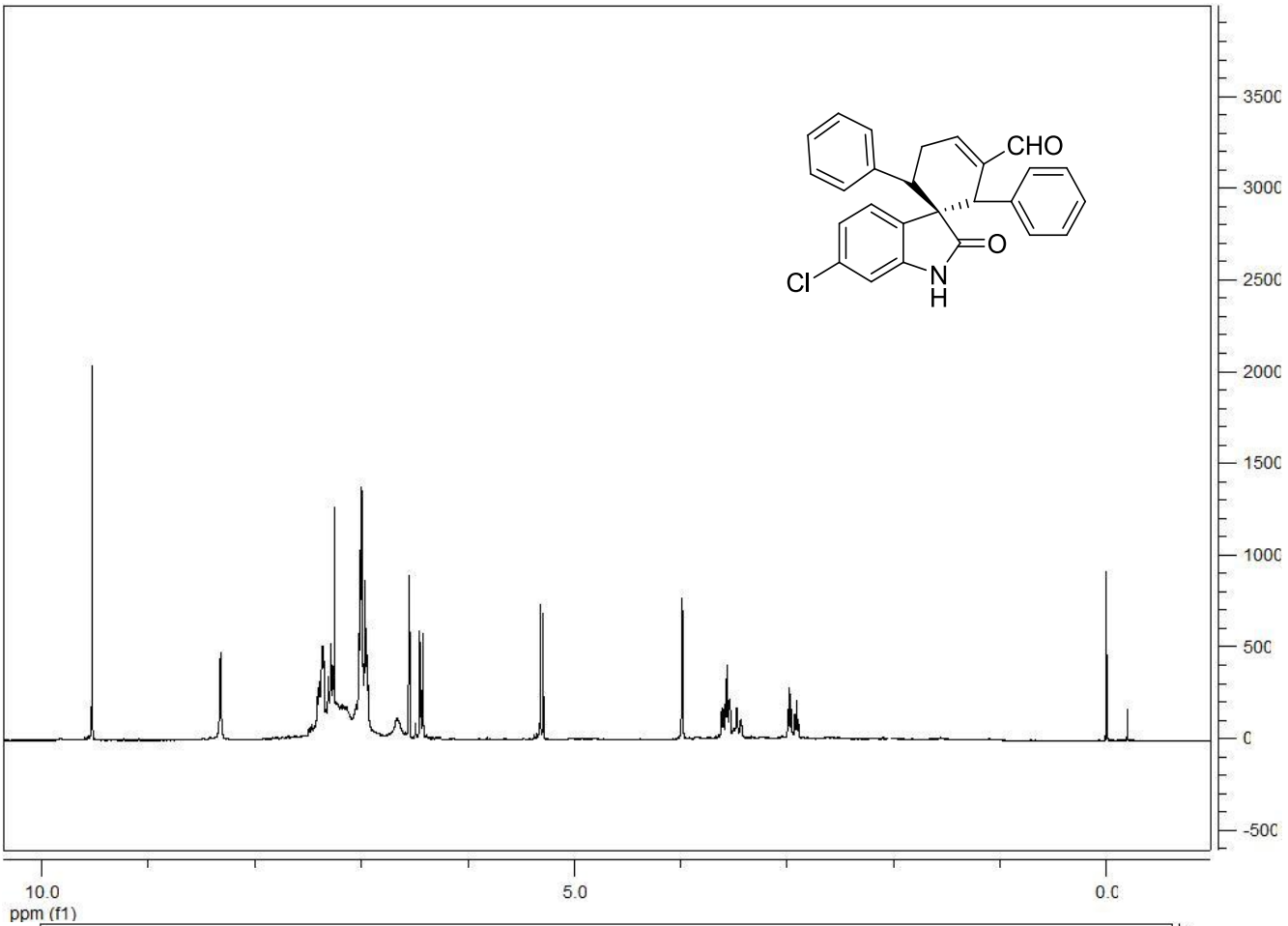
1 Det.A Ch1/254nm

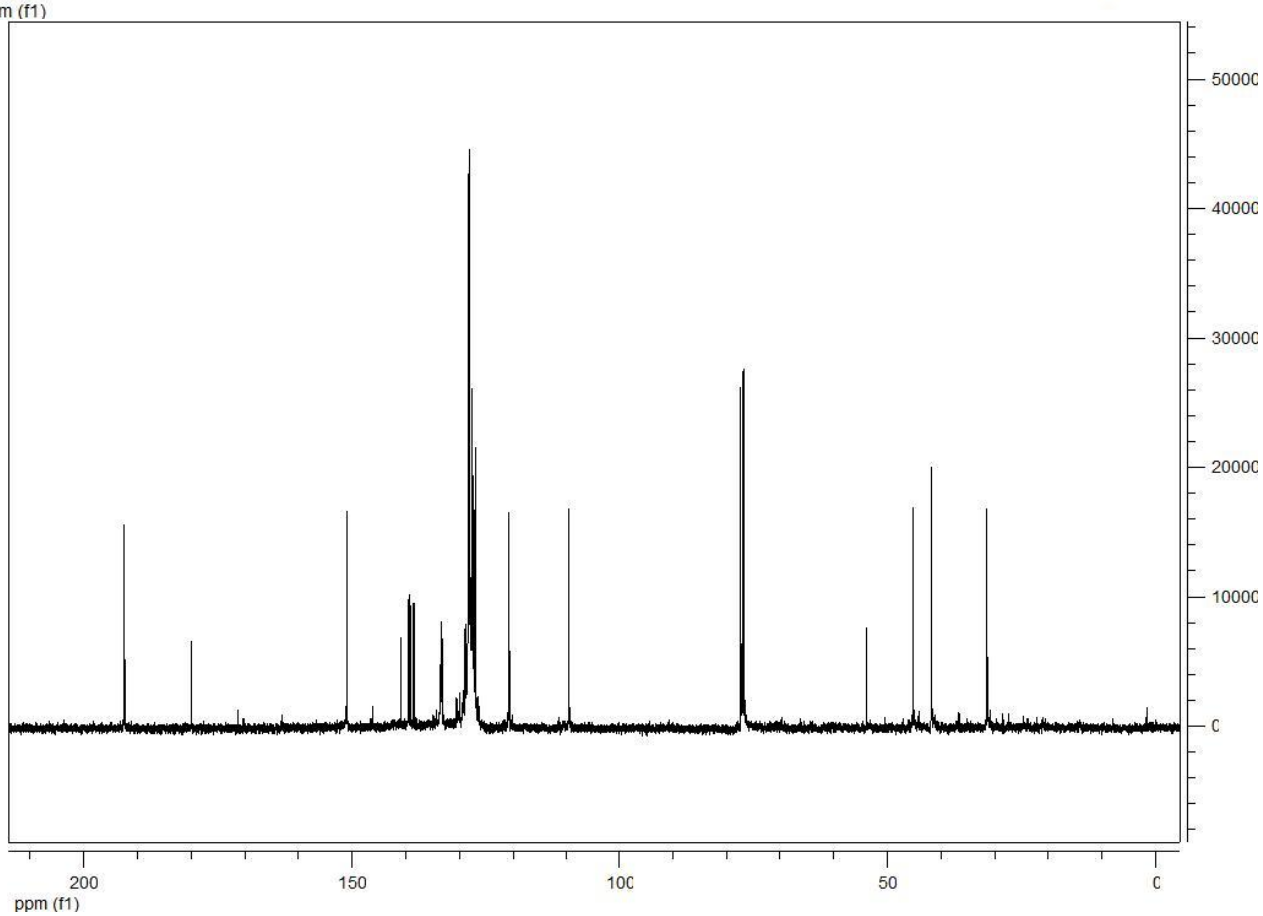
PeakTable

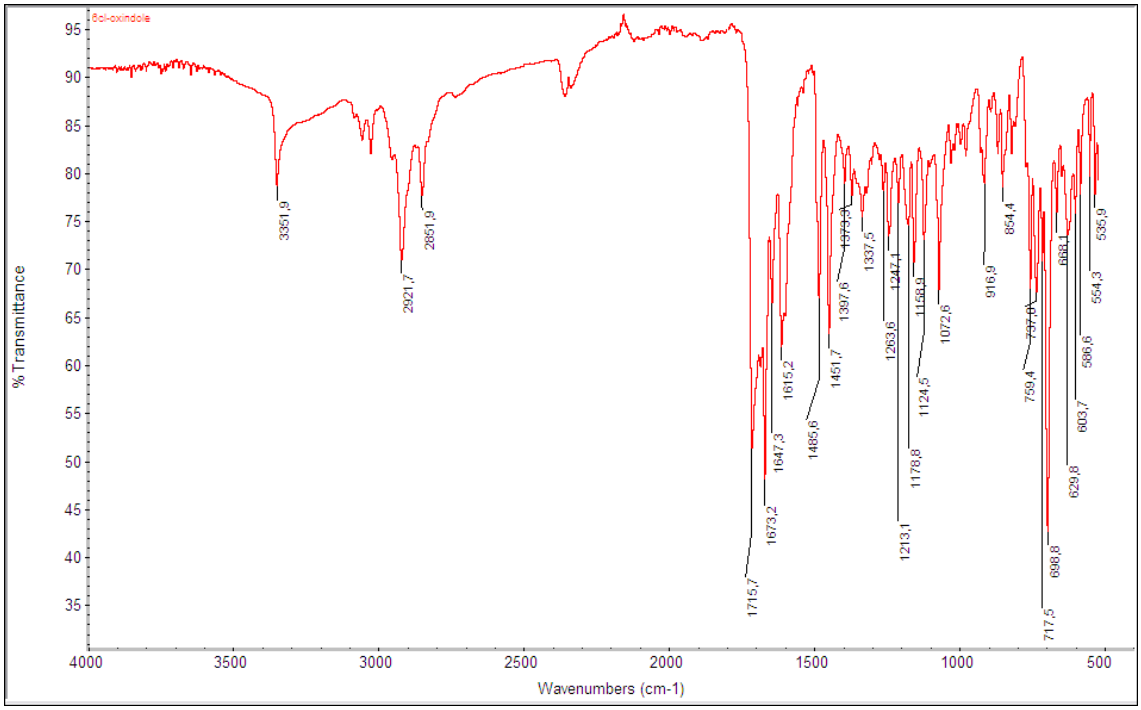
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.493	157844384	3798915	99.941	99.939
2	21.760	93220	2307	0.059	0.061
Total		157937604	3801222	100.000	100.000

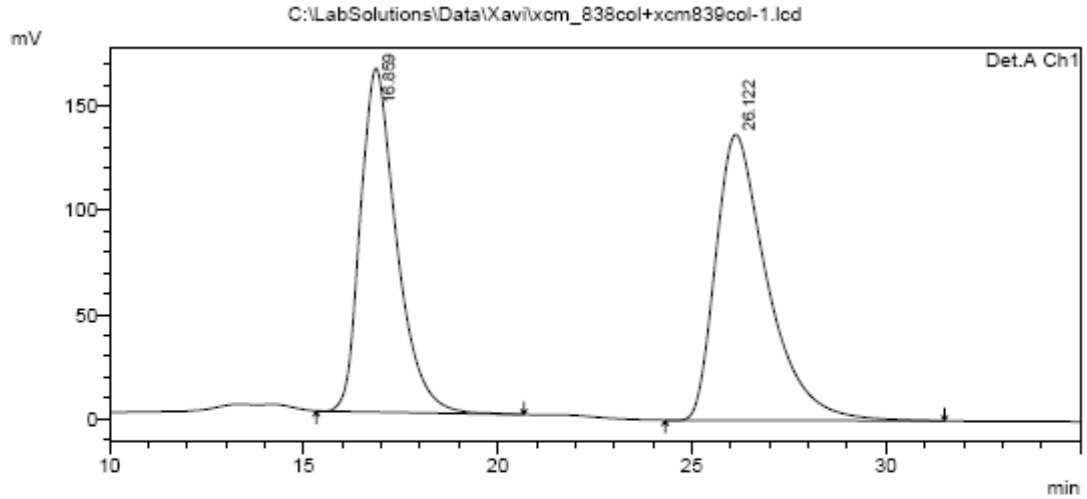
3i


CHO
O
Cl
N
H
3500
3000
2500
2000
1500
1000
500
0
-500
10.0
5.0
0.0
ppm (f1)


50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (f1)


8ol-oxindole
% Transmittance
Wavenumbers (cm-1)
95
90
85
80
75
70
65
60
55
50
45
40
35
4000
3500
3000
2500
2000
1500
1000
500
3351,9
2921,7
2851,9
1715,7
1673,2
1647,3
1615,2
1485,6
1451,7
1397,6
1373,3
1337,5
1263,6
1247,1
1213,1
1178,8
1158,9
1124,5
1072,6
916,9
854,4
759,4
737,0
717,5
698,8
668,1
629,8
603,7
586,6
554,3
535,9

<Chromatogram>



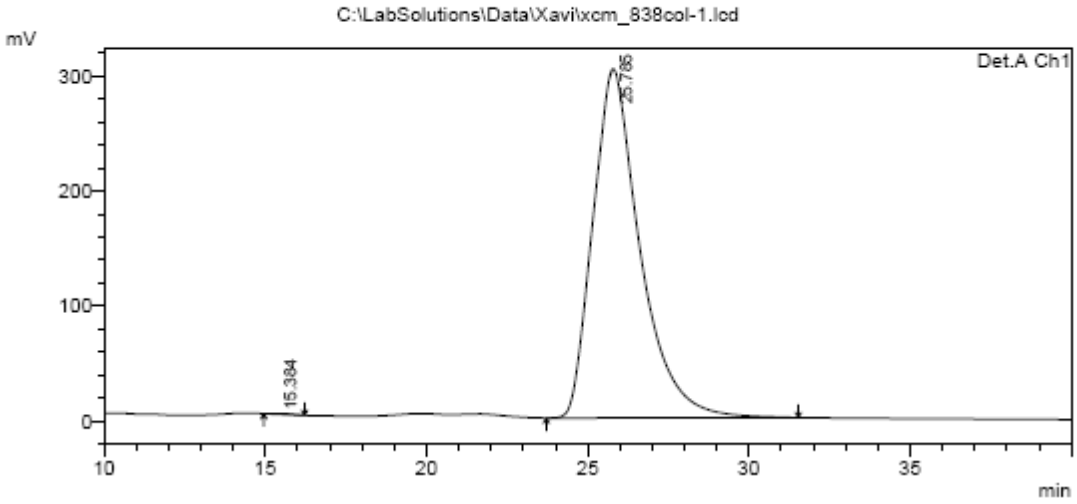
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.859	10686130	164738	45.835	54.606
2	26.122	12628253	136947	54.165	45.394
Total		23314383	301685	100.000	100.000

<Chromatogram>



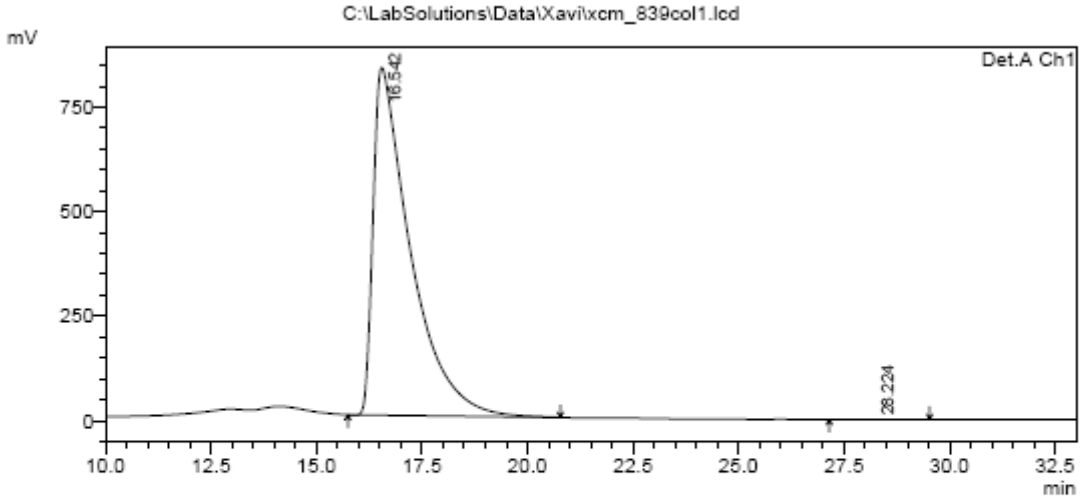
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.384	28011	505	0.091	0.166
2	25.785	30852535	303490	99.909	99.834
Total		30880546	303995	100.000	100.000

<Chromatogram>



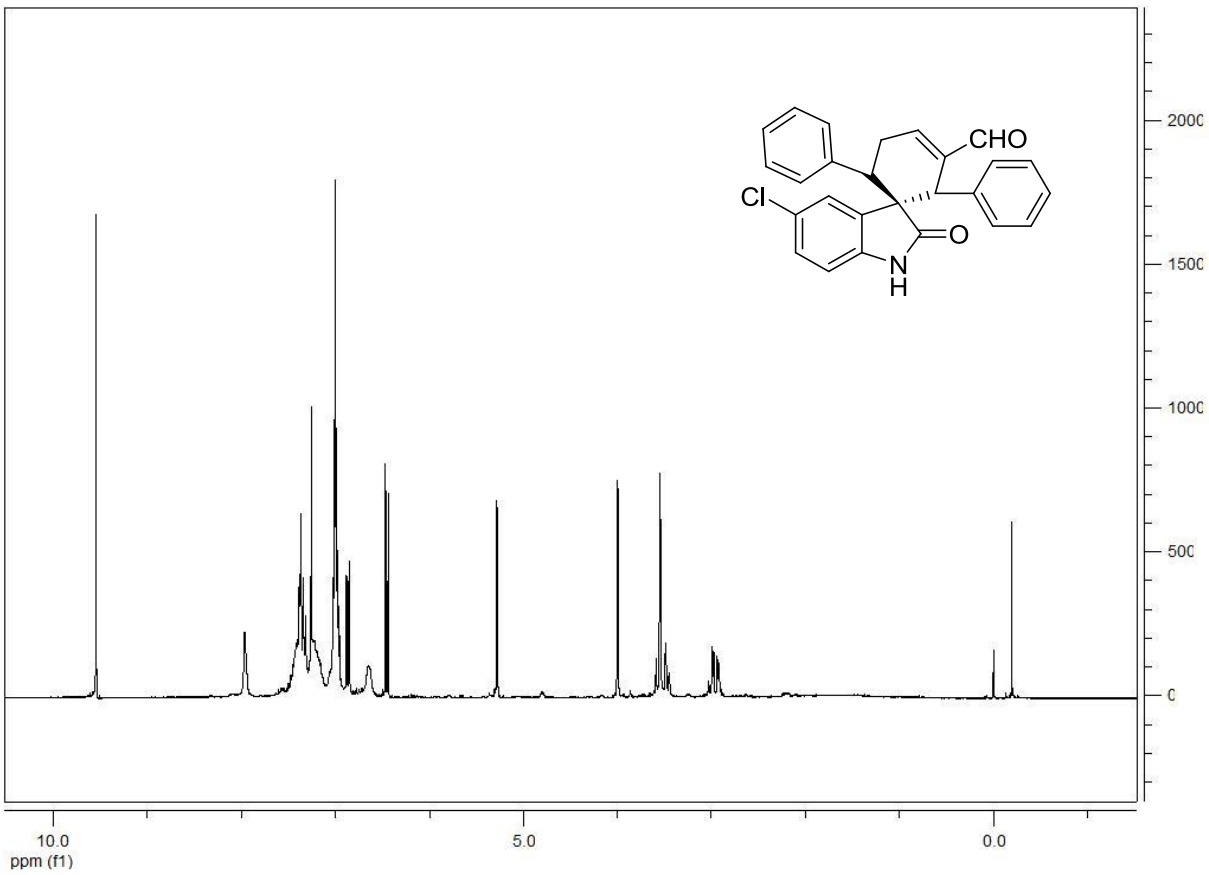
1 Det.A Ch1/254nm

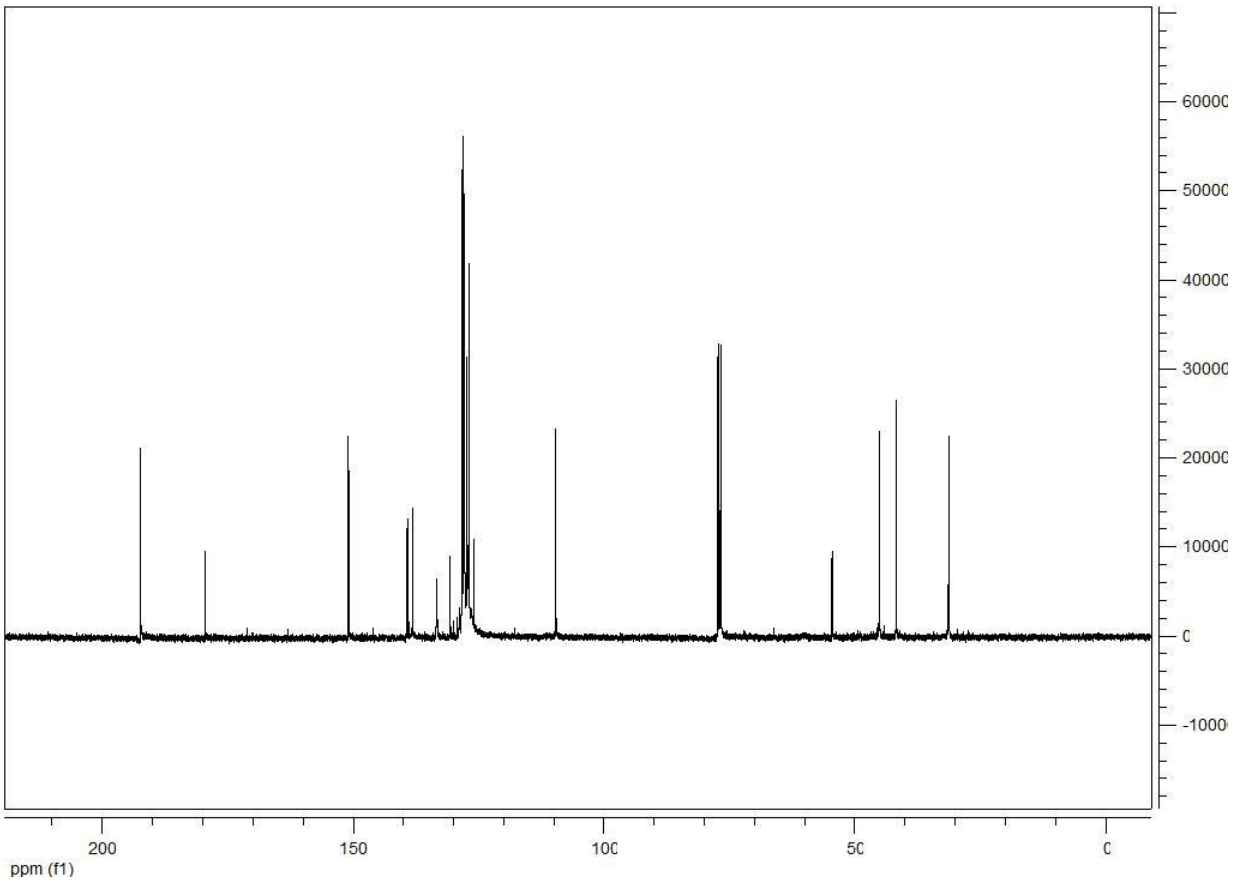
PeakTable

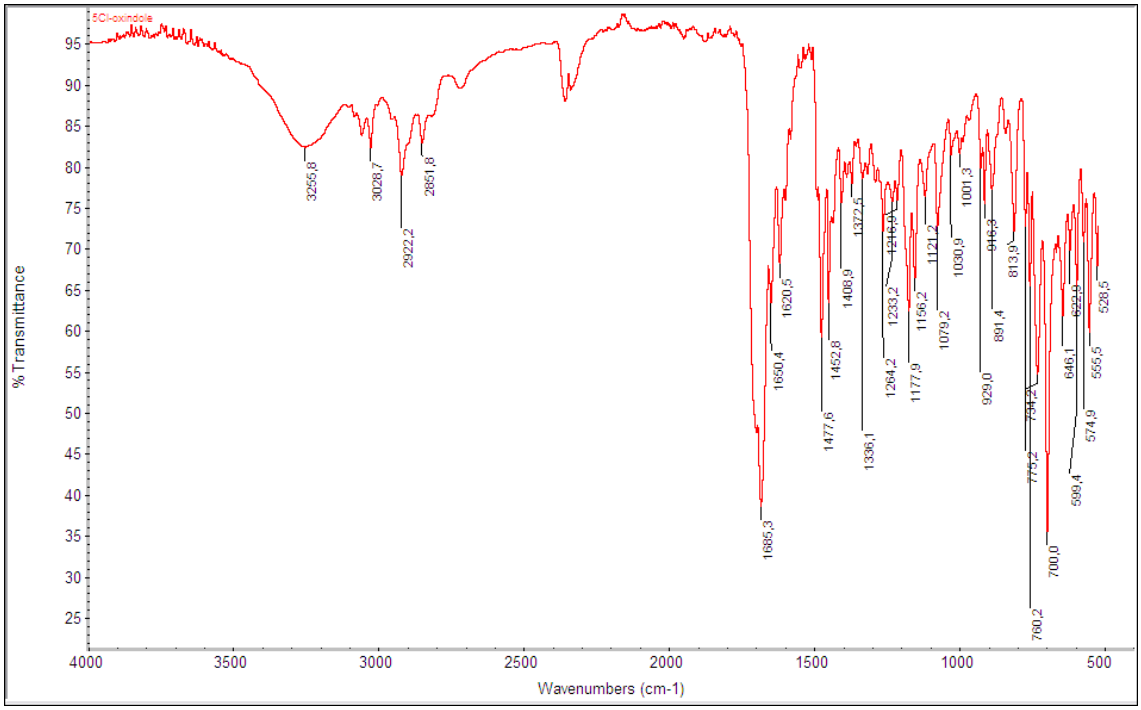
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.542	50940822	831369	99.915	99.923
2	28.224	43457	638	0.085	0.077
Total		50984279	832007	100.000	100.000

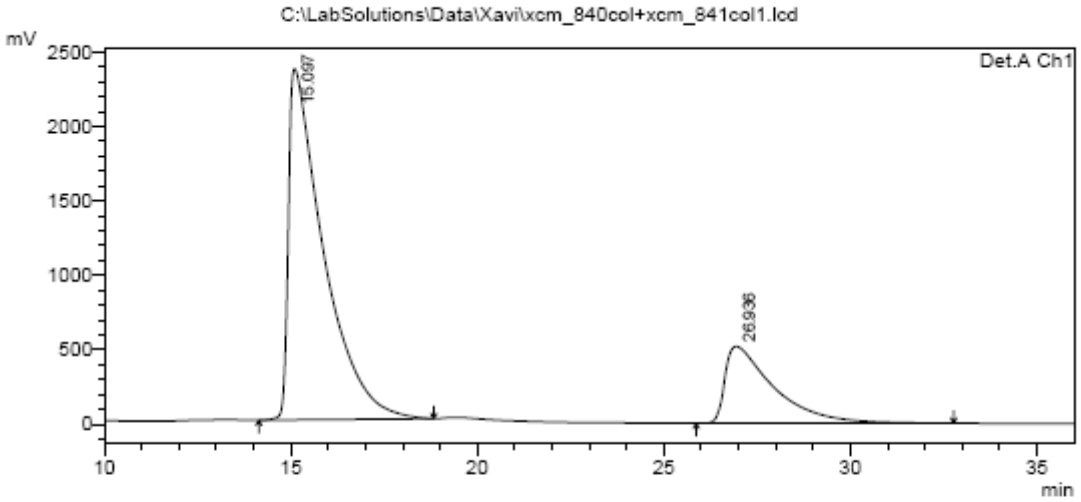
3l


CHO
Cl
O
N
H
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)


60000
50000
40000
30000
20000
10000
0
-10000
200
150
100
50
0
ppm (f1)


5Cl-oxindole
%Transmittance
Wavenumbers (cm-1)
3255,8
3028,7
2922,2
2851,8
1685,3
1650,4
1620,5
1477,6
1452,8
1408,9
1372,5
1336,1
1264,2
1233,2
1177,9
1156,2
1121,2
1079,2
1030,9
1001,3
929,0
891,4
813,9
775,2
734,2
700,0
646,1
622,9
599,4
574,9
555,5
528,5
760,2

<Chromatogram>



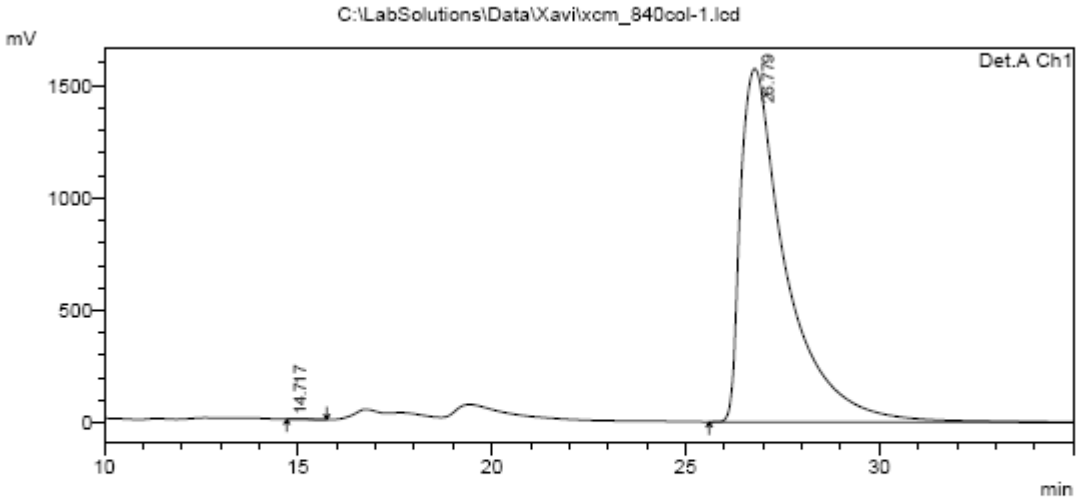
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.097	153463370	2358727	76.643	82.053
2	26.936	46766944	515920	23.357	17.947
Total		200230315	2874646	100.000	100.000

<Chromatogram>



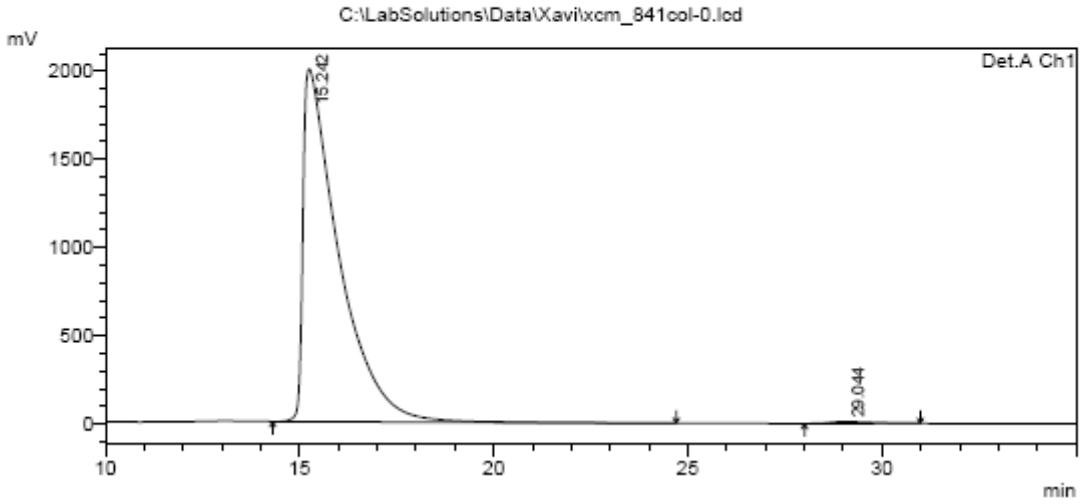
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.717	19727	11	0.015	0.001
2	26.779	128202823	1571239	99.985	99.999
Total		128222550	1571249	100.000	100.000

<Chromatogram>



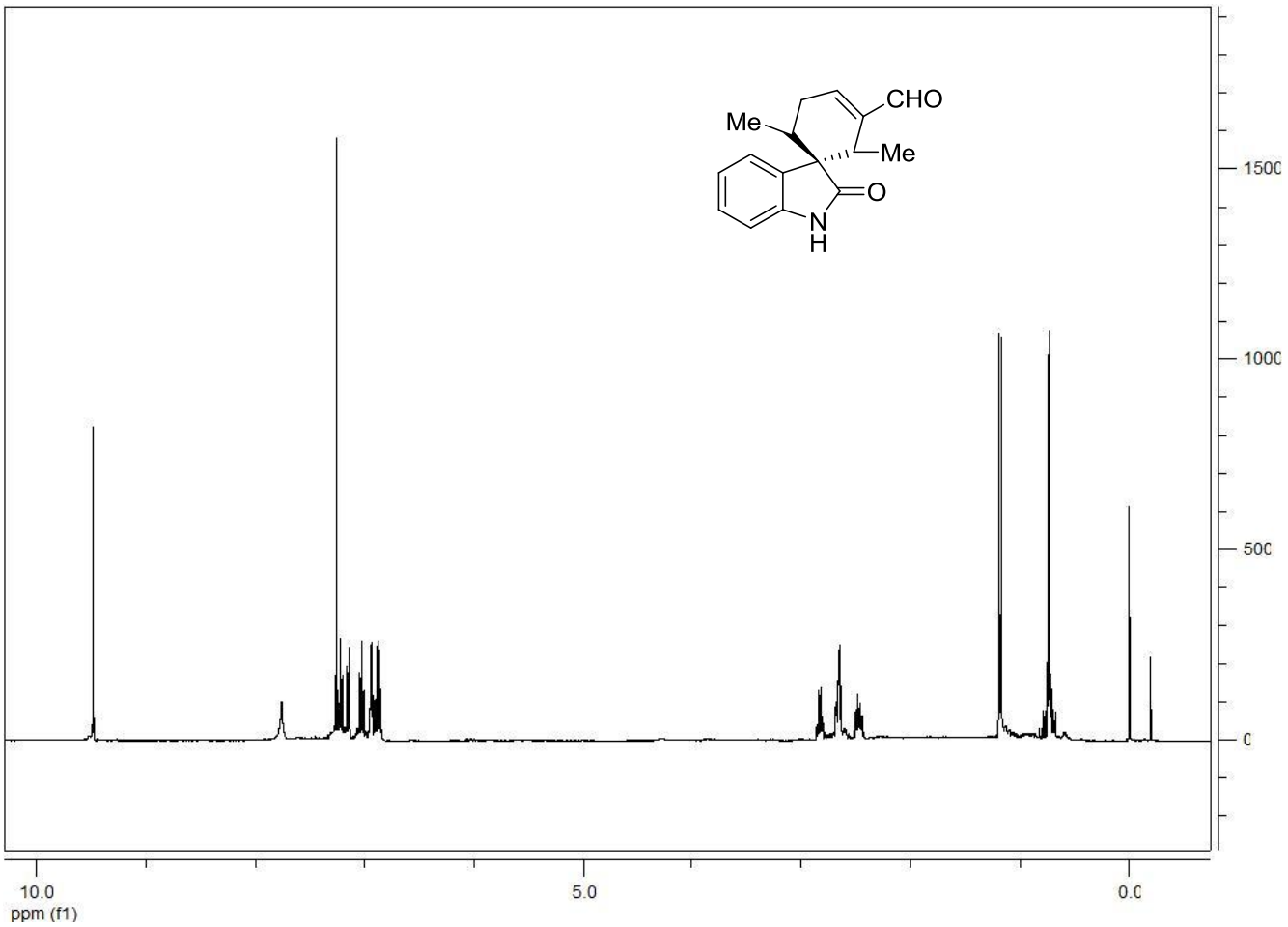
1 Det.A Ch1/254nm

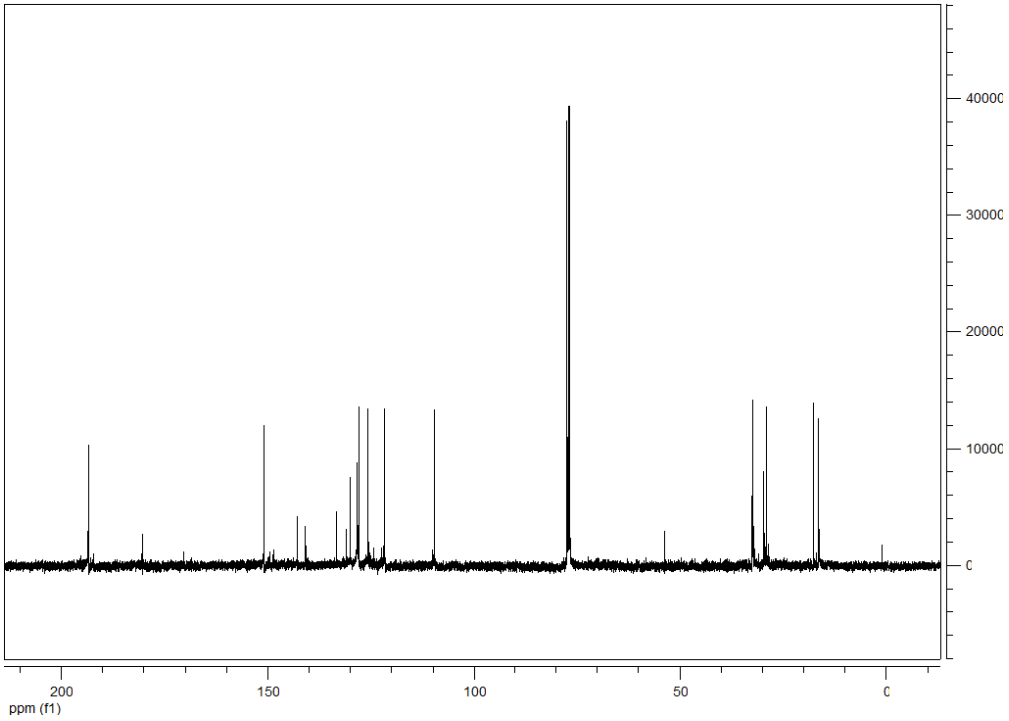
PeakTable

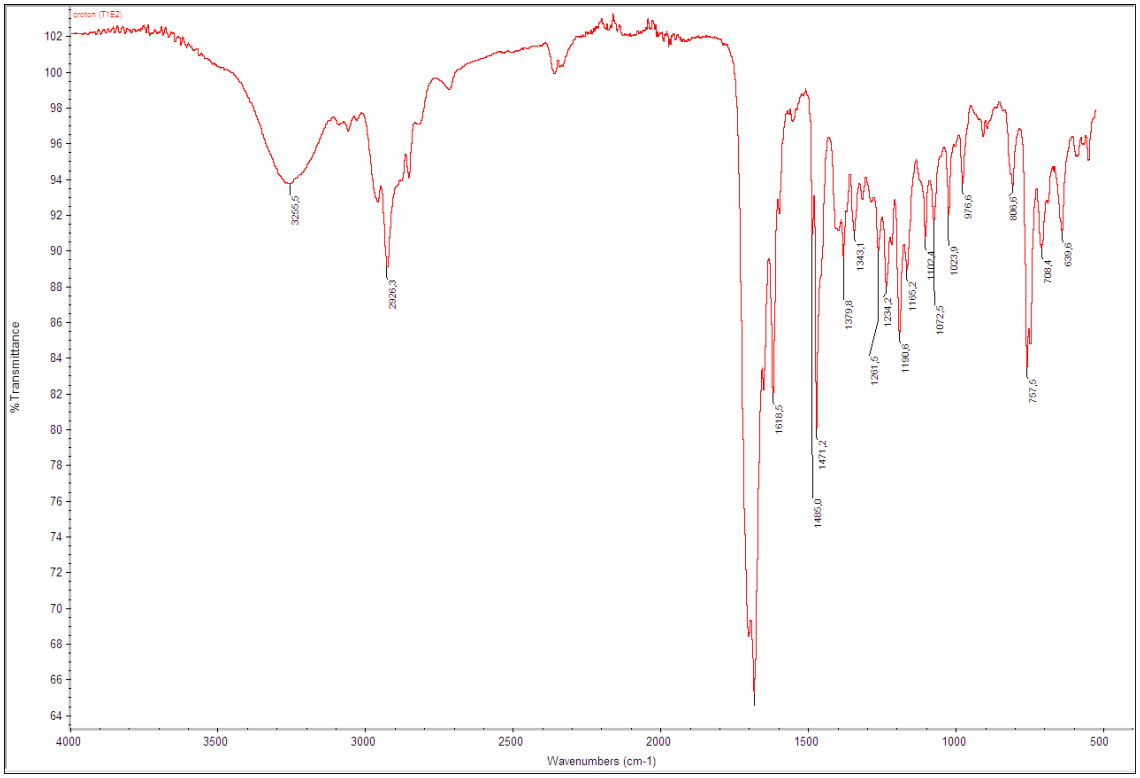
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.242	127639622	1998901	99.412	99.494
2	29.044	754654	10164	0.588	0.506
Total		128394276	2009065	100.000	100.000

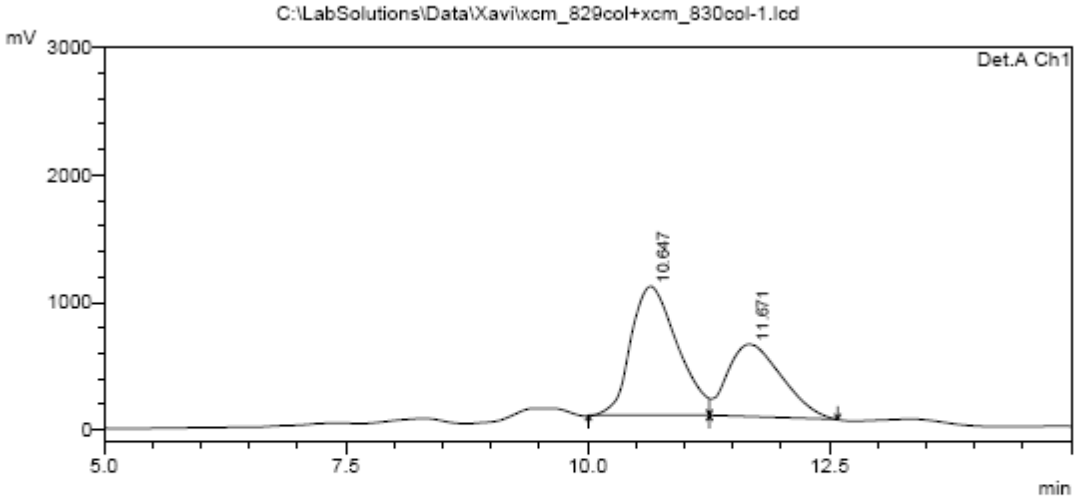
3b


CHO
Me
Me
O
N
H
1500
1000
500
0
10.0
ppm (f1)
5.0
0.0


40000
30000
20000
10000
0
200
ppm (f1)
150
100
50
0


croton (T1E2)
% Transmittance
Wavenumbers (cm-1)
3255,5
2926,3
1618,5
1485,0
1471,2
1379,8
1343,1
1261,5
1234,2
1190,6
1165,2
1102,4
1072,5
1023,9
976,6
806,8
757,6
708,4
639,6

<Chromatogram>



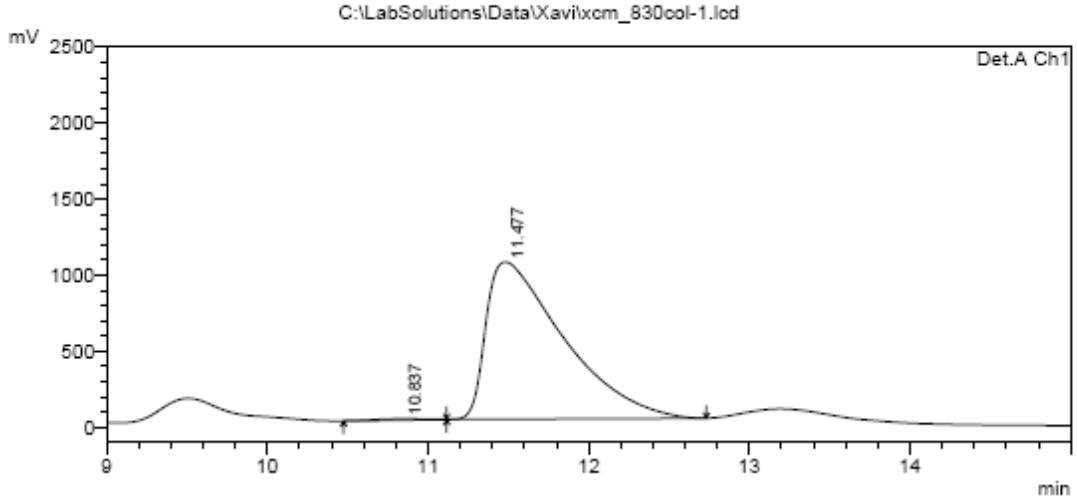
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.647	33808568	1011029	60.415	63.990
2	11.671	22152336	568940	39.585	36.010
Total		55960904	1579969	100.000	100.000

<Chromatogram>



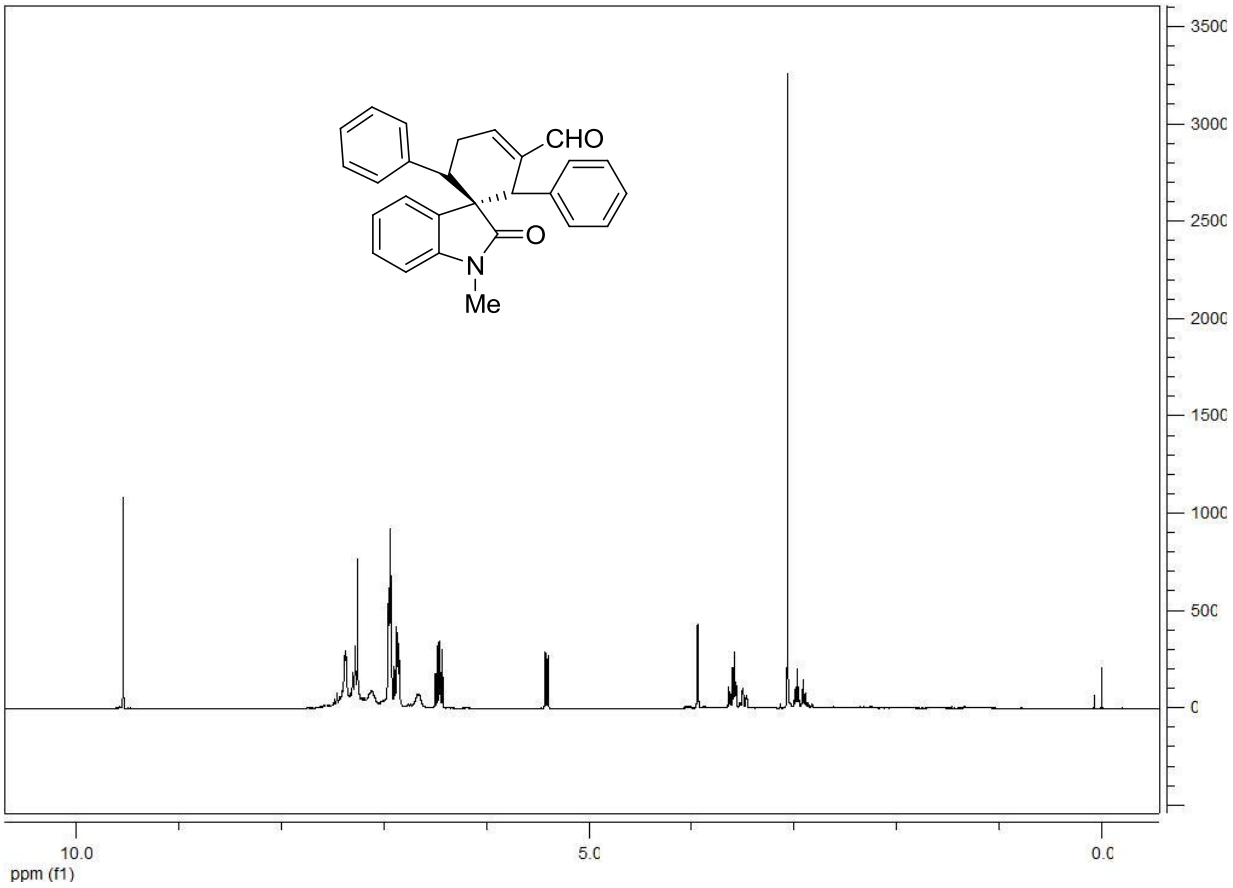
1 Det.A Ch1/254nm

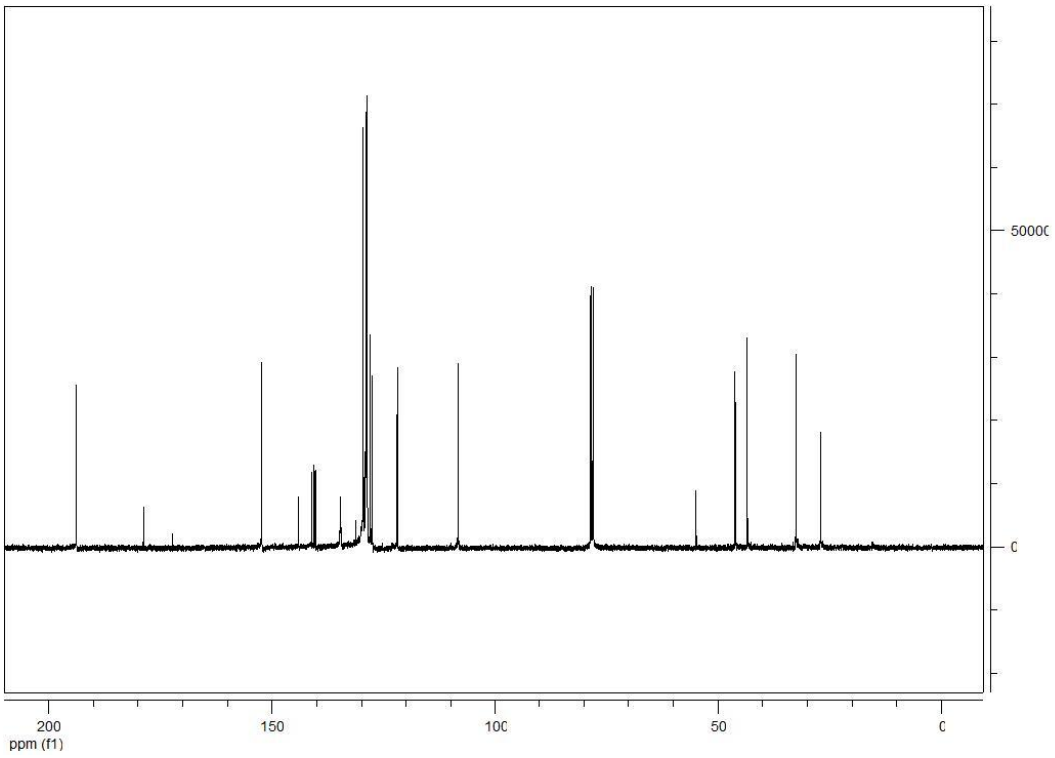
PeakTable

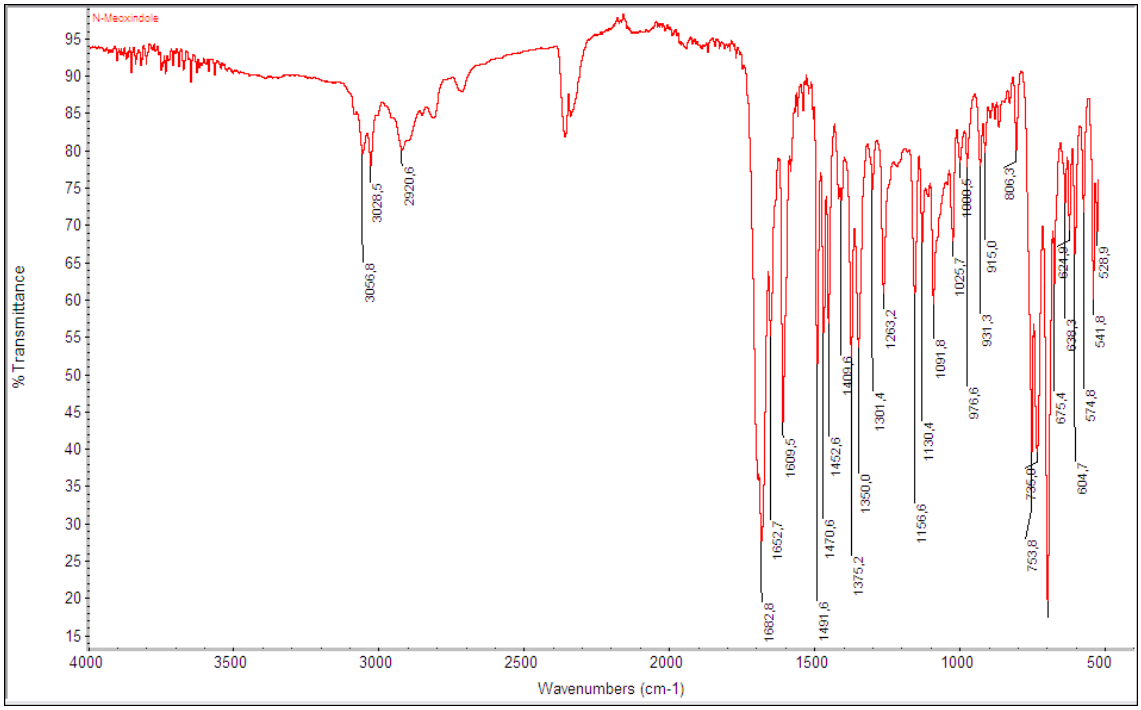
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.837	175906	8341	0.506	0.801
2	11.477	34583478	1033246	99.494	99.199
Total		34759384	1041587	100.000	100.000

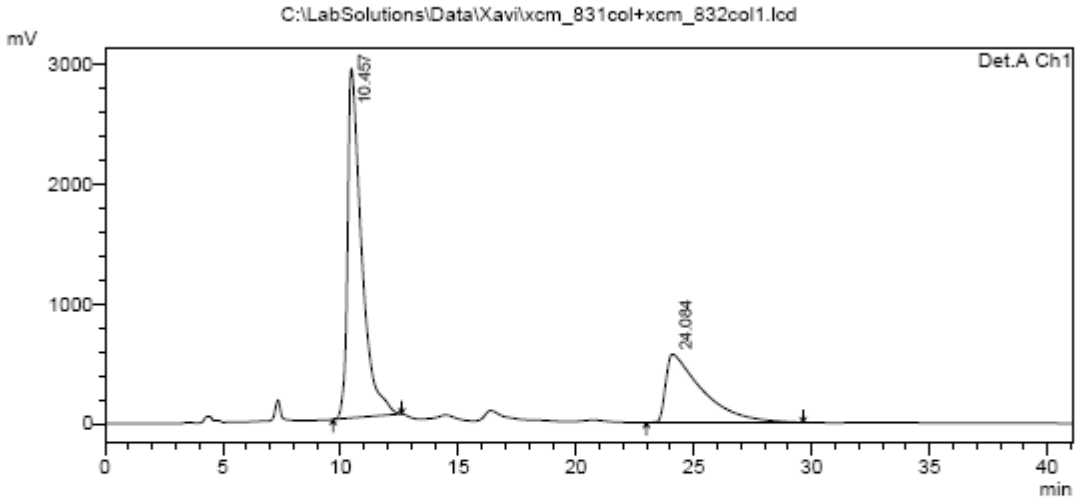
3k


CHO
O
N
Me
3500
3000
2500
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)


50000
0
200
150
100
50
0
ppm (f1)


N-Meoxindole
%Transmittance
Wavenumbers (cm-1)
4000
3500
3000
2500
2000
1500
1000
500
3056,8
3028,5
2920,6
1682,8
1652,7
1609,5
1491,6
1470,6
1452,6
1409,6
1375,2
1350,0
1301,4
1263,2
1156,6
1130,4
1091,8
1025,7
1000,5
976,6
931,3
915,0
806,3
753,8
735,0
675,4
638,3
624,0
604,7
574,8
541,8
528,9

<Chromatogram>



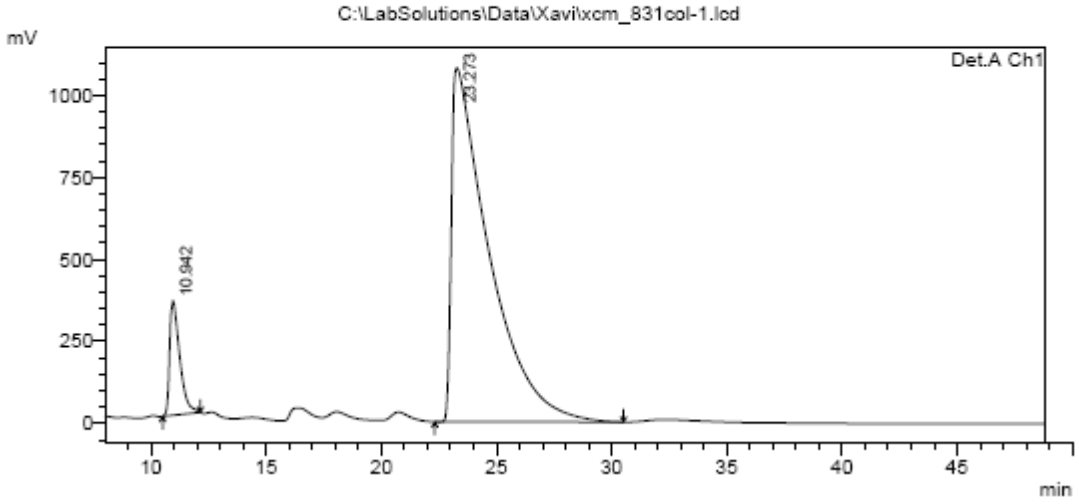
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.457	120530801	2915321	66.408	83.648
2	24.084	60968330	569910	33.592	16.352
Total		181499131	3485231	100.000	100.000

<Chromatogram>



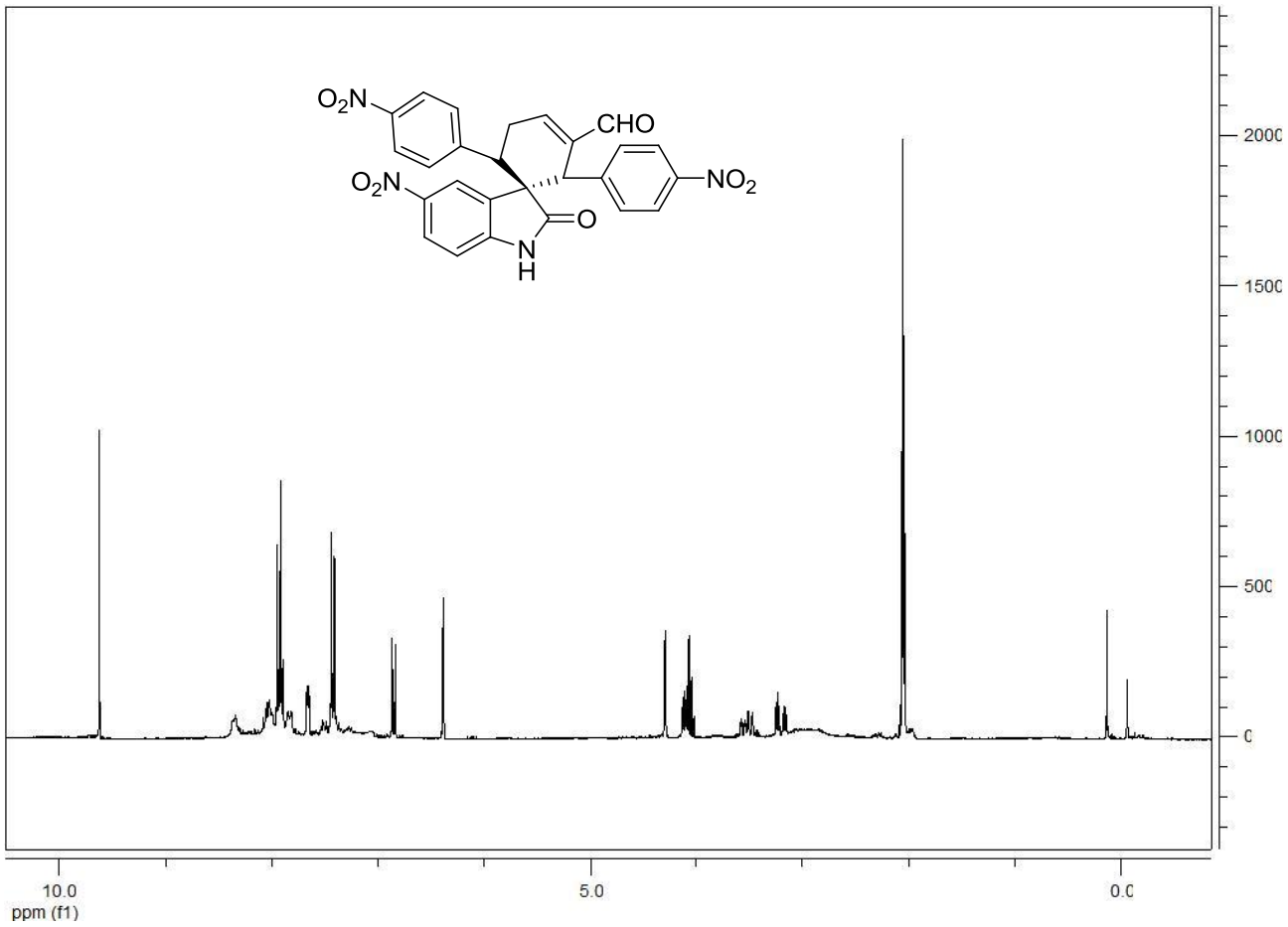
1 Det.A Ch1/254nm

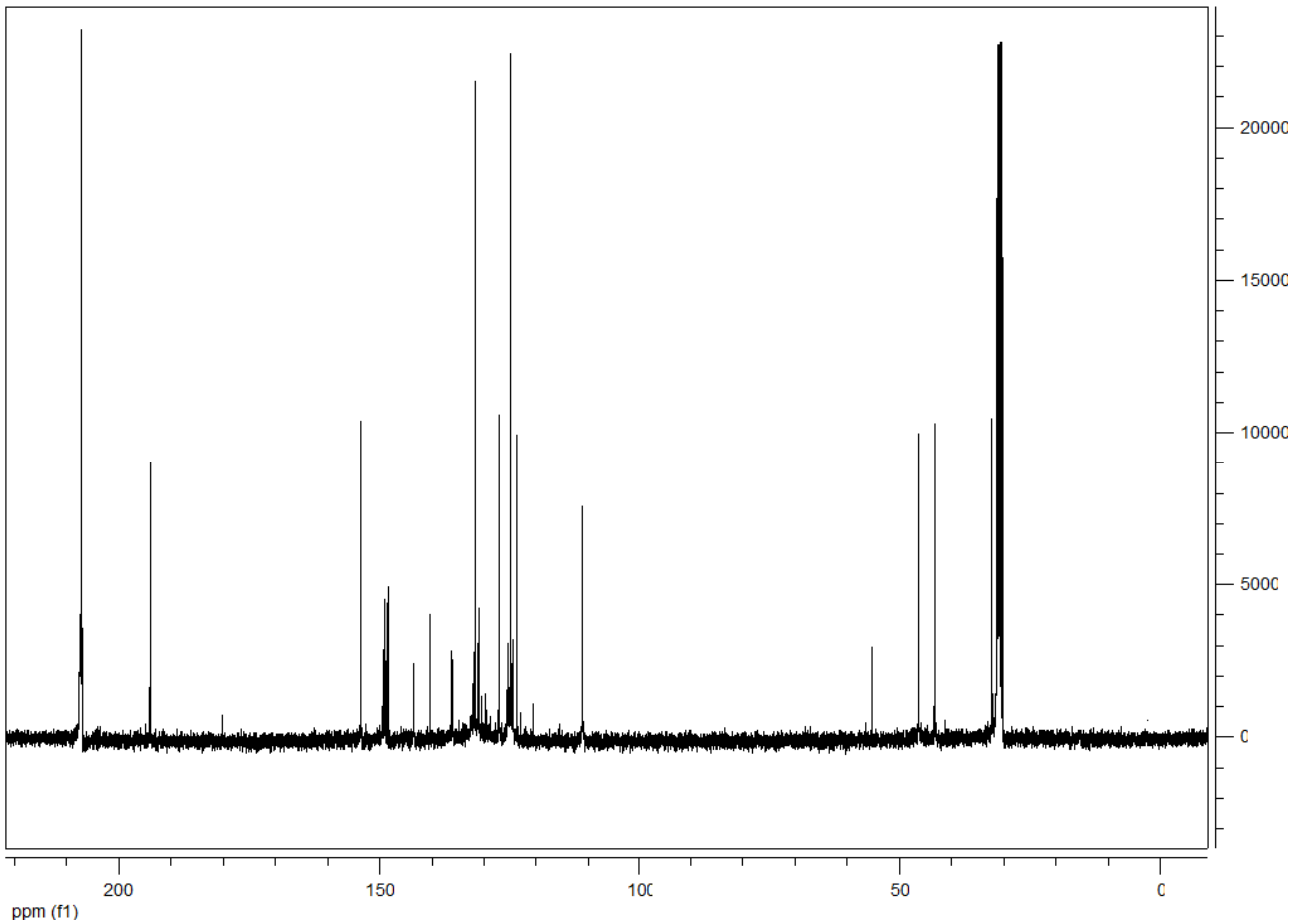
PeakTable

Detector A Ch1 254nm

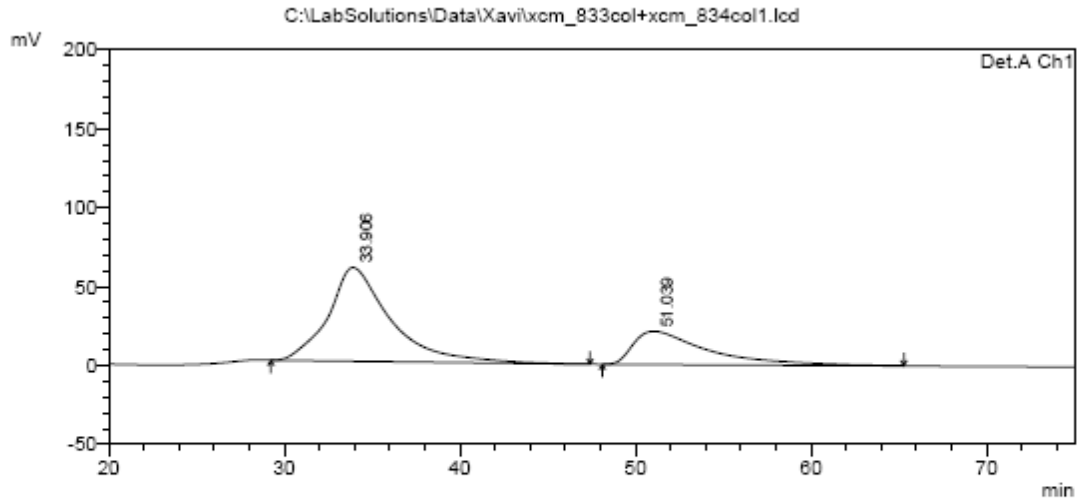
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.942	10672332	348866	8.033	24.440
2	23.273	122189074	1078564	91.967	75.560
Total		132861406	1427430	100.000	100.000

3h


O2N
CHO
O2N
NO2
O
N
H
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)


20000
15000
10000
5000
0
200
150
100
50
0
ppm (f1)

<Chromatogram>



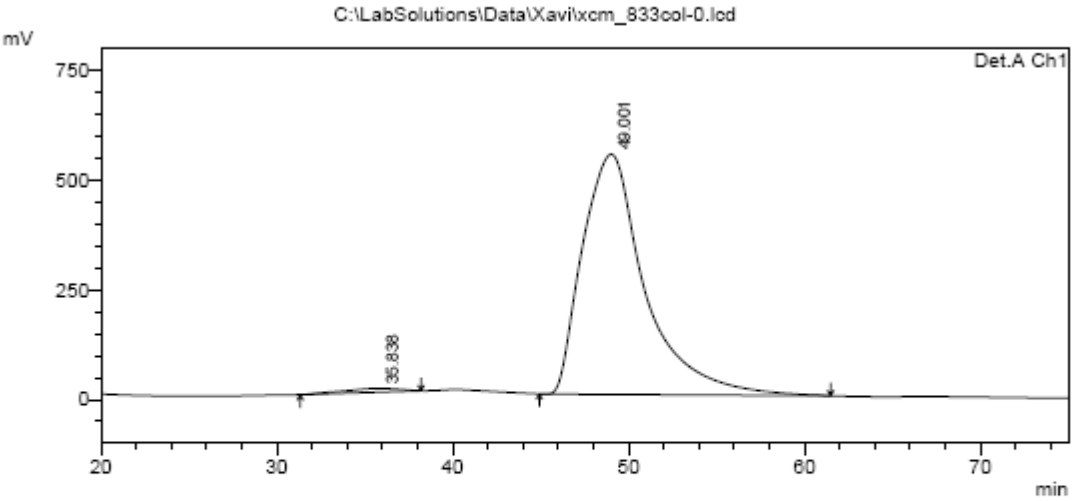
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.906	14608385	59355	70.293	73.777
2	51.039	6173604	21097	29.707	26.223
Total		20781988	80452	100.000	100.000

<Chromatogram>



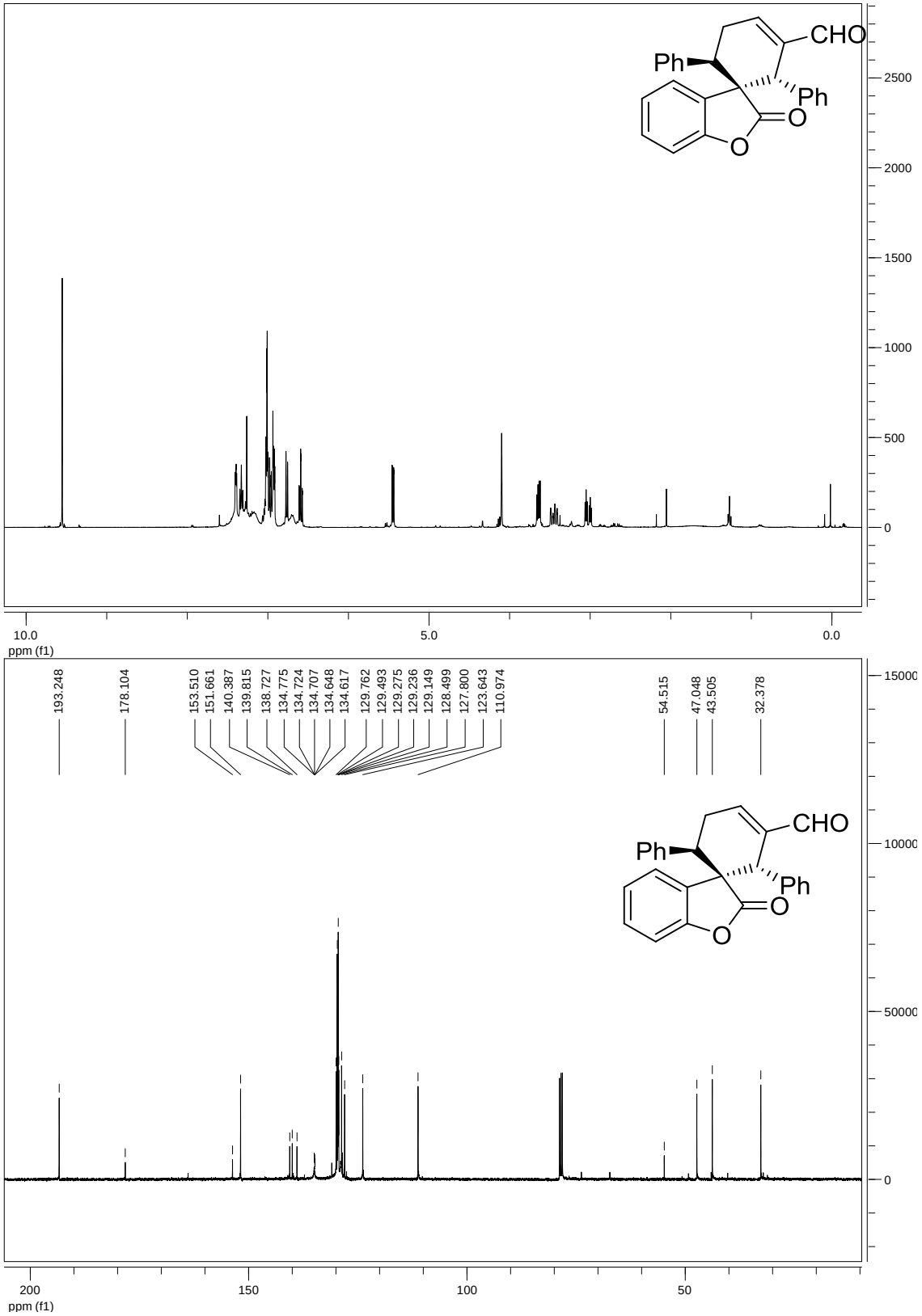
1 Det.A Ch1/254nm

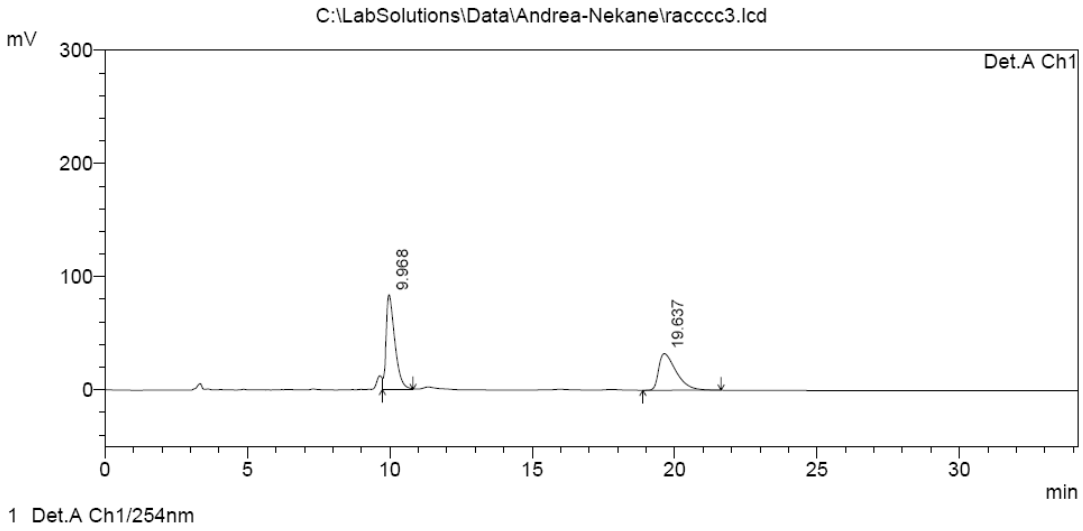
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.838	1885852	8402	1.374	1.510
2	49.001	135396829	547849	98.626	98.490
Total		137282681	556251	100.000	100.000

5a


CHO
Ph
Ph
O
O
2500
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)
193.248
178.104
153.510
151.661
140.387
139.815
138.727
134.775
134.724
134.707
134.648
134.617
129.762
129.493
129.275
129.236
129.149
128.499
127.800
123.643
110.974
54.515
47.048
43.505
32.378
CHO
Ph
Ph
O
O
15000
10000
50000
0
200
150
100
50
ppm (f1)

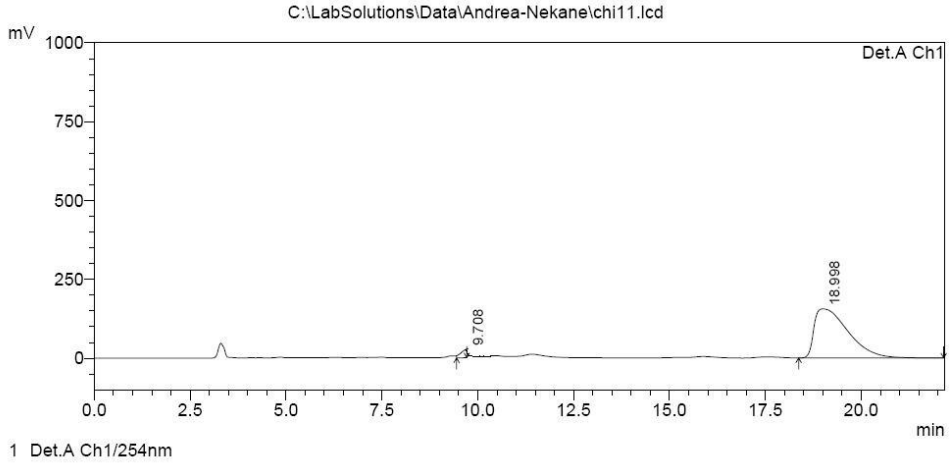


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.968	1789216	83822	56.520	72.169
2	19.637	1376394	32325	43.480	27.831
Total		3165610	116147	100.000	100.000

Cat-(*R*)

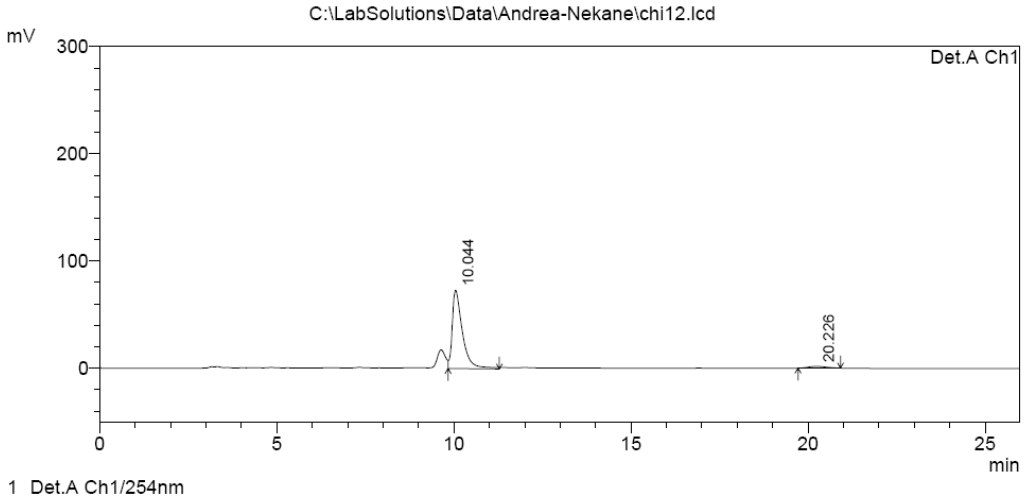


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.708	285600	27120	2.886	14.842
2	18.998	9608879	155611	97.114	85.158
Total		9894478	182731	100.000	100.000

Cat-(*S*)



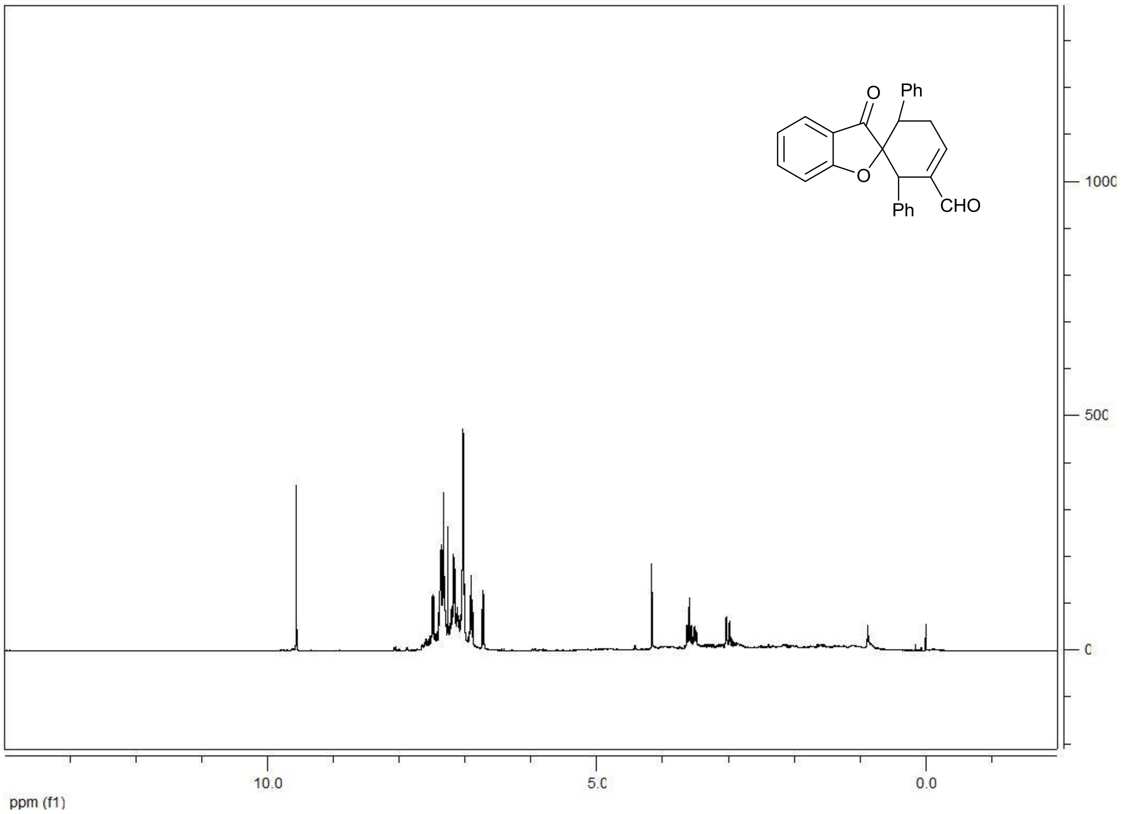
1 Det.A Ch1/254nm

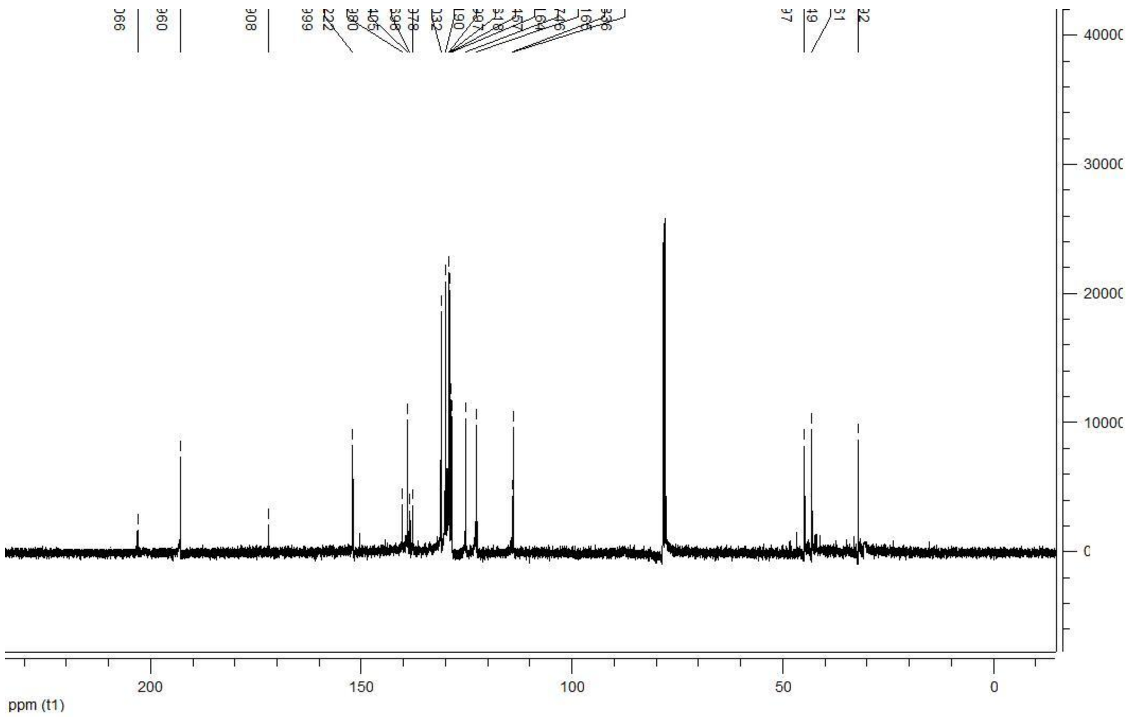
PeakTable

Detector A Ch1 254nm

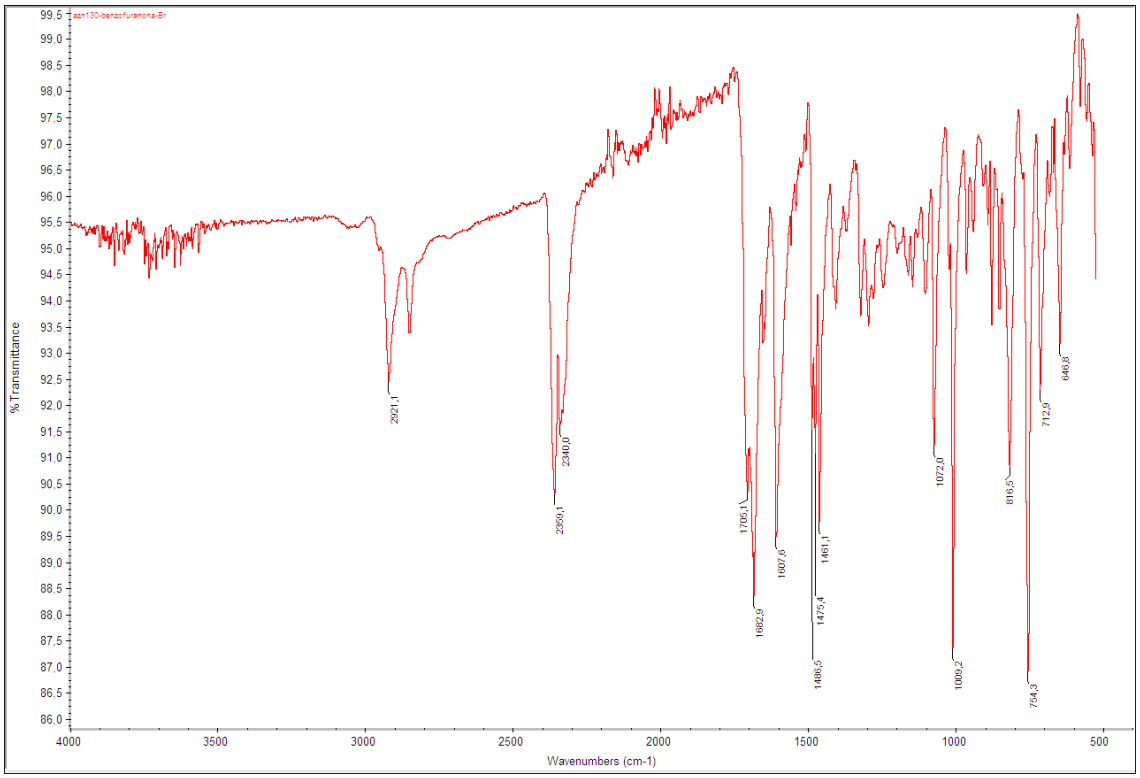
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.044	1470255	73113	96.362	97.846
2	20.226	55514	1609	3.638	2.154
Total		1525769	74722	100.000	100.000

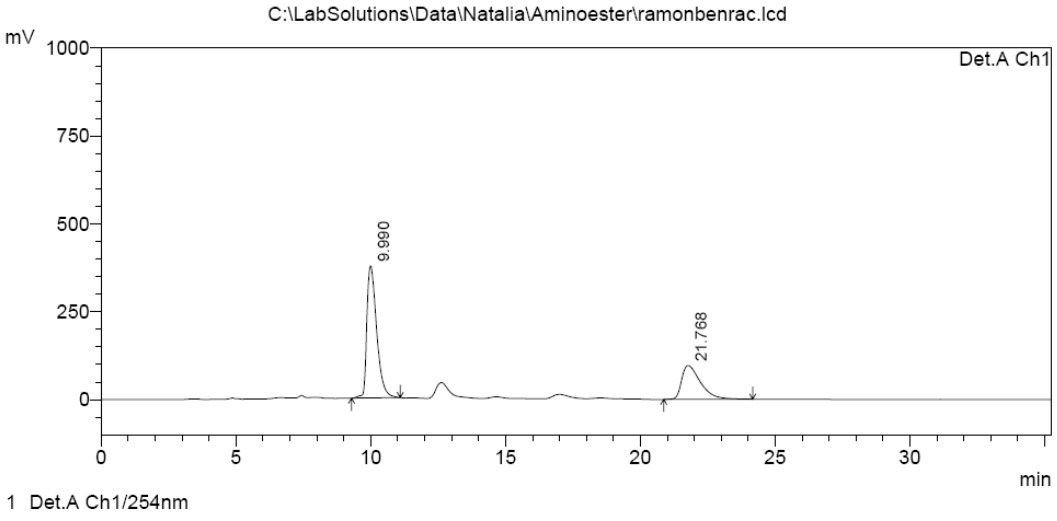
6a


O
Ph
O
Ph
CHO
1000
500
0
10.0
5.0
0.0
ppm (f1)


40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

IR



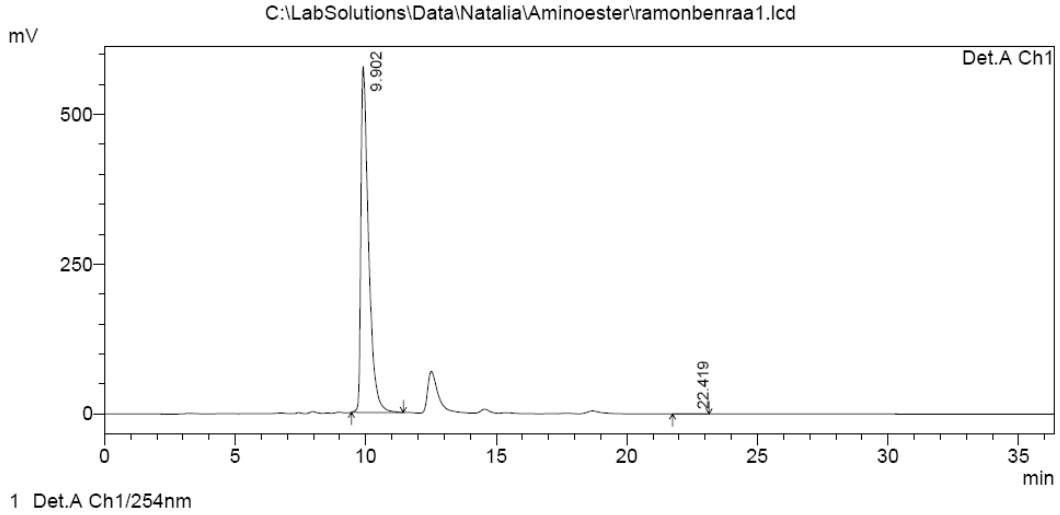


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.990	9511135	375462	67.307	79.674
2	21.768	4619752	95787	32.693	20.326
Total		14130887	471249	100.000	100.000

Cat-(*S*)

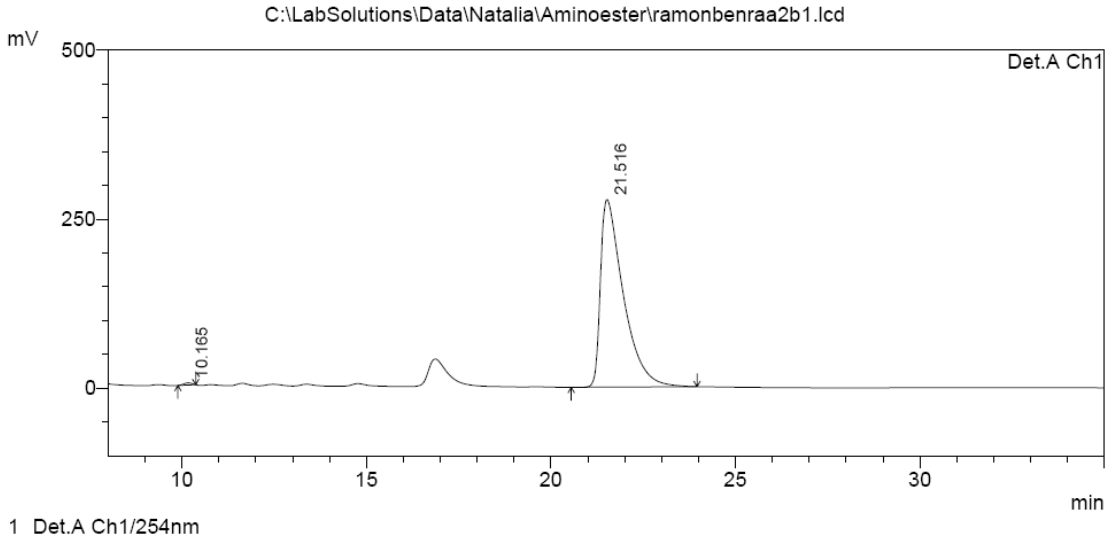


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.902	11832269	577383	99.921	99.961
2	22.419	9385	227	0.079	0.039
Total		11841654	577610	100.000	100.000

Cat-(*R*)

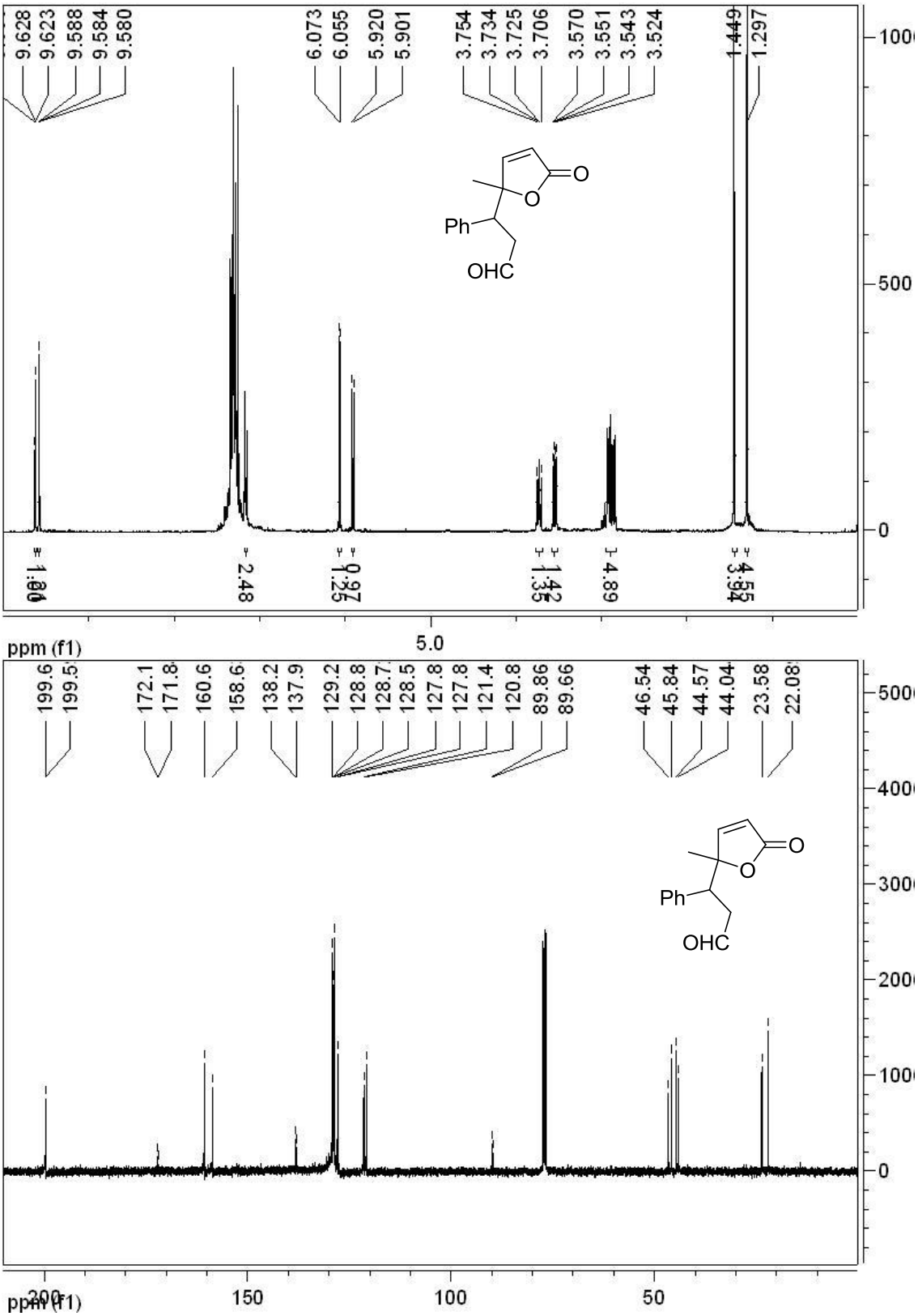


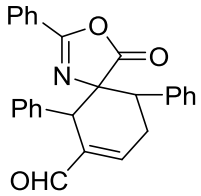
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.165	48608	3143	0.405	1.119
2	21.516	11954456	277665	99.595	98.881
Total		12003065	280808	100.000	100.000

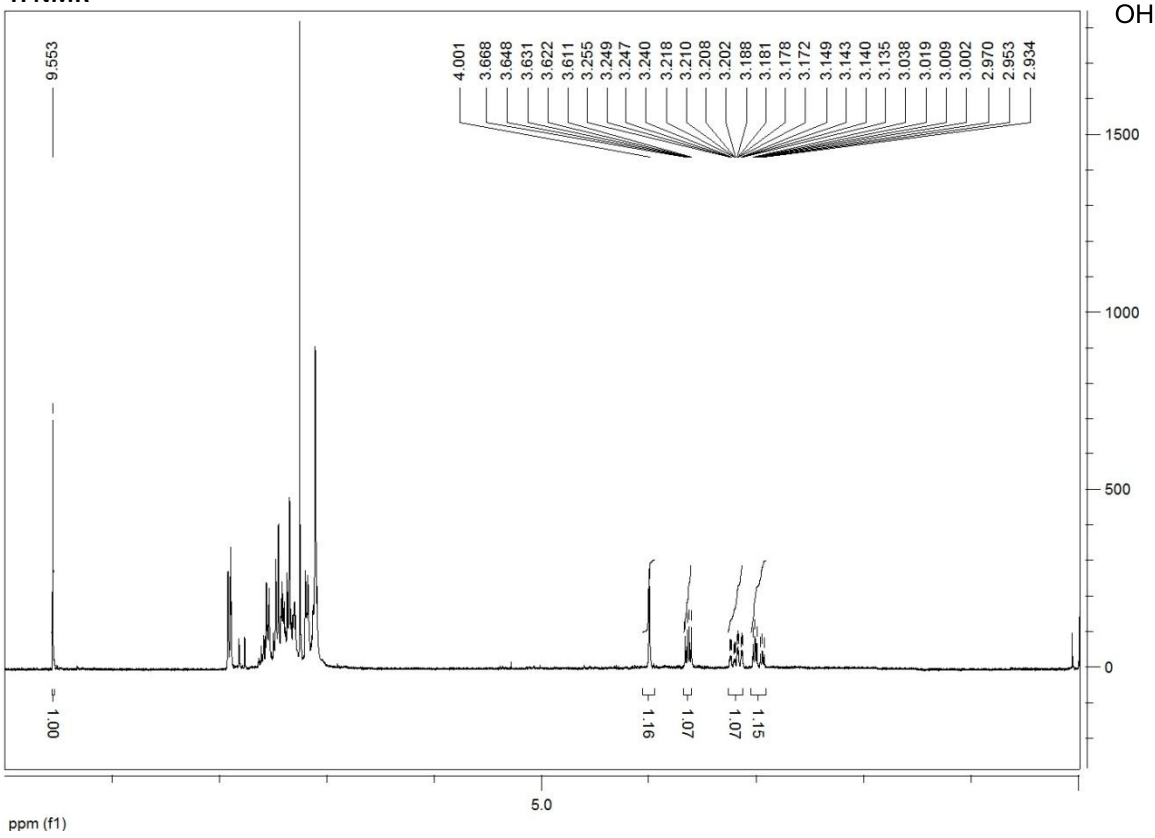
7a


9.628
9.623
9.588
9.584
9.580
6.073
6.055
5.920
5.901
3.754
3.734
3.725
3.706
3.570
3.551
3.543
3.524
1.449
1.297
O
O
Ph
OHC
1.80
2.48
0.92
1.25
1.42
1.33
4.89
3.94
4.55
ppm (f1)
5.0
199.6
199.5
172.1
171.8
160.6
158.6
138.2
137.9
129.2
128.8
128.7
128.5
127.8
127.8
121.4
120.8
89.86
89.66
46.54
45.84
44.57
44.04
23.58
22.08
O
O
Ph
OHC
ppm (f1)
150
100
50

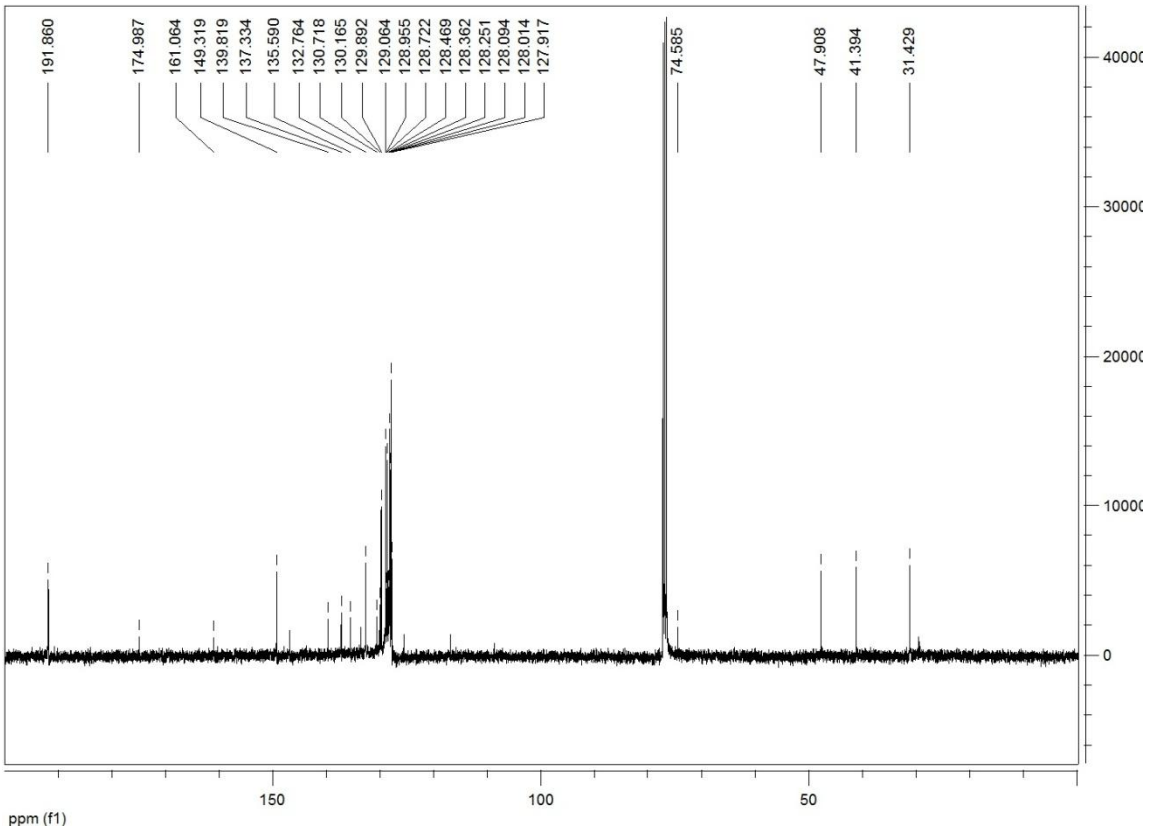


8a'

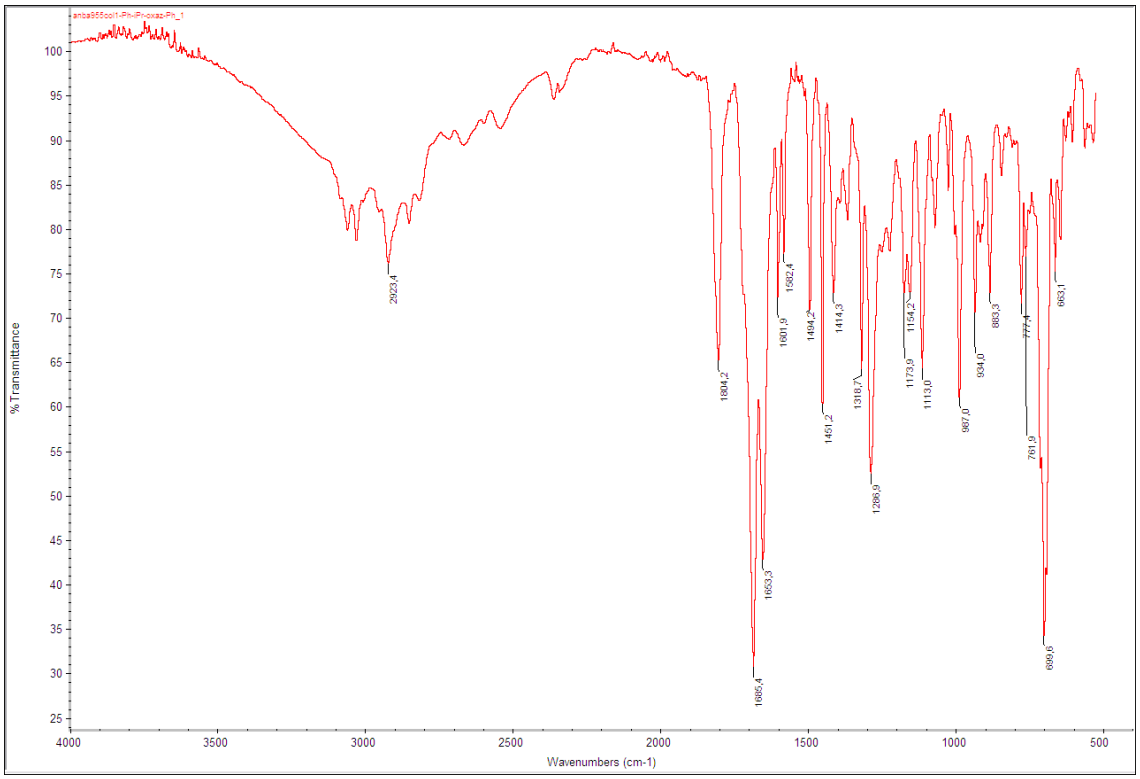
^{1}H NMR



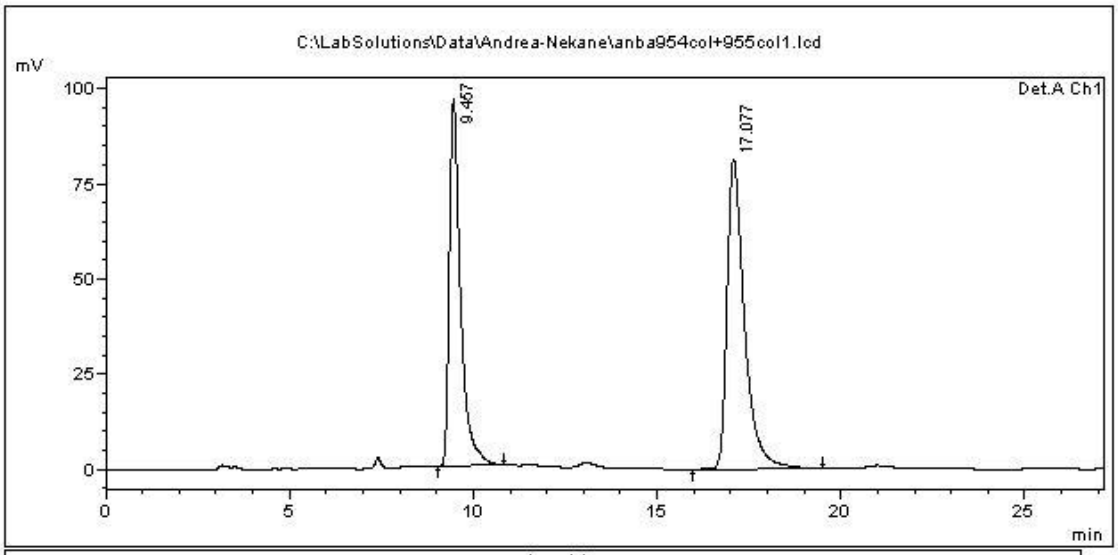
^{13}C NMR


191.860
174.987
161.064
149.319
139.819
137.334
135.590
132.764
130.718
130.165
129.892
129.064
128.955
128.722
128.469
128.362
128.251
128.094
128.014
127.917
74.585
47.908
41.394
31.429
40000
30000
20000
10000
0
150
100
50
ppm (f1)

IR


% Transmittance
Wavenumbers (cm-1)
4000
3500
3000
2500
2000
1500
1000
500
2923,4
1804,2
1685,4
1653,3
1601,9
1582,4
1494,2
1451,2
1414,3
1318,7
1286,9
1173,9
1154,2
1113,0
987,0
934,0
883,3
777,4
761,9
699,6
683,1

HPLC

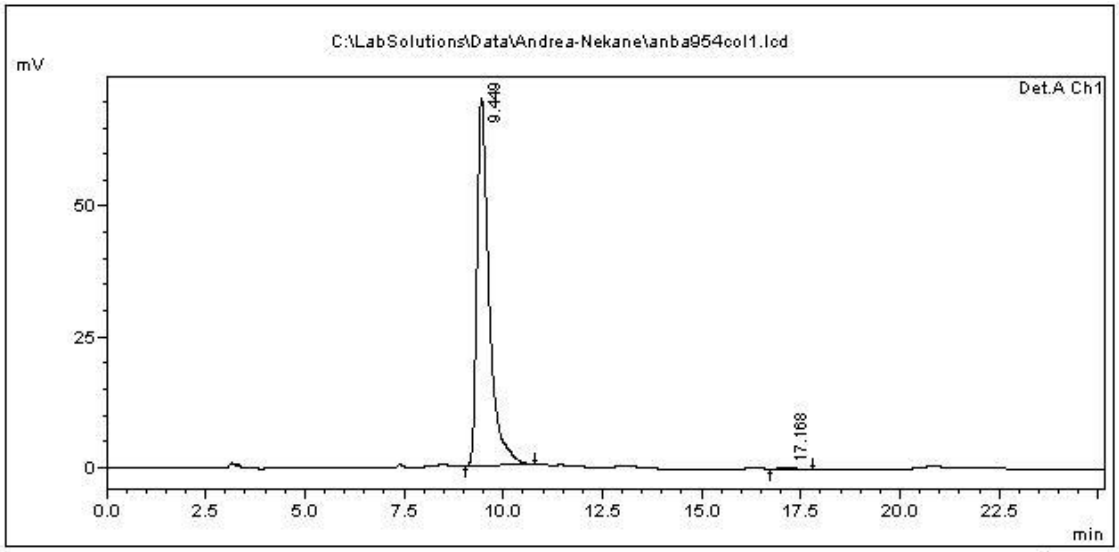


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	9.457	2059596	43.316
2	17.077	2695265	56.684
Total		4754862	100.000

(*S*)-Cat

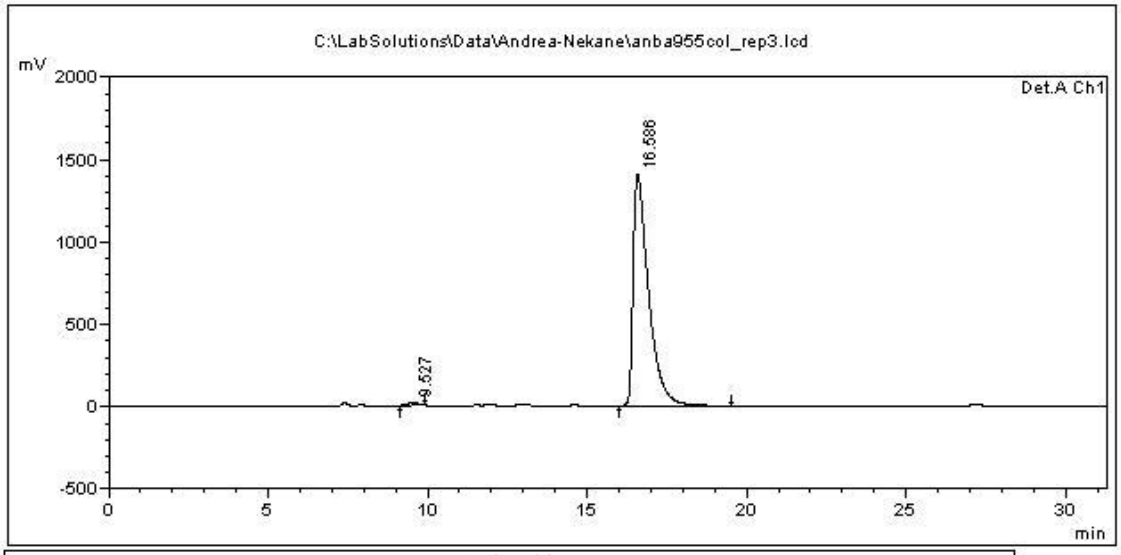


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	9.449	1497531	99.721
2	17.168	4193	0.279
Total		1501724	100.000

(*R*)-Cat



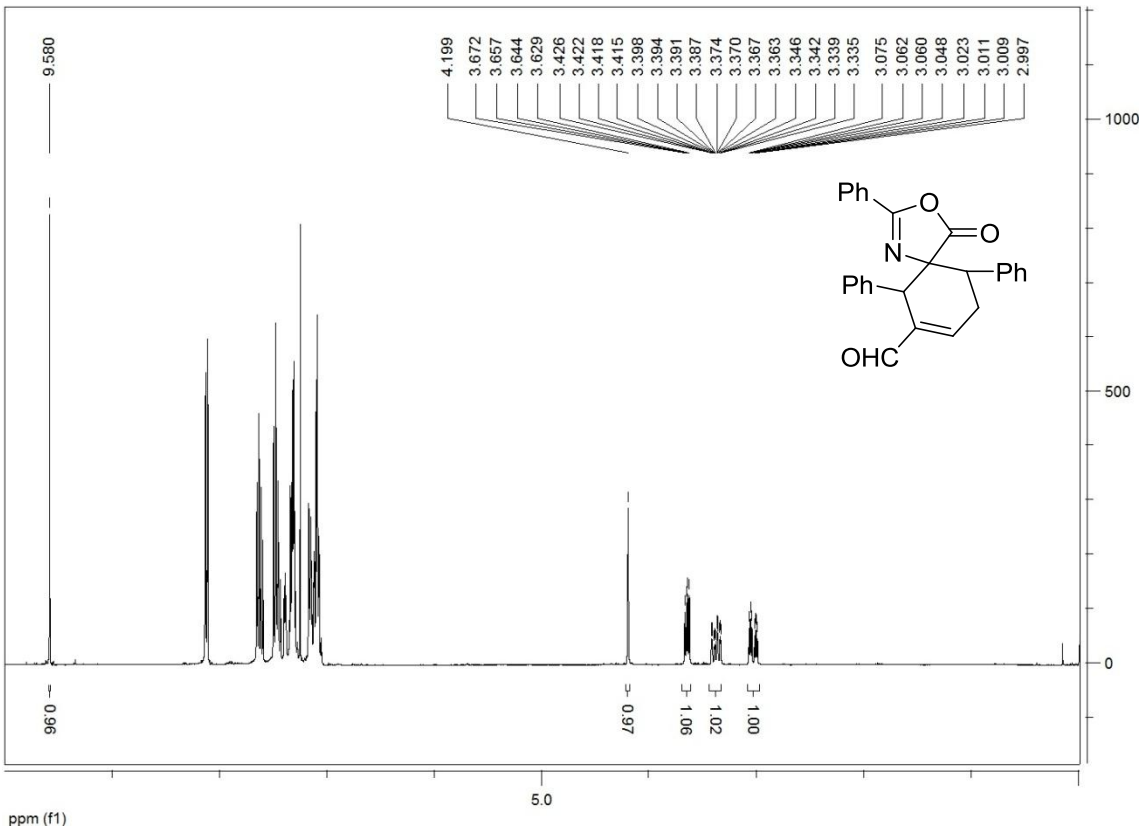
PeakTable

Detector A Ch1 254nm

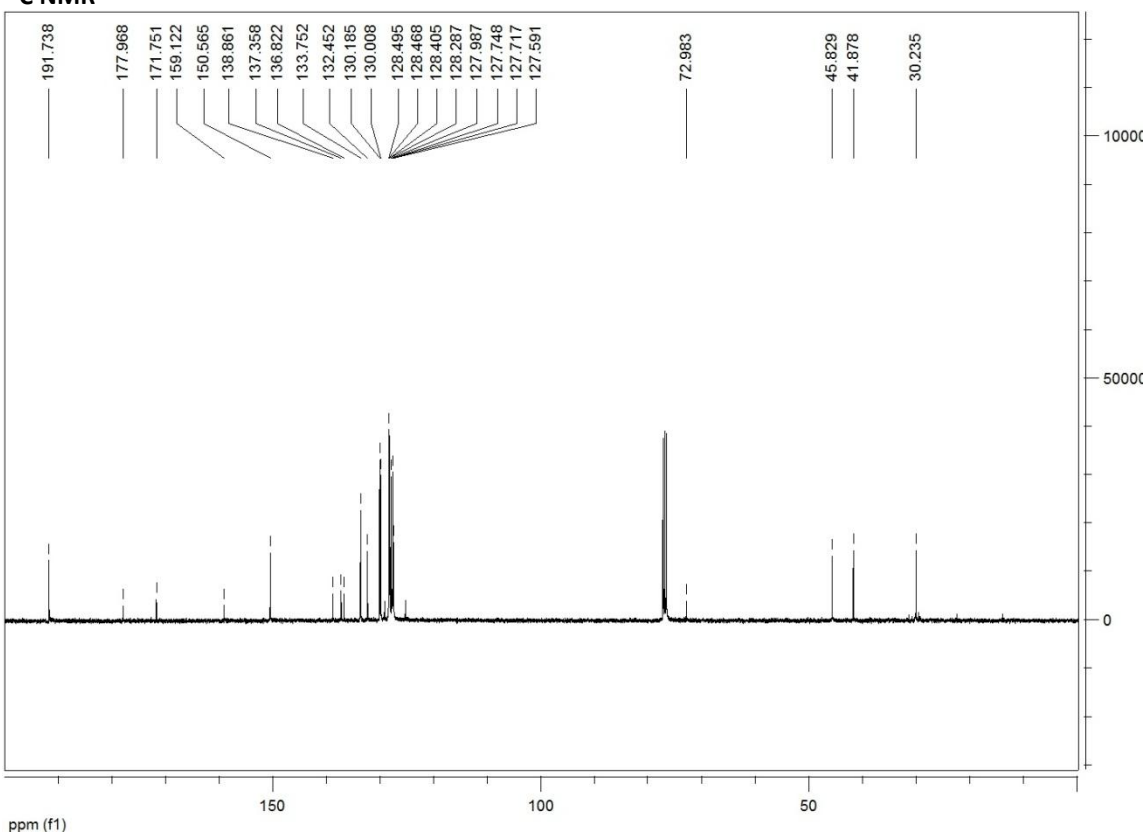
Peak#	Ret. Time	Area	Area %
1	9.527	386308	0.806
2	16.586	47526269	99.194
Total		47912577	100.000

8a

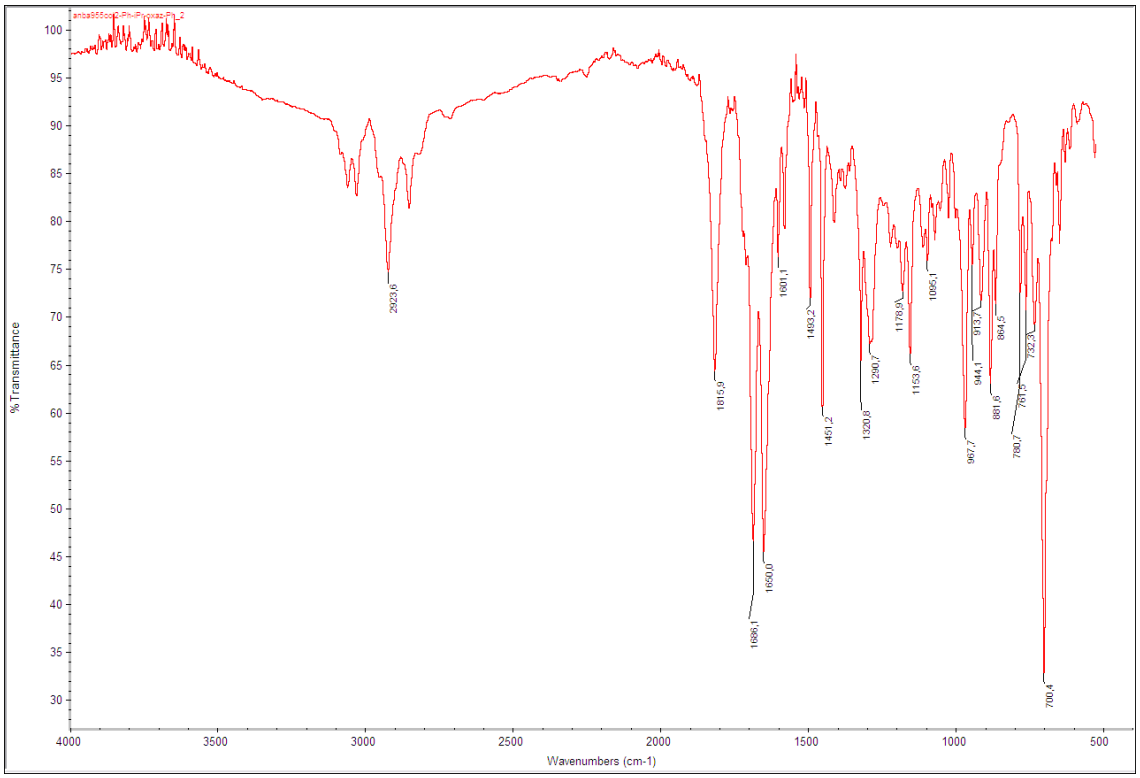
^{1}H NMR



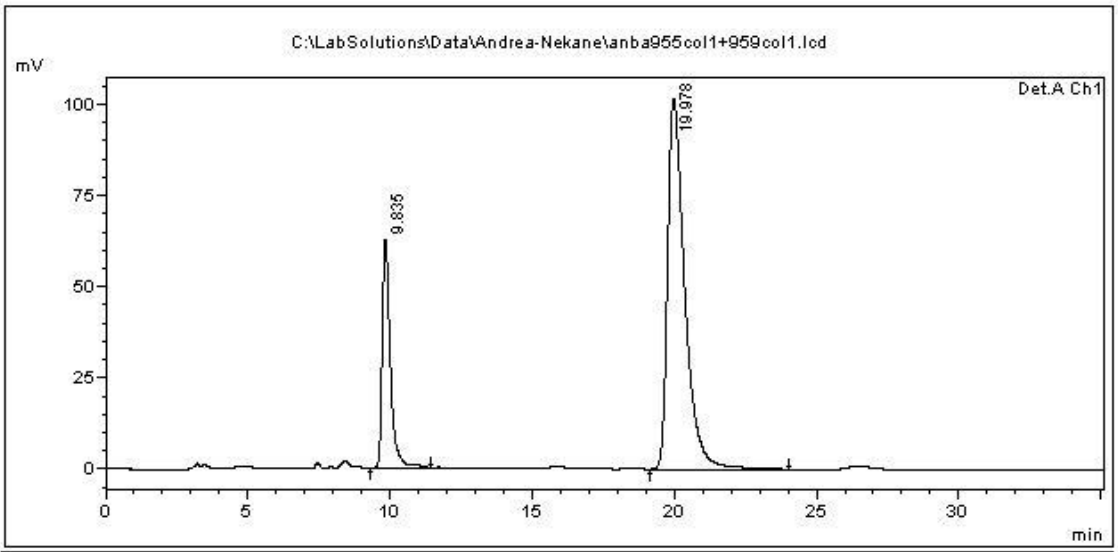
^{13}C NMR



IR



HPLC

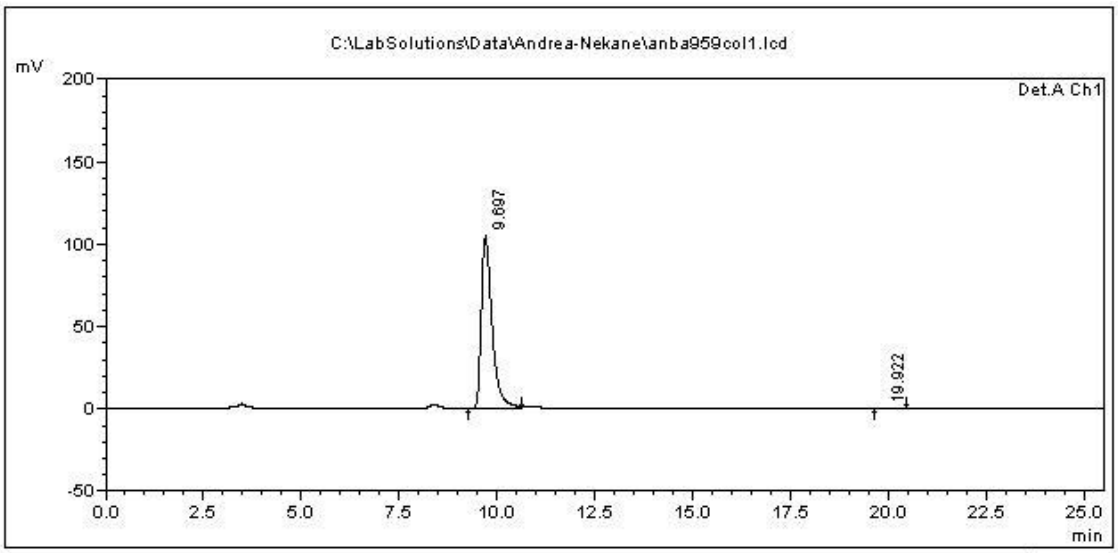


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.835	1258091	62832	22.869	38.242
2	19.978	4243267	101471	77.131	61.758
Total		5501358	164303	100.000	100.000

(*S*)-Cat.

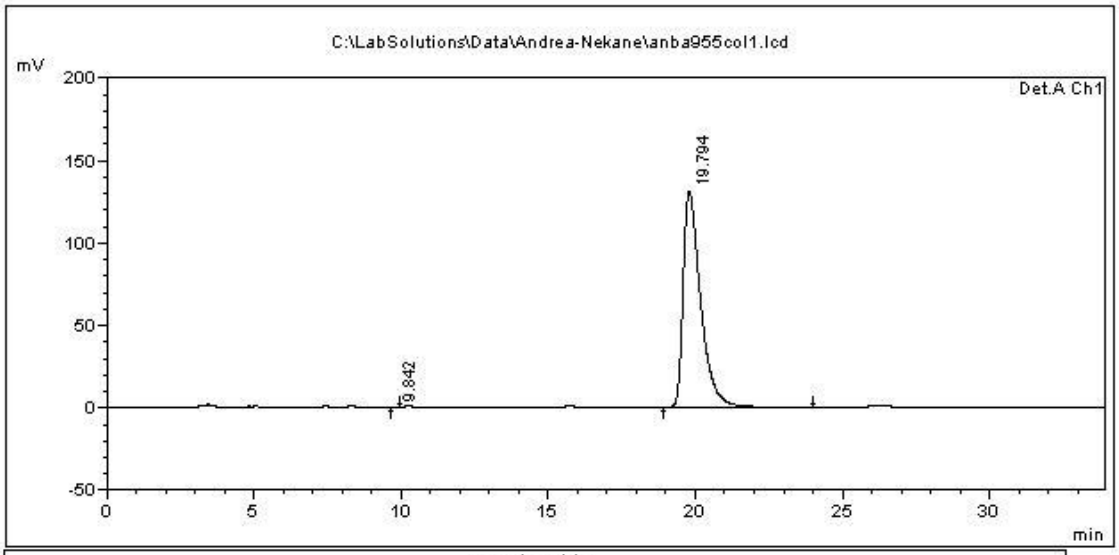


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	9.697	2032355	99.915
2	19.922	1721	0.085
Total		2034077	100.000

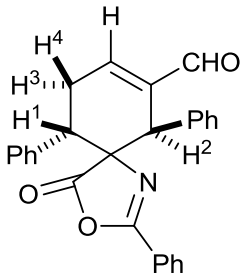
(*R*)-Cat.



PeakTable

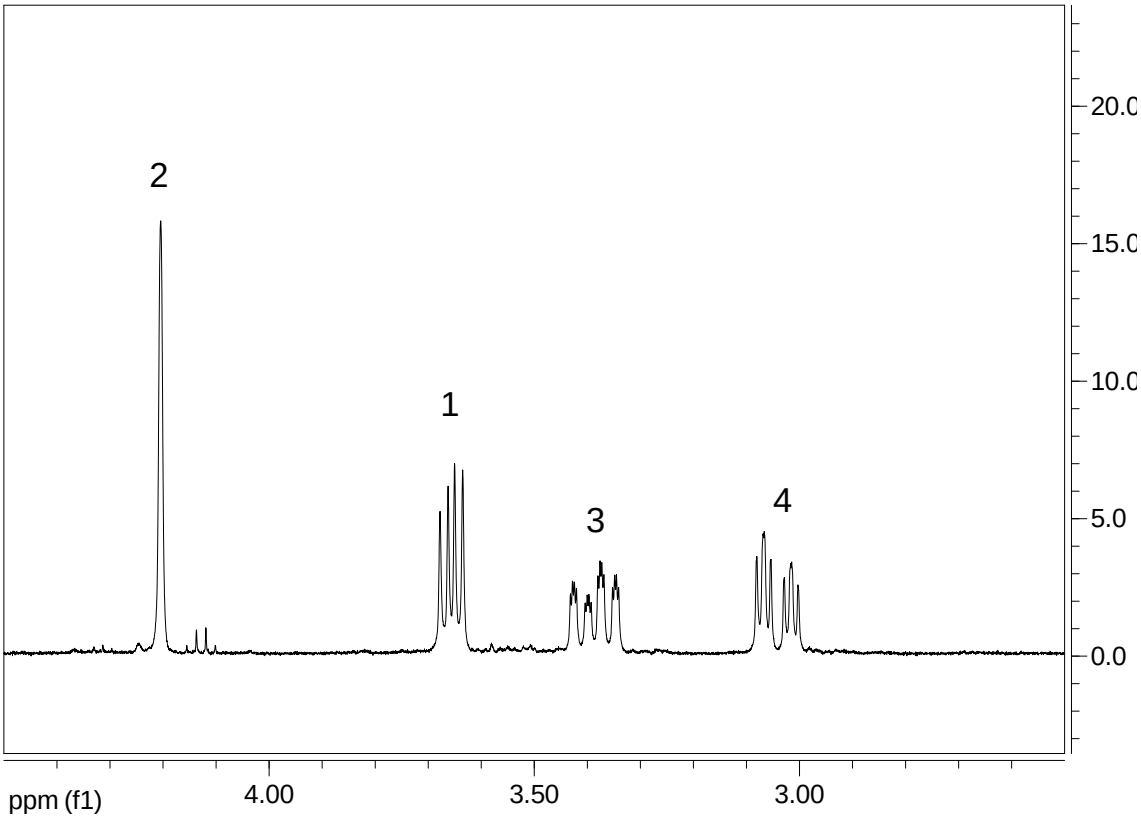
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	9.842	1116	0.020
2	19.794	5462410	99.980
Total		5463526	100.000

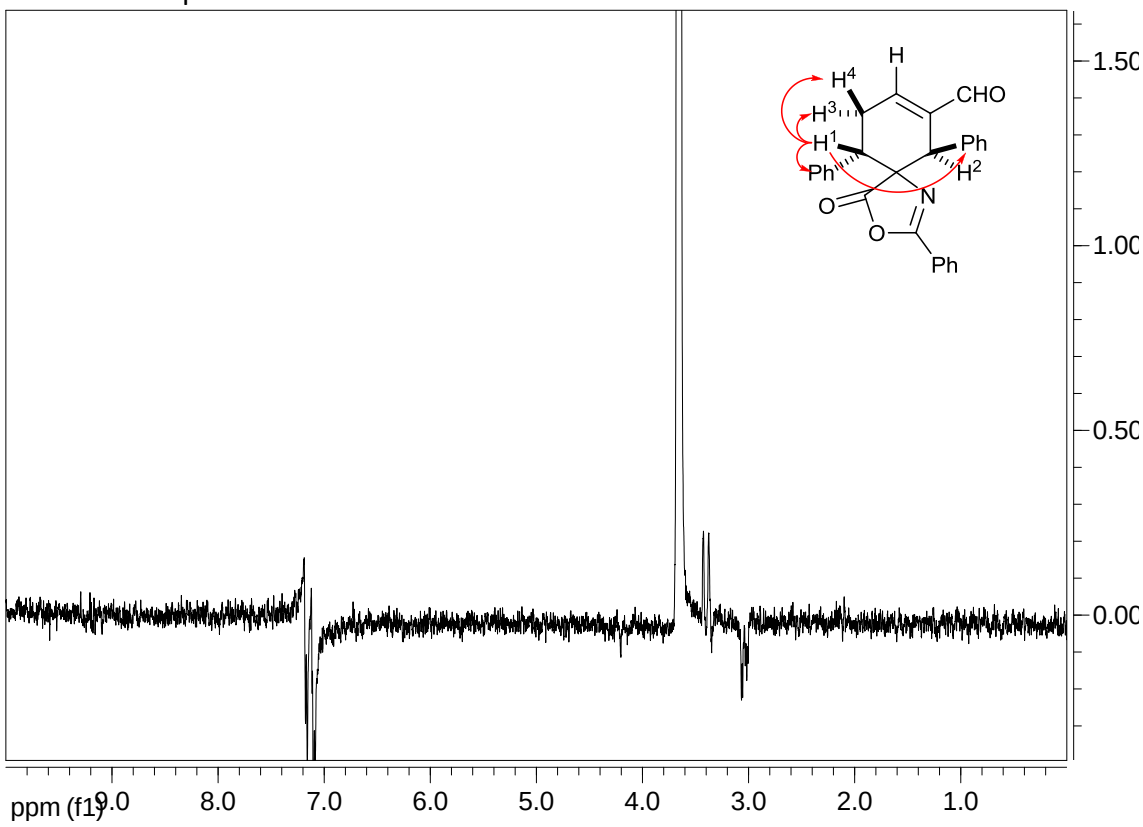


Compound **8a** (minor diastereomer):

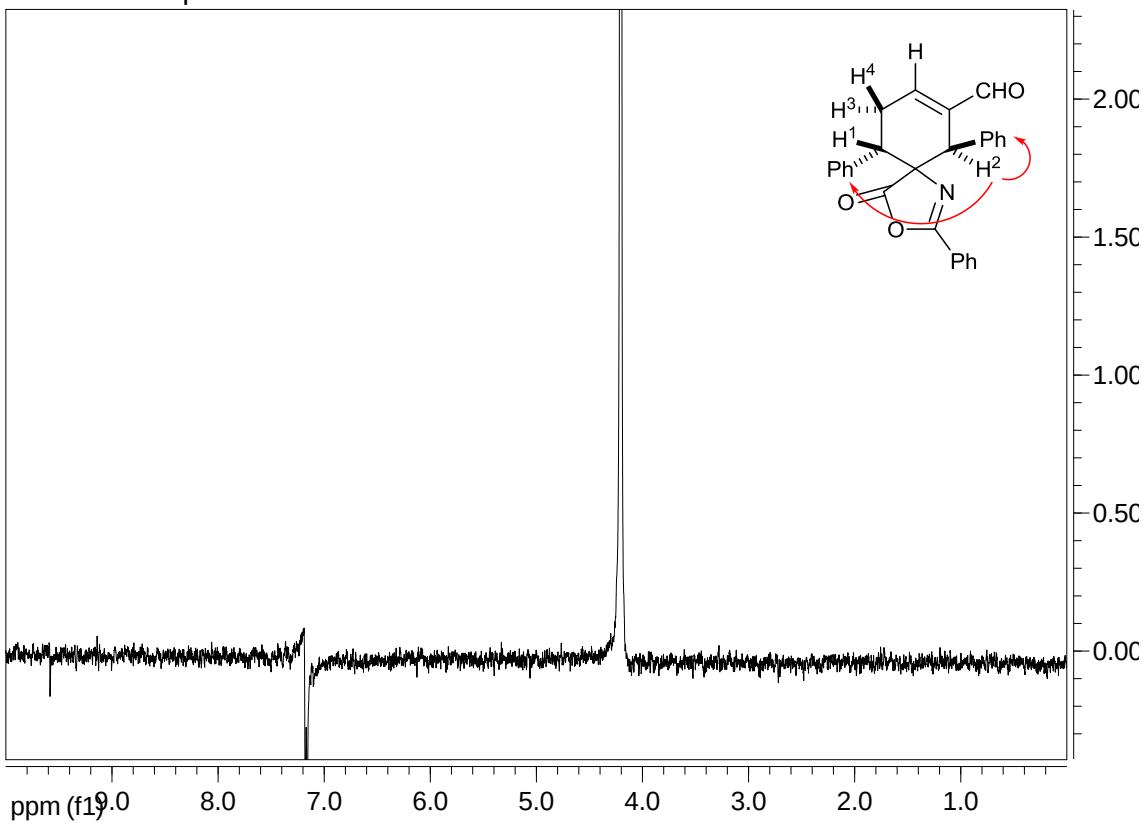
The *trans* relative stereochemistry between the two phenyl groups was readily secured by nOe experiments. Thus, irradiation of proton 1 (vide supra) leads to an enhancement of the intensities of the aromatic signals, and of those of protons 3 and 4. Irradiation of proton 2 leads only to an enhancement of the intensities of the aromatic signals. Irradiation of proton 3 leads to an enhancement of the intensities of both the olefinic hydrogen and of the aromatic protons.



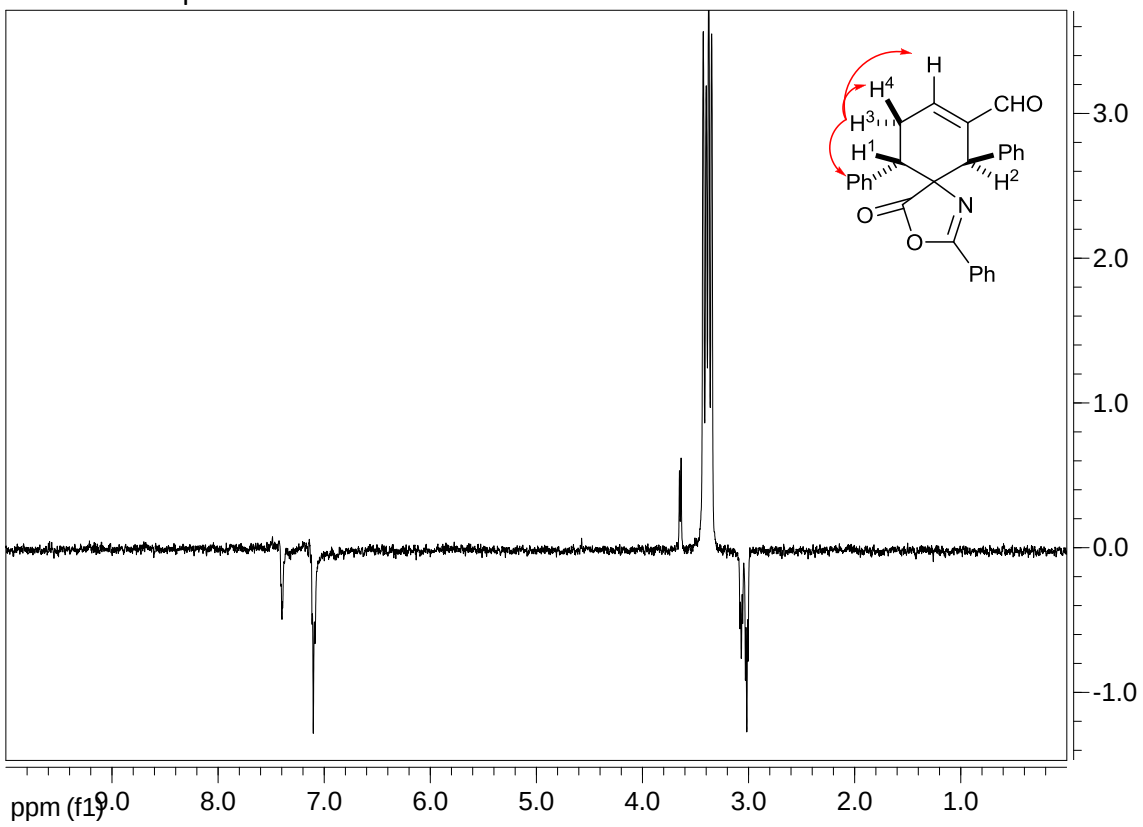
Irradiation of proton **1**:



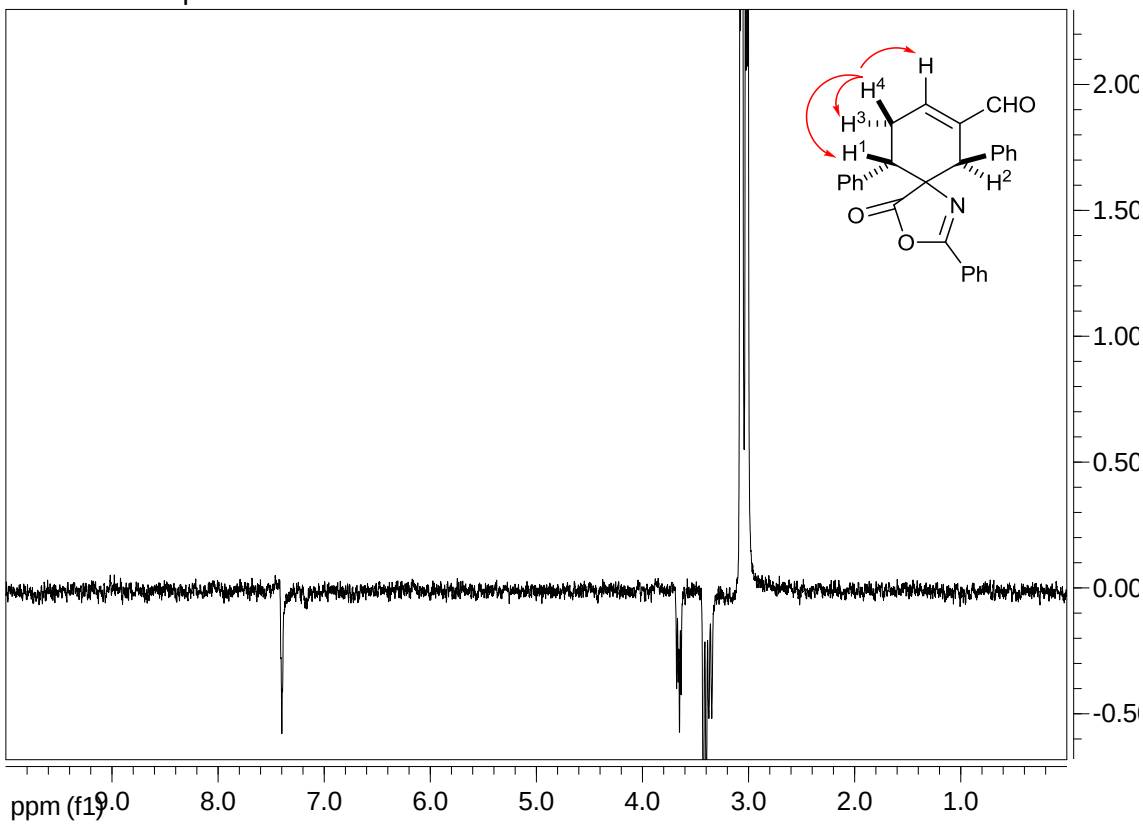
Irradiation of proton **2**:



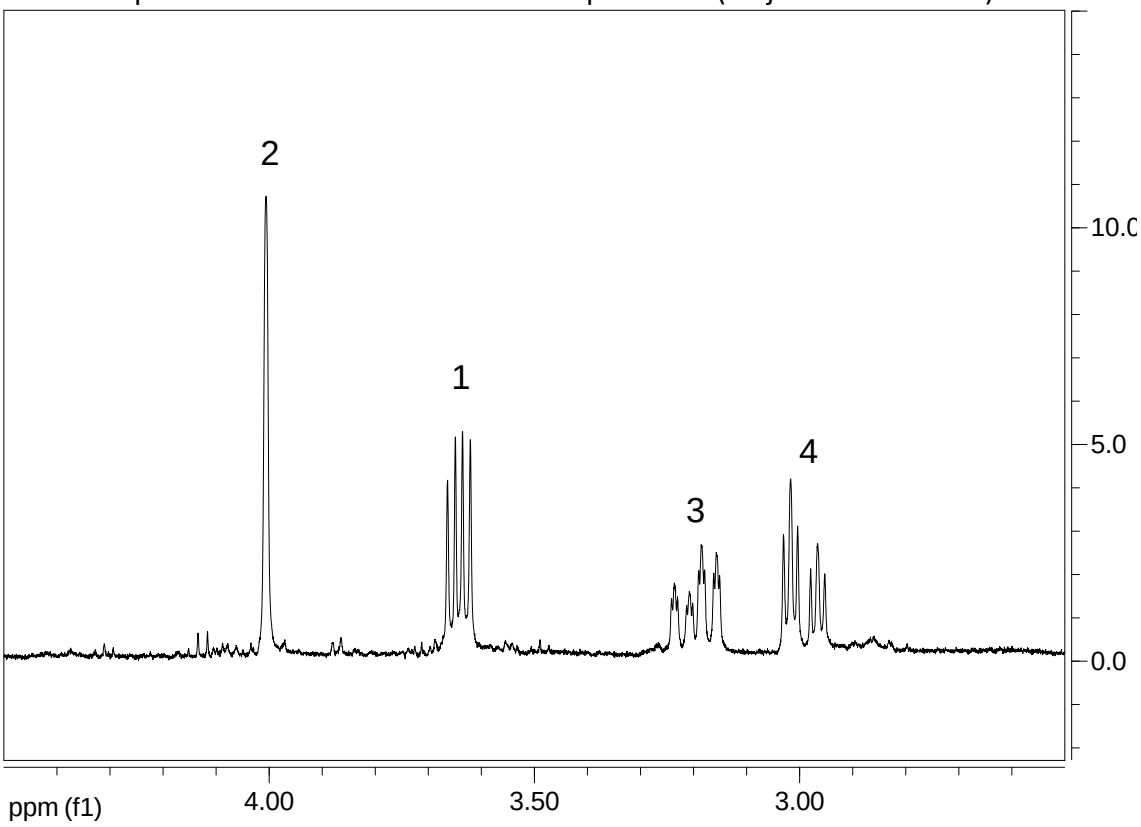
Irradiation of proton **3**:



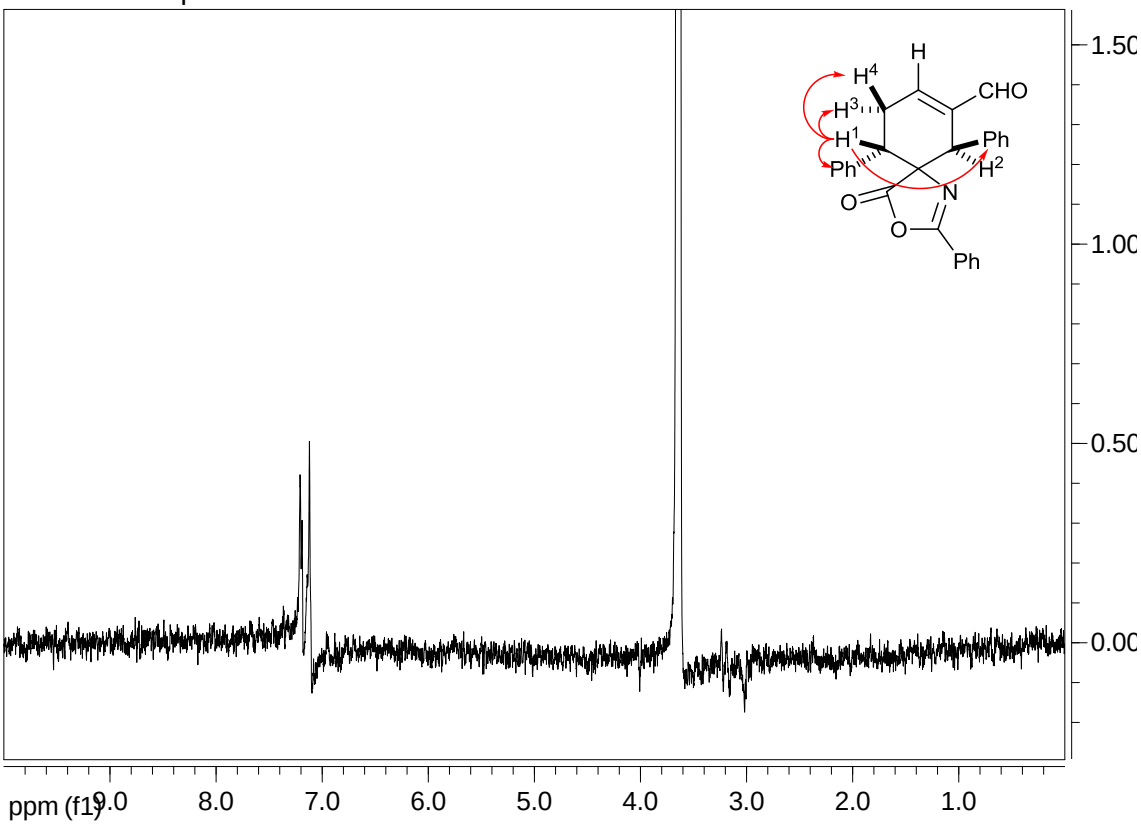
Irradiation of proton **4**:



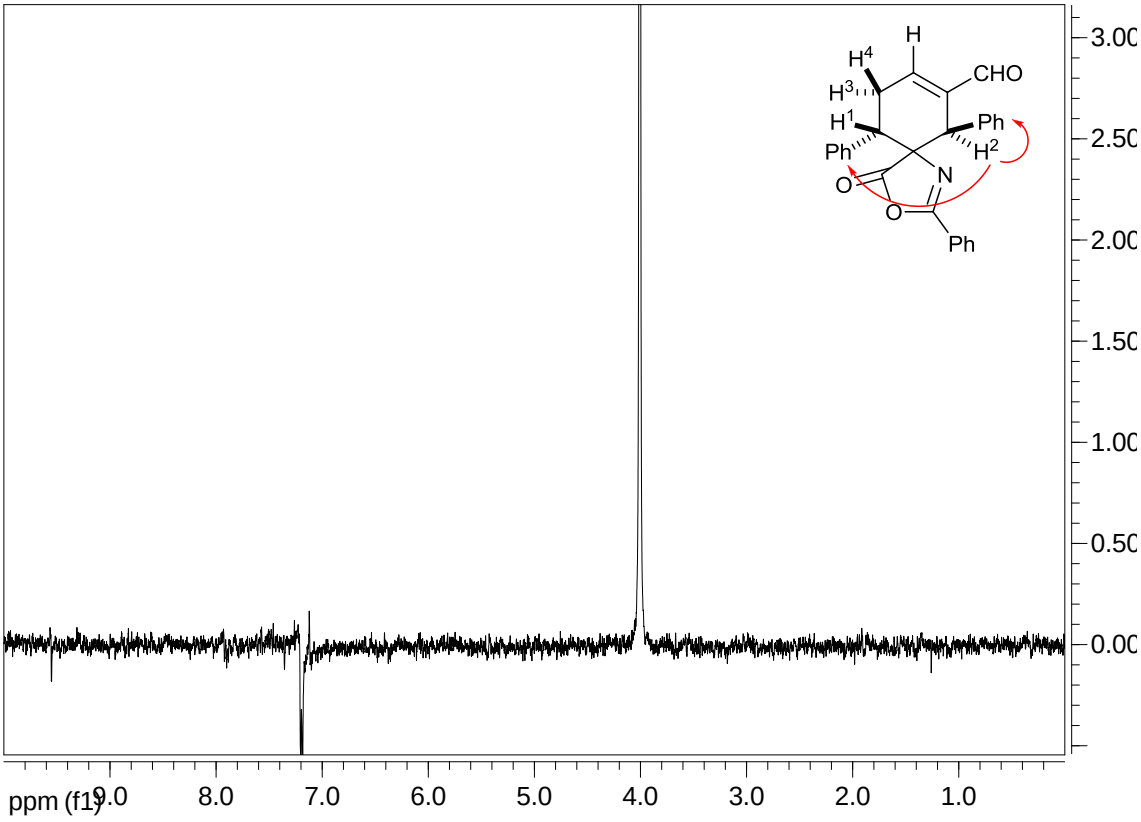
The same phenomena were observed in compound 8a (major diastereomer):



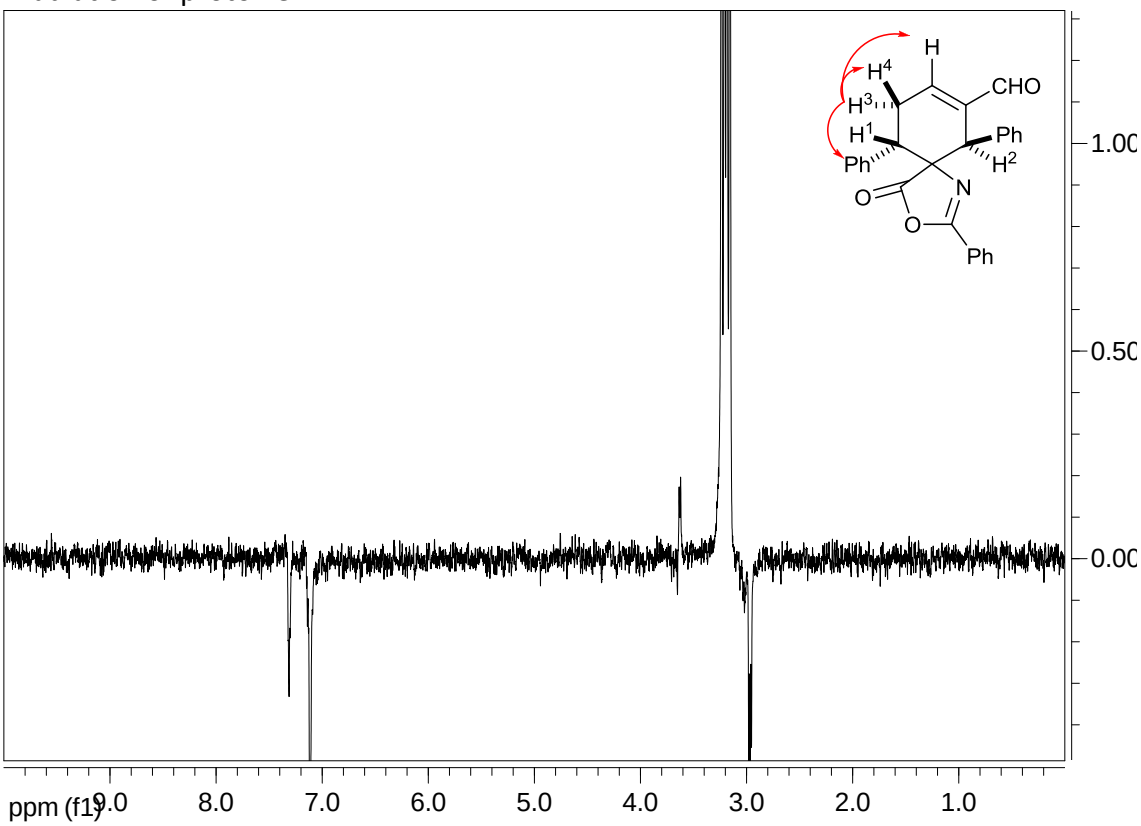
Irradiation of proton **1**:



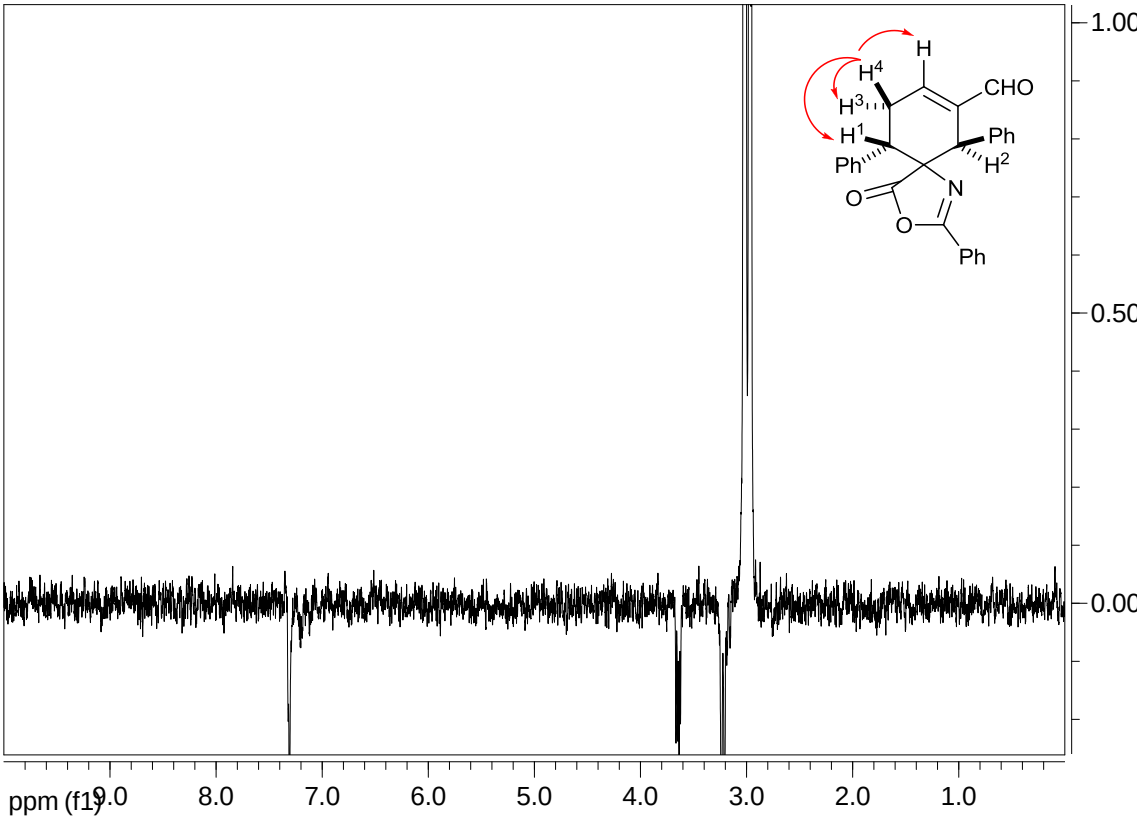
Irradiation of proton **2**:



Irradiation of proton **3**:

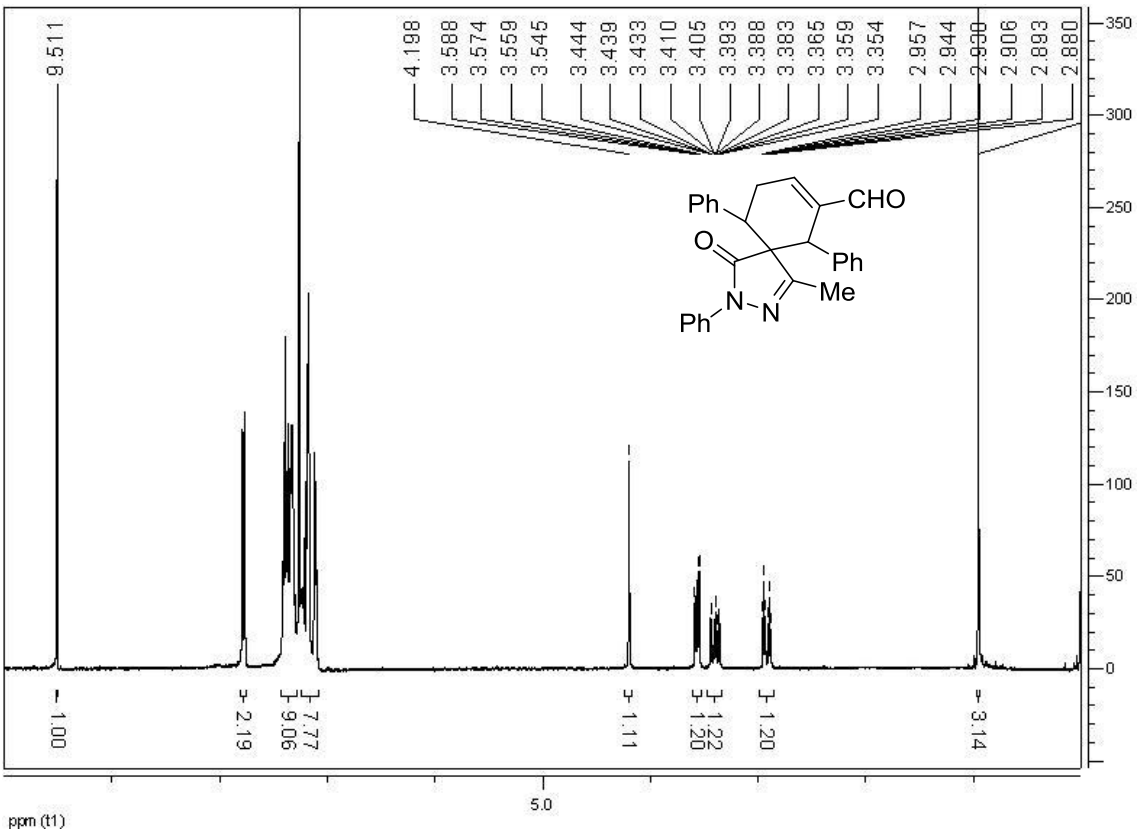


Irradiation of proton **4**:

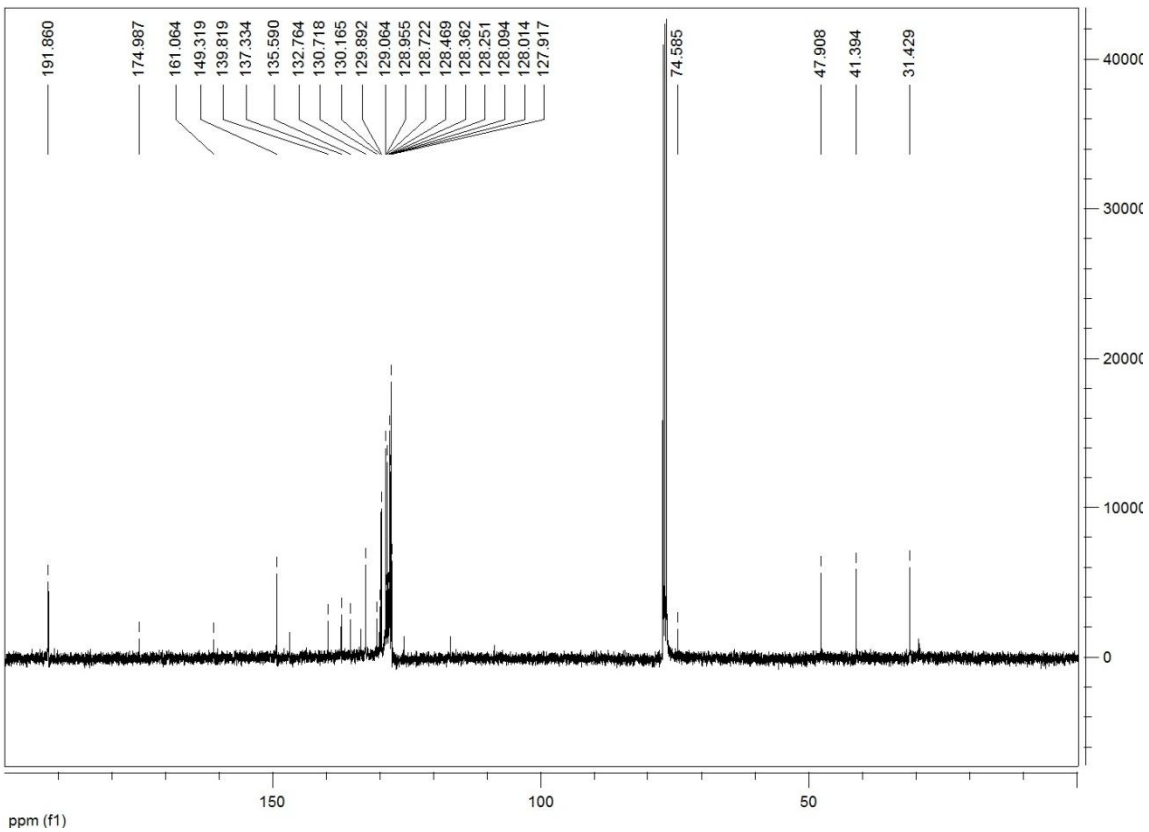


4a

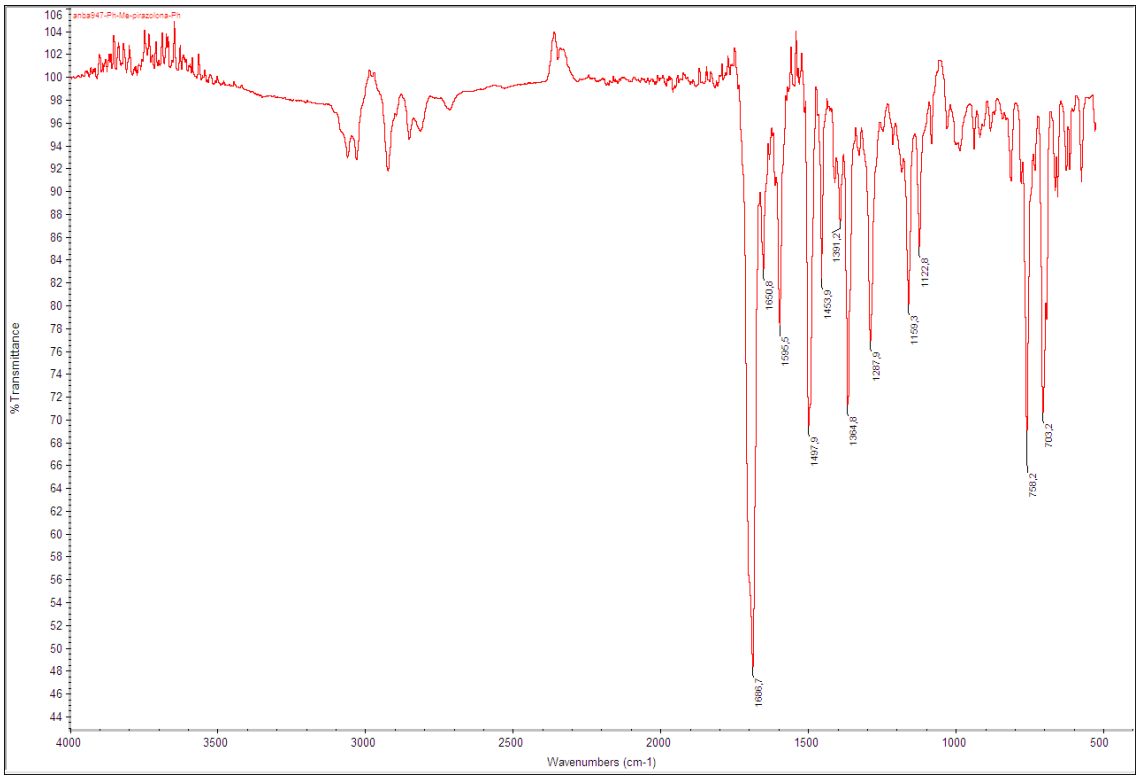
^{1}H NMR



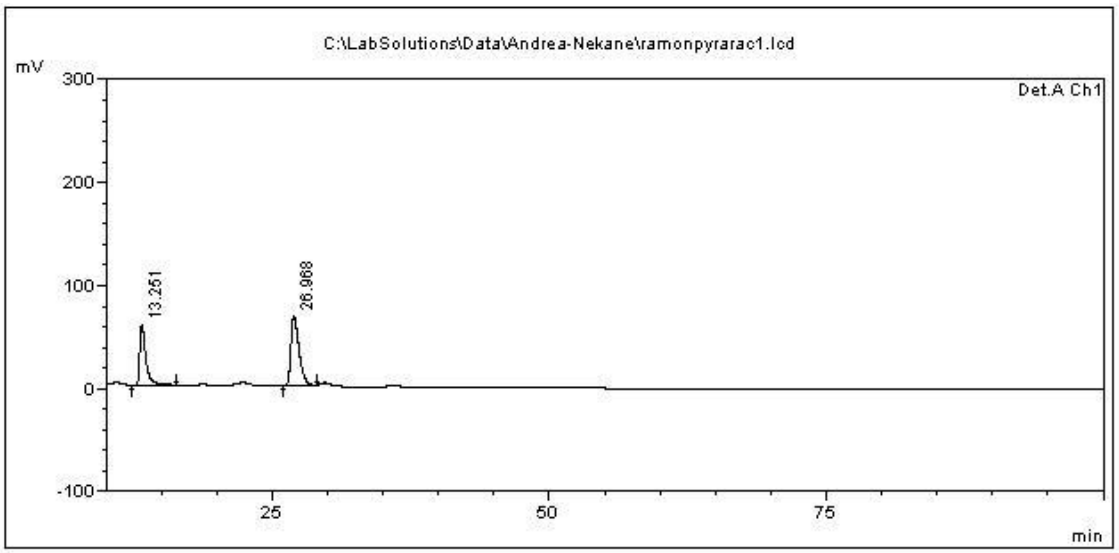
^{13}C NMR



IR



HPLC

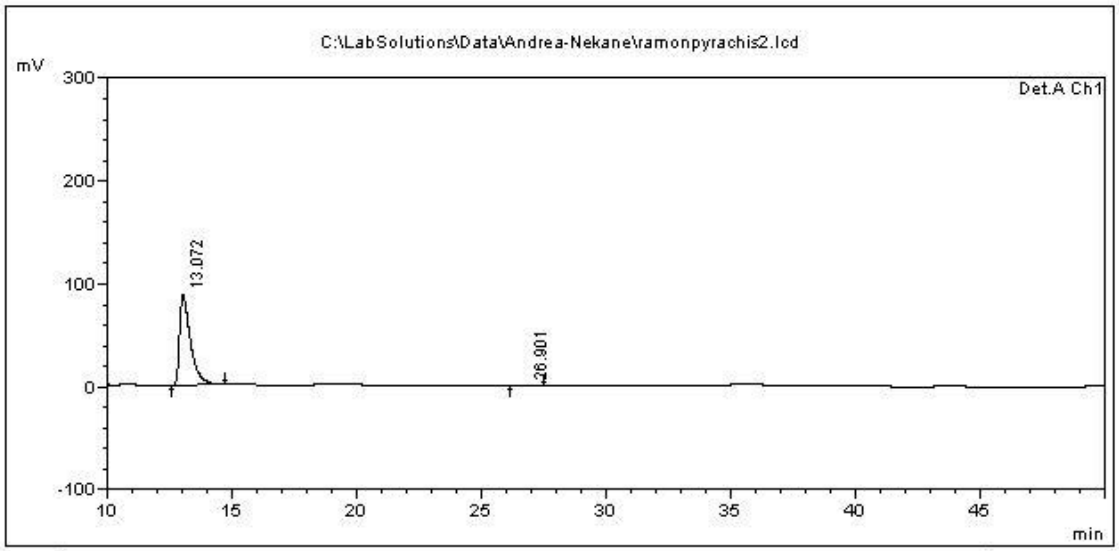


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.251	2270990	57966	39.606	46.027
2	26.968	3463012	67973	60.394	53.973
Total		5734002	125938	100.000	100.000

(*S*)-Cat.

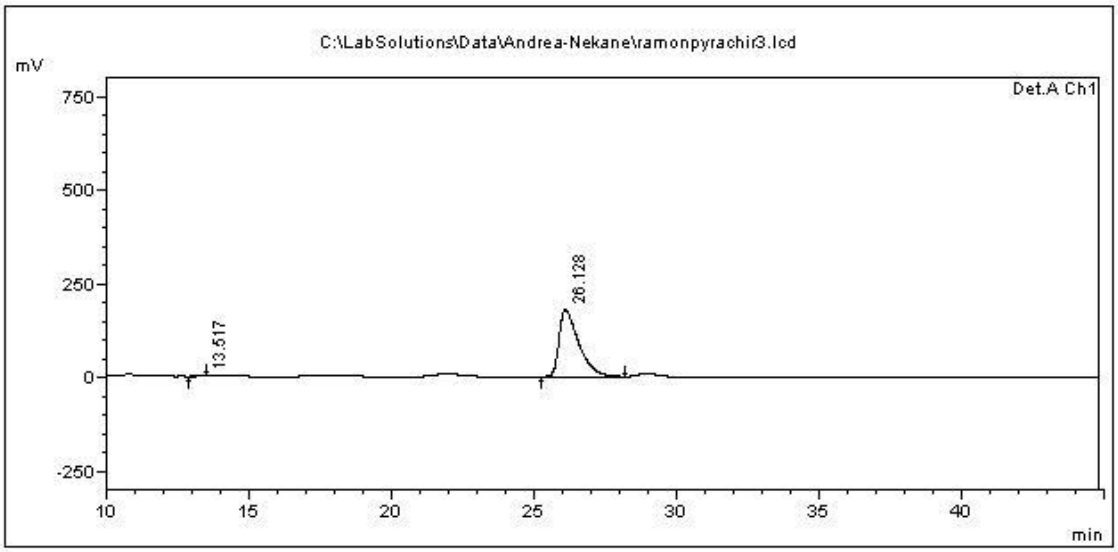


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	13.072	2664818	99.847
2	26.901	4070	0.153
Total		2668889	100.000

(*R*)-Cat.

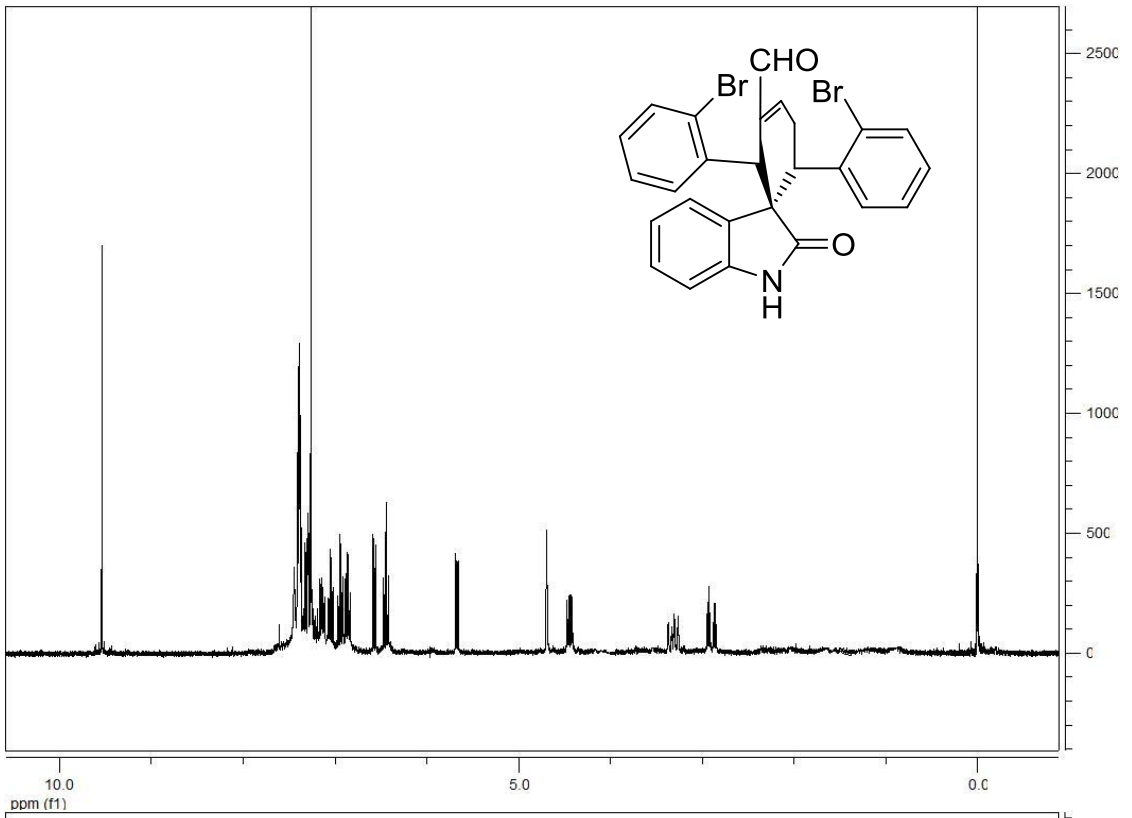


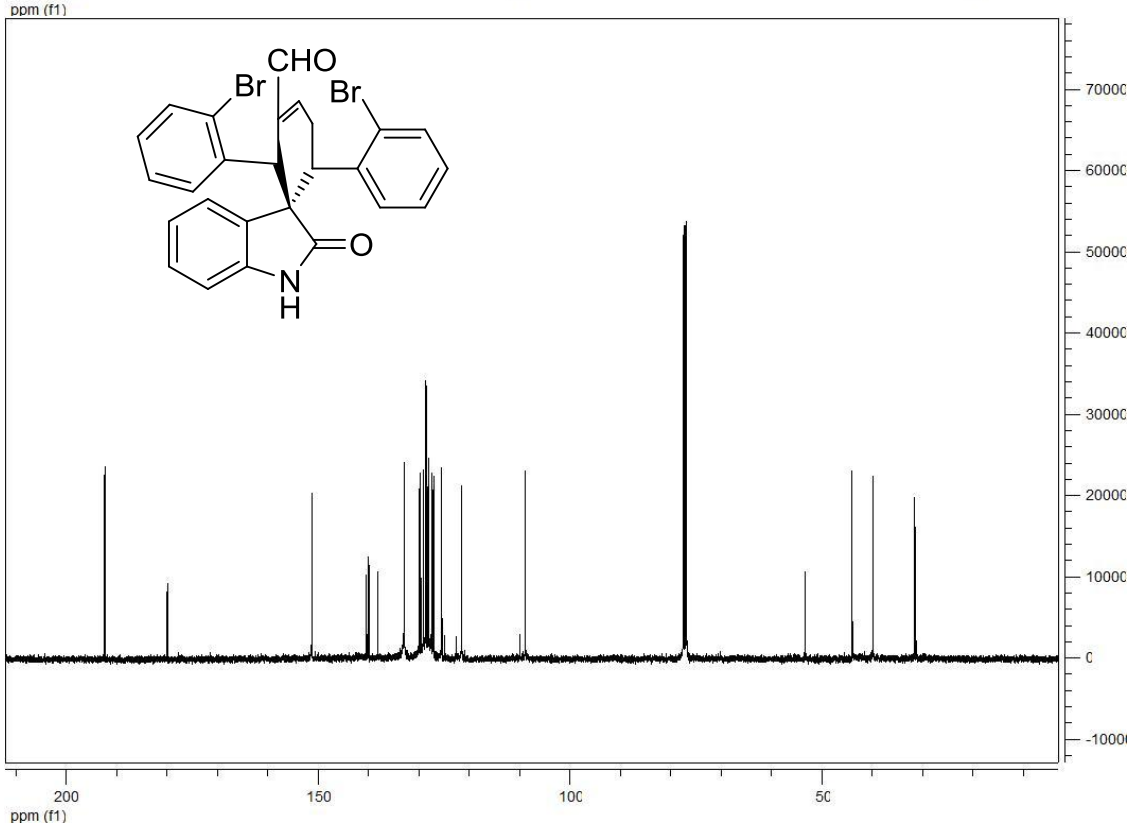
PeakTable

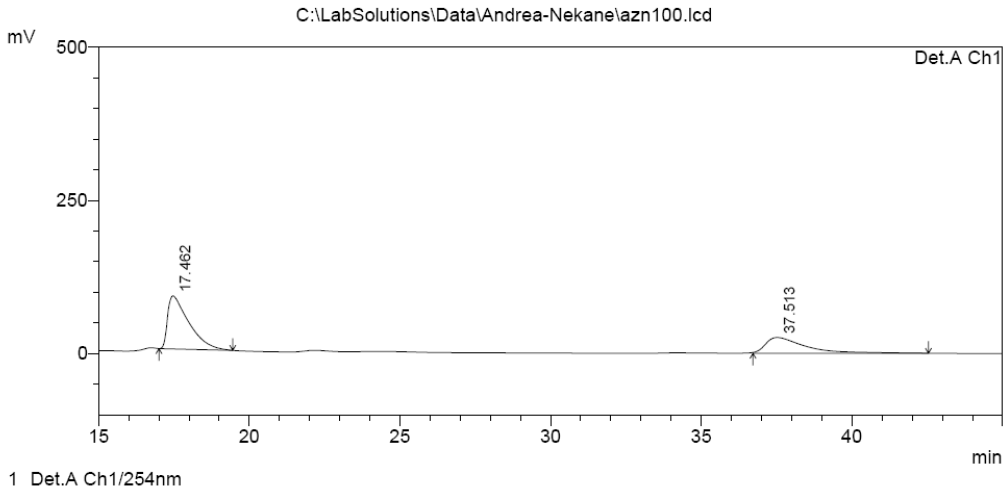
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	13.517	7962	0.093
2	26.128	8518875	99.907
Total		8526836	100.000

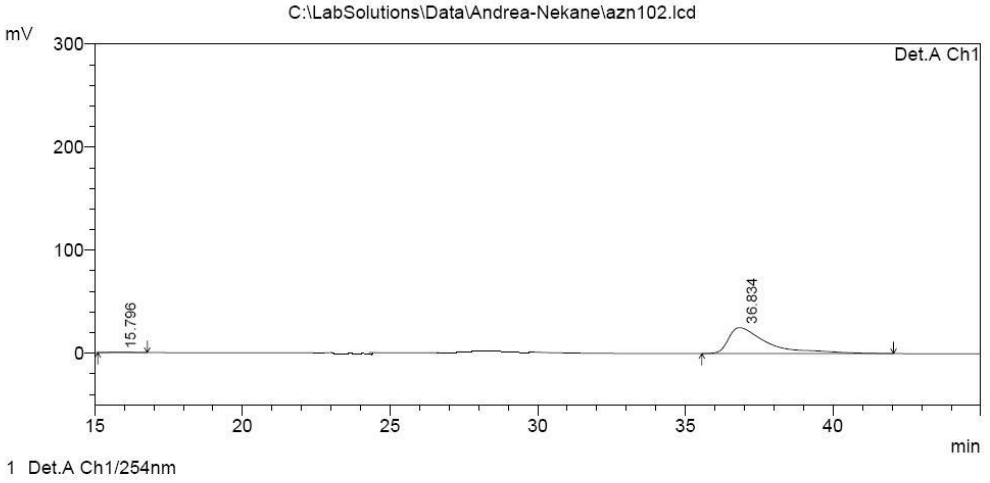
3f


CHO
Br
Br
O
N
H
2500
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)


CHO
Br
Br
O
N
H
70000
60000
50000
40000
30000
20000
10000
0
-10000
200
150
100
50
ppm (f1)



(*S*)-Catalyst

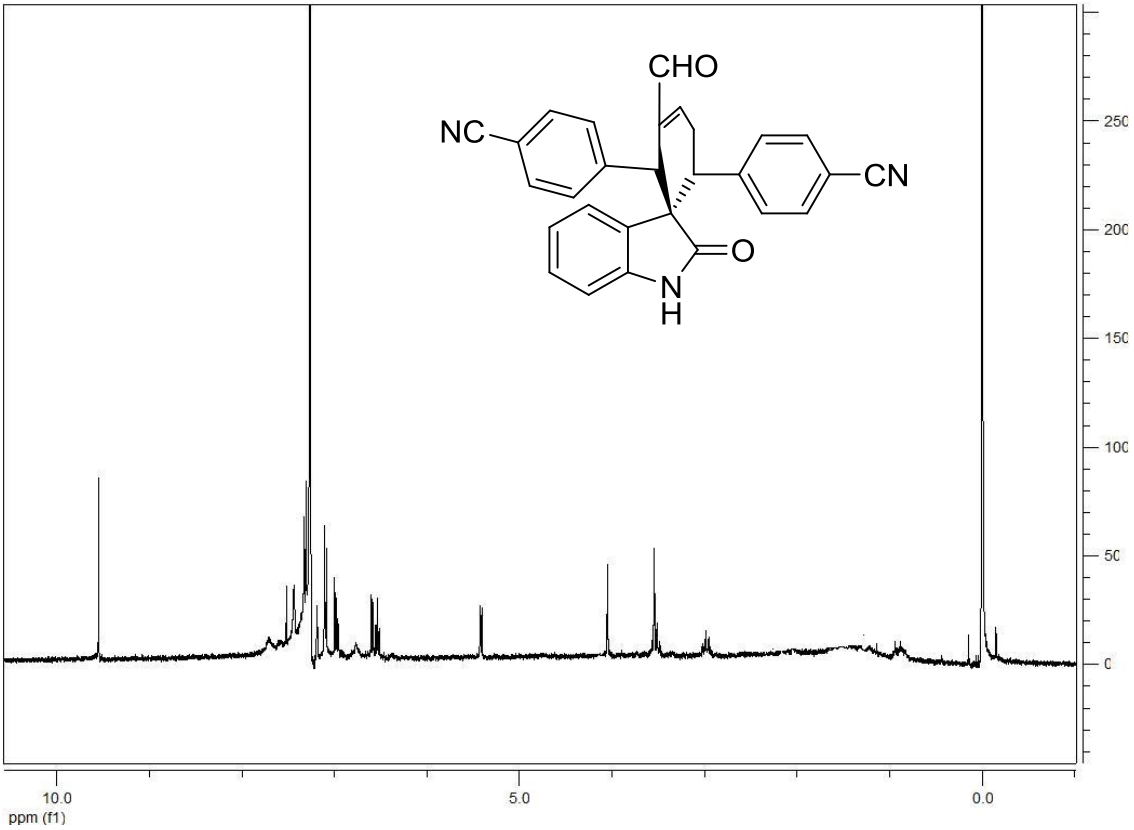


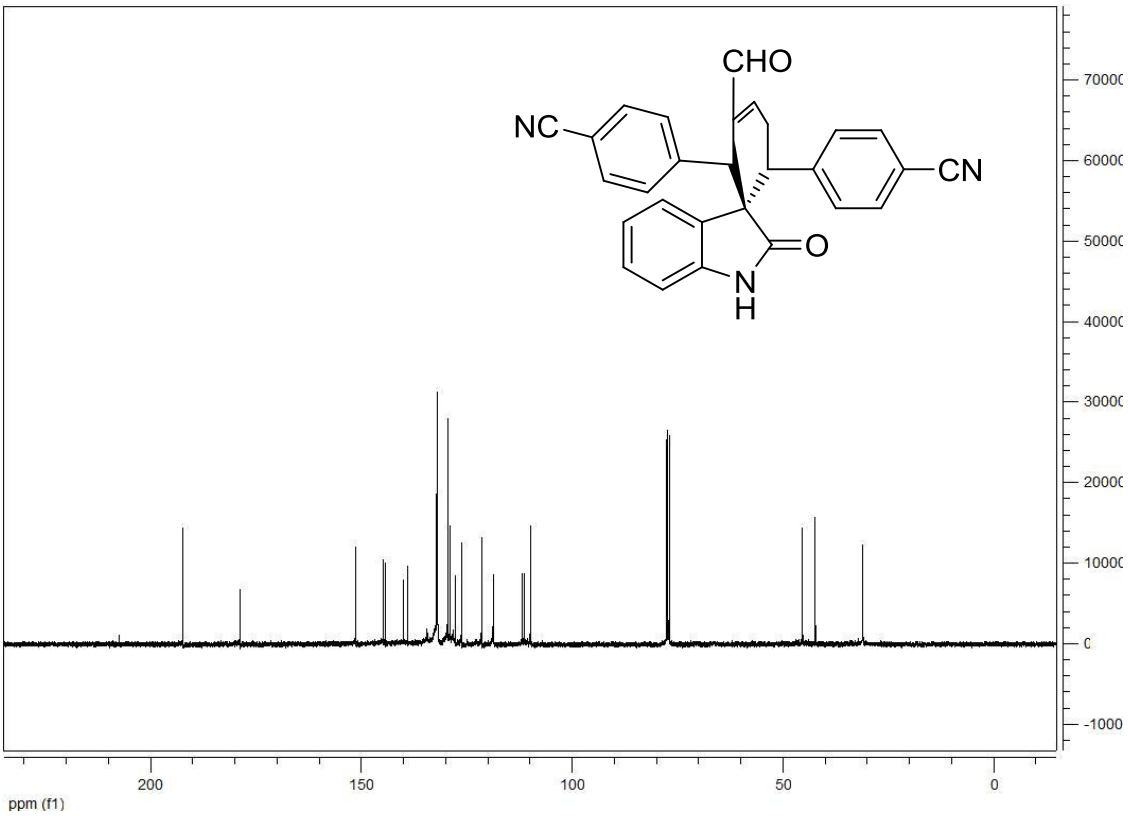
PeakTable

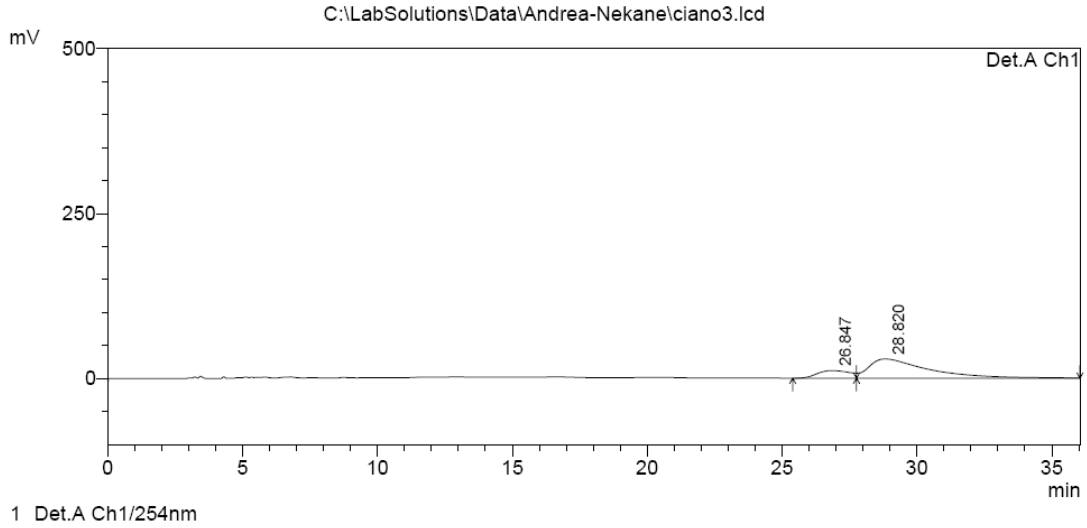
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.796	19510	289	0.838	1.135
2	36.834	2309058	25197	99.162	98.865
Total		2328568	25486	100.000	100.000

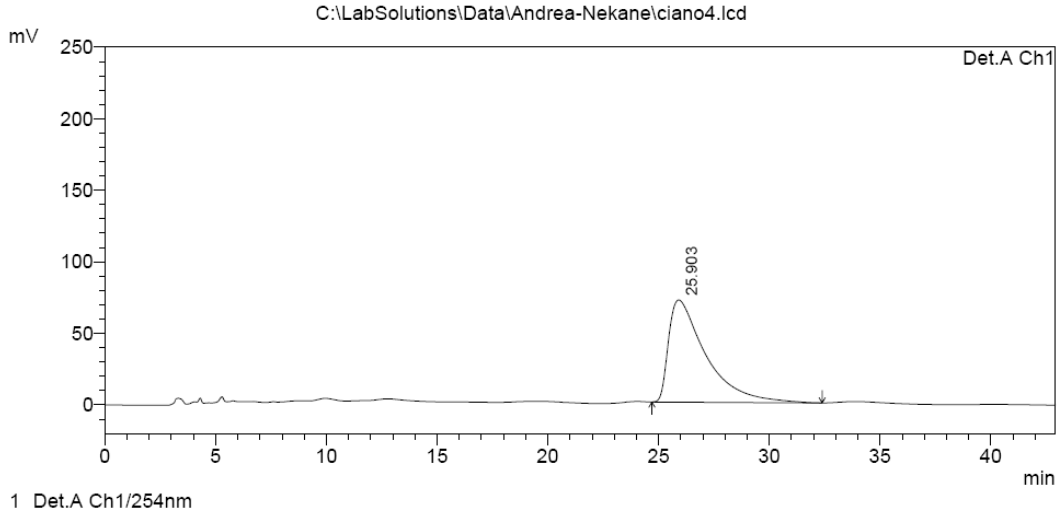
3e







(*S*)-Catalyst

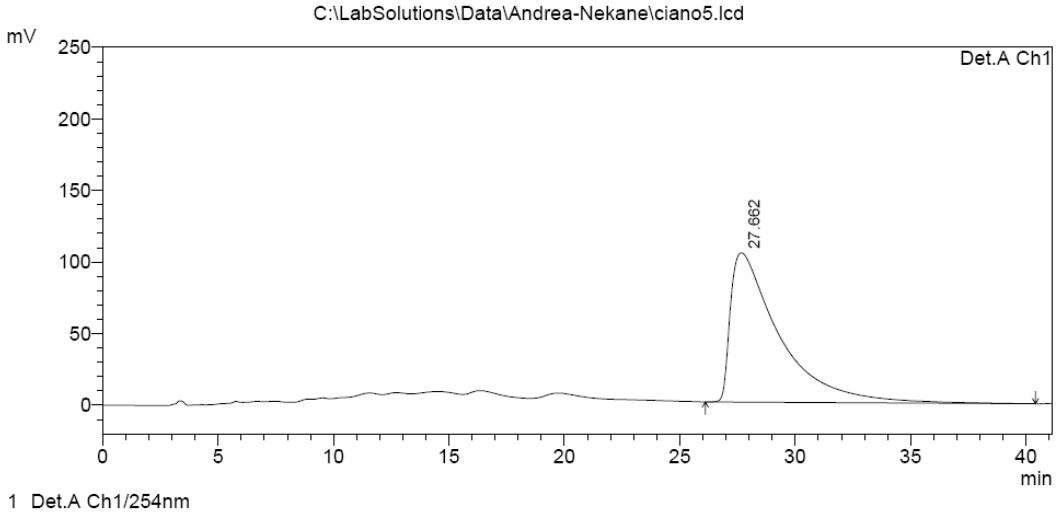


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.903	8367803	71449	100.000	100.000
Total		8367803	71449	100.000	100.000

(*R*)-Catalyst



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.662	15398153	104333	100.000	100.000
Total		15398153	104333	100.000	100.000

[i] For a review on the assignment of the absolute configurations of organic molecules by TD-DFT see: Bringmann, G.; Bruhn, T.; Maksimenka, K.; Hemberger, Y. *Eur. J. Org. Chem.* **2009**, 2717–2727, see also (a) Diedrich, C.; Grimme, S. *J. Phys. Chem. A* **2003**, *107*, 2524; (b) Casarini, D.; Lunazzi, L.; Mancinelli, M.; Mazzanti, A.; Rosini, C. *J. Org. Chem.* **2007**, *72*, 7667; (c) Goel, A.; Singh, F. V.; Kumar, V.; Reichert, M.; Goulder, T. A. M.; Bringmann, G. *J. Org. Chem.* **2007**, *72*, 7765. (d) Stephens, P. J.; Pan, J. J.; Devlin, F. J.; Cheeseman, J. R. *J. Nat. Prod.* **2008**, *71*, 285. (e) Gioia, C. Fini, F.; Mazzanti, A.; Bernardi, L.; Ricci, A. *J. Am. Chem. Soc.***2009**, *131*, 9614-9615. Bencivenni, G.; Wu, L.Y; Giannichi, B.; Mazzanti, A.; Pesciaioli, F.; Song, M-P.; Bartoli, G.; Melchiorre, P. *Angew. Chem. Int. Ed.* **2009**, *48*, 7200-7203.

[ii] Gaussian 03, Revision E.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A.; Gaussian, Inc., Wallingford CT, 2004.

[iii] Pescitelli, G.; Di pietro, S.; Cardellicchio, C.; Annunziata, M; capozzi, M.; Di Bari, L. *J.Org.Chem.* **2010**, *75*, 1143-1154

[iv] The use of a moderate basis set is dictated by the molecular size, and by the need of limiting the computational time (about 24-48 hours on a 8-core Xeon server)
[v] Stephens, P.J.; McCann, D.M.; Devlin, F.J., Cheeseman, J.R.; Frisch, M.J. *J.Am.Chem.Soc.* **2004**, *126*, 7514-7521
[vi] Gaussview 4.1.2, Semichem Inc., 2006