



Supporting Information

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## ***Supporting Information***

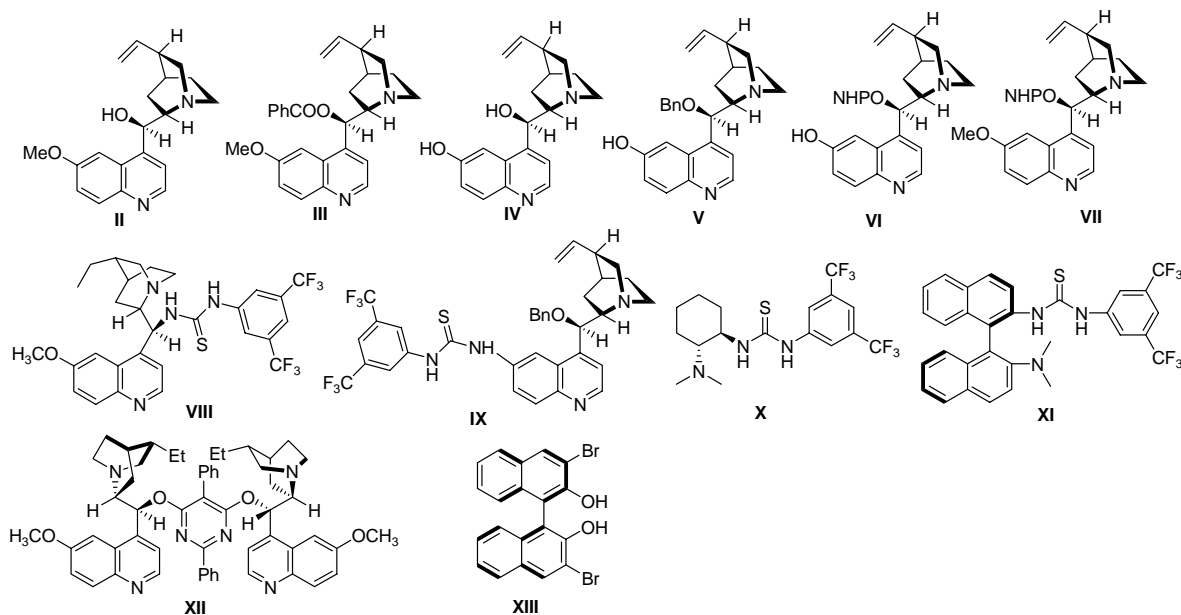
Hydrogen-bond Mediated Highly Stereoselective Cascade Michael-Michael Process via  
Dynamic Kinetic Resolution

*Jian Wang, Hexin Xie, Liansuo Zu, Hao Li, and Wei Wang\**

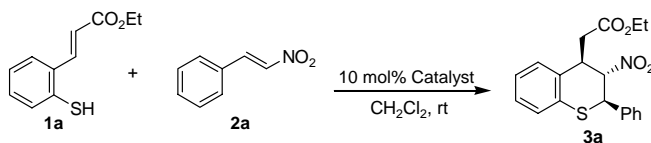
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**General Information:** Commercial reagents were used as received, unless otherwise stated. Merck 60 silica gel was used for chromatography, and Whatman silica gel plates with fluorescence F<sub>254</sub> indicator were used for thin-layer chromatography (TLC) analysis. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker Advance 500, and tetramethylsilane (TMS) was used as a reference. Data for <sup>1</sup>H are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet).

**Figure S1.** Structures of Other Organocatalysts Screened



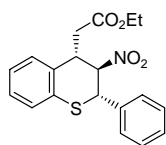
**Table S1:** Results of exploratory studies of asymmetric catalytic cascade Michael-Michael reaction of 3-(2-Mercapto-phenyl)-acrylic acid ethyl ester (**1a**) and *trans*- $\beta$ -nitrostyrene (**2a**).



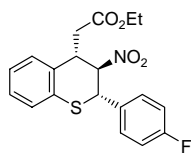
entry	catalyst	t (h)	% yield	% ee	dr
1	II	6	84	75	1:25
2 <sup>a</sup>	III	24	- <sup>b</sup>	-	-
3	IV	24	61	30	1:32
4	V	24	62	rac. <sup>c</sup>	1:17
5 <sup>a</sup>	VI	24	- <sup>b</sup>	-	-
6 <sup>a</sup>	VII	24	- <sup>b</sup>	-	-
7	VIII	2	91	87	16:1
8	IX	24	55	rac.	1:23
9	X	4	87	-83	17:1
10 <sup>a</sup>	XI	24	- <sup>b</sup>	-	-
11	XII	24	12	48	1:17
12 <sup>a</sup>	XIII	24	- <sup>b</sup>	-	-

<sup>a</sup> Reaction stopped at first step and did not generate Michael-Michael adducts. <sup>b</sup> No reaction. <sup>c</sup> Racemic mixture.

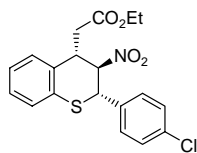
**Typical procedure for cascade Michael-Michael reaction:** A mixture of 3-(2-mercapto-phenyl)-acrylic acid ethyl ester **1a** (21 mg, 0.1 mmol), and *trans*- $\beta$ -nitrostyrene **2a** (15 mg, 0.1 mmol) and the catalyst **I** (3 mg, 0.002 mmol) in toluene (0.2 mL) was stirred at r.t. for 8 h. The crude product was purified by column chromatography on silica gel, eluted by hexane/EtOAc= 20:1 to afford 32 mg (90% yield) of the desired product as a clear oil.



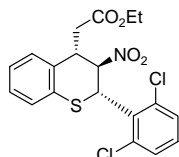
**(3-Nitro-2-phenyl-thiochroman-4-yl)-acetic acid ethyl ester (3a)** (Table 2, entry 1). The title compound was prepared according the typical procedure, as described above in 90% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.60-7.10 (m, 9H), 5.60 (dd, 1H,  $J$  = 10.5 Hz, 7.0 Hz), 4.58 (d, 1H,  $J$  = 10.5 Hz), 4.30-4.00 (m, 3H), 3.05 (dd, 1H,  $J$  = 17.0 Hz, 7.0 Hz), 2.76 (dd, 1H,  $J$  = 16.5 Hz, 5.0 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 170.3, 135.2, 135.0, 133.7, 129.1, 128.6, 128.0, 127.4, 126.5, 93.9, 61.0, 50.2, 42.0, 38.6, 14.0; HRMS (EI) calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_4\text{S}$  ( $\text{M} + \text{Na}^+$ ) 380.0932, found 380.0940; HPLC (Chiralcel OD-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 16.5 min,  $t_{\text{major}}$  = 14.7 min, ee = 97%, dr > 30:1;  $[\alpha]^{25}_{\text{D}}$  (major) = -88.6 ( $c$  = 0.9 in  $\text{CHCl}_3$ ).



**[2-(4-Fluoro-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3b)** (Table 2, entry 2). The title compound was prepared according the typical procedure, as described above in 92% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.40-7.31 (m, 2H), 7.30-7.15 (m, 4H), 7.10-7.00 (m, 2H), 5.57 (dd, 1H,  $J$  = 10.5 Hz, 7.0 Hz), 4.57 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 7.0 Hz), 3.05 (dd, 1H,  $J$  = 17.0 Hz, 6.5 Hz), 2.75 (dd, 1H,  $J$  = 17.0 Hz, 5.0 Hz), 1.20 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 170.3, 163.9, 162.0, 134.8, 133.4, 131.0, 129.8, 129.7, 128.5, 127.8, 127.5, 126.6, 116.3, 116.1, 93.9, 61.1, 49.4, 41.9, 38.4, 14.0; HRMS (EI) calcd for  $\text{C}_{19}\text{H}_{18}\text{FNO}_4\text{S}$  ( $\text{M} + \text{Na}^+$ ) 398.0938, found 398.0936; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 15.1 min,  $t_{\text{major}}$  = 16.9 min, ee = 97%, dr = 30:1;  $[\alpha]^{25}_{\text{D}}$  (major) = -73.4 ( $c$  = 1.5 in  $\text{CHCl}_3$ ).

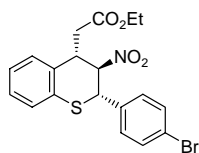


**[2-(4-Chloro-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3c)** (Table 2, entry 3). The title compound was prepared according the typical procedure, as described above in 99% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.41-7.10 (m, 8H), 5.57 (dd, 1H,  $J$  = 10.5 Hz, 7.5 Hz), 4.56 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.05 (dd, 1H,  $J$  = 16.5 Hz, 6.5 Hz), 2.75 (dd, 1H,  $J$  = 17.0 Hz, 5.0 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 170.3, 135.1, 134.8, 133.8, 133.2, 129.4, 129.3, 128.6, 127.9, 127.5, 126.7, 93.7, 61.1, 49.5, 41.9, 38.4, 14.0; HRMS (EI) calcd for  $\text{C}_{19}\text{H}_{19}\text{ClNO}_4\text{S}$  ( $\text{M} + \text{Na}^+$ ) 414.0543, found 414.0542; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 15.1 min,  $t_{\text{major}}$  = 17.0 min, ee = 97%, dr > 30:1;  $[\alpha]^{25}_{\text{D}}$  (major) = -99.7 ( $c$  = 0.8 in  $\text{CHCl}_3$ ).

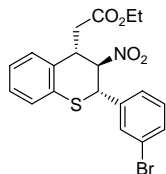


**[2-(2,6-Dichloro-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3d)** (Table 2, entry 4): The title compound was prepared according the typical procedure, as described above in 98% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.39-7.28 (m, 4H), 7.27-7.14 (m, 3H), 6.20 (dd, 1H,  $J$  = 10.5 Hz, 5.0 Hz), 5.54 (d, 1H,  $J$  = 10.5 Hz), 4.14 (q, 2H,  $J$  = 7.0 Hz), 4.08 (dd, 1H,  $J$  = 10.5 Hz, 5.5 Hz), 3.21 (dd, 1H,  $J$  = 17.5 Hz, 7.5 Hz), 2.81 (dd, 1H,  $J$  = 17.0 Hz, 6.0 Hz), 1.21 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,

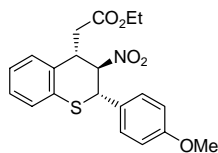
CDCl<sub>3</sub>, TMS):  $\delta$  = 170.7, 136.9, 135.8, 135.0, 134.5, 130.6, 130.5, 130.3, 139.2, 129.1, 128.7, 127.7, 127.3, 89.7, 61.1, 47.3, 42.7, 38.3, 14.1; HRMS (EI) calcd for C<sub>19</sub>H<sub>17</sub>Cl<sub>2</sub>NO<sub>4</sub>S (M + Na<sup>+</sup>) 448.0153, found 448.0158; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 14.2 min,  $t_{\text{major}}$  = 13.3 min, ee = 94%, dr = 16:1;  $[\alpha]_D^{25}$  (major) = -57.8 ( $c$  = 1.3 in CHCl<sub>3</sub>).



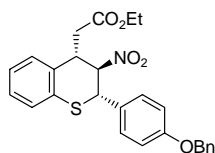
**[2-(4-Bromo-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3e)** (Table 2, entry 5). The title compound was prepared according to the typical procedure, as described above in 91% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 7.51-7.40 (m, 2H), 7.35-7.10 (m, 6H), 5.56 (dd, 1H,  $J$  = 10.5 Hz, 7.5 Hz), 4.55 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.05 (dd, 1H,  $J$  = 17.0 Hz, 6.5 Hz), 2.75 (dd, 1H,  $J$  = 17.0 Hz, 5.0 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 170.3, 134.8, 134.3, 133.2, 132.4, 129.6, 128.5, 127.9, 127.5, 126.7, 123.3, 93.6, 61.1, 49.5, 41.9, 38.4, 14.0; HRMS (EI) calcd for C<sub>19</sub>H<sub>18</sub>BrNO<sub>4</sub>S (M + Na<sup>+</sup>) 458.0038, found 458.0043; HPLC (Chiralcel OD-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 15.9 min,  $t_{\text{major}}$  = 17.6 min, ee = 97%, dr > 30:1;  $[\alpha]_D^{25}$  (major) = -75.5 ( $c$  = 1.1 in CHCl<sub>3</sub>).



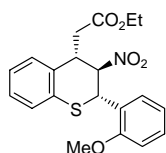
**[2-(3-Bromo-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3f)** (Table 2, entry 6). The title compound was prepared according to the typical procedure, as described above in 83% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 7.58-7.40 (m, 2H), 7.32-7.10 (m, 6H), 5.54 (dd, 1H,  $J$  = 10.5 Hz, 7.0 Hz), 4.53 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.05 (dd, 1H,  $J$  = 17.0 Hz, 7.0 Hz), 2.75 (dd, 1H,  $J$  = 17.0 Hz, 5.0 Hz), 1.19 (t, 3H,  $J$  = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 170.3, 137.6, 134.9, 133.2, 132.3, 131.0, 130.6, 128.6, 127.9, 127.6, 126.8, 126.6, 123.1, 93.5, 61.1, 49.6, 42.0, 38.5, 14.0; HRMS (EI) calcd for C<sub>19</sub>H<sub>18</sub>BrNO<sub>4</sub>S (M + Na<sup>+</sup>) 458.0038, found 458.0040; HPLC (Chiralcel OJ-H, *i*-propanol/hexane = 15/85, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 22.7 min,  $t_{\text{major}}$  = 23.6 min, ee = 97%, dr > 30:1;  $[\alpha]_D^{25}$  (major) = -71.4 ( $c$  = 1.1 in CHCl<sub>3</sub>).



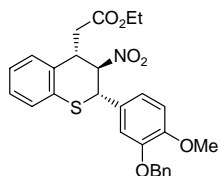
**[2-(4-Methoxy-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3g)** (Table 2, entry 7). The title compound was prepared according to the typical procedure, as described above in 88% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 7.40-7.10 (m, 6H), 6.92-6.83 (m, 2H), 5.57 (dd, 1H,  $J$  = 10.5 Hz, 7.5 Hz), 4.53 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.79 (s, 3H), 3.05 (dd, 1H,  $J$  = 17.0 Hz, 6.0 Hz), 2.74 (dd, 1H,  $J$  = 17.0 Hz, 5.0 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 170.4, 160.1, 134.8, 133.8, 129.1, 128.5, 127.8, 127.4, 126.9, 126.4, 114.5, 94.0, 61.0, 55.3, 49.6, 42.0, 38.6, 14.0; HRMS (EI) calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>5</sub>S (M + Na<sup>+</sup>) 410.1038, found 410.1029; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 19.2 min,  $t_{\text{major}}$  = 22.3 min, ee = 97%, dr > 30:1;  $[\alpha]_D^{25}$  (major) = -74.4 ( $c$  = 1.3 in CHCl<sub>3</sub>).



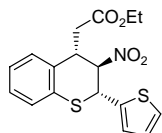
**[2-(4-Benzyloxy-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3h)** (Table 2, entry 8). The title compound was prepared according the typical procedure, as described above in 95% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.58-7.10 (m, 11H), 7.06-6.86 (m, 2H), 5.54 (dd, 1H,  $J$  = 10.5 Hz, 7.0 Hz), 5.03 (s, 2H), 4.54 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.05 (dd, 1H,  $J$  = 17.0 Hz, 6.5 Hz), 2.75 (dd, 1H,  $J$  = 17.0 Hz, 4.5 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 170.4, 159.3, 136.6, 134.8, 133.8, 129.2, 128.6, 128.5, 128.1, 127.8, 127.5, 127.4, 127.2, 126.4, 94.0, 61.0, 49.6, 42.0, 38.5, 14.0; HRMS (EI) calcd for  $\text{C}_{26}\text{H}_{25}\text{NO}_5\text{S}$  ( $\text{M} + \text{Na}^+$ ) 486.1351, found 486.1350; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 23.5 min,  $t_{\text{major}}$  = 38.1 min, ee = 97%, dr > 30:1;  $[\alpha]_{\text{D}}^{25}$  (major) = -88.0 ( $c$  = 1.7 in  $\text{CHCl}_3$ ).



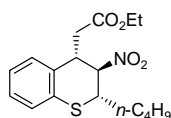
**[2-(2-Methoxy-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3i)** (Table 2, entry 9). The title compound was prepared according the typical procedure, as described above in 90% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.38-7.32 (m, 1H), 7.32-7.23 (m, 3H), 7.22-7.15 (m, 2H), 6.95 (t, 1H,  $J$  = 7.5 Hz), 6.89 (d, 1H,  $J$  = 8.5 Hz), 5.68 (dd, 1H,  $J$  = 10.0 Hz, 6.0 Hz), 5.09 (d, 1H,  $J$  = 10.0 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.03 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.80 (s, 3H), 3.04 (dd, 1H,  $J$  = 17.0 Hz, 7.0 Hz), 2.76 (dd, 1H,  $J$  = 17.0 Hz, 5.5 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 170.6, 157.2, 135.4, 134.3, 130.1, 128.8, 128.3, 127.4, 126.5, 123.8, 121.1, 111.5, 92.4, 61.0, 55.7, 44.6, 42.2, 38.5, 14.0; HRMS (EI) calcd for  $\text{C}_{20}\text{H}_{21}\text{NO}_5\text{S}$  ( $\text{M} + \text{Na}^+$ ) 410.1038, found 410.1044; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 16.2 min,  $t_{\text{major}}$  = 14.5 min, ee = 99%, dr > 30:1;  $[\alpha]_{\text{D}}^{25}$  (major) = -91.7 ( $c$  = 0.9 in  $\text{CHCl}_3$ ); HRMS (EI) calcd for  $\text{C}_{17}\text{H}_{18}\text{O}_6$  ( $\text{M} + \text{Na}^+$ ) 341.0996, found 341.0997.



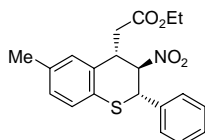
**[2-(3-Benzyloxy-4-methoxy-phenyl)-3-nitro-thiochroman-4-yl]-acetic acid ethyl ester (3j)** (Table 2, entry 10). The title compound was prepared according the typical procedure, as described above in 85% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 7.50-7.15 (m, 10H), 6.97-6.87 (m, 2H), 6.87-6.80 (m, 1H), 5.46 (dd, 1H,  $J$  = 10.0 Hz, 6.0 Hz), 5.09 (s, 2H), 4.49 (d, 1H,  $J$  = 10.5 Hz), 4.11 (q, 2H,  $J$  = 7.0 Hz), 4.02 (dd, 1H,  $J$  = 12.0 Hz, 6.5 Hz), 3.86 (s, 3H), 3.00 (dd, 1H,  $J$  = 17.0 Hz, 6.5 Hz), 2.75 (dd, 1H,  $J$  = 17.0 Hz, 5.0 Hz), 1.18 (t, 3H,  $J$  = 7.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  = 170.4, 134.9, 128.6, 128.0, 127.9, 127.5, 127.4, 126.4, 121.1, 113.8, 112.0, 94.1, 71.3, 61.0, 56.0, 49.9, 42.0, 38.5, 14.0; HRMS (EI) calcd for  $\text{C}_{27}\text{H}_{27}\text{NO}_6\text{S}$  ( $\text{M} + \text{Na}^+$ ) 516.1457, found 516.1461; HPLC (Chiralpak AD, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda$  = 254 nm):  $t_{\text{minor}}$  = 21.6 min,  $t_{\text{major}}$  = 26.1 min, ee = 92%, dr > 30:1;  $[\alpha]_{\text{D}}^{25}$  (major) = -89.5 ( $c$  = 1.5 in  $\text{CHCl}_3$ ).



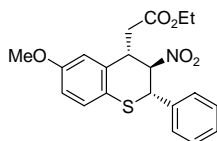
**(3-Nitro-2-thiophen-2-yl-thiochroman-4-yl)-acetic acid ethyl ester (3k)** (Table 2, entry 11). The title compound was prepared according the typical procedure, as described above in 97% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS): δ = 7.36-7.15 (m, 5H), 7.07 (d, 1H, *J* = 3.0 Hz), 6.95 (dd, 1H, *J* = 5.0 Hz, 3.5 Hz), 5.51 (dd, 1H, *J* = 10.0 Hz, 7.0 Hz), 4.96 (d, 1H, *J* = 10.0 Hz), 4.11 (q, 2H, *J* = 7.0 Hz), 4.04 (dd, 1H, *J* = 12.0 Hz, 6.5 Hz), 3.04 (dd, 1H, *J* = 17.0 Hz, 6.5 Hz), 2.75 (dd, 1H, *J* = 17.0 Hz, 5.0 Hz), 1.19 (t, 3H, *J* = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS): δ = 170.3, 137.8, 134.8, 128.6, 128.0, 127.6, 127.2, 126.8, 126.5, 94.8, 61.1, 45.3, 42.1, 38.5, 14.0; HRMS (EI) calcd for C<sub>17</sub>H<sub>17</sub>NO<sub>4</sub>S<sub>2</sub> (M + Na<sup>+</sup>) 386.0497, found 386.0498; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min, λ = 254 nm): t<sub>minor</sub> = 21.1 min, t<sub>major</sub> = 22.0 min, ee = 98%, dr > 30:1; [α]<sub>D</sub><sup>25</sup> (major) = -69.4 (*c* = 1.1 in CHCl<sub>3</sub>).



**(2-Butyl-3-nitro-thiochroman-4-yl)-acetic acid ethyl ester (3l)** (Table 2, entry 12). The title compound was prepared according the typical procedure, as described above in 32% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS): δ = 7.30-7.24 (m, 1H), 7.24-7.19 (m, 1H), 7.19-7.10 (m, 2H), 5.05 (dd, 1H, *J* = 9.5 Hz, 6.5 Hz), 4.11 (q, 2H, *J* = 7.0 Hz), 3.95 (dd, 1H, *J* = 12.5 Hz, 6.5 Hz), 3.55-3.43 (m, 1H), 2.94 (dd, 1H, *J* = 17.0 Hz, 7.0 Hz), 2.69 (dd, 1H, *J* = 17.0 Hz, 5.5 Hz), 1.80-1.66 (m, 1H), 1.65-1.50 (m, 1H), 1.45-1.22 (m, 4H), 1.19 (t, 3H, *J* = 7.0 Hz), 0.89 (t, 3H, *J* = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS): δ = 170.5, 135.6, 133.0, 128.7, 128.4, 127.4, 126.6, 93.6, 61.0, 46.5, 41.7, 38.1, 32.5, 31.2, 26.0, 22.3, 14.0, 13.9; HRMS (EI) calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>4</sub>S (M + Na<sup>+</sup>) 360.1245, found 360.1251; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 30/70, flow rate 0.5 mL/min, λ = 254 nm): t<sub>minor</sub> = 9.3 min, t<sub>major</sub> = 10.1 min, ee = 93%, dr > 30:1; [α]<sub>D</sub><sup>25</sup> (major) = -9.2 (*c* = 1.0 in CHCl<sub>3</sub>).

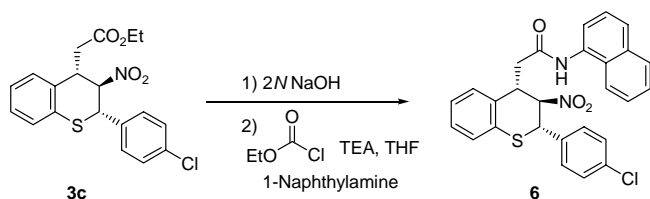


**(6-Methyl-3-nitro-2-phenyl-thiochroman-4-yl)-acetic acid ethyl ester (3m)** (Table 2, entry 13). The title compound was prepared according the typical procedure, as described above in 93% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS): δ = 7.45-7.30 (m, 4H), 7.16 (d, 1H, *J* = 8.0 Hz), 7.06 (s, 1H), 6.99 (d, 1H, *J* = 7.5 Hz), 5.58 (dd, 1H, *J* = 10.5 Hz, 7.5 Hz), 4.57 (d, 1H, *J* = 10.5 Hz), 4.11 (q, 2H, *J* = 7.0 Hz), 4.01 (dd, 1H, *J* = 11.5 Hz, 5.5 Hz), 3.02 (dd, 1H, *J* = 17.0 Hz, 6.5 Hz), 2.74 (dd, 1H, *J* = 17.0 Hz, 5.0 Hz), 2.30 (s, 1H), 1.20 (t, 3H, *J* = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS): δ = 170.4, 137.4, 135.3, 133.3, 131.8, 129.1, 128.3, 128.2, 128.0, 127.5, 93.9, 61.0, 50.2, 41.7, 38.6, 20.8, 14.0; HRMS (EI) calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>4</sub>S (M + Na<sup>+</sup>) 394.1089, found 394.1082; HPLC (Chiralpak AS-H, *i*-propanol/hexane = 7/93, flow rate 0.5 mL/min, λ = 254 nm): t<sub>minor</sub> = 22.4 min, t<sub>major</sub> = 20.9 min, ee = 99%, dr > 30:1; [α]<sub>D</sub><sup>25</sup> (major) = -117.3 (*c* = 0.7 in CHCl<sub>3</sub>).

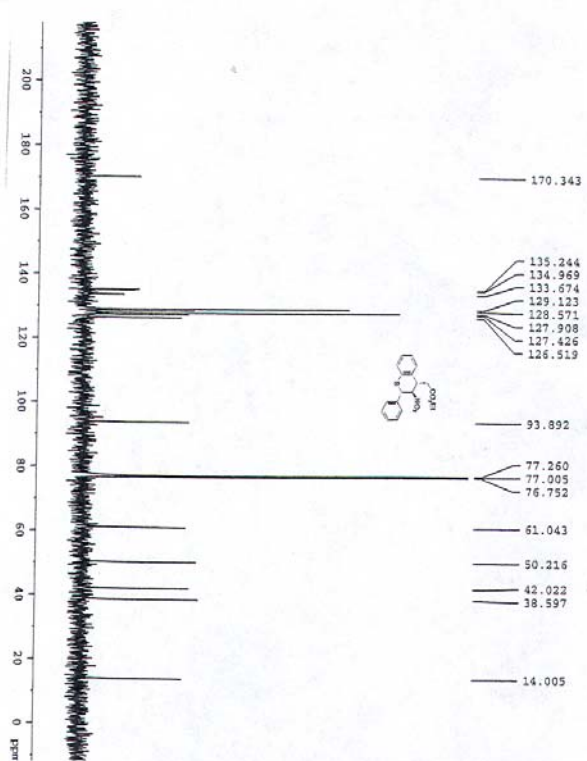
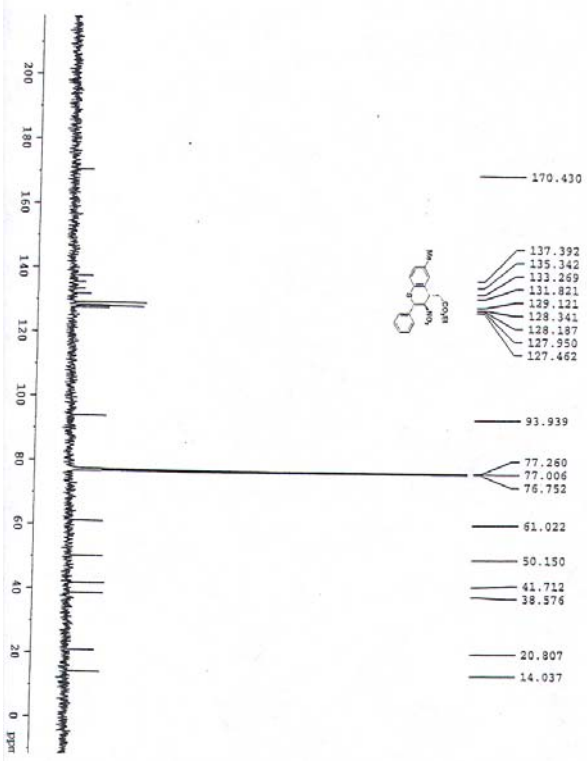
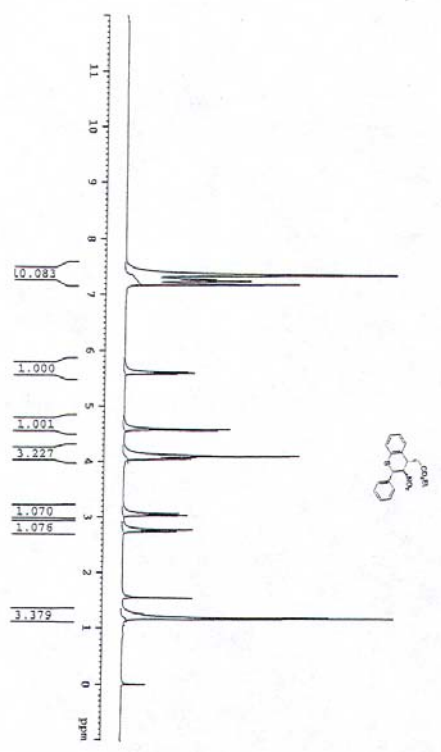


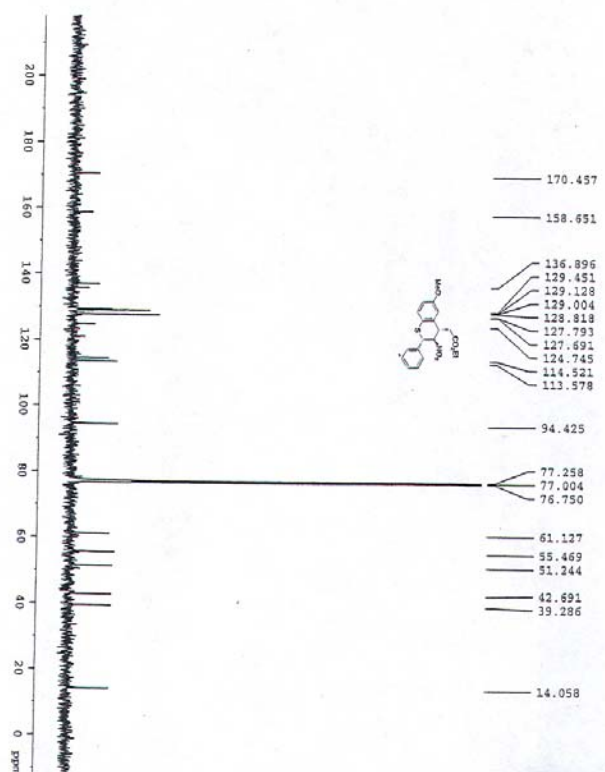
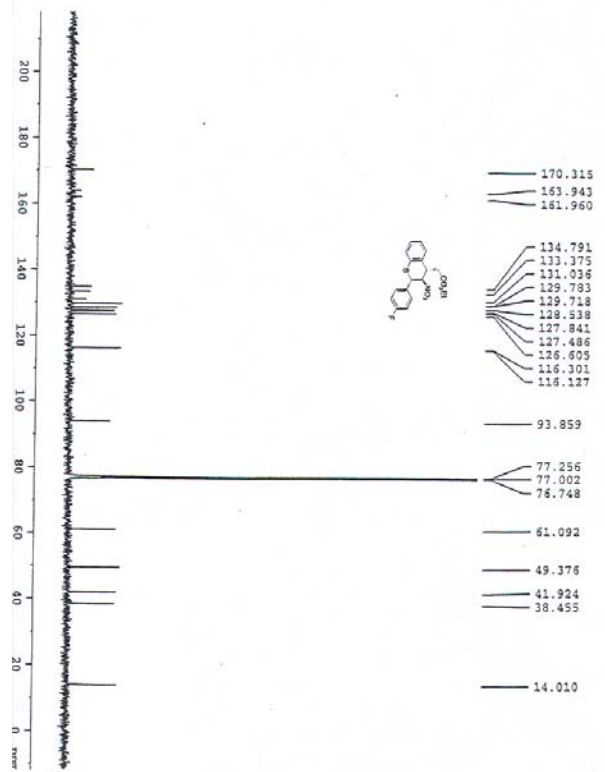
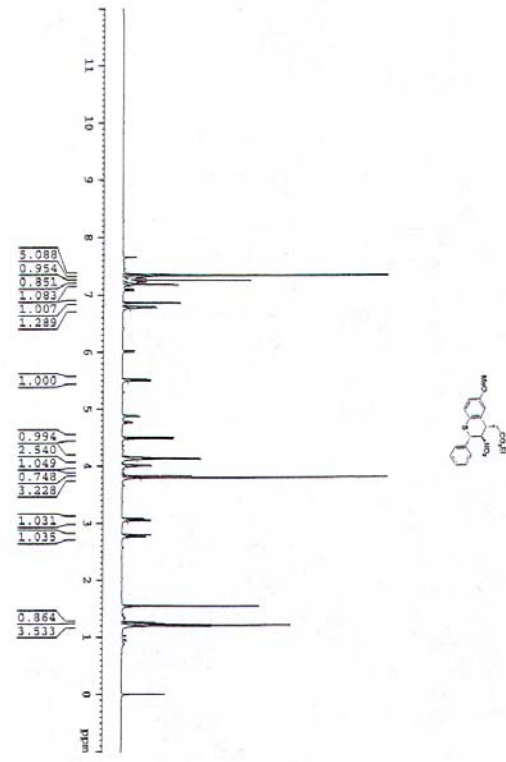
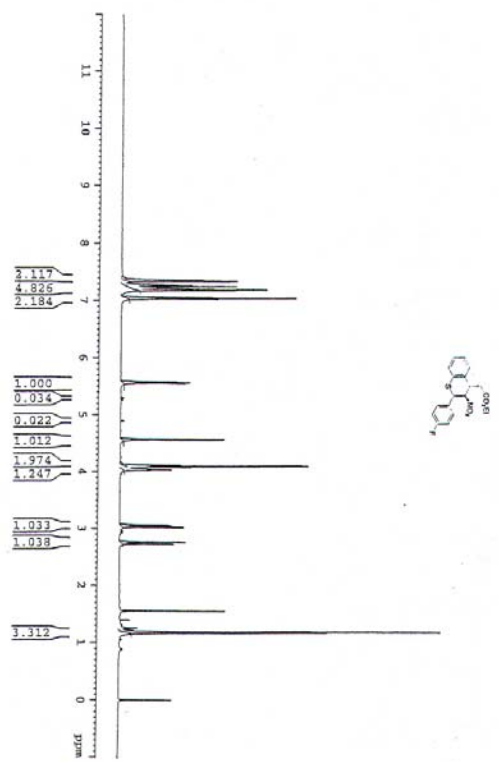
**(6-Methoxy-3-nitro-2-phenyl-thiochroman-4-yl)-acetic acid ethyl ester (3n)** (Table 2, entry 14). The title compound was prepared according the typical procedure, as described above in 42% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS): δ = 7.40-7.21 (m, 4H), 7.19 (d, 1H, *J* = 8.5 Hz), 6.86 (s, 1H), 6.78 (dd, 1H, *J* = 8.5 Hz, 2.5 Hz), 5.52 (dd, 1H, *J* = 10.5 Hz, 6.0 Hz), 4.49 (d, 1H, *J* = 10.5 Hz), 4.14 (q, 2H, *J* = 7.0 Hz), 4.01 (dd, 1H, *J* = 11.5 Hz, 5.5 Hz), 3.80 (s, 3H), 3.08 (dd, 1H, *J* = 16.5 Hz, 7.0 Hz), 2.77 (dd, 1H, *J* = 16.5 Hz, 5.0 Hz), 1.21 (t, 3H, *J* = 7.0 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, TMS): δ = 170.5, 158.7, 136.9, 129.5, 129.1, 129.0, 128.8, 127.8, 127.7, 124.7, 114.5, 113.6, 94.4, 61.1, 55.5, 51.2, 42.7, 39.3, 14.1; HRMS (EI) calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>5</sub>S (M + Na<sup>+</sup>) 410.1038, found 410.1035; HPLC (Chiralpak AS-H, *i*-

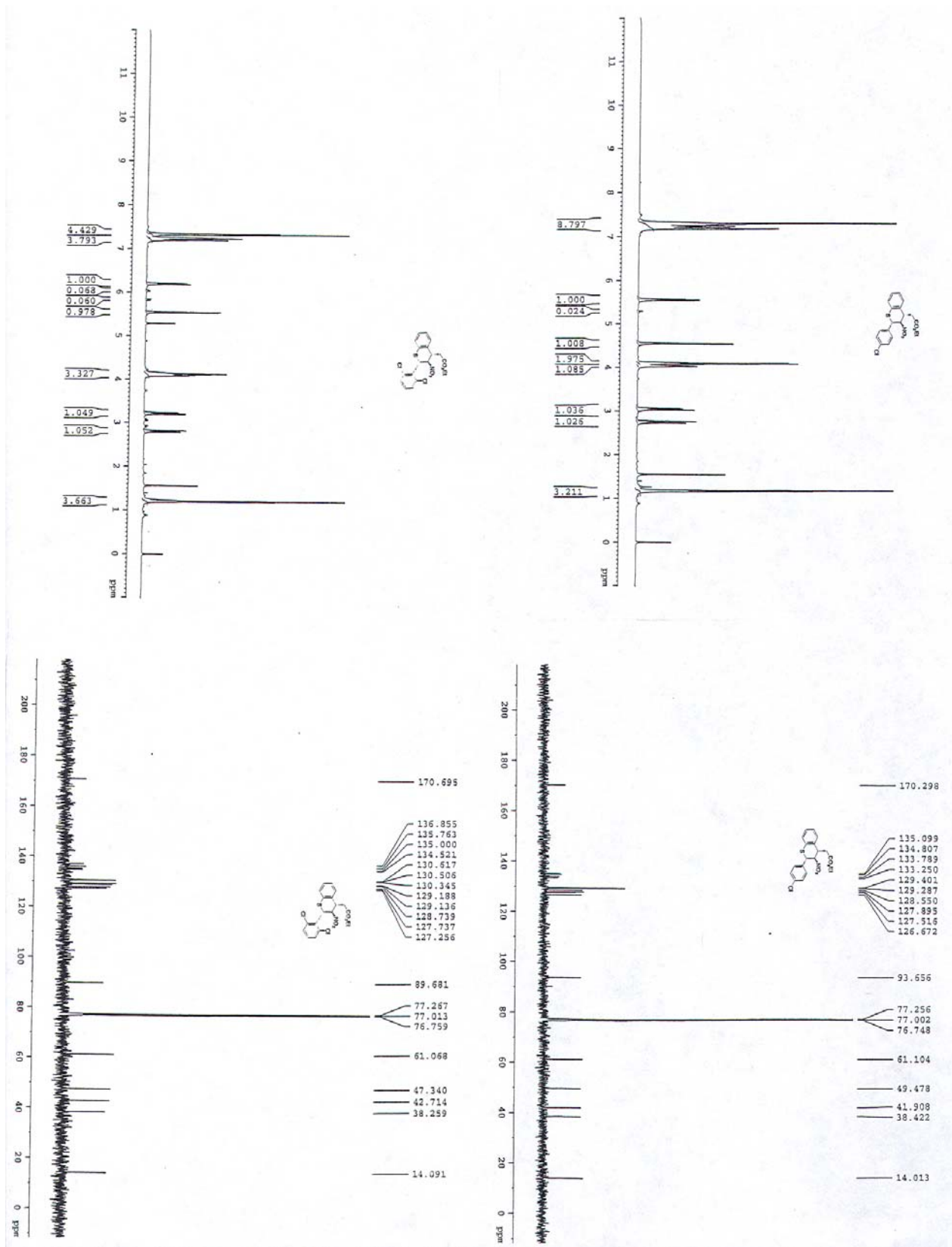
propanol/hexane = 30/70, flow rate 0.5 mL/min,  $\lambda = 254$  nm):  $t_{\text{minor}} = 18.8$  min,  $t_{\text{major}} = 21.4$  min, ee = 97%, dr > 30:1;  $[\alpha]_D^{25}$  (major) =  $-85.1$  ( $c = 0.9$  in  $\text{CHCl}_3$ ).

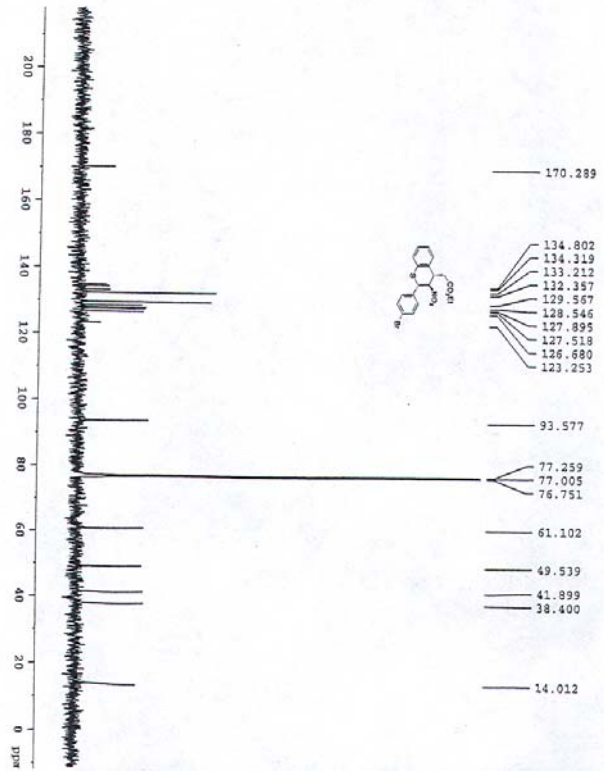
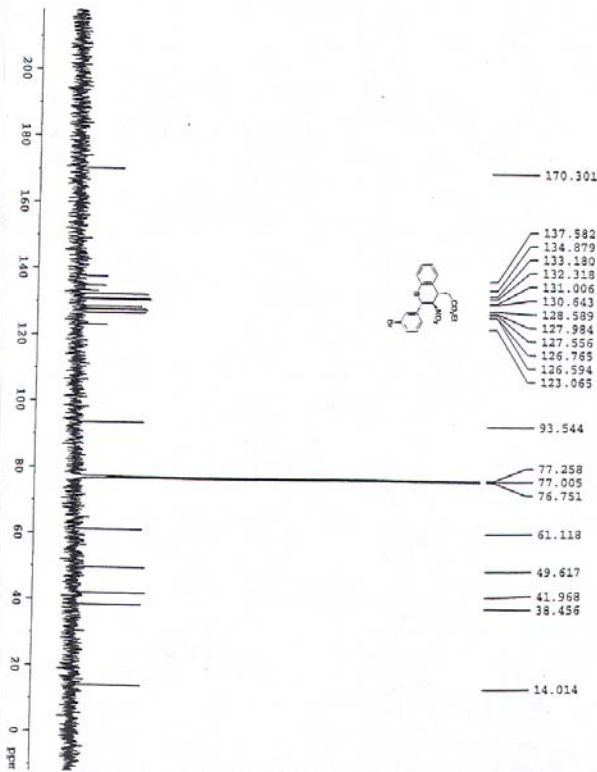
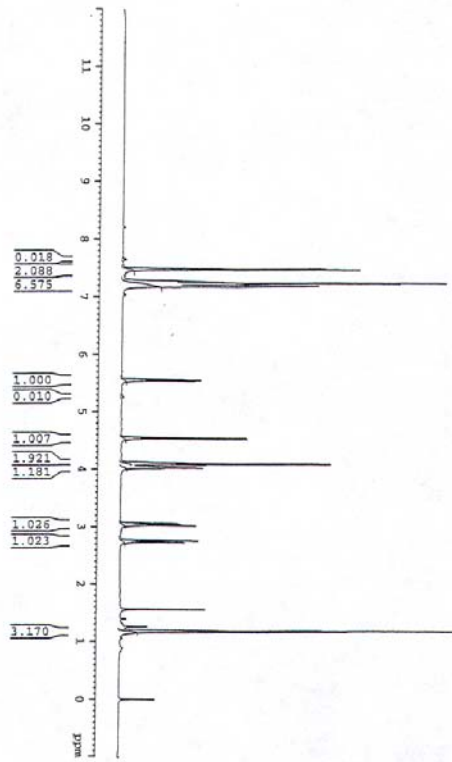
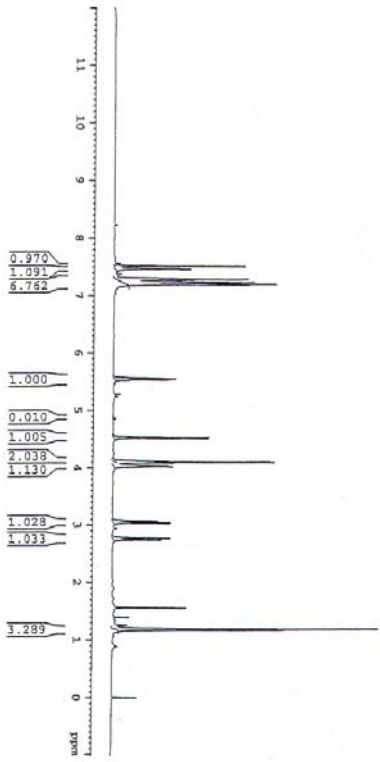


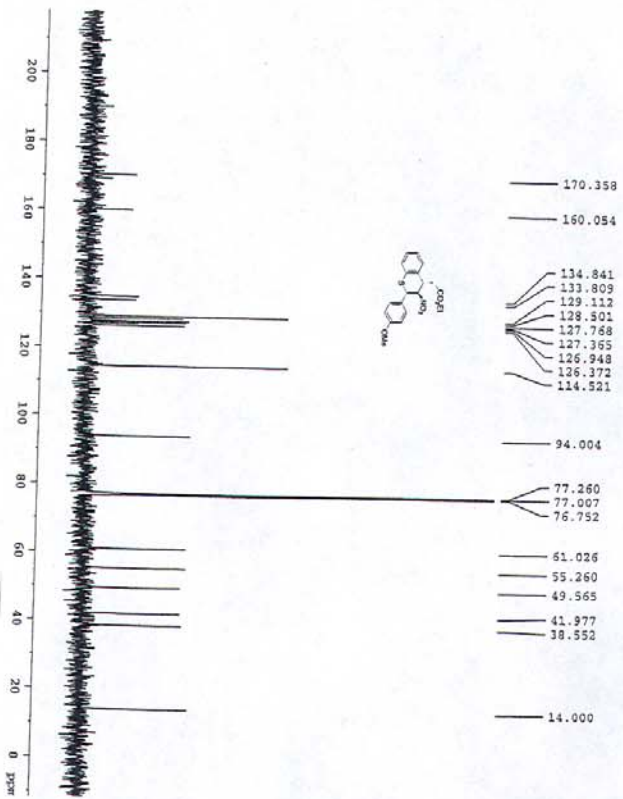
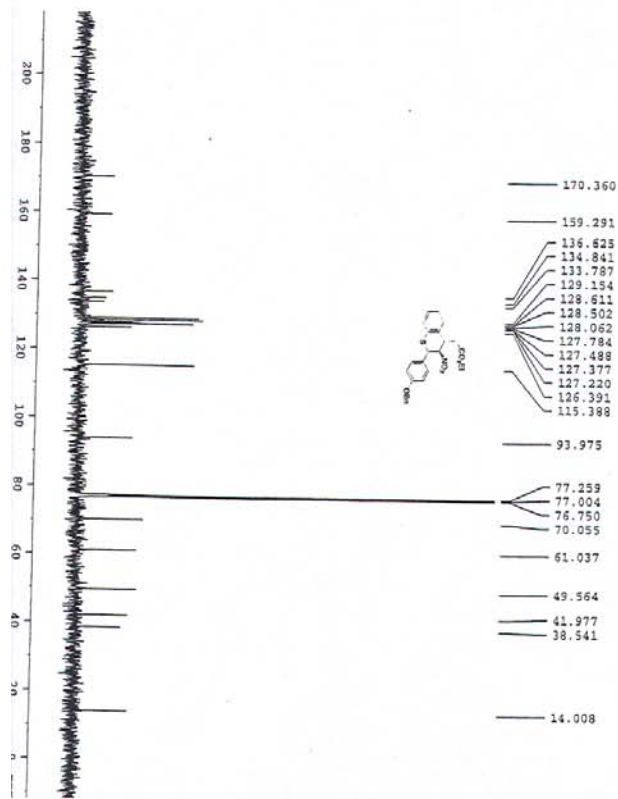
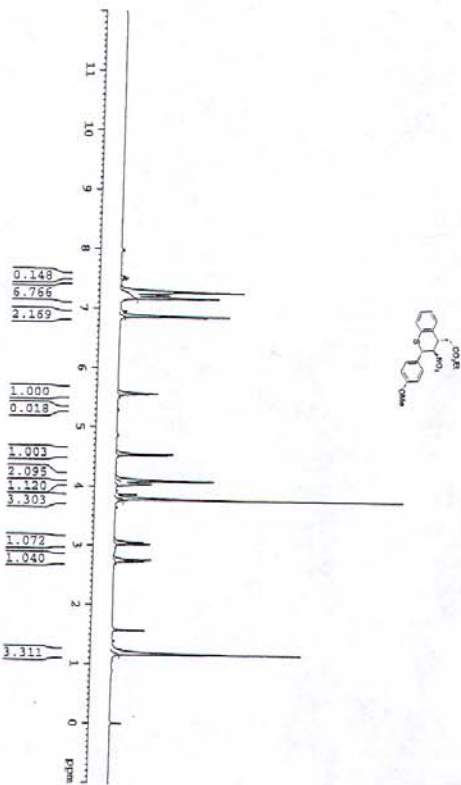
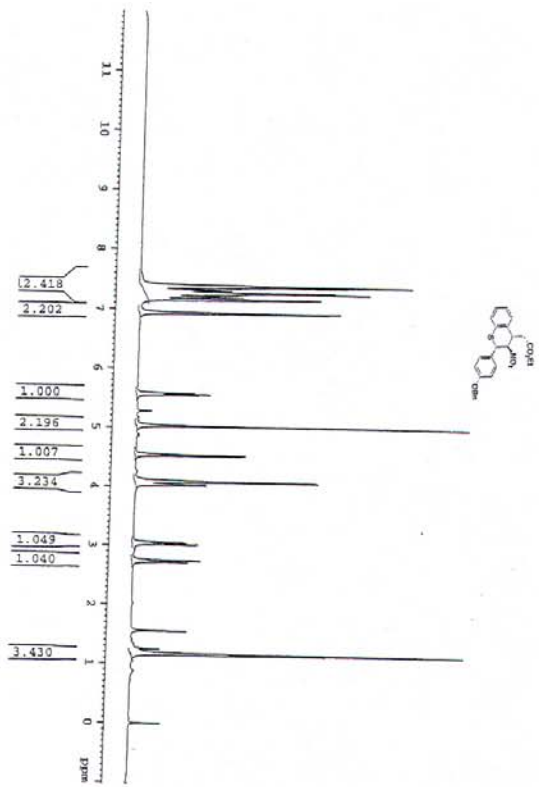
**2-[2-(4-Chloro-phenyl)-3-nitro-thiochroman-4-yl]-N-naphthalen-1-yl-acetamide (6)** (for x-ray analysis): Compound **3c** (163 mg, 0.45 mmol) was hydrolyzed by 2N NaOH at rt. After 3 h, the reaction mixture was extracted by  $\text{CH}_2\text{Cl}_2$  ( $3 \times 30$  mL) and the combined organic layer was concentrated and used to next step. Then, ethyl chloroformate (55  $\mu\text{L}$ , 0.68 mmol) was added slowly to the above compound in 20 mL of THF following the addition of naphthalen-1-ylamine (129 mg, 0.9 mmol) and triethyl amine (125  $\mu\text{L}$ , 0.9 mmol). After stirring for overnight, the concentrated reaction mixture was purified by column chromatography on silica gel, eluted by hexane/EtOAc = 15:1 to afford a white solid with 69% overall yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta = 7.90\text{-}7.80$  (m, 1H), 7.80-7.65 (m, 2H), 7.55-7.32 (m, 6H), 7.31-7.10 (m, 6H), 5.77 (dd, 1H,  $J = 12.0$  Hz, 4.5 Hz), 4.60 (d, 1H,  $J = 10.5$  Hz), 4.65-4.50 (m, 1H), 3.21 (dd, 1H,  $J = 15.5$  Hz, 5.0 Hz), 3.03 (dd, 1H,  $J = 15.5$  Hz, 5.0 Hz);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , TMS):  $\delta = 168.1, 135.1, 134.1, 133.8, 133.6, 129.4, 129.3, 129.1, 128.7, 128.4, 127.9, 127.7, 127.5, 127.0, 126.5, 126.4, 126.1, 125.6, 121.8, 120.6, 93.7, 49.6, 42.5, 41.5$ .

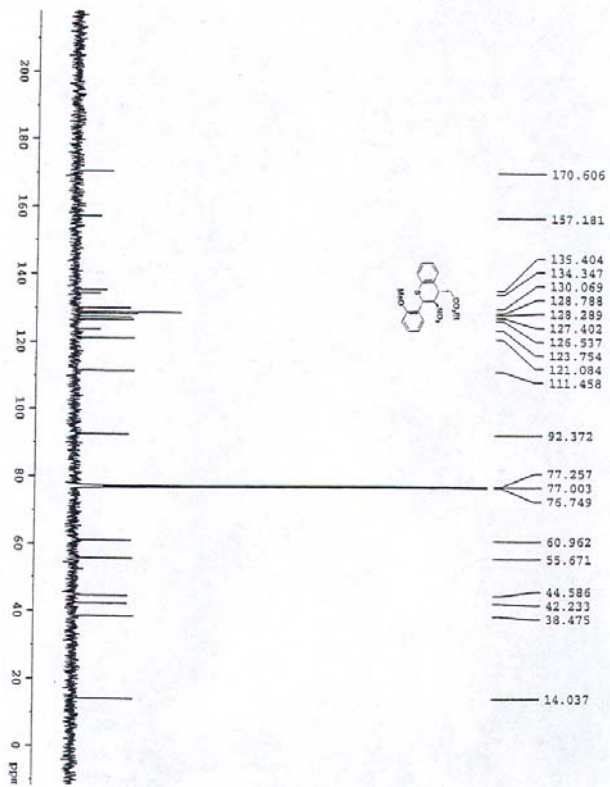
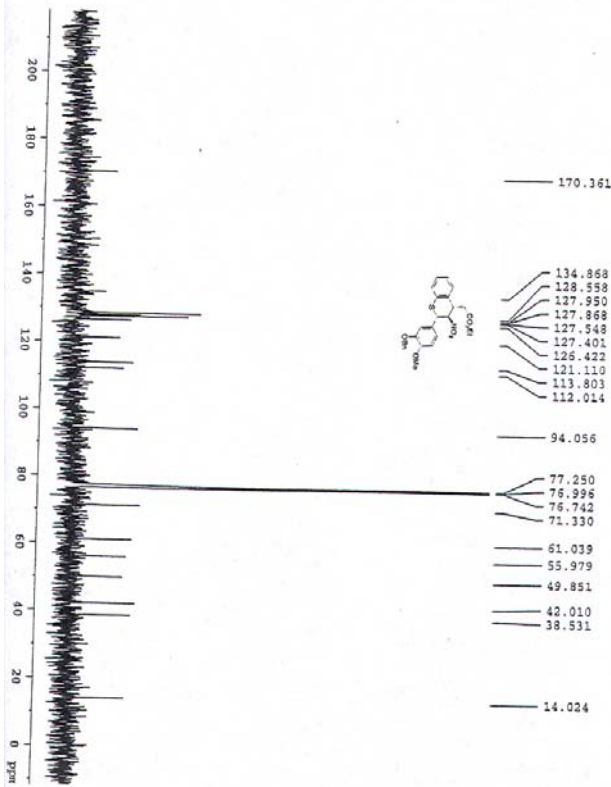
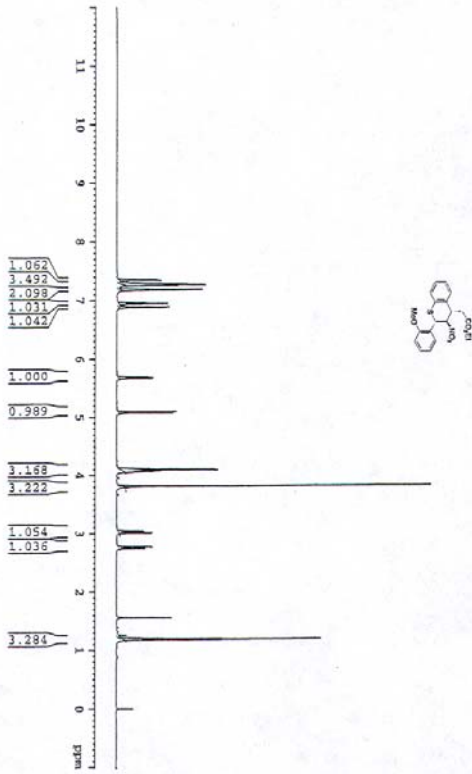
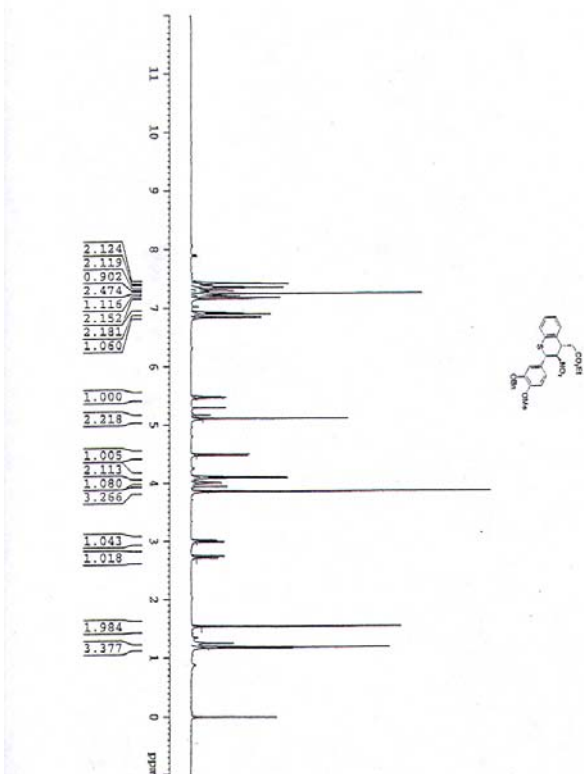


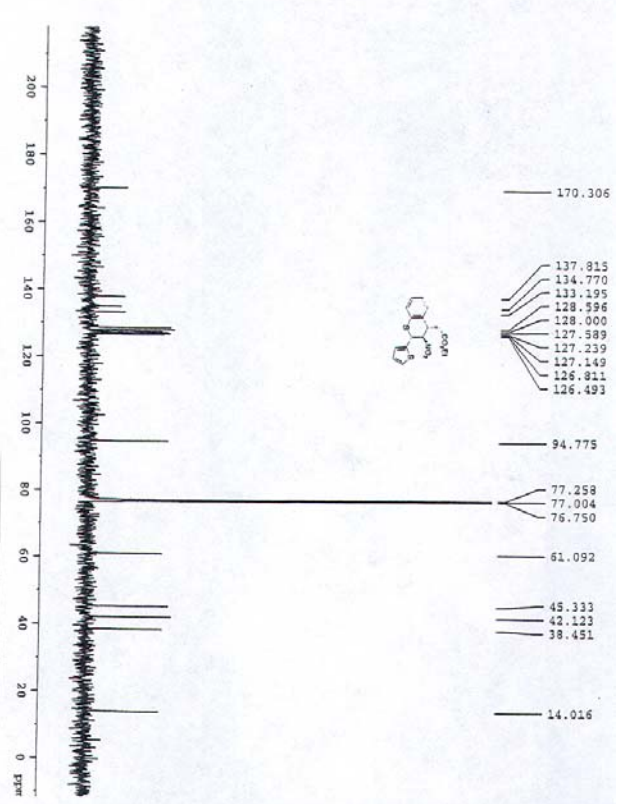
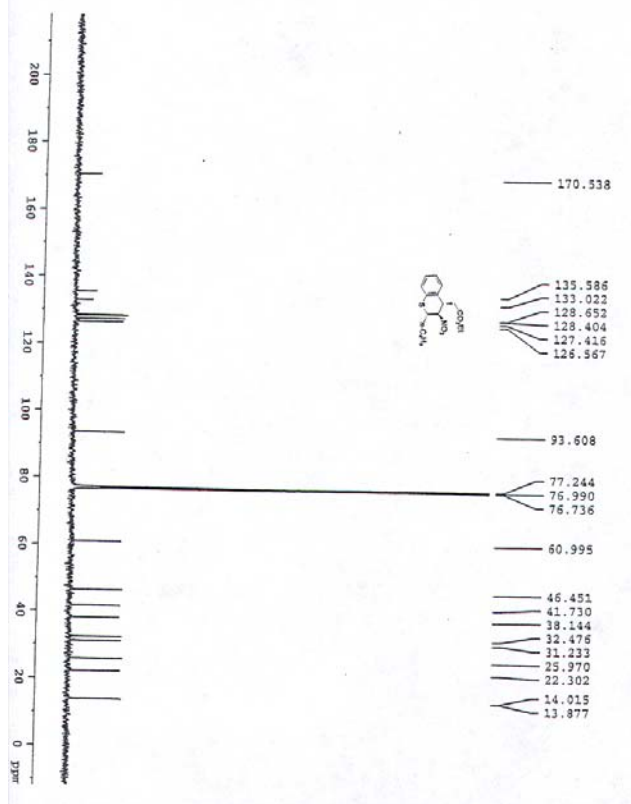
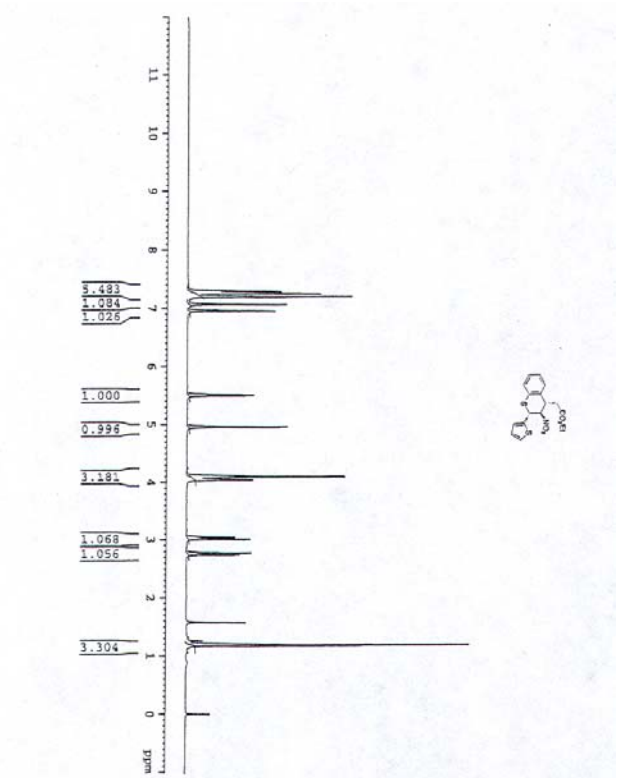
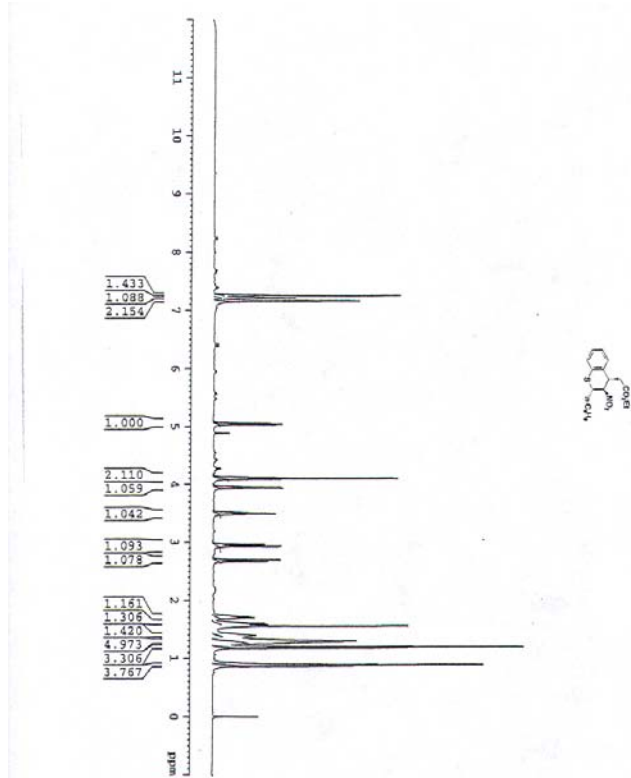






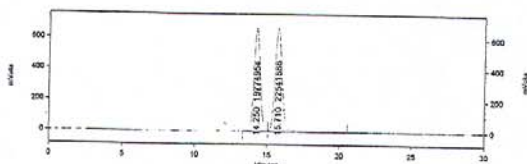






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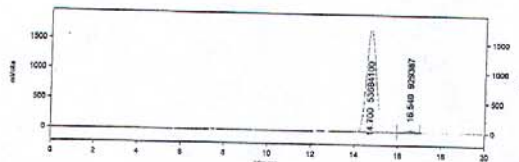
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Totals			42316840	100.000

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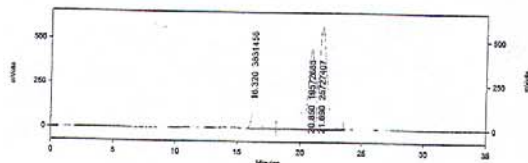
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Totals			34613487	100.000

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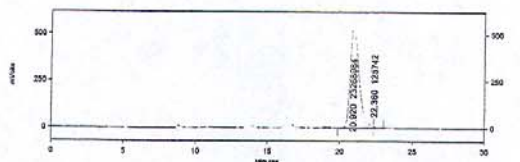
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SPD-10Avp Chl-254nm Results	PK #	RT	Area	Area %
	1	16.330	3821156	7.798
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Totals			49131548	100.000

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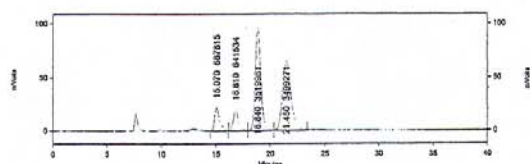
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Totals			23394726	100.000

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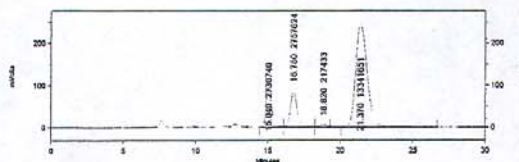
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Totals			8348581	100.000

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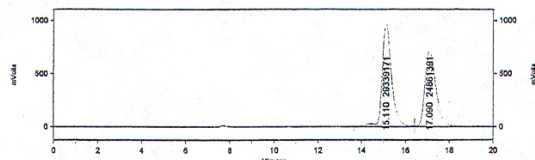
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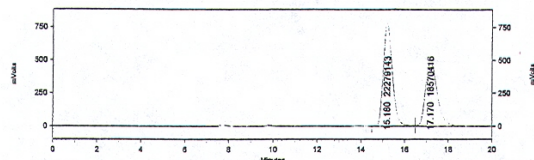
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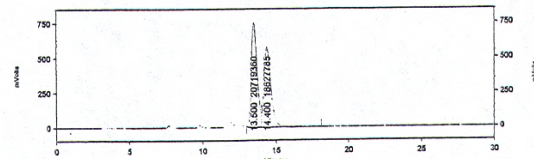
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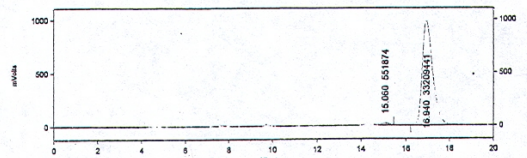
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SPD-10Avp Chl-254nm Results			
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1	13.500	20719360	52.658
2	14.400	18627785	47.342
Totals		39347145	100.000

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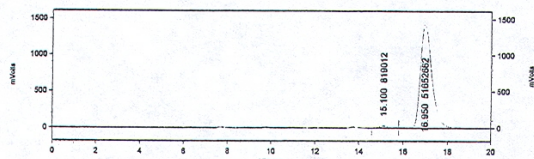
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SPD-10Avp Chl-254nm Results			
PK #	RT	Area	Area %
1	15.060	551874	1.635
2	16.940	33209441	98.365
Totals		33761315	100.000

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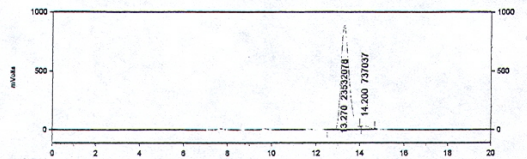
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SPD-10Avp Chl-254nm Results			
PK #	RT	Area	Area %
1	15.100	819012	1.561
2	16.950	51652662	98.439
Totals		52471674	100.000

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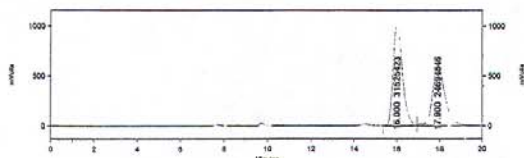
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SPD-10Avp Chl-254nm Results			
PK #	RT	Area	Area %
1	13.270	23532078	96.963
2	14.200	737037	3.037
Totals		24269115	100.000

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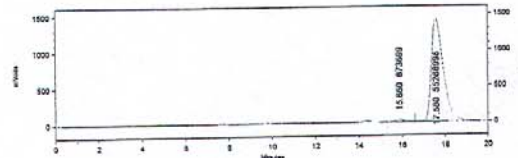
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Sample ID: jvw78a



SPD-10Avp				
Chl-254nm Results				
PK #	RT	Area	Area %	
1	16.000	31525423	36.073	
2	17.900	24694846	43.925	
Totals		56220269	100.000	

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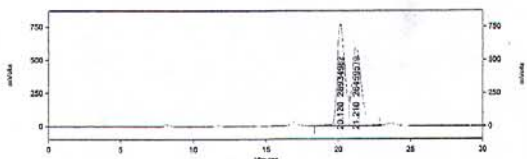
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Sample ID: jvw77a



SPD-10Avp				
Chl-254nm Results				
PK #	RT	Area	Area %	
1	15.860	873699	1.356	
2	17.580	55248998	98.444	
Totals		56142697	100.000	

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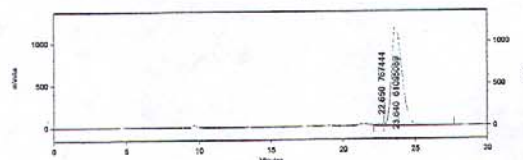
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Sample ID: jvw84a



SPD-10Avp				
Chl-254nm Results				
PK #	RT	Area	Area %	
1	20.120	28934382	32.234	
2	21.210	26493579	47.766	
Totals		55394561	100.000	

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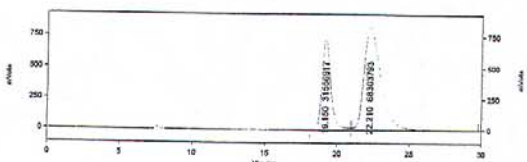
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Sample ID: jvw83a



SPD-10Avp				
Chl-254nm Results				
PK #	RT	Area	Area %	
1	22.850	787444	1.241	
2	23.840	61095089	98.759	
Totals		61882533	100.000	

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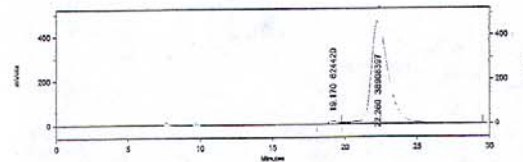
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Sample ID: jvw80a



SPD-10Avp				
Chl-254nm Results				
PK #	RT	Area	Area %	
1	19.150	31559317	31.801	
2	22.210	68303793	68.199	
Totals		99860710	100.000	

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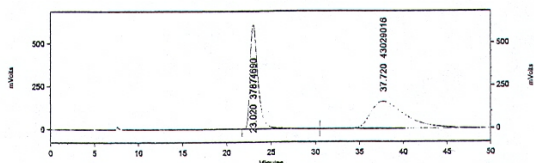
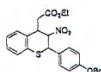
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Sample ID: jvw79a



SPD-10Avp				
Chl-254nm Results				
PK #	RT	Area	Area %	
1	19.170	924420	1.379	
2	22.260	38908397	98.421	
Totals		39832817	100.000	

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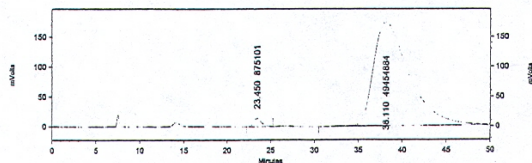
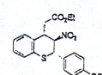
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Date Acquired: 5/10/2007 8:59:04 AM Date Printed: 05/25/2007 12:27:56 PM  
Sample ID: jvw86e



SPD-10Avp Chl-254nm Results				
PK #	RT	Area	Area %	
1	23.020	37874690	46.815	
2	37.720	43029016	53.185	
Totals		80903706	100.000	

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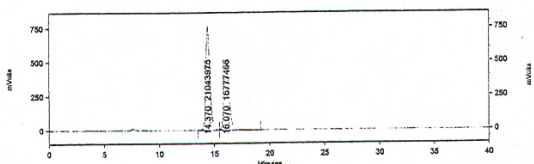
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Sample ID: jvw85e



SPD-10Avp Chl-254nm Results				
PK #	RT	Area	Area %	
1	23.450	875101	1.739	
2	38.110	49454884	98.261	
Totals		50329985	100.000	

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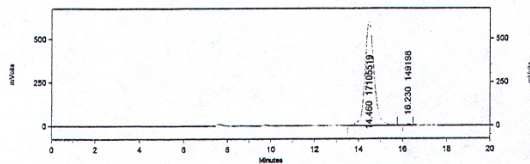
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Date Acquired: 5/12/2007 10:02:12 AM Date Printed: 05/25/2007 12:30:20 PM  
Sample ID: jvw28e



SPD-10Avp Chl-254nm Results				
PK #	RT	Area	Area %	
1	14.370	21043975	55.640	
2	16.070	16777466	44.360	
Totals		37821441	100.000	

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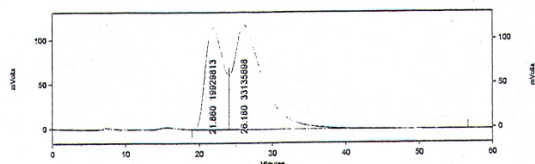
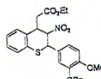
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Sample ID: jvw27e



SPD-10Avp Chl-254nm Results				
PK #	RT	Area	Area %	
1	14.460	17105519	99.135	
2	16.230	149198	0.865	
Totals		17254717	100.000	

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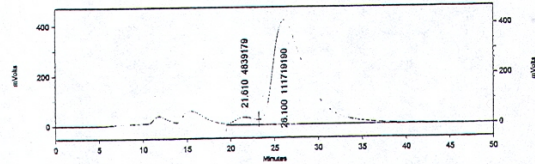
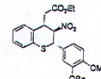
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Sample ID: jvw30e



SPD-10Avp Chl-254nm Results				
PK #	RT	Area	Area %	
1	21.860	19929813	37.357	
2	26.180	33135898	62.443	
Totals		53065711	100.000	

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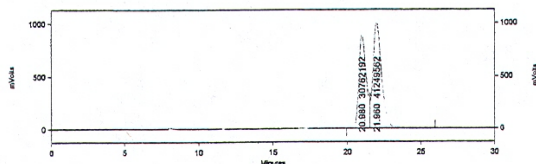
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SPD-10Avp Chl-254nm Results				
PK #	RT	Area	Area %	
1	21.610	4839179	4.152	
2	26.100	111719190	95.848	
Totals		116558369	100.000	

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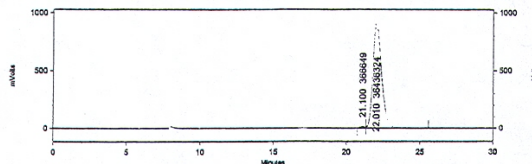
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Sample ID: jvw88a



SPD-10Avp				
Chi-254nm Results				
PK #	RT	Area	Area %	
1	20.980	30762192	42.718	
2	21.960	41249562	57.282	
Totals		72011754	100.000	

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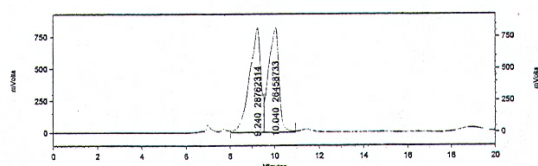
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Sample ID: jvw87a



SPD-10Avp				
Chi-254nm Results				
PK #	RT	Area	Area %	
1	21.100	366649	0.996	
2	22.010	36436324	99.004	
Totals		36802973	100.000	

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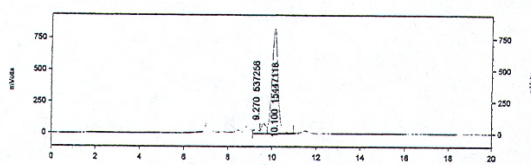
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Sample ID: jvw92a



SPD-10Avp				
Chi-254nm Results				
PK #	RT	Area	Area %	
1	9.240	28762314	52.086	
2	10.040	26458733	47.914	
Totals		55221047	100.000	

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Method Name: C:\EZStart\Projects\WeiWang\sl1119.met  
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Sample ID: jvw91a



SPD-10Avp				
Chi-254nm Results				
PK #	RT	Area	Area %	
1	9.270	537256	3.261	
2	10.100	15447118	96.639	
Totals		15984374	100.000	