Electronic Supplementary Information

Enantioselective monofluoromethylation of aldehydes with 2-fluoro-1,3-benzodithiole-1,1,3,3-tetraoxide catalyzed by a bifunctional cinchona alkaloid-derived thiourea-titanium complex

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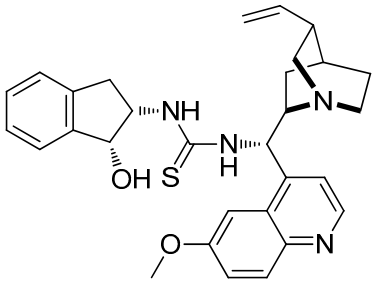
1 General information:

All reactions were performed in oven- and flame-dried glassware under a positive pressure of nitrogen. Solvents were transferred *via* syringe and were introduced into the reaction vessels through a rubber septum. All of the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or $KMnO_4$ in water/heat. Column chromatography was carried out on a column packed with silica gel 60N spherical neutral size 63-210 μm. The ^{1}H NMR (300 MHz) and ^{19}F NMR (282 MHz) spectra were recorded on a Varian Mercury 300. ^{13}C NMR (150.9 MHz) spectra was recorded on a BRUKER 600 UltraShieldTR. Chemical shifts (δ) are expressed in ppm downfield from internal TMS or $CHCl_3$, $(CH_3)_2CO$ or CH_2Cl_2. HPLC analyses were performed on a JASCO U-2080 Plus and SHIMADZU LC-2010AHT using 4.6 x 250 mm CHIRALPAK IA, IB, IC and IF column. Mass spectra were recorded on a SHIMAZU LCMS-2010EV (ESI-MS). Optical rotations were measured on a HORIBA SEPA-300. Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer

2 Preparation of chiral thiourea catalysts:

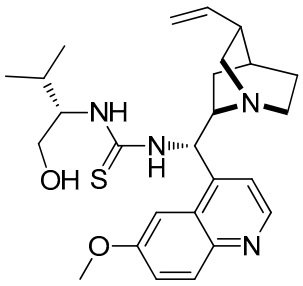
Chiral thiourea catalysts **I**–**III** were known compounds, **IV-VIII** were synthesized by known method. [1]



1-((1*R*,2*S*)-1-hydroxy-2,3-dihydro-1H-inden-2-yl)-3-((1*S*)-(6-methoxyquinolin-4-yl)((5*R*)-5-vinylquinuclidin-2-yl)methyl)thiourea (IV)

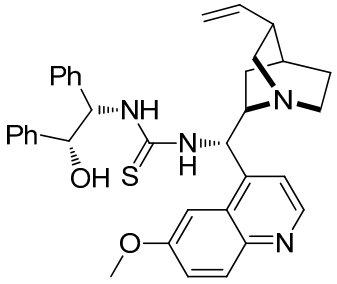
white solid, mp 157–160 °C, $[\alpha]_D^{25}$ –121.9 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.73 (s, 1H), 7.27-7.30 (m, 3H),

6.89-7.12 (m, 3H), 5.62-5.73 (m, 2H), 4.97 (t, *J* = 9.6 Hz, 2H), 4.63 (s, 1H), 4.32 (d, *J* = 7.8 Hz, 1H), 3.96 (s, 3H), 3.43 (d, *J* = 8.4 Hz, 2H), 3.05-3.20 (m, 3H), 2.71-2.85 (m, 2H), 2.56 (s, 1H), 2.27 (s, 1H), 1.89 (d, *J* = 11.1 Hz, 1H), 1.57-1.65 (m, 2H), 1.26-1.34 (m, 2H), 1.01-1.18 (m, 2H), 0.80-0.87 (m, 1H); **^{13}C NMR** (150.9 MHz, CD_3OD) δ 159.8, 159.7, 148.3, 145.2, 142.4, 141.4, 131.2, 128.8, 126.1, 125.3, 123.9, 115.1, 74.0, 56.6, 56.5, 49.7, 42.8, 40.6, 40.5, 34.75, 28.8, 28.5, 26.9, 26.7, 26.1; **HRMS** (ESI) found: m/z 515.2498 $[M+H]^+$; calcd. for $C_{30}H_{34}N_4O_2S$+H 515.2481; **IR** (KBr): ν 3435, 2903, 1626, 1574, 1509, 1474, 1242, 1089, 826, 743 cm^{-1}.



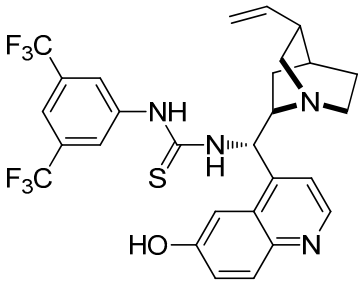
1-((*S*)-1-hydroxy-3-methylbutan-2-yl)-3-((1*S*)-(6-methoxyquinolin-4-yl)((5*R*)-5-vinylquinuclidin-2-yl)methyl)thiourea

white solid, mp 135–137 °C, $[\alpha]_D^{25}$ –146.4 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.74 (d, *J* = 7.8 Hz, 1H), 8.03 (d, *J* = 9.3 Hz, 1H), 7.27-7.42 (m, 3H), 5.67-5.74 (m, 1H), 5.00 (t, *J* = 9.3 Hz, 2H), 4.25 (d, *J* = 7.8 Hz, 1H), 3.92 (s, 3H), 3.38-3.74 (m, 3H), 3.16-3.28 (m, 2H), 2.63-2.83 (m, 3H), 2.34 (s, 1H), 1.92 (d, *J* = 9.6 Hz, 2H), 1.56-1.68 (m, 6H), 1.26-1.41 (m, 2H), 1.04-1.20 (m, 2H), 0.72-0.97 (m, 3H); **^{13}C NMR** (150.9 MHz, CD_3OD) δ 159.8, 159.6, 148.2, 145.1, 142.4, 131.1, 130.1, 123.7, 115.0, 104.1, 62.1, 56.6, 56.5, 49.7, 42.5, 40.6, 34.7, 30.0, 29.8, 28.8, 28.5, 26.7, 26.0, 19.7, 18.8; **HRMS** (ESI) found: m/z 469.2664 $[M+H]^+$; calcd. for $C_{26}H_{36}N_4O_2S$+H 469.2637; **IR** (KBr): ν 3326, 2903, 2851, 1624, 1574, 1541, 1508, 1242, 1228, 919 cm^{-1}.



1-((1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl)-3-((1*S*)-(6-methoxyquinolin-4-yl)((5*R*)-5-vinylquinuclidin-2-yl)methyl)thiourea

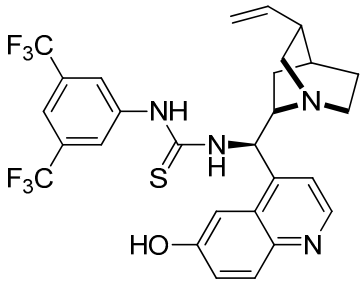
white solid, mp 120–122 °C, $[\alpha]_D^{25}$ –47.1 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.60 (d, *J* = 3.6 Hz, 1H), 7.96 (d, *J* = 9.3 Hz, 1H), 7.26-6.90 (m, 13H), 5.59-5.65 (m, 1H), 5.26 (s, 1H), 4.94 (t, *J* = 6.3 Hz, 2H), 4.75 (d, *J* = 6.3 Hz, 1H), 4.32 (d, *J* = 7.8 Hz, 1H), 4.15 (d, *J* = 6.3 Hz, 1H), 3.95 (s, 3H), 3.45 (s, 1H), 2.42-2.59 (m, 2H), 1.55-1.60 (m, 5H), 1.24-1.36 (m, 2H), 1.04-1.13 (m, 2H), 0.84-0.87 (m, 1H); **^{13}C NMR** (150.9 MHz, CD_3OD) δ 183.2, 159.8, 159.5, 148.2, 145.0, 142.8, 142.4, 131.1, 129.6, 129.0 (d, *J* = 7.5 Hz), 128.6 (d, *J* = 21.1 Hz), 128.1, 127.5, 123.7, 115.1, 104.2, 79.0, 76.2, 65.1, 62.7, 61.8, 56.8, 56.6, 40.6, 34.7, 28.7, 28.4, 27.0, 26.7, 26.0; **HRMS** (ESI) found: m/z 579.2790 $[M+H]^+$; calcd. for $C_{35}H_{38}N_4O_2S$+H 579.2794; **IR** (KBr): ν 3327, 3061, 2929, 2851, 1568, 1515, 1498, 1453, 1028, 704 cm^{-1}.



1-(3,5-bis(trifluoromethyl)phenyl)-3-((1*S*)-(6-hydroxyquinolin-4-yl)((5*R*)-5-vinylquinuclidin-2-yl)methyl)thiourea

brown solid, mp 170–172 °C, $[\alpha]_D^{25}$ –85.0 (*c* 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, CD_3OD) δ 8.62 (d, *J* = 4.5 Hz, 1H), 8.13 (s, 2H), 7.92 (d, *J* = 9.0 Hz, 2H), 7.60 (s, 1H), 7.51 (d, *J* = 4.8 Hz, 1H), 7.38 (d, *J* = 9.3 Hz, 1H), 6.19 (d, *J* = 10.8 Hz, 1H), 5.75-5.87 (m, 1H), 4.94-5.04 (m, 3H), 3.42 (m, 1H), 2.77-2.80 (m, 3H), 2.35 (s, 1H), 1.64-1.77 (m, 4H), 1.31-1.37 (m, 2H), 0.96-1.03 (m, 2H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ

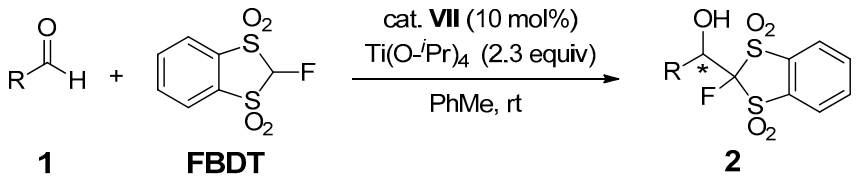
–63.0 (s, 6F); **^{13}C NMR** (150.9 MHz, CD_3OD) δ 182.3, 157.7, 147.5, 144.2, 143.0, 142.4, 132.7 (q, *J* = 33.2 Hz), 131.21, 130.5, 124.7 (q, *J* = 271.6 Hz), 123.6, 123.3, 117.7, 115.0, 106.9, 56.5, 42.5, 28.7, 28.4, 26.3; **HRMS** (ESI) found: m/z 581.1803 $[M+H]^+$; calcd. for $C_{28}H_{26}F_6N_4O_2S$+H 581.1810; **IR** (KBr): ν 2954, 1715, 1515, 1472, 1383, 1278, 1179, 1133, 850, 681 cm^{-1}.



1-(3,5-bis(trifluoromethyl)phenyl)-3-((1*R*)-(6-hydroxyquinolin-4-yl)((5*R*)-5-vinyl quinuclidin-2-yl)methyl)thiourea

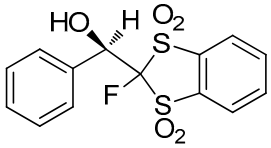
brown solid, mp 155–157 °C, $[\alpha]_D^{25}$ +40.7 (*c* 0.5, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.80 (dd, *J* = 4.5 Hz, *J* = 55.5 Hz, 1H), 8.15-8.23 (m, 1H), 8.01 (d, *J* = 7.2 Hz, 3H), 7.46-7.58 (m, 3H), 5.88-5.93 (m, 1H), 5.35-5.39 (m, 3H), 3.77-3.80 (m, 1H), 3.60 (s, 1H), 3.17-3.29 (m, 3H), 2.62 (s, 1H), 2.37-2.41 (m, 1H), 2.05-2.17 (m, 2H), 1.79-1.91 (m, 3H), 1.52 (s, 1H), 1.24-1.28 (m, 1H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –63.0 (s, 6F); **^{13}C NMR** (150.9 MHz, $CDCl_3$) δ 180.5, 169.5, 150.1, 149.2, 146.9, 146.7, 137.4, 131.8 (q, *J* = 19.6 Hz), 125.2, 123.2 (q, *J* = 273.1 Hz), 118.1, 60.6, 49.0, 46.5, 26.6, 24.5, 24.0, 21.3; **HRMS** (ESI) found: m/z 581.1807 $[M+H]^+$; calcd. for $C_{28}H_{26}F_6N_4O_2S$+H 581.1810; **IR** (KBr): ν 3235, 3044, 1761, 1619, 1547, 1513, 1472, 1383, 1278, 681 cm^{-1}.

3 General procedure for the enantioselective addition of monofluoromethylation of aldehydes:



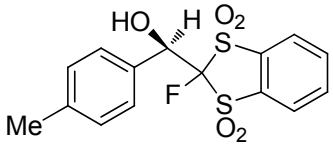
To a solution of catalyst **VII** (0.01 mmol) and FBDT (0.1 mmol) in toluene (1 mL) was added Ti(O-^{i}Pr)$_4$ (0.23 mmol) under N_2. Then the correspounding aldehydes **1** (0.15 mmol or 0.5 mmol) were added to the mixture. The resulting mixture was stirred at room temperature until the reaction completed (detected by TLC). Purification by column chromatography on silica gel (*n*-hexane / ethyl acetate =8:1–2:1) afforded the product **2**.

2a, **2b**, **2c**, **2d**, **2i** and **2k** are known compounds.[2]



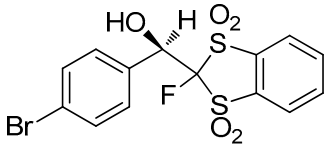
(*R*)-2-fluoro-2-(hydroxy(phenyl)methyl)benzodithiole-1,1,3,3-tetraoxide (2a)

28.7 mg, white solid, 84% yield, 91% ee, $[\alpha]_D^{25}$ –92.8 (*c* 0.5, $(CH_3)_2CO$), **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.05 (dd, *J* = 3.9 Hz, *J* = 26.7 Hz, 1H), 6.31 (d, *J* = 3.9 Hz, 1H), 7.45-7.47 (m, 3H), 7.68-7.69 (m, 2H), 8.18-8.33 (m, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –165.9 (d, *J* = 27.6 Hz, 1F); **HPLC** (DAICEL Chiralpak IA, *n*-hexane / *i*-PrOH (IPA) = 70:30, 1.0 mL / min, 254 nm) t_R (major) = 21.4 min, t_R (minor) = 15.2 min.



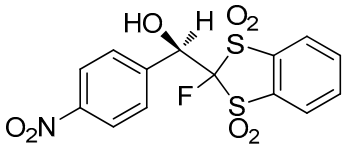
(*R*)-2-fluoro-2-(hydroxy(p-tolyl)methyl)benzodithiole-1,1,3,3-tetraoxide (2b)

29.6 mg, white solid, 83% yield, 60% ee, $[\alpha]_D^{25}$ –37.2 (*c* 0.5, $(CH_3)_2CO$), **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 2.36 (s, 3H), 5.99 (d, *J* = 27.0 Hz, 1H), 6.20 (d, *J* = 6.0 Hz, 1H), 7.26 (d, *J* = 7.2 Hz, 2H), 7.55 (d, *J* = 27.0 Hz, 2H), 8.15-8.31 (m, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –166.0 (d, *J* = 26.8 Hz, 1F); **HPLC** (DAICEL Chiralpak IA, *n*-hexane / *i*-PrOH (IPA) = 70:30, 1.0 mL / min, 254 nm) t_R (major) = 26.3 min, t_R (minor) = 18.5 min.



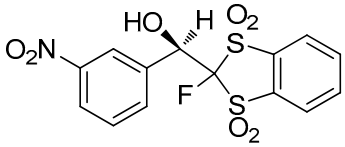
(*R*)-2-((4-bromophenyl)(hydroxy)methyl)-2-fluorobenzodithiole-1,1,3,3-tetraoxide(2c)

34.1 mg, white solid, 81% yield, 56% ee, $[\alpha]_D^{25}$ –72.6 (*c* 1.0, $(CH_3)_2CO$), **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.04 (dd, *J* = 6.6 Hz, *J* = 26.4 Hz, 1H), 6.47 (d, *J* = 6.6 Hz, 1H), 7.61-7.68 (m, 4H), 8.16-8.33 (m, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –166.1 (d, *J* = 26.8 Hz, 1F); **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 90:10, 1.0 mL / min, 254 nm) t_R (major) = 25.5 min, t_R (minor) = 18.7 min.



(*R*)-2-fluoro-2-(hydroxy(4-nitrophenyl)methyl)benzodithiole-1,1,3,3-tetraoxide (2d)

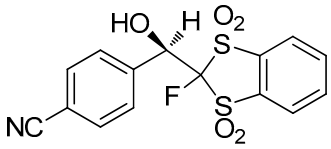
35.2 mg, white solid, 91% yield, 60% ee, $[\alpha]_D^{25}$ –39.2 (*c* 0.5, $(CH_3)_2CO$), **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.25 (d, *J* = 25.8 Hz, 1H), 6.78 (s, 1H) 7.99 (d, *J* = 7.8 Hz, 2H), 8.20-8.34 (m, 3H), 8.35-8.38 (m, 3H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –165.6 (d, *J* = 25.9 Hz, 1F); **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 90:10, 1.0 mL / min, 254 nm) t_R (major) = 50.1 min, t_R (minor) = 41.6 min.



(*R*)-2-fluoro-2-(hydroxy(3-nitrophenyl)methyl)benzodithiole-1,1,3,3-tetraoxide (2e)

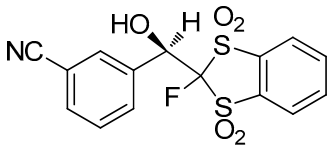
34.4 mg, white solid, mp 188–190 °C, 89% yield, 96% ee, $[\alpha]_D^{25}$ –19.6 (*c* 0.3, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.27 (dd, *J* = 4.8 Hz, *J* = 26.1 Hz, 1H), 6.78 (d, *J* = 6.3 Hz, 1H), 7.82 (t, *J* = 7.8 Hz, 1H), 8.12-8.24 (m, 4H), 8.33-8.37 (m, 2H), 8.57 (s, 1H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –165.8 (d, *J* = 24.8 Hz, 1F); **^{13}C**

NMR (150.9 MHz, $(CD_3)_2SO$) δ 147.6, 137.4, 137.3, 137.1 (d, J = 3.0 Hz), 135.2, 135.0, 133.7, 130.2, 124.5, 124.1, 123.9, 123.2, 105.0 (d, J = 274.6 Hz), 67.7 (d, J = 16.6 Hz); **HRMS** (ESI) found: m/z 409.9777 $[M+Na]^+$; calcd. for $C_{14}H_{10}FNO_7S_2$+Na 409.9780; **IR** (KBr): ν 3510, 3089, 1525, 1360, 1189, 1162, 1137, 1105, 588, 519 cm^{-1}; **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 85:15, 1.0 mL / min, 254 nm) t_R (major) = 28.0 min, t_R (minor) = 19.6 min.



(*R*)-4-((2-fluoro-1,1,3,3-tetraoxidobenzodithiol-2-yl)(hydroxy)methyl)benzonitrile (2f)

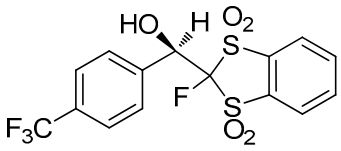
32.0 mg, white solid, mp 192–194 °C, 87% yield, 67% ee, $[\alpha]_D^{25}$ –16.2 (*c* 0.5, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.18 (dd, J = 3.6 Hz, J = 2.61 Hz, 1H), 6.67 (d, J = 3.6 Hz, 1H), 7.90-7.94 (m, 4H), 8.21-8.27 (m, 3H), 8.33-8.35 (m, 1H);; **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –165.7 (d, J = 26.8 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2CO$) δ 140.9, 137.7, 137.5, 136.8, 135.5, 133.1 (d, J = 1.5 Hz), 124.6, 124.3, 118.9, 114.1, 106.1 (d, J = 276.1 Hz), 69.5 (d, J = 16.6 Hz); **HRMS** (ESI) found: m/z 389.9878 $[M+Na]^+$; calcd. for $C_{15}H_{10}FNO_5S_2$+Na 389.9882; **IR** (KBr): ν 3388, 3081, 3010, 2236, 1705, 1445, 1364, 1188, 1052, 775 cm^{-1}; **HPLC** (DAICEL Chiralpak ID, *n*-hexane / *i*-PrOH (IPA) = 70:30, 1.0 mL / min, 254 nm) t_R (major) = 20.7 min, t_R (minor) = 15.4 min.



(*R*)-3-((2-fluoro-1,1,3,3-tetraoxidobenzodithiol-2-yl)(hydroxy)methyl)benzonitrile (2g)

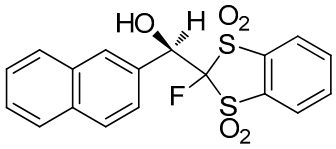
32.3 mg, white solid, mp 225–227 °C, 88% yield, 80% ee, $[\alpha]_D^{25}$ –20.1 (*c* 0.5, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.16 (dd, J = 6.6 Hz, J = 26.1 Hz, 1H),

6.65 (d, J = 6.3 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.85-7.91 (m, 1H), 8.03 (d, J = 10.2 Hz, 1H), 8.20-8.34 (m, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –165.9 (d, J = 25.7 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2SO$) δ 137.4, 137.1, 136.5, 135.0, 133.7, 133.5, 133.4, 132.2, 129.9, 124.1, 123.9, 118.4, 111.4, 105.0 (d, J = 274.6 Hz), 67.7 (d, J = 16.6 Hz); **HRMS** (ESI) found: m/z 389.9880 $[M+Na]^+$; calcd. for $C_{15}H_{10}FNO_5S_2$+Na 389.9882; **IR** (KBr): ν 3367, 3086, 2244, 1444, 1361, 1190, 1163, 1137, 772, 693 cm^{-1}; **HPLC** (DAICEL Chiralpak IF, *n*-hexane / *i*-PrOH (IPA) = 60:40, 1.0 mL / min, 254 nm) t_R (major) = 26.9 min, t_R (minor) = 10.7 min.



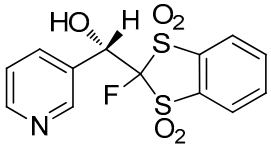
(*R*)-2-fluoro-2-(hydroxy(4-(trifluoromethyl)phenyl)methyl)benzodithiole-1,1,3,3-tetraoxide (2h)

34.9 mg, white solid, mp 138–140 °C, 85% yield, 67% ee, $[\alpha]_D^{25}$ –41.3 (*c* 0.3, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.15 (dd, J = 3.3 Hz, J = 25.8 Hz, 1H), 6.58 (d, J = 3.3 Hz, 1H), 7.85 (dd, J = 7.8 Hz, J = 26.7 Hz, 4H), 8.16-8.32 (m, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –60.6 (s, 3F), –163.2 (d, J = 25.7 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2CO$) δ 140.3, 137.7, 137.5, 137.0, 135.6, 131.8 (q, J = 31.7 Hz), 130.4 (d, J = 1.5 Hz), 126.2, 126.0, 125.2 (q, J = 250.5 Hz), 124.6, 106.3 (d, J = 276.1 Hz), 69.6 (d, J = 16.6 Hz); **HRMS** (ESI) found: m/z 432.9798 $[M+Na]^+$; calcd. for $C_{15}H_{10}F_4O_5S_2$+Na 432.9803; **IR** (KBr): ν 3497, 3214, 3084, 1702, 1445, 1363, 1324, 1265, 1188, 692 cm^{-1}; **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 80:20, 1.0 mL / min, 254 nm) t_R (major) = 6.6 min, t_R (minor) = 5.8 min.



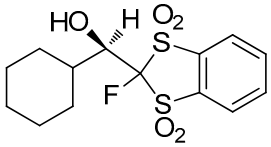
(*R*)-2-fluoro-2-(hydroxy(naphthalen-2-yl)methyl)benzodithiole-1,1,3,3-tetraoxide (2i)

32.1 mg, white solid, 82% yield, 42% ee, $[\alpha]_D^{25}$ –50.1 (*c* 0.5, $(CH_3)_2CO$), **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.24 (dd, *J* = 6.3 Hz, *J* = 26.7 Hz, 1H), 6.49 (d, *J* = 6.6 Hz, 1H), 7.56-7.60 (m, 2H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.95-8.02 (m, 3H), 8.14-8.31 (m, 4H), 8.32 (d, *J* = 7.2 Hz, 1H); **^{19}F NMR** (282MHz, $(CD_3)_2CO$) δ –165.6 (d, *J* = 26.8 Hz, 1F); **HPLC** (DAICEL Chiralpak IC, hexane / *i*PrOH (IPA) = 85:15, 1.0 mL / min, 254 nm) t_R (major) = 25.8 min, t_R (minor) = 19.0 min.



(*S*)-2-fluoro-2-(hydroxy(pyridin-3-yl)methyl)benzodithiole-1,1,3,3-tetraoxide (2j)

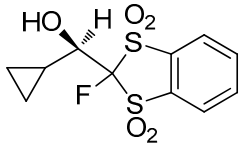
26.8 mg, white solid, mp 178–180 °C, 78% yield, 60% ee, $[\alpha]_D^{25}$ +11.3 (*c* 0.5, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 6.16 (dd, *J* = 6.6 Hz, *J* = 25.8 Hz, 1H), 6.28 (d, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 6.3 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.93 (t, *J* = 7.8 Hz, 1H), 8.19-8.31 (m, 4H), 8.66 (d, *J* = 4.2 Hz, 1H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –164.7 (d, *J* = 26.8 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2SO$) δ 155.0, 148.7, 137.3, 137.0, 134.9, 134.5, 124.3, 123.9, 123.8, 123.0, 105.9 (d, *J* = 276.1 Hz), 70.2 (d, *J* = 18.1 Hz); **HRMS** (ESI) found: m/z 365.9877 $[M+Na]^+$; calcd. for $C_{13}H_{10}FNO_5S_2$+Na 365.9882; **IR** (KBr): ν 3151, 2824, 1597, 1573, 1482, 1436, 1362, 1188, 1163, 761, 553 cm^{-1}; **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 70:30, 1.0 mL / min, 254 nm) t_R (major) = 25.5 min, t_R (minor) = 40.6 min.



(*R*)-2-(cyclohexyl(hydroxy)methyl)-2-fluorobenzodithiole-1,1,3,3-tetraoxide (2k)

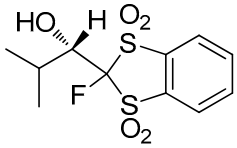
29.9 mg, white solid, 86% yield, 44% ee, $[\alpha]_D^{25}$ –10.5 (*c* 0.5, $(CH_3)_2CO$), **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 1.20-1.37 (m, 4H), 1.14-2.05 (m, 7H), 4.81 (d, *J* = 31.8 Hz, 1H), 5.62 (brs, 1H), 8.25 (d, *J* = 14.7 Hz, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –163.0 (d, *J* = 30.7 Hz, 1F); **HPLC** (DAICEL Chiralpak IC, hexane / *i*PrOH (IPA) =

85:15, 1.0 mL / min, 254 nm) t_R (major) = 11.1 min, t_R (minor) = 8.8 min.



(*R*)-2-(cyclopropyl(hydroxy)methyl)-2-fluorobenzodithiole1,1,3,3-tetraoxide (2l)

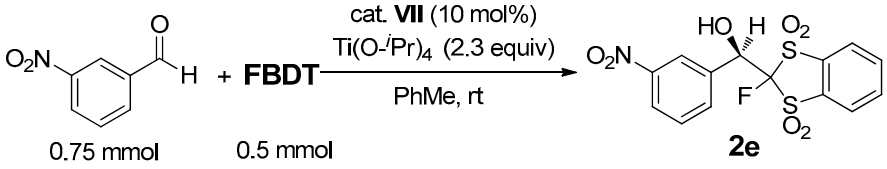
24.2 mg, white solid, mp 165–168 °C, 79% yield, 37% ee, $[\alpha]_D^{25}$ –18.6 (*c* 0.5, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 0.69-0.75 (m, 4H), 1.38-1.40 (m, 1H), 4.31 (tt, *J* = 7.8 Hz, 15.9 Hz, 1H), 5.73 (d, *J* = 7.5 Hz, 1H), 8.23 (d, *J* = 13.5 Hz, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –164.7 (d, *J* = 26.8 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2CO$) δ 137.5, 137.2, 135.8, 124.4, 124.2, 122.1 107.3 (q, *J* = 271.6 Hz), 72.0 (q, *J* = 18.1 Hz), 12.7 (q, *J* = 4.5 Hz), 4.6, 3.6; **HRMS** (ESI) found: m/z 328.9933 $[M+Na]^+$; calcd. for $C_{11}H_{11}FO_5S_2$+Na 328.9933; **IR** (KBr): ν 3463, 3376, 3087, 3014, 1442, 1358, 1264, 1191, 768, 576 cm^{-1}; **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 85:15, 1.0 mL / min, 254 nm) t_R (major) = 21.2 min, t_R (minor) = 19.5 min.



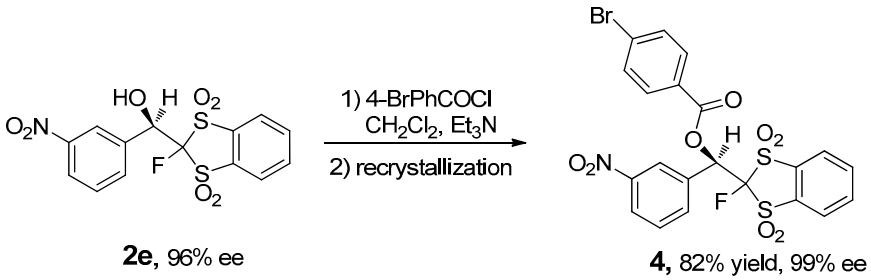
(*S*)-2-fluoro-2-(1-hydroxy-2-methylpropyl)benzodithiole-1,1,3,3-tetraoxide (2m)

22.5 mg, white solid, mp 140–142 °C, 73% yield, 32% ee, $[\alpha]_D^{25}$ +7.3 (*c* 0.5, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 1.14-1.18 (m, 6H), 2.05-2.38 (m, 1H), 4.86 (dd, *J* = 8.4 Hz, 21.9 Hz, 1H), 5.65 (d, *J* = 8.4 Hz, 1H), 8.22-8.28 (m, 4H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –164.7 (d, *J* = 30.7 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2CO$) δ 137.6, 137.3, 173.2, 135.5, 124.5, 12.3, 108.0 (q, *J* = 276.1 Hz), 70.8 (q, *J* = 18.1 Hz), 31.3, 21.3, 15.8 (q, *J* = 6.0 Hz); **HRMS** (ESI) found: m/z 331.0086 $[M+Na]^+$; calcd. for $C_{11}H_{13}FO_5S_2$+Na 331.0086; **IR** (KBr): ν 3471, 2983, 1443, 1359, 1344, 1192, 1160, 1124, 769, 554 cm^{-1}; **HPLC** (DAICEL Chiralpak IC, *n*-hexane / *i*-PrOH (IPA) = 85:15, 1.0 mL / min, 254 nm) t_R (major) = 9.8 min, t_R (minor) = 8.7 min.

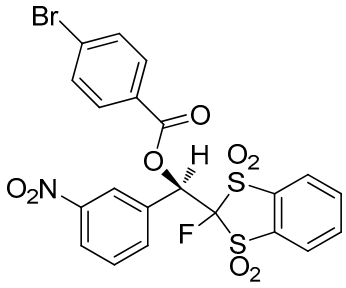
4 A large-scale addition, Further transformation, and X-ray analysis:



To a solution of catalyst **VII** (0.05 mmol) and FBDT (0.5 mmol) in toluene (5 mL) was added $Ti(O\text{-}^{i}Pr)_4$ (1.15 mmol) under N_2. Then the correspounding 3-nitrobenzaldehyde (0.75mmol) was added to the mixture. The resulting mixture was stirred at room temperature until the reaction completed (detected by TLC). The reaction system was concentrated under reduced pressure and purification by column chromatography on silica gel (*n*-hexane / ethyl acetate =8:1–1.5:1) afforded the product **2e** as white soild (172.4 mg, 89% yield and 96% ee).



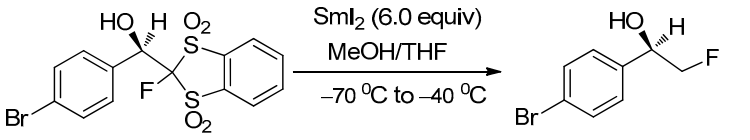
To a solution of **2e** (0.39mmol, 150 mg) in CH_2Cl_2 (10 mL) was directly dropped a mixture of 4-bromobenzoyl chloride (103.1mg, 0.47 mmol, 1.2 equiv) and Et_3N (108.6 μL, 0.78 mmol, 2.0 eqiuv) in CH_2Cl_2 (5 mL) at 0 ^{o}C, then stirring was maintained overnight at room temperature. The resulting mixture was poured into water and extracted with ethyl acetate. The organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel to afford the product **4**. Recrystallization of this product from acetone/*n*-hexane furnished acicular crystal.



(*R*)-(2-fluoro-1,1,3,3-tetraoxidobenzodithiol-2-yl)(3-nitrophenyl)methyl-4-bromo benzoate (4)

white solid, mp 240–242 °C, 99% ee, $[\alpha]_D^{25}$ –9.3 (*c* 0.2, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 7.29 (d, *J* = 25.2 Hz, 1H), 7.82-7.90 (m, 2H), 8.11 (d, *J* = 7.8 Hz, 2H), 8.23-8.42 (m, 7H), 8.60 (s, 1H); **^{19}F NMR** (282 MHz, $(CD_3)_2CO$) δ –161.5 (d, *J* = 25.7 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2CO$) δ 163.9, 149.4, 138.4, 138.2, 136.1, 135.8, 135.3, 133.2, 132.8, 131.6, 130.7, 128.0, 126.4, 125.1, 124.9, 124.6, 104.5 (d, *J* = 276.1 Hz), 70.9 (d, *J* = 16.6 Hz); **HRMS** (ESI) found: m/z 591.9148 $[M+Na]^+$; calcd. for $C_{21}H_{13}BrFO_8S_2$+Na 591.9150; **IR** (KBr): ν 3091, 2982, 1741, 1590, 1536, 1364, 1164, 1089, 1011, 586 cm^{-1}; **HPLC** (DAICEL Chiralpak IA, *n*-hexane / *i*-PrOH (IPA) = 60:40, 1.0 mL / min, 254 nm) t_R (major) = 32.8 min, t_R (minor) = 21.4 min.

5 Procedure for the desulfonylation of 1,2-Adducts 2c:

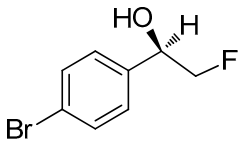


2c, 80% ee

3c, 73% yield, 80% ee

To a solution of 1,2-adduct (30.0 mg, 0.07 mmol) in MeOH (3.0 mL), SmI_2 in THF (4.2 ml, 0.42mmol) was added at –70 °C under nitrogen atmosphere and warmed to –40 °C. After the starting material was completely consumed, the reaction mixture was quenched with saturated NH_4Cl solution and saturated $Na_2S_2O_4$ solution. The aqueous layer was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was

purified by silica gel chromatography eluting with ethyl acetate in hexane (1 : 4) to give **3c** as colorless oil.



(*R*)-1-(4-bromophenyl)-2-fluoroethanol (3c)

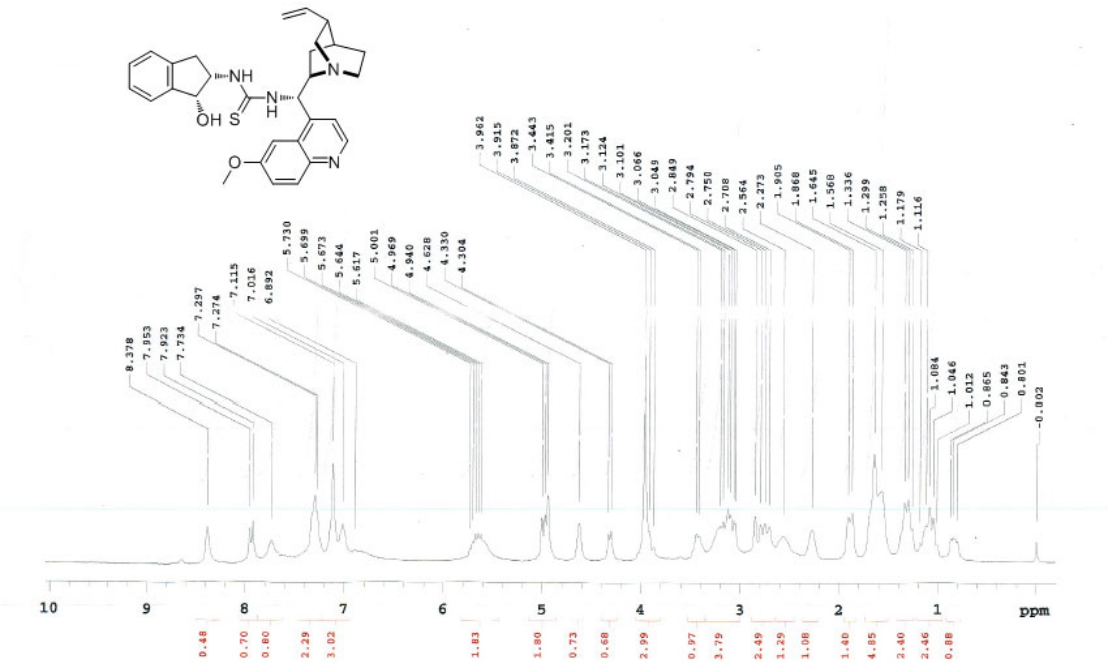
11.2 mg, colorless oil, 73%, 80% ee, $[\alpha]_D^{25}$ −10.5 (*c* 0.5, $(CH_3)_2CO$); **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 4.31-4.56 (m, 2H), 8.11 (d, *J* = 7.8 Hz, 2H), 4.96 (s, 2H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 7.8 Hz, 2H); **^{19}F NMR** (282 MHz, $CDCl_3$) δ –221.7 (dt, *J* = 13.3 Hz, 47.1 Hz, 1F); **^{13}C NMR** (150.9 MHz, $(CD_3)_2CO$) δ 140.9 (d, *J* = 7.5 Hz), 132.0, 129.4, 121.8, 87.7 (d, *J* = 175.0 Hz), 72.2 (d, *J* = 19.6 Hz); **HRMS** (ESI) found: m/z 216.9669 $[M–H]^-$; calcd. for $C_{21}H_{13}BrFO_8S_2$–H 216.9665; **IR** (KBr): ν 3394, 2952, 1593, 1488, 1403, 1090, 1010, 896, 822, 526 cm^{-1}; **HPLC** (DAICEL Chiralpak IF, *n*-hexane / *i*-PrOH (IPA) = 99:1, 1.0 mL / min, 254 nm) t_R (major) = 43.4 min, t_R (minor) = 39.9 min.

5. References:

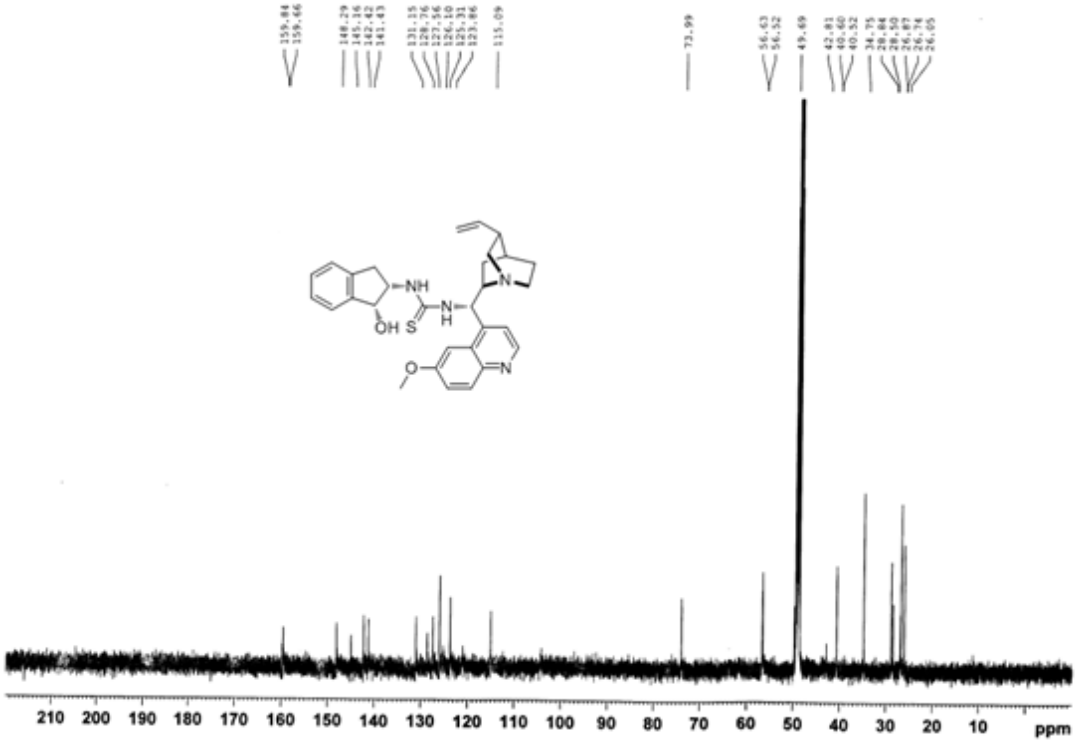
1 (a) H. Brunner, P. Schmidt, *Eur. J. Org. Chem.* **2000**, 2119–2133; (b) W. Chen, W. Du, Y.-Z. Duan, Y. Wu, S.-Y. Yang, Y-C. Chen, *Angew. Chem. Int. Ed.*, **2007**, *46*, 7667–7670; (c) P. S. Mukund, I. Kennosuke, *J. Am. Chem. Soc.* **2007**, 129, 8064–8065.

2 T. Furukawa, Y. Goto, J. Kawazoe, E. Tokunaga, S. Nakamura, Y. Yang, H. Du, A. Kakehi, M. Shiro, N. Shibata, *Angew. Chem. Int. Ed.*, **2010**, *49*, 1642–1647.

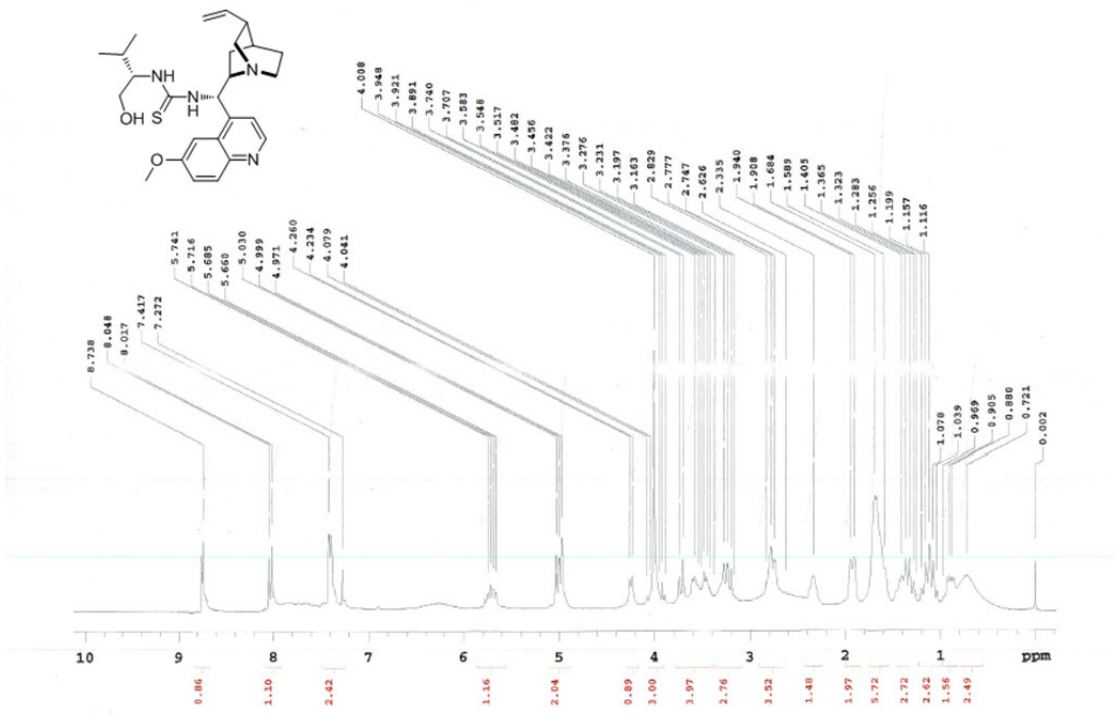
6 NMR Spectra and HPLC Charts for the Addition Adducts:



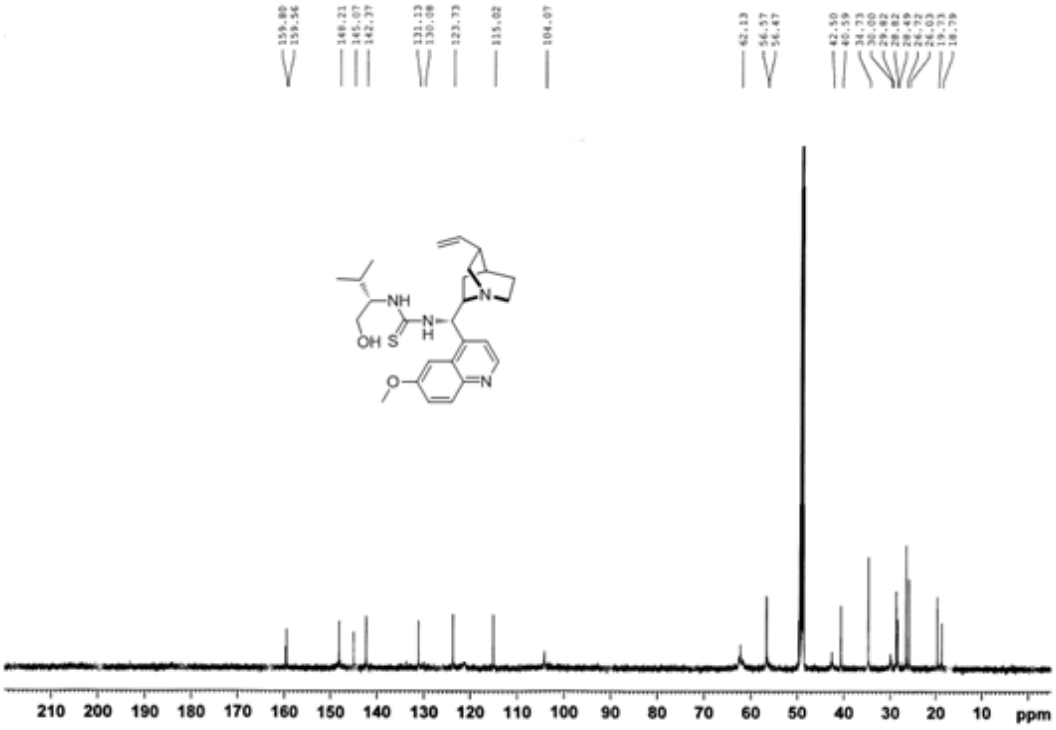
IV ^{1}H NMR



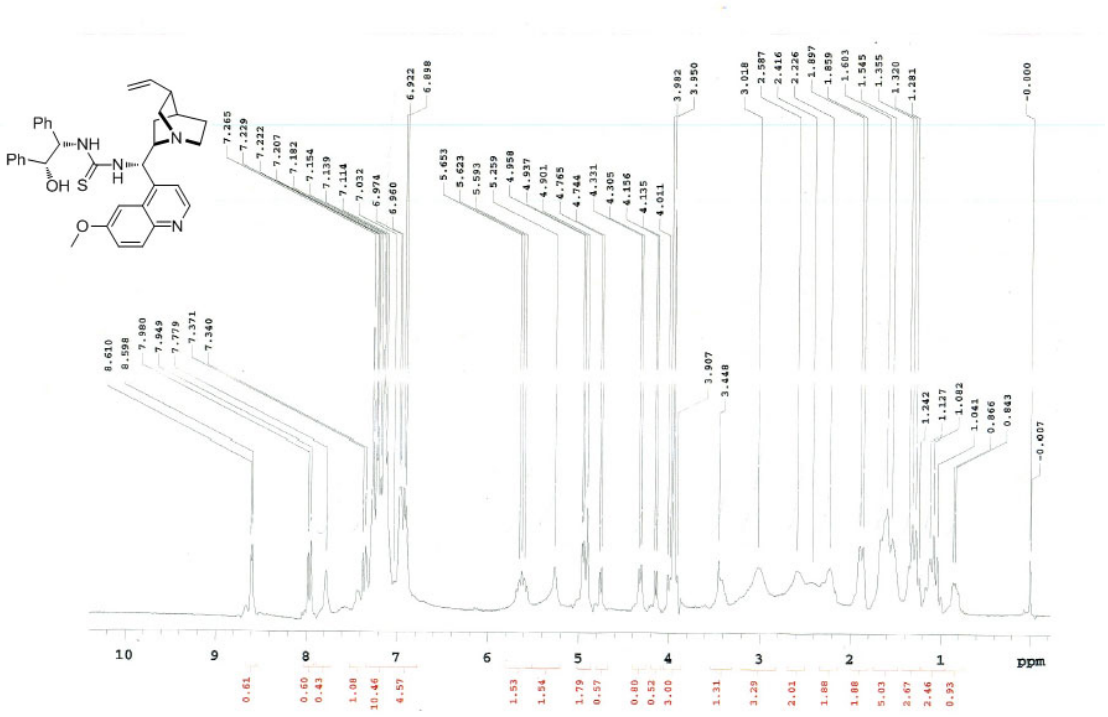
IV ^{13}C NMR



V ^{1}H NMR



V ^{13}C NMR



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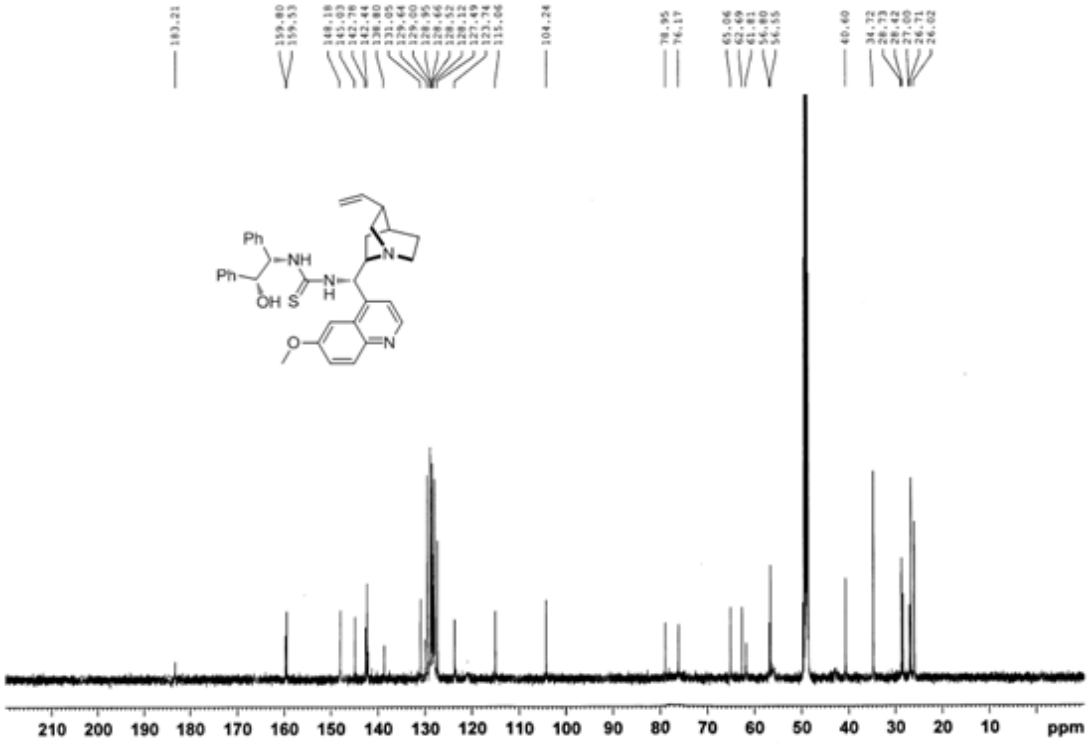
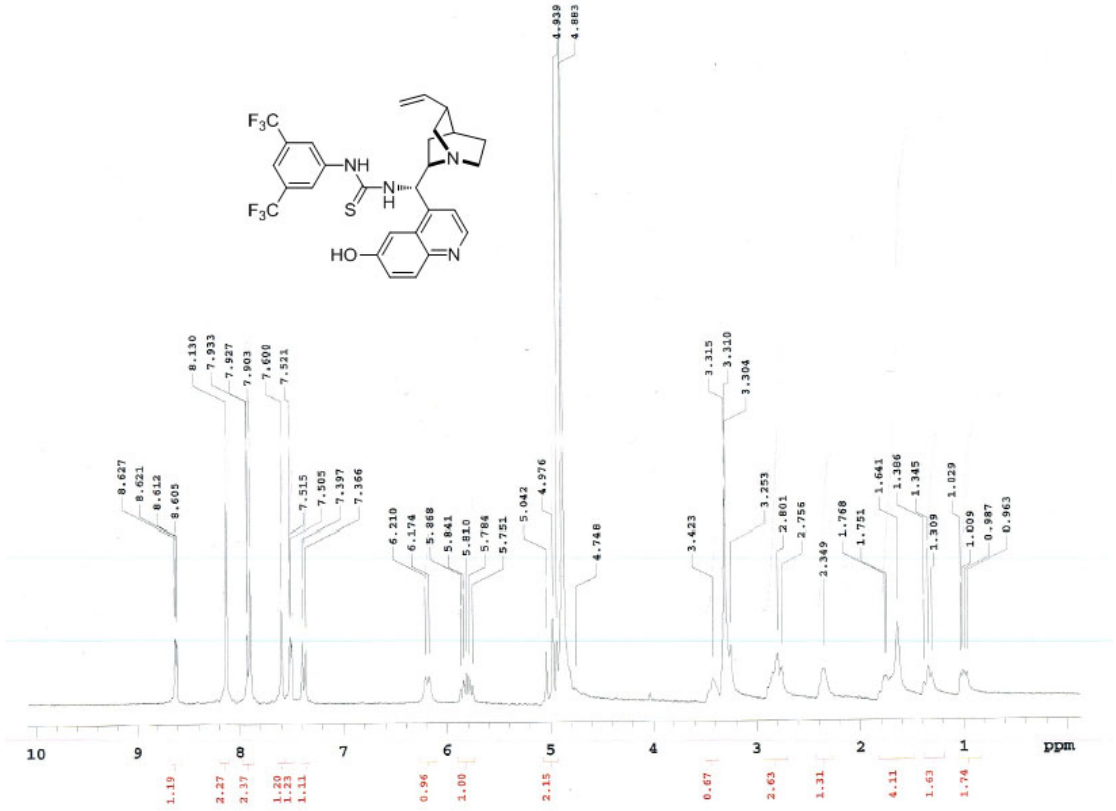
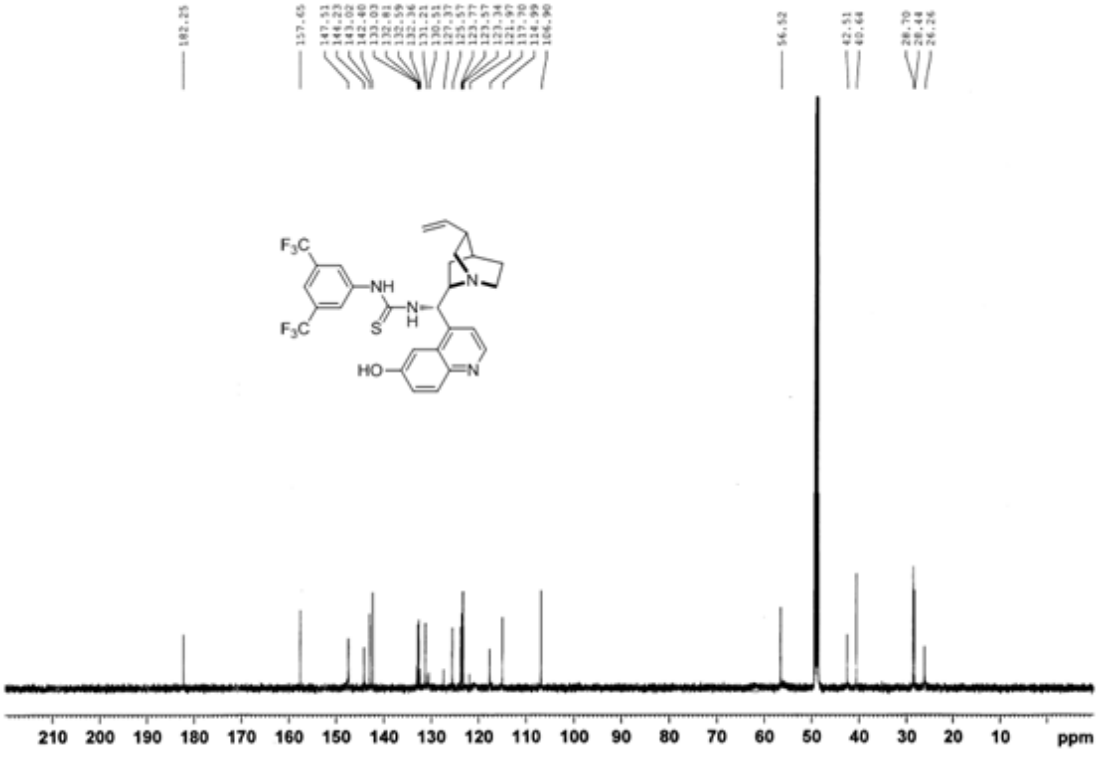


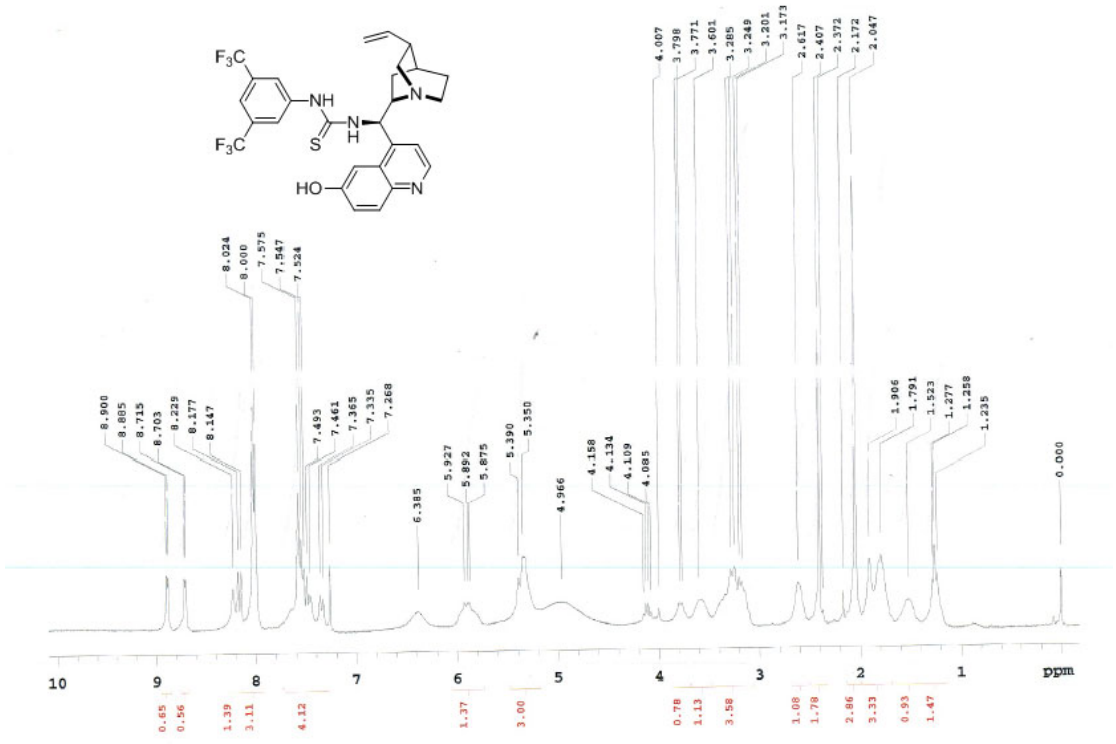
VI ^{13}C NMR



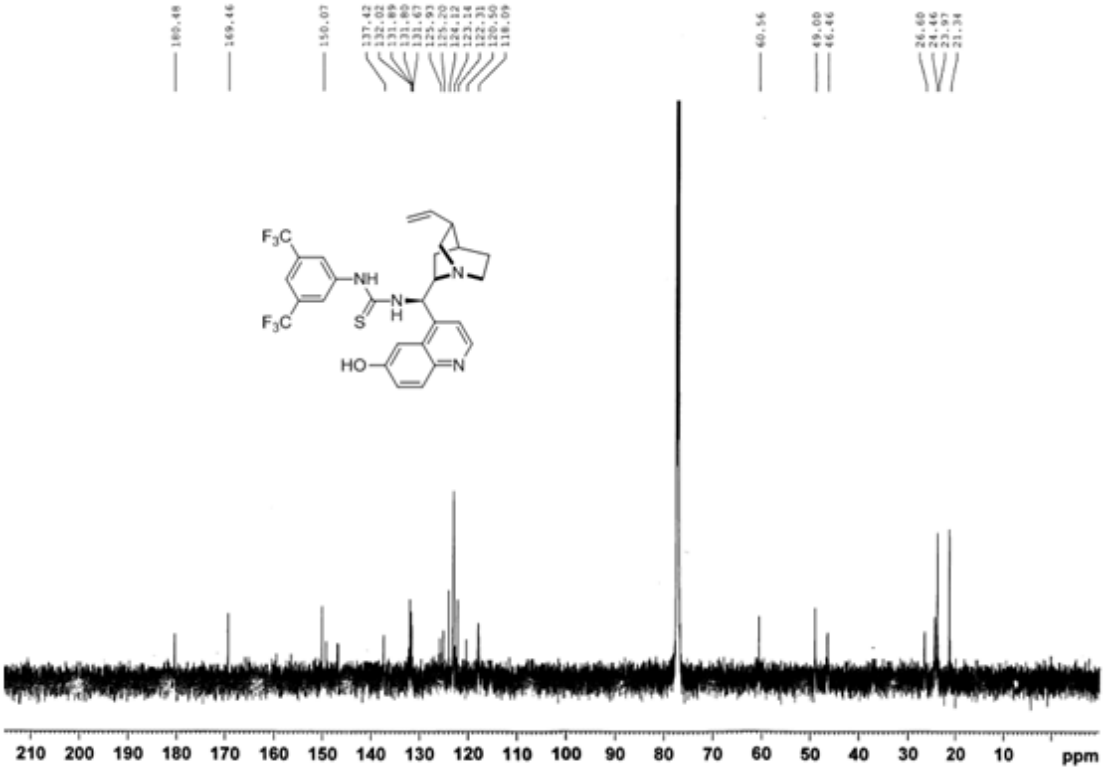
VII ^{1}H NMR



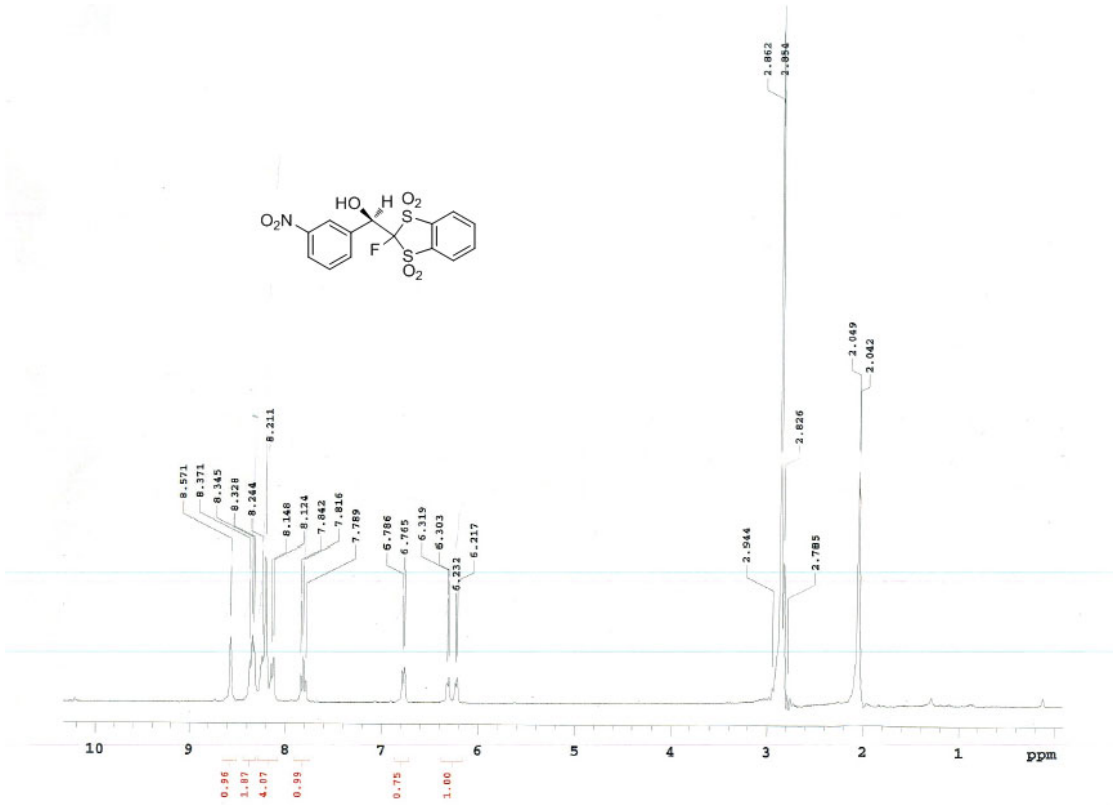
VII ^{13}C NMR



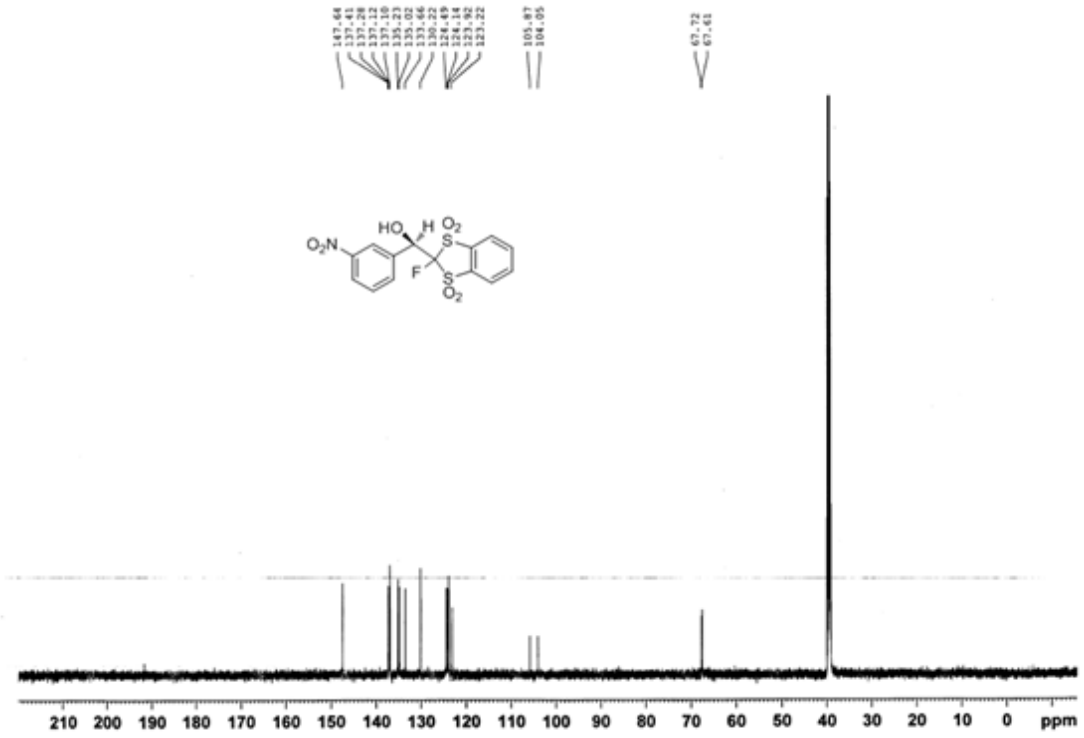
VIII ^{1}H NMR



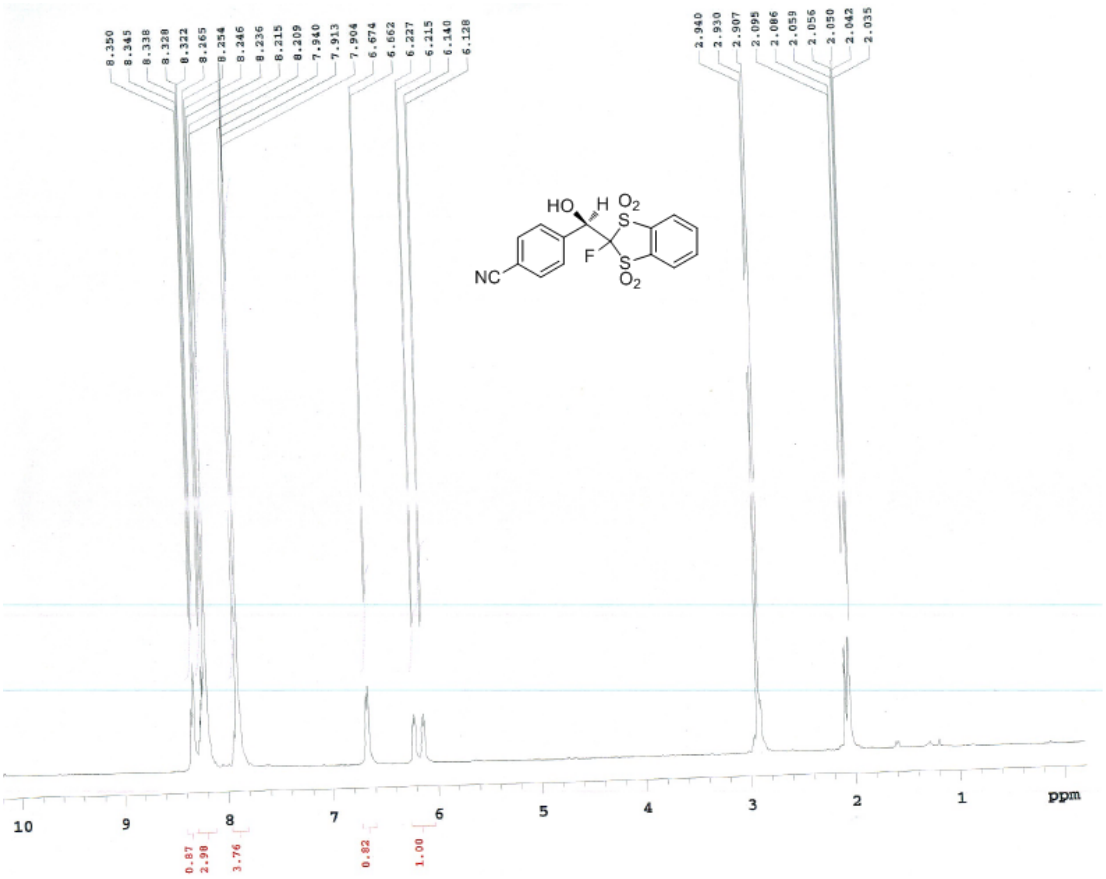
VIII ^{13}C NMR



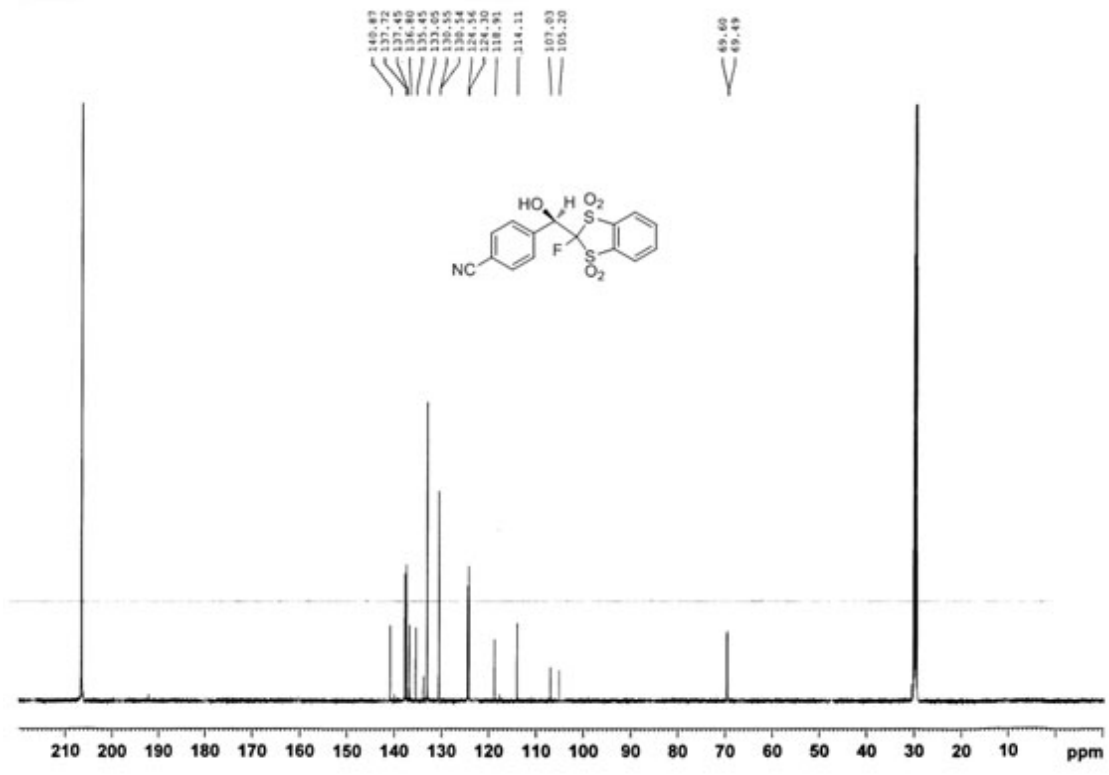
2e ^{1}H NMR



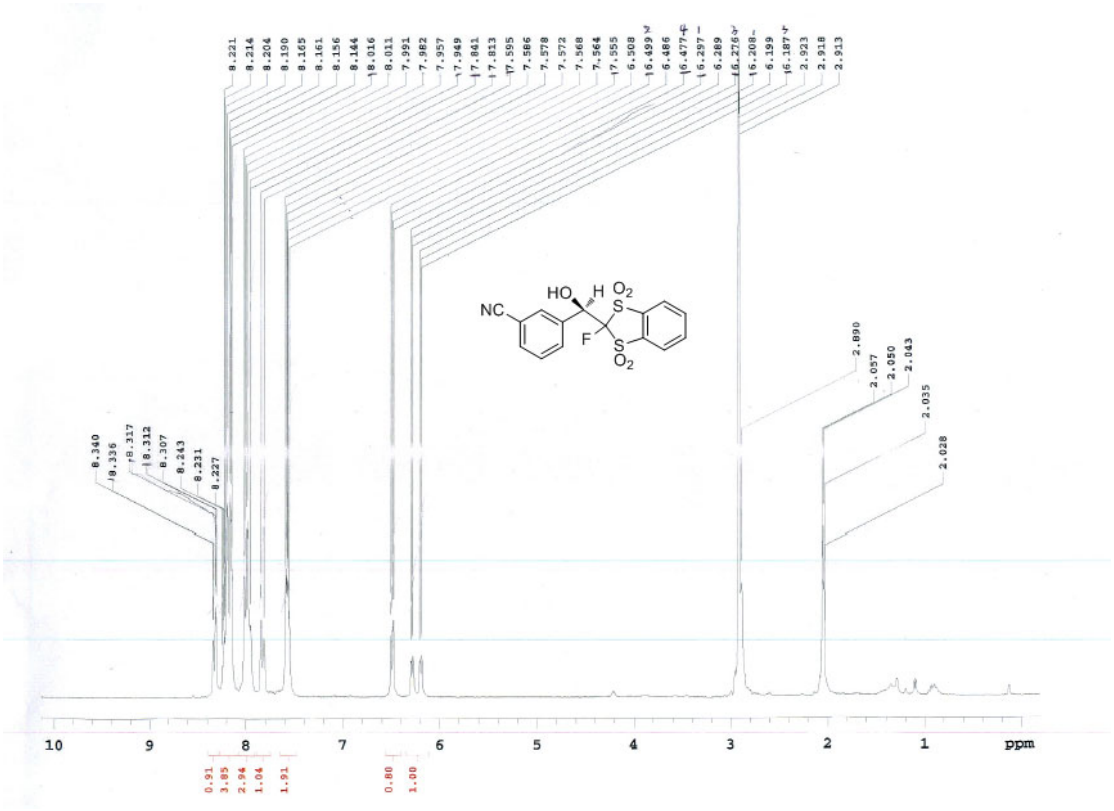
2e ^{13}C NMR



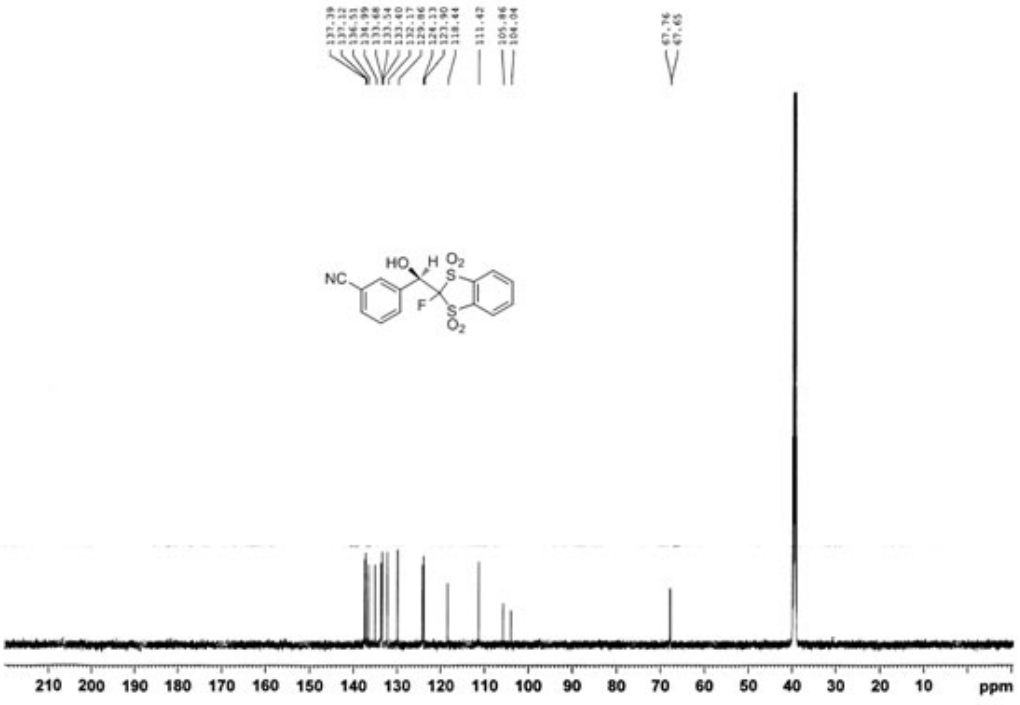
2f ^{1}H NMR



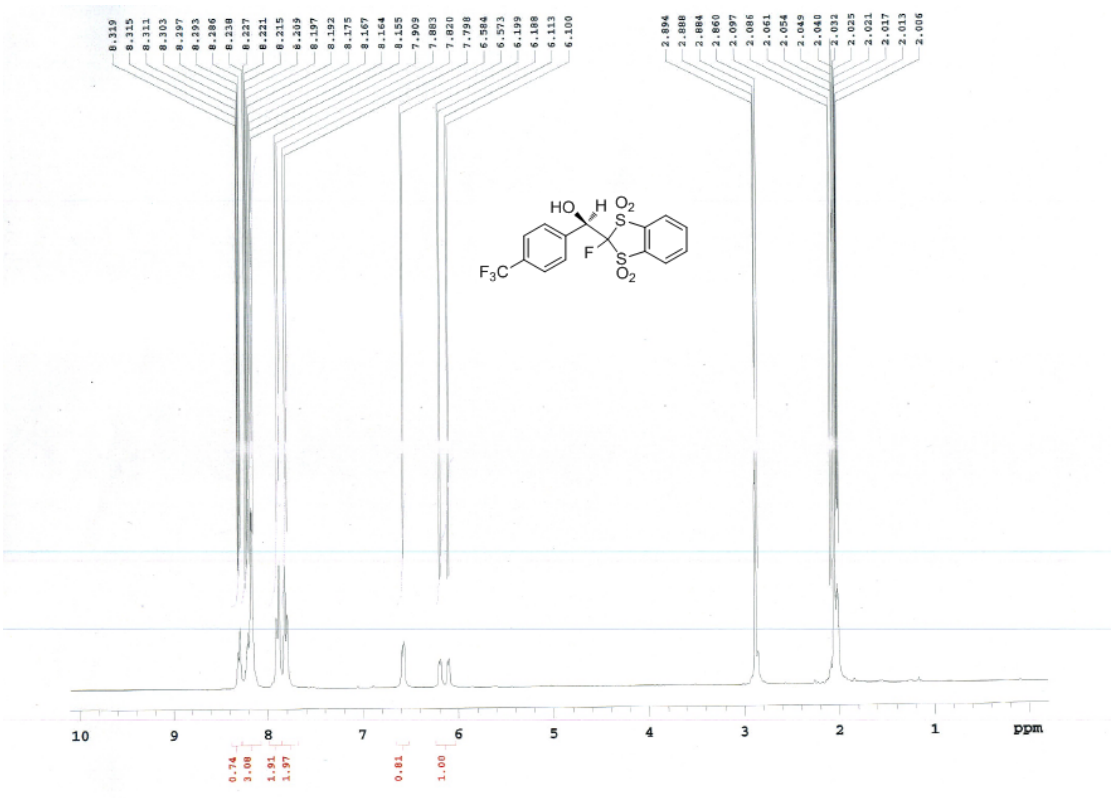
2f ^{13}C NMR



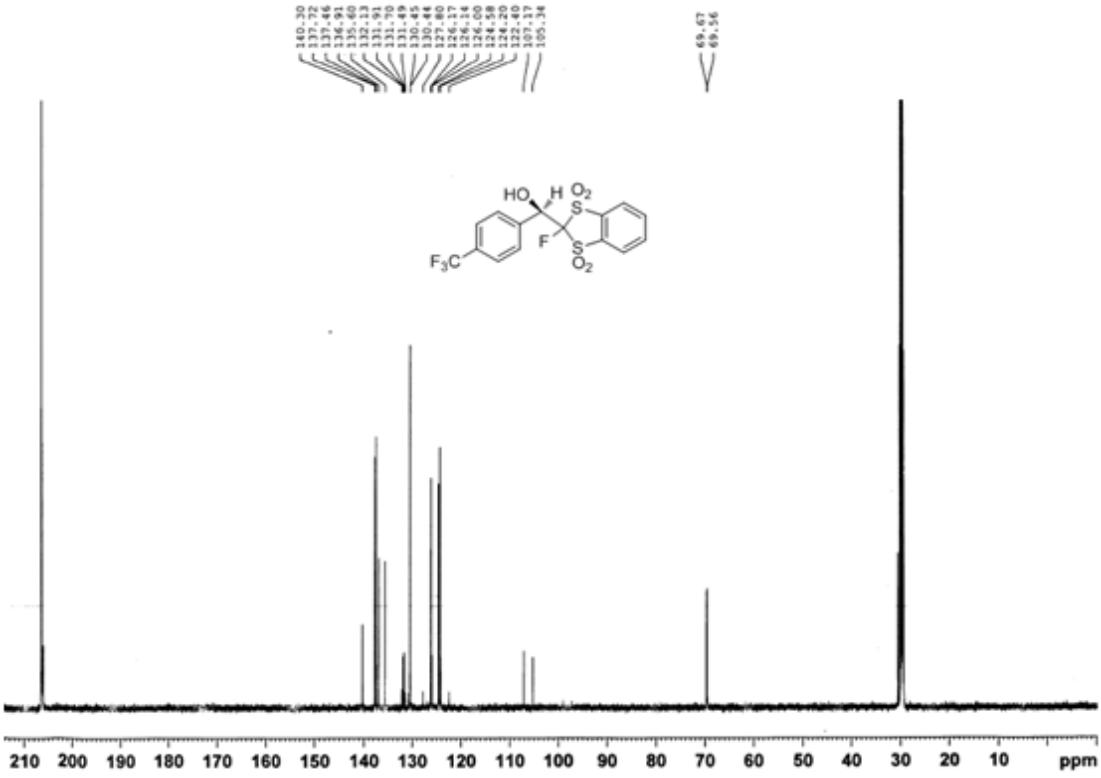
2g ^{1}H NMR



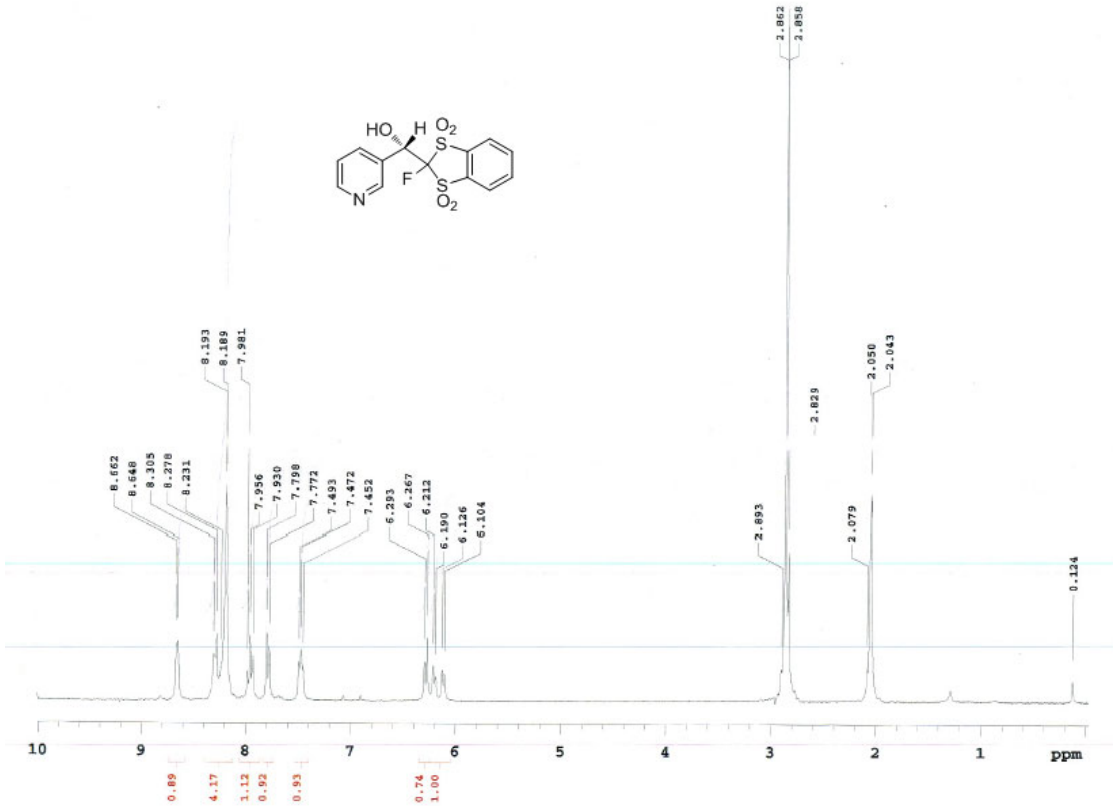
2g ^{13}C NMR



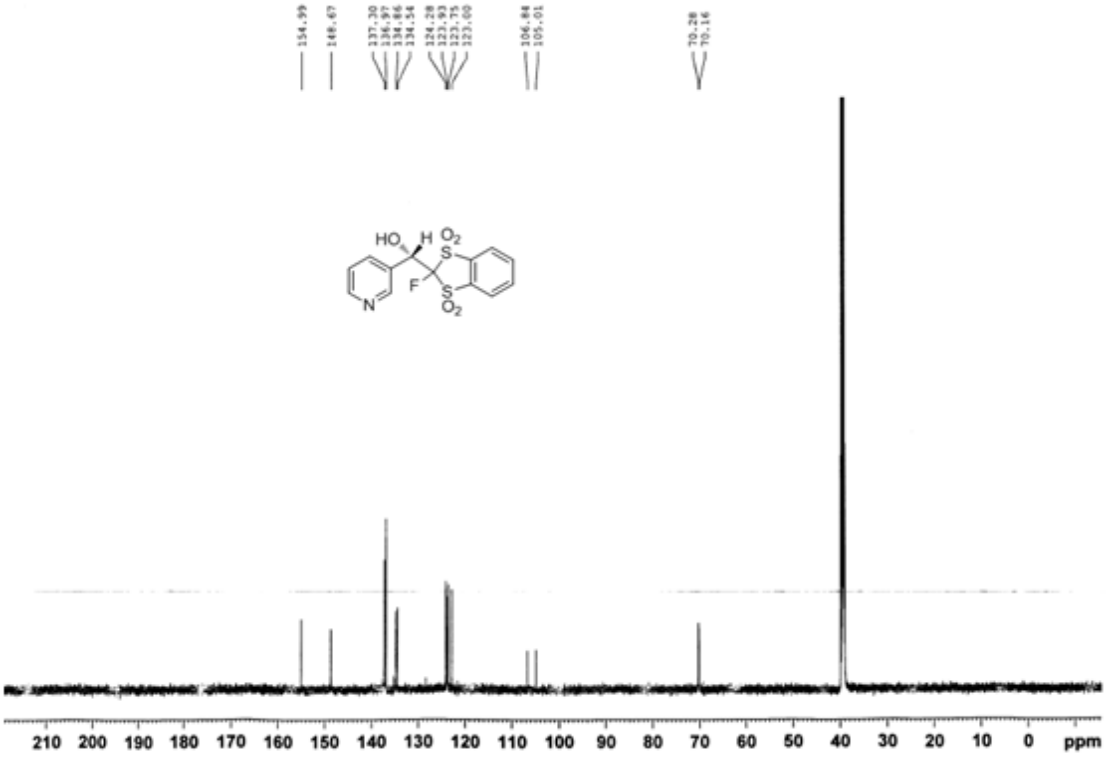
2h ^{1}H NMR



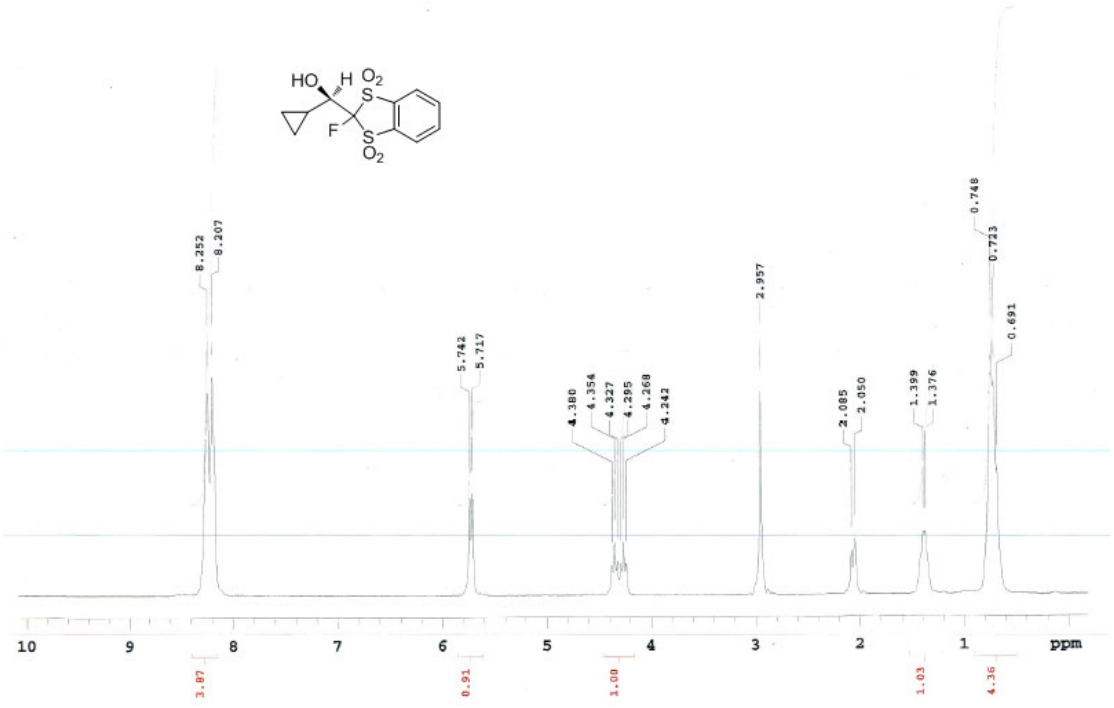
2h ^{13}C NMR



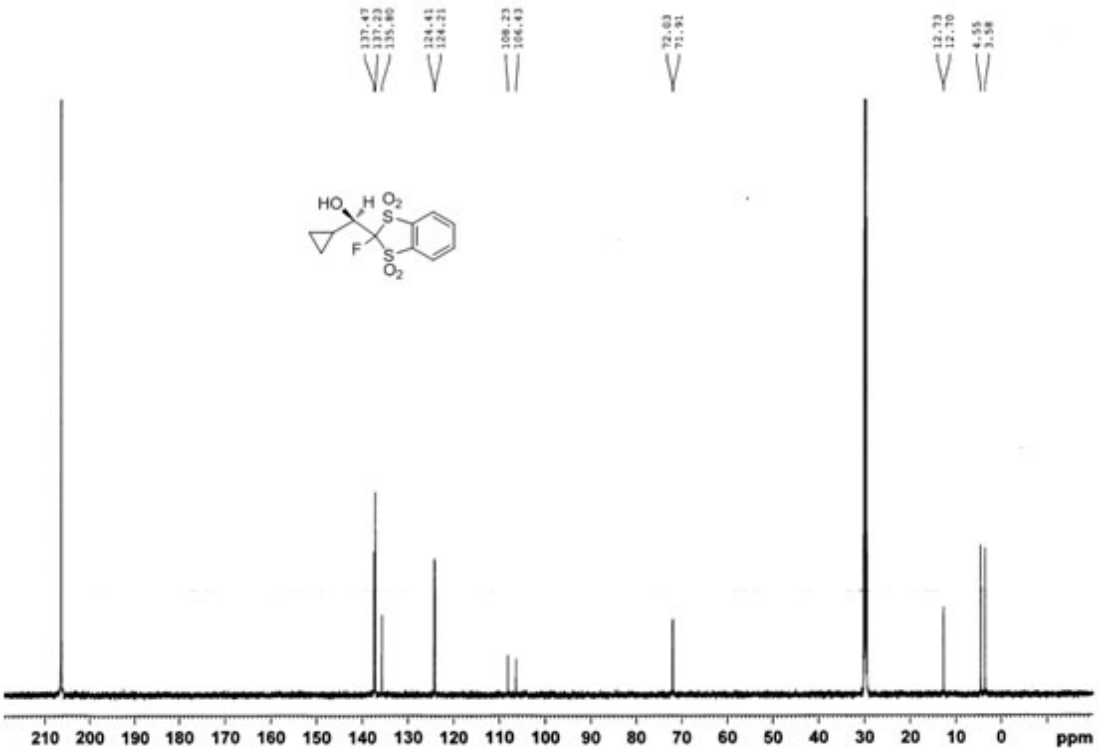
2j ^{1}H NMR



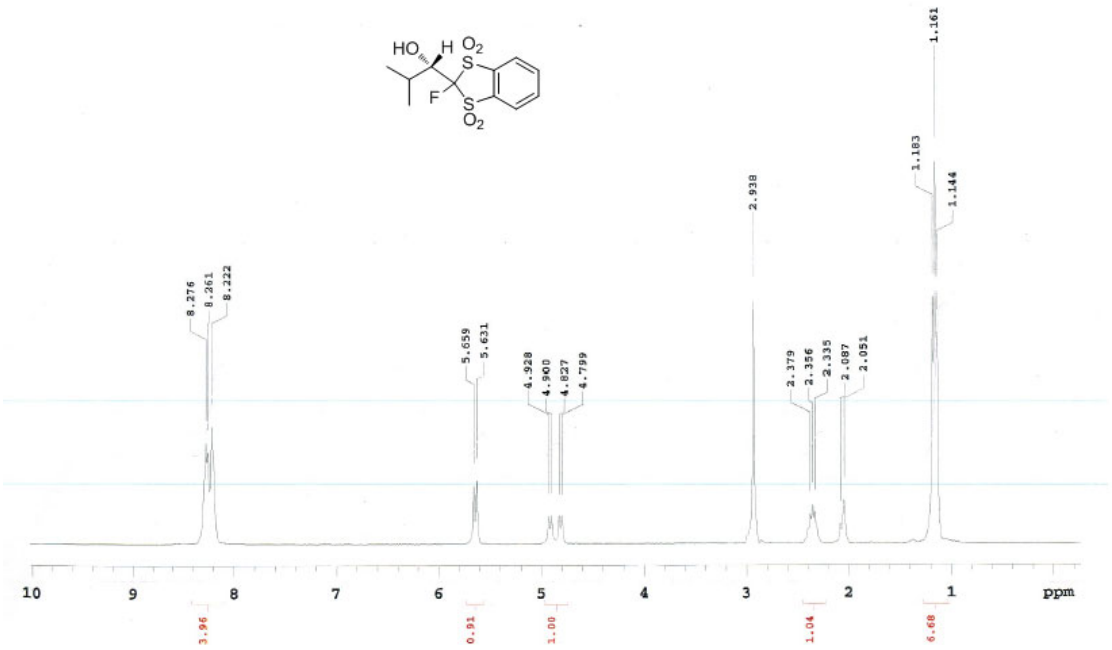
2j ^{13}C NMR



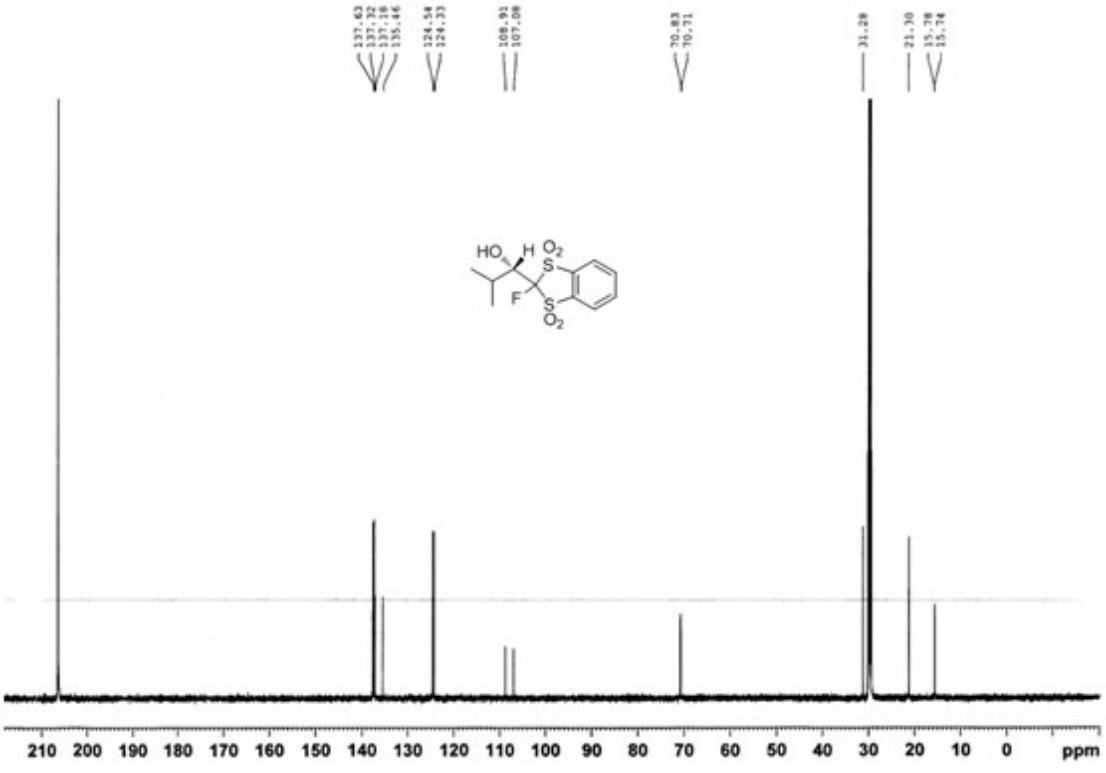
2l ^{1}H NMR



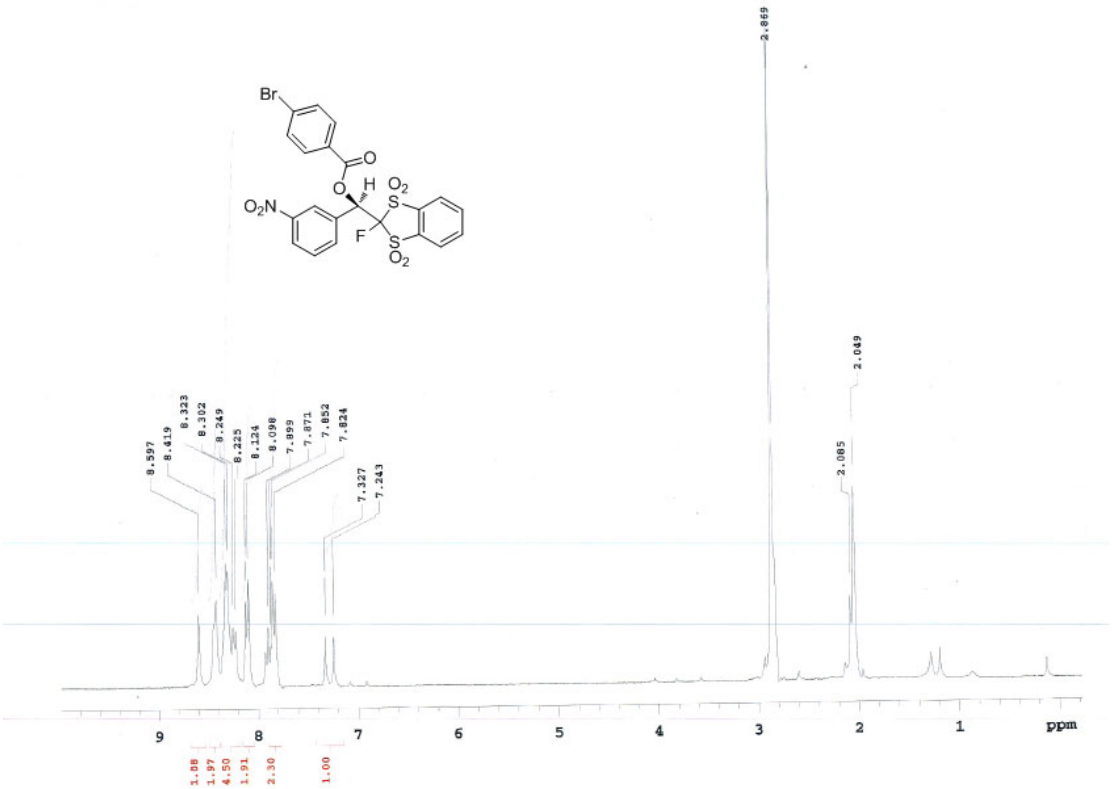
2l ^{13}C NMR



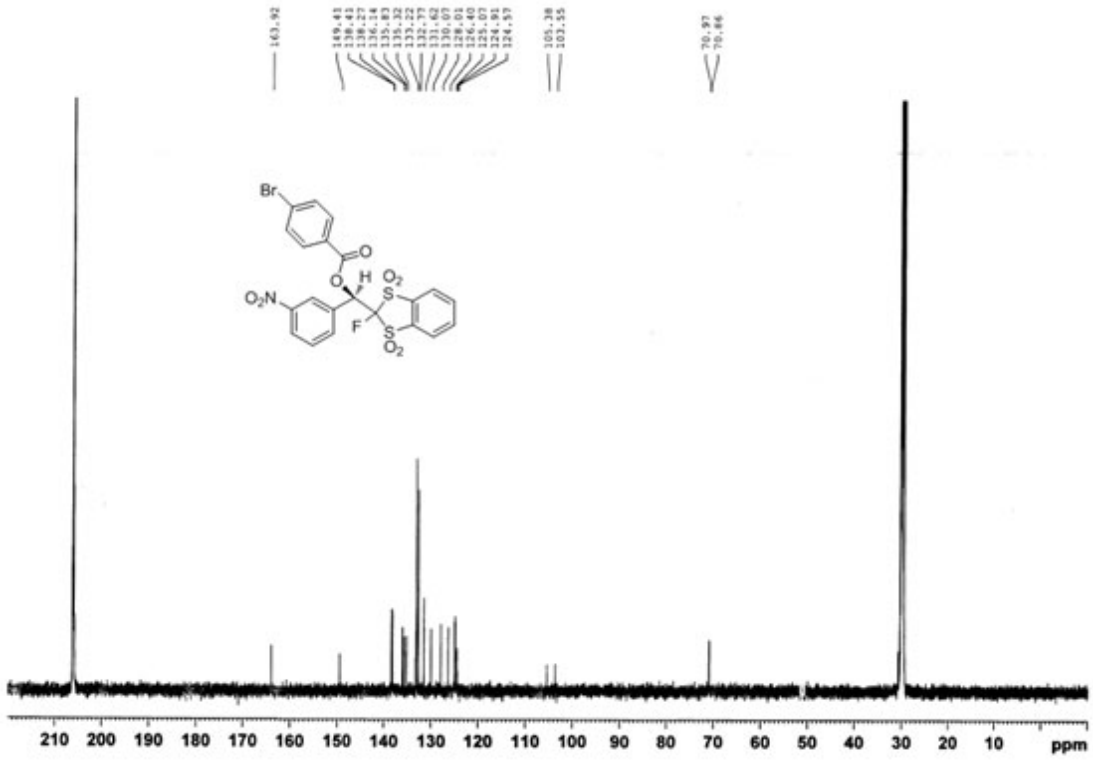
2m ^{1}H NMR



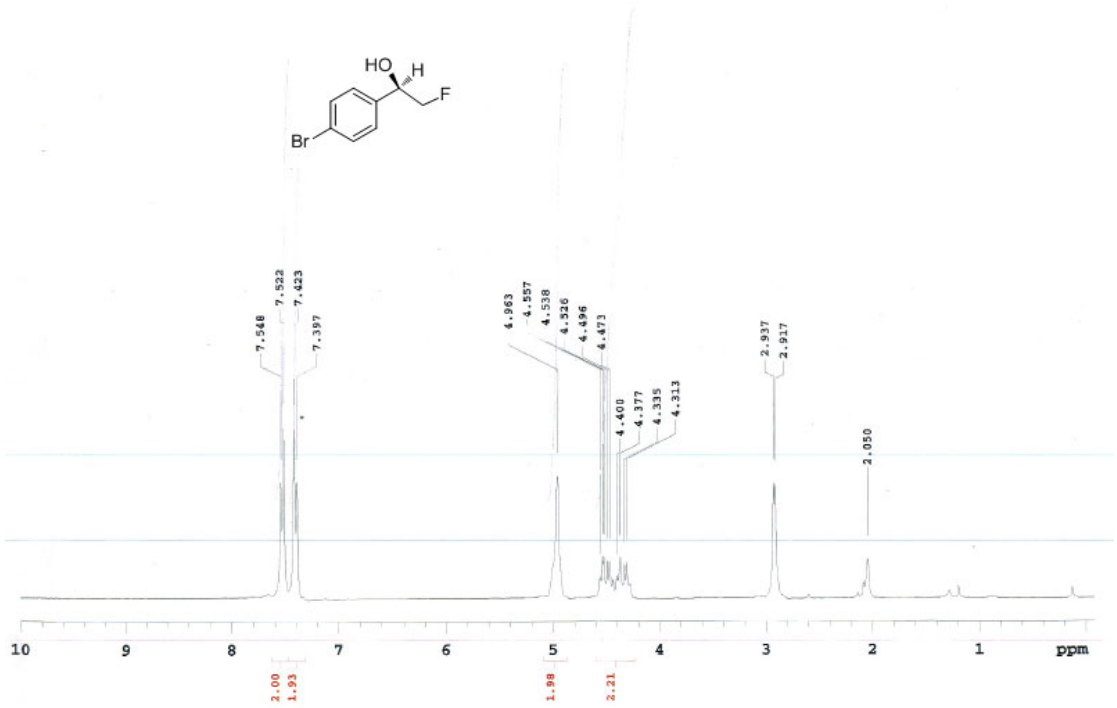
2m ^{13}C NMR



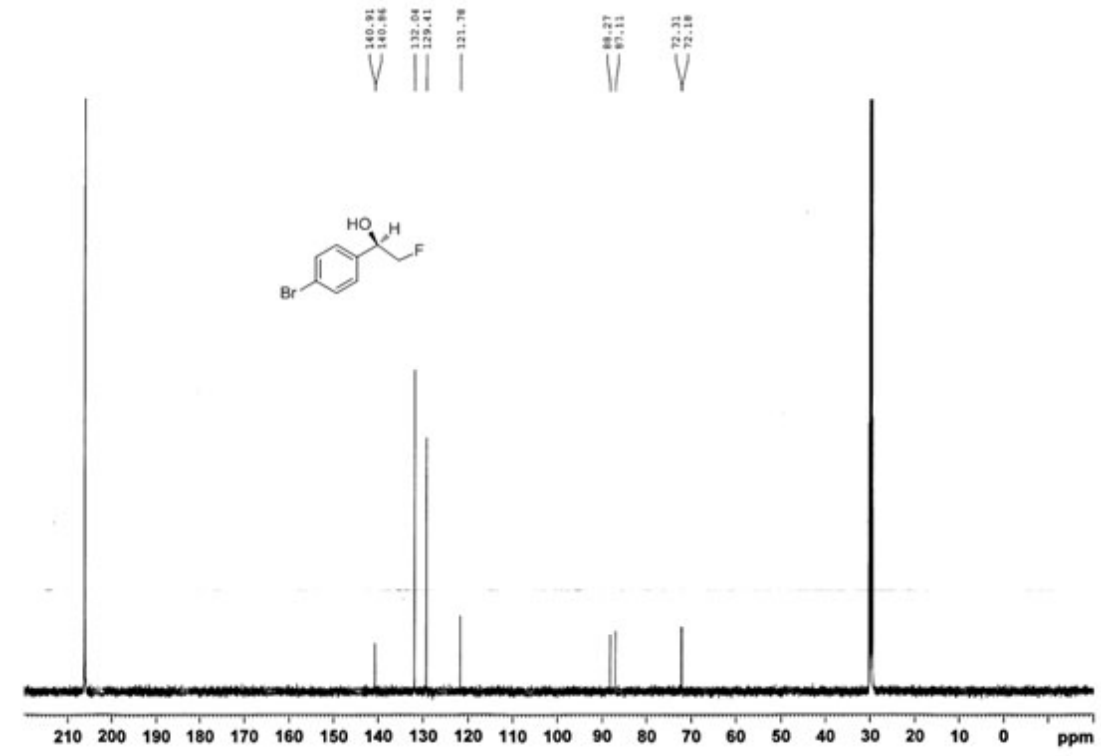
4 ^{1}H NMR



4 ^{13}C NMR

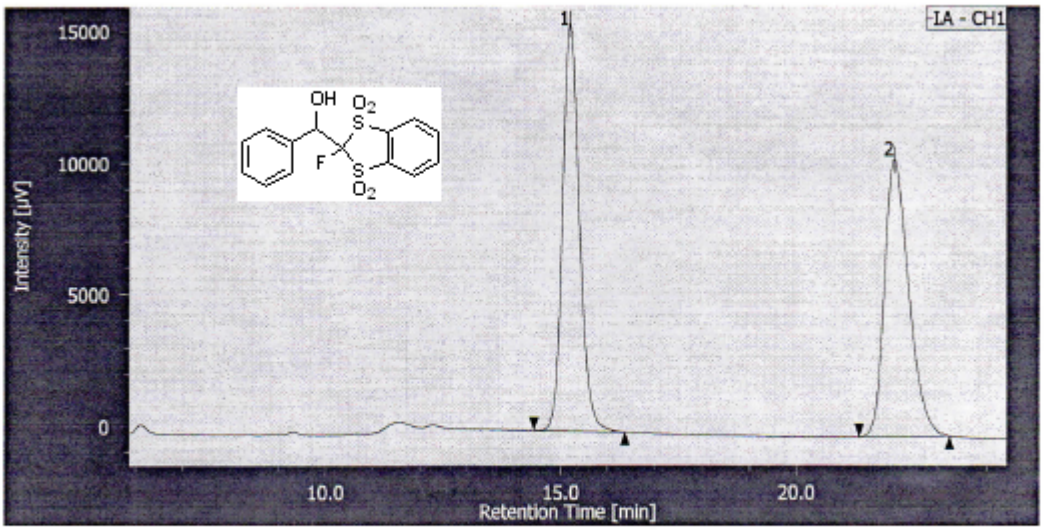


3c ^{1}H NMR



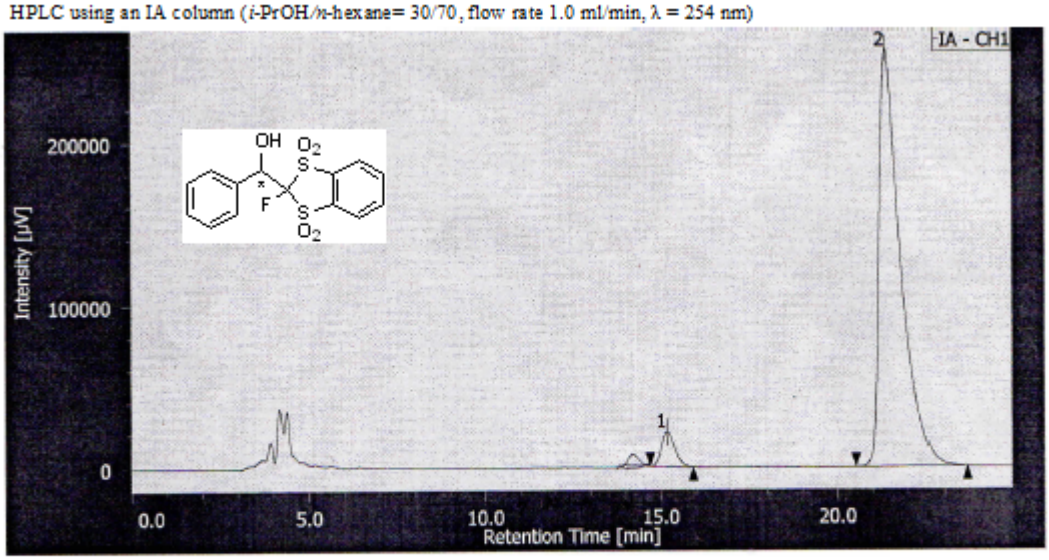
3c ^{13}C NMR

HPLC using an IA column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



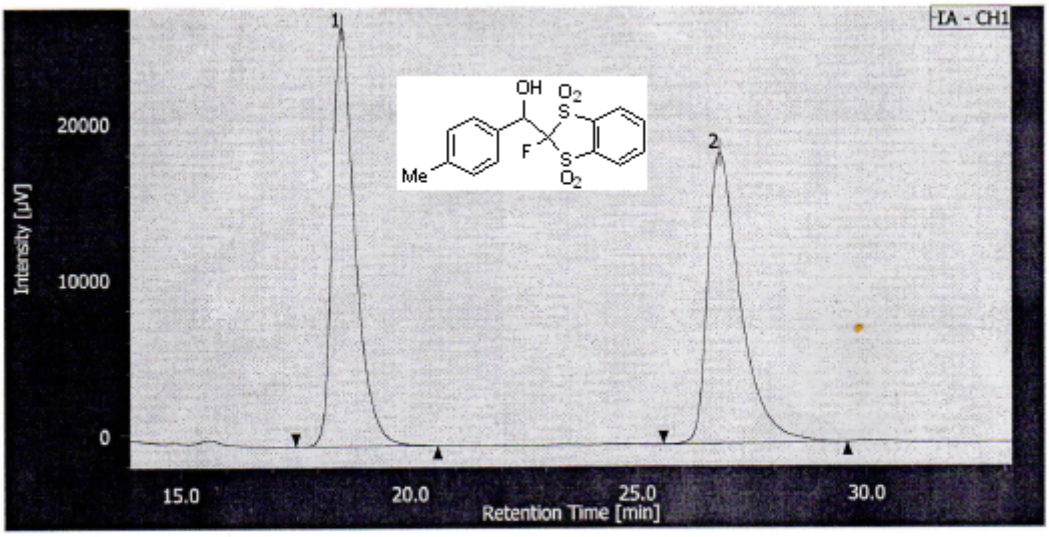
Peak	tR (min)	Area (%)	Height (%)
1	15.192	50.568	59.546
2	22.067	49.432	40.454

HPLC using an IA column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



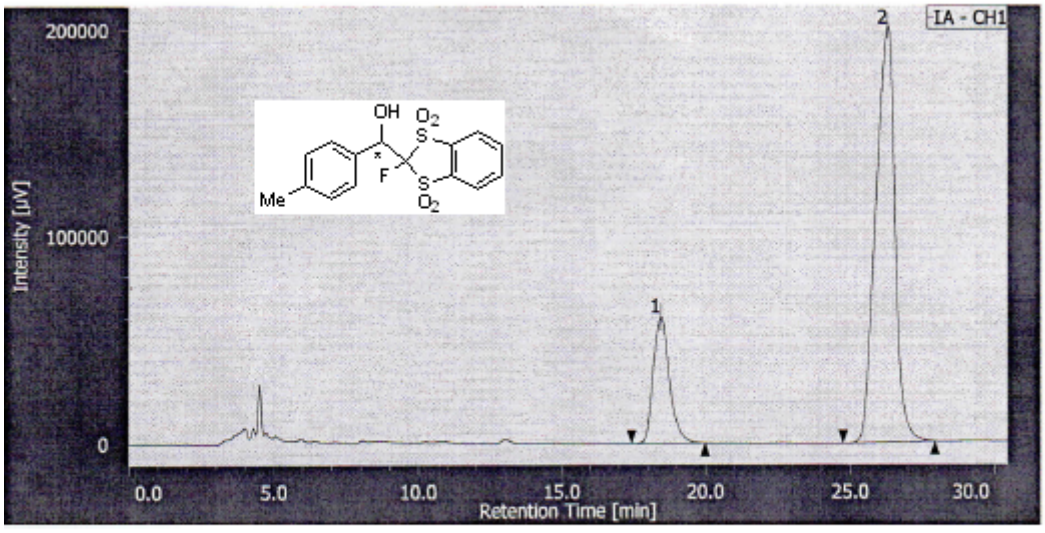
Peak	tR (min)	Area (%)	Height (%)
1	15.175	4.751	7.541
2	21.350	95.249	92.459

HPLC using an IA column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



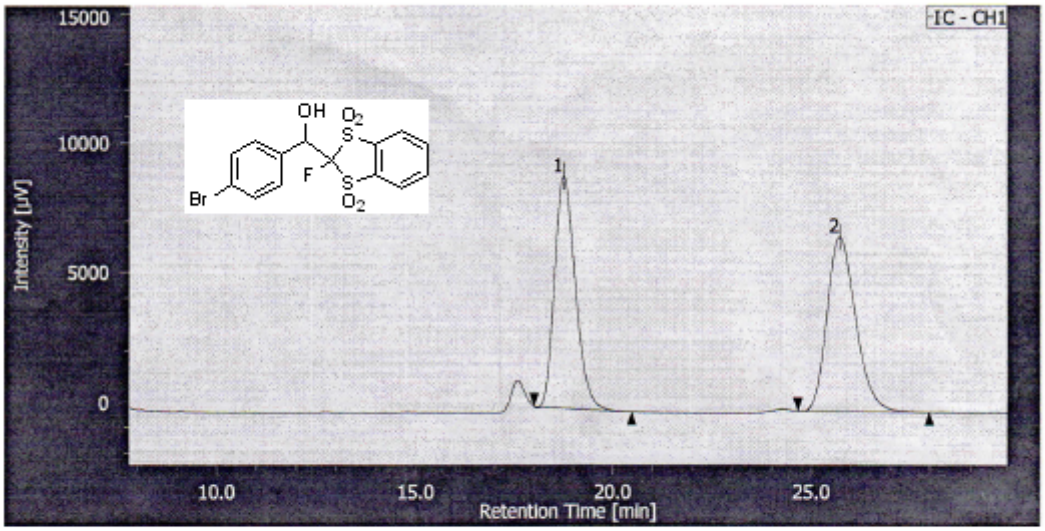
Peak	tR (min)	Area (%)	Height (%)
1	18.508	49.981	58.964
2	26.792	50.019	41.036

HPLC using an IA column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



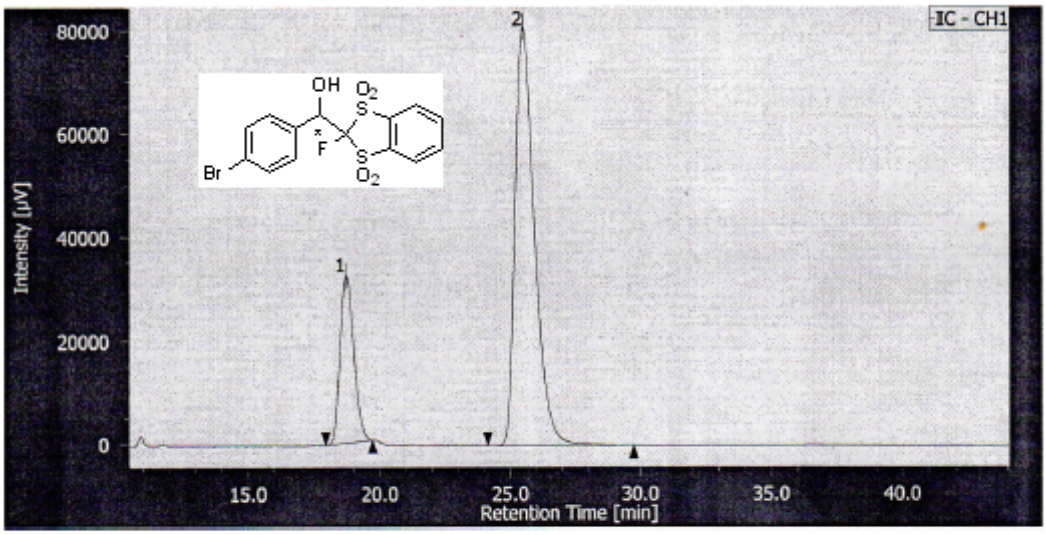
Peak	tR (min)	Area (%)	Height (%)
1	18.458	20.233	23.283
2	26.300	79.767	76.717

HPLC using an IC column (*i*-PrOH/*n*-hexane= 10/90, flow rate 1.0 ml/min, λ = 254 nm)



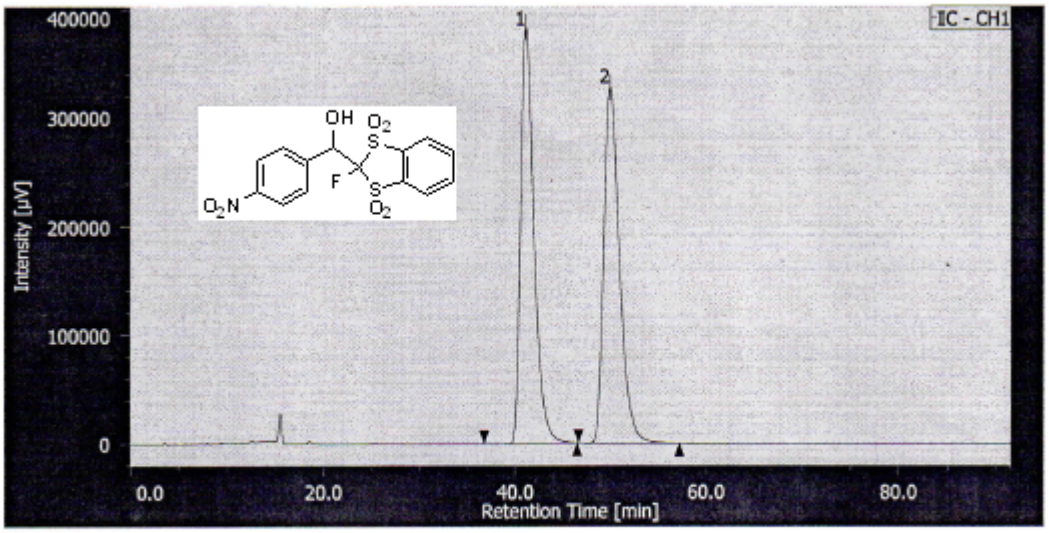
Peak	tR (min)	Area (%)	Height (%)
1	18.742	49.263	57.071
2	25.708	50.764	42.929

HPLC using an IC column (*i*-PrOH/*n*-hexane= 10/90, flow rate 1.0 ml/min, λ = 254 nm)



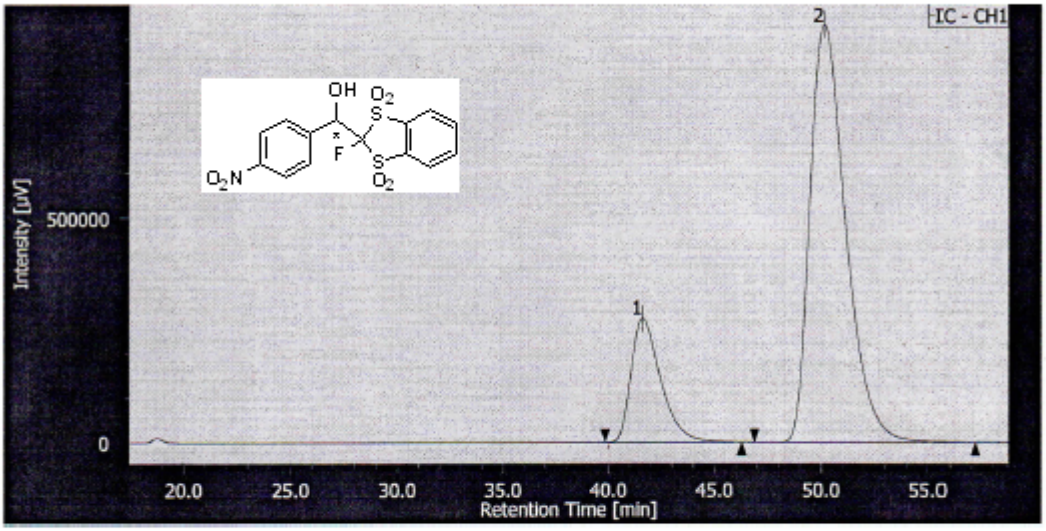
Peak	tR (min)	Area (%)	Height (%)
1	18.708	21.788	28.498
2	25.467	78.212	71.502

HPLC using an IC column (*i*-PrOH/*n*-hexane= 10/90, flow rate 1.0 ml/min, λ = 254 nm)



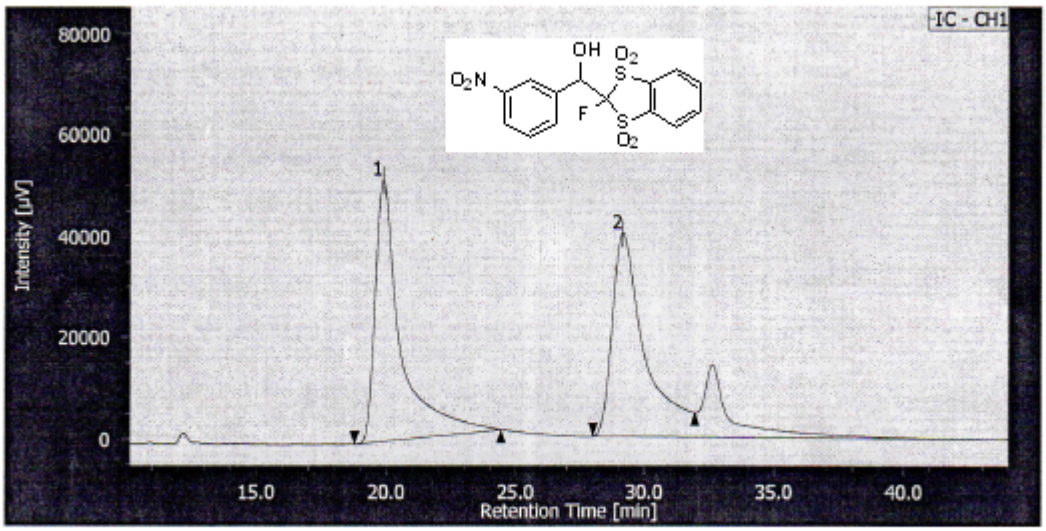
Peak	tR (min)	Area (%)	Height (%)
1	41.108	49.958	54.012
2	49.958	50.042	45.988

HPLC using an IC column (*i*-PrOH/*n*-hexane= 10/90, flow rate 1.0 ml/min, λ = 254 nm)



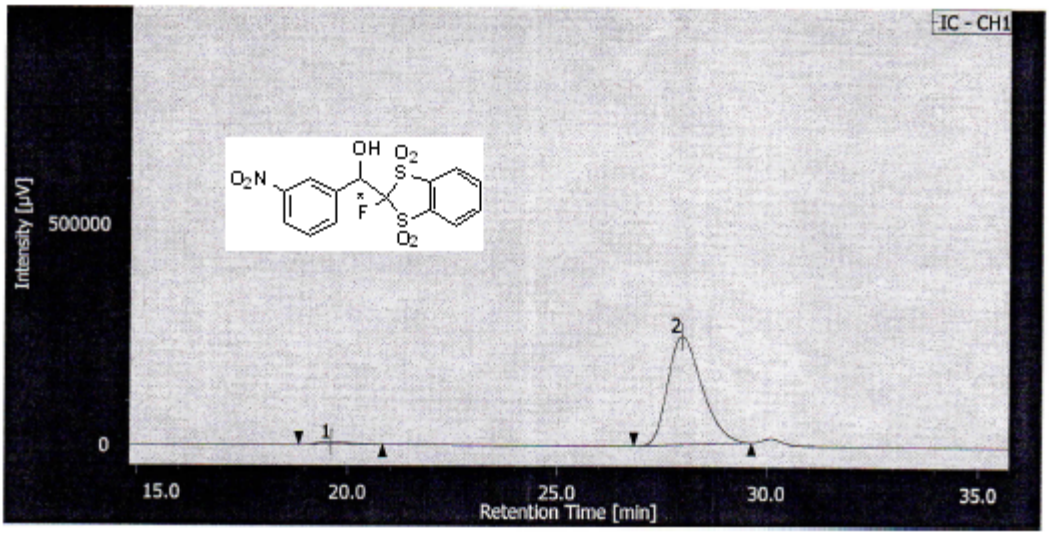
Peak	tR (min)	Area (%)	Height (%)
1	41.608	19.794	22.745
2	50.125	80.206	77.255

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



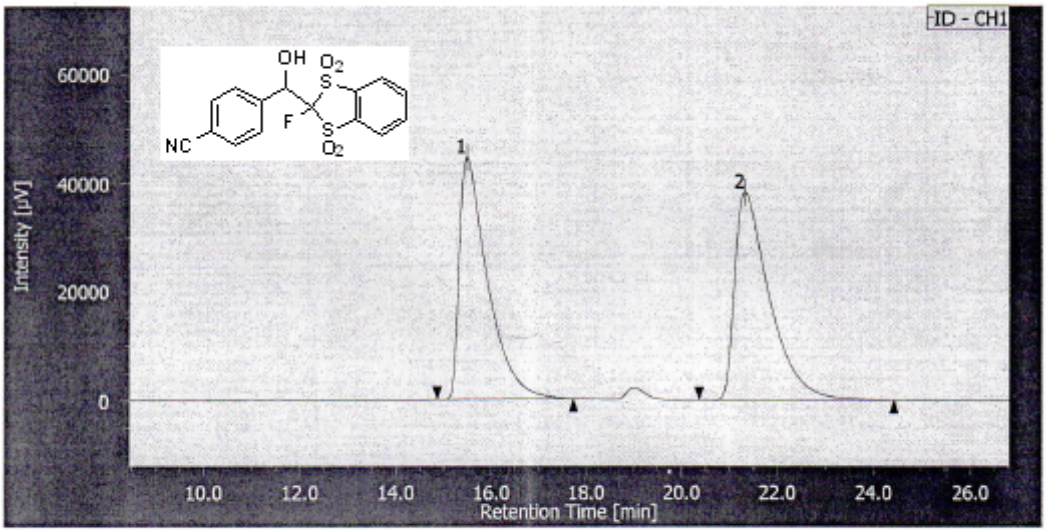
Peak	tR (min)	Area (%)	Height (%)
1	19.142	50.678	56.046
2	27.558	49.322	43.954

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



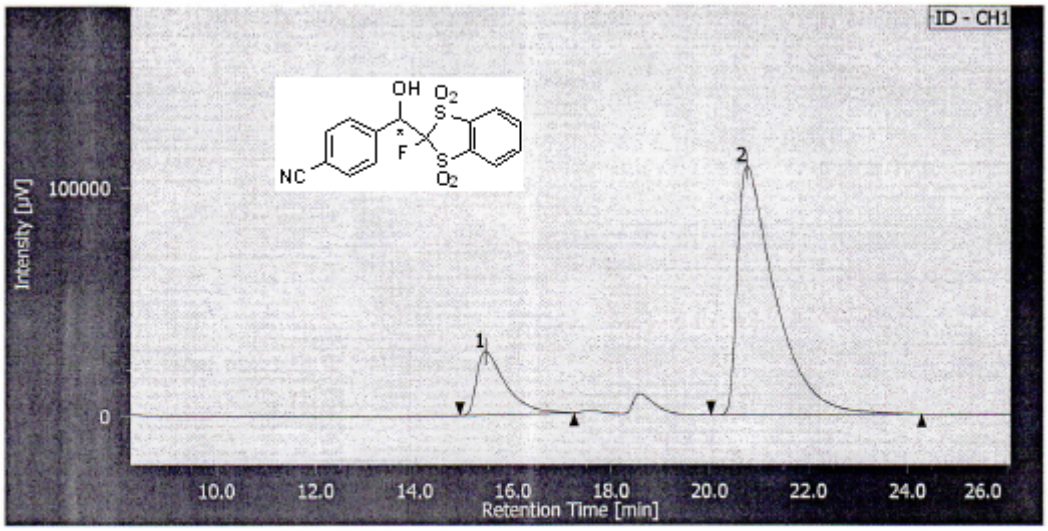
Peak	tR (min)	Area (%)	Height (%)
1	19.617	2.103	2.365
2	27.975	97.897	97.635

HPLC using an ID column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



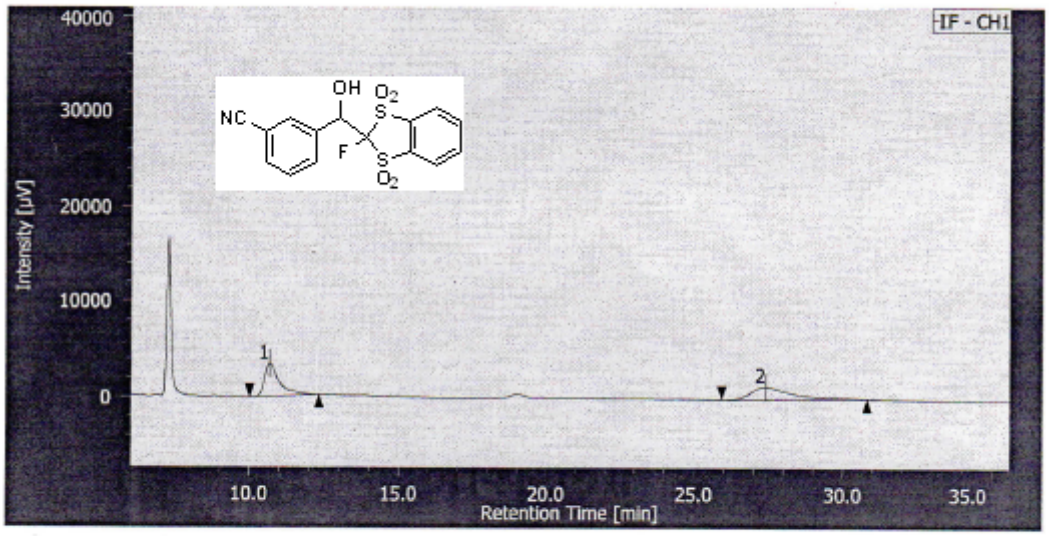
Peak	tR (min)	Area (%)	Height (%)
1	15.483	48.958	53.773
2	21.325	51.042	46.227

HPLC using an ID column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



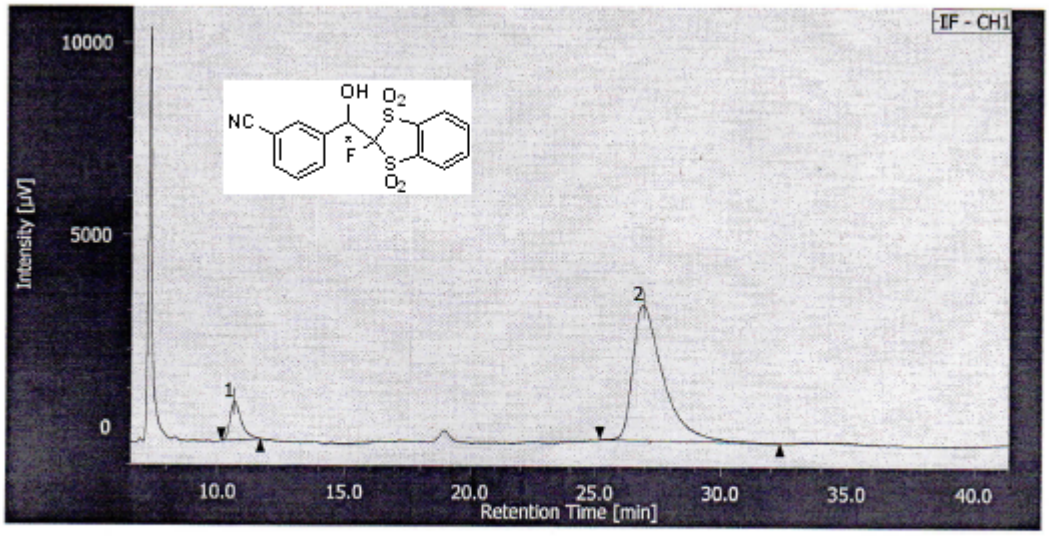
Peak	tR (min)	Area (%)	Height (%)
1	15.433	16.656	20.344
2	20.750	83.344	79.656

HPLC using an IF column (*i*-PrOH/*n*-hexane= 40/60, flow rate 1.0 ml/min, λ = 254 nm)



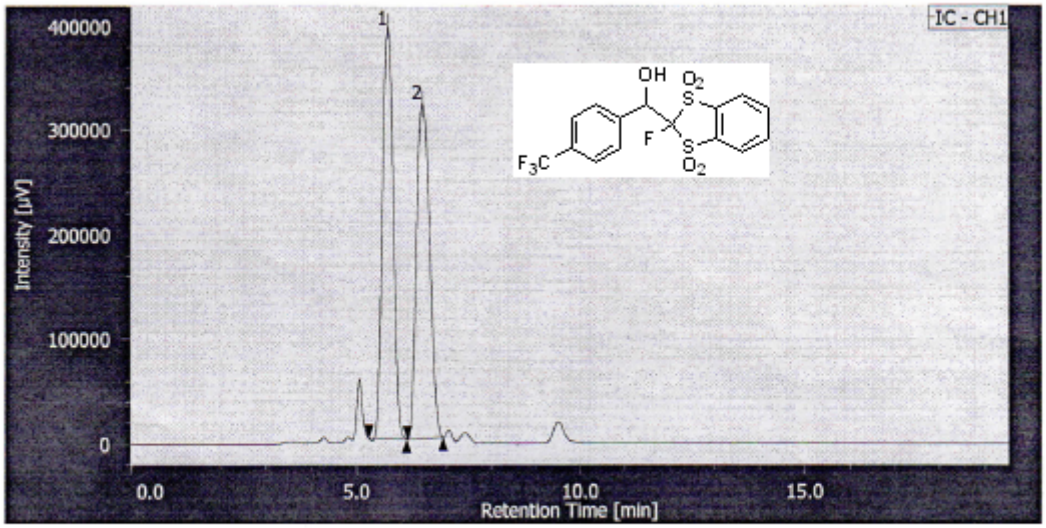
Peak	tR (min)	Area (%)	Height (%)
1	10.675	49.599	72.677
2	27.408	50.401	27.323

HPLC using an IF column (*i*-PrOH/*n*-hexane= 40/60, flow rate 1.0 ml/min, λ = 254 nm)



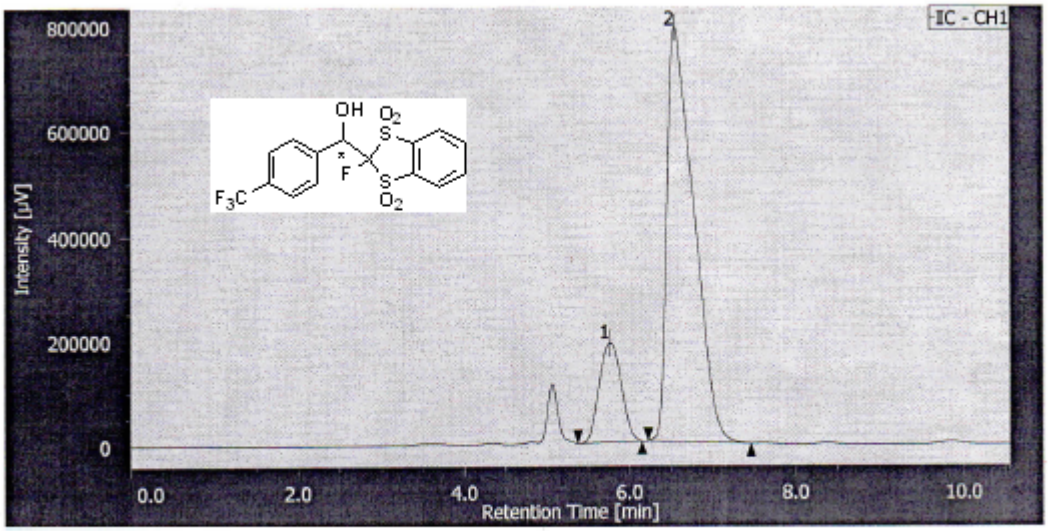
Peak	tR (min)	Area (%)	Height (%)
1	10.675	9.832	22.763
2	26.917	90.168	77.237

HPLC using an IC column (*i*-PrOH/*n*-hexane= 20/80, flow rate 1.0 ml/min, λ = 254 nm)



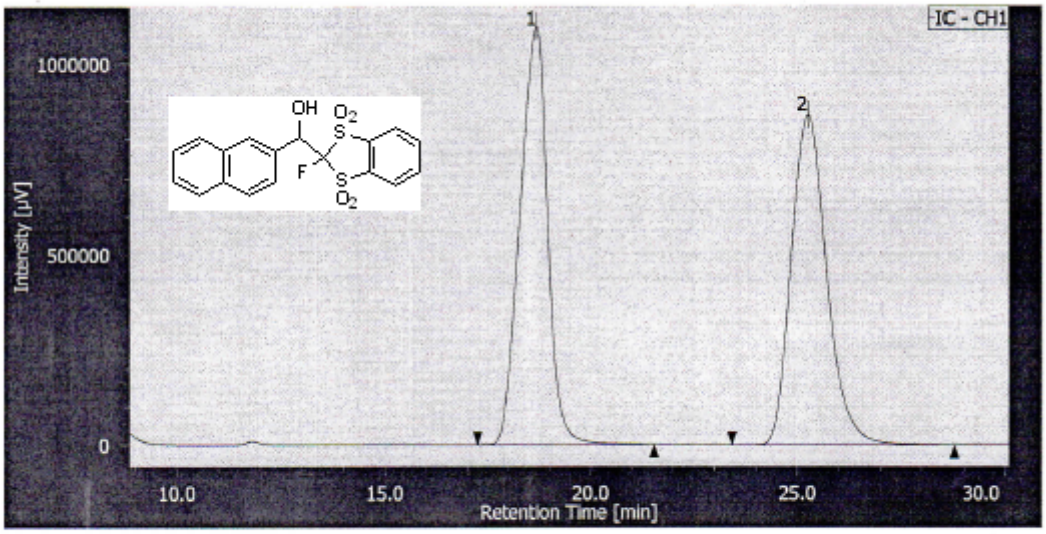
Peak	tR (min)	Area (%)	Height (%)
1	5.683	49.879	55.255
2	6.458	50.121	44.745

HPLC using an IC column (*i*-PrOH/*n*-hexane= 20/80, flow rate 1.0 ml/min, λ = 254 nm)



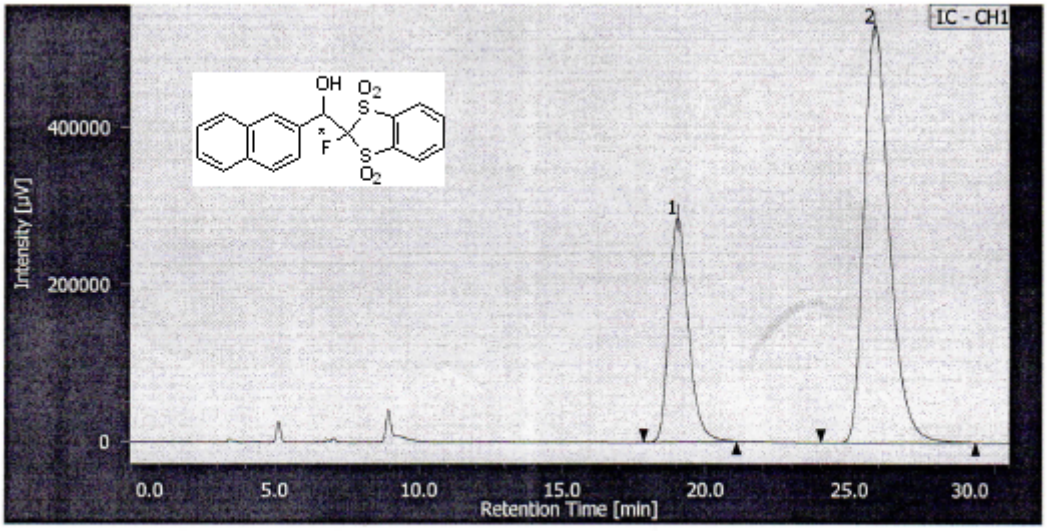
Peak	tR (min)	Area (%)	Height (%)
1	5.767	16.665	19.327
2	6.550	83.335	80.673

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



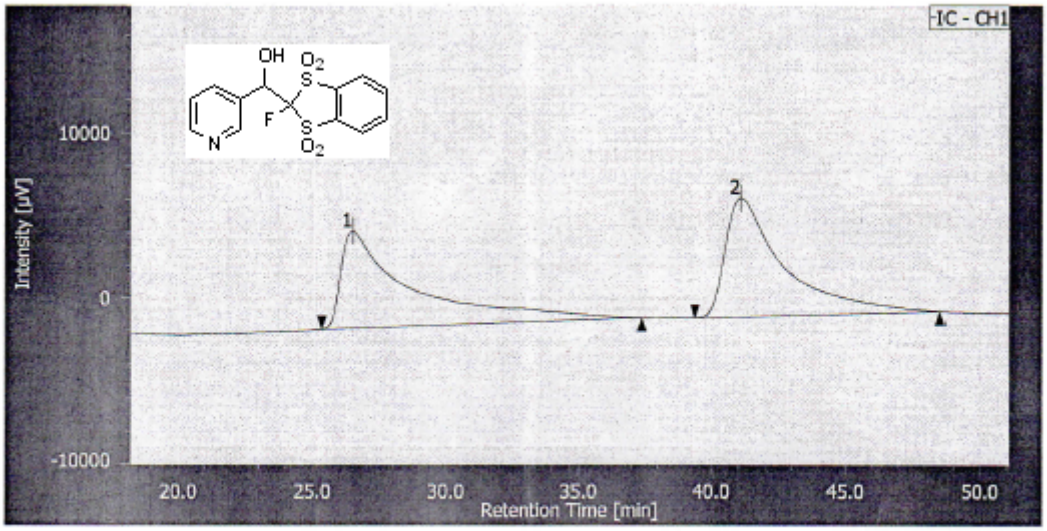
Peak	tR (min)	Area (%)	Height (%)
1	18.683	49.963	55.992
2	25.250	50.037	44.008

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



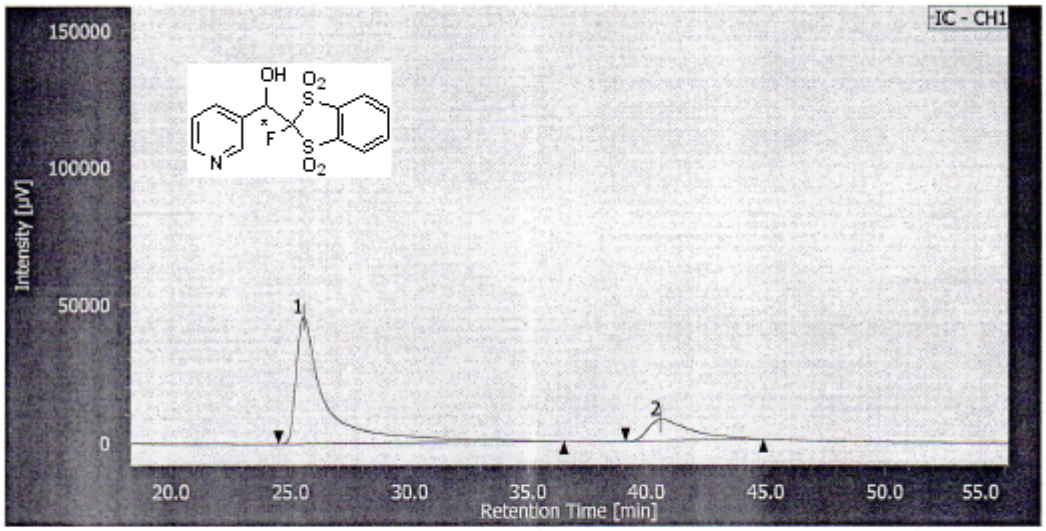
Peak	tR (min)	Area (%)	Height (%)
1	19.025	28.937	34.934
2	25.858	71.063	65.066

HPLC using an IC column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



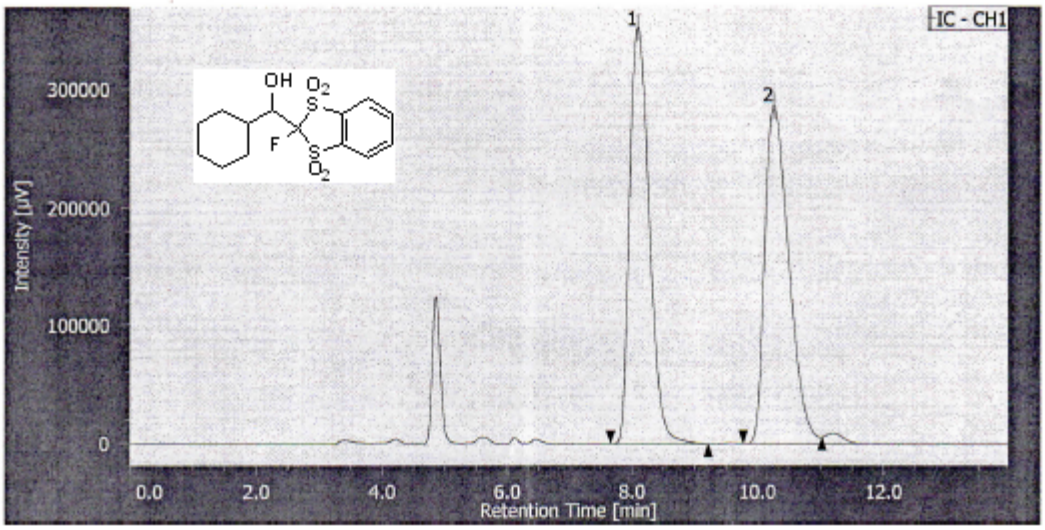
Peak	tR (min)	Area (%)	Height (%)
1	26.508	49.717	44.946
2	41.075	50.283	55.054

HPLC using an IC column (*i*-PrOH/*n*-hexane= 30/70, flow rate 1.0 ml/min, λ = 254 nm)



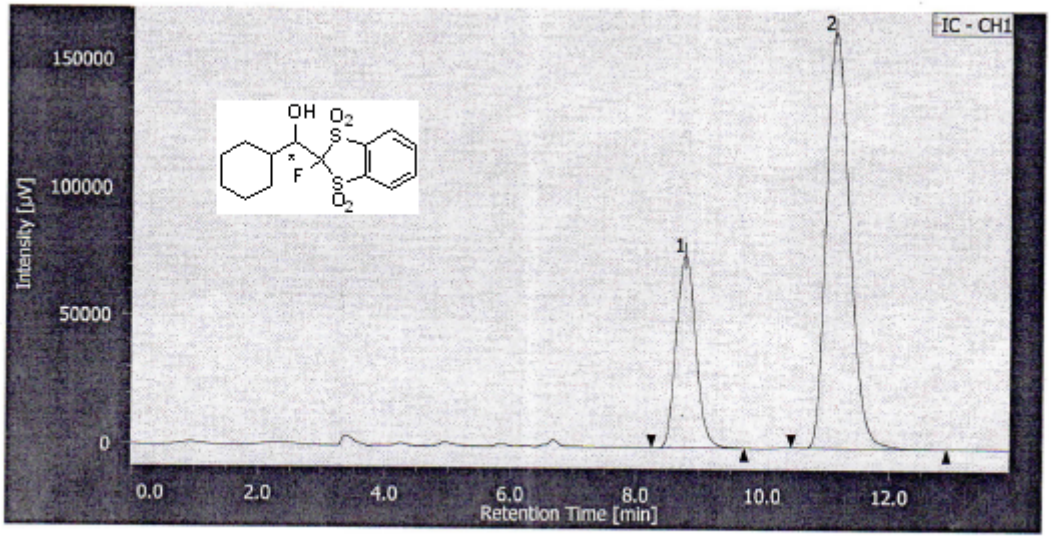
Peak	tR (min)	Area (%)	Height (%)
1	25.542	80.262	85.454
2	40.617	19.738	14.546

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



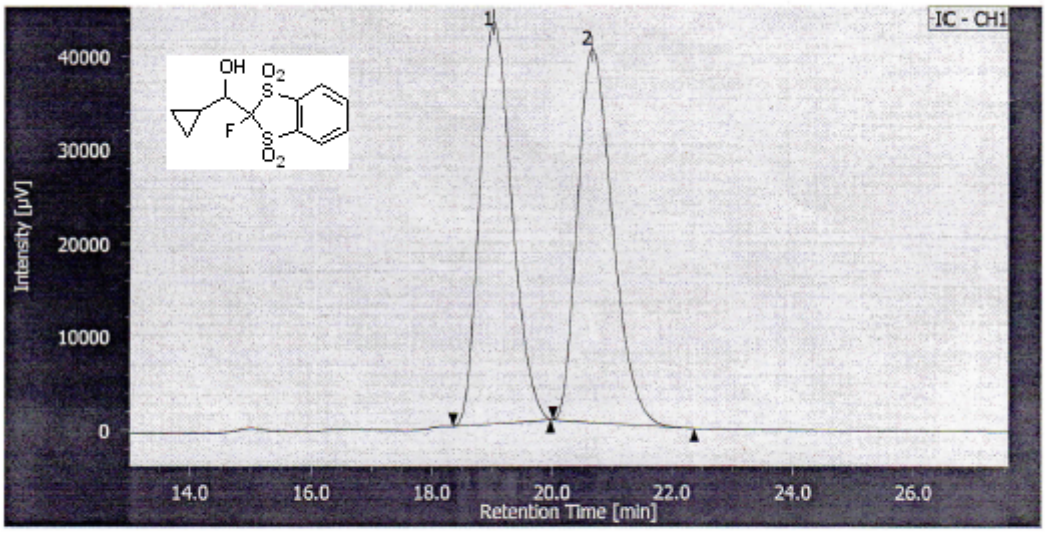
Peak	tR (min)	Area (%)	Height (%)
1	8.083	50.261	55.287
2	10.250	49.739	44.713

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



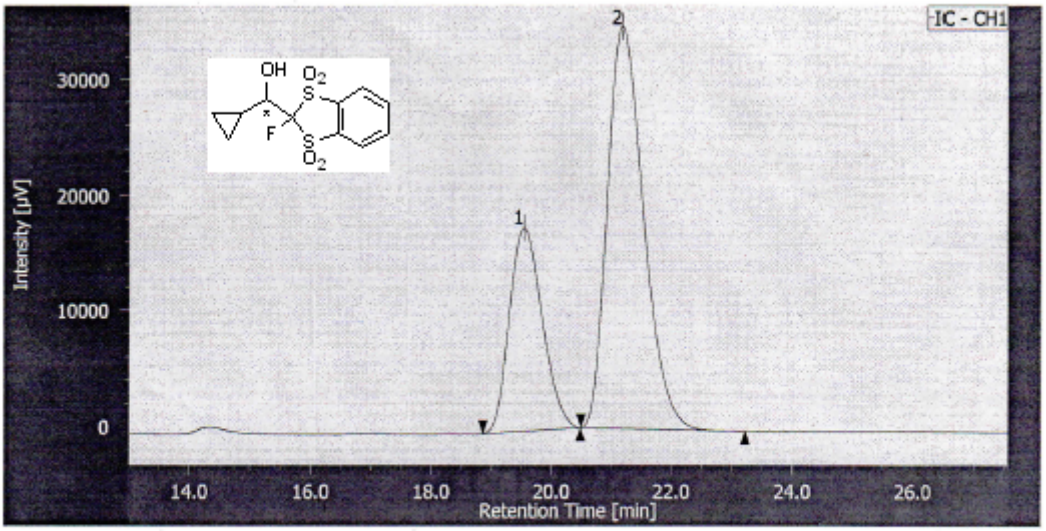
Peak	tR (min)	Area (%)	Height (%)
1	8.758	27.977	31.567
2	11.117	72.023	68.433

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



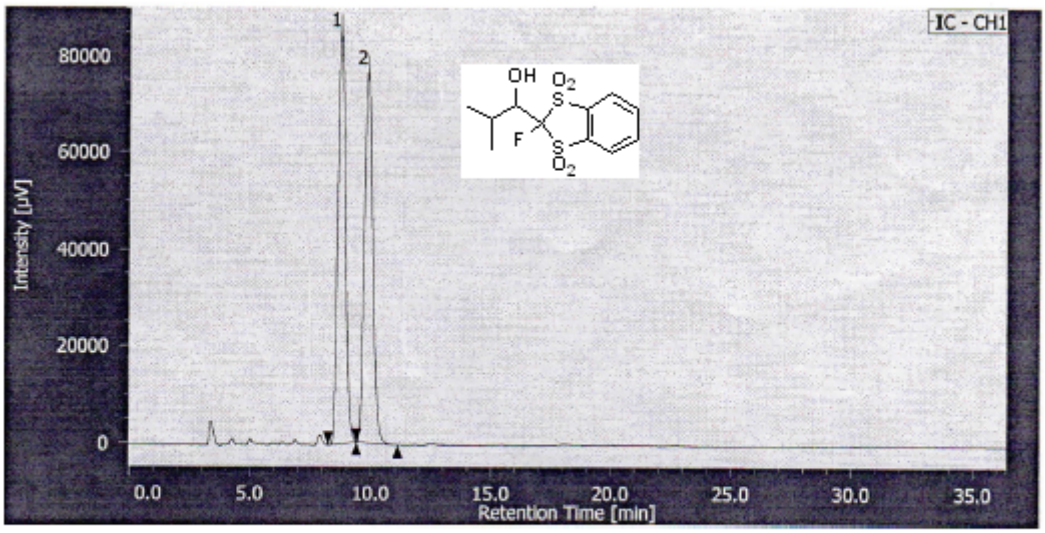
Peak	tR (min)	Area (%)	Height (%)
1	19.017	49.834	51.840
2	20.667	50.166	48.160

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



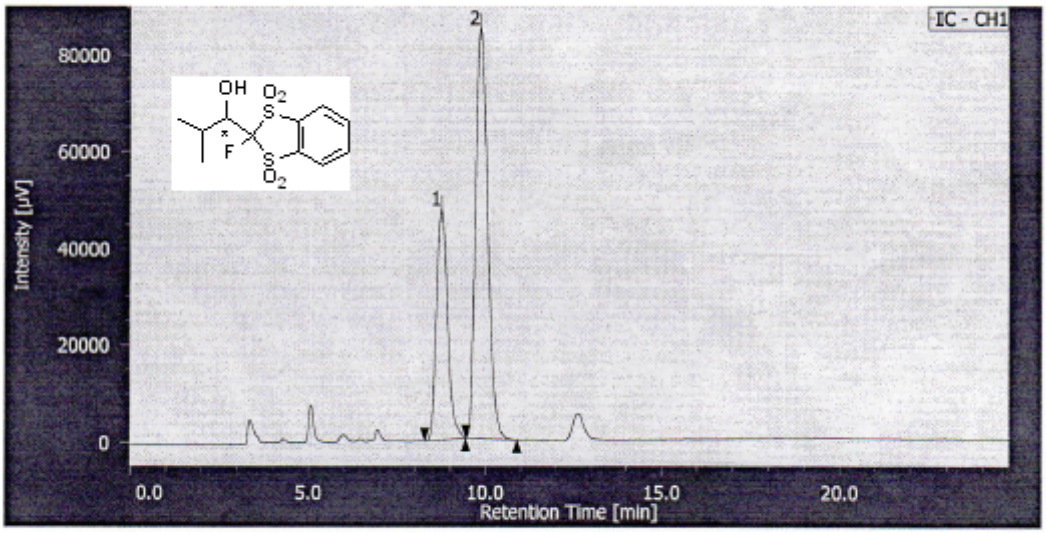
Peak	tR (min)	Area (%)	Height (%)
1	19.542	31.478	33.544
2	21.183	68.522	66.456

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



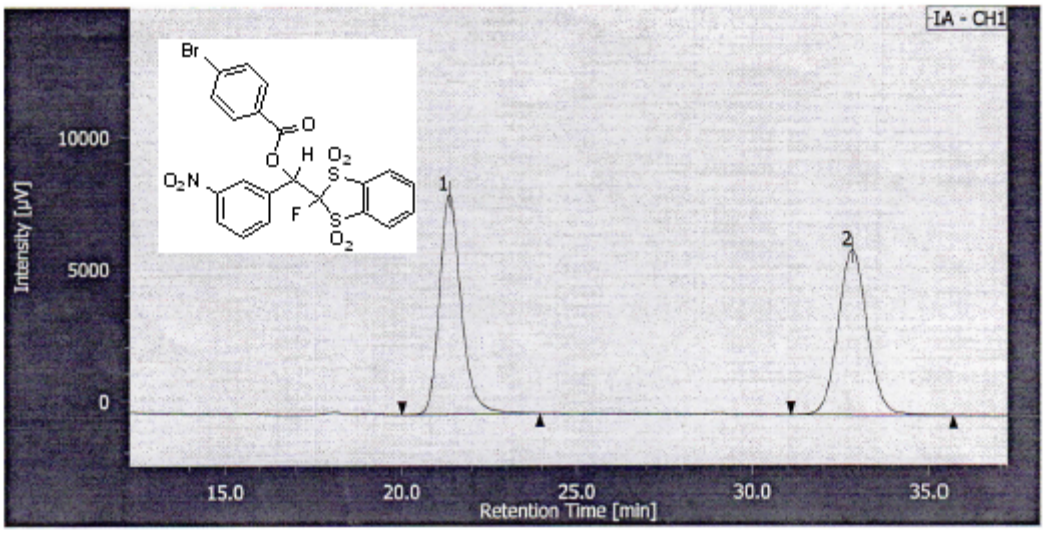
Peak	tR (min)	Area (%)	Height (%)
1	8.733	49.949	52.645
2	9.842	50.051	47.355

HPLC using an IC column (*i*-PrOH/*n*-hexane= 15/85, flow rate 1.0 ml/min, λ = 254 nm)



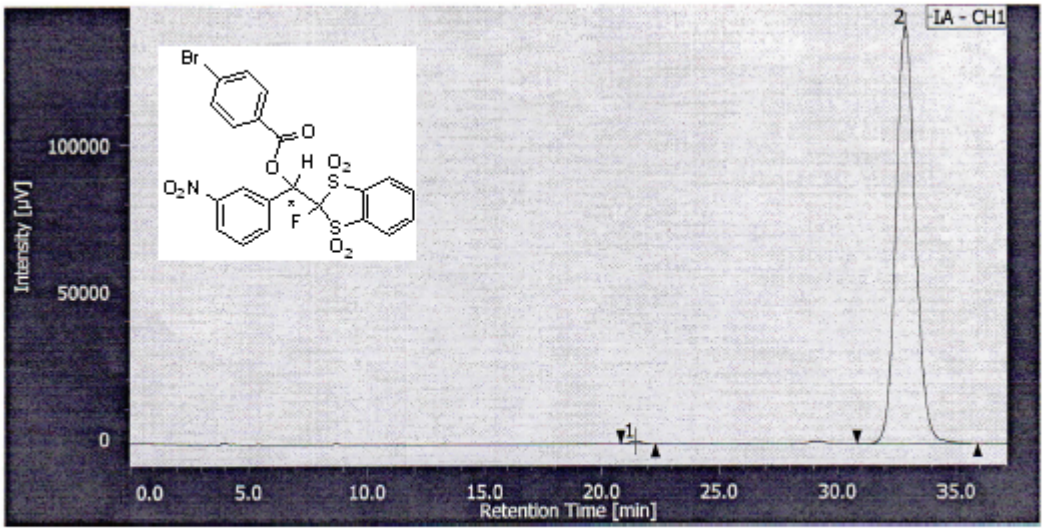
Peak	tR (min)	Area (%)	Height (%)
1	8.742	33.938	35.913
2	9.842	66.062	64.087

HPLC using an IA column (*i*-PrOH/*n*-hexane= 40/60, flow rate 1.0 ml/min, λ = 254 nm)



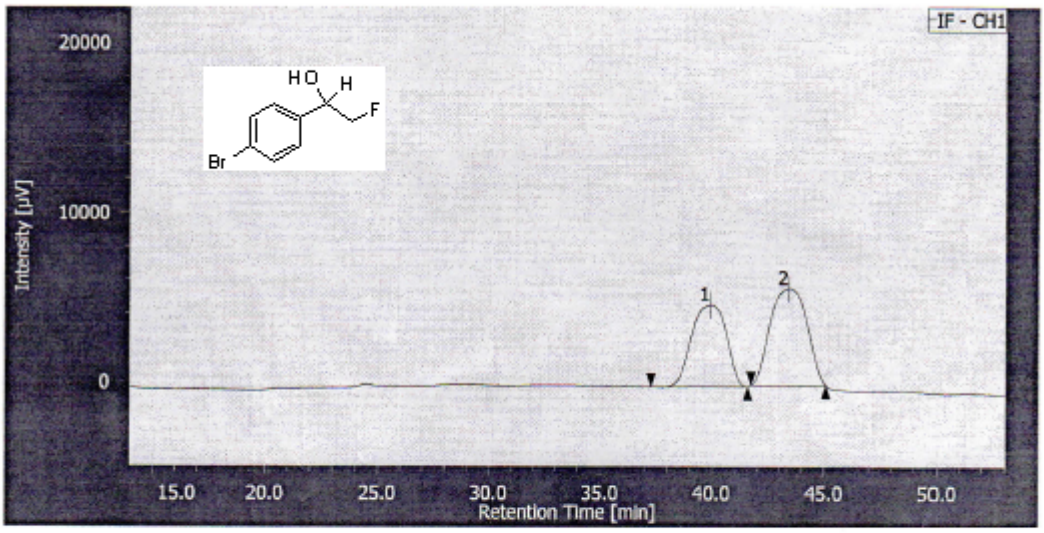
Peak	tR (min)	Area (%)	Height (%)
1	21.342	50.056	57.140
2	32.817	49.944	42.860

HPLC using an IA column (*i*-PrOH/*n*-hexane= 40/60, flow rate 1.0 ml/min, λ = 254 nm)



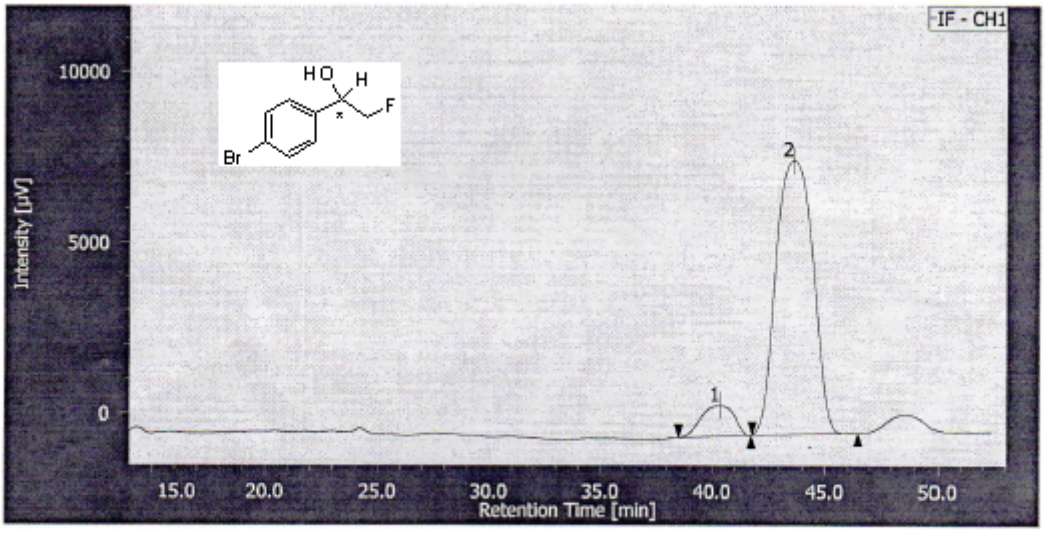
Peak	tR (min)	Area (%)	Height (%)
1	21.433	0.423	0.620
2	32.875	99.577	99.380

HPLC using an IF column (*i*-PrOH/*n*-hexane= 1/99, flow rate 1.0 ml/min, λ = 254 nm)



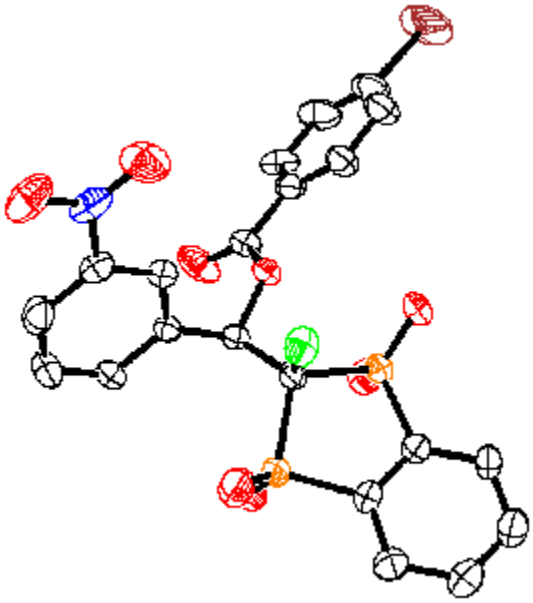
Peak	tR (min)	Area (%)	Height (%)
1	39.933	44.262	45.740
2	43.433	55.738	54.260

HPLC using an IF column (*i*-PrOH/*n*-hexane= 1/99, flow rate 1.0 ml/min, λ = 254 nm)



Peak	tR (min)	Area (%)	Height (%)
1	40.358	9.179	10.133
2	43.625	90.821	89.867

7 X-Ray report of 4:



The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 956341.