Synthesis and radio-protective effects of novel benzyl naphthyl sulfoxide (sulfone) derivatives transformed from Ex-RAD

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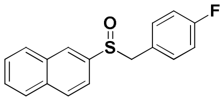
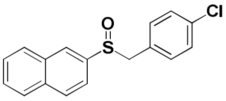
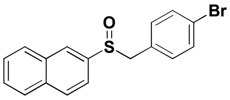
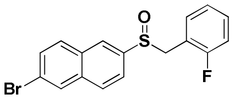
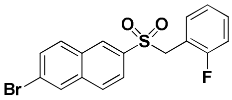
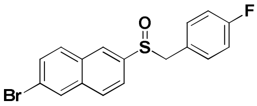
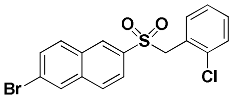
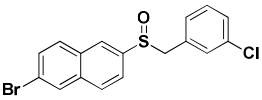
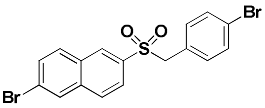
Supplementary Materials

1.The survival rates in some compounds (40μM) pretreated cells after irradiation

Table 1

The survival rates in some compounds pretreated cells after irradiation.

Compound (40μM)	Structure	Survival Rate（%）
Vehicle control	-	43.7±3.4
8d		67.0±0.7
8g		66.9±1.8
8j		59.1±1.6
8l		50.5±5.8
9l		55.2±1.6
8n		83.9±5.3
9o		62.4±3.3
8p		52.9±2.1

9t		55.6±5.5
Ex-RAD	-	60.4±1.3

2. Synthetic procedures

2.1. *6-bromo-2-naphthol* (**2**)

To a solution of 2-naphthol (20.10g, 140mmol) in acetic acid (60mL) was added Br_2 (14mL) in acetic acid (14mL). The reaction mixture was refluxed for 3h during which three portions of Sn (2×3.56g, 2×0.03mol and 14.56g, 0.12mol) were added. Then, the mixture was cooled to 50℃, and the formed Sn salts were filtered and discarded. The remaining solution was poured into cold water (400mL) where the product precipitated as a pink powder.

Obtained in 92.9% yield, pink solid, m.p. 125~127℃. ^{1}H NMR data was according to the literature[1]. ^{1}H NMR (400MHz , $CDCl_3$) *δ* (ppm): 7.92 (s, H, ArH), 7.67 (d, 1H, *J* = 9.6 Hz, ArH), 7.56 (d, 1H, *J* = 8.8Hz, ArH), 7.49 (d, 1H, *J* = 8.9 Hz, ArH), 7.12 (s, 2H, ArH), 5.03 (s, 1H, OH).

2.2. *6-O-(2-bromonaphthyl)-dimethylthiocarbamate* (**3**)

The previously prepared 6-bromo-2-naphthol (500mg, 2.24mmol) was dissolved in DMF (10mL) and added to a solution of sodium hydride (55% moistened with oil, 193 mg, 6.72mmol) in DMF (8mL) at 0℃. The ice bath was taken away and the mixture was stirred for 30 min. Then dimethyl carbamoyl chloride (830mg, 6.72mmol) was added and it was stirred for 2h at 80℃ and 15h at room temperature. The reaction mixture was then extracted with 1% aqueous NaOH (100mL) and TBME (100mL). The aqueous phase was washed with TBME (2×50mL). The combined organic phases were washed with brine and 5% aqueous HCl (100mL), dried with anhydrous Na_2SO_4 and the solvents evaporated. The crude was purified by column chromatography to give the product.

Obtained in 46.6% yield, colorless solid, m.p. 129~131℃. Characterization data was according to the literature[1]. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.01 (d, *J* = 1.6 Hz, 1H), 7.76 (d, *J* = 8.9 Hz, 1H), 7.67 (d, J = 8.7 Hz, 1H), 7.55 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.47 (d, *J* =

2.2 Hz, 1H), 7.26 (dd, *J* = 9.0, 2.3 Hz, 1H), 3.49 (s, 3H), 3.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 188.0, 152.3, 133.0, 132.5, 130.3, 129.8, 128.5, 124.1, 120.0, 43.8, 39.2; HRMS (ESI): calcd. for $C_{13}H_{13}BrNOS$ $[M+H]^+$: 309.9896, found 309.9896.

2.3. *6-S-(2-bromonaphthyl)-dimethylthiocarbamate* (**4**)

The compound **3** (3.21g, 10.35mmol) prepared in the previous step was melted and kept at 220℃ for 6h and the product was purified by column chromatography, eluting with DCM. After recrystallization in methanol, the product was obtained as yellow crystals.

Obtained in 63.9% yield, yellow solid, m.p. 112~114℃. Characterization data was according to the literature[1]. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.03–7.96 (m, 2H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.68 (d, *J* = 8.7 Hz, 1H), 7.59–7.53 (m, 2H), 3.12 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.6, 135.1, 134.2, 133.3, 131.8, 129.8, 129.7, 129.5, 127.4, 126.8, 121.0, 36.9; HRMS (EI): calcd. for $C_{13}H_{13}BrNOS$ $[M+H]^+$: 309.9896, found 309.9893.

2.4. *6-bromonaphtalene-2-thiol* (**5b**)

A solution of the **4** (3.48 g, 11.2mmol) in MeOH (250mL) was saturated with Ar. Then solid KOH (5.22 g, 93.0mmol) was added and it was heated to 80℃ for 2.5h. The reaction mixture was then quenched with 1M aqueous HCl (250mL) at 0℃ and it was extracted with CH_2Cl_2 (300mL). The aqueous phase was washed with CH_2Cl_2 (2×100mL). The combined organic phases were washed with brine, dried with anhydrous Na_2SO_4 and the solvents evaporated to give the product as a beige solid.

Obtained in 89.2% yield, beige solid, m.p. 160~162℃. Characterization data was according to the literature[1]. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.93 (s, 1H), 7.70 (s, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 3.60 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 132.8, 132.6, 130.5, 130.2, 129.5, 129.2, 128.8, 128.1, 127.3, 119.8; HRMS (EI): calcd. for $C_{10}H_7BrS$ $[M^+]$: 238.9525, found 238.9348.

2.5. *General procedure for the synthesis of compounds* (**7a~7t)**

5a or **5b** (2.56mmol) was dissolved in a mixture of ethanol (12mL), sodium hydroxide (3mmol) and H_2O (0.6mL). The mixture was heated to reflux, and solution of benzylic halides (3mmol) in ethanol (1.5mL) was added dropwise. After refluxing the mixture for 3h, it was cooled to room temperature and diluted with H_2O (50mL). The resulting precipitate was filtered to give the corresponding intermediates (**7a~7t**).

benzyl(naphthalen-2-yl)sulfane (**7a**). Obtained in 100% yield, white solid, m.p. 89~90℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.80-7.87 (m, 4H), 7.40-7.50 (m, 5H), 7.30 (t, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 4.37 (s, 2H).

(2-fluorobenzyl)(naphthalen-2-yl)sulfane (**7b**). Obtained in 93.0% yield, white solid. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.82-7.88 (m, 4H), 7.40-7.52 (m, 4H), 7.26-7.32 (m, 1H), 7.17(t, J = 8.0 Hz, 1H), 7.10 (t, J = 8.0 Hz, 1H), 4.37 (s, 2H).

(3-fluorobenzyl)(naphthalen-2-yl)sulfane (**7c**). Obtained in 97.6% yield, white solid. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.81-7.88 (m, 4H), 7.44-7.52 (m, 3H), 7.30-7.35 (q, J = 8.0 Hz, 2H), 7.24(d, J = 8.0 Hz, 1H), 7.05 (t, J = 8.0 Hz, 1H), 4.39 (s, 2H).

(4-fluorobenzyl)(naphthalen-2-yl)sulfane (**7d**). Obtained in 95.5% yield, white solid, m.p. 77~79℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.81-7.87 (m, 4H), 7.42-7.50 (m, 5H), 7.12 (t, J = 8.0 Hz, 2H), 4.36 (s, 2H).

(2-chlorobenzyl)(naphthalen-2-yl)sulfane (**7e**). Obtained in 86.7% yield, white solid, m.p. 75~76℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.79-7.89 (m, 4H), 7.38-7.49 (m, 5H), 7.18-7.27 (m, 2H), 4.38 (s, 2H).

(3-chlorobenzyl)(naphthalen-2-yl)sulfane (**7f**). Obtained in 96.3% yield, white solid, m.p. 62~63℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.77-7.84 (m, 4H), 7.41-7.48 (m, 4H), 7.23-7.33 (m, 3H), 4.34 (s, 2H).

(4-chlorobenzyl)(naphthalen-2-yl)sulfane (**7g**). Obtained in 100% yield, white solid, m.p. 90~92℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.80-7.87 (m, 4H), 7.40-7.52 (m, 5H), 7.34 (d, J = 8.0 Hz, 2H), 4.37 (s, 2H).

(2-bromobenzyl)(naphthalen-2-yl)sulfane (**7h**). Obtained in 92.3% yield, white solid, m.p. 73~74℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.83-7.89 (m, 4H), 7.63 (d, J = 8.0 Hz, 1H), 7.42-7.53 (m, 4H), 7.28 (t, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 4.42 (s, 2H).

(3-bromobenzyl)(naphthalen-2-yl)sulfane (**7i**). Obtained in 91.9% yield, white solid, m.p. 69~71℃. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.80-7.86 (m, 4H), 7.62 (s, 1H), 7.39-7.49 (m, 5H), 7.24 (t, J = 8.0 Hz, 1H), 4.37 (s, 2H).

(4-bromobenzyl)(naphthalen-2-yl)sulfane (**7j**). Obtained in 91.9% yield, white solid, m.p.

99~100℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.76-7.86 (m, 4H), 7.40-7.49 (m, 5H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.31 (s, 2H).

benzyl(6-bromonaphthalen-2-yl)sulfane (**7k**). Obtained in 78.9% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.15 (s, 1H), 7.88 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 1H), 4.37 (s, 2H).

(6-bromonaphthalen-2-yl)(2-fluorobenzyl)sulfane (**7l**). Obtained in 51.4% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.17 (s, 1H), 7.91 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.26-7.31 (m, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 4.37 (s, 2H).

(6-bromonaphthalen-2-yl)(3-fluorobenzyl)sulfane (**7m**). Obtained in 47.4% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.16 (s, 1H), 7.89 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.30-7.36 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.05 (t, *J* = 8.0 Hz, 1H), 4.40 (s, 2H).

(6-bromonaphthalen-2-yl)(4-fluorobenzyl)sulfane (**7n**). Obtained in 76.5% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.15 (s, 1H), 7.87 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.42-7.45 (m, 2H), 7.12 (t, *J* = 8.0 Hz, 2H), 4.40 (s, 2H).

(6-bromonaphthalen-2-yl)(2-chlorobenzyl)sulfane (**7o**). Obtained in 51.9% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.16 (s, 1H), 7.90 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.28-7.32 (m, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 4.38 (s, 2H).

(6-bromonaphthalen-2-yl)(3-chlorobenzyl)sulfane (**7p**). Obtained in 57.9% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.17 (s, 1H), 7.91 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.28-7.33 (m, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 8.0 Hz, 1H), 4.39 (s, 2H).

(6-bromonaphthalen-2-yl)(4-chlorobenzyl)sulfane (**7q**). Obtained in 75.5% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.15 (s, 1H), 7.86 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.41-7.45 (m, 2H), 7.11 (t, *J* = 8.0 Hz, 2H), 4.41 (s, 2H).

(6-bromonaphthalen-2-yl)(2-bromobenzyl)sulfane (**7r**). Obtained in 53.5% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.15 (s, 1H), 7.89 (s, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.29-7.34 (m, 1H), 7.17 (t, J = 8.0 Hz, 1H), 7.10 (t, J = 8.0 Hz, 1H), 4.37 (s, 2H).

(6-bromonaphthalen-2-yl)(4-bromobenzyl)sulfane (**7t**). Obtained in 68.0% yield, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.17 (s, 1H), 7.90 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.42-7.45 (m, 2H), 7.10 (t, J = 8.0 Hz, 2H), 4.39 (s, 2H).

2.6. *General procedure for the synthesis of compounds* (**8a~8r**)

To a ice cold solution of **7a~7r** (1.0mmol) in 50mL acetic acid was added 2.0mmol 30% H_2O_2, then the mixture was stirred at room temperature for about 3~5h. After completion of reaction (monitored by TLC), the mixture was poured into ice water, the formed white precipitate was filtered, washed with water and dried under vacuum to get the target compounds (**8a~8r**).

2-(benzylsulfinyl)naphthalene (**8a**). Obtained in 94.3% yield, white solid, m.p. 200~201℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.99-8.09(m, 4H), 7.61-7.68(m, 3H), 7.10-7.26(m, 5H), 4.37(d, J=12.4Hz, 1H), 4.16(d, J=12.9Hz, 1H).

2-((2-fluorobenzyl)sulfinyl)naphthalene (**8b**). Obtained in 90.9% yield, white solid, m.p. 117~119℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.98-8.09(m, 4H), 7.59-7.67(m, 3H), 7.05-7.35(m, 4H), 4.40(d, J=12.9Hz, 1H), 4.26(d, J=12.9Hz, 1H).

2-((3-fluorobenzyl)sulfinyl)naphthalene (**8c**). Obtained in 87.5% yield, white solid, m.p. 185~187℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.99-8.10(m, 4H), 7.60-7.68(m, 3H), 6.90-7.30(m, 4H), 4.42 (d, J=12.9Hz, 1H), 4.20 (d, J=12.9Hz, 1H).

2-((2-chlorobenzyl)sulfinyl)naphthalene (**8e**). Obtained in 73.7% yield, white solid, m.p. 106~107℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.01-8.11(m, 4H), 7.62-7.66(m, 3H), 7.22-7.45(m, 4H), 4.45 (d, J=12.9Hz, 1H), 4.35 (d, J=12.9Hz, 1H).

2-((3-chlorobenzyl)sulfinyl)naphthalene (**8f**). Obtained in 86.8% yield, white solid, m.p. 142~143℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.00-8.11(m, 4H), 7.61-7.68(m, 3H), 7.01-7.34(m, 4H), 4.43 (d, J=12.9Hz, 1H), 4.18 (d, J=12.9Hz, 1H).

2-((2-bromobenzyl)sulfinyl)naphthalene (**8h**). Obtained in 75.8% yield, white solid, m.p.

90~92℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.02-8.12(m, 4H), 7.62-7.66(m, 4H), 7.21-7.33(m, 3H), 4.43 (d, *J*=12.9Hz, 1H), 4.35 (d, *J*=12.9Hz, 1H).

2-((3-bromobenzyl)sulfinyl)naphthalene (**8i**). Obtained in 93.9% yield, white solid, m.p. 127~129℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.10(d, *J*=8.7Hz, 1H), 7.99-8.04(m, 3H), 7.60-7.68(m, 3H), 7.46(d, *J*=8.1Hz, 1H), 7.29(s, 1H), 7.20(t, *J*=7.9Hz, 1H), 7.07(d, *J*=7.9Hz, 1H), 4.42 (d, *J*=12.9Hz, 1H), 4.16 (d, *J*=12.9Hz, 1H).

2-(benzylsulfinyl)-6-bromonaphthalene (**8k**). Obtained in 92.3% yield, white solid, m.p. 198~200℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.33(s, 1H), 8.05-8.08(m, 2H), 7.97(d, *J*=8.7Hz, 1H), 7.70-7.75(m, 2H), 7.06-7.28(m, 5H), 4.38(d, *J*=12.9Hz, 1H), 4.16(d, *J*=12.9Hz, 1H).

2-bromo-6-((3-fluorobenzyl)sulfinyl)naphthalene (**8m**). Obtained in 81.8% yield, white solid, m.p. 156~158℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.34(s, 1H), 7.97-8.09(m, 3H), 7.70-7.75(m, 2H), 6.86-7.29(m, 4H), 4.44(d, *J*=12.9Hz, 1H), 4.20(d, *J*=12.9Hz, 1H).

2-bromo-6-((2-chlorobenzyl)sulfinyl)naphthalene (**8o**). Obtained in 63.0% yield, white solid, m.p. 138~140℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.34(s, 1H), 7.98-8.09(m, 3H), 7.67-7.76(m, 2H), 7.20-7.43(m, 4H), 4.45(d, *J*=12.9Hz, 1H), 4.36(d, *J*=12.9Hz, 1H).

2-bromo-6-((4-chlorobenzyl)sulfinyl)naphthalene (**8q**). Obtained in 82.6% yield, white solid, m.p. 205~207℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.30(s, 1H), 7.93-8.04(m, 3H), 7.65-7.73(m, 2H), 7.26(d, *J*=8.4Hz, 2H), 7.02(d, *J*=8.4Hz, 2H), 4.39(d, *J*=13.2Hz, 1H), 4.14(d, *J*=12.9Hz, 1H).

2-bromo-6-((2-bromobenzyl)sulfinyl)naphthalene (**8r**). Obtained in 50.0% yield, white solid, m.p. 136~138℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.35(s, 1H), 8.00-8.12(m, 3H), 7.61-7.77(m, 3H), 7.19-7.31(m, 3H), 4.45(d, *J*=12.8Hz, 1H), 4.37(d, *J*=12.8Hz, 1H).

2.7. *General procedure for the synthesis of compounds* (**9a~9t**)

To a ice cold solution of **7a~7t** (1.0mmol) in 50mL acetic acid was added 6.0mmol 30% H_2O_2, then the mixture was heated to 50℃ and stirred for about 2~5h. After completion of reaction (monitored by TLC), the mixture was poured into ice water, the formed white precipitate was filtered, washed with water and dried under vacuum to get the target compounds (**9a~9t**).

2-(benzylsulfonyl)naphthalene (**9a**). Obtained in 87.8% yield, white solid, m.p.

201~203℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.37(s, 1H), 8.06-8.14(m, 3H), 7.66-7.77(m, 3H), 7.15-7.30(m, 5H), 4.76(s, 2H).

2-((2-fluorobenzyl)sulfonyl)naphthalene (**9b**). Obtained in 94.7% yield, white solid, m.p. 173~175℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.39(s, 1H), 8.08-8.16(m, 3H), 7.67-7.78(m, 3H), 7.08-7.41(m, 4H), 4.78(s, 2H).

2-((3-fluorobenzyl)sulfonyl)naphthalene (**9c**). Obtained in 94.1% yield, white solid, m.p. 207~208℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.40(s, 1H), 8.07-8.16(m, 3H), 7.67-7.77(m, 3H), 6.98-7.33(m, 4H), 4.83(s, 2H).

2-((4-fluorobenzyl)sulfonyl)naphthalene (**9d**). Obtained in 88.2% yield, white solid, m.p. 229~231℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.38(s, 1H), 8.07-8.16(m, 3H),, 7.67-7.77(m, 3H), 7.09-7.22(m, 4H), 4.78(s, 2H).

2-((2-chlorobenzyl)sulfonyl)naphthalene (**9e**). Obtained in 87.5% yield, white solid, m.p. 101~103℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.38(s, 1H), 8.08-8.16(m, 3H),, 7.67-7.76(m, 3H), 7.29-7.37(m, 4H), 4.87(s, 2H).

2-((3-chlorobenzyl)sulfonyl)naphthalene (**9f**). Obtained in 80.5% yield, white solid, m.p. 182~183℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.40(s, 1H), 8.15(d, J=8.7Hz, 2H), 8.09(d, J=8.1Hz, 1H), 7.67-7.77(m, 3H), 7.26-7.39(m, 3H), 7.11(d, J=7.9Hz, 1H), 4.82(s, 2H).

2-((4-chlorobenzyl)sulfonyl)naphthalene (**9g**). Obtained in 81.4% yield, white solid, m.p. 239~241℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.40(s, 1H), 8.07-8.17(m, 3H), 7.67-7.77(m, 3H), 7.35(d, J=8.7Hz , 2H), 7.18(d, J=8.4Hz , 2H), 4.81(s, 2H).

2-((2-bromobenzyl)sulfonyl)naphthalene (**9h**). Obtained in 90.2% yield, white solid, m.p. 99~100℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.38(s, 1H), 8.08-8.17(m, 3H), 7.67-7.78(m, 3H), 7.56(d, J=8.1Hz , 1H), 7.26-7.38(m, 3H), 4.88(s, 2H).

2-((3-bromobenzyl)sulfonyl)naphthalene (**9i**). Obtained in 82.9% yield, white solid, m.p. 158~160℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.40(s, 1H), 8.16(d, J=8.4Hz, 2H), 8.09(d, J=7.6Hz, 1H), 7.68-7.78(m, 3H), 7.51(d, J=7.9Hz, 1H), 7.39(s, 1H), 7.24(t, J=7.6Hz, 1H), 7.15(d, J=7.9Hz, 1H), 4.81(s, 2H).

2-((4-bromobenzyl)sulfonyl)naphthalene (**9j**). Obtained in 79.5% yield, white solid, m.p. 244~246℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.40(s, 1H), 8.07-8.17(m, 3H), 7.69-7.76(m, 3H), 7.49(d, *J*=8.3Hz, 2H), 7.12(d, *J*=8.5Hz, 2H), 4.79(s, 2H).

2-(benzylsulfonyl)-6-bromonaphthalene (**9k**). Obtained in 92.3% yield, white solid, m.p. 205~207℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.40(m, 2H), 8.09-8.12(m, 2H), 7.78-7.83(m, 2H), 7.13-7.29(m, 5H), 4.77(s, 2H).

2-bromo-6-((3-fluorobenzyl)sulfonyl)naphthalene (**9m**). Obtained in 70.0% yield, white solid, m.p. 186~188℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.42(d, *J*=8.2Hz, 2H), 8.11-8.14(m, 2H), 7.79-7.84(m, 2H), 6.96-7.33(m, 4H), 4.83(s, 2H).

2-bromo-6-((4-fluorobenzyl)sulfonyl)naphthalene (**9n**). Obtained in 88.5% yield, white solid, m.p. 207~209℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.41(s, 2H), 8.11-8.14(m, 2H), 7.77-7.84(m, 2H), 7.09-7.20(m, 4H), 4.79(s, 2H).

2-bromo-6-((3-chlorobenzyl)sulfonyl)naphthalene (**9p**). Obtained in 77.3% yield, white solid, m.p. 178~180℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.42(d, *J*=7.6Hz, 2H), 8.14(d, *J*=8.7Hz, 2H), 7.80-7.84(m, 2H), 7.25-7.37(m, 3H), 7.09(d, *J*=7.8Hz, 1H), 4.83(s, 2H).

2-bromo-6-((4-chlorobenzyl)sulfonyl)naphthalene (**9q**). Obtained in 87.5% yield, white solid, m.p. 200~202℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.42(d, *J*=8.7Hz, 2H), 8.11-8.15(m, 2H), 7.79-7.84(m, 2H), 7.35(d, *J*=8.4Hz, 2H), 7.17(d, *J*=8.4Hz, 2H), 4.82(s, 2H).

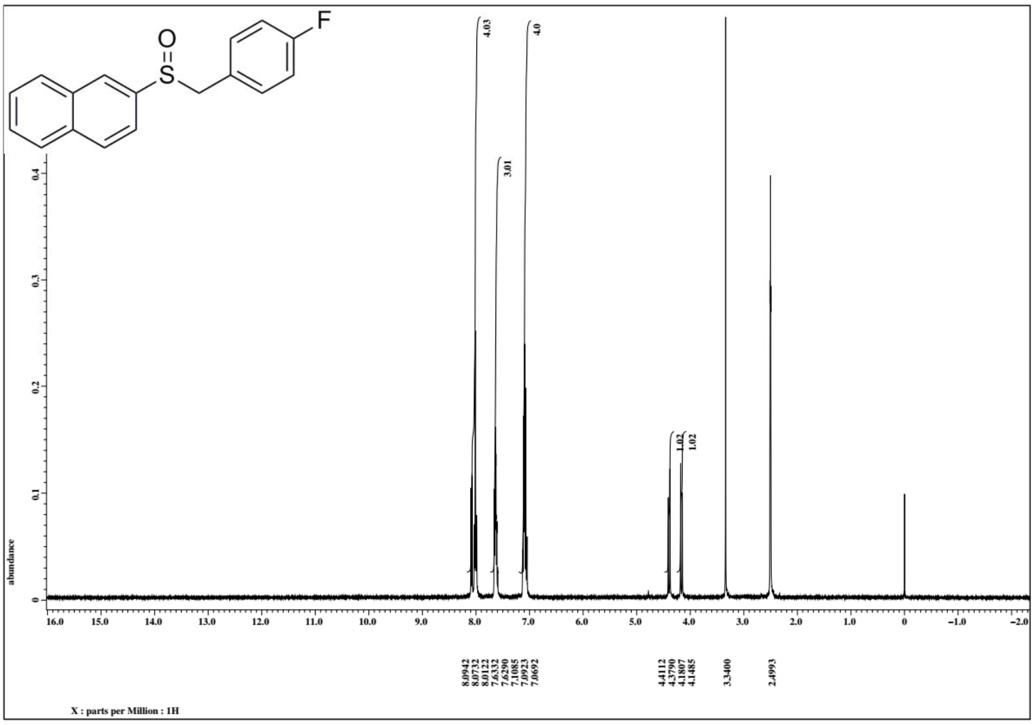
2-bromo-6-((2-bromobenzyl)sulfonyl)naphthalene (**9r**). Obtained in 78.5% yield, white solid, m.p. 131~133℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.41(s, 2H), 8.06-8.14(m, 2H), 7.71-7.84(m, 2H), 7.55(d, *J*=8.1Hz, 1H), 7.25-7.37(m, 3H), 4.88(s, 2H).

References

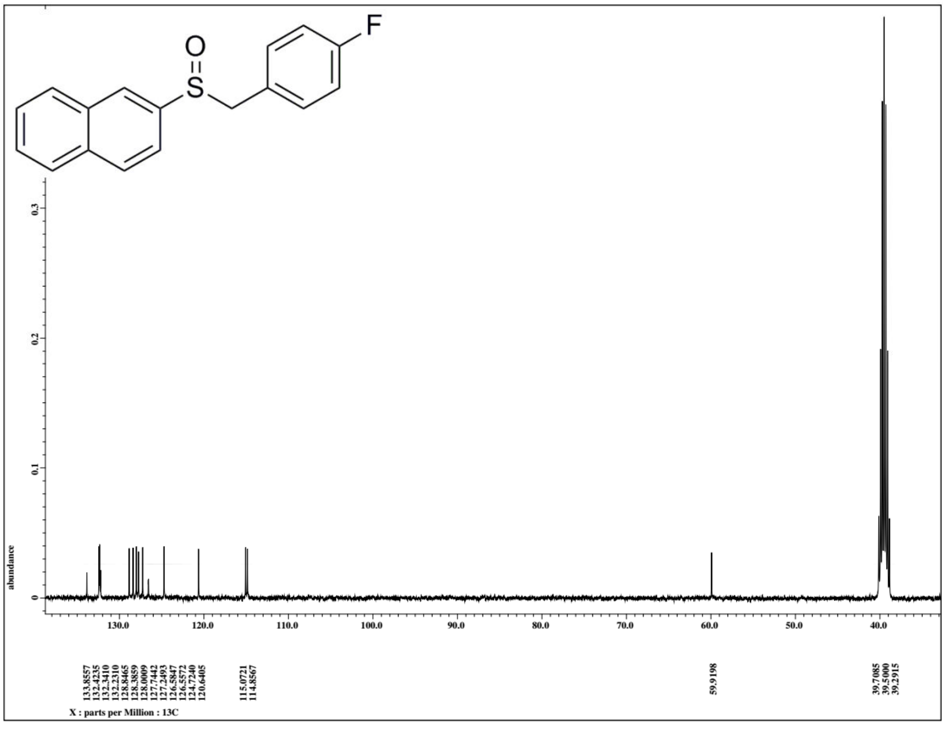
1. Sergio G, Roman H, Songmei Wu, et al. *Euro. J. Org. Chem.* **2010**, 833 - 845.

3. Copies of ^{1}H-NMR and ^{13}C-NMR for target compounds（8d, 8g, 8j, 8l, 9l, 8n, 9o, 8p and 9t）

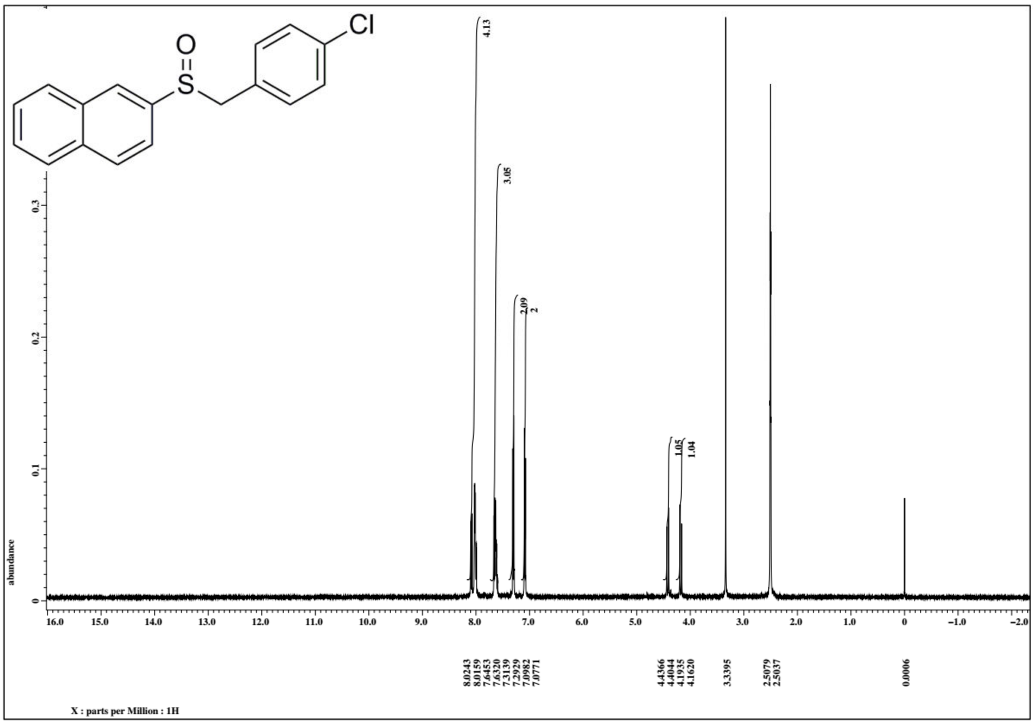
^{1}H-NMR of Compound 8d:



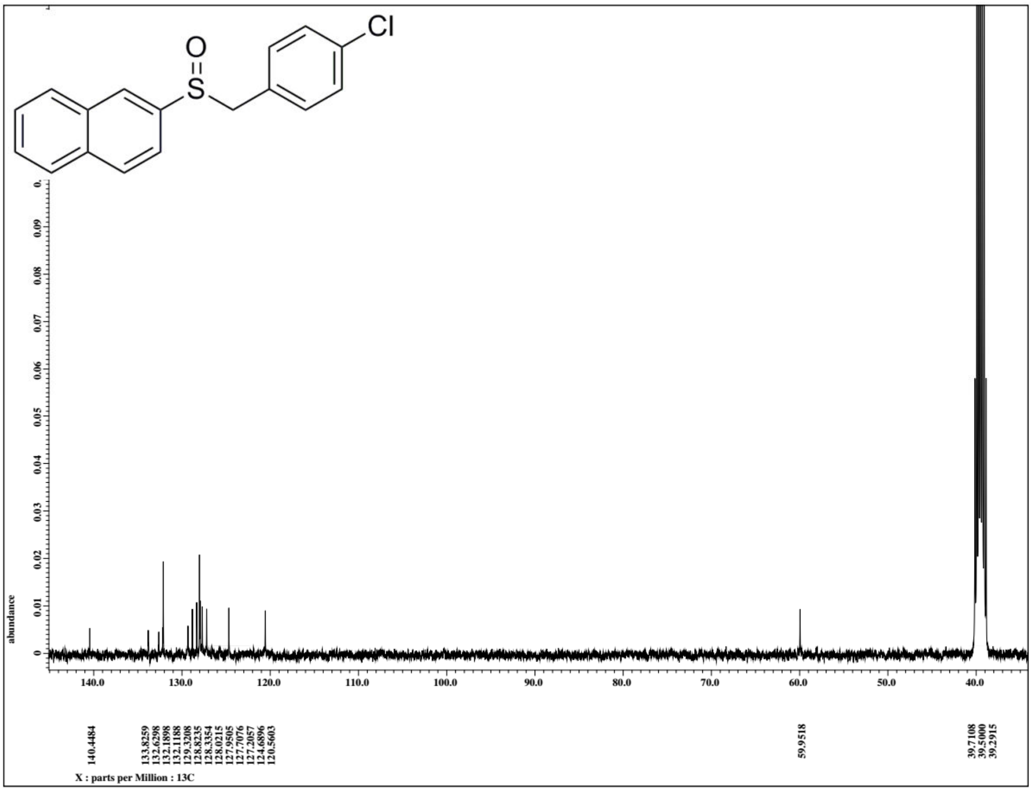
^{1}C-NMR of Compound 8d:



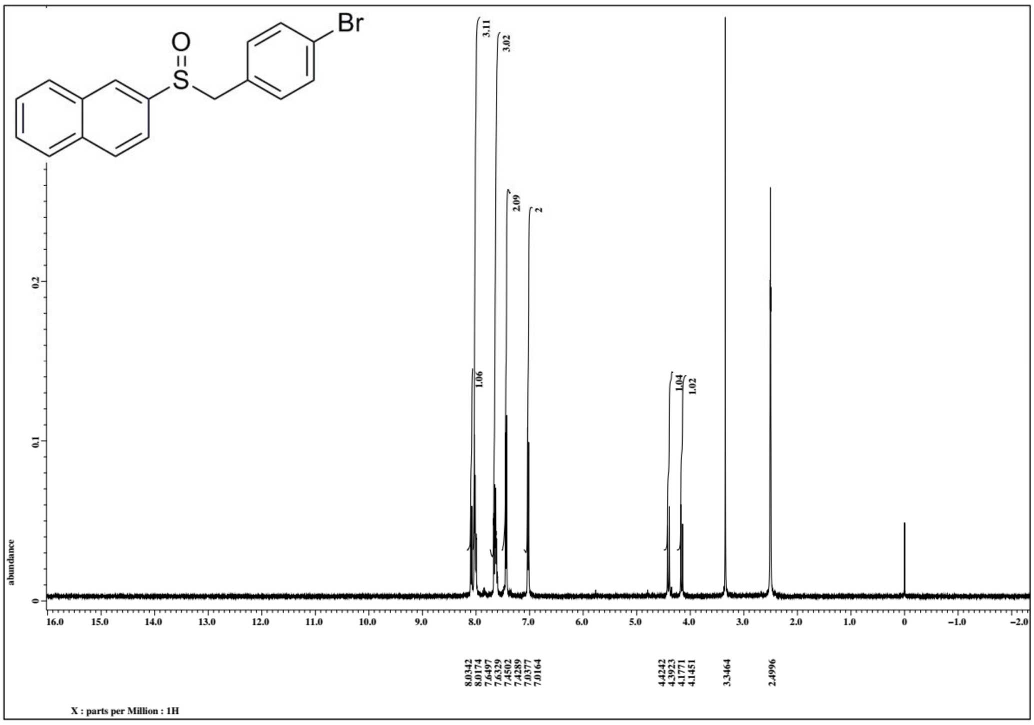
^{1}H-NMR of Compound 8g:



^{1}C-NMR of Compound 8g:



^{1}H-NMR of Compound 8j:



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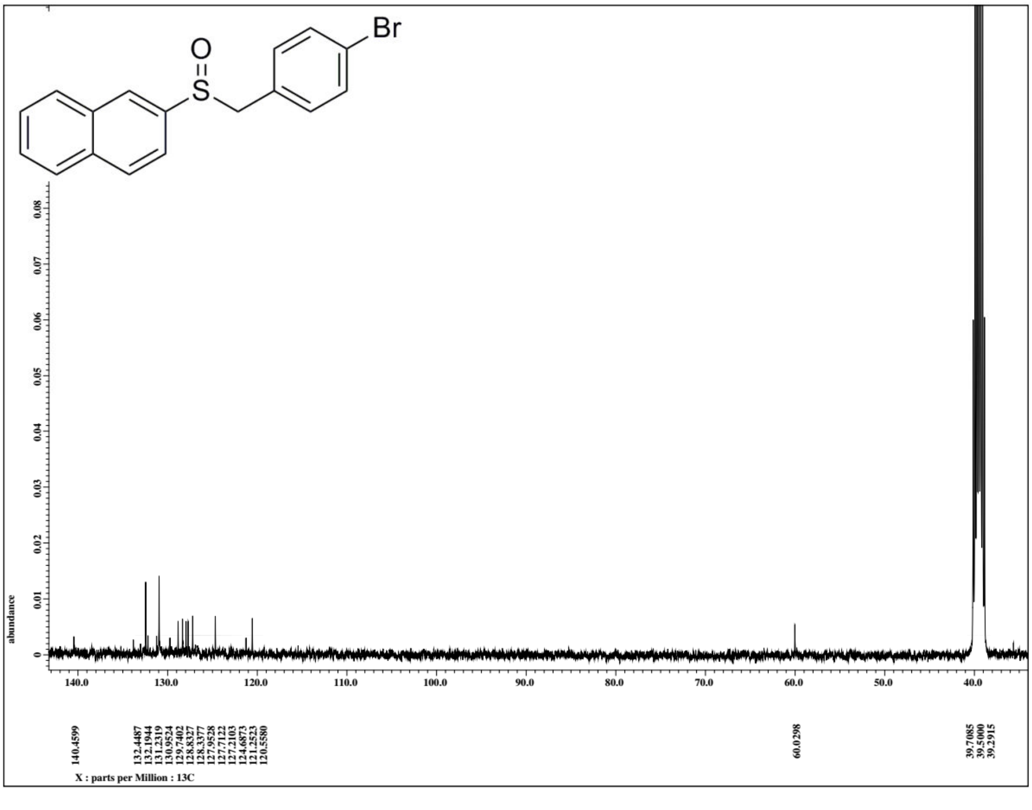

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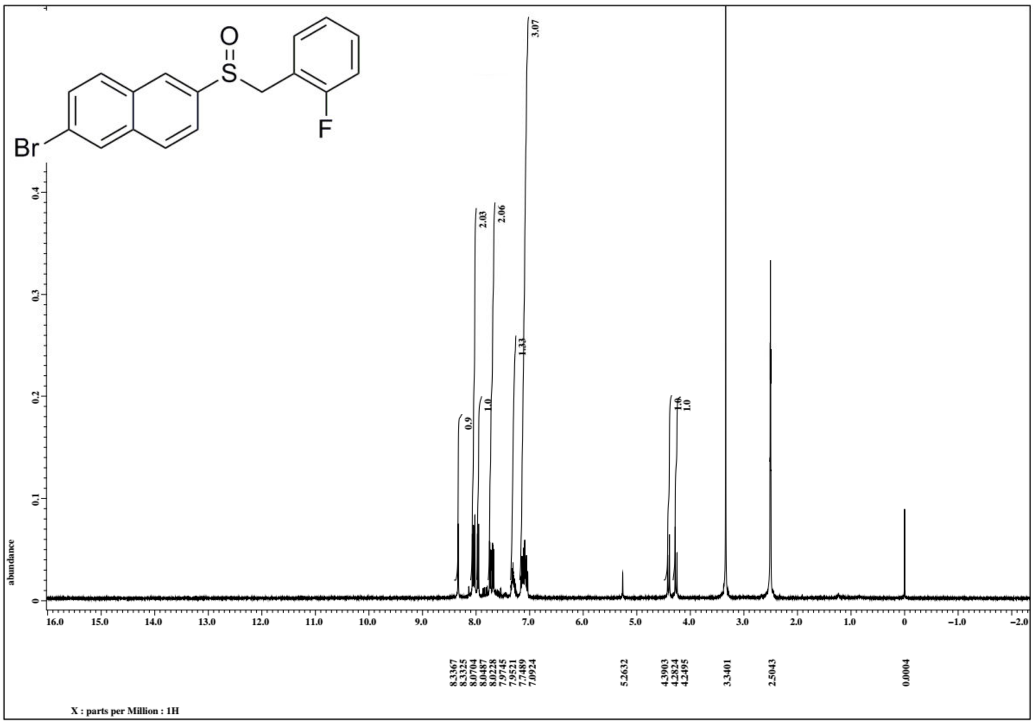

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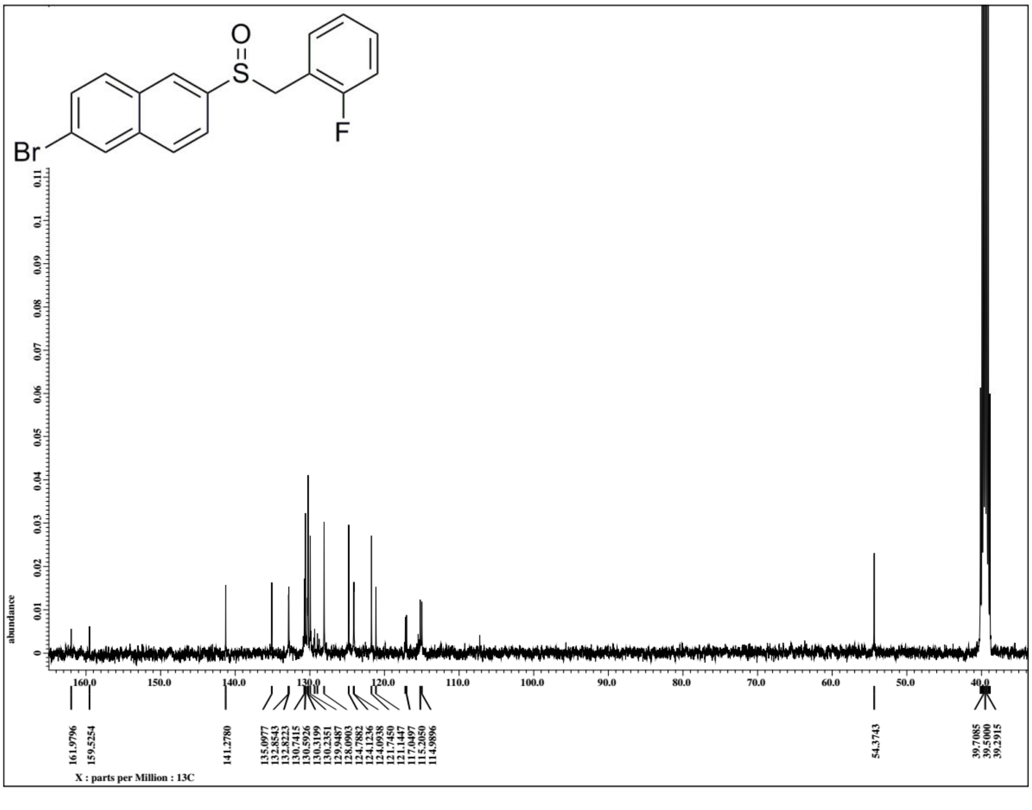

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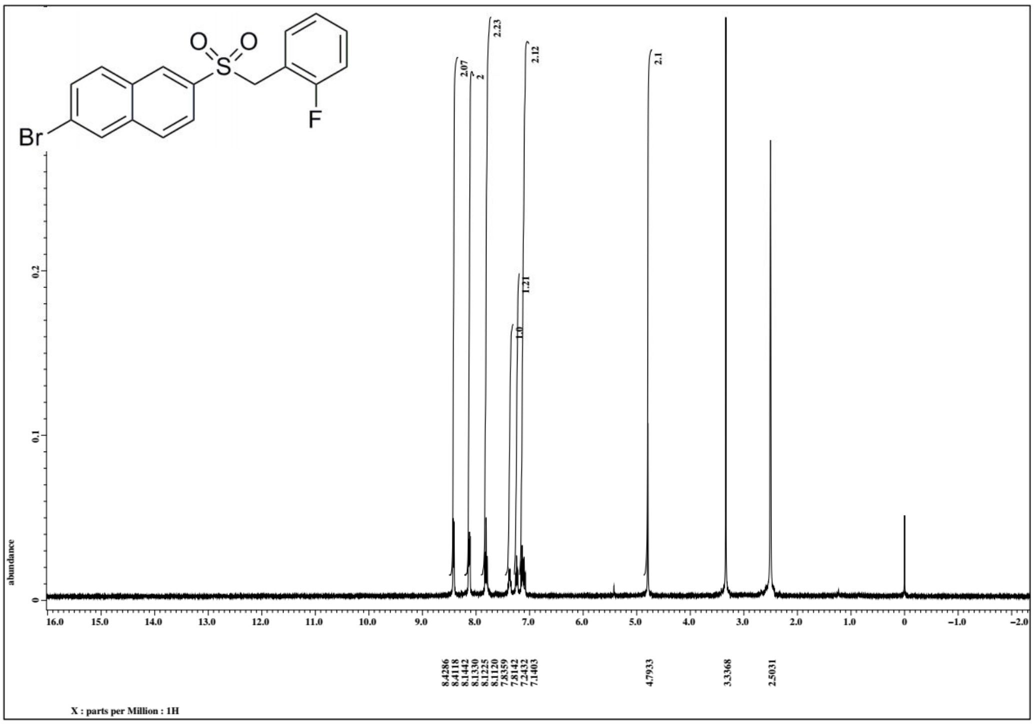

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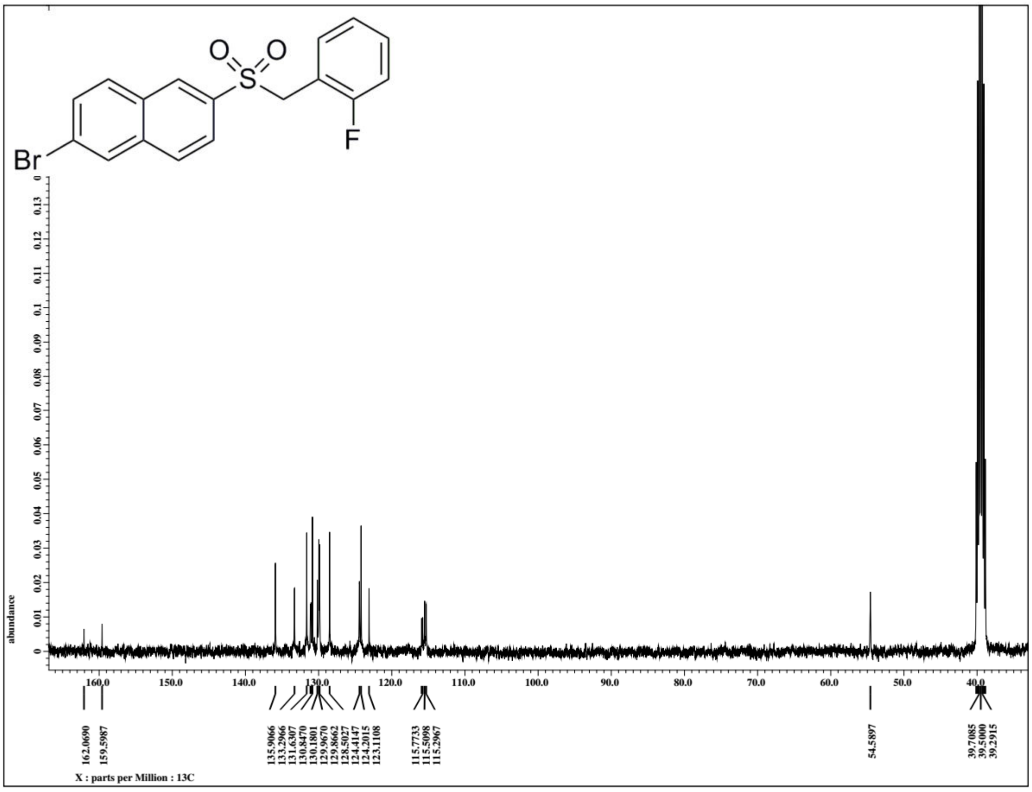

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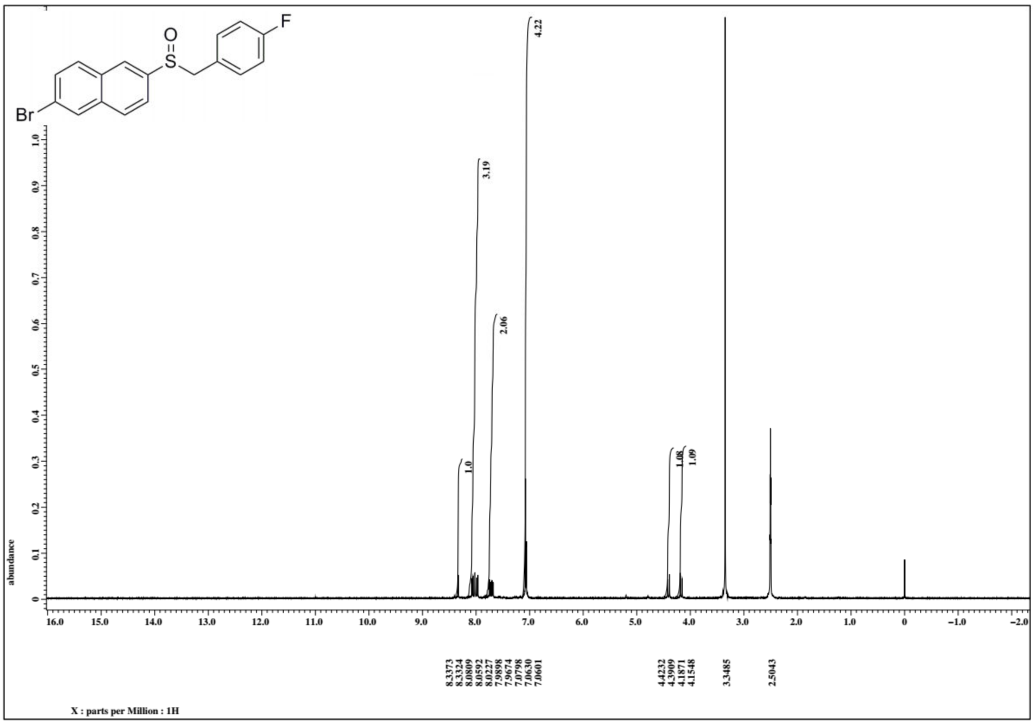

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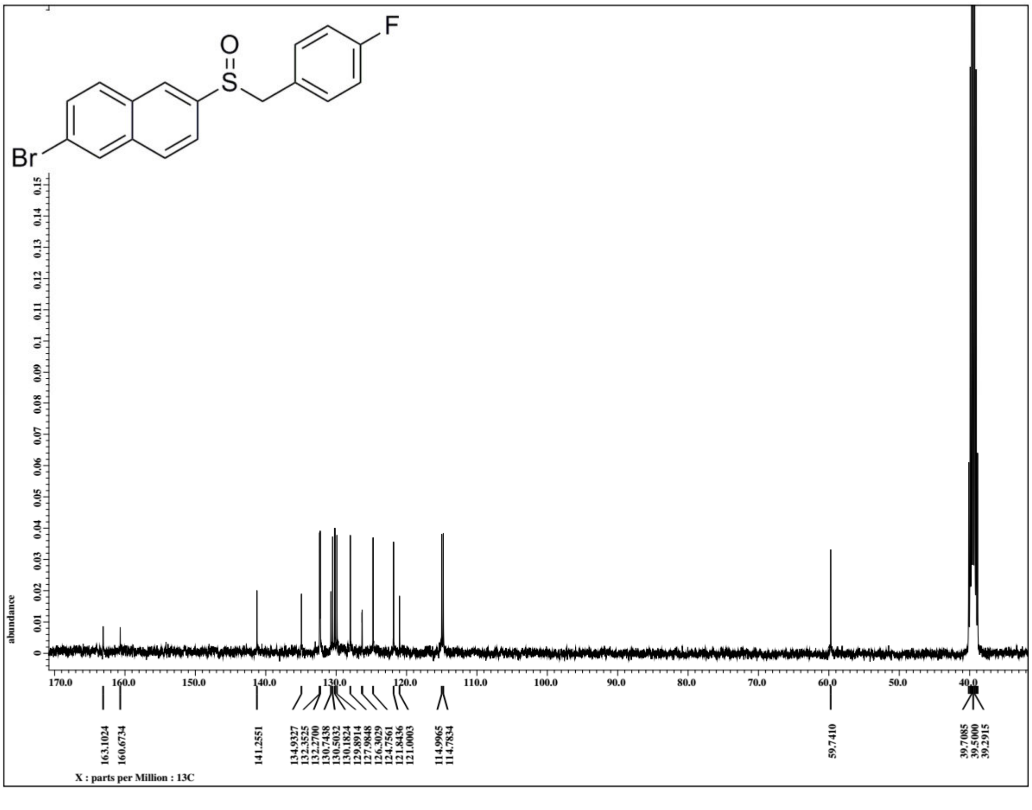

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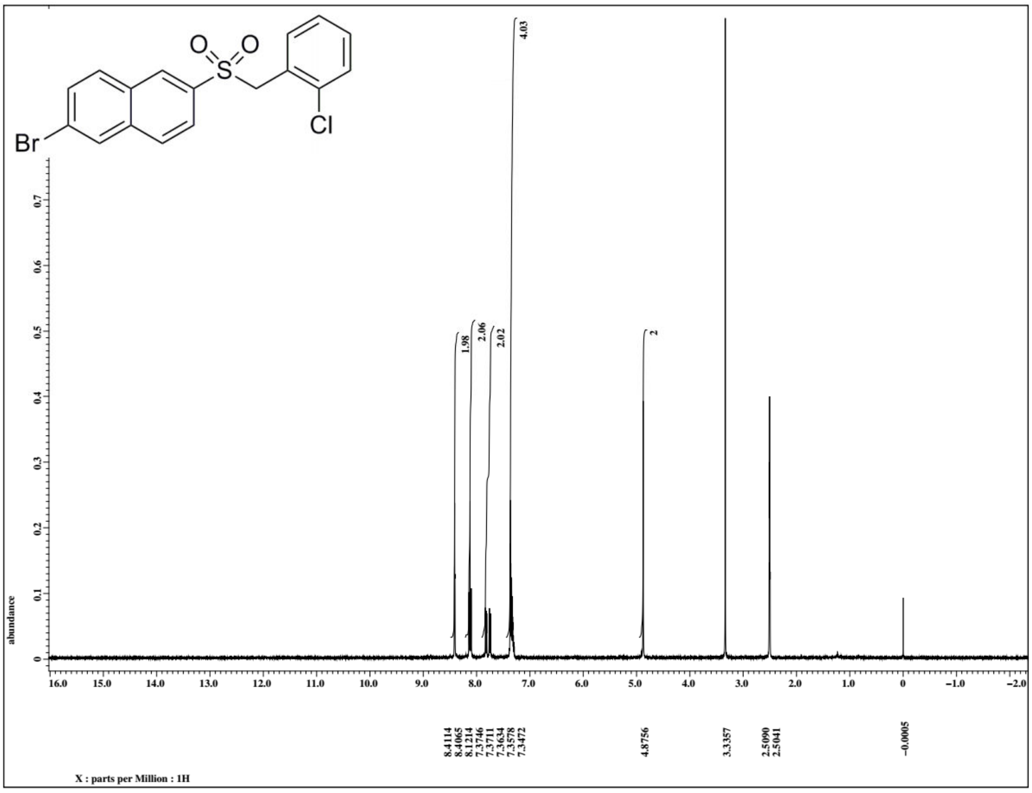

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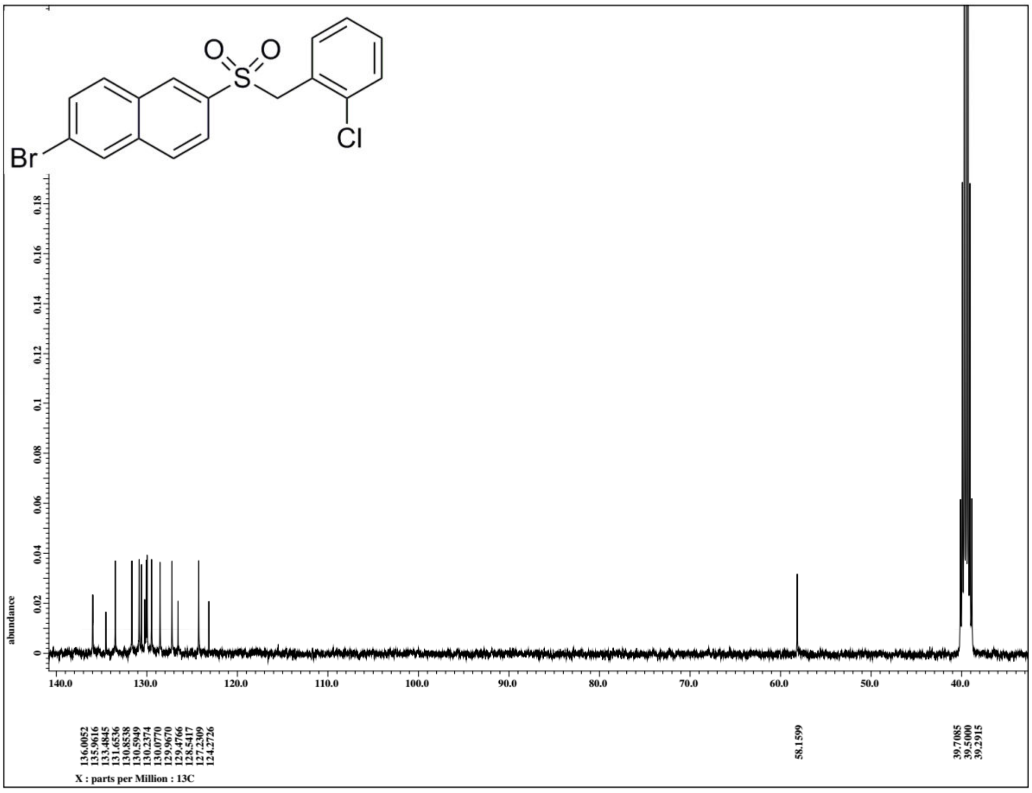

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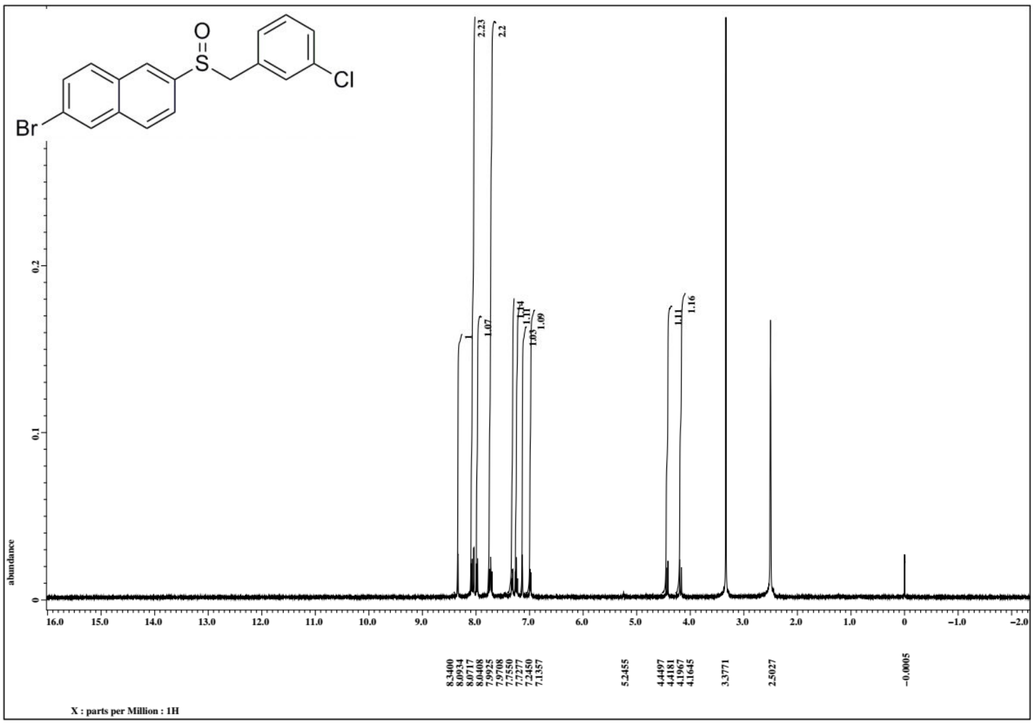

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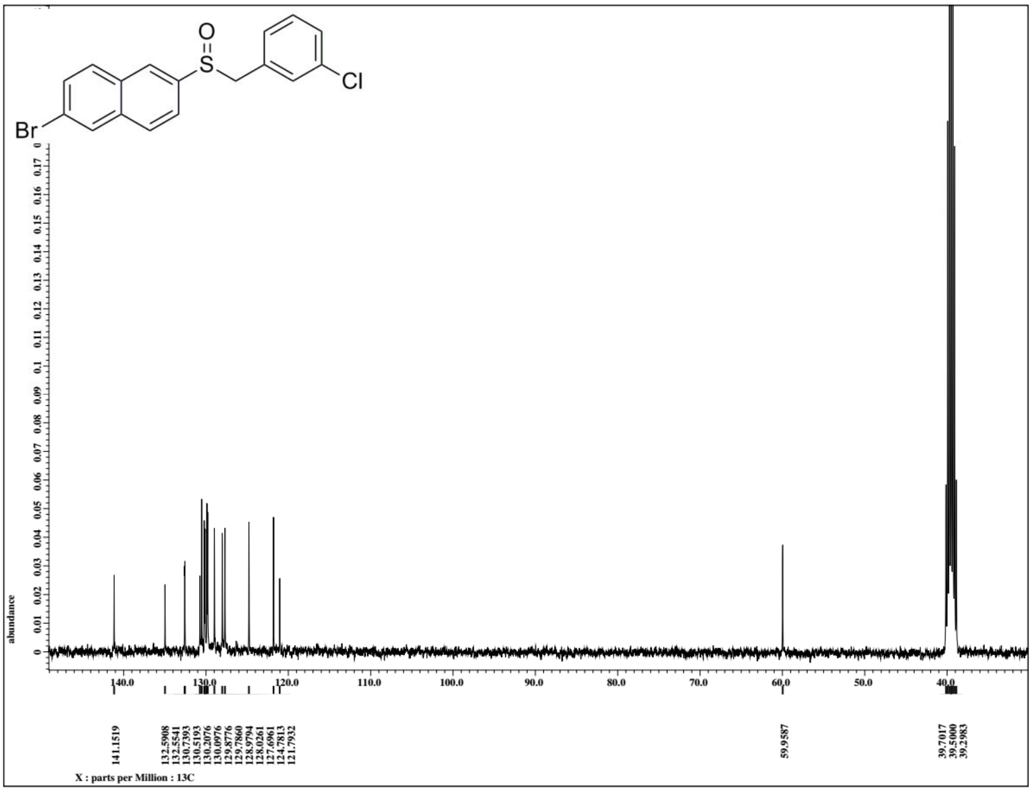
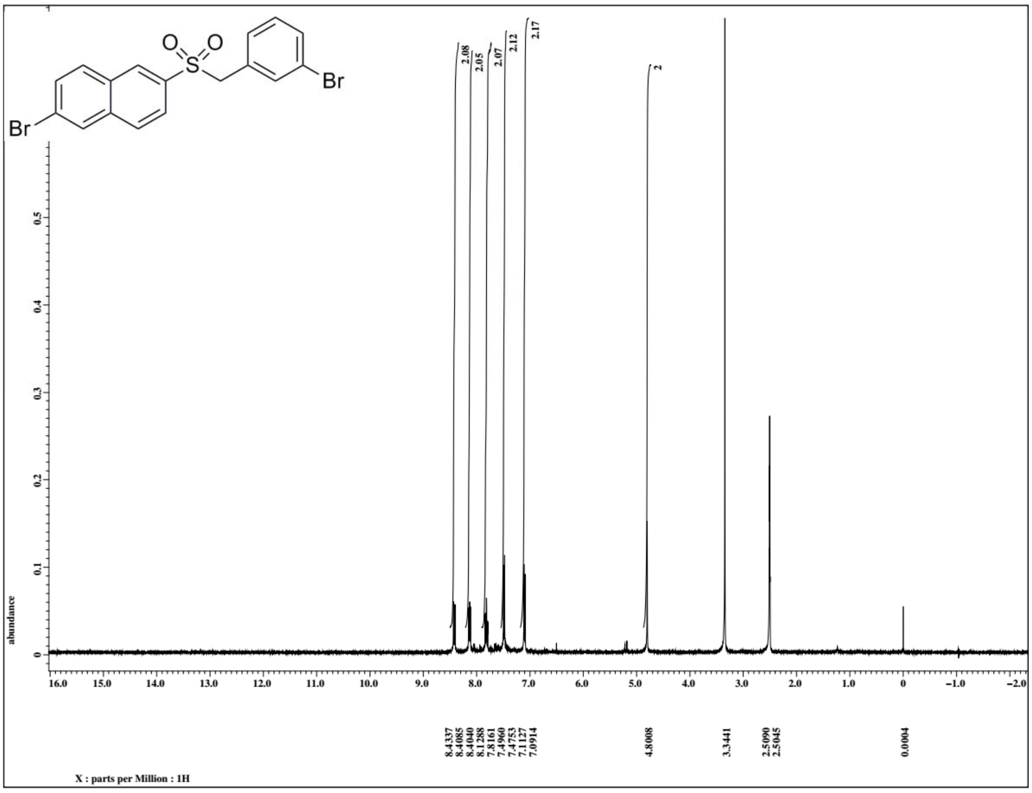


^{1}H-NMR of Compound 9t:



^{1}C-NMR of Compound 9t: