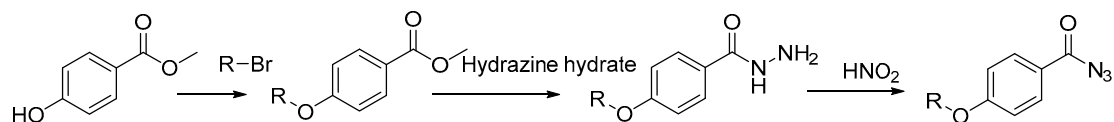


Figure S1. Comparison of the BIRB-796 molecular docking conformation (green) with the actual conformation (blue).

1. Process for synthesis of 1a-1o

4-methoxybenzoyl azide (**1a**): To a acetone solution of methyl 4-hydroxybenzoate (1.2 g, 7.22 mmol) were added K_2CO_3 (2 g, 8.67 mmol, 1.2 equiv) and dimethyl sulfate (1.18 g, 9.39 mmol, 1.3 equiv) and refluxed for 2 hours. The solvent acetone was then removed by vacuum evaporation to give a white solid (methyl 4-methoxybenzoate) which was used directly in the next step without purification. To a solution of the white solid in dichloromethane and water (25 mL, DCM: H_2O = 1: 4), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.25 g, 18.05 mmol, 2 equiv) were added slowly at $0^\circ C$. The resulting mixture was stirred for 15 mins at $0^\circ C$. The reaction mixture was then concentrated, dissolved in EtOAc (30 mL) and dried over anhydrous $MgSO_4$. The crude product was purified by flash column chromatography (20% ethyl acetate in petroleum ether) to give **1a** as a light yellow oil (0.54 g, 34 % yield). 1H NMR (600 MHz, $DMSO-d_6$) δ 7.27-7.21 (2H, $J=8.5$ Hz, d), 6.84-6.72 (2H, $J=8.5$ Hz, d), 3.97-3.46 (3H, $J=7.4$ Hz, t).

General Procedure for the formation of **1b-1o**



To a DMF solution of methyl 4-hydroxybenzoate were added NaH (60%, 1.2 equiv) and haloalkane (1.3 equiv) slowly at $0^\circ C$. The resulting mixture was brought to $60^\circ C$ and stirred for 2 hours. The solvent DMF was then removed by vacuum evaporation. The remaining mixture was added to a ethanol solution of hydrazine hydrate and reflux overnight. The solvent ethanol was removed by vacuum evaporation to give a white solid which was used directly in the next step without purification. To a mixed solution of the white solid in dichloromethane and water (25 mL, DCM: H_2O = 1: 4), hydrochloric acid (10%, 1.5 equiv) and sodium nitrite (2 equiv) were added slowly at $0^\circ C$. The resulting mixture was stirred for 15 mins at $0^\circ C$. The reaction mixture was then

concentrated, dissolved in EtOAc (30 mL) and dried over anhydrous MgSO₄. The crude product was purified by flash column chromatography (20% ethyl acetate in petroleum ether) to give **1b-1o**.

4-ethoxybenzoyl azide (**1b**): Following the general procedure, bromoethane (1.40 g, 12.82 mmol, 1.3 equiv) hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.15 g, 16.65 mmol, 2 equiv) gave **1b** as a light yellow oil (0.57 g, 36 % yield). ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.25-7.20 (2H, *J*=8.5 Hz, m), 6.85-6.71 (2H, *J*=8.5 Hz, d), 3.51-3.46 (2H, *J*=4.9 Hz, d), 1.70 (3H, *J*=7.4 Hz, t).

4-propoxybenzoyl azide (**1c**): Following the general procedure, 1-bromopropane (1.58 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.50 g, 15.45 mmol, 2 equiv) gave **1c** as a light yellow oil (0.63 g, 33 % yield). ¹H NMR (600 MHz, DMSO-*d*₆): δ 7.20-7.14 (2H, d, *J* = 7.7 Hz), 6.89-6.79 (2H, m), 3.94 (2H, t, *J* = 4.9 Hz), 1.90-1.74 (2H, m), 1.7 (t, *J*=7.4 Hz, 3H). 4-butoxybenzoyl azide (**1d**): Following the general procedure, 1-bromobutane (1.76 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1 g, 14.41 mmol, 2 equiv) gave **1d** as a light yellow oil (0.61 g, 38 % yield). ¹H NMR (600 MHz, DMSO-*d*₆): δ, 7.24-7.15 (2H, d, *J* = 7.7 Hz), 6.84-6.79 (2H, m), 3.94 (2H, t, *J* = 4.9 Hz), 1.90-1.74 (2H, m), 1.70-1.52 (2H, m), 1.44-1.32 (t, *J*=7.4 Hz, 3H). 4-(sec-butoxy)benzoyl azide (**1e**): Following the general procedure, 1-bromo-2-methylbutane (1.76 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1 g, 14.41 mmol, 2 equiv) gave **1e** as a light yellow oil (0.52 g, 33 % yield). ¹H NMR (600 MHz, DMSO-*d*₆): δ, 7.24-7.15 (2H, d, *J* = 8.5 Hz), 6.84-6.79 (2H, d, *J* = 8.5 Hz), 4.04 (1H, d, *J* = 4.9 Hz), 1.90-1.72 (3H, d, *J* = 6 Hz), 1.63-1.59 (2H, m), 1.44-1.32 (t, *J*=7.4 Hz, 3H). 4-(pentyloxy)benzoyl azide (**1f**): Following the general procedure, 1-bromopentane (1.94 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (0.93 g, 13.50 mmol, 2 equiv) gave **1f** as a light yellow oil (0.49 g, 30 % yield). ¹H NMR (600 MHz, DMSO-*d*₆): δ 7.66-7.12 (2H, d, *J* = 8.5 Hz), 6.99-6.83 (2H, d, *J* = 8.5 Hz), 3.95 (2H, t, *J* = 6.5 Hz), 1.73-1.66 (d, 2 H), 1.35-1.27 (d, 4 H), 0.89 (t, *J*=7.2 Hz, 3 H). 4-(2-methoxyethoxy)benzoyl azide (**1g**): Following the general procedure, 1-bromo-2-methoxyethane (1.78 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (0.98 g, 14.27 mmol, 2 equiv) gave **1g** as a light yellow oil (0.56 g, 35 % yield). ¹H NMR (600 MHz, DMSO-*d*₆): δ, 7.22-7.17 (d, *J*=8.5 Hz, 2 H), 6.81-6.73 (d, *J*=8.5 Hz, 2 H), 4.03 (2H, t, *J* = 6.5 Hz), 3.70 (2H, t, *J* = 6.7 Hz), 3.40 (3H, s, *J* = 6.9 Hz).

4-isopropoxybenzoyl azide (**1h**): Following the general procedure, 2-bromopropane (1.58 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.07 g, 15.45 mmol, 2 equiv) gave **1h** as a light yellow oil (0.67 g, 45 % yield). ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.33-7.17 (d, *J*=8.8 Hz, 2 H), 6.84-6.78 (d, *J*=9.0 Hz, 2 H), 3.84-3.68 (m, 1 H), 1.22 (d, *J*=6.0 Hz, 6 H).

3-chlorobenzoyl azide (**1i**): Following the general procedure, methyl 3-chlorobenzoate (1.5 g, 8.79 mmol, 1 equiv) hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.21 g, 17.59 mmol, 2 equiv) gave **1i** as a light yellow oil (1.07 g, 66 % yield). ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.80 (d, *J*=9.0 Hz, 2 H), 7.64-7.56 (d, *J*=9.0 Hz, 2 H). 2-chlorobenzoyl azide (**1j**): Following the general procedure, methyl 2-chlorobenzoate (1.5 g, 8.79 mmol, 1 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.21 g, 17.59 mmol, 2 equiv) gave **1j** as a light yellow oil (1.09 g, 68 % yield). ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.98-7.76 (m, 2H), 7.56 -7.33 (m, 2H).

4-bromobenzoyl azide (**1k**): Following the general procedure, methyl 3-bromobenzoate (1.5 g, 6.98 mmol, 1 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (0.96 g, 13.95 mmol, 2 equiv) gave **1k** as a light yellow solid (0.93 g, 59 % yield). M.p. 46-47°C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.98 (s, 1H), 7.76 (d, *J*=9.0 Hz, 1H), 7.56 (d, *J*=9.0 Hz, 1H), 7.33 (m, 1H).

4-fluorobenzoyl azide (**1l**): Following the general procedure, methyl 3-fluorobenzoate (1.5 g, 9.73 mmol, 1 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.34 g, 19.49 mmol, 2 equiv) gave **1l** as a light yellow solid (1 g, 61 % yield). M.p. 39-41°C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.78 (s, 1H), 7.64 (d, *J*=9.0 Hz, 1H), 7.56 (d, *J*=9.0 Hz, 1H), 7.24 (m, 1H).

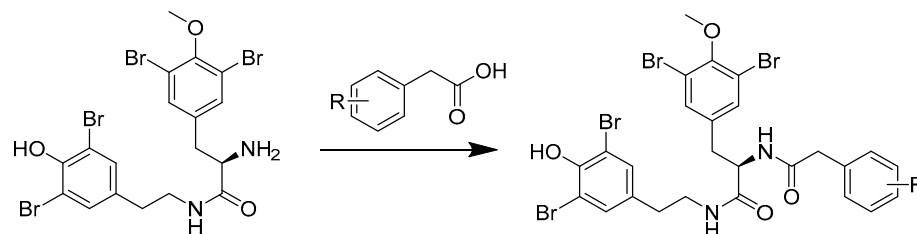
2-fluorobenzoyl azide (**1m**): Following the general procedure, methyl 2-fluorobenzoate (1.5 g, 9.73 mmol, 1 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.34 g, 19.49 mmol, 2 equiv) gave **1m** as a light yellow oil (0.87 g, 54 % yield). M.p. 32-34°C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.84-7.81 (d, *J*=8.5 Hz, 1 H), 7.71-7.61 (d, *J*=8.5 Hz, 1 H), 7.42 (d, *J*=8.5 Hz, 2 H).

4-methylbenzoyl azide (**1n**): Following the general procedure, methyl 3-methylbenzoate (1.5 g, 9.99 mmol, 1 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (1.38 g, 19.98 mmol, 2 equiv) gave **1n** as a light yellow oil (0.93 g, 57 % yield). M.p. 33-34°C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.79 (s, 1H), 7.72 (d, *J*=8.5 Hz, 1H), 7.31 (d, *J*=8.5 Hz, 1H), 3.46 (s, 3H), 2.24 (s, 3 H).

3-(3-morpholinopropyl)benzoyl azide (**1o**): Following the general procedure, T 4-(3-bromopropyl)morpholine (2.67 g, 12.82 mmol, 1.3 equiv), hydrochloric acid (10%, 4 mL, 1.5 equiv) and sodium nitrite (0.74 g, 10.74 mmol, 2 equiv) gave **1o** as a light yellow solid (0.44 g, 28 % yield). M.p. 49-51°C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.85-7.80 (d, *J*=8.5 Hz, 2 H), 7.35-7.21 (d, *J*=8.5 Hz, 2 H), 4.48-4.32 (t, *J*=4.9 Hz, 1 H), 3.35-3.26 (t, *J*=5.7 Hz, 4 H), 3.04-2.87 (t, *J*=5.7 Hz, 4 H), 2.85 (m, 2 H), 2.39 (m, 2 H).

2. General Procedure for the formation of 4a-4o

To a DMF solution of **3a-3o** was added EDCI (1.1 equiv) and HOBt (1.1 equiv) at 0°C. The resulting mixture was brought to room temperature and stirred for 30 mins. Then (R) -2-amino-N-(3,5-dibromo-4-hydroxyphenethyl) -3- (3,5-dibromo-4-methoxyphenyl) propanamide (**2q**, 0.9 equiv) was added to the mixture and continue stirred for 1 hour. The reaction mixture was quenched with water and filtered. The crude product was recrystallized with ethanol (18 mL) to give **4a-4o**.



Compound No.	R	Compound No.	R
4A	4-methyl ether	4H	4-isopropoxy ether
4B	4-ethyl ether	4I	3-Cl
4C	4-propyl ether	4J	2-Cl
4D	4-butyl ether	4K	4-Br
4E	4-sec-butyl ether	4L	4-F

4F	4-pentyl ether	4M	2-F
4G	4-(2-methoxyethoxy ether)	4N	4-methy
		4O	4-(3-morpholinopropoxy ether)

(3,5-dibromo-4-methoxyphenyl) -2- [2- (4-methoxy) Phenyl] aminoacetyl] propionamide (4a)

Following the general procedure, **3a** (0.25 g, 1.20 mmol) gave **4a** as a white solid (0.45 g, 46% yield). m.p.: 151-153°C. $[\alpha]_D^{20}$ -8.25 (c 0.66, MeOH). ¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.0 (C=O), 169.0 (C=O), 152.2 (=C-O), 149.3(C-O), 138.0 (C-N), 132.8 (C-Br), 131.9 (C-Br), 129.3 (-C=), 127.2 (-C=), 117.3 (-C=), 115.1 (-C=), 112.2 (-C=), 70.2 (-C=), 60.7 (-O-CH₃), 54.2 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 37.0 (CH₂), 33.7 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-ethoxy Phenyl) aminoacetyl] propionamide (4b)

Following the general procedure, **3b** (0.25 g, 1.39 mmol) gave **4b** as a white solid (0.58 g, 53% yield). mp: 177-180°C. $[\alpha]_D^{20}$ -8.92 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (d, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 170.0 (C=O), 168.6 (C=O), 155.8 (=C-O), 153.5 (=C-O), 150.3 (C-O), 137.0 (C-N), 133.9 (C-N), 132.6 (C-Br), 129.2 (C-Br), 126.7 (-C=), 119.8 (-C=), 114.8 (-C=), 112.5 (-C=), 70.42 (-C=), 63.4 (-O-CH₃), 45.5 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 34.5 (CH₂), 32.0 (CH₂), 15.1 (CH₃).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-propoxy Phenyl) aminoacetyl] propanamide (4c)

Following the general procedure, **3c** gave **4c** as a white solid (0.55 g, 53% yield). mp: 171-173 °C. $[\alpha]_D^{20}$ -9.35 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (d, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 170.0 (C=O), 169.0 (C=O), 155.7 (=C-O), 153.7 (=C-O), 138.0 (C-N), 133.8 (C-N), 132.8 (C-Br), 130.2 (C-Br), 128.3 (-C=), 119.9 (-C=), 117.6 (-C=), 114.9 (-C=), 69.4 (-C=), 60.7 (-O-CH₃), 40.4 (CH₂), 34.7 (CH₂), 22.5 (CH₂), 10.8 (CH₃).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-butoxy Phenyl) aminoacetyl] propionamide (4d)

Following the general procedure, **3d** (0.25 g, 1.20 mmol) gave **4d** as a white solid (0.41 g, 42%

yield). mp: 191-194 °C. $[\alpha]_D^{20}$ -8.25 (c 10.98, MeOH).

$^1\text{H NMR}$ (600 MHz, DMSO- d_6) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, $J=8.5$ Hz, 2 H), 6.71 - 6.85 (d, $J=8.5$ Hz, 2 H), 6.28 (d, $J=8.5$ Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, $J=12.1, 5.7$ Hz, 1 H), 2.85 (dd, $J=13.5, 4.0$ Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, $J=4.9$ Hz, 2 H).

$^{13}\text{C NMR}$ (150 MHz, DMSO- d_6) δ 171.0 (C=O), 170.0 (C=O), 155.7 (=C-O), 153.7 (=C-O), 149.3 (C-O), 134.6 (C-N), 133.9 (C-N), 132.7 (C-Br), 130.1 (C-Br), 128.2(-C=), 119.8(-C=), 114.7(-C=), 112.3(-C=), 67.6 (-O-CH₃), 40.7 (CH₂), 34.5 (CH₂), 31.2 (CH₂), 19.1 (CH₂), 14.1 (CH₃).

(R)-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-sec-Phenyl)aminoacetyl] propionamide (4e)

Following the general procedure, 3e (0.25 g, 1.20 mmol) gave 4D as a white solid (0.49 g, 50% yield). mp: 160-166 °C. $[\alpha]_D^{20}$ -6.39 (c 0.66, MeOH).

$^1\text{H NMR}$ (600 MHz, DMSO- d_6) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, $J=8.5$ Hz, 2 H), 6.71 - 6.85 (d, $J=8.5$ Hz, 2 H), 6.28 (d, $J=8.5$ Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, $J=12.1, 5.7$ Hz, 1 H), 2.85 (dd, $J=13.5, 4.0$ Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, $J=4.9$ Hz, 2 H).

$^{13}\text{C NMR}$ (150 MHz, DMSO- d_6) δ 171.1 (C=O), 170.6 (C=O), 156.6 (=C-O), 152.19 (=C-O), 149.4 (C-O), 138.0 (C-N), 134.2 (C-N), 133.8 (C-Br), 132.8 (C-Br), 130.2 (-C=), 128.3 (-C=), 117.3 (-C=), 115.7 (-C=), 112.2 (-C=), 74.4 (-C=), 60.7 (-O-CH₃), 54.1 (CH₂), 41.6 (CH₂), 40.4 (CH₂), 37.0 (CH₂), 33.7 (CH₂), 28.9 (CH₂), 19.5 (CH₃), 9.9 (CH₃).

(R)-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-pentyl Phenyl)aminoacetyl] propionamide (4F)

Following the general procedure, 3f (0.25 g, 1.13 mmol) gave 4F as a white solid (0.51 g, 55% yield). mp: 174-178 °C. $[\alpha]_D^{20}$ -6.71 (c 0.66, MeOH).

$^1\text{H NMR}$ (600 MHz, DMSO- d_6) δ 8.25 (d, $J=8.7$ Hz, 1 H), 8.09 (t, $J=5.6$ Hz, 1 H), 7.51 (s, 2 H), 7.35 - 7.41 (d, 2 H), 6.95 - 7.01 (d, $J=8.5$ Hz, 2 H), 6.72 - 6.78 (d, $J=8.7$ Hz, 2 H), 4.33 - 4.42 (m, 1 H), 3.89 (t, $J=6.5$ Hz, 2 H), 3.72 - 3.78 (m, 3 H), 3.30 - 3.38 (m, 2 H), 3.15 - 3.27 (m, 2 H), 2.81 (dd, $J=13.6, 3.9$ Hz, 1 H), 2.54 - 2.67 (m, 3 H), 1.68 (quin, $J=6.8$ Hz, 2 H), 1.29 - 1.41 (m, 4 H), 0.89 (t, $J=7.1$ Hz, 3 H).

$^{13}\text{C NMR}$ (150 MHz, DMSO- d_6) δ 171.0 (C=O), 170.6 (C=O), 157.5 (=C-O), 152.1 (=C-O), 149.4 (C-O), 137.9 (C-N), 133.8 (C-N), 132.8 (C-Br), 130.2 (C-Br), 128.3 (-C=), 117.2 (-C=), 114.4 (-C=), 112.2 (-C=), 67.7 (-C=), 60.7 (-O-CH₃), 54.0 (CH₂), 41.6 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 37.0 (CH₂), 33.7 (CH₂), 28.8 (CH₂), 28.1 (CH₂), 22.3 (CH₂), 14.3 (CH₃).

(R)-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-pentyl Phenyl)aminoacetyl] propanamide (4g)

Following the general procedure, 3g (0.25 g, 1.19 mmol) gave 4g as a white solid (0.62 g, 61% yield). mp: 181-183 °C. $[\alpha]_D^{20}$ -6.91 (c 0.66, MeOH).

$^1\text{H NMR}$ (600 MHz, DMSO- d_6) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, $J=8.5$ Hz, 2 H), 6.71 - 6.85 (d, $J=8.5$ Hz, 2 H), 6.28 (d, $J=8.5$ Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, $J=12.1, 5.7$ Hz, 1 H), 2.85 (dd, $J=13.5, 4.0$ Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, $J=4.9$ Hz, 2 H).

$^{13}\text{C NMR}$ (150 MHz, DMSO- d_6) δ 170.1 (C=O), 168.7 (C=O), 155.4 (=C-O), 153.5 (=C-O),

149.3(C-O), 134.6 (C-N), 132.7 (C-N), 128.25 (C-Br), 119.7 (C-Br), 114.9 (-C=), 112.3 (-C=), 70.4 (-C=), 66.0 (-C=), 54.5 (-O-CH₃), 40.3 (CH₂), 39.5 (CH₂), 34.50 (CH₂), 31.2 (CH₂), 22.5 (CH₂), 10.8 (CH₂)

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-isopropyl Phenyl) aminoacetyl] propionamide (4h)

Following the general procedure, 3H (0.25 g, 1.29 mmol) gave 4h as a white solid (0.57 g, 55% yield). mp: 169-173 °C. $[\alpha]_D^{20}$ -8.75 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.2 (C=O), 170.0 (C=O), 155.7 (=C-O), 153.7 (=C-O), 137.0 (C-O), 133.8 (C-N), 133.4 (C-N), 127.0 (C-Br), 119.9 (C-Br), 117.6 (-C=), 114.9 (-C=), 69.4 (-C=), 54.2 (-O-CH₃), 40.4 (CH₂), 34.7 (CH₂), 22.5 (CH₃), 10.8 (CH₃).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (3-chlorophenyl) Aminoacetyl] propionamide (4i)

Following the general procedure, 3i (0.25 g, 1.47 mmol) gave 4i as a white solid (0.55 g, 59% yield). m.p.: 208-213 °C. $[\alpha]_D^{20}$ -8.16 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.40 (d, *J*=8.5 Hz, 1 H), 8.13 (t, *J*=5.6 Hz, 1 H), 7.46 - 7.52 (d, 2 H), 7.38 (s, 2 H), 7.23 - 7.27 (d, 2 H), 7.19 (s, 1 H), 6.98 - 7.09 (d, 1 H), 4.37 - 4.43 (m, 1 H), 3.75 (s, 3 H), 3.42 - 3.48 (m, 1 H), 3.40 (s, 1 H), 3.31 - 3.37 (m, 2 H), 2.81 (dd, *J*=13.7, 4.1 Hz, 1 H), 2.55 - 2.68 (m, 3 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 172.2 (C=O), 170.4 (C=O), 155.6 (=C-O), 152.6 (=C-O), 149.4 (C-O), 140.98 (C-N), 138.08 (C-N), 132.2 (C-Cl), 128.8 (C-Br), 122.0 (C-Br), 118.6 (-C=), 115.2 (-C=), 113.2 (-C=), 70.7 (-C=), 54.5(-O-CH₃), 40.3 (CH₂), 39.5 (CH₂), 34.6 (CH₂), 21.6 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (2-chlorophenyl) Aminoacetyl] propionamide (4J)

Following the general procedure, 3j (0.25 g, 1.47 mmol) gave 4j as a white solid (0.49 g, 52% yield). m.p.: 186-193 °C. $[\alpha]_D^{20}$ -8.67 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 9.68 (br. s., 1 H), 8.35 (d, *J*=8.7 Hz, 1 H), 8.11 (t, *J*=5.6 Hz, 1 H), 7.54 (s, 2 H), 7.40 (s, 2 H), 7.35 (dd, *J*=7.7, 1.5 Hz, 1 H), 7.17 - 7.24 (d, 2 H), 7.11 - 7.15 (d, 1 H), 4.44 (ddd, *J*=10.5, 8.8, 4.0 Hz, 1 H), 3.72 - 3.79 (m, 3 H), 3.49 - 3.60 (m, 2 H), 3.31 - 3.41 (m, 2 H), 2.63 - 2.68 (m, 2 H), 2.57 - 2.63 (m, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.0 (C=O), 169.0 (C=O), 152.2 (=C-O), 149.4 (=C-O), 138.0 (C-O), 134.4 (C-N), 134.3 (C-N), 133.9 (C-Cl), 133.9 (C-Br), 132.8 (C-Br), 132.0 (-C=), 129.3 (-C=), 128.7 (-C=), 127.2 (-C=), 117.3 (-C=), 112.2 (-C=), 60.7 (-O-CH₃), 54.2, 40.3 (CH₂), 39.5 (CH₂), 37.0 (CH₂), 33.7 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-bromophenyl) Aminoacetyl] propionamide (4k).

Following the general procedure, 3k (0.25 g, 1.16 mmol) gave 4k as a white solid (0.49 g, 51% yield). m.p.: 221-225 °C. $[\alpha]_D^{20}$ -10.13 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 9.68 (br. s., 1 H), 8.37 (d, *J*=8.7 Hz, 1 H), 8.12 (t, *J*=5.6 Hz, 1 H), 7.49 (s, 2 H), 7.37 - 7.43 (d, 4 H), 7.05 (d, *J*=8.3 Hz, 2 H), 4.33 - 4.46 (m, 1 H), 3.75 (s, 3 H), 3.42 (d, *J*=13.9 Hz, 1 H), 3.29 - 3.38 (m, 2 H), 3.19 (dq, *J*=12.6, 6.3 Hz, 1 H), 2.81 (dd, *J*=13.6, 4.0 Hz, 1 H), 2.55 - 2.68 (m, 3 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.7 (C=O), 155.8 (C=O), 153.7 (=C-O), 149.4 (=C-O), 133.9 (C-O), 132.6 (C-N), 130.1 (C-N), 128.0 (C-Br), 119.8 (C-Br), 114.9 (-C=), 112.5 (-C=), 67.9 (-C=), 60.7 (-O-CH₃), 40.3 (CH₂), 39.5 (CH₂).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-fluorophenyl) aminoacetyl] propionamide (4l)**

Following the general procedure, 3l (0.25 g, 1.62 mmol) gave 4l as a white solid (0.64 g, 52% yield). m.p. : 186-189 °C. [α]_D²⁰-7.72 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.0 (C=O), 170.2 (C=O), 162.0 (=C-O), 160.4 (=C-O), 152.2 (C-O), 149.3 (C-N), 137.9 (C-N), 134.3 (C-F), 133.8 (C-Br), 132.8 (C-Br), 131.0 (-C=), 130.9 (-C=), 117.3 (-C=), 115.2 (-C=), 115.0 (-C=), 112.2 (-C=), 60.7(-O-CH₃), 54.0 (CH₂), 41.5 (CH₂), 37.0 (CH₂), 33.6 (CH₂).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(2-fluorophenyl) aminoacetyl] propionamide (4m)**

Following the general procedure, 3m (0.25 g, 1.62 mmol) gave 4m as a white solid (0.69 g, 56% yield). m.p. : 181-183 °C. [α]_D²⁰-8.05 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.6 (C=O), 170.6 (C=O), 155.8 (=C-O), 153.7 (=C-O), 152.0 (C-O), 139.8 (C-N), 133.8 (C-N), 133.4 (C-F), 130.3 (C-Br), 128.3 (C-Br), 119.9 (-C=), 117.6 (-C=), 112.9 (-C=), 67.9 (-C=), 60.7 (-O-CH₃), 40.3 (CH₂), 39.5 (CH₂).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-methylbenzene Yl) aminoacetyl] propionamide (4n)**

Following the general procedure, 3n (0.25 g, 1.62 mmol) gave 4n as a white solid (0.69 g, 56% yield). m.p. : 230-233 °C. [α]_D²⁰-9.96 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 9.64 (br. s., 1 H), 8.27 (d, *J*=8.7 Hz, 1 H), 8.09 (t, *J*=5.6 Hz, 1 H), 7.51 (s, 2 H), 7.39 (s, 2 H), 7.00 - 7.04 (d, *J*=7.9 Hz, 2 H), 6.94 - 6.98 (d, *J*=7.9 Hz, 2 H), 4.32 - 4.45 (m, 1 H), 3.76 (s, 3 H), 3.39 (d, *J*=13.9 Hz, 1 H), 3.34 (dd, *J*=13.5, 6.7 Hz, 1 H), 3.27 (d, *J*=13.9 Hz, 1 H), 3.13 - 3.23 (m, 1 H), 2.80 (dd, *J*=13.6, 4.0 Hz, 1 H), 2.54 - 2.67 (m, 3 H), 2.19 - 2.25 (m, 3 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.2 (C=O), 170.6 (C=O), 155.6 (=C-O), 140.9 (=C-O), 138.0 (C-O), 132.2 (C-N), 128.8 (C-N), 122.0 (C-Br), 118.6 (C-Br), 115.2 (-C=), 113.2 (-C=), 67.9 (-C=),

60.4 (-O-CH₃), 54.8 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 34.7 (CH₂), 22.3 (CH₃).

(R)-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-(2-Methyl ether)) aminoacetyl] propionamide (4o)

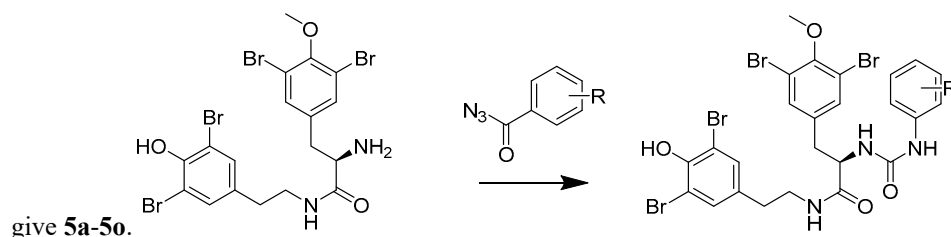
Following the general procedure, 3o (0.25 g, 0.90 mmol) gave 4o as a white solid (0.44 g, 45% yield). m.p.: 232-235 °C. $[\alpha]_D^{20}$ -8.59 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 170.0 (C=O), 169.0 (C=O), 155.7 (=C-O), 153.7 (=C-O), 137.9 (C-O), 133.8 (C-O), 132.8 (C-N), 130.2 (C-N), 128.3 (C-Br), 119.9 (C-Br), 117.6 (-C=), 114.9 (-C=), 74.6 (-C=), 69.4 (-C=), 60.7 (-O-CH₃), 57.4 (CH₂), 34.7 (CH₂), 22.5 (CH₂), 10.8 (CH₃).

3. General Procedure for the formation of 5a-5o

Aryl azide **1a-1o** was added into 1,2-dichloroethane and stirred for 30 mins at 80°C. To the solution of **1a-1o** in 1,2-dichloroethane, (R)-2-amino-N-(3,5-dibromo-4-hydroxy-phenethyl)-3-(3,5-dibromo-4-methoxyphenyl)propanamide (**2q**, 0.65 g, 1.03 mmol, 0.9 equiv) was added and stirred for 2 hours at 80°C. The reaction mixture was then concentrated and recrystallized with DCM (20 mL) to



Compound No.	R	5H	4-isopropoxy ether
5A	4-methyl ether	5I	3-Cl
5B	4-ethyl ether	5J	2-Cl
5C	4-propyl ether	5K	4-Br
5D	4-butyl ether	5L	4-F
5E	4-sec-butyl ether	5M	2-F
5F	4-pentyl ether	5N	4-methy
5G	4-(2-methoxyethoxy ether	5O	4-(3-morpholinoproxy ether

(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-methoxy) Phenyl] ureido] propionamide (5A):

Following the general procedure, **1a** (0.25 g, 1.14 mmol) gave **5a** as a white solid (0.19 g, 21% yield). M.p.: 149-150°C. $[\alpha]_D^{20}$ -14.31 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.5 (C=O), 155.1 (C=O), 153.8 (=C-O), 152.2 (=C-O), 137.8

(C-O), 133.9 (C-O), 132.7 (C-O), 119.8 (C-N), 117.3 (C-N), 114.9 (C-Br), 112.4 (C-Br), 67.9 (-O-CH₃), 54.25 (CH₂), 40.35 (CH₂), 39.55 (CH₂).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-ethoxy Phenyl) ureido] propionamide (5b)**

Following the general procedure, 1b (0.25 g, 1.31 mmol) gave 5b as a white solid (0.31 g, 29% yield). mp: 194-203 °C. $[\alpha]_D^{20}$ -19.14 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.42 (s, 1 H), 8.18 (t, *J*=5.6 Hz, 1 H), 7.44 (s, 2 H), 7.40 (s, 2 H), 7.15 - 7.23 (d, 2 H), 6.74 - 6.81 (d, 2 H), 6.26 (d, *J*=8.5 Hz, 1 H), 4.38 (td, *J*=8.5, 5.1 Hz, 1 H), 3.93 (q, *J*=7.0 Hz, 2 H), 3.73 - 3.76 (m, 3 H), 3.32 (dq, *J*=13.1, 6.8 Hz, 3 H), 2.84 (dd, *J*=13.7, 4.9 Hz, 1 H), 2.52 - 2.66 (m, 3 H), 1.28 (t, *J*=7.0 Hz, 3 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 158.3 (C=O), 154.7 (C=O), 152.6 (=C-O), 149.8 (=C-O), 143.0 (=C-O), 136.1 (C-O), 130.3 (C-O), 129.8 (C-N), 129.6 (C-N), 123.1 (C-N), 122.6 (C-Br), 120.9 (C-Br), 117.7 (-C=), 115.8 (-C=), 111.4 (-C=), 67.8 (-O-CH₃), 41.6 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 29.2 (CH₃).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-propoxy Phenyl) ureido] propionamide (5c)**

Following the general procedure, 1c (0.25 g, 1.22 mmol) gave 5c as a white solid (0.33 g, 34% yield). mp: 173-176 °C. $[\alpha]_D^{20}$ -15.38 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 172.3 (C=O), 155.2 (C=O), 153.7 (=C-O), 152.2 (=C-O), 138.2 (C-O), 133.9 (C-N), 132.3 (C-N), 119.8 (C-N), 117.3 (C-Br), 114.9 (C-Br), 113.0 (-C=), 67.9 (-O-CH₃), 54.1 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 34.5 (CH₂), 22.5 (CH₂), 10.8 (CH₃).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-butoxy Phenyl) ureido] propionamide (5d)**

Following the general procedure, 1d (0.25 g, 1.14 mmol) gave 5d as a white solid (0.22 g, 24% yield). mp: 185-188 °C. $[\alpha]_D^{20}$ -10.88 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 172.1 (C=O), 155.7 (C=O), 153.5 (=C-O), 149.3 (=C-O), 137.9 (C-O), 134.6 (C-N), 132.7 (C-N), 119.8 (C-N), 117.4 (C-Br), 114.9 (C-Br), 112.3 (-C=), 66.0 (-O-CH₃), 55.1 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 34.5 (CH₂), 31. (CH₂)₂, 22.5 (CH₂), 10.8 (CH₃).

***(R)*-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-sec- Phenyl) ureido] propionamide (5E)**

Following the general procedure, 1e (0.25 g, 1.14 mmol) gave 5e as a white solid (0.27g, 29% yield). mp: 174-176 °C. $[\alpha]_D^{20}$ -14.37 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20

- 7.25 (d, $J=8.5$ Hz, 2 H), 6.71 - 6.85 (d, $J=8.5$ Hz, 2 H), 6.28 (d, $J=8.5$ Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, $J=12.1, 5.7$ Hz, 1 H), 2.85 (dd, $J=13.5, 4.0$ Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, $J=4.9$ Hz, 2 H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 171.8 (C=O), 155.8 (C=O), 153.7 (=C-O), 151.8 (=C-O), 136.1 (C-O), 133.9 (C-N), 132.6 (C-N), 119.8 (C-N), 117.3 (C-Br), 114.9 (C-Br), 112.5 (-C=), 67.9 (-O-CH₃), 60.7 (CH₂), 40.3 (CH₂), 39.5 (CH₂), 34.5 (CH₂), 28.9 (CH₂), 28.1 (CH₂), 22.3 (CH₃), 14.3 (CH₃).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-pentyl Phenyl) ureido] propionamide (5f)

Following the general procedure, 1f (0.25 g, 1.07 mmol) gave 5f as a white solid (0.33 g, 34% yield). mp: 186-193 °C. $[\alpha]_D^{20}$ -14.89 (c 0.66, MeOH).

^1H NMR (600 MHz, DMSO- d_6) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, $J=8.5$ Hz, 2 H), 6.71 - 6.85 (d, $J=8.5$ Hz, 2 H), 6.28 (d, $J=8.5$ Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, $J=12.1, 5.7$ Hz, 1 H), 2.85 (dd, $J=13.5, 4.0$ Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, $J=4.9$ Hz, 2 H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 171.5 (C=O), 155.1 (C=O), 153.8 (=C-O), 152.2 (=C-O), 137.8 (C-O), 133.9 (C-N), 132.7 (C-N), 119.8 (C-N), 117.3 (C-Br), 114.9 (C-Br), 112.4 (-C=), 68.0 (-O-CH₃), 60.7 (CH₂), 54.1 (CH₂), 38.0 (CH₂), 33.7 (CH₂), 28.8, (CH₂), 28.1 (CH₂), 22.3 (CH₂), 14.3 (CH₃).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4- (3-Morpholinopropyl) phenyl) ureido] propionamide (5g)

Following the general procedure, 1g (0.25 g, 1.13 mmol) gave 5g as a white solid (0.37 g, 39% yield). mp: 179-182 °C. $[\alpha]_D^{20}$ -10.44 (c 0.66, MeOH).

^1H NMR (600 MHz, DMSO- d_6) δ 8.49 (s, 1 H), 8.18 (t, $J=5.2$ Hz, 1 H), 7.45 (s, 2 H), 7.29 (s, 2 H), 7.14 - 7.25 (d, $J=8.8$ Hz, 2 H), 6.65 - 6.84 (d, $J=8.8$ Hz, 2 H), 6.34 (d, $J=8.5$ Hz, 1 H), 4.27 - 4.45 (m, 1 H), 3.92 (t, $J=6.2$ Hz, 2 H), 3.75 (s, 3 H), 3.50 - 3.61 (m, 4 H), 3.29 (dq, $J=13.2, 6.6$ Hz, 1 H), 3.10 - 3.21 (m, 1 H), 2.85 (dd, $J=13.6, 4.6$ Hz, 1 H), 2.70 (dd, $J=13.5, 8.6$ Hz, 1 H), 2.54 (br. s., 2 H), 2.39 (t, $J=7.2$ Hz, 2 H), 2.35 (br. s., 4 H), 1.82 (quin, $J=6.7$ Hz, 2 H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 171.5 (C=O), 155.2 (C=O), 153.7 (=C-O), 152.2 (=C-O), 137.8 (C-O), 133.86 (C-N), 132.3 (C-N), 119.8 (C-Br), 113.0 (C-Br), 66.6 (-O-CH₃), 66.3 (CH₂), 60.7 (CH₂), 55.3 (CH₂), 53.8 (CH₂), 38.0 (CH₂), 33.8 (CH₂), 26.3 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4-isopropyl Phenyl) ureido] propionamide (5h)

Following the general procedure, 1h (0.25 g, 1.22 mmol) gave 5h as a white solid (0.25 g, 26% yield). mp: 175-177 °C. $[\alpha]_D^{20}$ -10.91 (c 0.66, MeOH).

^1H NMR (600 MHz, DMSO- d_6) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, $J=8.5$ Hz, 2 H), 6.71 - 6.85 (d, $J=8.5$ Hz, 2 H), 6.28 (d, $J=8.5$ Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, $J=12.1, 5.7$ Hz, 1 H), 2.85 (dd, $J=13.5, 4.0$ Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, $J=4.9$ Hz, 2 H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 169.1 (C=O), 155.7 (C=O), 153.7 (=C-O), 149.3 (=C-O), 134.6 (C-O), 133.9 (C-N), 132.7 (C-N), 119.8 (C-N), 117.2 (C-Br), 114.9 (C-Br), 112.3 (-C=), 69.4 (-O-CH₃), 40.7 (CH₂), 34.5 (CH₂), 22.5 (CH₂), 10.8 (CH₃).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4- (3-Chlorophenyl)) ureido] propionamide (5i)

Following the general procedure, 1i (0.25 g, 1.38 mmol) gave 5i as a white solid (0.31 g, 29% yield). mp: 205-207 °C. $[\alpha]_D^{20}$ -10.75 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 172.3 (C=O), 155.2 (C=O), 153.7 (=C-O), 152.6 (=C-O), 138.2 (C-O), 133.9 (C-N), 132.3 (C-N), 119.7 (C-N), 117.9 (C-Br), 114.2 (C-Br), 112.9 (-C=), 60.7 (-O-CH₃), 54.0 (CH₂), 37.0 (CH₂), 33.7 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4- (2-Chlorophenyl)) ureido] propionamide (5j)

Following the general procedure, 1j (0.25 g, 1.38 mmol) gave 5j as a white solid (0.33 g, 31% yield). mp: 224-226 °C. $[\alpha]_D^{20}$ -20.89 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.2 (C=O), 155.7 (C=O), 153.7 (=C-O), 149.3 (=C-O), 132.7 (C-O), 130.0 (C-N), 119.8 (C-N), 117.2 (C-Br), 114.9 (C-Br), 112.3 (-C=), 60.7 (-O-CH₃), 54.0 (CH₂), 34.5 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4- (4-Bromophenyl)) ureido] propionamide (5k)

Following the general procedure, 1k (0.25 g, 1.11 mmol) gave 5k as a white solid (0.31 g, 34% yield). mp: 217-219 °C. $[\alpha]_D^{20}$ -10.46 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 9.05 (br. s., 1 H), 8.21 (s, 1 H), 7.47 (s, 2 H), 7.31 - 7.38 (d, 4 H), 7.19 (s, 2 H), 6.68 (br. s., 1 H), 4.39 (d, *J*=4.9 Hz, 1 H), 3.74 (s, 3 H), 3.25 (s, 1 H), 3.11 (br. s., 1 H), 2.88 (d, *J*=4.7 Hz, 1 H), 2.71 - 2.78 (m, 1 H), 2.42 - 2.54 (m, 4 H)

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.2 (C=O), 154.9 (C=O), 152.2 (=C-O), 140.1 (=C-O), 137.8 (C-O), 133.9 (C-N), 131.7 (C-N), 120.0 (C-N), 117.3 (C-Br), 114.0 (C-Br), 112.7 (-C=), 60.7 (-O-CH₃), 54.3 (CH₂), 41.1 (CH₂), 37.9 (CH₂), 33.9 (CH₂).

(R) -N- (3,5-dibromo-4-hydroxybenzene) -3- (3,5-dibromo-4-methoxyphenyl) -2- [2- (4- (4-Fluorophenyl)) ureido] propionamide (5l)

Following the general procedure, 1l (0.25 g, 1.51 mmol) gave 5l as a white solid (0.44 g, 38% yield). mp: 180-183 °C. $[\alpha]_D^{20}$ -17.09 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (m, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 172.0 (C=O), 155.1 (C=O), 152.0 (=C-O), 139.6 (=C-O),

137.0 (C-O), 133.4 (C-F), 129.4 (C-N), 127.8 (C-N), 122.9 (C-N), 121.4 (C-Br), 117.6 (C-Br), 114.0 (-C=), 112.0 (-C=), 60.7 (-O-CH₃), 54.0 (CH₂), 34.5 (CH₂).

(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-(2-Fluorophenyl))ureido] propionamide (5m)

Following the general procedure, **1m** (0.25 g, 1.11 mmol) gave **5m** as a white solid (0.35 g, 31% yield). mp: 177-180 °C. $[\alpha]_D^{20}$ -16.07 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.52 (br. s., 1 H), 8.22 (t, *J*=5.2 Hz, 1 H), 8.02 (td, *J*=8.3, 1.3 Hz, 1 H), 7.47 (s, 2 H), 7.23 (br. s., 2 H), 7.15 (ddd, *J*=11.5, 8.2, 1.1 Hz, 1 H), 6.98 - 7.07 (m, 2 H), 6.88 - 6.94 (m, 1 H), 4.40 (td, *J*=8.5, 5.1 Hz, 1 H), 3.75 (s, 3 H), 3.22 - 3.33 (m, 1 H), 3.14 (dd, *J*=12.3, 5.6 Hz, 1 H), 2.88 (dd, *J*=13.7, 4.9 Hz, 1 H), 2.70 (dd, *J*=13.7, 8.7 Hz, 1 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.0 (C=O), 152.2 (C=O), 149.4 (=C-O), 138.0 (=C-O), 134.3 (C-O), 133.6 (C-F), 132.8 (C-N), 131.9 (C-N), 129.3 (C-N), 127.2 (C-Br), 117.3 (C-Br), 112.2 (-C=), 60.7 (-O-CH₃), 54.2 (CH₂), 37.0 (CH₂), 33.7 (CH₂).

(R)-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-(4-Methylphenyl))ureido] propionamide (5n)

Following the general procedure, **1n** (0.25 g, 1.55 mmol) gave **5n** as a white solid (0.43 g, 36% yield). mp: 208-213 °C. $[\alpha]_D^{20}$ -11.50 (c 0.66, MeOH).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.59 (s, 1 H), 8.19 (t, *J*=5.6 Hz, 1 H), 7.46 (s, 2 H), 7.18 - 7.27 (m, 4 H), 7.00 (d, *J*=8.3 Hz, 2 H), 6.41 (d, *J*=8.5 Hz, 1 H), 4.38 (td, *J*=8.5, 5.1 Hz, 1 H), 3.75 (s, 3 H), 3.27 (dd, *J*=13.4, 6.6 Hz, 1 H), 3.11 - 3.18 (m, 1 H), 2.86 (dd, *J*=13.7, 4.9 Hz, 1 H), 2.71 (dd, *J*=13.7, 8.5 Hz, 1 H), 2.20 (s, 3 H)

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.1 (C=O), 155.6 (C=O), 152.3 (=C-O), 140.1 (=C-O), 137.8 (C-N), 133.9 (C-N), 131.7 (C-N), 120.0 (C-Br), 117.3 (C-Br), 112.5 (-C=), 60.7 (-O-CH₃), 54.3 (CH₂), 37.9 (CH₂), 33.9 (CH₃).

(R)-N-(3,5-dibromo-4-hydroxybenzene)-3-(3,5-dibromo-4-methoxyphenyl)-2-[2-(4-(2-Methyl ethyl ether))ureido] propionamide (5o)

Following the general procedure, **1o** (0.25 g, 0.86 mmol) gave **5o** as a white solid (0.29 g, 38% yield). mp: 211-214 °C. $[\alpha]_D^{20}$ -13.35 (c 0.66, MeOH).

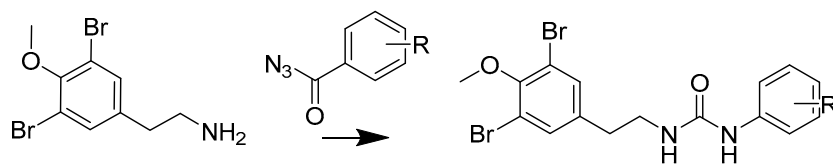
¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 171.0 (C=O), 162.1 (C=O), 160.4 (=C-O), 152.2 (=C-O), 149.3 (C-N), 137.9 (C-N), 134.3 (C-N), 133.8 (C-Br), 132.8 (C-Br), 130.9 (-C=), 117.2 (-C=), 115.2 (-C=), 112.2 (-C=), 60.7 (-O-CH₃), 58.0 (-O-CH₃), 54.5 (CH₂), 37.0 (CH₂), 33.7 (CH₂).

3. General Procedure for the formation of 6a-6o

The aryl azide **1a-1o** was added into 1,2-dichloroethane and stirred for 30 mins at 80°C. To the solution of **1a** in 1,2-dichloroethane, 2-(3,5-dibromo-4-methoxyphenyl)ethan-1-amine (**2p**, 0.51 g, 1.64 mmol, 0.9 equiv) was added and stirred for 2 hours at 80°C. The reaction mixture was then

concentrated and recrystallized with DCM (20 mL) to give **6a-6o**.



Compound No.	R	6H	4-isopropoxy ether
6A	4-methyl ether	6I	3-Cl
6B	4-ethyl ether	6J	2-Cl
6C	4-propyl ether	6K	4-Br
6D	4-butyl ether	6L	4-F
6E	4-sec-butyl ether	6M	2-F
6F	4-pentyl ether	6N	4-methy
6G	4-(2-methoxyethoxy ether	6O	4-(3-morpholinopropoxy ether

1-(3,5-dibromo-4-methoxyphenyl)-3-(4-methoxyphenyl) urea (6a)

Following the general procedure, **1a** (0.4 g, 1.82 mmol) gave **6a** as a white solid (0.44 g, 49% yield). M.p.: 151-155°C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.28 (s, 1 H), 7.43 - 7.60 (m, 2 H), 7.17 - 7.35 (m, 2 H), 6.69 - 6.87 (m, 2 H), 6.06 (t, *J*=5.6 Hz, 1 H), 3.77 (s, 3 H), 3.69 (s, 3 H), 3.30 - 3.32 (m, 2 H), 2.71 ppm (t, *J*=6.9 Hz, 2 H)

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.8 (C=O), 154.3 (=C-O), 133.9 (C-N), 133.4 (C-N), 119.8 (C-Br), 117.5 (C-Br), 114.2 (-C=), 60.7 (-O-CH₃), 55.5 (CH₂), 40.5 (CH₂), 34.7 (CH₂).

1-(3,5-dibromo-4-methoxyphenyl)-3-(4-ethoxyphenyl) urea (6b)

Following the general procedure, **1b** (0.4 g, 2.09 mmol) gave **6b** as a white solid (0.46 g, 47% yield). mp: 176-180 ° C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7 (C=O), 153.6 (=C-O), 152.0 (=C-O), 139.8 (C-N), 133.8 (C-N), 133.4 (C-Br), 114.8 (-C=), 63.4 (-O-CH₃), 60.7 (-O-CH₃), 40.5 (CH₂), 34.7 (CH₂), 15.1 (CH₃).

1-(3,5-dibromo-4-methoxyphenyl)-3-(4-propoxyphenyl) urea (6c)

Following the general procedure, **1c** (0.4 g, 1.95 mmol) gave **6c** as a white solid (0.39 g, 41% yield). mp: 197-199 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.21 (s, 1 H), 7.54 (s, 2 H), 7.14 - 7.27 (m, 2 H), 6.73 - 6.84 (m, 2 H), 5.99 (s, 1 H), 3.84 (t, *J*=6.5 Hz, 2 H), 3.77 (s, 3 H), 2.71 (t, *J*=6.9 Hz, 2 H), 1.60 - 1.76 (m, 2 H), 0.96 (t, *J*=7.4 Hz, 3 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7 (C=O), 153.7 (=C-O), 133.8 (=C-O), 133.4 (C-N), 119.9 (C-N), 117.6 (C-Br), 114.9 (-C=), 69.4 (-O-CH₃), 60.7 (CH₂), 34.7 (CH₂), 22.5 (CH₂), 10.8 (CH₃).

1- (3,5-dibromo-4-methoxyphenyl) -3- (4-butoxyphenyl) urea (6d)

Following the general procedure, 1d (0.4 g, 1.82 mmol) gave 6d as a white solid (0.50 g, 55% yield). mp: 150-156 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.21 (s, 1 H), 7.54 (s, 2 H), 7.19 - 7.28 (d, *J*=9.0 Hz, 2 H), 6.74 - 6.89 (d, *J*=9.0 Hz, 2 H), 6.00 (t, *J*=5.6 Hz, 1 H), 3.88 (t, *J*=6.5 Hz, 2 H), 3.77 (s, 3 H), 3.27 - 3.32 (m, 2 H), 2.71 (t, *J*=6.8 Hz, 2 H), 1.59 - 1.71 (m, 2 H), 1.42 (sxt, *J*=7.4 Hz, 2 H), 0.92 (t, *J*=7.3 Hz, 3 H)

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7 (C=O), 153.8 (=C-O), 152.0 (=C-O), 139.8 (C-N), 133.4 (C-N), 119.9 (C-Br), 117.6 (-C=), 114.9 (-C=), 67.6 (-O-CH₃), 60.7 (CH₂), 40.5 (CH₂), 34.7 (CH₂), 31.2 (CH₂), 19.1 (CH₂), 14.1 (CH₃).

1- (3,5-dibromo-4-methoxyphenyl) -3- (4-secutoxyphenyl) urea (6e)

Following the general procedure, 1e (0.4 g, 1.82 mmol) gave 6e as a white solid (0.49 g, 54% yield). mp: 160-164 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.21 (s, 1 H), 7.43 - 7.60 (m, 2 H), 7.16 - 7.31 (d, *J*=9.0 Hz, 2 H), 6.69 - 6.89 (d, *J*=8.8 Hz, 2 H), 6.00 (t, *J*=5.6 Hz, 1 H), 4.19 - 4.29 (m, 1 H), 3.77 (s, 3 H), 3.30 - 3.33 (m, 2 H), 2.71 (t, *J*=6.9 Hz, 2 H), 1.46 - 1.66 (m, 2 H), 1.18 (d, *J*=6.0 Hz, 3 H), 0.90 (t, *J*=7.4 Hz, 3 H)

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.8 (C=O), 153.7 (=C-O), 152.0 (=C-O), 139.8 (C-N), 133.8 (C-N), 133.4 (C-Br), 119.9 (-C=), 67.9 (-O-CH₃), 60.7 (CH₂), 40.5 (CH₂), 34.7 (CH₂), 28.9 (CH₂), 28.1 (CH₂), 22.3 (CH₃), 14.3 (CH₃).

1- (3,5-dibromo-4-methoxyphenyl) -3- (4-n-pentylphenyl) urea (6f)

Following the general procedure, 1f (0.4 g, 1.71 mmol) gave 6f as a white solid (0.35 g, 40% yield). mp: 184-186 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.23 (s, 1 H), 7.47 - 7.62 (m, 2 H), 7.17 - 7.30 (m, 2 H), 6.71 - 6.86 (m, 2 H), 6.02 (t, *J*=4.7 Hz, 1 H), 3.87 (t, *J*=6.5 Hz, 2 H), 3.73 - 3.81 (m, 3 H), 3.30 - 3.33 (m, 2 H), 2.71 (t, *J*=6.9 Hz, 2 H), 1.63 - 1.70 (m, 2 H), 1.28 - 1.42 (m, 4 H), 0.89 (t, *J*=7.2 Hz, 3 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.8 (C=O), 153.7 (=C-O), 133.9 (=C-O), 132.6 (C-N), 119.8 (C-N), 114.9 (C-Br), 112.5 (-C=), 67.9 (-O-CH₃), 60.7 (CH₂), 34.7 (CH₂), 28.9 (CH₂), 28.1 (CH₂), 22.3 (CH₂), 14.3 (CH₃).

1- (3,5-dibromo-4-methoxyphenyl) -3- [4- (3-morpholinopropyl) phenyl] urea (6g)

Following the general procedure, 1g (0.4 g, 1.81 mmol) gave 6g as a white solid (0.44 g, 48% yield). m.p.: 169-172 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7 (C=O), 153.5 (=C-O), 149.3 (=C-O), 134.6 (C-N), 132.7 (C-N), 119.8 (C-Br), 114.9 (-C=), 66.1 (-O-CH₃), 55.0 (CH₂), 34.5 (CH₂).

1- (3,5-dibromo-4-methoxyphenyl) -3- (4-isopropylphenyl) urea (6h)

Following the general procedure, 1h (0.4 g, 1.95 mmol) gave 6h as a white solid (0.53 g, 56% yield). m.p.: 166-168 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.24 (s, 1 H), 7.47 - 7.57 (m, 2 H), 7.16 - 7.35 (d, *J*=8.8 Hz, 2 H), 6.72 - 6.85 (d, *J*=9.0 Hz, 2 H), 6.02 (t, *J*=5.6 Hz, 1 H), 4.47 (dt, *J*=12.0, 6.0 Hz, 1 H), 3.68 - 3.84 (m, 3 H), 3.30 - 3.34 (m, 2 H), 2.71 (t, *J*=6.9 Hz, 2 H), 1.22 (d, *J*=6.0 Hz, 6 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7 (C=O), 153.7 (=C-O), 149.3 (=C-O), 133.9 (C-N), 132.7 (C-N), 119.8 (C-Br), 114.9 (-C=), 69.4 (-O-CH₃), 60.7 (CH₂), 34.5 (CH₂), 22.5 (CH₂), 10.8 (CH₃).

1-(3,5-dibromo-4-methoxyphenyl)-3-[4-(3-chlorophenyl)] urea (6i)

Following the general procedure, 1i (0.4 g, 2.20 mmol) gave 6i as a white solid (0.49 g, 48% yield). mp: 169-172 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 152.9 (C=O), 140.0 (=C-O), 138.3 (C-N), 129.0 (C-N), 122.9 (C-Cl), 119.0 (C-Br), 115.7 (-C=), 21.6 (CH₂).

1-(3,5-dibromo-4-methoxyphenyl)-3-[4-(2-chlorophenyl)] urea (6j)

Following the general procedure, 1j (0.4 g, 2.20 mmol) gave 6j as a white solid (0.53 g, 52% yield). mp: 211-215 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.09 (dd, *J*=8.3, 1.3 Hz, 1 H), 8.00 (s, 1 H), 7.56 (s, 2 H), 7.38 (dd, *J*=8.0, 1.4 Hz, 1 H), 7.20 - 7.26 (m, 1 H), 6.99 (t, *J*=5.6 Hz, 1 H), 6.95 (td, *J*=7.7, 1.6 Hz, 1 H), 3.77 (s, 3 H), 3.33 - 3.38 (m, 2 H), 2.73 (t, *J*=6.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.1 (C=O), 152.0 (=C-O), 139.6 (C-N), 137.0 (C-N), 133.4 (C-Cl), 129.4 (C-Br), 127.8 (-C=), 122.9 (-C=), 60.7 (-O-CH₃), 34.5 (CH₂).

1-(3,5-dibromo-4-methoxyphenyl)-3-[4-(4-bromophenyl)] urea (6k)

Following the general procedure, 1k (0.4 g, 1.77 mmol) gave 6k as a white solid (0.37 g, 41% yield). 74% yield, mp: 204-207 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.59 (s, 1 H), 7.54 (s, 2 H), 7.32 - 7.39 (m, 4 H), 6.17 (t, *J*=5.6 Hz, 1 H), 3.77 (s, 3 H), 3.30 - 3.33 (m, 2 H), 2.72 (t, *J*=6.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.2 (C=O), 152.0 (=C-O), 139.6 (C-N), 133.4 (C-N), 128.6 (C-Br), 124.7 (C-Br), 117.6 (-C=), 115.2 (-C=), 55.4 (-O-CH₃), 34.6 (CH₂).

1-(3,5-dibromo-4-methoxyphenyl)-3-[4-(4-fluorophenyl)] urea (6l)

Following the general procedure, 1l (0.4 g, 2.42 mmol) gave 6l as a white solid (0.49 g, 45% yield). mp: 191-195 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.6 (C=O), 141.0 (=C-O), 138.0 (C-N), 132.2 (C-N), 128.8 (C-F), 122.0 (C-Br), 118.6 (-C=), 115.2 (-C=), 67.9 (-O-CH₃), 60.4 (CH₂), 34.7 (CH₂), 22.3 (CH₂).

1-(3,5-dibromo-4-methoxyphenyl)-3-[4-(2-fluorophenyl)] urea (6m)

Following the general procedure, 1m (0.4 g, 2.42 mmol) 1m gave 6m as a white solid (0.55 g, 51% yield). mp: 190-196 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.24 - 8.33 (m, 1 H), 8.10 (t, *J*=7.7 Hz, 1 H), 7.51 - 7.61 (m, 2 H), 7.16 (ddd, *J*=11.7, 8.2, 1.3 Hz, 1 H), 7.00 - 7.09 (m, 1 H), 6.87 - 6.95 (m, 1 H), 6.59 (t, *J*=5.6 Hz, 1 H), 3.69 - 3.81 (m, 3 H), 3.35 (q, *J*=6.8 Hz, 2 H), 2.72 (t, *J*=6.8 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.1 (C=O), 152.0 (=C-O), 139.6 (C-N), 137.0 (C-N), 133.4(C-F), 129.4 (C-Br), 127.8 (-C=), 122.9 (-C=), 60.7 (-O-CH₃), 34.5 (CH₂).

1- (3,5-dibromo-4-methoxyphenyl) -3- [4- (4-methylphenyl)] urea (6n)

Following the general procedure, 1n (0.4 g, 2.48 mmol) 1n gave 6n as a white solid (0.51 g, 46% yield). mp: 205-210 °C.

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

¹³C NMR (150 MHz, DMSO-*d*₆) δ 153.0 (C=O), 137.6 (=C-O), 130.9 (C-N), 129.5 (C-N), 118.6 (C-Br), 53.2, 20.7 (CH₃).

1- (3,5-dibromo-4-methoxyphenyl) -3- [4- (2-methylethyl ether)] urea (6o)

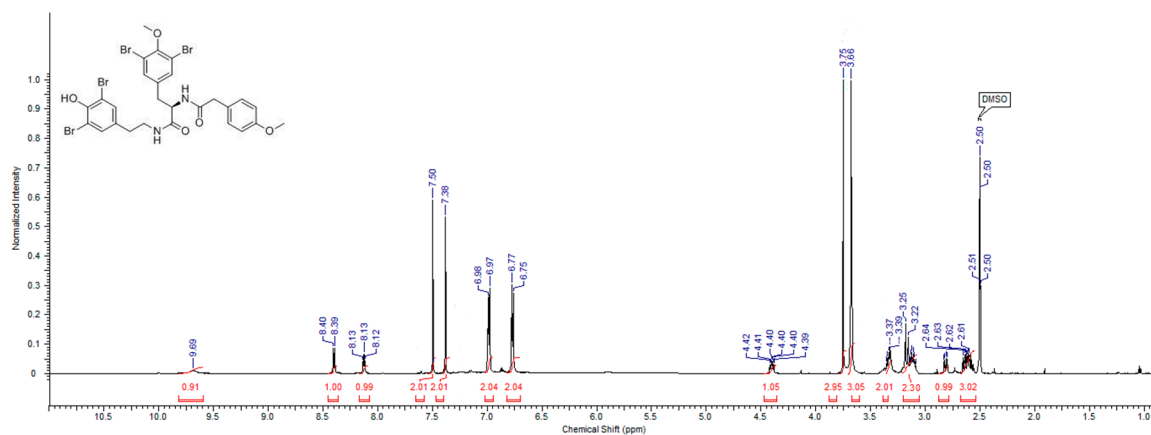
Following the general procedure, 1o (0.4 g, 1.38 mmol) 1o gave 6o as a white solid (0.37 g, 47% yield). m.p.: 201-209 °C

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.44 (s, 1 H), 8.19 (br. s., 1 H), 7.45 (s, 2 H), 7.39 (s, 2 H), 7.20 - 7.25 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.85 (d, *J*=8.5 Hz, 2 H), 6.28 (d, *J*=8.5 Hz, 1 H), 4.32 - 4.48 (m, 1 H), 3.75 (s, 3 H), 3.68 (s, 3 H), 3.26 - 3.35 (m, 1 H), 3.20 (dd, *J*=12.1, 5.7 Hz, 1 H), 2.85 (dd, *J*=13.5, 4.0 Hz, 1 H), 2.69 - 2.78 (m, 1 H), 2.60 (d, *J*=4.9 Hz, 2 H).

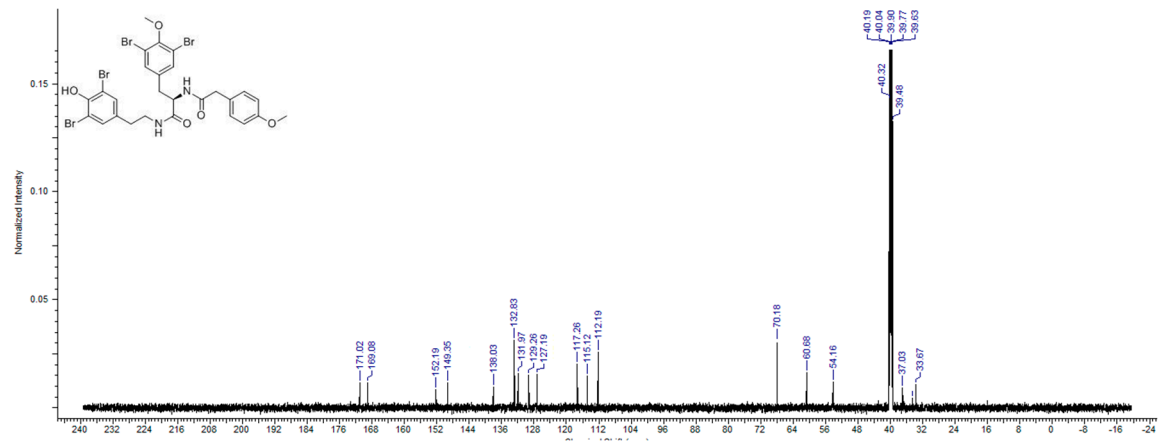
¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7 (C=O), 153.7 (=C-O), 149.3 (=C-O), 134.6 (C-N), 133.9 (C-N), 132.7 (C-Br), 119.8 (-C=), 71.9 (-O-CH₃), 67.6 (-O-CH₃), 34.5(CH₂).

4. spectrum of the derivatives

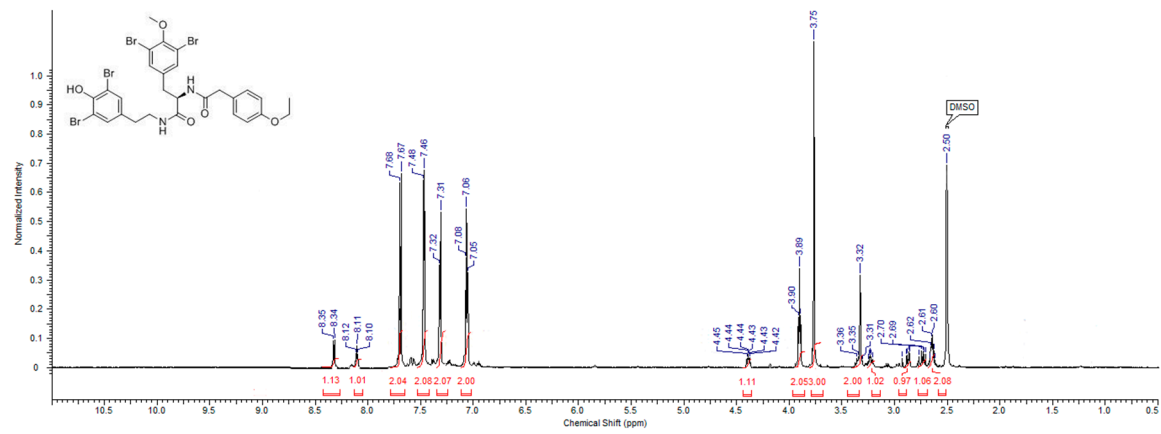
4.1



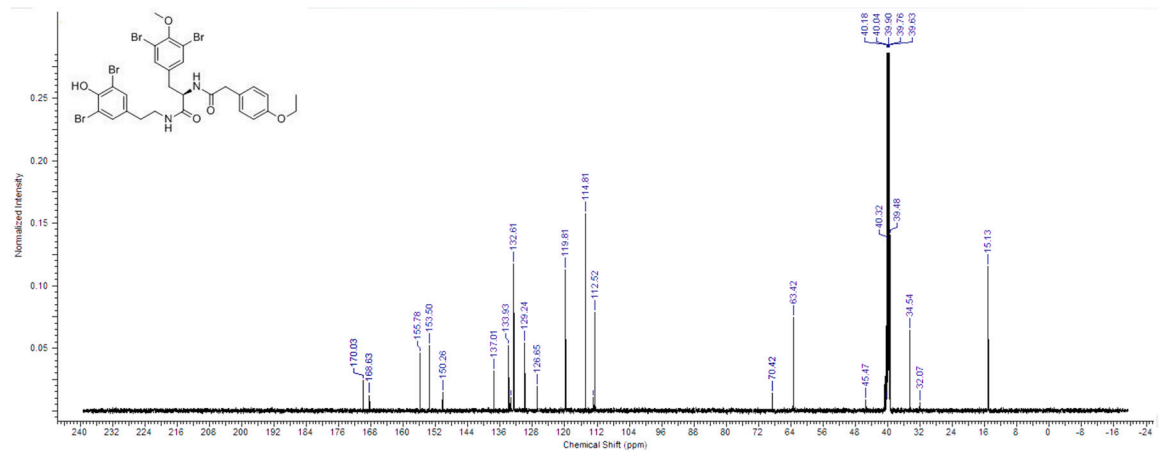
4A ¹H-NMR



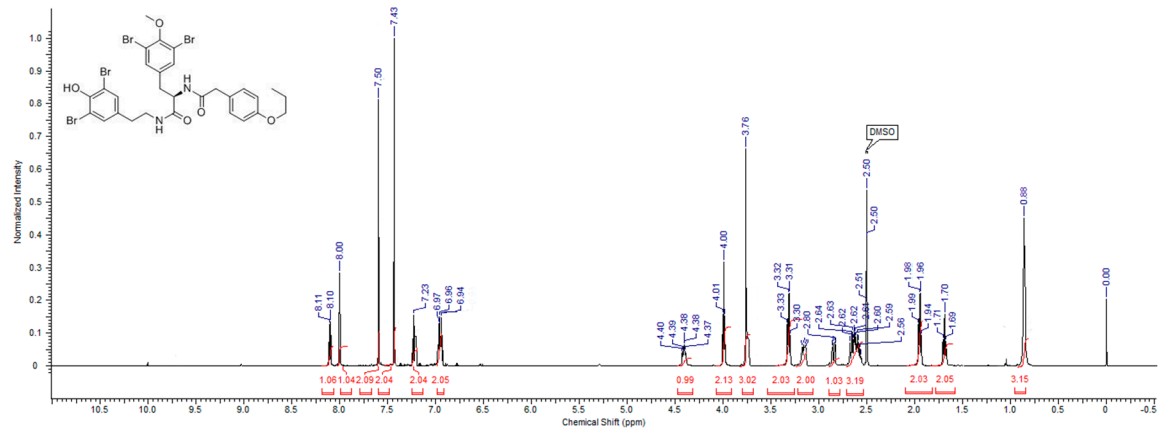
4A ¹³C-NMR



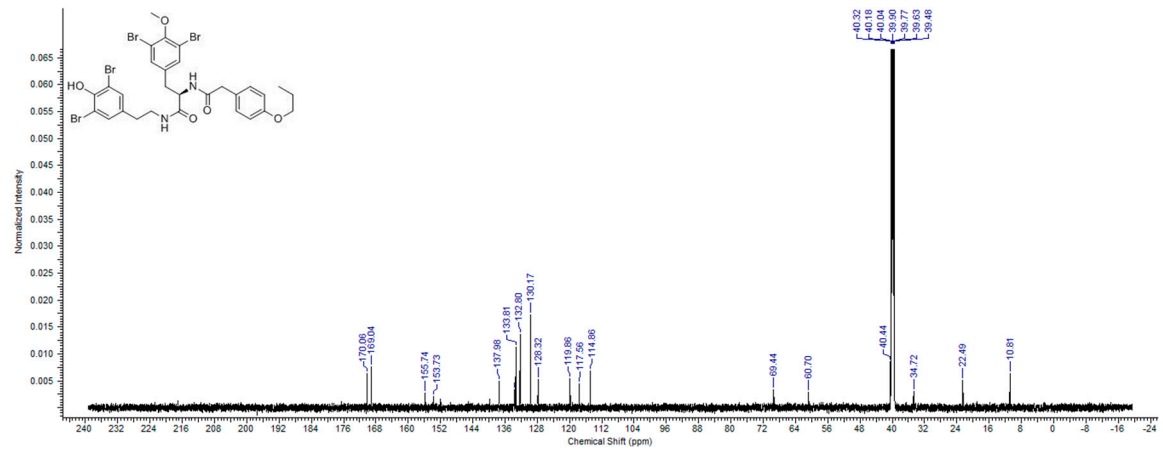
4B ¹H-NMR



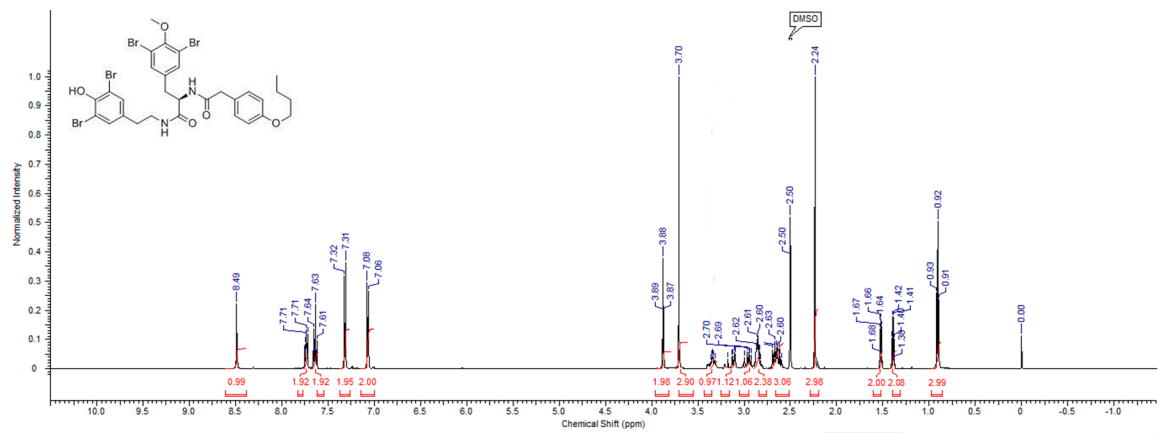
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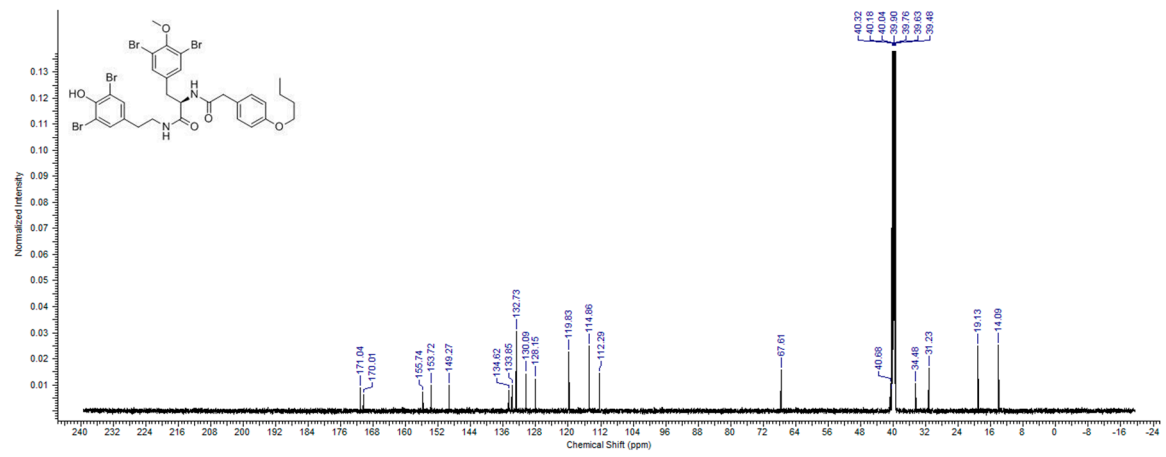
4c ¹H-NMR



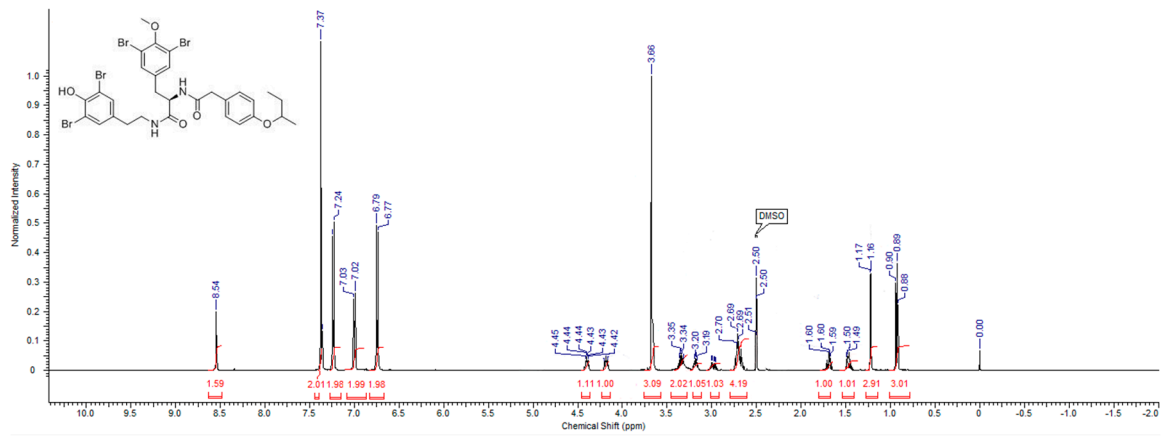
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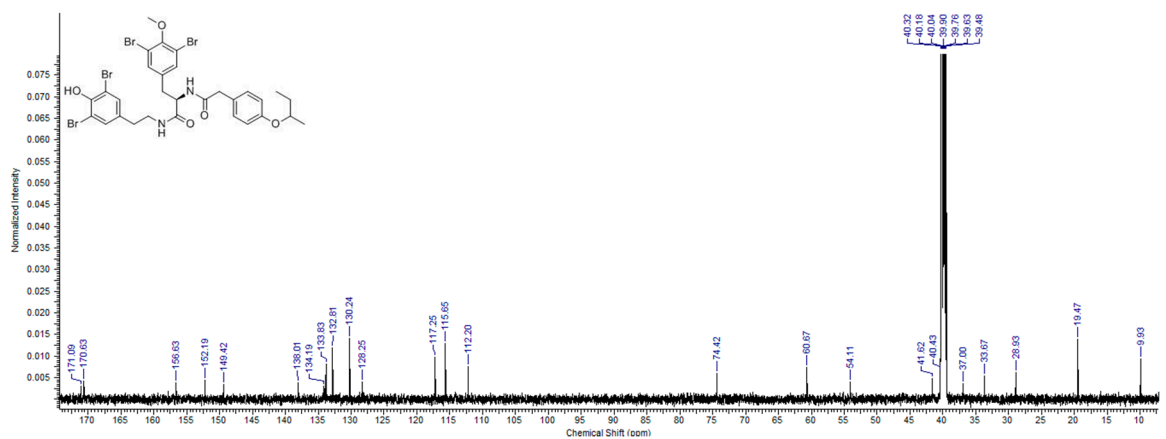
4D ¹H-NMR



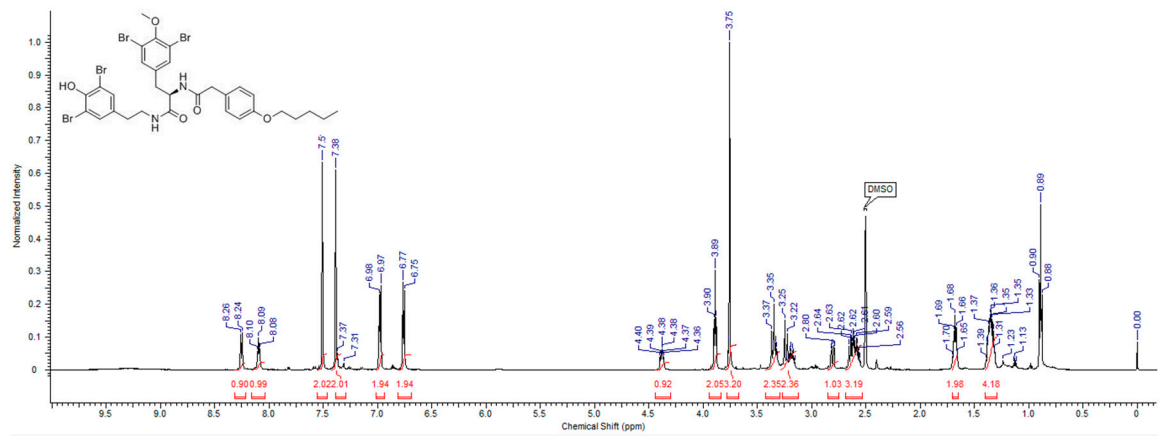
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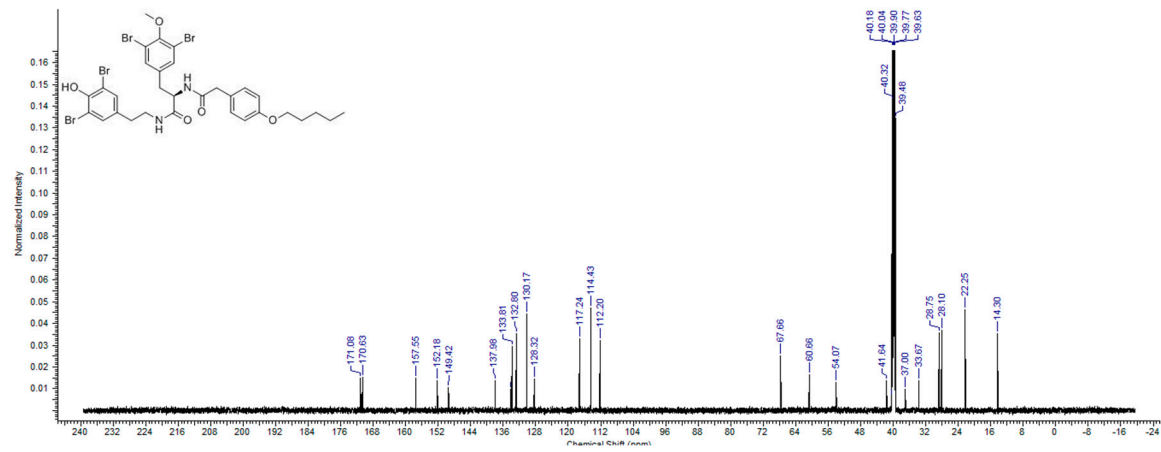
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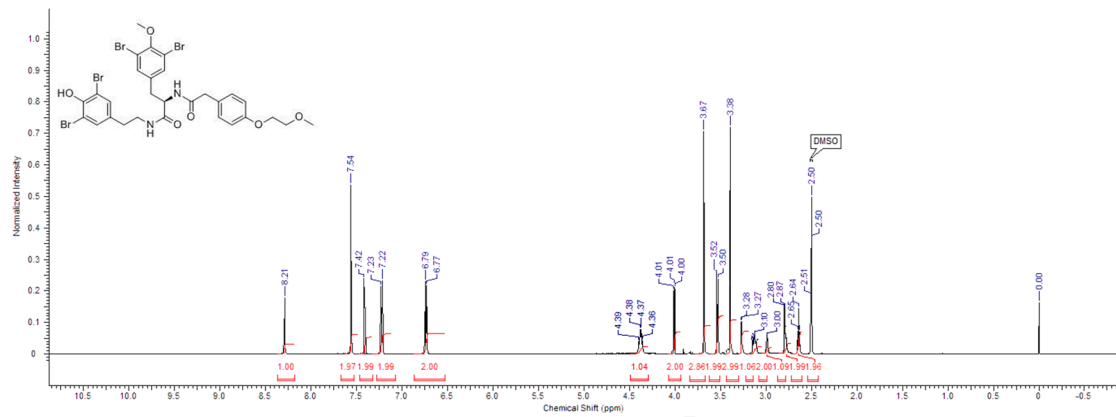
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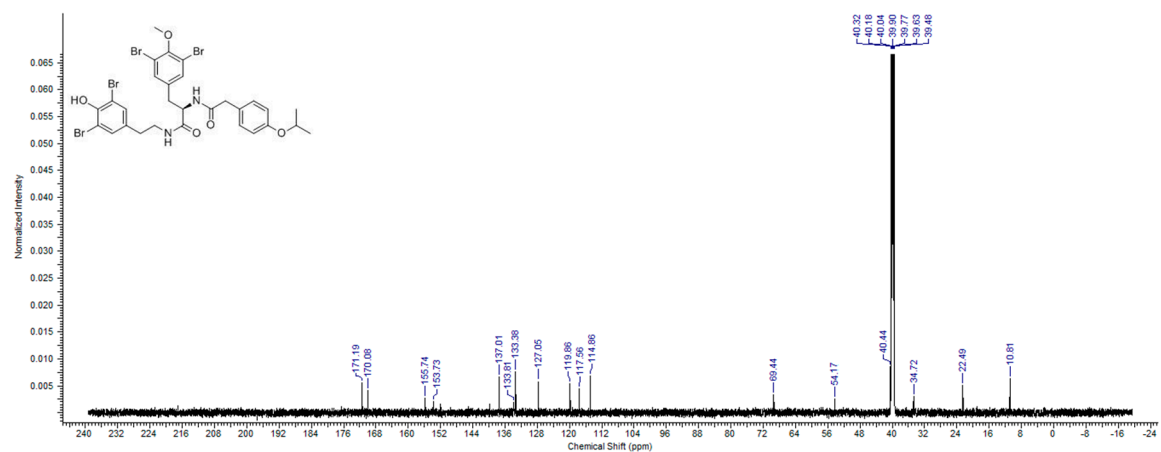
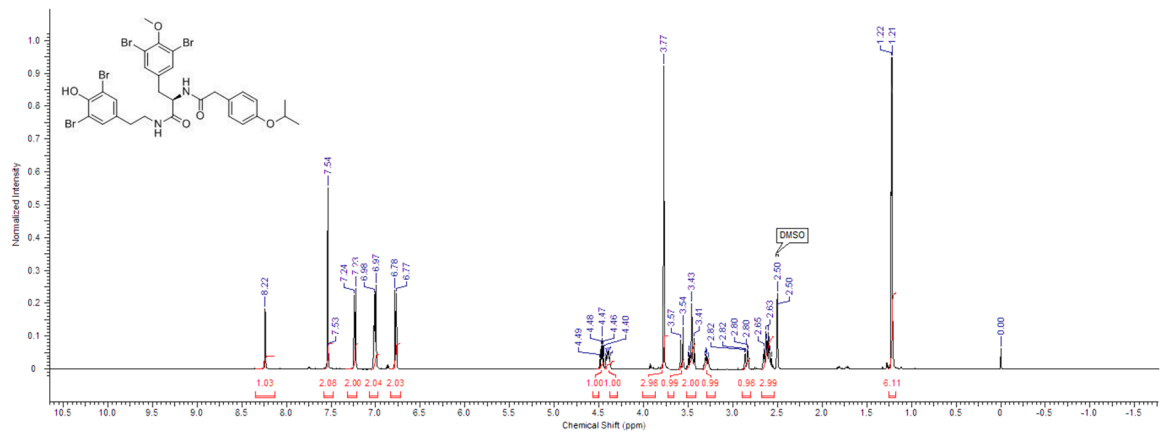
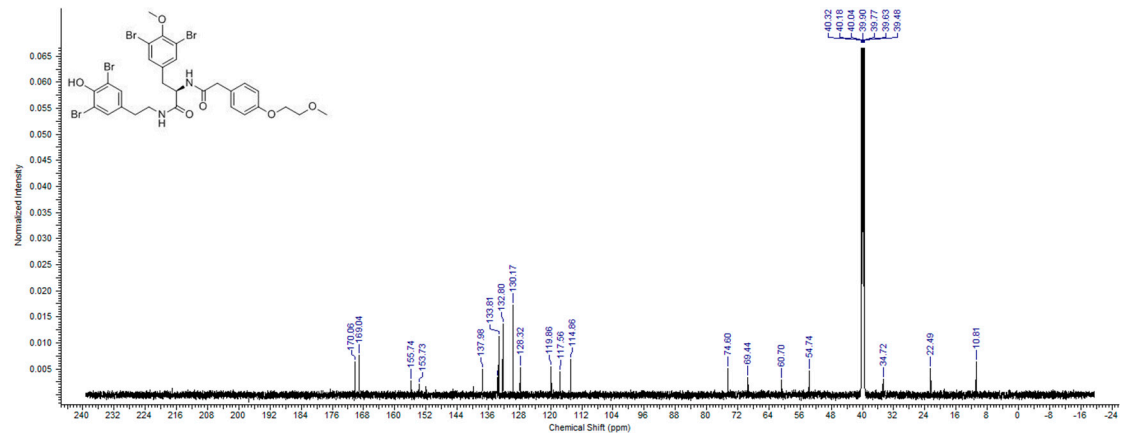
4F ¹H-NMR

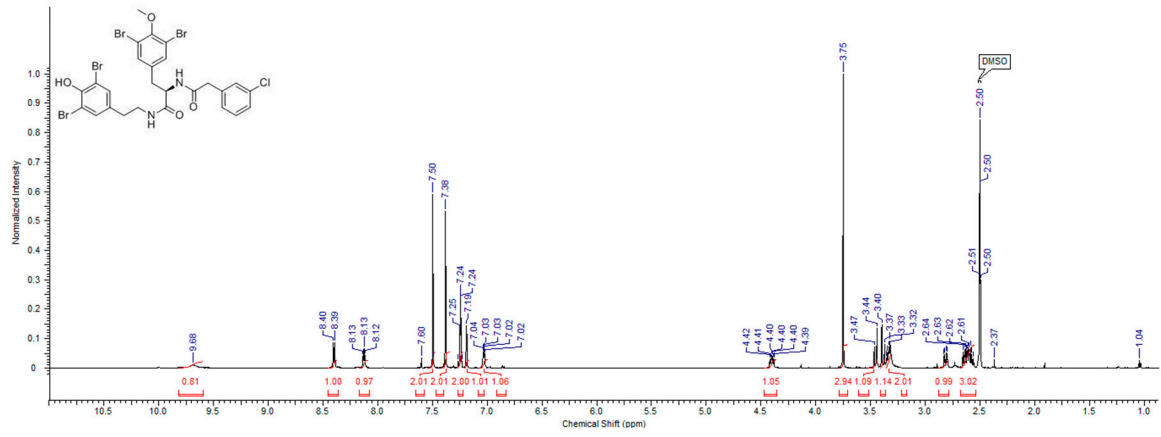


4F ¹³C-NMR

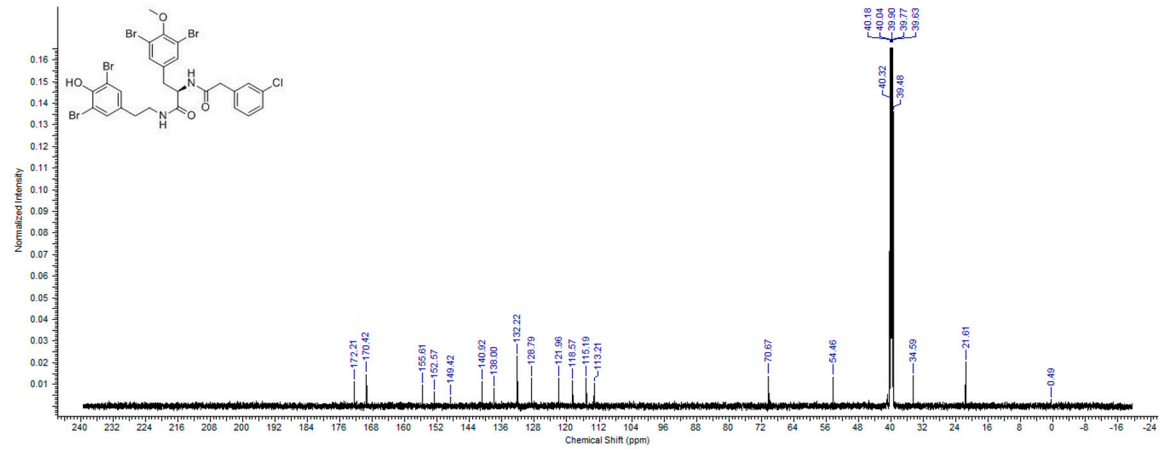


4G ¹H-NMR

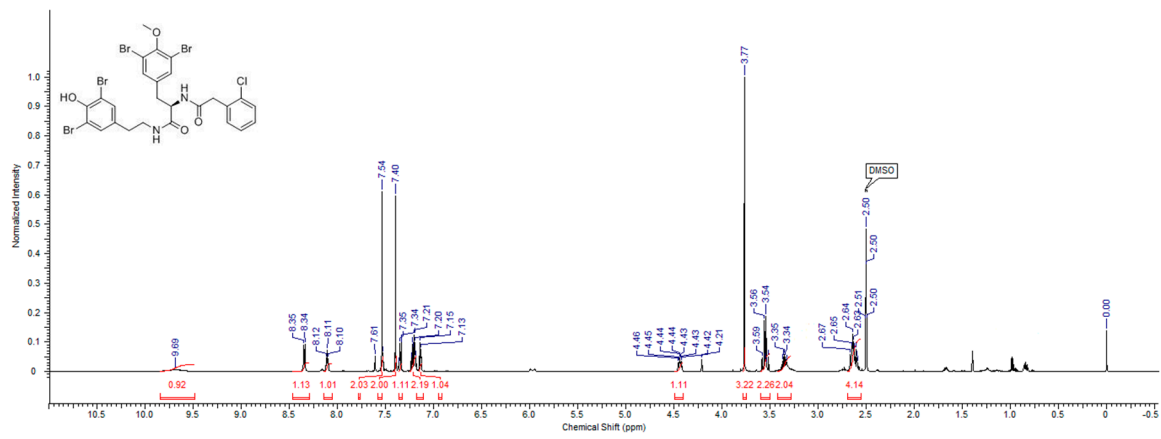




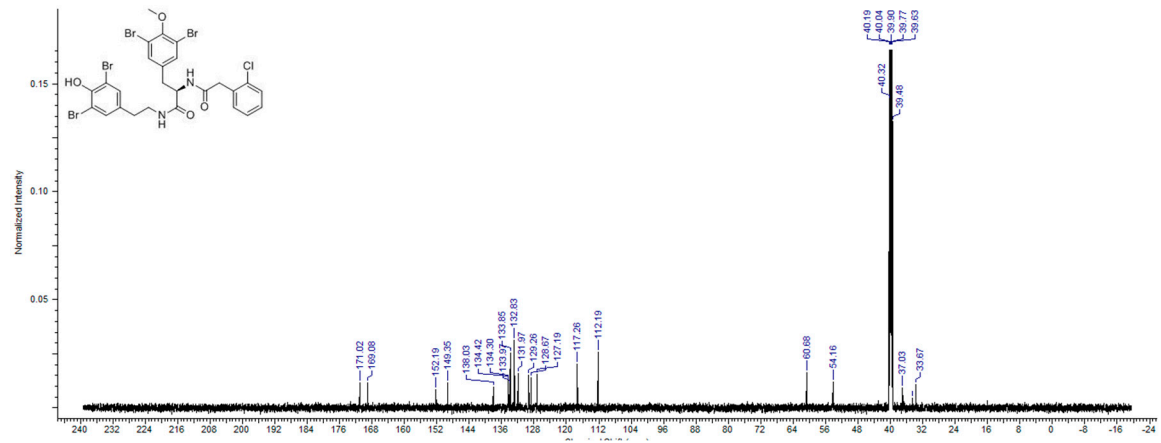
4I ¹H-NMR



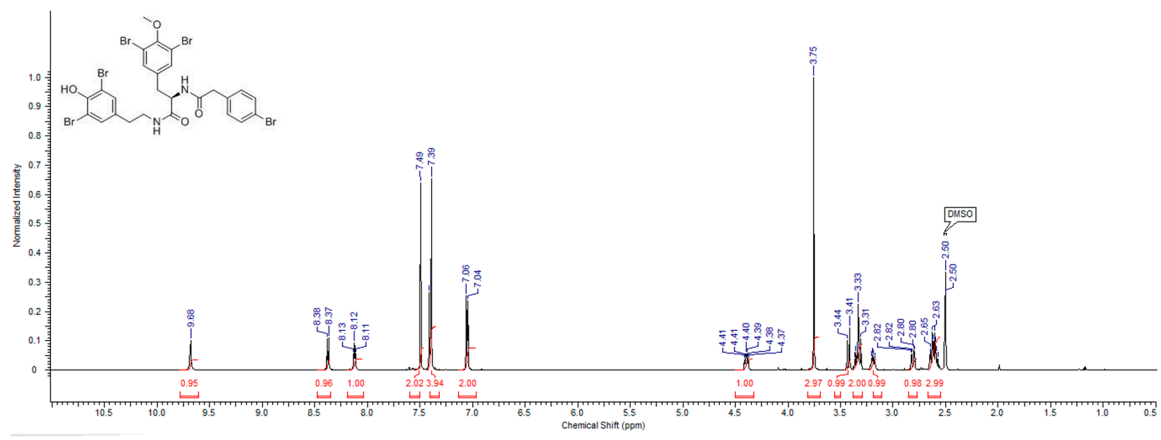
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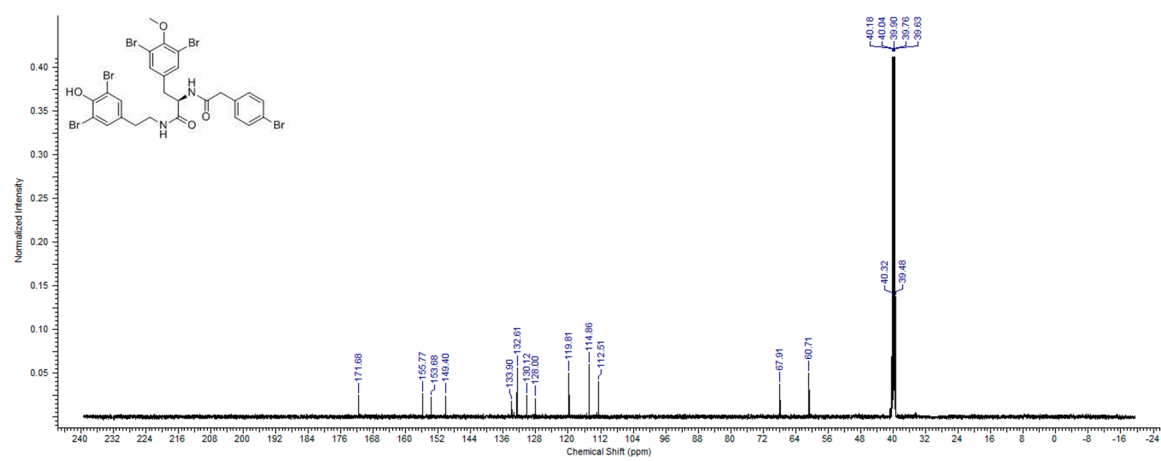
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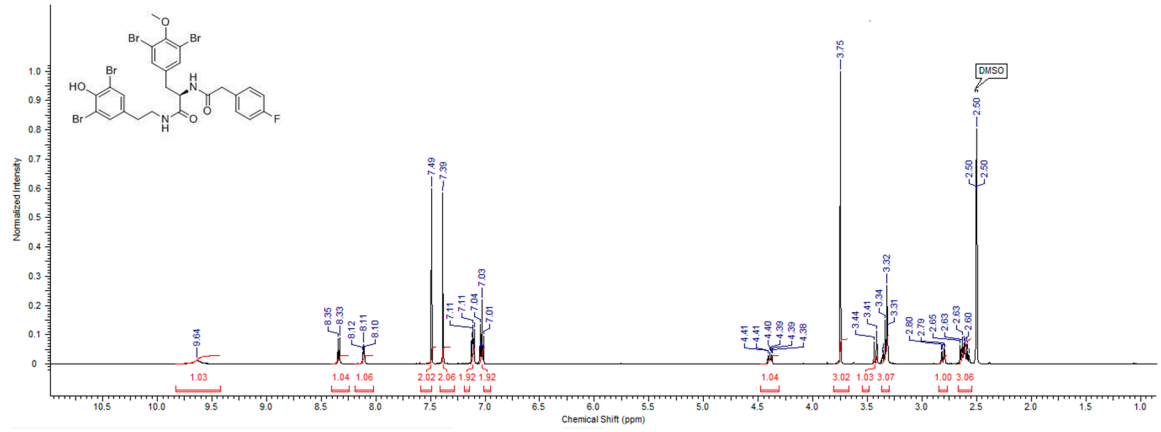
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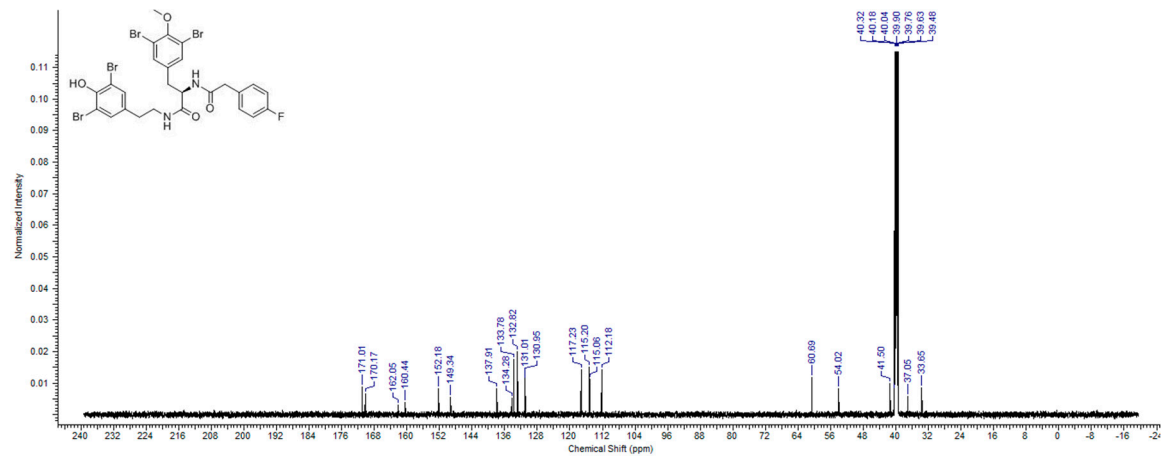
4K ¹H-NMR



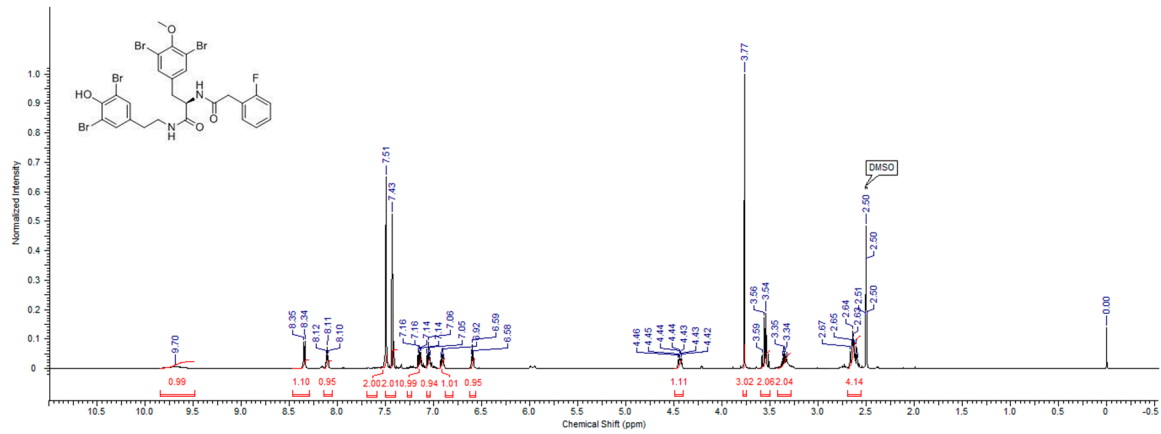
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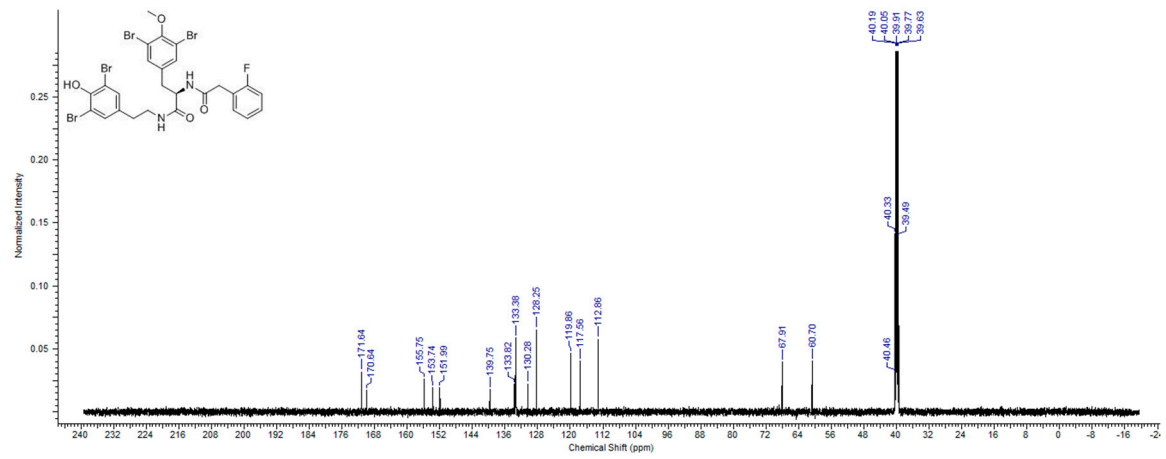
4L ¹H-NMR



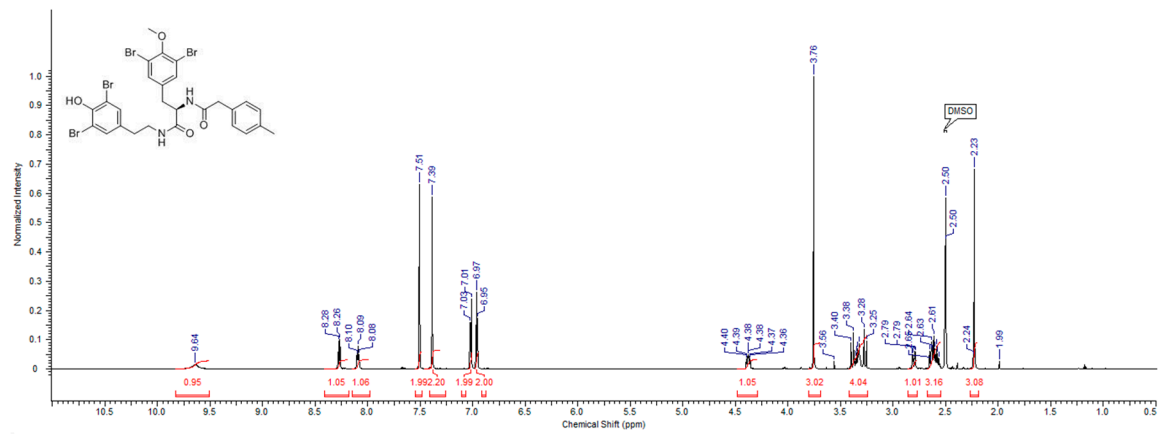
4L ¹³C-NMR



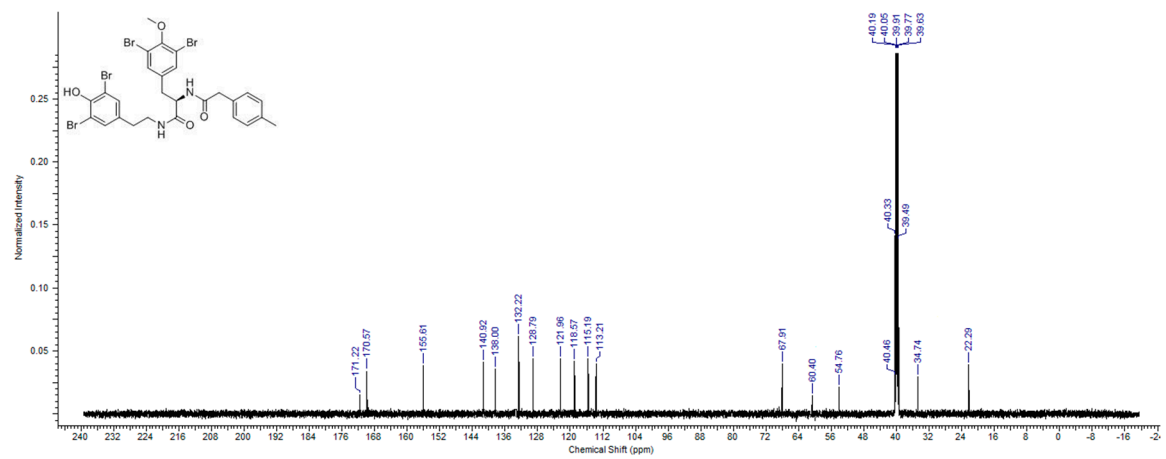
4M ¹H-NMR



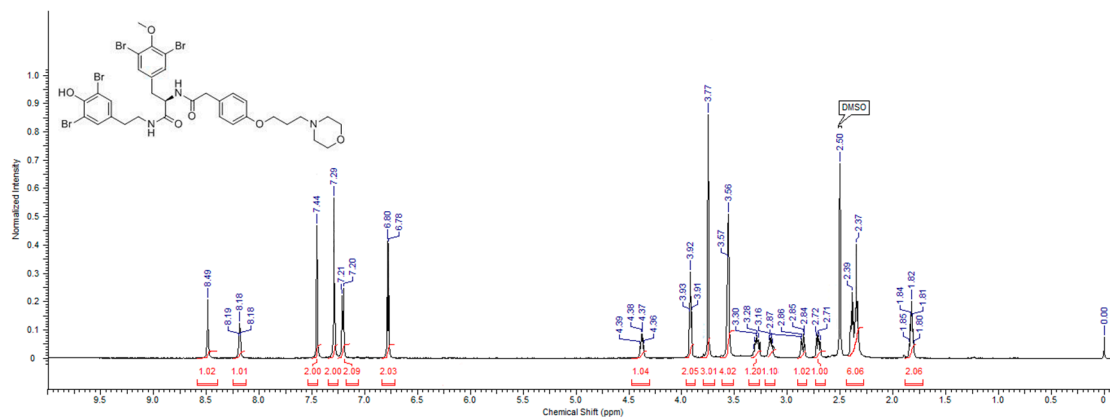
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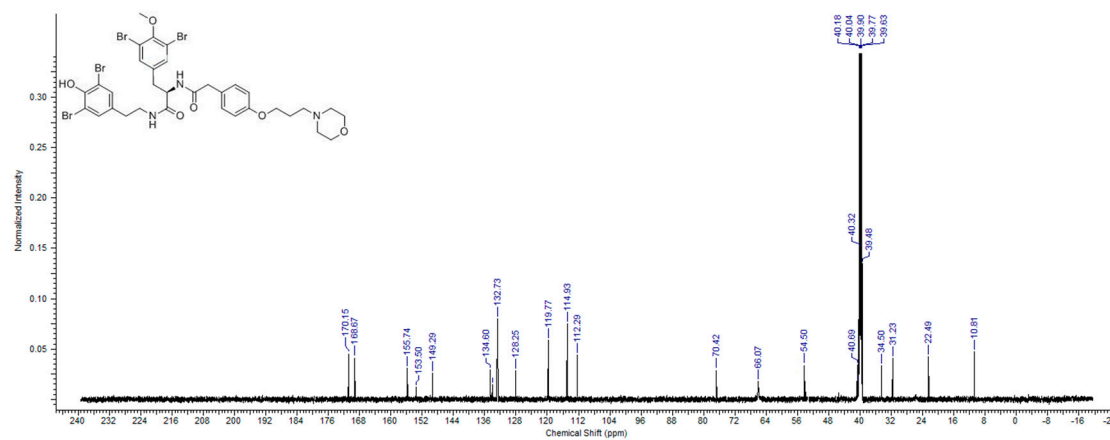
4N ¹H-NMR



4N ¹³C-NMR

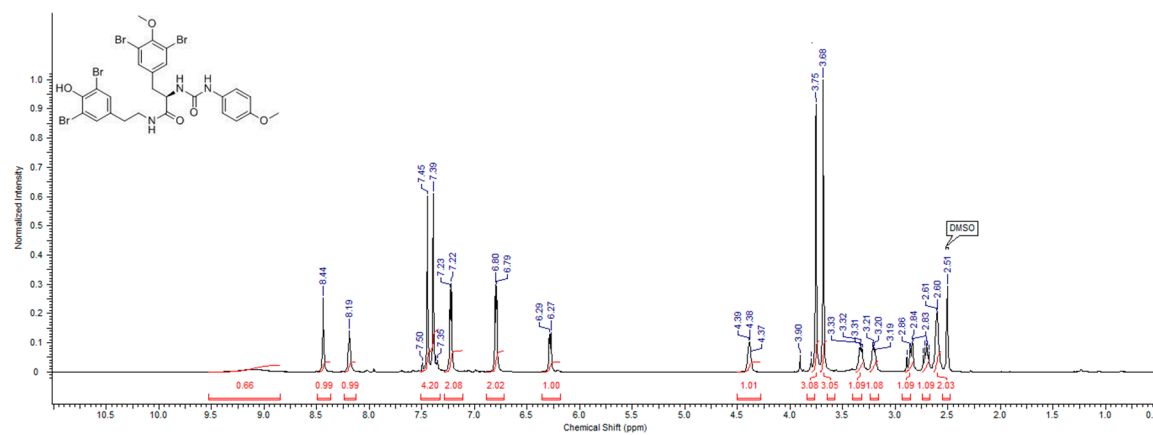


40 ¹H-NMR

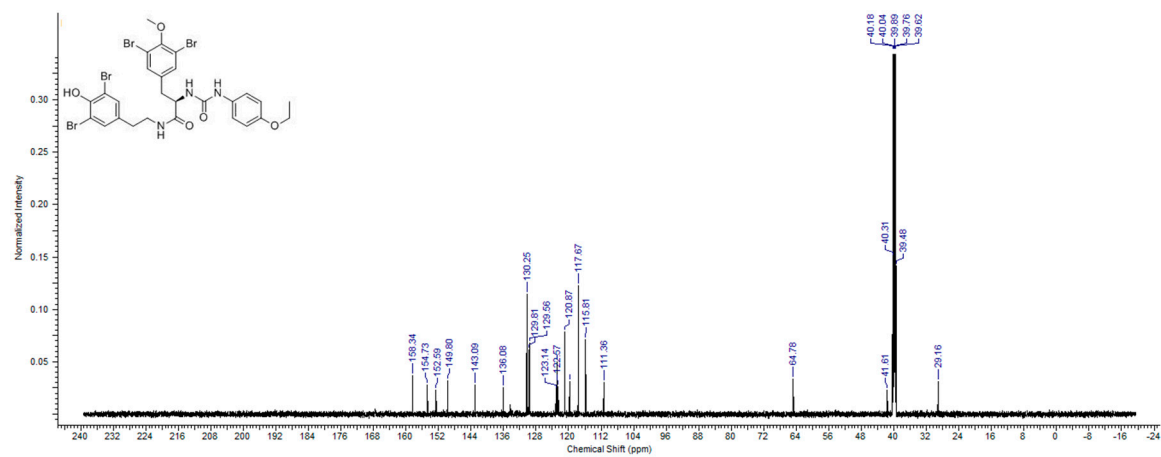
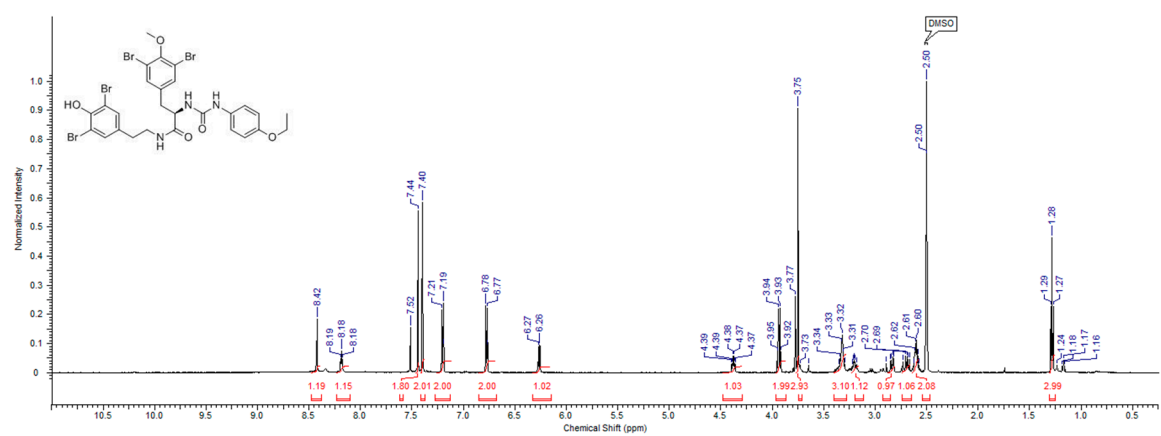
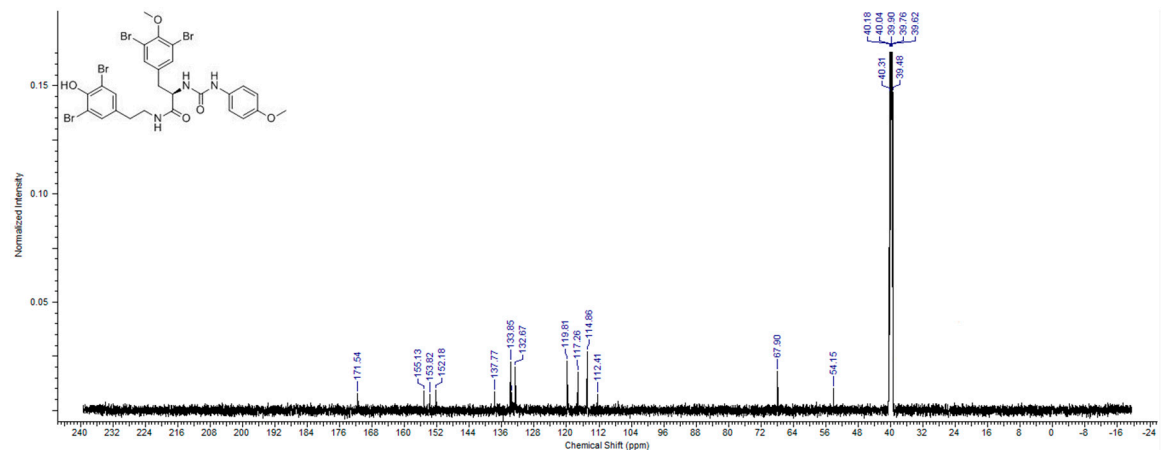


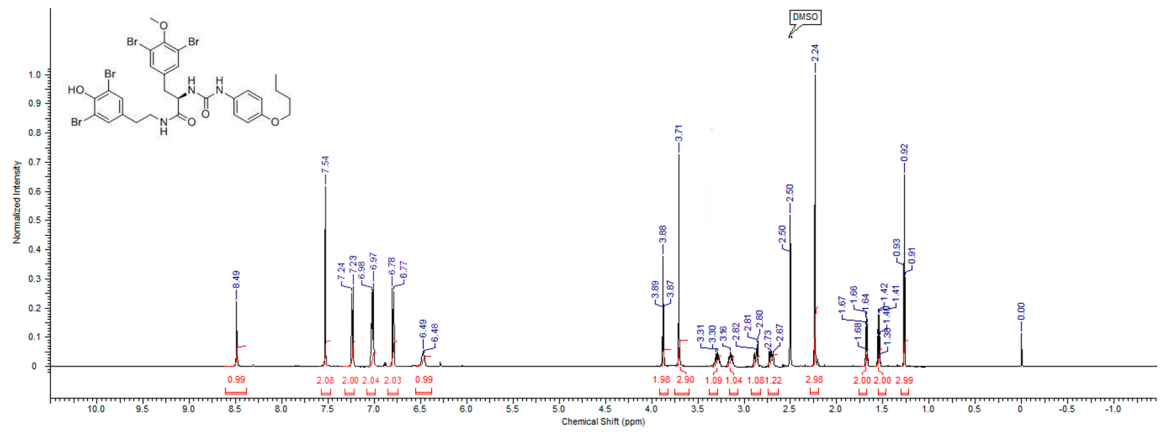
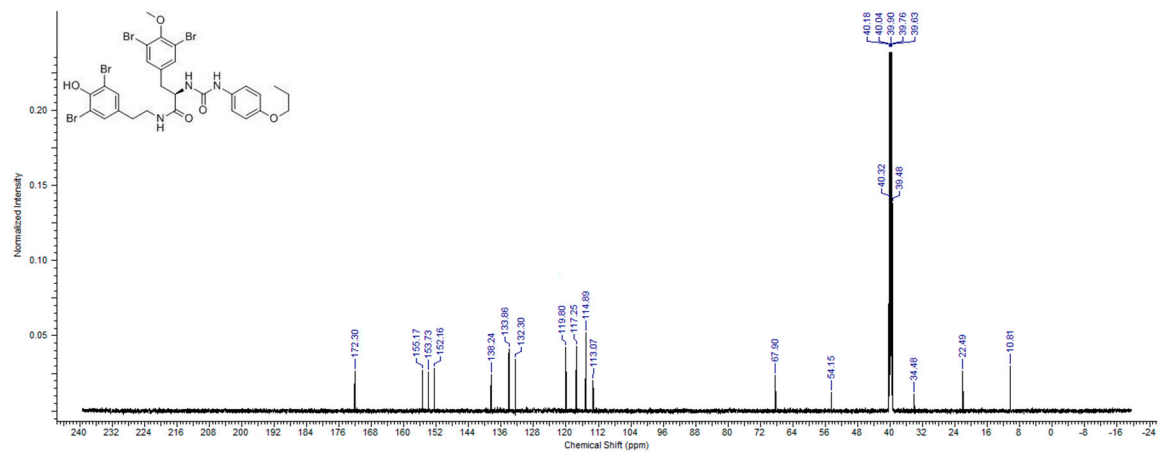
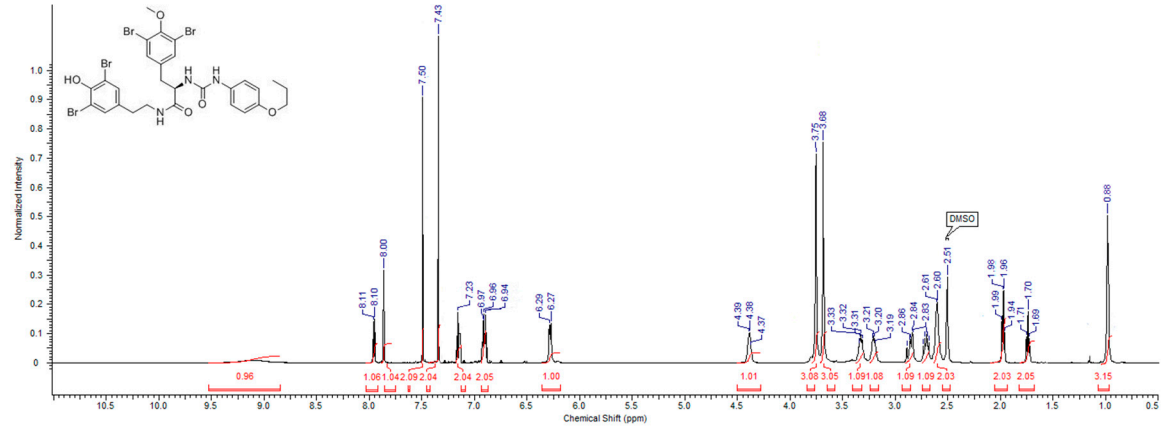
40 ¹³C-NMR

2.2

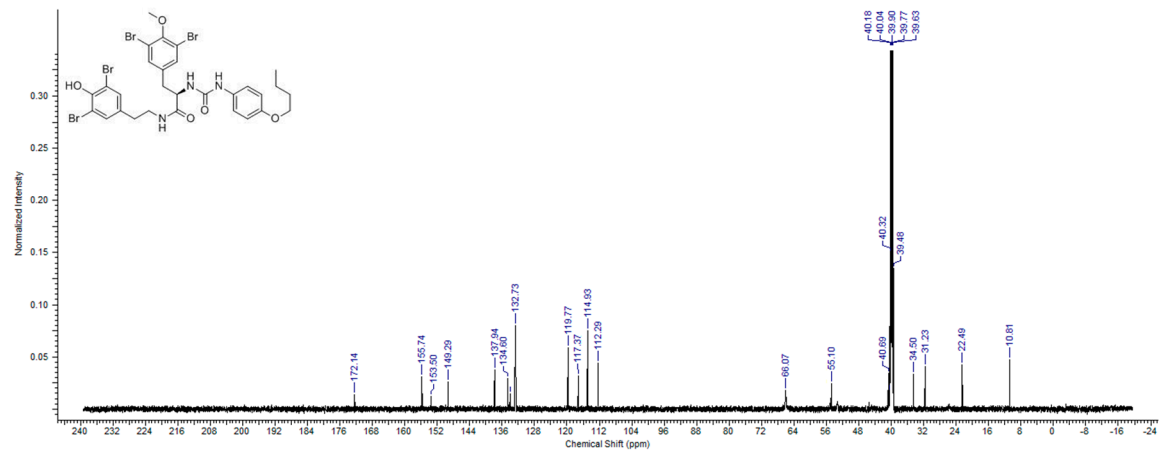


5A ¹H-NMR

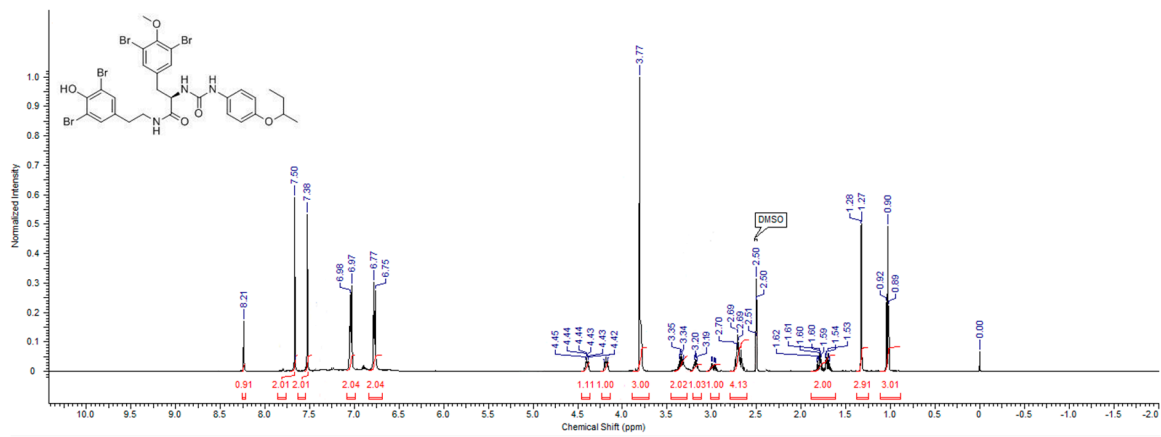




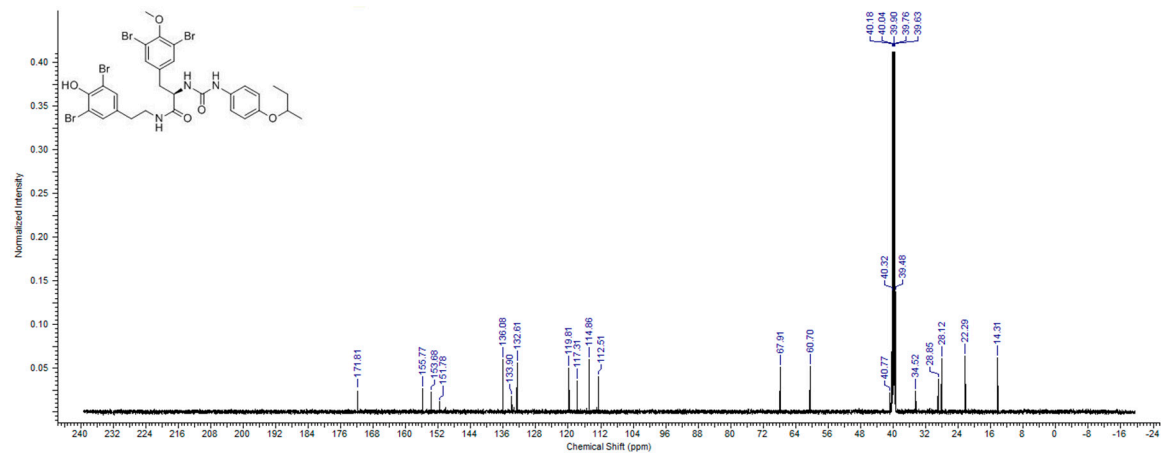
5D ¹H-NMR



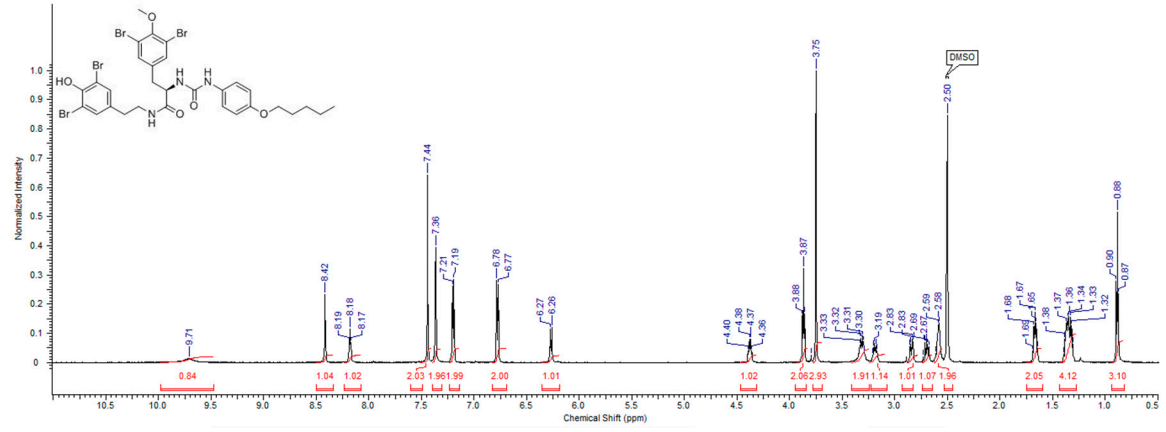
5D ¹³C-NMR



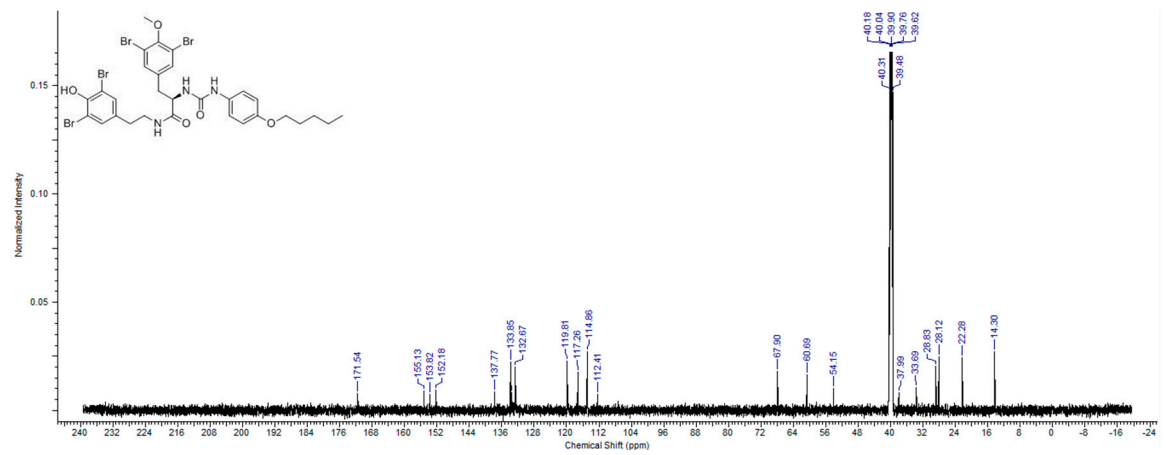
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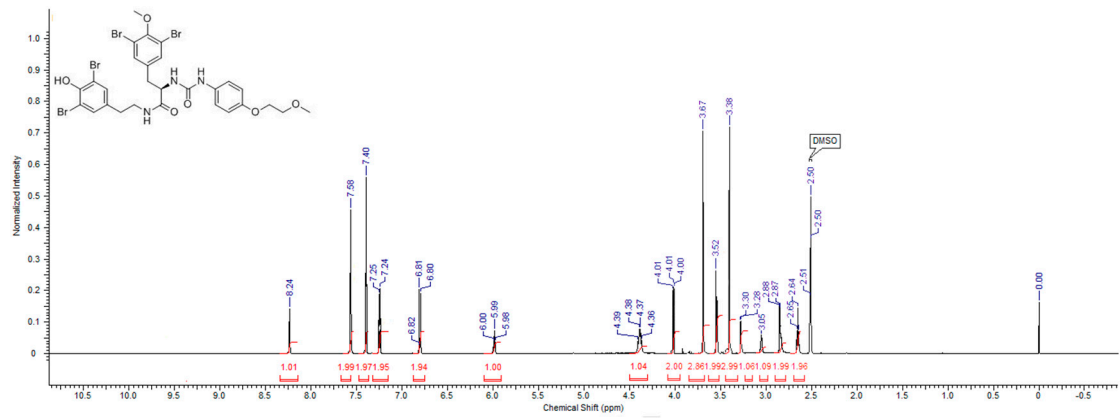
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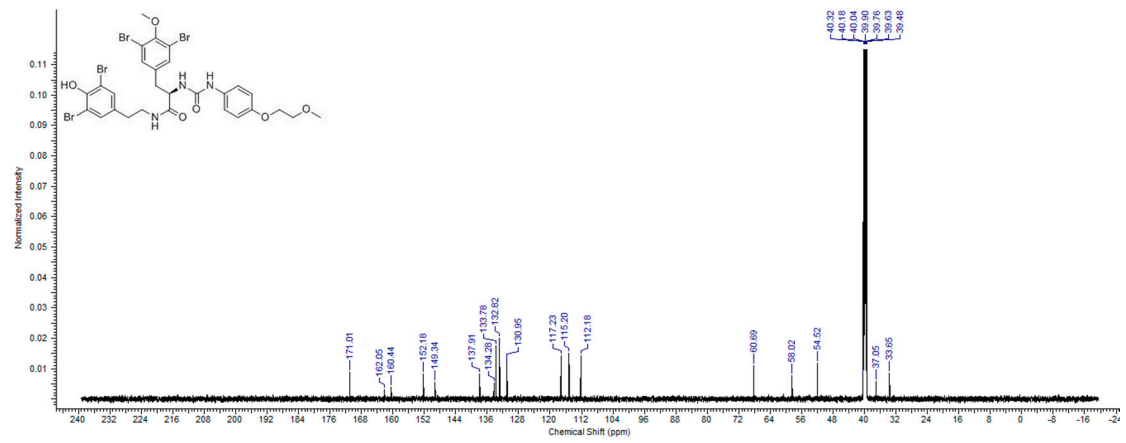
5F ¹H-NMR



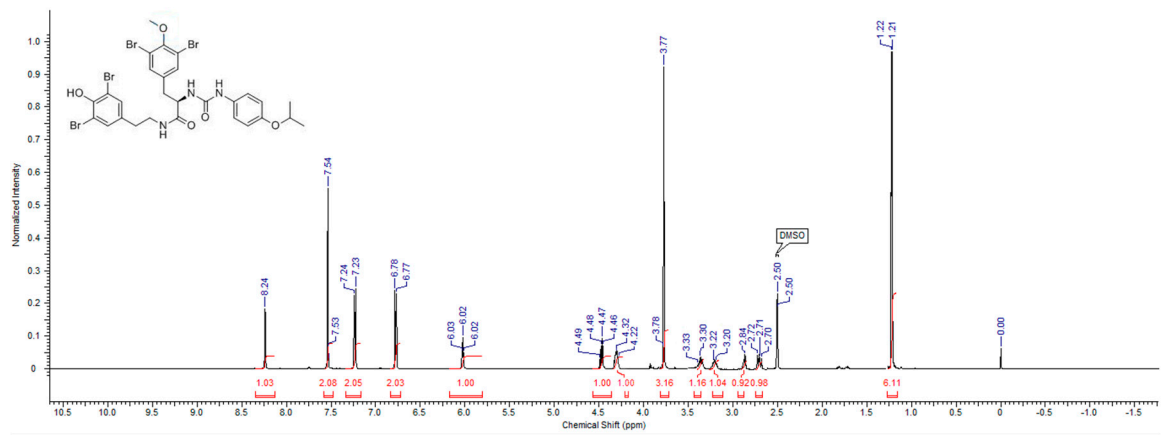
5F ¹³C-NMR



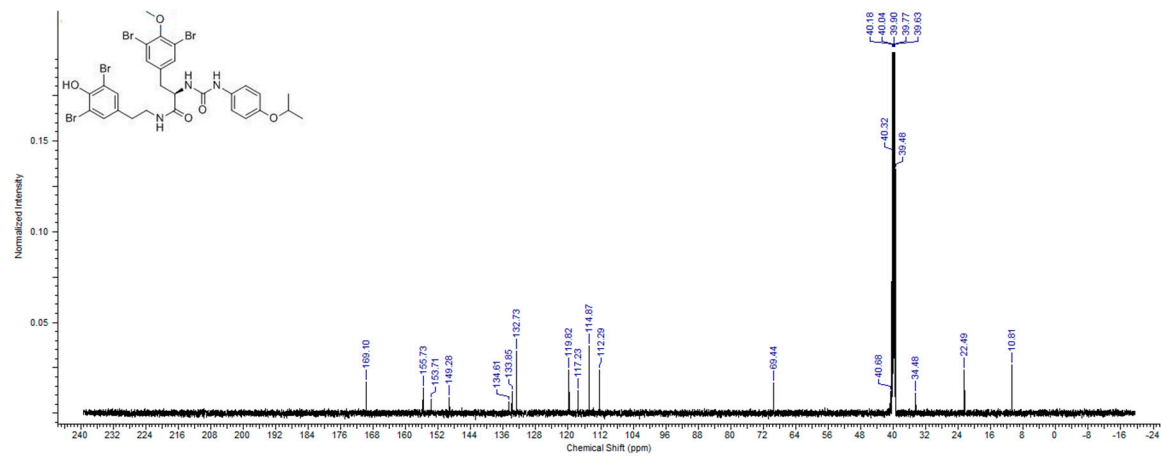
5G ¹H-NMR



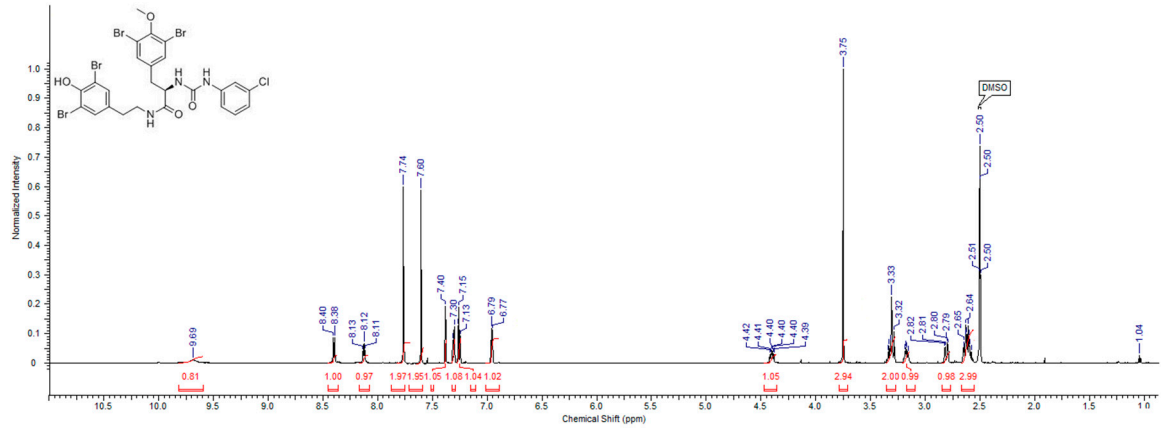
5G ^{13}C -NMR



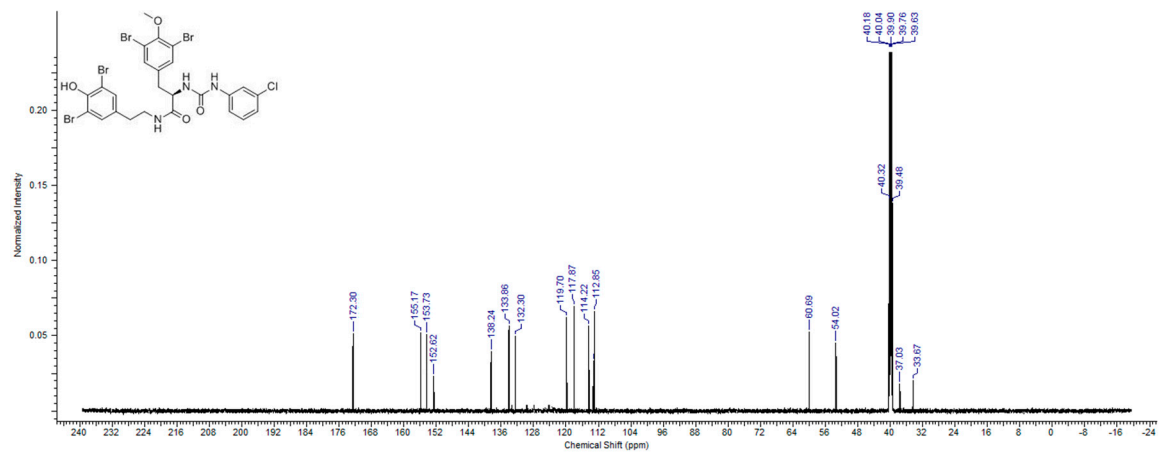
5H ^1H -NMR



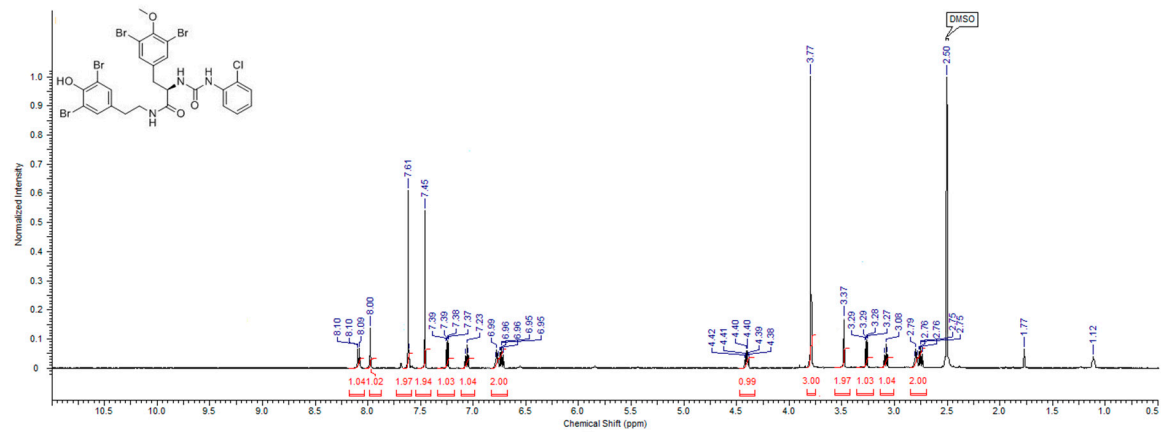
5H ^{13}C -NMR



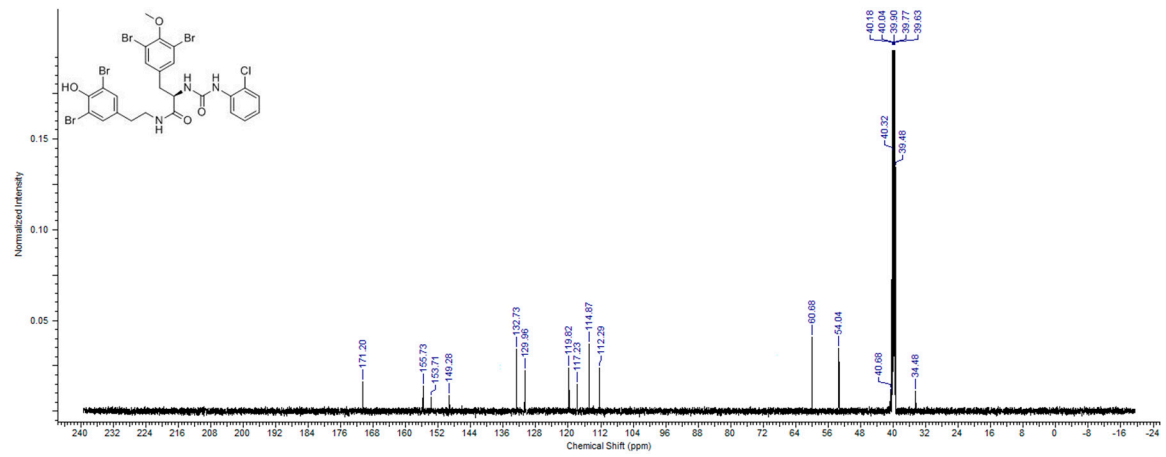
5I ¹H-NMR



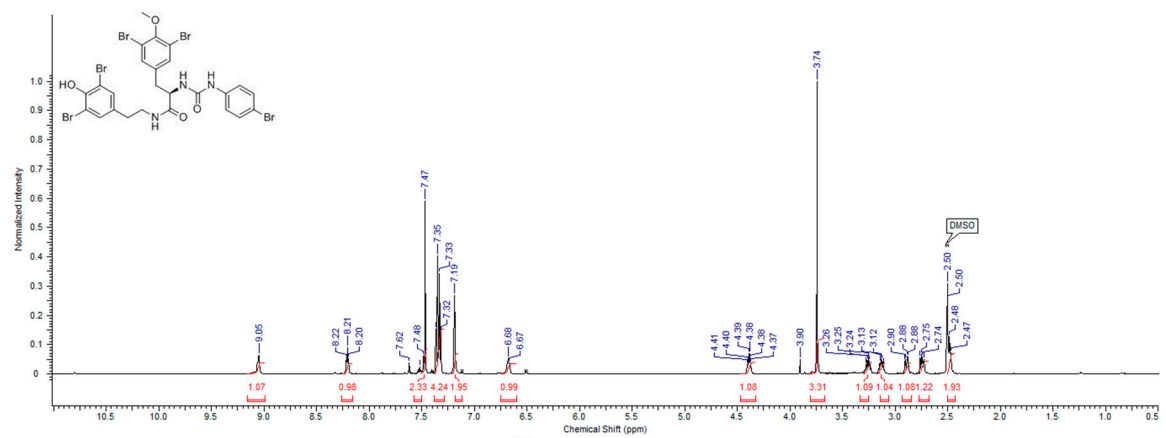
5I ¹³C-NMR



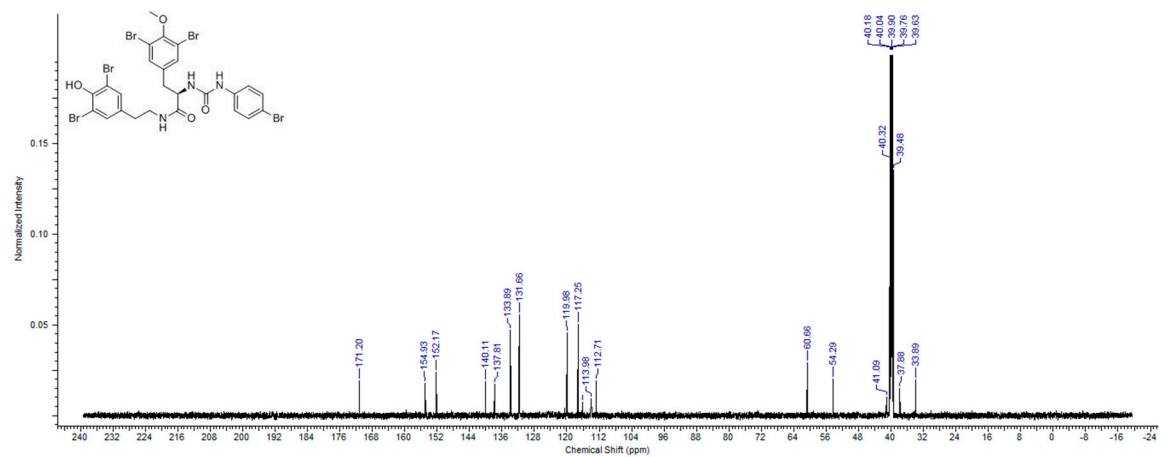
5J ¹H-NMR



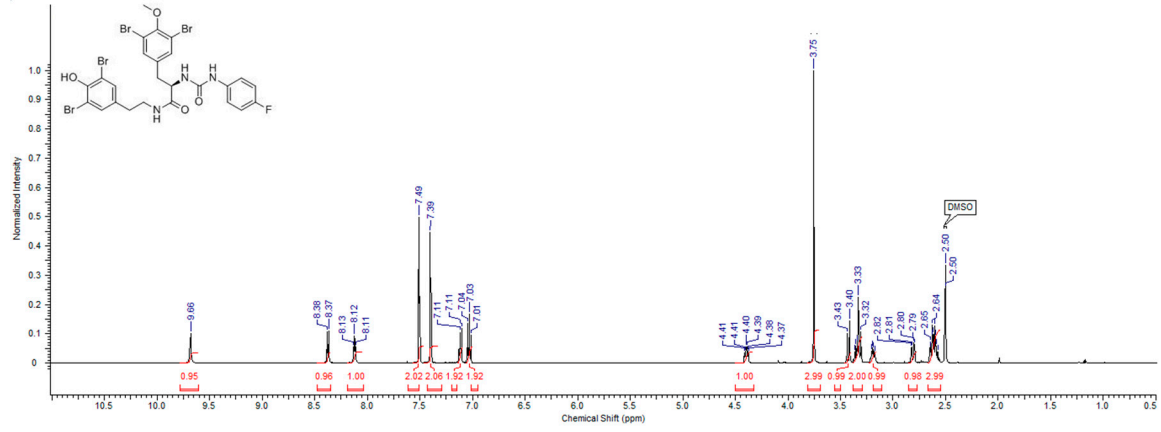
5J ¹³C-NMR



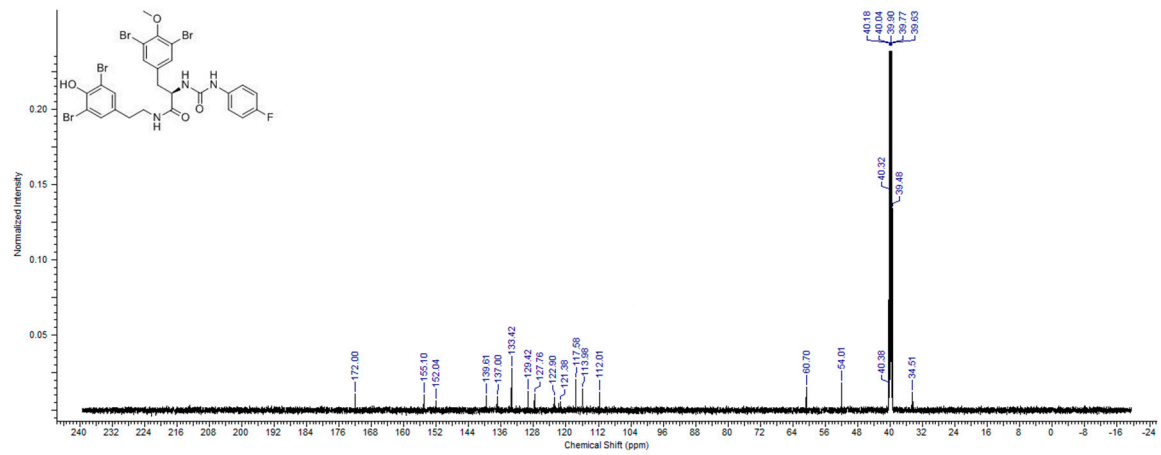
5K ¹H-NMR



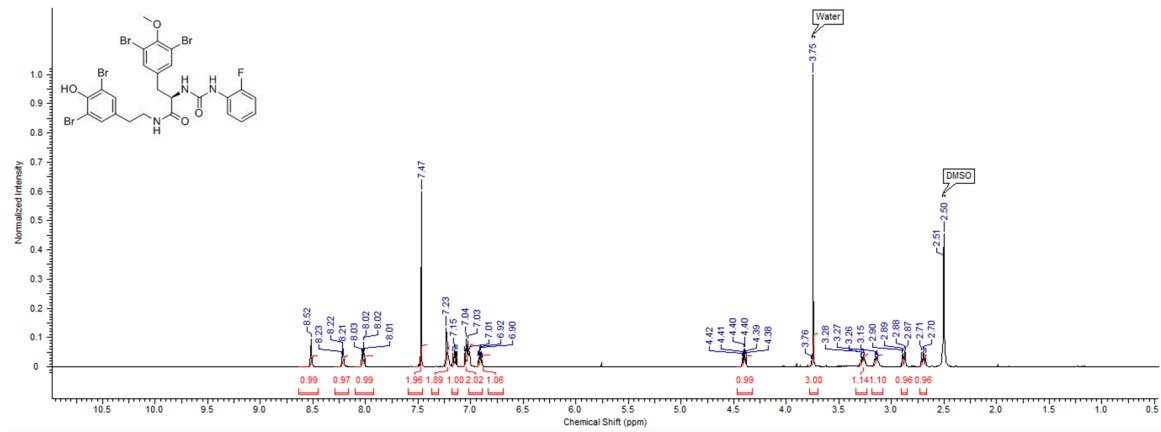
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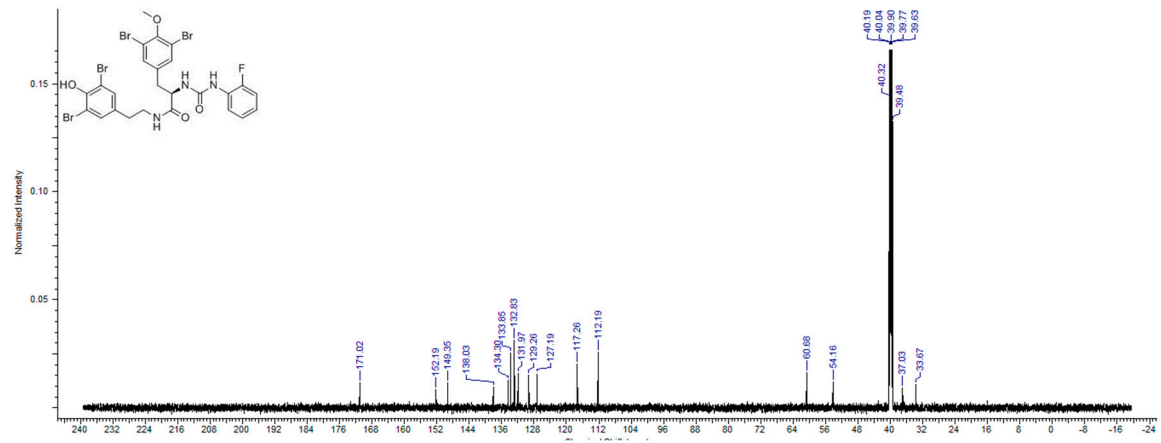
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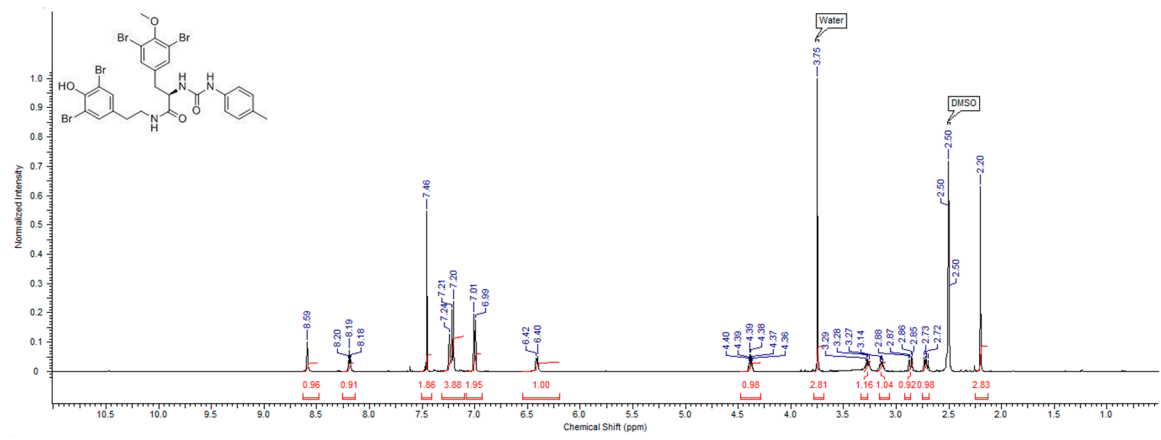
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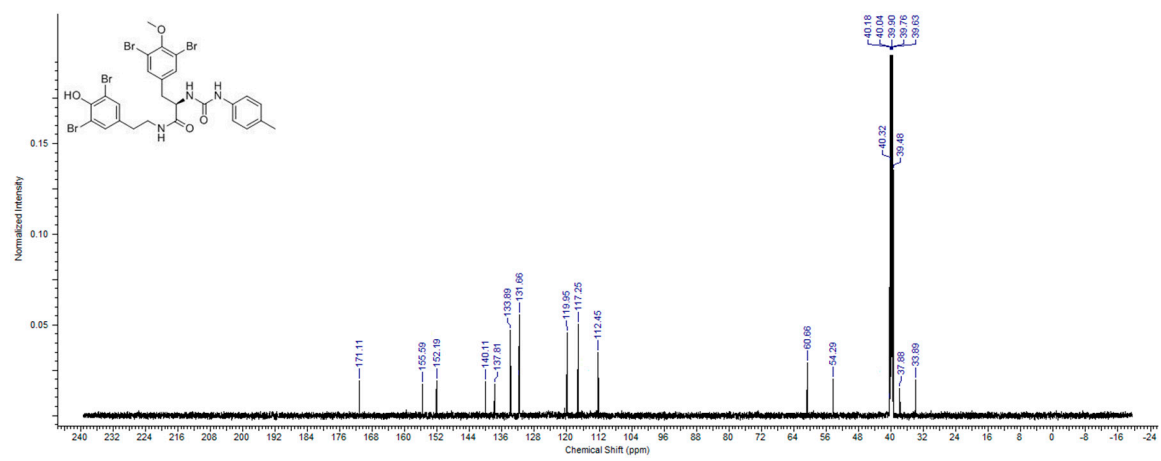
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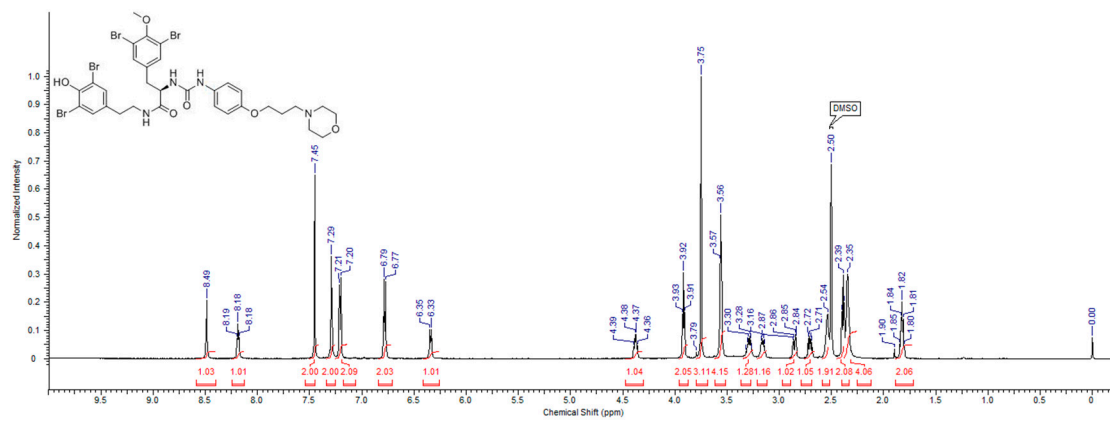
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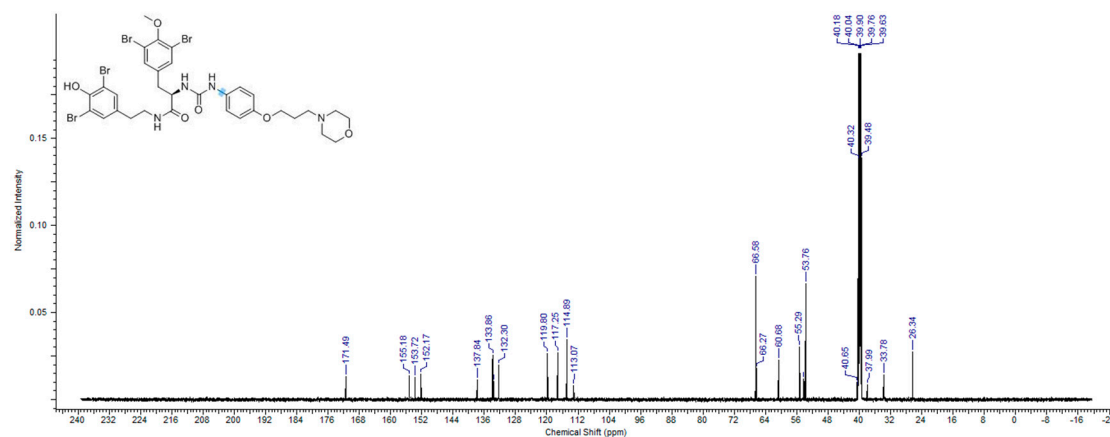
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5N ¹³C-NMR

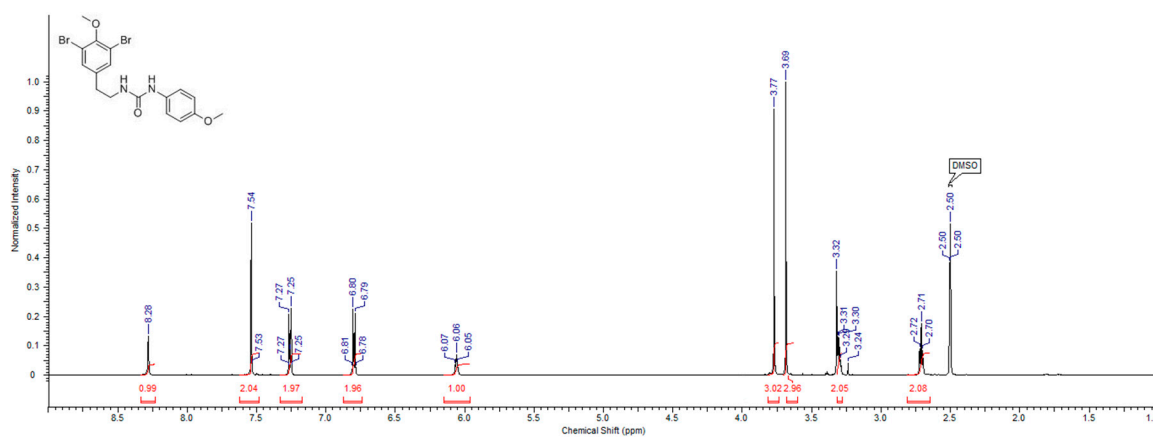


50 ¹H-NMR

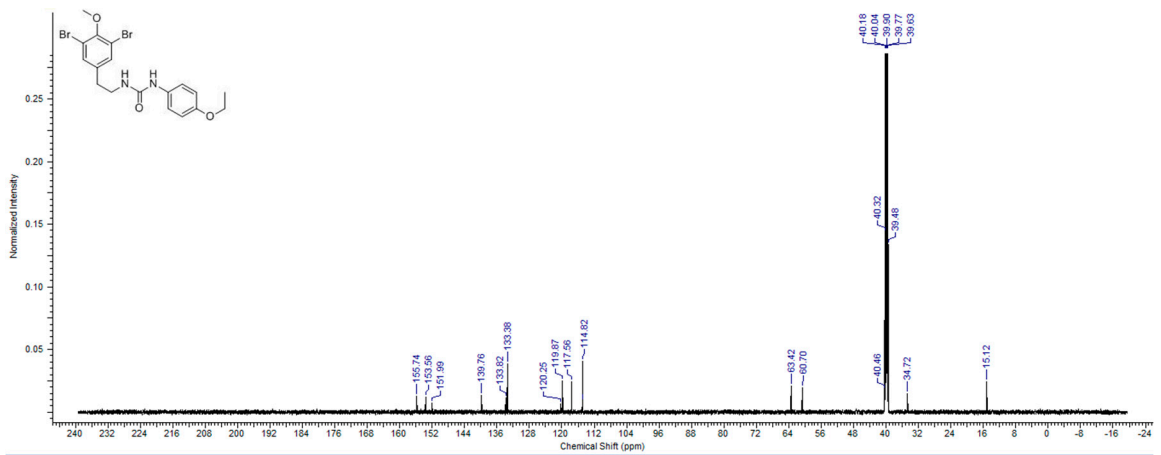
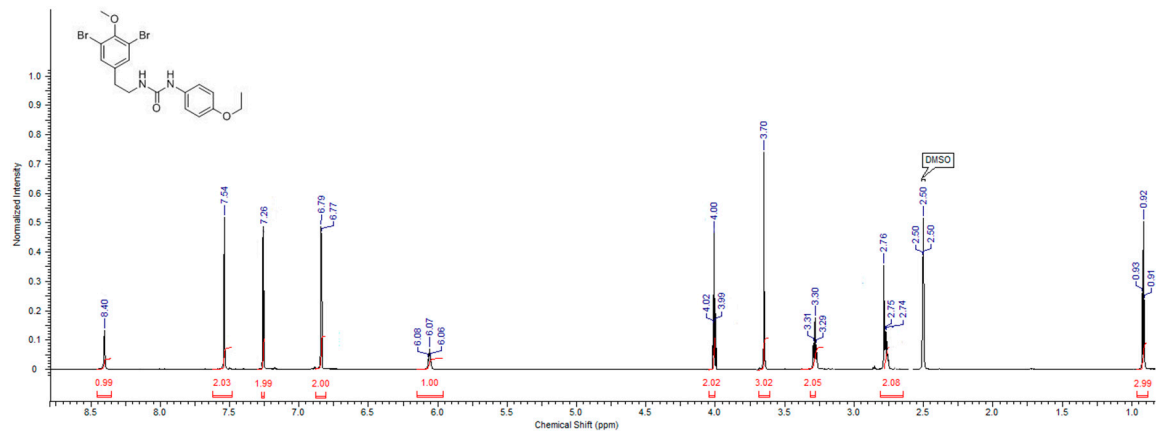
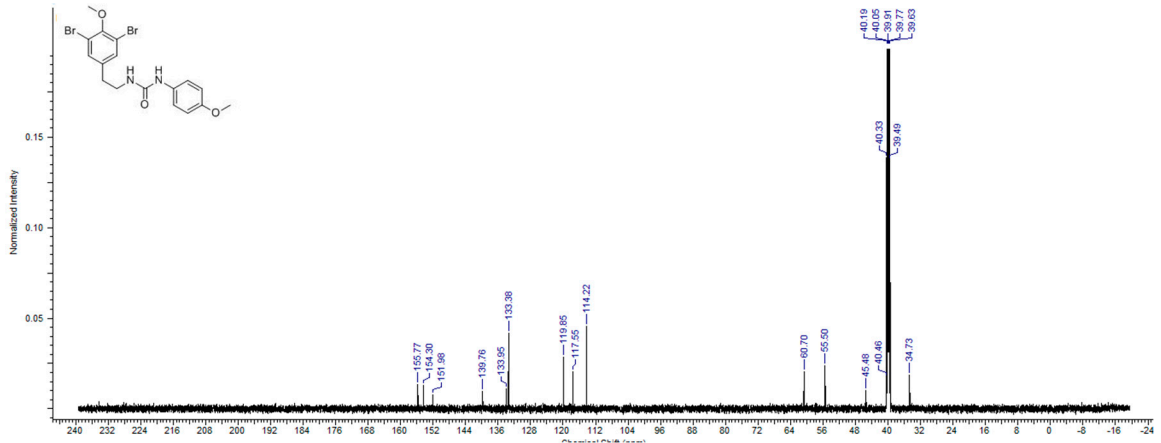


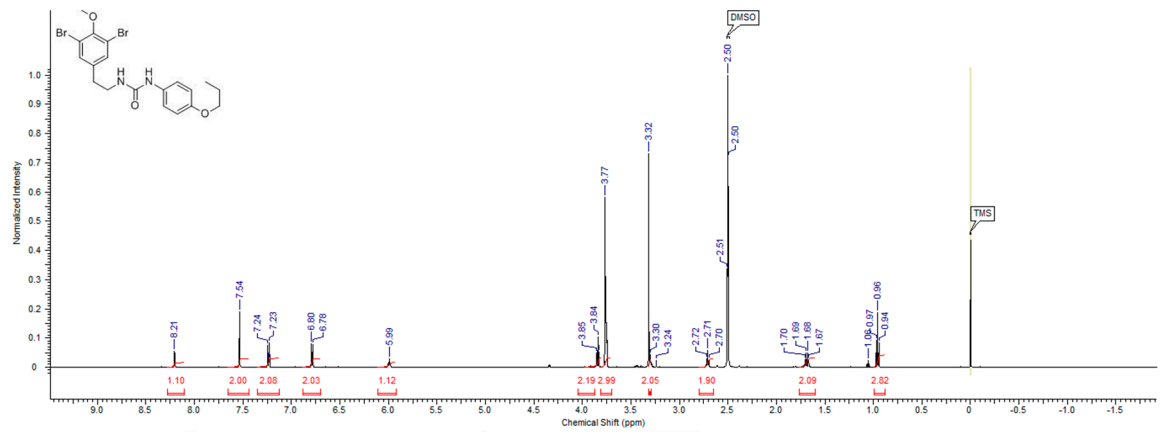
50 ¹³C-NMR

2.3

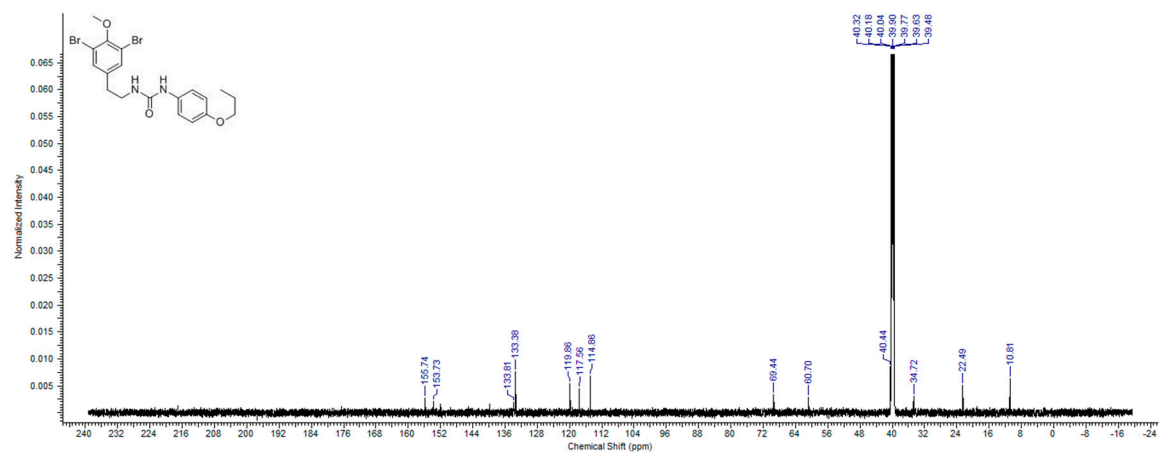


6A ¹H-NMR

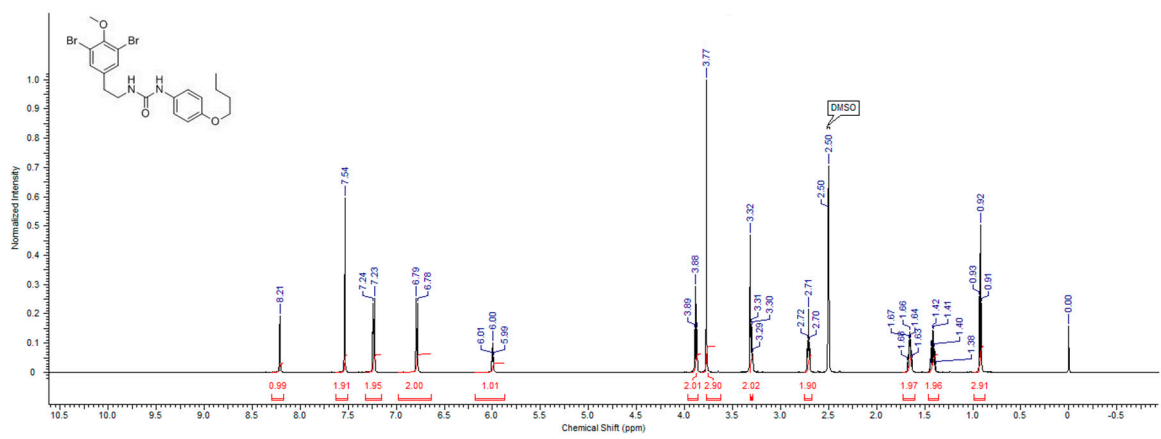




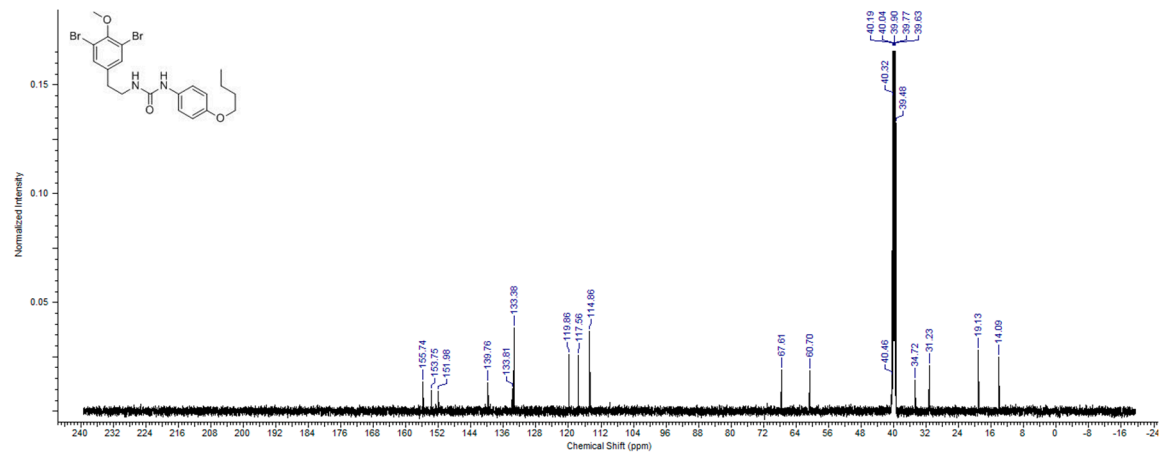
6C ¹H-NMR



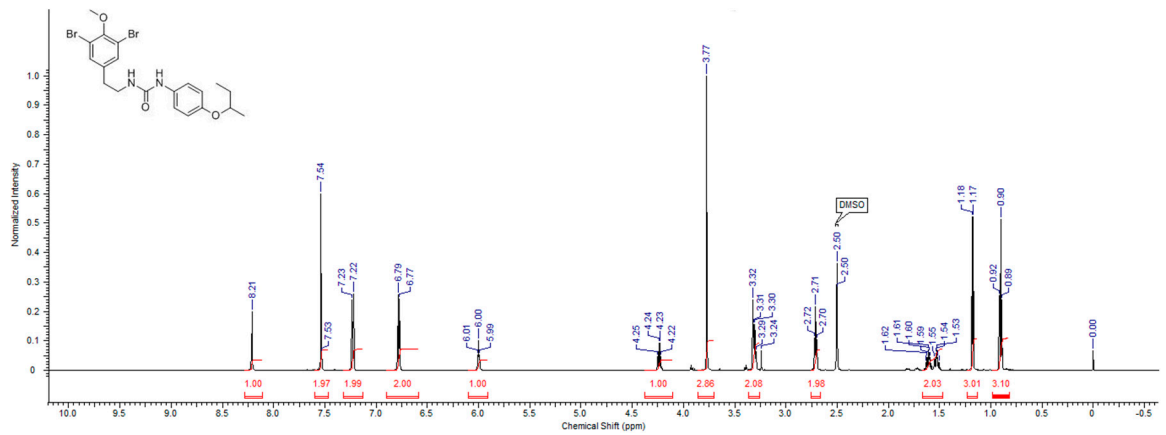
6C ¹³C-NMR



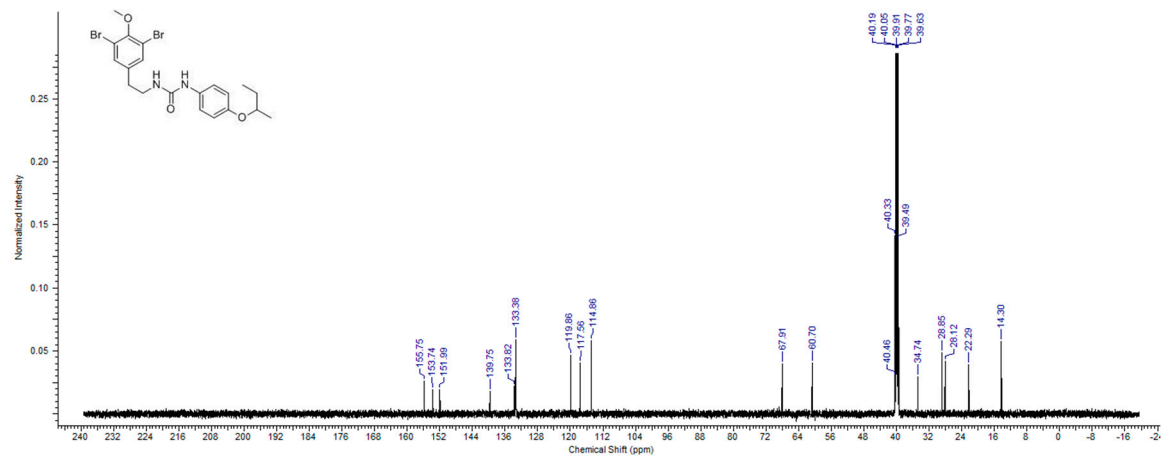
6D ¹H-NMR



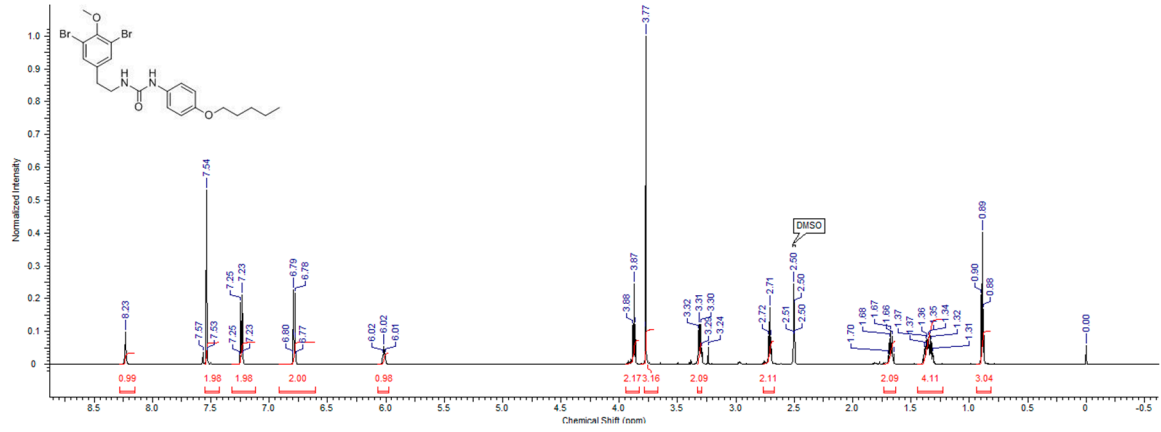
6D ^{13}C -NMR



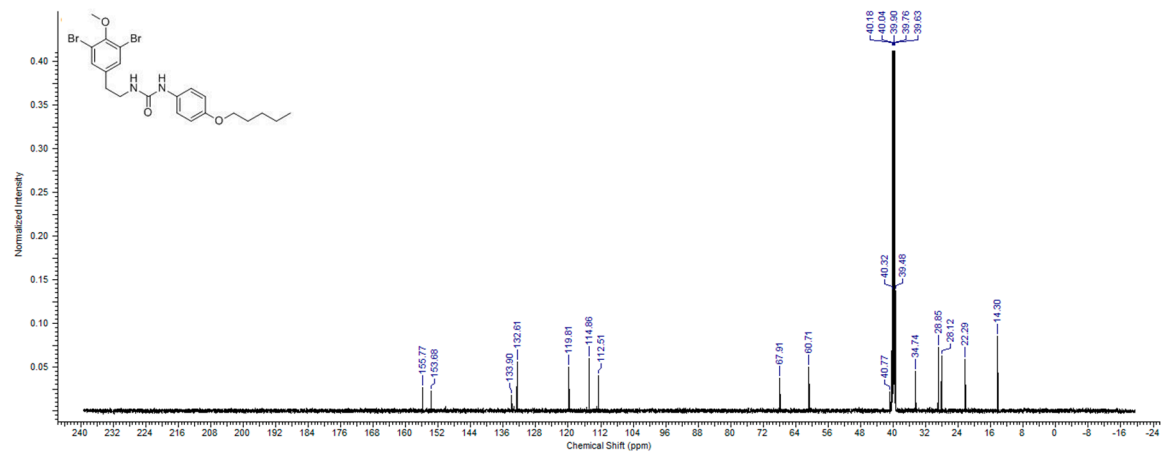
6E ^1H -NMR



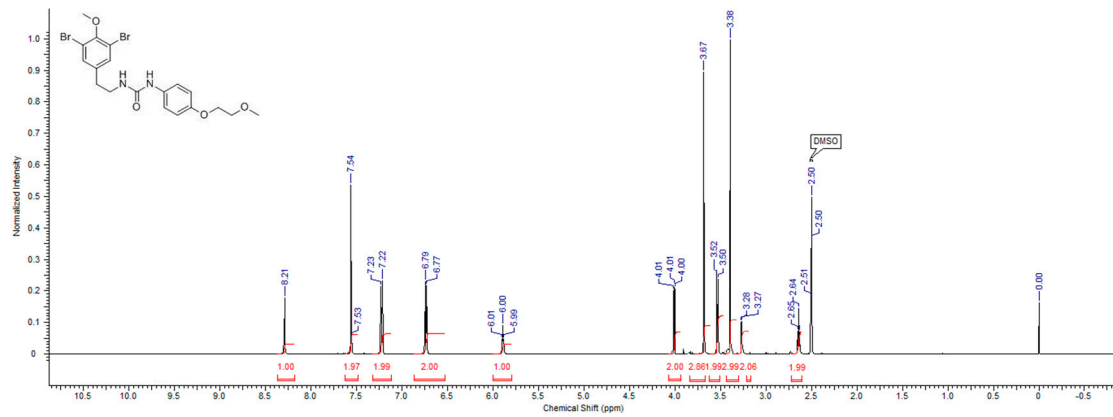
6E ^{13}C -NMR



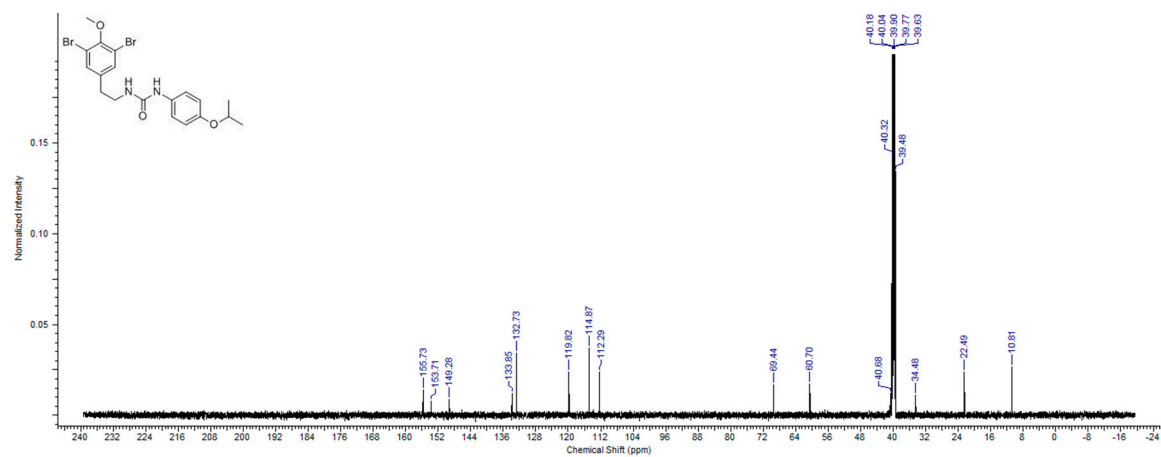
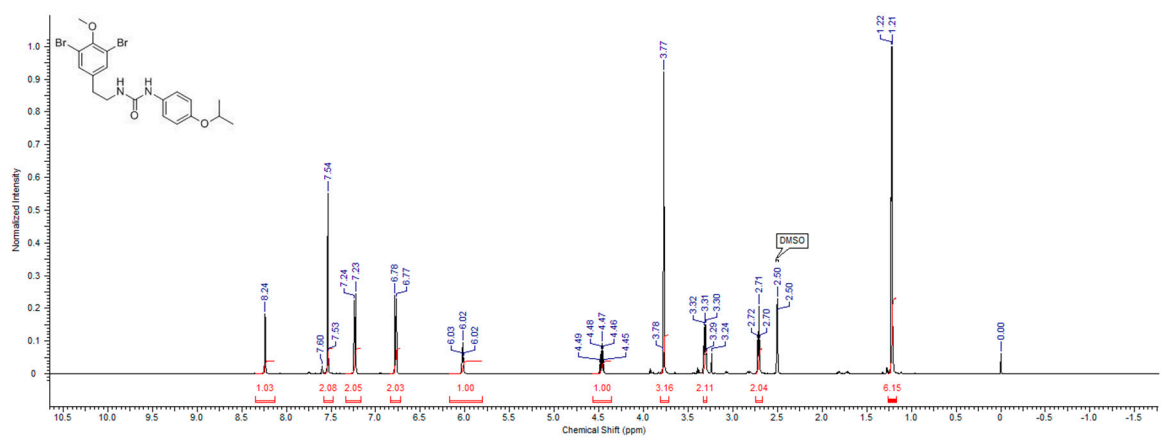
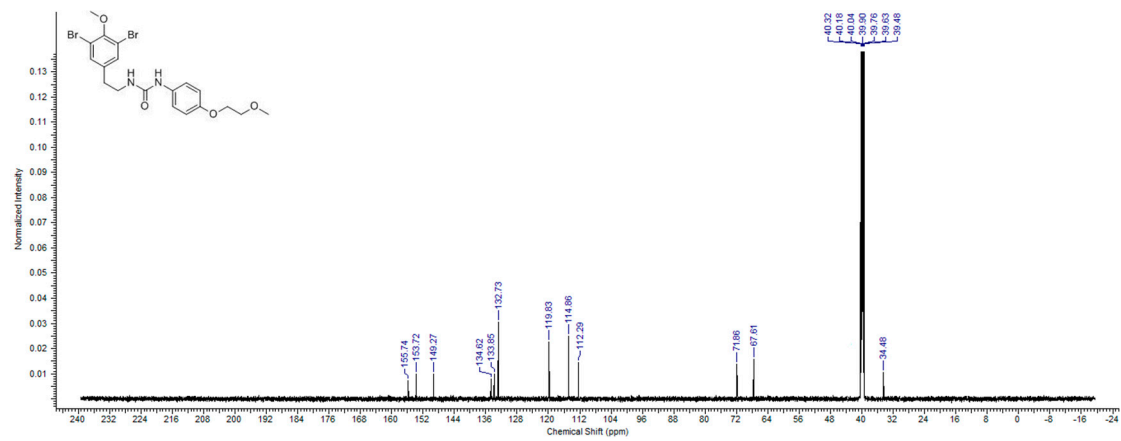
6F ¹H-NMR

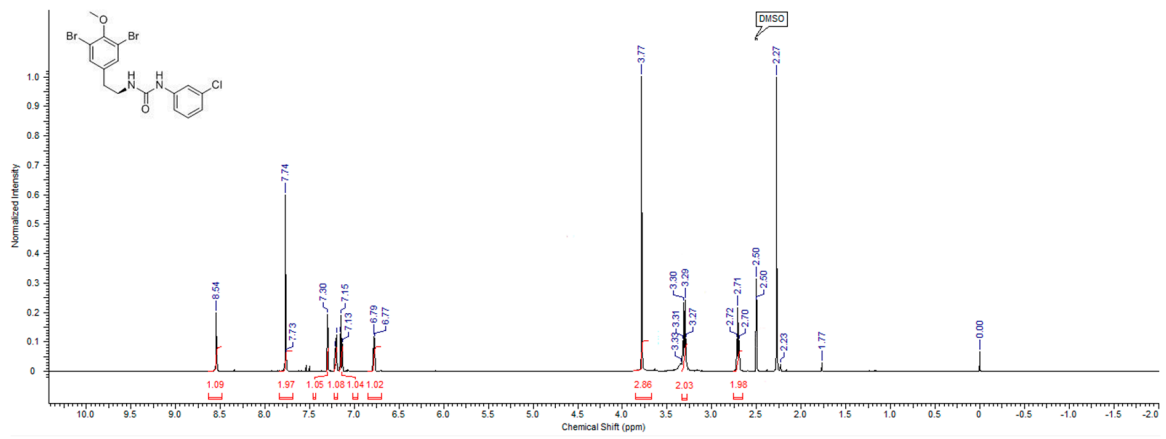


6F ¹³C-NMR

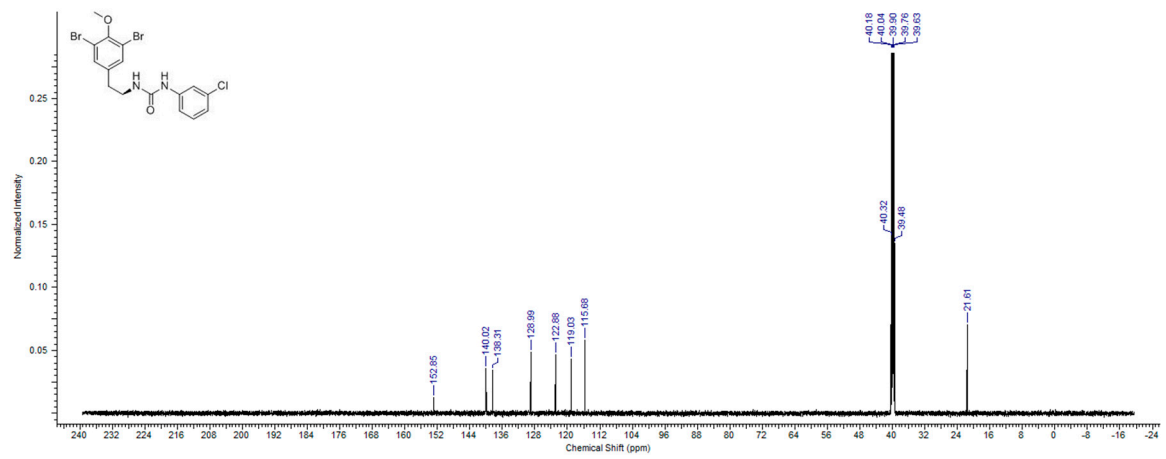


6G ¹H-NMR

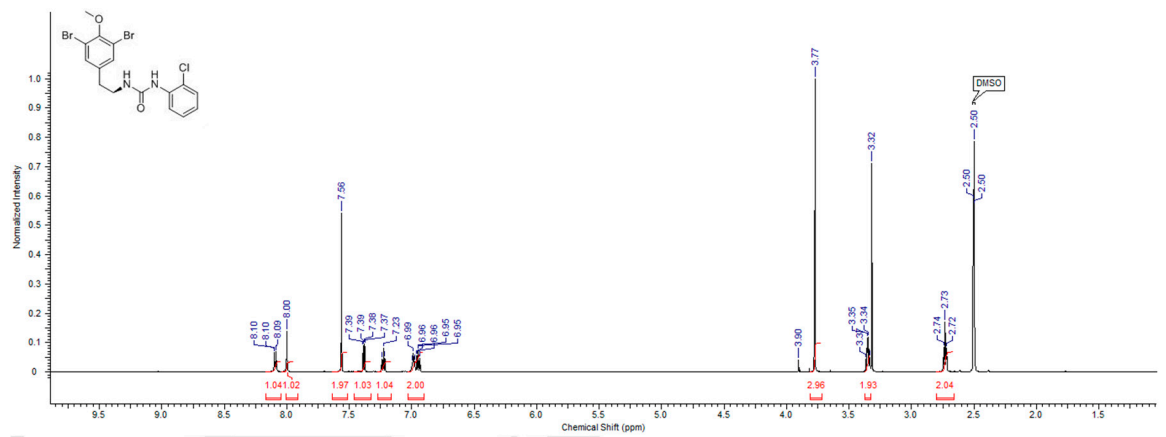




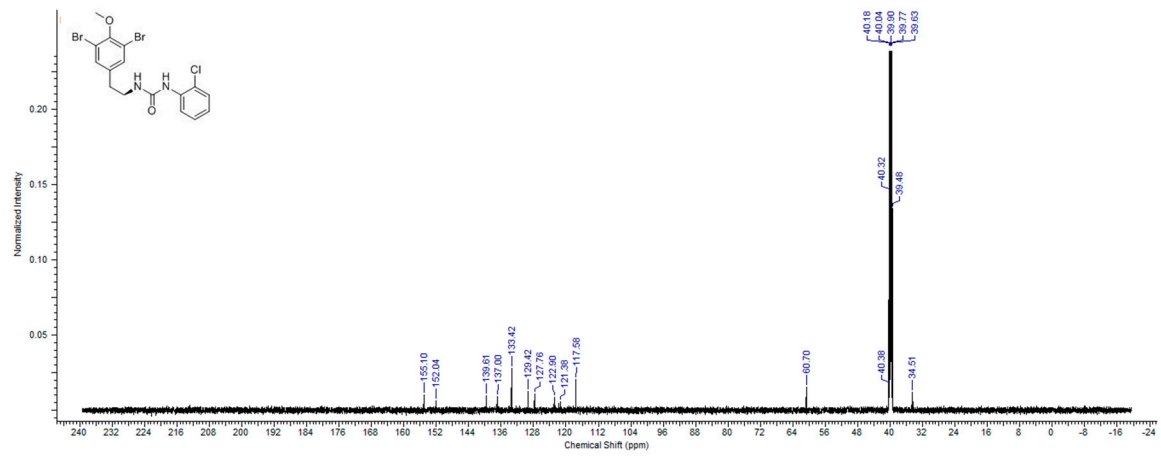
6I ¹H-NMR



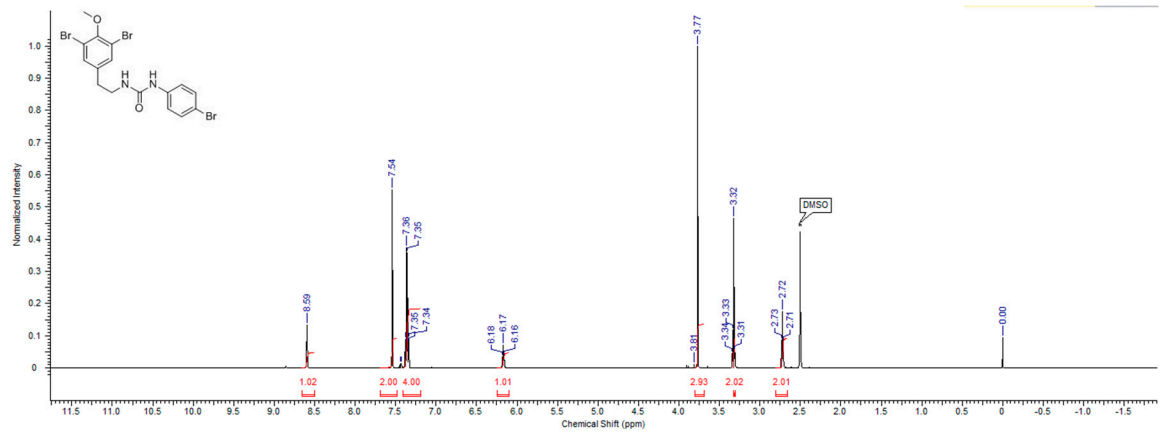
6I ¹³C-NMR



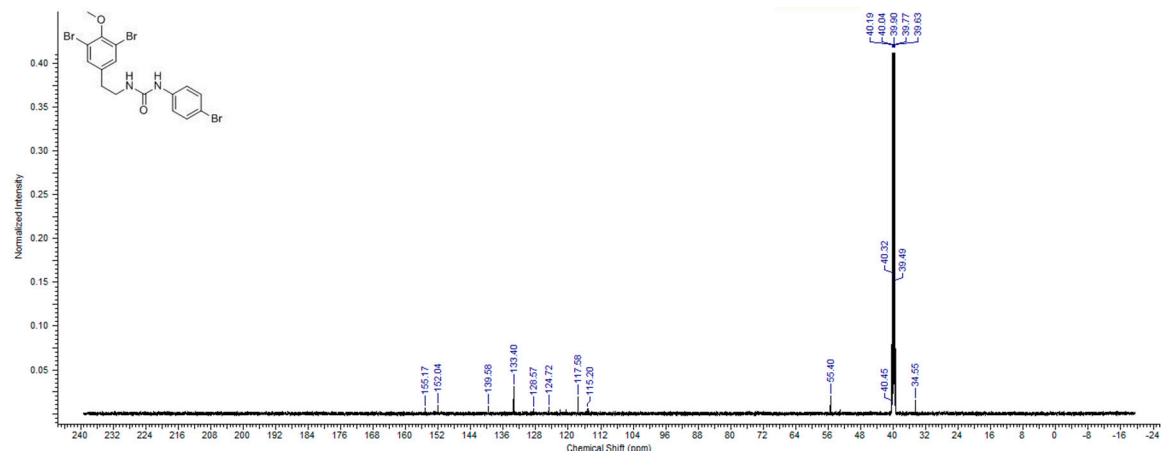
6J ¹H-NMR



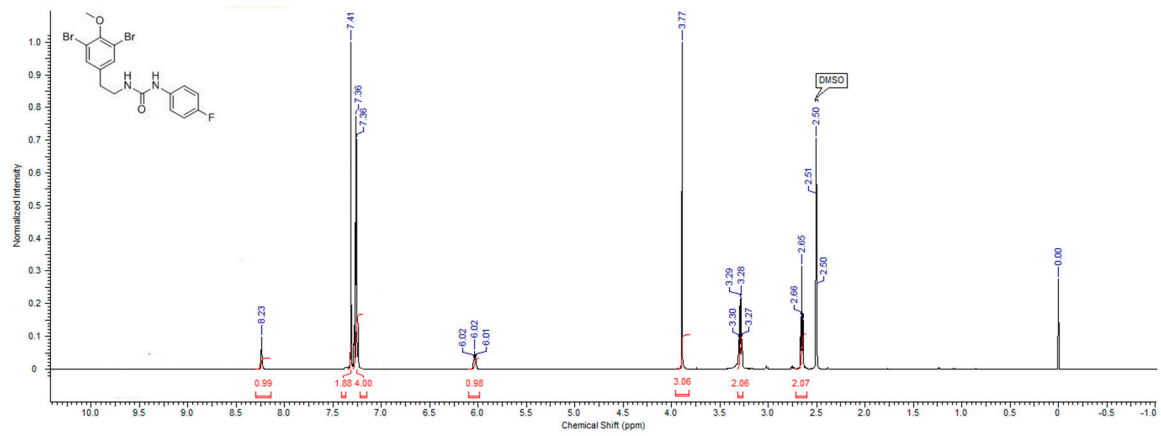
6J ^{13}C -NMR



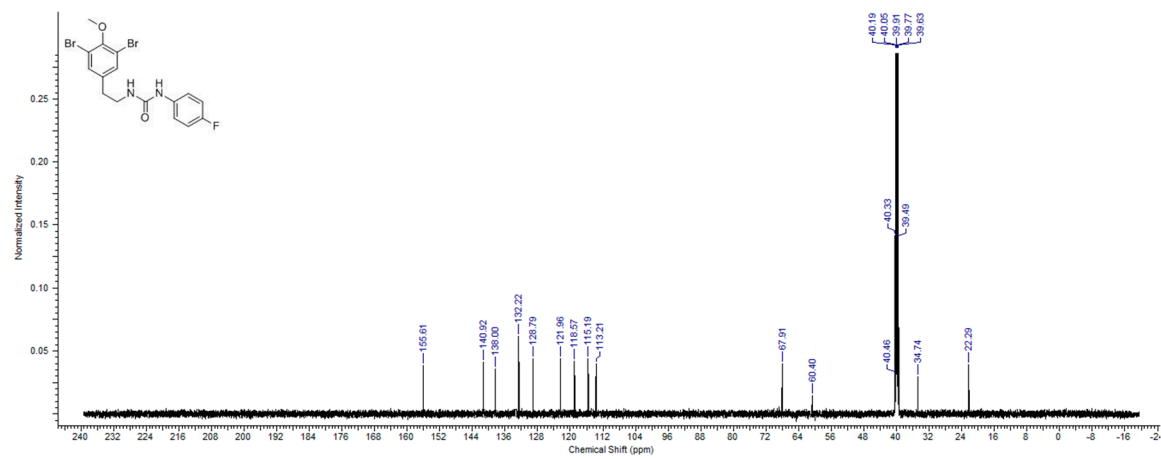
6K ^1H -NMR



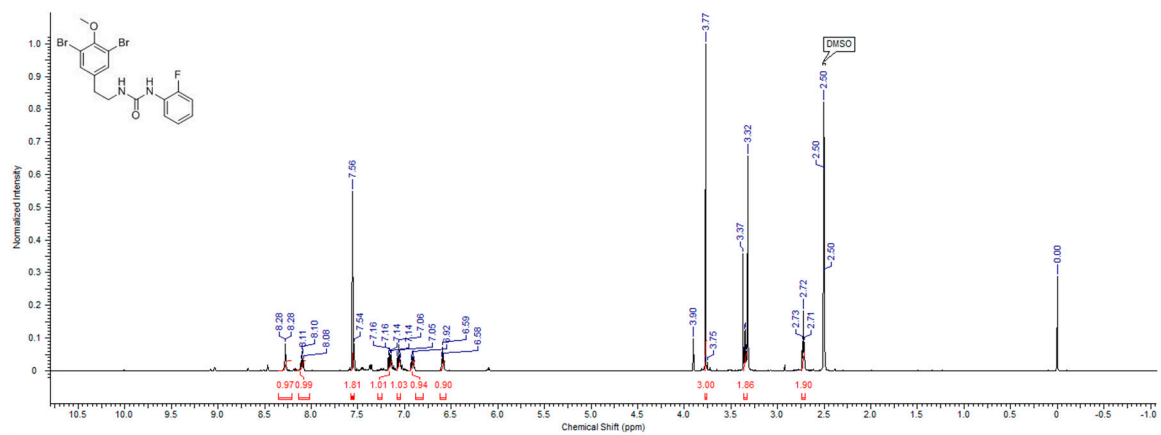
6K ^{13}C -NMR



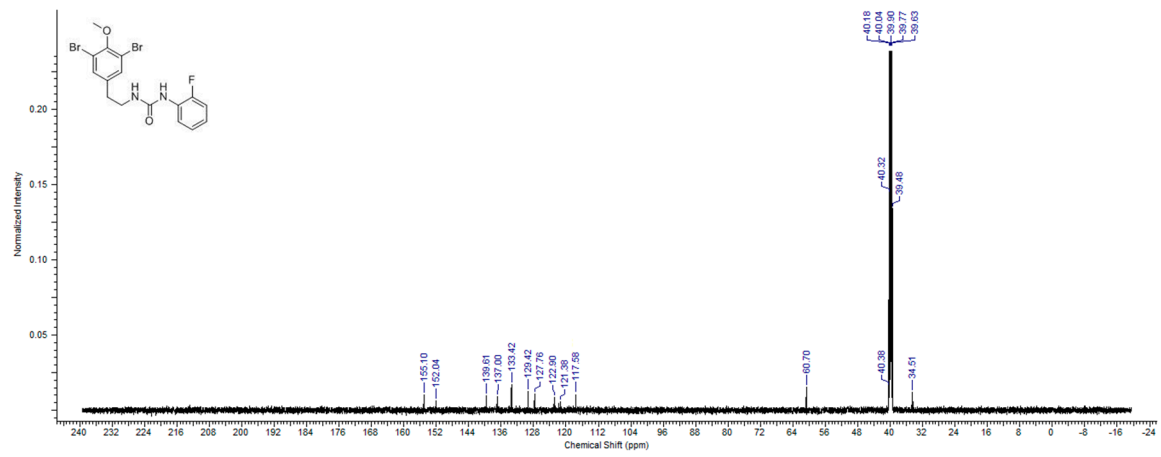
6L ¹H-NMR



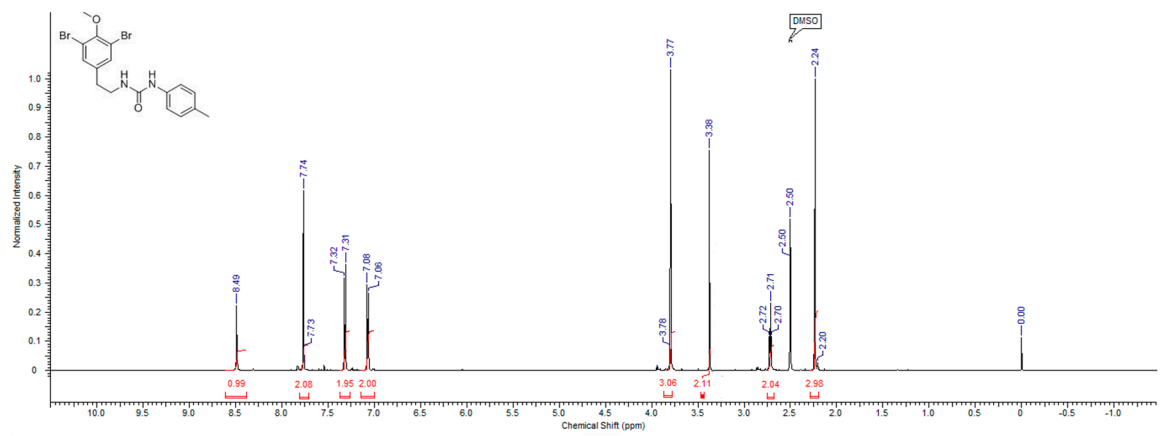
6L ¹³C-NMR



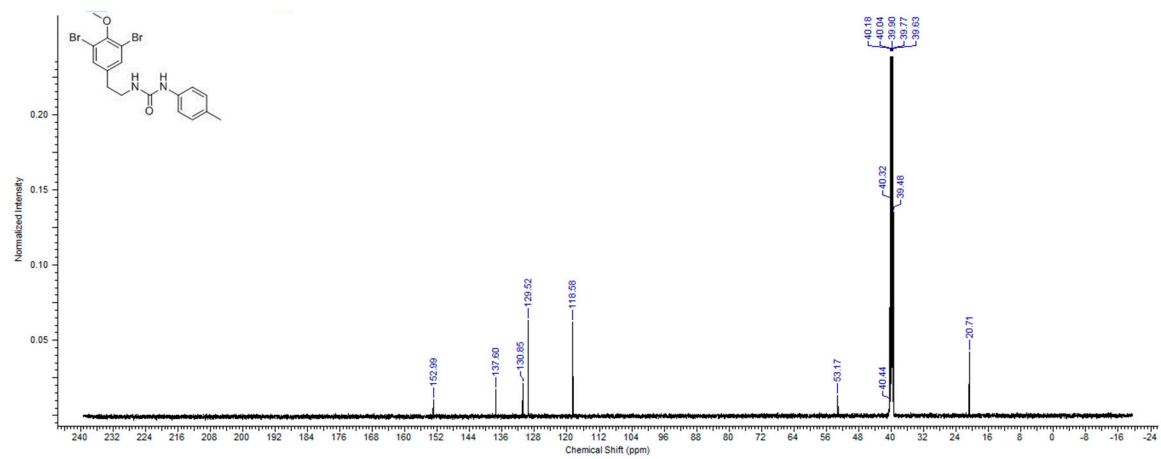
6M ¹H-NMR



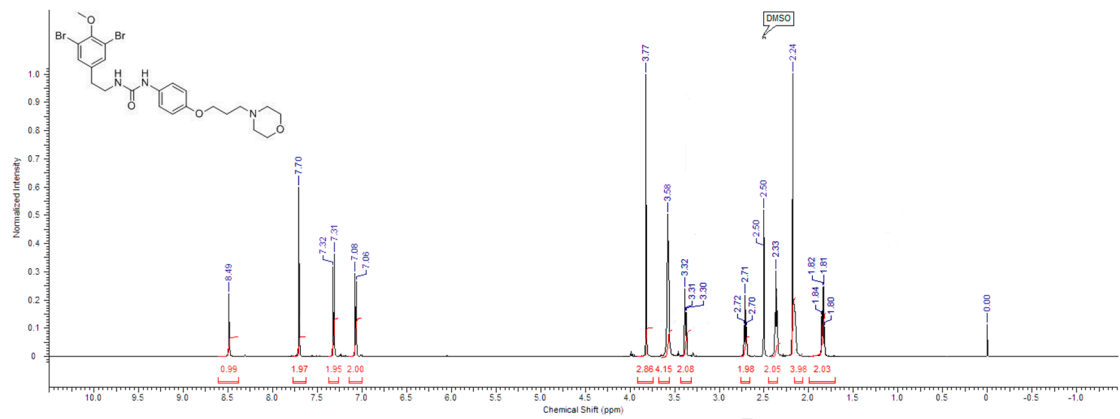
6M ¹³C-NMR



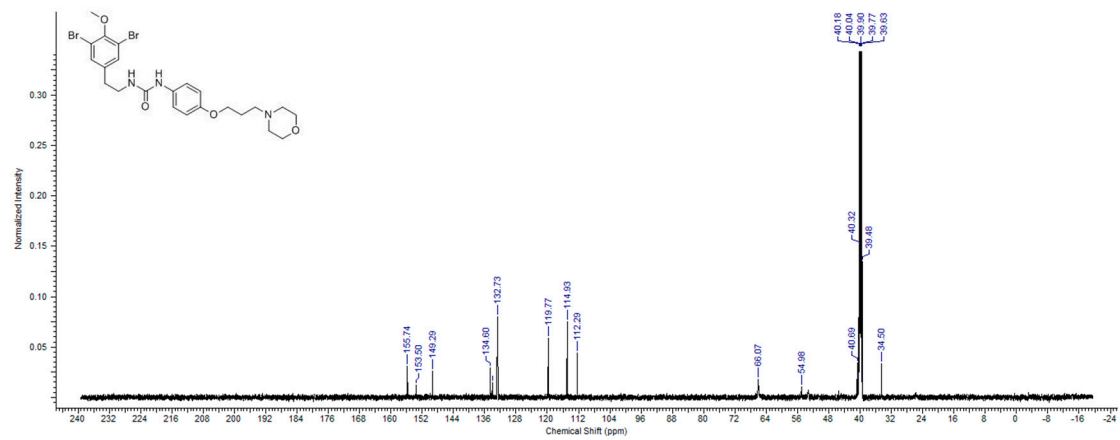
6N ¹H-NMR



6N ¹³C-NMR

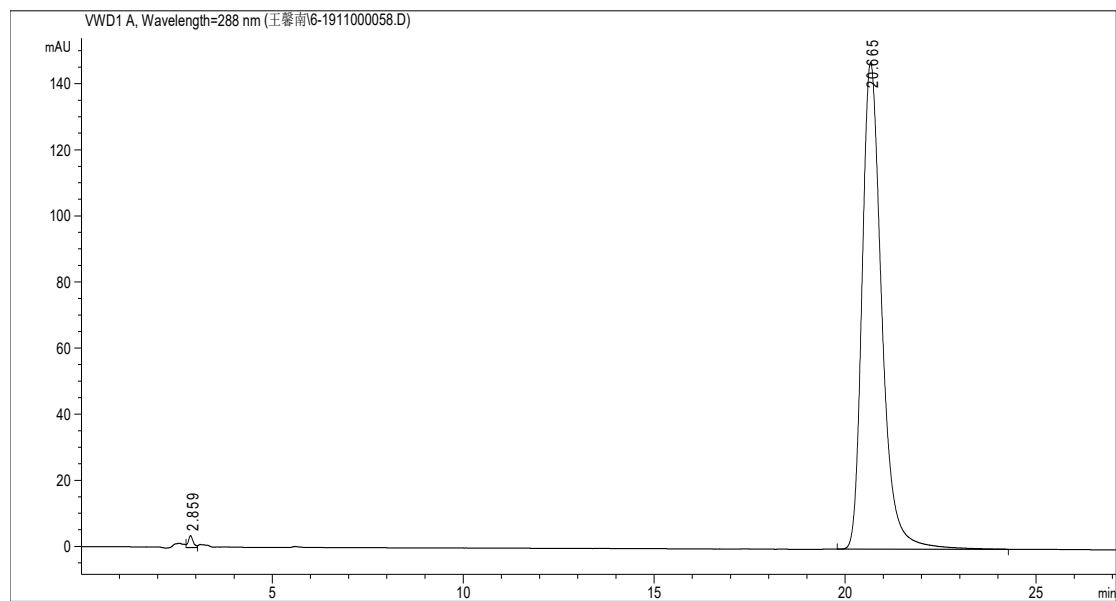


60 ¹H-NMR



60 ¹³C-NMR

4.2 HPLC data of 60



HPLC data for the purity of 60 (MeOH:H₂O=1:1)

