Supplementary Information

Novel Non-peptidic Small Molecule Inhibitors of Secreted Aspartic Protease 2 (SAP2) for the Treatment of Resistant Fungal Infections

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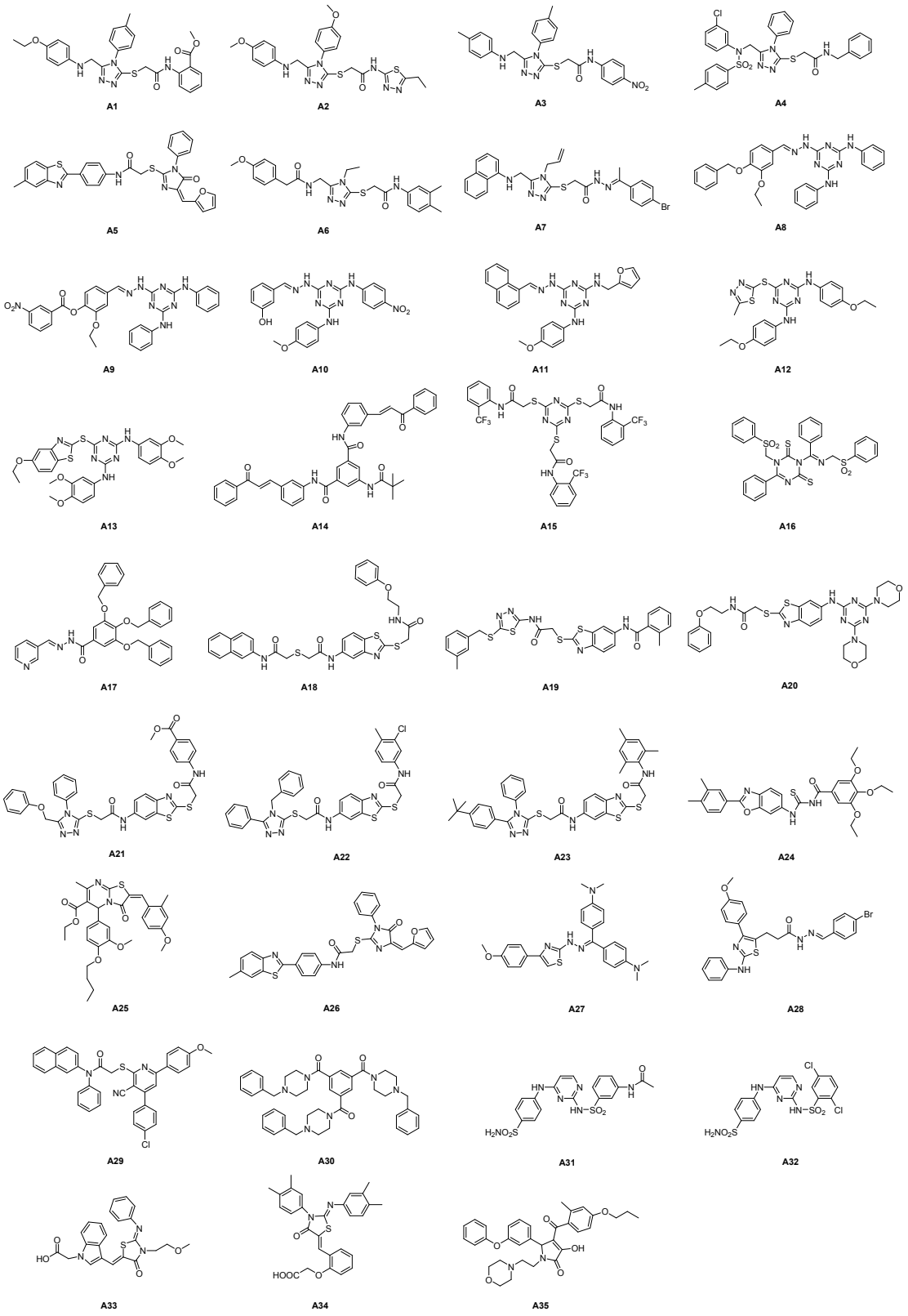


Figure S1. Chemical structures of compounds selected from virtual screening

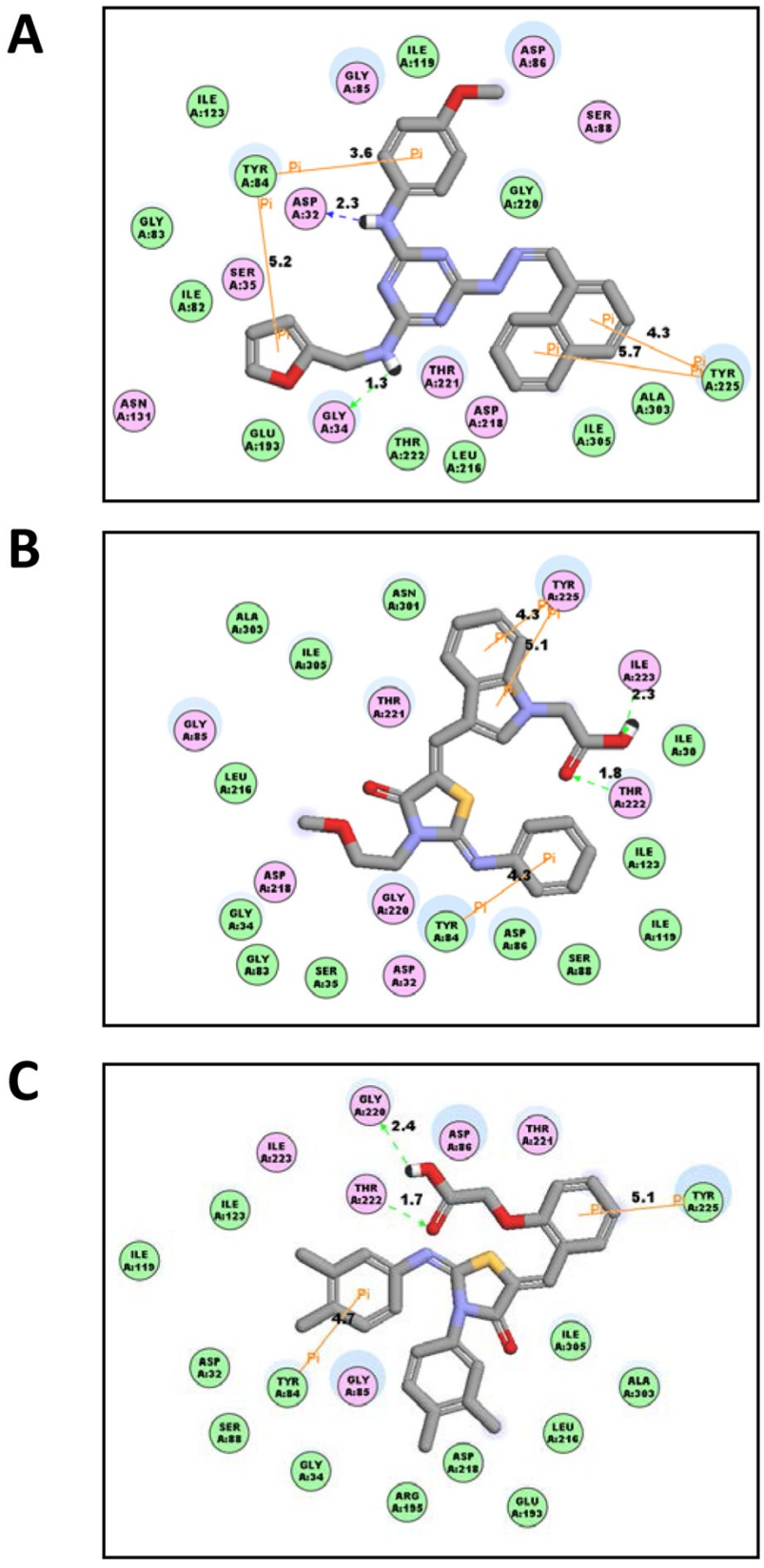


Figure S2. Schematic representation of the proposed interactions between inhibitors **A12 (3) (A)**, **A39 (4) (C)** and **A40 (5) (D)** and the active site of *C. albicans* SAP2.

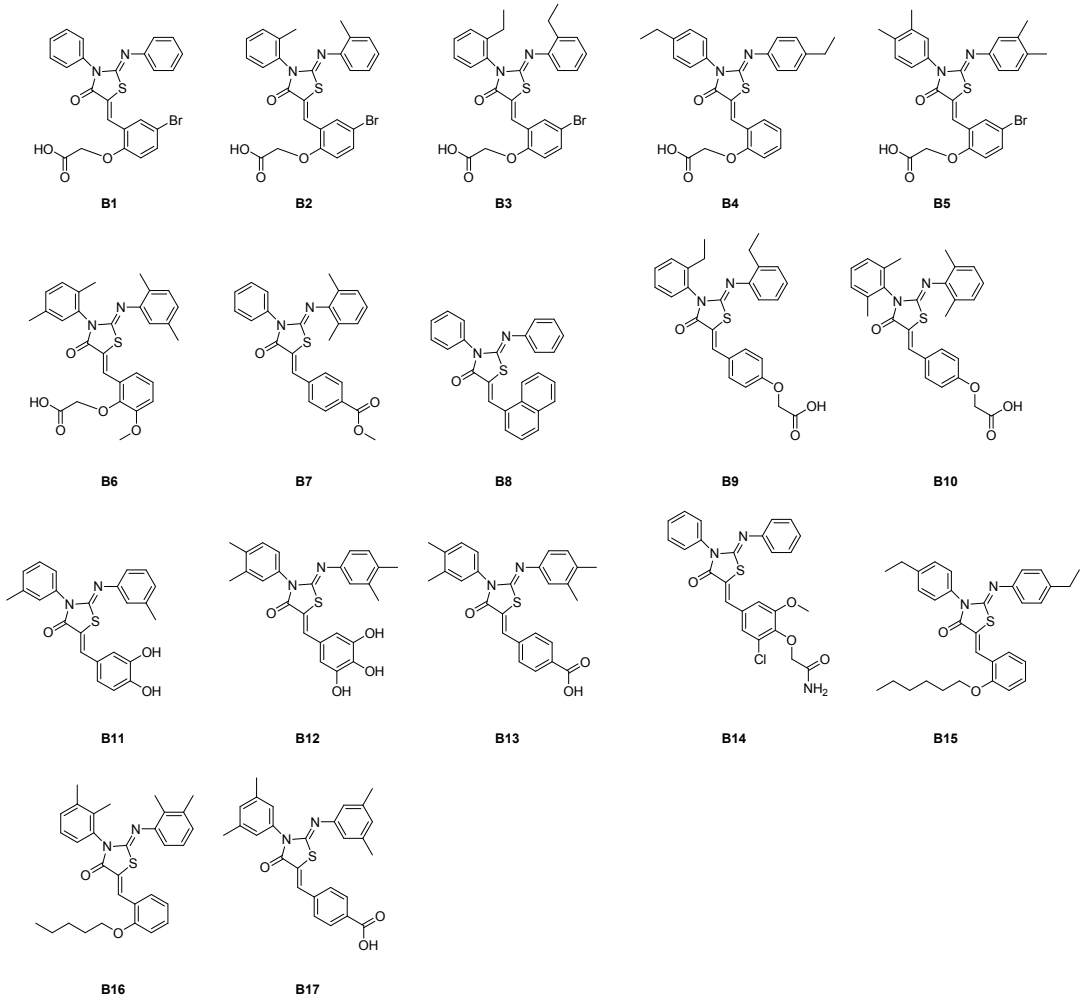


Figure S3. Chemical structures of hit 5 analogues by similarity search from the Specs database.

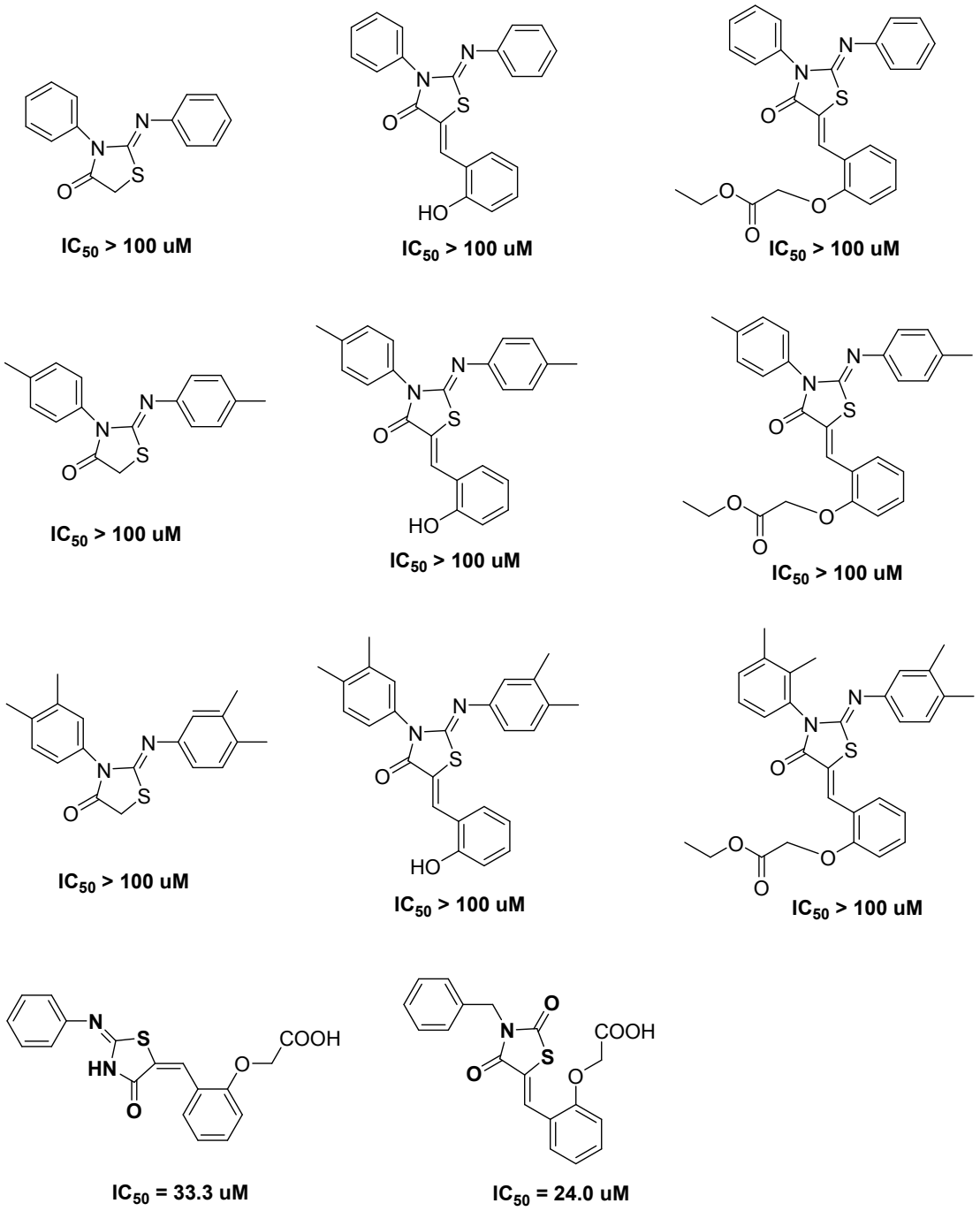


Figure S4. Chemical structures and SAP2 inhibitory activity of A, B, C-ring modified analogues.

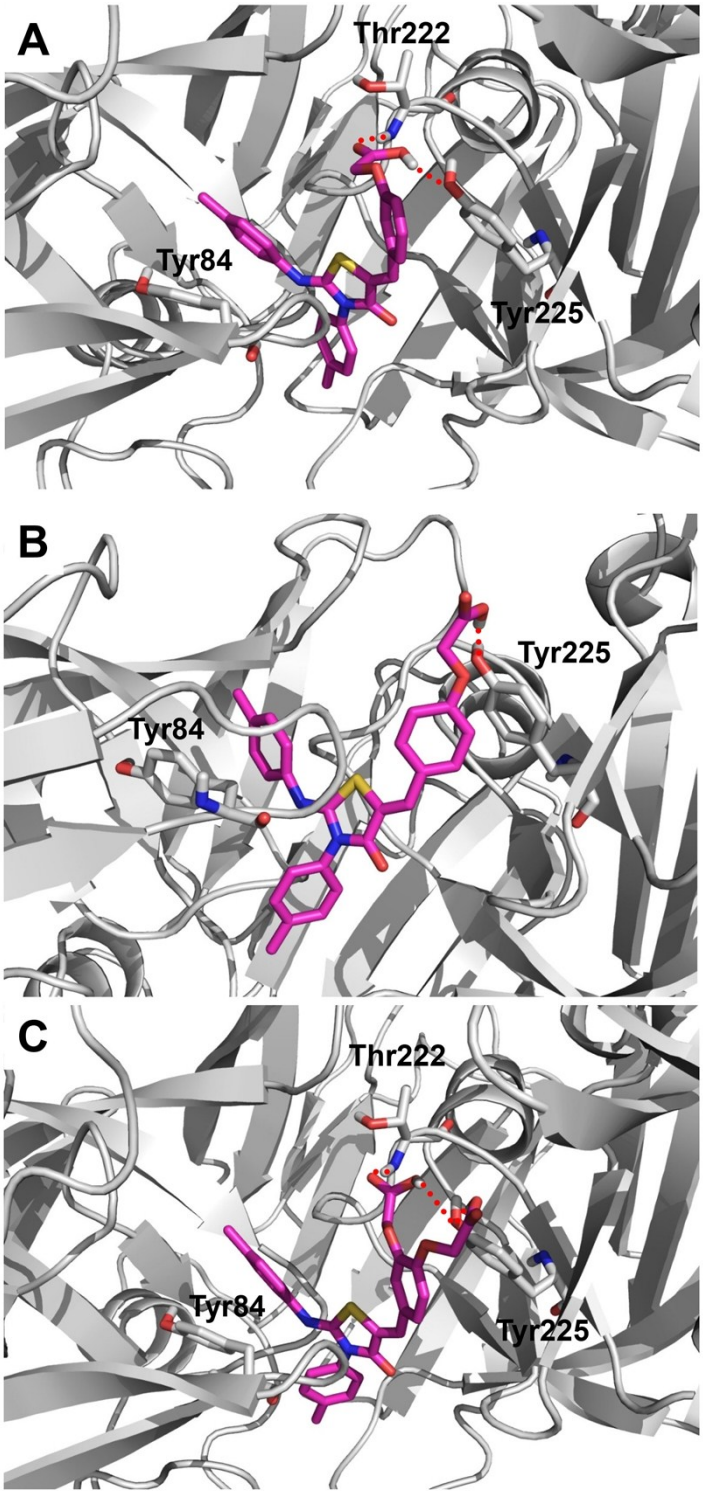


Figure S5. Proposed binding poses of inhibitor **23e (A)**, **23f (B)** and **23g (C)** in the active site of *C. albicans* SAP2.

Table S1. Matrix of RMSD values obtained by the docking methods selection.

RMSD < 1.0	1.0 < RMSD < 2.0	2.0 < RMSD < 4.0	4.0 < RMSD

		AutoDock		MVD		GOLD	
Ligand	PDB code	First Cluster	Most Pop Cluster	MolDock Score[grid]	MolDock Score	GoldSore	ChemPLP
A70450	1ZAP	0.91	0.92	1.85	1.80	0.28	6.24
A70450	1EAG	1.25	1.25	0.98	0.95	0.33	3.05

Table S2. Chemical structures, GOLD docking scores, compound rankings and SAP2 inhibitory activities of 45 compounds selected from virtual screening.

Compounds	**M.W.**	**Goldscore**	**Rank**	**Inhibition rate (100 μM)**	**IC_{50} (μM)**
A1	531.63	84.24	130	21%	nd[a]
A2	511.62	86.63	52	20%	nd
A3	488.56	82.3	245	35%	nd
A4	681.17	87.86	39	4%	nd
A5	550.65	81.64	294	35%	nd
A6	467.58	83.02	191	7%	nd
A7	549.49	81.89	273	12%	nd
A8	531.61	91.48	16	61%	52.96
A9	590.59	90.11	25	42%	nd
A10	472.43	90.26	24	17%	nd
A11	465.51	92.05	15	58%	77.18
A12	481.59	91.32	18	35%	nd
A13	592.69	95.75	5	45%	nd

A14	675.77	80.06	481	37%	nd
A15	780.71	81.2	337	28%	nd
A16	632.8	86.08	66	-[b]	nd
A17	543.61	84.47	122	-	nd
A18	616.77	83.24	181	14%	nd
A19	577.76	85.7	71	-	nd
A20	608.73	80.12	475	48%	nd
A21	696.82	87.15	45	10%	nd
A22	671.25	84.48	120	39%	nd
A23	706.94	88.62	35	36%	nd
A24	533.64	80.63	405	27%	nd
A25	550.67	84.81	108	42%	nd
A26	550.65	81.62	295	45%	nd
A27	471.62	80.24	456	67%	83.55
A28	535.46	83.33	173	55%	96.26
A29	612.14	81.79	279	-	nd
A30	684.87	80.66	401	9%	nd
A31	462.5	80.05	482	30%	nd
A32	474.34	80.21	462	53%	93.55
A33	435.5	85.04	102	100%	36.37
A34	486.58	86.91	48	100%	13.78
A35	556.65	89.12	30	45%	nd
PepstatinA				100%	0.021

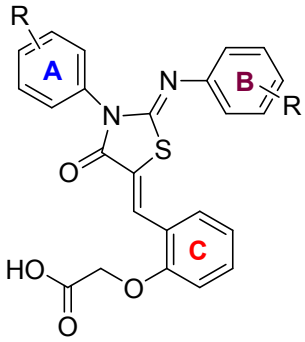
a. “nd” = “not determined”; b. “–” means compounds with high fluorescence and precise results cannot be determined.

Table S3. SAP2 inhibitory activity of hit **5** analogues from SPECS database

Compound	Inhibition rate[a]	IC_{50} (μM)	Compound	Inhibition rate (100 μM)	IC_{50} (μM)
B1	90%	36.47	**B10**	79%	39.14
B2 (6)	100%	10.18	**B11**	4%	nd
B3	100%	11.28	**B12**	9%	nd
B4	100%	12.32	**B13**	7%	nd
B5	80%	40.35	**B14**	12%	nd
B6	98%	21.45	**B15**	3%	nd
B7	11%	nd[b]	**B16**	5%	nd
B8	5%	nd	**B17**	13%	nd
B9	67%	49.50	**PepA**	100%	0.018

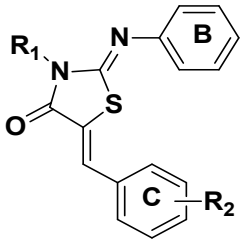
a. The inhibition rate was determined at the concentration of 100 μM. b. nd = not determined.

Table S4. SAP2 inhibitory activity of A, B-ring di-substituted analogues of hit **5**



Compounds	R	IC_{50} (μM)
12a	H	18.82
12b	4-Me	9.14
12c	3-Me	77.33
12d	2-Me	23.09
12e	2,4-diMe	20.55
12f	2,5-diMe	40.64
12g	4-F	68.79
12h	3-F	42.51
12i	2-F	27.45
12j	4-Cl	22.93
12k	3-Cl	31.19
12l	2-Cl	26.3
12m	4-Br	59.19
12n	3-Br	43.21
12o	2-Br	58.07
12p	4-OMe	19.49
12q	3-OMe	44.86
12r	4-OEt	25.12
12s	3-OEt	60.8
12t	2-OEt	30.62
1	-	0.016

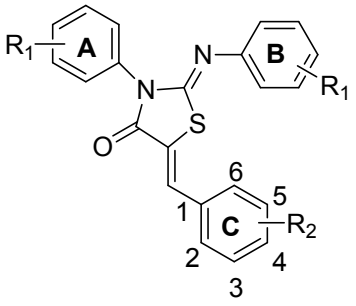
Table S5. SAP2 inhibitory activity of A -ring modified analogues of hit **5**



$R_1 = OCH_2COOH$

Compounds	R_1	R_2	IC_{50} (μM)
18a	-CH_2CH_2OH	2-OCH_2COOH	46.90
18b	-CH_2CH_2OH	3-OCH_2COOH	53.19
18c	-CH_2CH_2OH	4-OCH_2COOH	59.06
18d	-$CH_2CH_2CH_2OH$	2-OCH_2COOH	54.09
18e	-$CH_2CH_2CH_2OH$	3-OCH_2COOH	56.58
18f	-$CH_2CH_2CH_2OH$	4-OCH_2COOH	77.30
1	-	-	0.016

Table S6. SAP2 inhibitory activity of the thiazolidinone inhibitors



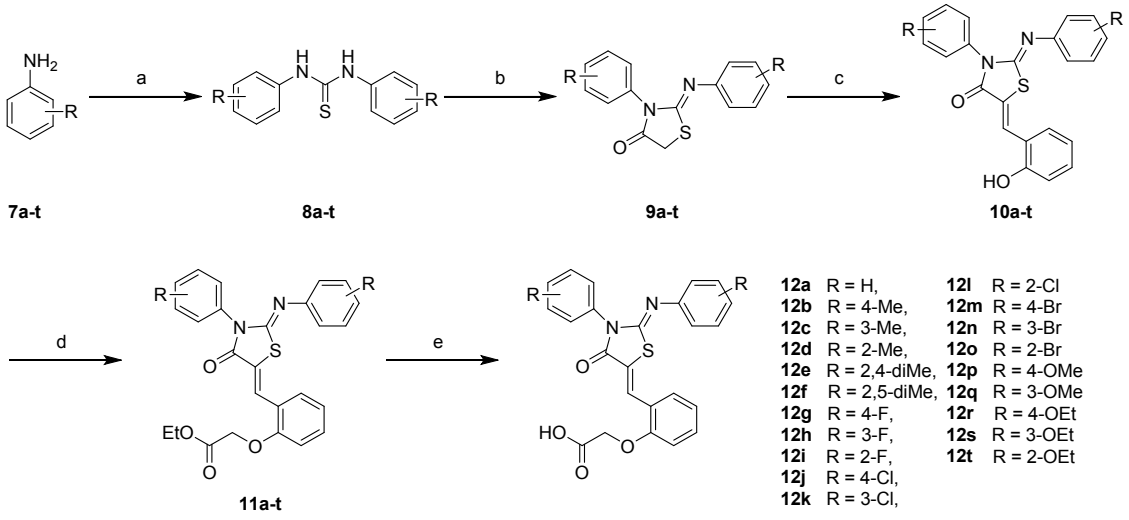
Compounds	R_1	R_2	IC_{50} (μM)
23a	H	3-OCH_2COOH	35.24
23b	H	4-OCH_2COOH	98.62
23c	H	3,4-di-OCH_2COOH	23.27
23d	H	2,4-di-OCH_2COOH	9.418
23e	4-Me	3-OCH_2COOH	11.62
23f	4-Me	4-OCH_2COOH	15.17

23g	4-Me	3,4-di-OCH_2COOH	4.41
23h	4-Me	2,4-di-OCH_2COOH	0.86
23i	4-OEt	3-OCH_2COOH	41.59
23j	4-OEt	4-OCH_2COOH	93.16
23k	4-OEt	3,4-di-OCH_2COOH	5.82
23l	4-OEt	2,4-di-OCH_2COOH	3.03
23m	3,4-di-Me	3,4-OCH_2COOH	17.36
23n	3,4-di-Me	2,4-di-OCH_2COOH	2.76
23o	2,5-di-Me	3,4-diOCH_2COOH	8.16
23p	2,5-di-Me	2,4-diOCH_2COOH	5.8
23q	4-F	3,4-di-OCH_2COOH	12.64
23r	4-F	2,4-di-OCH_2COOH	13.8
23s	4-Cl	3,4-di-OCH_2COOH	3.39
23t	4-Cl	2,4-di-OCH_2COOH	7.16
23u	4-Br	3,4-di-OCH_2COOH	5.67
23v	4-Br	2,4-di-OCH_2COOH	2.25
23w	4-OMe	3,4-di-OCH_2COOH	7.22
23x	4-OMe	2,4-di-OCH_2COOH	5.64
1	-	-	0.016

Experimental Protocols

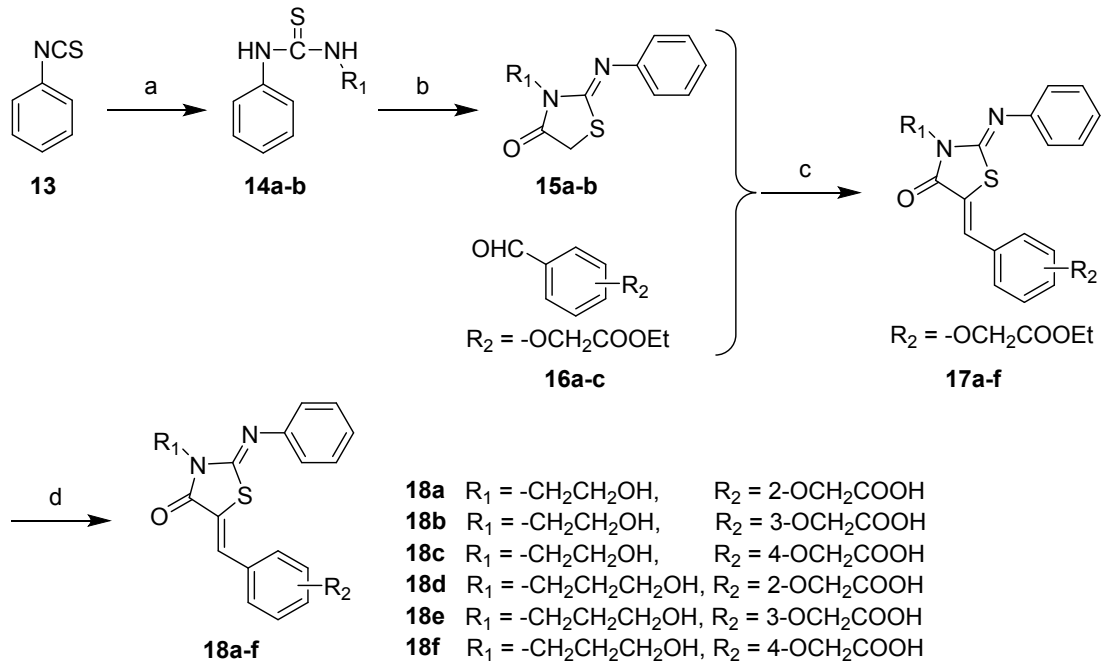
Synthetic methods and characterization data for target compounds.

Scheme 1. Synthesis of compounds 12a-t.



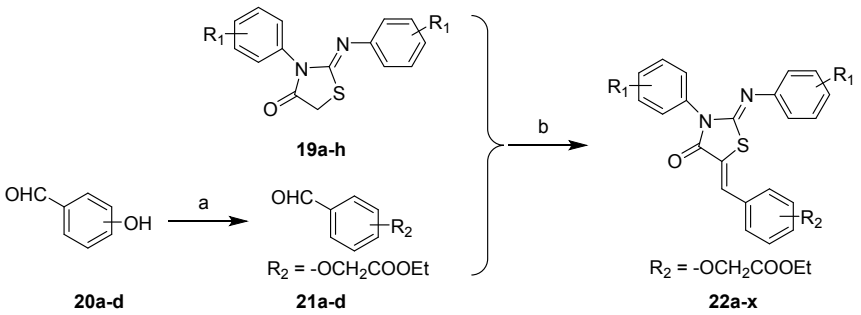
Reagents and conditions: (a) CS_2, sulfur, triethanolamine, water, reflux, 6 h, yield 35-81%; (b) $ClCH_2COOEt$, NaOAc, absolute alcohol, reflux, 10 h, yield 39-72%; (c) 2-hydroxybenz-aldehyde, piperidine, absolute alcohol, 60 ºC, 6 h, yield 75-95%; (d) $BrCH_2COOEt$, acetone, reflux, 4 h, yield 73-92%; (e) $LiOH{\cdot}H_2O$, THF: MeOH: H_2O = 3: 2: 1, rt, 0.5-6 h, yield 66-95%.

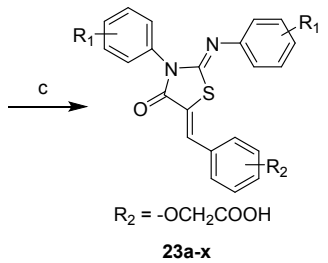
Scheme 2. Synthesis of Compounds 18a-f.



Reagents and conditions: (a) Ethanolamine or 3-amino-1-propanol, THF, rt, 30 min, yield 53-67%; (b) $ClCH_2COOEt$, NaOAc, absolute alcohol, reflux, 10 h, yield 38-45%; (c) piperidine, absolute alcohol, 60 ºC, 6 h, yield 35-80%; (d) $LiOH{\cdot}H_2O$, THF: MeOH: H_2O = 3: 2: 1, rt, 30 min, yield 54-83%.

Scheme 3. Synthesis of Compounds 23a-x.





23a	R_1 = H,	R_2 = 3-OCH_2COOH	**23m**	R_1 = 3,4-diMe,	R_2 = 3,4-diOCH_2COOH
23b	R_1 = H,	R_2 = 4-OCH_2COOH	**23n**	R_1 = 3,4-diMe,	R_2 = 2,4-diOCH_2COOH
23c	R_1 = H,	R_2 = 3,4-diOCH_2COOH	**23o**	R_1 = 2,5-diMe,	R_2 = 3,4-diOCH_2COOH
23d	R_1 = H,	R_2 = 2,4-diOCH_2COOH	**23p**	R_1 = 2,5-diMe,	R_2 = 2,4-diOCH_2COOH
23e	R_1 = 4-Me,	R_2 = 3-OCH_2COOH	**23q**	R_1 = 4-F,	R_2 = 3,4-diOCH_2COOH
23f	R_1 = 4-Me,	R_2 = 4-OCH_2COOH	**23r**	R_1 = 4-F,	R_2 = 2,4-diOCH_2COOH
23g	R_1 = 4-Me,	R_2 = 3,4-diOCH_2COOH	**23s**	R_1 = 4-Cl,	R_2 = 3,4-diOCH_2COOH
23h	R_1 = 4-Me,	R_2 = 2,4-diOCH_2COOH	**23t**	R_1 = 4-Cl,	R_2 = 2,4-diOCH_2COOH
23i	R_1 = 4-OEt,	R_2 = 3-OCH_2COOH	**23u**	R_1 = 4-Br,	R_2 = 3,4-diOCH_2COOH
23j	R_1 = 4-OEt,	R_2 = 4-OCH_2COOH	**23v**	R_1 = 4-Br,	R_2 = 2,4-diOCH_2COOH
23k	R_1 = 4-OEt,	R_2 = 3,4-diOCH_2COOH	**23w**	R_1 = 4-OMe,	R_2 = 3,4-diOCH_2COOH
23l	R_1 = 4-OEt,	R_2 = 2,4-diOCH_2COOH	**23x**	R_1 = 4-OMe,	R_2 = 2,4-diOCH_2COOH

Reagents and conditions: (a) $BrCH_2COOEt$, acetone, K_2CO_3, rt, 12 h, yield 72-90%; (b) piperidine, absolute alcohol, 60 ºC, 6 h, yield 42-86%; (c) $LiOH{\cdot}H_2O$, THF: MeOH: H_2O = 3: 2: 1, rt, 0.5-6 h, yield 60-93%.

General. Reagents were purchased from commercial sources and were used without further purification unless otherwise stated. Oxygen or water sensitive reactions were performed under the nitrogen atmosphere. ^{13}C-NMR and ^{1}H-NMR spectra were recorded on Bruker AVANCE600, or AVANCE300 spectrometer (Bruker Company, Germany), operating at the indicated frequencies and $CDCl_3$ or DMSO-d_6 as solvents. Chemical shift was expressed in ppm (δ). The mass spectra were recorded on an Esquire 3000 LC-MS mass spectrometer. Melting points (m.p.) were determined by microscope melting-point apparatus with aromatic temperature control system (XT4A). Flash chromatography was performed on 200-300 mesh silica gel with the

indicated solvent systems (Qingdao Haiyang Chemical, China). Chemical purities were analyzed by HPLC using MeOH/H_2O as the mobile phase with a flow rate of 0.6 mL/min on a C18 column. All final compounds exhibited the purity greater than 98%.

1,3-Diphenylthiourea (8a). A mixture of aniline (2.33 g, 25.0 mmol, 2 equiv), water (50 mL), carbon disulfide (1.24 g, 16.25 mmol, 1.3 equiv), triethanolamine (2.5 mL) and sulfer power (100 mg) was stirred under reflux for 6 h. After being cooled to room temperature, precipitates were formed, which were separated by filtration and washed with cold water to give compound **8a** (1.46 g, yield 51%) as a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 9.78 (s, 2H), 7.47 (d, J = 7.8 Hz, 4H), 7.38-7.26 (m, 4H), 7.17-7.05 (m, 2H). ESI-MS (m/z): 229.28 [M+H].

Intermediates **8b-t** were prepared using a similar protocol described for **8a**.

3-Phenyl-2-(phenylimino)thiazolidin-4-one (9a). To a stirred suspension of thiourea **8a** (1.14 g, 4.0 mmol, 1 equiv) and anhydrous sodium acetate (1.64 g, 20.0 mmol, 5 equiv) in absolute ethanol (20 mL) was added ethyl chloroacetate (0.85 mL, 0.98 g, 8.0 mmol, 2 equiv). The mixture was stirred at 60 ºC for 6 h. After being cooled to room temperature, the precipitates were collected by filtration, and washed with ethanol to give the crude product, which was recrystallized from EtOAc to give compound **9a** (0.68 g, yield 64%) as an orange solid and used directly for subsequent reactions without further purification. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 7.59-7.47 (m, 2H), 7.46-7.37 (m, 3H), 7.36-7.25 (m, 2H), 7.08 (t, J = 7.8 Hz, 1H), 6.92-6.81 (m, 2H), 4.15 (s, 2H). ESI-MS (m/z): 269.35 [M+H].

Intermediates **9b-u** were prepared using a similar protocol described for **9a**.

5-(2-Hydroxybenzylidene)-3-phenyl-2-(phenylimino)thiazolidin-4-one (10a). A mixture of compound **9a** (0.3 g, 1.12 mmol, 1 equiv), salicyladehyde (0.16 g, 1.35 mmol, 1.2 equiv), piperidine (0.095 g, 1.12 mmol, 1 equiv) was dissolved in absolute ethanol (5 mL). The mixture was stirred at 60 ºC for 8 h. The solvent was removed under the reduced pressure and the residue was purified by flash chromatography (Hexane: EtOAc = 5:1) to give compound **10a** as a light yellow solid (0.39 g, yield 95%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 10.46 (s, 1H), 8.02 (s, 1H), 7.62-7.45 (m, 5H), 7.41-7.32 (m, 2H), 7.31-7.21 (m, 2H), 7.14 (t, J = 7.6 Hz, 1H), 7.00-6.87 (m,

4H). ESI-MS (m/z): 373.39 [M+H].

Intermediates **10b-t** were prepared were prepared using a similar protocol described for **10a**.

Ethyl 2-(2-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy) acetate (11a). Intermediate **10a** (0.2 g, 0.54 mmol, 1 equiv), K_2CO_3 (0.033 g, 0.81 mmol, 1.5 equiv) and ethyl bromoacetate (0.099 g, 0.59 mmol, 1.1 equiv) in acetone (5 mL) were stirred at under reflux for 6 h. The solvent was removed under the reduced pressure. H_2O (30 mL) and EtOAc (50 mL) were added and the mixture was shaken. The aqueous phase was extracted with the EtOAc (50 mL×2). The organic phase was washed with brine, dried with anhydrous Na_2SO_4, and evaporated under the reduced pressure. The residue was purified by flash chromatography (Hexane : EtOAc = 10:1) to give compound **11a** as a light yellow solid (0.18 g, yield 73%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 8.07 (s, 1H), 7.62-7.44 (m, 5H), 7.43-7.30 (m, 4H), 7.22-7.02 (m, 3H), 7.01-6.90 (m, 2H), 4.94 (s, 2H), 4.16 (dd, J = 14.02, 7.06 Hz, 2H), 1.20 (t, J = 7.31 Hz, 3H). ESI-MS (m/z): 459. 40 [M+H].

Intermediates **11b-t** were prepared using a similar protocol described for **11a**.

Ethyl 2-(2-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12a). Compound **11a** (0.1 g, 0.22 mmol, 1 equiv) and LiOH·H_2O (0.014 g, 0.33 mmol, 1.5 equiv) in mixed solvent (THF: MeOH: H_2O = 3: 2: 1, 5 mL) were stirred at room temperature for 3 h. The solvent was removed under the reduced pressure. H_2O (20 mL) was added and the mixture was adjusted to pH 2.0-3.0 by 1M HCl. the precipitates were collected by filtration, and washed with cold water. The crude product was purified by flash chromatography (CH_2Cl_2 : MeOH = 100:5) to afford target compound **12a** as a light yellow solid (62 mg, yield 66%). m.p.: 249-251 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.25 (br s, 1H), 8.10 (s, 1H), 7.56-7.36 (m, 9H), 7.16 (t, J = 7.42 Hz, 1H), 7.08 (t, J = 7.62 Hz, 1H), 7.02 (d, J = 8.42 Hz, 1H), 6.97 (d, J = 7.22 Hz, 2H), 4.81 (s, 2H). ^{13}C-NMR (75 MHz, DMSO-d_6) δ: 172.22, 167.90, 158.84, 152.93, 150.23, 137.31, 134.03, 131.74 (2C), 131.35 (2C), 131.03, 130.85 (2C), 130.41, 127.46, 127.06, 124.50, 123.69, 123.11 (2C), 120.45, 114.97, 67.35. HRMS (ESI, positive) m/z calcd for $C_{24}H_{19}N_2O_4S$ (M + H) 431.1060, found

431.1060.

Compounds **12b-t** were prepared using a similar protocol described for **12a**.

Ethyl 2-(2-((4-oxo-3-(*p*-tolyl)-2-(*p*-tolylimino)thiazolidin-5-ylidene)methyl) phenoxy)acetic acid (12b). Light yellow solid (yield: 74%), m.p.: 245-247 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.18 (br s, 1H), 8.08 (s, 1H), 7.44-7.31 (m, 6H), 7.17 (d, J = 8.01 Hz, 2H), 7.08 (t, J = 7.39 Hz, 1H), 7.03 (d, J = 8.32 Hz, 1H), 6.86 (d, J = 8.32 Hz, 2H), 4.83 (s, 2H), 2.38 (s, 3H), 2.29 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 160.79, 165.60, 156.40, 152.59, 150.35, 145.40, 138.22, 137.20, 133.73, 132.41, 131.62, 130.44, 129.48, 129.10, 128.19, 128.08, 124.79, 122.24, 121.48, 121.42, 120.61, 118.18, 112.59, 64.84, 20.74, 20.45. HRMS (ESI, positive) m/z calcd for $C_{26}H_{23}N_2O_4S$ (M + H) 459.1373, found 459.1381.

Ethyl 2-(2-((4-oxo-3-(*o*-tolyl)-2-(*o*-tolylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12d). Light yellow solid (yield: 76%), m.p.: 227-228 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.17 (br s, 1H), 8.12 (s, 1H), 7.52-7.32 (m, 6H), 7.23 (d, J = 7.36 Hz, 1H), 7.19 (t, J = 7.71 Hz, 1H), 7.11-7.00 (m, 3H), 6.86 (d, J = 7.36 Hz, 1H), 4.84 (s, 2H), 2.25 (s, 3H), 2.04 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.78, 165.28, 156.43, 149.51, 146.51, 135.97, 134.26, 131.78, 130.72, 130.59, 129.37, 129.07, 128.91, 128.10, 127.00, 126.78, 125.19, 124.81, 122.06, 121.46, 121.36, 119.66, 112.61. 64.84, 17.27, 17.06. HRMS (ESI, positive) m/z calcd for $C_{26}H_{23}N_2O_4S$ (M + H) 459.1373, found 459.1381.

1-(2-hydroxyethyl)-3-phenylthiourea (14a). To a solution of compound **13** (6.75 g, 50 mmol, 1 equiv) in THF (20 mL) was added ethanolamine (3.66 g, 1.2 mmol, 1.2 equiv) dropwisely. The mixture was stirred for 30 min under room temperature, and then the solvent was evaporated under vacuum. The crude product was purified by column chromatography (Hexane : EtOAc = 6:1) to afford compound **14a** as a white solid (5.2 g, yield 53%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 9.67 (br s, 1H), 7.77 (s, 1H), 7.45 (dd, J = 8.20, 1.49 Hz, 2H), 7.31 (t, J = 7.20 Hz, 2H), 7.12-7.06 (m, 1H), 4.79 (s, 1H), 3.54-3.39 (m, 4H). HRMS (ESI, positive) m/z calcd for $C_9H_{14}N_2OS$ (M + H) 197.0743, found 197.0739.

Intermediates **14b** were prepared using a similar protocol described for **14a**.

The synthesis of **15a-b** was similar to that of **9a**.

***(Z)*-3-(2-hydroxyethyl)-2-(phenylimino)thiazolidin-4-one (15a).** Light yellow solid (yield: 38%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 7.36 (t, J = 7.33 Hz, 2H), 7.13 (t, J = 7.33 Hz, 1H), 6.93 (d, J = 7.28 Hz, 2H), 4.87 (s, 1H), 4.01 (s, 2H), 3.81 (t, J = 6.58 Hz, 2H), 3.62 (t, J = 6.17 Hz, 2H). ESI-MS (m/z): 237.07 [M+H].

***(Z)*-3-(3-hydroxypropyl)-2-(phenylimino)thiazolidin-4-one (15b).** Light yellow solid (yield: 45%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 7.36 (t, J = 7.67 Hz, 2H), 7.13 (t, J = 7.31 Hz, 1H), 6.93 (dd, J = 8.35, 1.23 Hz, 2H), 4.55 (s, 1H), 4.01 (s, 2H), 3.79 (t, J = 7.26 Hz, 2H), 3.48 (t, J = 6.19 Hz, 2H), 1.79 (m, 2H). ESI-MS (m/z): 251.34 [M+H].

Intermediates **17a-f** were synthesized using a similar protocol of **10a.**

Ethyl 2-(2-((*Z*)-((*Z*)-3-(2-hydroxyethyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetate (17a). Light yellow solid (yield: 86%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.04 (s, 1H), 7.46-7.31 (m, 4H), 7.17 (t, J = 7.38 Hz, 1H), 7.10-6.98 (m, 4H), 4.94 (s, 2H), 4.93 (s, 1H), 4.17 (dd, J = 14.23, 7.11 Hz, 2H), 3.98 (t, J = 6.25 Hz, 2H), 3.71 (dd, J = 12.42, 6.04 Hz, 2H), 1.21 (t, J = 7.21 Hz, 3H). ESI-MS (m/z): 427.47 [M+H].

Ethyl 2-(3-((*Z*)-((*Z*)-3-(2-hydroxyethyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetate (17b). Light yellow solid (yield: 49%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.72 (s, 1H), 7.46-7.33 (m, 3H), 7.20 (t, J = 7.71 Hz, 1H), 7.15-6.97 (m, 4H), 6.93 (dd, J = 8.13, 1.10 Hz, 1H), 4.86 (s, 1H), 4.79 (s, 2H), 4.09 (dd, J = 14.11, 7.05 Hz, 2H), 3.98 (t, J = 6.17 Hz, 2H), 3.71 (dd, J = 12.20, 6.06 Hz, 2H), 1.17 (t, J = 7.21 Hz, 3H). ESI-MS (m/z): 427.43 [M+H].

Ethyl 2-(4-((*Z*)-((*Z*)-3-(2-hydroxyethyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetate (17c). Light yellow solid (yield: 63%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.71 (s, 1H), 7.53-7.38 (m, 4H), 7.20 (t, J = 7.46 Hz, 1H), 7.08-6.99 (m, 4H), 4.93 (s, 1H), 4.83 (s, 2H), 4.16 (dd, J = 14.05, 7.03 Hz, 2H), 3.97 (t, J = 6.22 Hz, 2H), 3.71 (dd, J = 11.62, 5.67 Hz, 2H), 1.20 (t, J = 7.15 Hz, 3H). ESI-MS (m/z): 427.26 [M+H].

Ethyl 2-(2-((*Z*)-((*Z*)-3-(3-hydroxypropyl)-4-oxo-2-(phenylimino)thiazolidin-5-

ylidene)methyl)phenoxy)acetate (17d). Light yellow solid (yield: 77%).^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.04 (s, 1H), 7.45-7.40 (m, 4H), 7.19 (t, J = 7.33 Hz, 1H), 7.10-6.98 (m, 4H), 4.94 (s, 2H), 4.57 (s, 1H), 4.17 (dd, J = 14.15, 7.14 Hz, 2H), 3.97 (t, J = 7.19 Hz, 2H), 3.71 (dd, J = 11.36, 6.07 Hz, 2H), 1.88 (m, 2H), 1.21 (t, J = 7.15 Hz, 3H). ESI-MS (m/z): 441.42 [M+H].

Ethyl 2-(3-((*Z*)-((*Z*)-3-(3-hydroxypropyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetate (17e). Light yellow solid (yield: 35%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.72 (s, 1H), 7.47-7.35 (m, 3H), 7.20 (t, J = 7.45 Hz, 1H), 7.14-6.97 (m, 5H), 4.79 (s, 2H), 4.57 (s, 1H), 4.09 (dd, J = 14.22, 7.22 Hz, 2H), 3.97 (t, J = 7.22 Hz, 2H), 3.51 (dd, J = 11.46, 6.10 Hz, 2H), 1.87 (m, 2H), 1.17 (t, J = 7.06 Hz, 3H). ESI-MS (m/z): 441.42 [M+H].

Ethyl 2-(4-((*Z*)-((*Z*)-3-(3-hydroxypropyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetate (17f). Light yellow solid (yield: 53%).^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.71 (s, 1H), 7.48 (d, J = 8.79 Hz, 2H), 7.42 (t, J = 7.47 Hz, 2H), 7.20 (t, J = 7.47 Hz, 1H), 7.08-6.98 (m, 4H), 4.83 (s, 2H), 4.56 (s, 1H), 4.16 (dd, J = 14.06, 7.3 Hz, 2H), 3.96 (t, J = 7.03 Hz, 2H), 3.51 (dd, J = 11.52, 6.08 Hz, 2H), 1.87 (m, 2H), 1.20 (t, J = 7.15 Hz, 3H). ESI-MS (m/z): 441.40 [M+H].

The synthesis of **18a-f** was similar to that of **12a**.

2-(2-((*Z*)-((*Z*)-3-(2-hydroxyethyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (18a). Light yellow solid (yield: 83%), m.p.: 206-207 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.13 (br s, 1H), 8.04 (s, 1H), 7.45-7.31 (m, 4H), 7.19 (t, J = 7.46 Hz, 1H), 7.09-6.98 (m, 4H), 4.94 (s, 1H), 4.84 (s, 2H), 3.98 (t, J = 6.21 Hz, 2H), 3.71 (dd, J = 11.87, 5.94 Hz, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.77, 165.89, 156.36, 150.05, 147.86, 131.55, 129.43, 128.03, 124.73, 124.58, 122.22, 121.52, 121.39, 120.97, 112.57, 64.84, 57.06, 45.07. ESI-MS (m/z): 399.35 [M+H].

2-(4-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (18b). Light yellow solid (yield: 89%), m.p.: 290-291 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.02 (br s, 1H), 7.72 (s, 1H), 7.43-7.41 (m, 3H), 7.40-7.18 (m, 1H), 7.12-6.97 (m, 5H), 4.94 (s, 1H), 4.70 (s, 2H), 4.01-

3.97 (m, 2H), 3.73-3.32 (m,2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.39, 170.21, 166.12, 150.95, 149.50, 148.29, 147.79, 135.56, 130.93, 129.89, 129.50, 129.15, 129.03, 127.05, 125.22, 123.37, 121.32, 119.40, 117.08, 114.45, 65.64, 65.42. ESI-MS (m/z): 431.46 [M+H].

2,2'-((4-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (18c). Light yellow solid (yield: 61%), m.p.: 250-251 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.07 (s, 1H), 7.68 (s, 1H), 7.47-7.38 (m, 4H), 7.17 (t, J = 7.2 Hz, 1H), 7.02-6.99 (m, 4H), 4.91 (s, 1H), 4.71 (s, 2H), 3.96 (t, J = 6.0 Hz, 2H), 3.69 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.21, 166.53, 159.50, 150.55, 148.44, 132.09, 130.35, 129.96, 126.78, 125.21, 121.49, 119.07, 115.80, 64.93, 57.54, 45.53. ESI-MS (m/z): 505.36 [M+H].

2-(2-(*(Z)*-(*(Z)*-3-(3-hydroxypropyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (18d). Light yellow solid (yield: 67%), m.p.: 146-147 ºC。^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.13 (br s, 1H), 8.04 (s, 1H), 7.45-7.29 (m, 4H), 7.19 (t, J = 7.42 Hz, 1H), 7.09-6.98 (m, 4H), 4.84 (s, 2H), 4.56 (t, J = 4.96 Hz, 1H), 3.97 (t, J = 7.03 Hz, 2H), 3.51 (dd, J = 10.85, 5.92 Hz, 2H), 1.87 (m, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.30, 166.26, 156.86, 150.47, 148.40, 132.09, 129.93, 128.55, 125.25, 125.09, 122.66, 121.87, 121.48, 113.06, 65.32, 59.13, 30.72. ESI-MS (m/z): 413.33 [M+H].

2-(3-(*(Z)*-(*(Z)*-3-(3-hydroxypropyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (18e). Pale yellow solid (yield: 69%), m.p.: 149-151 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.03 (br s, 1H), 7.69 (s, 1H), 7.41-7.35 (m, 3H), 7.17-7.05 (m, 3H), 7.01 (dd, J = 1.2, 0.6 Hz, 2H), 6.95 (dd, J = 6.6, 2.4 Hz, 1H), 4.68 (s, 2H), 4.57 (t, J = 4.81 Hz, 1H), 3.95 (t, J = 7.2 Hz, 2H), 3.50 (t, J = 6.6 Hz, 2H), 1.87-1.85 (m, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.40, 166.17, 158.53, 150.20, 148.29, 135.15, 130.82, 130.33, 129.97, 125.34, 125.26, 121.47, 116.91, 116.25, 64.89, 59.12, 30.70. ESI-MS (m/z): 413.29 [M+H].

2-(4-(*(Z)*-(*(Z)*-3-(3-hydroxypropyl)-4-oxo-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (18f). Light yellow solid (yield: 79%), m.p.: 190-191 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.11 (br s, 1H), 7.68 (s, 1H), 7.46-

7.38 (m, 4H), 7.17 (t, *J* = 7.20 Hz, 1H), 7.01-6.99 (m, 4H), 4.70 (s, 2H), 4.56 (s, 1H), 3.94 (t, *J* = 7.20 Hz, 2H), 3.49 (t, *J* = 6.6 Hz, 2H), 1.87-1.83 (m, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.21, 166.39, 159.51, 150.47, 148.47, 132.11, 130.42, 129.95, 126.75, 125.22, 121.49, 118.95, 115.79, 64.94, 59.13, 30.74. ESI-MS (m/z): 413.21 [M+H].

Ethyl 2-(3-formylphenoxy)acetate (21a). 3-hydroxybenzaldehyde (12.2 g, 10 mmol, 1 equiv), ethyl bromoacetate (18.4 g, 11 mmol, 1.1 equiv) and K_2CO_3 (15.2 g, 11 mmol, 1.1 equiv) in acetone (100 mL) was stirred at room temperature for 12 h. Then, unorganic salts were discarded by filtration. The filtrate was concentrated under reduced pressure to afford the crude product, which was purified by column chromatography (hexane : EtOAc = 5:1) to achieve compound **21a** (13.5 g, yield 75%) as a white solid. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 9.95 (s, 1H), 7.53-7.41 (m, 2H), 7.34 (s, 1H), 7.24-7.18 (m, 1H), 4.67 (s, 2H), 4.26 (dd, *J* = 14.17, 7.45 Hz, 2H), 1.29 (t, *J* = 7.38 Hz, 3H). ESI-MS (m/z): 209.33 [M+H].

Intermediates **21b-d** were synthesized according to a similar protocol described for **21a**.

Ethyl 2-(4-formylphenoxy)acetate (21b). White solid (yield: 90%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 9.89 (s, 1H), 7.84 (dd, *J* = 6.89, 1.92 Hz, 2H), 7.00 (dd, *J* = 6.94, 1.92 Hz, 2H), 4.70 (s, 2H), 4.28 (dd, *J* = 14.36, 7.10 Hz, 2H), 1.30 (t, *J* = 7.21 Hz, 3H). ESI-MS (m/z): 209.19 [M+H].

Diethyl 2,2'-((4-formyl-1,2-phenylene)bis(oxy))diacetate (21c). White solid (yield: 66%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 9.84 (s, 1H), 7.48 (dd, *J* = 8.26, 1.77 Hz, 1H), 7.37 (d, *J* = 1.80 Hz, 1H), 6.93 (d, *J* = 8.21 Hz, 1H), 4.80 (s, 2H), 4.77 (s, 2H), 4.28 (dd, *J* = 14.22, 7.10 Hz, 4H), 1.48-1.22 (m, 6H). ESI-MS (m/z): 311.32 [M+H].

Diethyl 2,2'-((4-formyl-1,3-phenylene)bis(oxy))diacetate (21d). White solid (yield: 79%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 10.39 (s, 1H), 7.85 (d, *J* = 8.84 Hz, 1H), 6.53 (dd, *J* = 8.70, 2.18 Hz, 1H), 6.42 (d, *J* = 2.21 Hz, 1H), 4.71 (s, 2H), 4.66 (s, 2H), 4.28 (dd, *J* = 14.22, 7.18 Hz, 4H), 1.30 (t, *J* = 7.17 Hz, 6H). ESI-MS (m/z): 311.25 [M+H].

The synthesis of **22a-x** were similar to that of **10a**.

Ethyl 2-(3-((*Z*)-((*Z*)-4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetate (22a). Light yellow solid (yield: 49%). ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 7.79 (s, 1H), 7.58-7.46 (m, 5H), 7.43-7.37 (m, 3H), 7.20-7.13 (m, 3H), 7.04-6.95 (m, 3H), 4.81 (s, 2H), 4.10 (dd, J = 14.33, 6.97 Hz, 2H), 1.18 (t, J = 7.36 Hz, 3H). ESI-MS (m/z): 459. 64 [M+H].

Ethyl 2-(4-((*Z*)-((*Z*)-4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl) phenoxy)acetate (22b). Light yellow solid (yield: 65%). ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 7.78 (s, 1H), 7.58-7.47 (m, 7H), 7.41-7.37 (m, 2H), 7.19-7.15 (m, 1H), 7.07 (dd, J = 7.03, 2.12 Hz, 2H), 6.98 (dd, J = 8.20, 1.20 Hz, 2H), 4.84 (s, 2H), 4.17 (dd, J = 14.21, 7.03 Hz, 2H), 1.21 (t, J = 7.04 Hz, 3H). ESI-MS (m/z): 459.49 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene) methyl)-1,3-phenylene)bis(oxy))diacetate (22d) Light yellow solid (yield: 63%). ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 8.04 (s, 1H), 7.58-7.44 (m, 5H), 7.40-7.30 (m, 3H), 7.16 (t, J = 7.38 Hz, 1H), 6.97 (d, J = 7.55 Hz, 2H), 6.71-6.66 (m, 2H), 4.97 (s, 2H), 4.83 (s, 2H), 4.16 (dd, J = 14.03, 7.15 Hz, 4H), 1.21 (t, J = 7.15 Hz, 6H). ESI-MS (m/z): 561.69 [M+H].

Ethyl 2-(3-((*Z*)-((*Z*)-4-oxo-3-(p-tolyl)-2-(p-tolylimino)thiazolidin-5-ylidene) methyl)phenoxy)acetate(22e) Light yellow solid (yield: 49%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.76 (s, 1H), 7.49-7.29 (m, 5H), 7.23-7.11 (m, 4H), 7.02 (d, J = 8.0 Hz, 1H), 6.86 (d, J = 8.11 Hz, 2H), 4.81 (s, 2H), 4.10 (dd, J = 14.05, 7.03 Hz, 2H), 2.38 (s, 3H), 2.30 (s, 3H), 1.18 (t, J = 7.06 Hz, 3H). ESI-MS (m/z): 487.61 [M+H].

Ethyl 2-(4-((*Z*)-((*Z*)-4-oxo-3-(p-tolyl)-2-(p-tolylimino)thiazolidin-5-ylidene) methyl)phenoxy)acetate (22f). Light yellow solid (yield: 65%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.75 (s, 1H), 7.52 (d, J = 8.86 Hz, 2H), 7.39 (d, J = 8.44 Hz, 2H), 7.34 (d, J = 8.23 Hz, 2H), 7.19 (d, J = 8.02 Hz, 2H), 7.07 (dd, J = 7.02, 1.89 Hz, 2H), 6.86 (d, J = 8.25 Hz, 2H), 4.84 (s, 2H), 4.17 (dd, J = 14.17, 7.08 Hz, 2H), 2.38 (s, 3H), 2.30 (s, 3H), 1.21 (t, J = 7.16 Hz, 3H). ESI-MS (m/z): 487.37 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-4-oxo-3-(p-tolyl)-2-(p-tolylimino)thiazolidin-5-ylidene) methyl)-1,2-phenylene)bis(oxy))diacetate (22g). Light yellow solid (yield: 53%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.72 (s, 1H), 7.42-7.30 (m, 4H), 7.22-7.09 (m, 4H),

7.05 (d, *J* = 8.70 Hz, 1H), 6.85 (dd, *J* = 6.42, 1.74 Hz, 2H), 4.87 (s, 2H), 4.81 (s, 2H), 4.16 (dd, *J* = 14.24, 7.30 Hz, 2H), 4.04 (dd, *J* = 14.18, 7.09 Hz, 2H), 2.38 (s, 3H), 2.30 (s, 3H), 1.21 (t, *J* = 7.19 Hz, 3H), 1.15 (t, *J* = 7.00 Hz, 3H). ESI-MS (m/z): 589.51 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-4-oxo-3-(p-tolyl)-2-(p-tolylimino)thiazolidin-5-ylidene) methyl)-1,3-phenylene)bis(oxy))diacetate (22h). Light yellow solid (yield: 65%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.02 (s, 1H), 7.43-7.27 (m, 5H), 7.17 (d, *J* = 8.35 Hz, 2H), 6.85 (d, *J* = 8.19 Hz, 2H), 6.69 (d, *J* = 8.70 Hz, 2H), 4.97 (s, 2H), 4.84 (s, 2H), 4.16 (dd, *J* = 14.12, 7.06 Hz, 4H), 2.38 (s, 3H), 2.29 (s, 3H), 1.21 (t, *J* = 7.19 Hz, 6H). ESI-MS (m/z): 589.68 [M+H].

Ethyl 2-(3-((Z)-((*Z*)-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)phenoxy)acetate (22i). Light yellow solid (yield: 42%).^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.75 (s, 1H), 7.29-7.12 (m, 4H), 7.10-6.99 (m, 4H), 6.94-6.88 (m, 2H), 6.84 (d, *J* = 8.19 Hz, 2H), 4.74 (s, 2H), 4.16-4.04 (m, 6H), 1.42-1.25 (m, 9H). ESI-MS (m/z): 547.45 [M+H].

Ethyl 2-(4-((*Z*)-((*Z*)-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)phenoxy)acetate (22j). Light yellow solid (yield: 69%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.74 (s, 1H), 7.32 (d, *J* = 8.48 Hz, 2H), 7.24 (d, *J* = 8.48 Hz, 2H), 7.10-7.01 (m, 4H), 6.84 (d, *J* = 8.97 Hz, 2H), 6.78 (d, *J* = 8.97 Hz, 2H), 4.74 (s, 2H), 4.20-4.04 (m, 6H), 1.41-1.25 (m, 9H). ESI-MS (m/z): 547.62 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22k). Light yellow solid (yield: 81%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.70 (s, 1H), 7.40 (dd, *J* = 6.82, 1.99 Hz, 2H), 7.22-7.01 (m, 5H), 6.93 (dd, *J* = 6.67, 2.38 Hz, 2H), 6.89 (dd, *J* = 6.67, 2.38 Hz, 2H), 4.87 (s, 2H), 4.82 (s, 2H), 4.23-3.94 (m, 8H), 1.45-1.08 (m, 12H). ESI-MS (m/z): 649.93 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22l). Light yellow solid (yield: 85%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.01 (s, 1H), 7.40 (dd, *J*

= 6.71, 2.00 Hz, 2H), 7.31 (d, *J* = 8.43 Hz, 1H), 7.06 (dd, *J* = 6.91, 2.02 Hz, 2H), 6.92 (dd, *J* = 6.57, 2.41 Hz, 2H), 6.88 (dd, *J* = 6.55, 2.46 Hz, 2H), 6.72-6.66 (m, 2H), 4.97 (s, 2H), 4.84 (s, 2H), 4.27-3.95 (m, 8H), 1.43-1.15 (m, 12H). ESI-MS (m/z): 649.51 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(3,4-dimethylphenyl)-2-((3,4-dimethylphenyl)imino) -4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22m). Light yellow solid (yield: 74%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.70 (s, 1H), 7.34-7.15 (m, 4H), 7.12 (d, *J* = 8.25 Hz, 2H), 7.04 (d, *J* = 8.57 Hz, 1H), 6.74 (d, *J* = 1.63 Hz, 1H), 6.68 (dd, *J* = 2.17, 7.86 Hz, 1H), 4.87 (s, 2H), 4.81 (s, 2H), 4.16 (dd, *J* = 14.14, 6.90 Hz, 2H), 4.02 (dd, *J* = 14.17, 7.08 Hz, 2H), 2.22 (s, 6H), 2.20 (s, 6H), 1.21 (t, *J* = 6.95 Hz, 3H), 1.14 (t, *J* = 7.17 Hz, 3H). ESI-MS (m/z): 617.61 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(3,4-dimethylphenyl)-2-((3,4-dimethylphenyl)imino) -4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22n). Light yellow solid (yield: 86%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.10 (s, 1H), 7.34-7.23 (m, 3H), 7.20 (dd, *J* = 7.95, 2.04 Hz, 1H), 7.11 (d, *J* = 7.95 Hz, 1H), 6.73 (d, *J* = 2.04 Hz, 1H), 6.71-6.64 (m, 3H), 4.97 (s, 2H), 4.83 (s, 2H), 4.16 (dd, *J* = 14.20, 7.05 Hz, 4H), 2.28 (s, 6H), 2.20 (s, 6H), 1.21 (t, *J* = 7.18 Hz, 6H). ESI-MS (m/z): 617.72 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(2,5-dimethylphenyl)-2-((2,5-dimethylphenyl)imino) -4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22o). Light yellow solid (yield: 63%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.74 (s, 1H), 7.32 (d, *J* = 7.76 Hz, 1H), 7.23 (d, *J* = 9.77 Hz, 2H), 7.20-7.08 (m, 3H), 7.04 (d, *J* = 8.62 Hz, 1H), 6.88 (d, *J* = 7.47 Hz, 1H), 6.67 (s, 1H), 4.86 (s, 2H), 4.81 (s, 2H), 4.16 (dd, *J* = 13.80, 6.90 Hz, 2H), 4.00 (dd, *J* = 14.09, 7.19 Hz, 2H), 2.34 (s, 3H), 2.26 (s, 3H), 2.17 (s, 3H), 1.99 (s, 3H), 1.20 (t, *J* = 7.19 Hz, 3H), 1.14 (t, *J* = 7.19 Hz, 3H). ESI-MS (m/z): 617.57 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(2,5-dimethylphenyl)-2-((2,5-dimethylphenyl)imino) -4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22p). Light yellow solid (yield: 69%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.04 (s, 1H), 7.36-7.19 (m, 4H), 7.11 (d, *J* = 8.06 Hz, 1H), 6.87 (d, *J* = 7.62 Hz, 1H), 6.71-6.62 (m, 3H), 4.97

(s, 2H), 4.83 (s, 2H), 4.20-4.14 (m, 4H), 2.34 (s, 3H), 2.25 (s, 3H), 2.17 (s, 3H), 1.99 (s, 3H), 1.24-1.18 (m, 6H). ESI-MS (m/z): 617.35 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-fluorophenyl)-2-((4-fluorophenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22q). Light yellow solid (yield: 46%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.75 (s, 1H), 7.65-7.58 (m, 2H), 7.39 (t, J = 8.37 Hz, 2H), 7.27-7.12 (m, 4H), 7.08-6.95 (m, 3H), 4.87 (s, 2H), 4.82 (s, 2H), 4.16 (dd, J = 14.04, 7.02 Hz, 2H), 4.04 (dd, J = 14.29, 7.02 Hz, 2H), 1.21 (t, J = 7.27 Hz, 3H), 1.16 (t, J = 7.27 Hz, 3H). ESI-MS (m/z): 597.48 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-fluorophenyl)-2-((4-fluorophenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22r). Light yellow solid (yield: 56%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.05 (s, 1H), 7.64-7.58 (m, 2H), 7.44-7.17 (m, 5H), 7.03-6.97 (m, 2H), 6.72-6.67 (m, 2H), 4.98 (s, 2H), 4.84 (s, 2H), 4.16 (dd, J = 14.22, 7.11 Hz, 4H), 1.21 (t, J = 7.11 Hz, 6H). ESI-MS (m/z): 597.46 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-chlorophenyl)-2-((4-chlorophenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22s). Light yellow solid (yield: 64%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.76 (s, 1H), 7.67-7.56 (m, 4H), 7.44 (dd, J = 6.63, 2.11 Hz, 2H), 7.23-6.97 (m, 5H), 4.87 (s, 2H), 4.82 (s, 2H), 4.17 (dd, J = 14.27, 7.14 Hz, 2H), 4.04 (dd, J = 14.27, 7.14 Hz, 2H), 1.21 (t, J = 7.28 Hz, 3H), 1.16 (t, J = 7.28 Hz, 3H). ESI-MS (m/z): 629.64 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-chlorophenyl)-2-((4-chlorophenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22t). Light yellow solid (yield: 70%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.06 (s, 1H), 7.66-7.57 (m, 4H), 7.43 (dd, J = 8.55, 2.03 Hz, 2H), 7.32 (d, J = 8.58 Hz, 1H), 7.01 (dd, J = 6.61, 2.04 Hz, 2H), 6.72- 6.67 (m, 2H), 4.98 (s, 2H), 4.84 (s, 2H), 4.16 (dd, J = 14.46, 7.23 Hz, 4H), 1.21 (t, J = 7.22 Hz, 6H). ESI-MS (m/z): 631.35 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-bromophenyl)-2-((4-bromophenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22u). Light yellow solid (yield: 77%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.77 (s, 1H), 7.76-7.71 (m, 2H), 7.61-7.49 (m, 4H), 7.22-6.90 (m, 5H), 4.87 (s, 2H), 4.82 (s, 2H), 4.17 (dd, J

= 14.28, 7.00 Hz, 2H), 4.04 (dd, *J* = 14.28, 7.29 Hz, 2H), 1.21 (t, *J* = 7.25 Hz, 3H), 1.16 (t, *J* = 7.07 Hz, 3H). ESI-MS (m/z): 719.34 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-bromophenyl)-2-((4-bromophenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22v). Light yellow solid (yield: 55%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.06 (s, 1H), 7.76 (dd, *J* = 6.65, 1.96 Hz, 2H), 7.61-7.48 (m, 4H), 7.32 (d, *J* = 8.80 Hz, 1H), 6.95 (dd, *J* = 6.61, 1.95 Hz, 2H), 6.73-6.66 (m, 2H), 4.98 (s, 2H), 4.84 (s, 2H), 4.20-4.12 (m, 4H), 1.24-1.18 (m, 6H). ESI-MS (m/z): 719.53 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetate (22w). Light yellow solid (yield: 49%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.71 (s, 1H), 7.42 (dd, *J* = 6.80, 2.17 Hz, 2H), 7.21-7.02 (m, 5H), 6.97-6.88 (m, 4H), 4.87 (s, 2H), 4.82 (s, 2H), 4.16 (dd, *J* = 14.54, 7.27 Hz, 2H), 4.04 (dd, *J* = 14.23, 7.07 Hz, 2H), 3.82 (s, 3H), 3.76 (s, 3H), 1.21 (t, *J* = 7.19 Hz, 3H), 1.15 (t, *J* = 6.88 Hz, 3H). ESI-MS (m/z): 621.42 [M+H].

Diethyl 2,2'-((4-((*Z*)-((*Z*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)imino)-4-oxothiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetate (22x). Light yellow solid (yield: 68%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 8.02 (s, 1H), 7.42 (dd, *J* = 6.88, 2.14 Hz, 2H), 7.32 (d, *J* = 8.37 Hz, 1H), 7.08 (dd, *J* = 6.86, 2.18 Hz, 2H), 6.97- 6.87 (m, 4H), 6.72-6.65 (m, 2H), 4.97 (s, 2H), 4.84 (s, 2H), 4.16 (dd, *J* = 14.19, 7.16 Hz, 4H), 3.82 (s, 3H), 3.75 (s, 3H), 1.21 (t, *J* = 7.08 Hz, 6H). ESI-MS (m/z): 621.67 [M+H].

Titled compounds **23a-x** was prepared in a similar manner to that described for **12a**

2-(3-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (23a). Light yellow solid (yield: 69%), m.p.: 252-253 ºC. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 13.02 (br s, 1H), 7.79 (s, 1H), 7.61-7.47 (m, 5H), 7.45-7.32 (m, 3H), 7.20-7.12 (m, 3H), 7.04-6.95 (m, 3H), 4.71 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.88, 165.46, 158.09, 150.31, 147.80, 134.96, 134.67, 130.40, 130.19, 129.44, 129.02, 128.72, 128.51, 124.80, 121.79, 120.75, 116.49, 115.84, 64.43. HRMS (ESI, positive) m/z calcd for $C_{24}H_{19}N_2O_4S$ (M + H)

431.1060, found 431.1058.

2,2'-((4-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23d). Light yellow solid (yield: 80%), m.p.: 254-255 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.12 (br s, 2H), 8.05 (s, 1H), 7.61-7.45 (m, 5H), 7.42-7.28 (m, 3H), 7.17 (t, J = 7.47 Hz, 1H), 6.98 (dd, J = 8.49, 1.22 Hz, 2H), 6.70-6.63 (m, 2H), 4.86 (s, 2H), 4.73 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.66, 169.58, 165.72, 160.78, 158.01, 150.74, 148.00, 135.07, 129.39, 128.98, 128.62, 128.53, 124.95, 124.64, 120.81, 118.40, 115.56, 107.21, 100.27, 65.06, 64.67. HRMS (ESI, positive) m/z calcd for $C_{26}H_{22}N_2O_7S$ (M + H) 505.1064, found 505.1077.

2,2'-((4-((4-oxo-3-(*p*-tolyl)-2-(*p*-tolylimino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23h). Light yellow solid (yield: 90%)), m.p.: 230-231 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.07 (br s, 2H), 8.02 (s, 1H), 7.44-7.27 (m, 5H), 7.17 (d, J = 8.24 Hz, 2H), 6.85 (d, J = 8.32 Hz, 2H), 6.70-6.62 (m, 2H), 4.86 (s, 2H), 4.73 (s, 2H), 2.38 (s, 3H), 2.29 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 165.88, 161.49, 158.79, 150.69, 145.56, 138.09, 133.58, 132.55, 129.83, 129.46, 129.02, 128.23, 125.38, 120.65, 117.25, 114.73, 106.98, 20.74, 20.45. HRMS (ESI, positive) m/z calcd for $C_{28}H_{26}N_2O_7S$ (M + H) 533.1377, found 533.1394.

2,2'-((4-((4-oxo-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23k). Light yellow solid (yield: 88%), m.p.: 213-214 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.02 (br s, 2H), 7.70 (s, 1H), 7.40 (d, J = 8.56 Hz, 2H), 7.23 (d, J = 1.92 Hz, 1H), 7.11-7.02 (m, 4H), 6.94-6.89 (m, 4H), 4.76 (s, 2H), 4.73 (s, 2H), 4.09 (dd, J = 13.92, 7.14 Hz, 2H), 4.01 (dd, J = 13.92, 6.78 Hz, 2H), 1.37-1.31 (m, 6H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.92, 169.73, 165.79, 158.40, 155.70, 153.53, 150.15, 148.91, 147.30, 140.75, 132.88, 129.98, 129.58, 127.49, 126.67, 122.95, 121.96, 119.84, 119.08, 116.45, 115.02, 114.60, 114.50, 113.94, 65.14, 64.93, 63.34, 63.10, 14.68, 14.58. HRMS (ESI, positive) m/z calcd for $C_{30}H_{30}N_2O_9S$ (M + H) 593.1588, found 533.1586.

2,2'-((4-((4-oxo-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23l). Light yellow solid (yield: 82%), m.p.: 204-205 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.10 (br s, 2H),

8.01 (s, 1H), 7.40 (dd, *J* = 6.85, 2.04 Hz, 2H), 7.31 (d, *J* = 8.78 Hz, 1H), 7.05 (dd, *J* = 6.91, 2.04 Hz, 2H), 6.96-6.85 (m, 4H), 6.71-6.61 (m, 2H), 4.86 (s, 2H), 4.72 (s, 2H), 4.09 (dd, *J* = 13.88, 6.68 Hz, 2H), 4.01 (dd, *J* = 14.04, 7.02 Hz, 2H), 1.37-1.31 (m, 6H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.23, 166.38, 159.56, 158.90, 156.18, 150.90, 141.46, 132.16, 130.38, 130.09, 127.98, 126.85, 122.39, 119.11, 115.83, 115.53, 115.11, 65.04, 63.83, 63.60, 15.21, 15.10. HRMS (ESI, positive) m/z calcd for $C_{30}H_{30}N_2O_9S$ (M + H) 593.1588, found 593.1596.

2,2'-((4-((4-oxo-3-(3,4-dimethylphenyl)-2-((3,4-dimethylphenyl)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23n). Light yellow solid (yield: 89%), m.p.: 264-265 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.08 (br s, 2H), 8.01 (s, 1H), 7.33-7.18 (m, 4H), 7.12 (d, *J* = 7.84 Hz, 1H), 6.73 (d, *J* = 2.10 Hz, 1H), 6.70-6.62 (m, 3H), 4.86 (s, 2H), 4.73 (s, 2H), 2.28 (s, 6H), 2.20 (s, 6H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.67, 169.59, 165.82, 160.67, 157.95, 150.29, 145.81, 137.25, 137.05, 136.94, 132.70, 132.39, 130.22, 129.88, 129.40, 129.05, 125.69, 124.61, 121.88, 118.61, 117.79, 115.66, 107.12, 100.25, 65.03, 64.64, 19.37, 19.28, 19.05, 18.76. HRMS (ESI, positive) m/z calcd for $C_{30}H_{30}N_2O_7S$ (M + H) 561.1690, found 561.1690.

2,2'-((4-((4-oxo-3-(2,5-dimethylphenyl)-2-((2,5-dimethylphenyl)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23p). Light yellow solid (yield: 84%), m.p.: 251-252 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.11 (br s, 2H), 8.04 (s, 1H), 7.35-7.18 (m, 4H), 7.10 (d, *J* = 7.73 Hz, 1H), 6.87 (dd, *J* = 6.71, 1.05 Hz, 1H), 6.70-6.60 (m, 3H), 4.86 (s, 2H), 4.72 (s, 2H), 2.33 (s, 3H), 2.25 (s, 3H), 2.18 (s, 3H), 1.99 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.66, 169.56, 165.49, 160.79, 158.01, 149.49, 146.54, 136.28, 135.90, 134.15, 132.71, 130.48, 130.44, 129.95, 129.46, 129.28, 125.46, 125.33, 125.00, 120.22, 118.44, 115.47, 107.21, 100.24, 65.03, 64.64, 20.54, 20.32, 16.85, 16.66. HRMS (ESI, positive) m/z calcd for $C_{30}H_{30}N_2O_7S$ (M + H) 561.1690, found 561.1697.

2,2'-((4-((4-oxo-3-(4-chlorophenyl)-2-((4-chlorophenyl)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23s). Light yellow solid (yield: 60%), m.p.: 242-243 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.03 (br s, 2H),

7.76 (s, 1H), 7.32-7.22 (m, 4H), 7.10 (d, J = 1.25 Hz, 1H), 6.88-6.86 (m, 1H), 6.68-6.64 (m, 3H), 4.86 (s, 2H), 4.72 (s, 2H), 2.34 (s, 3H), 2.25 (m, 3H), 2.18 (s, 3H), 2.00 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.89, 169.70, 165.42, 151.20, 149.09, 147.30, 146.59, 138.52, 133.74, 133.33, 130.87, 130.41, 129.36, 129.05, 128.88, 128.58, 126.41, 125.47, 123.06, 122.75, 119.80, 118.48, 116.47, 113.95, 65.10, 64.89. HRMS (ESI, positive) m/z calcd for $C_{26}H_{20}Cl_2N_2O_7S$ (M + H) 573.0285, found 573.0298.

2,2'-((4-((4-oxo-3-(4-chlorophenyl)-2-((4-chlorophenyl)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23t). Light yellow solid (yield: 65%), m.p.: 249-251 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.15 (br s, 2H), 8.06 (s, 1H), 7.66-7.57 (m, 4H), 7.43 (dd, J = 6.64, 2.15 Hz, 2H), 7.32 (d, J = 8.59 Hz, 1H), 7.01 (dd, J = 6.58, 2.03 Hz, 2H), 6.72-6.62 (m, 2H), 4.86 (s, 2H), 4.73 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.65, 169.59, 165.54, 160.92, 158.09, 151.52, 146.81, 133.74, 133.30, 130.40, 129.51, 129.35, 129.04, 128.82, 125.38, 122.75, 117.95, 115.41, 107.27, 100.27, 65.09, 64.69. HRMS (ESI, positive) m/z calcd for $C_{26}H_{20}Cl_2N_2O_7S$ (M + H) 573.0285, found 573.0285.

2,2'-((4-((4-oxo-3-(4-bromophenyl)-2-((4-bromophenyl)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23u). Light yellow solid (yield: 74%), m.p.: 240-241 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.05 (br s, 2H), 7.77 (s, 1H), 7.76-7.74 (m, 2H), 7.57-7.41 (m, 4H), 7.24 (d, J = 2.05 Hz, 1H), 7.11 (dd, J = 8.44, 2.05 Hz, 1H), 7.03 (d, J = 8.70 Hz, 1H), 7.01 (dd, J = 6.65, 2.05 Hz, 2H), 4.76 (s, 2H), 4.73 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.91, 169.71, 165.37, 151.08, 149.10, 147.30, 146.99, 138.97, 134.19, 132.27, 132.02, 131.47, 130.89, 130.74, 126.38, 123.17, 123.01, 121.88, 120.20, 118.47, 117.06, 116.53, 113.96, 113.32, 65.11, 64.90. HRMS (ESI, positive) m/z calcd for $C_{26}H_{20}Br_2N_2O_7S$ (M + H) 662.9254, found 662.9264.

2,2'-((4-((4-oxo-3-(4-bromophenyl)-2-((4-bromophenyl)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23v). Light yellow solid (yield: 82%), m.p.: 260-261 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.10 (br s, 1H), 8.06 (s, 1H), 7.43 (dd, J = 6.65, 2.12 Hz, 2H), 7.59-7.51 (m, 4H), 7.32 (d, J = 8.77 Hz,

1H), 6.95 (dd, *J* = 6.64, 2.02 Hz, 2H), 6.71-6.63 (m, 2H), 4.86 (s, 2H), 4.73 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ:169.64, 169.57, 165.48, 160.91, 158.08, 151.39, 147.21, 134.19, 132.26, 132.00, 130.72, 129.51, 125.37, 123.16, 121.85, 117.96, 117.00, 115.41, 107.30, 100.27, 65.06, 64.66. HRMS (ESI, positive) m/z calcd for $C_{26}H_{20}Br_2N_2O_7S$ (M + H) 662.9254, found 662.9260.

2,2'-((4-((4-oxo-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23w). Light yellow solid (yield: 89%), m.p.: 126-127 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 7.70 (s, 1H), 7.43 (dd, *J* = 6.80, 2.00 Hz, 2H), 7.23 (d, *J* = 1.73 Hz, 1H), 7.13-7.00 (m, 4H), 6.97-6.90 (m, 4H), 4.76 (s, 2H), 4.72 (s, 2H), 3.82 (s, 3H), 3.76 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.92, 169.74, 165.79, 159.13, 156.40, 150.22, 148.91, 147.28, 140.87, 130.00, 127.65, 126.65, 122.91, 119.06, 116.46, 114.56, 114.20, 113.91, 65.15, 64.95, 55.37, 55.14. HRMS (ESI, positive) m/z calcd for $C_{28}H_{26}N_2O_9S$ (M + H) 565.1275, found 565.1278.

2,2'-((4-((4-oxo-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23x). Light yellow solid (yield: 91%), m.p.: 220-221 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.10 (br s, 2H), 8.02 (s, 1H), 7.42 (dd, *J* = 6.73, 2.02 Hz, 2H), 7.31 (d, *J* = 8.75 Hz, 1H), 7.08 (dd, *J* = 6.90, 2.19 Hz, 2H), 6.97-6.88 (m, 4H), 6.70-6.62 (m, 2H), 4.86 (s, 2H), 4.73 (s, 2H), 3.82 (s, 3H), 3.75 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 169.67, 169.59, 165.91, 160.66, 159.11, 157.96, 156.35, 150.62, 141.10, 129.60, 128.38, 127.66, 124.50, 121.91, 118.60, 115.66, 114.55, 114.19, 107.14, 100.26, 65.04, 64.65, 55.37, 55.15. HRMS (ESI, positive) m/z calcd for $C_{28}H_{26}N_2O_9S$ (M + H) 565.1275, found 565.1293.

Ethyl 2-(2-((4-oxo-3-(*m*-tolyl)-2-(*m*-tolylimino)thiazolidin-5-ylidene)methyl) phenoxy)acetic acid (12c). Light yellow solid (yield: 78%), m.p.: 178-180 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.18 (br s, 1H), 8.09 (s, 1H), 7.45-7.24 (m, 7H), 7.08 (t, *J* = 7.59 Hz, 1H), 7.03 (d, *J* = 8.22 Hz, 1H), 6.97 (d, *J* = 7.58 Hz, 1H), 6.76 (d, *J* = 8.48 Hz, 2H), 4.84 (s, 2H), 2.39 (s, 3H), 2.29 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6)

δ: 170.30, 166.07, 156.91, 150.82, 148.36, 139.32, 139.04, 135.42, 132.17, 129.86, 129.69, 129.32, 128.62, 126.06, 125.89, 125.48, 122.68, 121.95, 121.88, 118.09, 113.09, 65.36, 21.41, 21.30. ESI-MS (m/z): 459.56 [M+H].

Ethyl 2-(2-((4-oxo-3-(2,4-dimethylphenyl)-2-((2,4-dimethylphenyl)imino)thiazol-idin-5-ylidene)methyl)phenoxy)acetic acid (12e). Light yellow solid, yield: 85%, m.p.: 125-127 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.11 (br s, 1H), 8.09 (s, 1H), 7.41-7.32 (m, 3H), 7.25 (s, 1H), 7.18 (d, J = 7.8 Hz, 1H), 7.09-6.98 (m, 4H), 6.73 (d, J = 7.78 Hz, 1H), 4.84 (s, 2H), 2.35 (s, 3H), 2.25 (s, 3H), 2.18 (s, 3H), 1.99 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.31, 165.88, 165.93, 149.95, 144.62, 139.33, 136.03, 134.18, 132.19, 131.73, 129.26, 129.14, 128.57, 128.04, 127.70, 125.42, 122.59, 121.91, 119.99, 113.08, 65.35, 21.17, 20.92, 17.72, 17.51. ESI-MS (m/z): 485.12 [M-H].

Ethyl 2-(2-((4-oxo-3-(2,5-dimethylphenyl)-2-((2,5-dimethylphenyl)imino)thiazol -idin-5-ylidene)methyl)phenoxy)acetic acid (12f). Light yellow solid (yield: 89%), m.p.: 230-231 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.13 (br s, 1H), 8.09 (s, 1H), 7.45-7.20 (m, 5H), 7.10 (t, J = 8.20 Hz, 2H), 7.03 (d, J = 8.20 Hz, 1H), 6.87 (d, J = 7.46 Hz, 1H), 6.66 (s, 1H), 4.85 (s, 2H), 2.34 (s, 3H), 2.25 (s, 3H), 2.19 (s, 3H), 1.99 (s, 3H). ESI-MS (m/z): 487.65 [M+H].

Ethyl 2-(2-((4-oxo-3-(4-fluorophenyl)-2-((4-fluorophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12g). Light yellow solid (yield: 83%), m.p.: 225-226 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.13 (br s, 1H), 8.10 (s, 1H), 7.68-7.56 (m, 2H), 7.45-7.32 (m, 4H), 7.22 (t, J = 8.77 Hz, 2H), 7.12-6.96 (m, 4H), 4.85 (s, 2H). ESI-MS (m/z): 467.14 [M+H].

Ethyl 2-(2-((4-oxo-3-(3-fluorophenyl)-2-((3-fluorophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12h). Light yellow solid (yield: 88%), m.p.: 189-190 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.14 (br s, 1H), 8.13 (s, 1H), 7.59-7.33 (m, 6H), 7.15-6.96 (m, 4H), 6.89-6.81 (m, 2H), 4.83 (s, 2H). ESI-MS (m/z): 465.19 [M-H].

Ethyl 2-(2-((4-oxo-3-(2-fluorophenyl)-2-((2-fluorophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12i). Light yellow solid (yield: 76%), m.p.:

205-206 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.21 (br s, 1H), 8.16 (s, 1H), 7.75-7.35 (m, 6H), 7.32-7.18 (m, 3H), 7.14-7.01 (m, 3H), 4.84 (s, 2H). ESI-MS (m/z): 467.14 [M+H].

Ethyl 2-(2-((4-oxo-3-(4-chlorophenyl)-2-((4-chlorophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12j). Light yellow solid (yield: 90 %), m.p.: 244-245 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.13 (br s, 1H), 8.16 (s, 1H), 7.67-7.58 (m, 3H), 7.50-7.29 (m, 5H), 7.10 (t, J = 7.49 Hz, 1H), 7.05 (d, J = 8.36 Hz, 1H), 7.01 (dd, J = 6.72, 1.85 Hz, 2H), 4.85 (s, 2H). ESI-MS (m/z): 499.33 [M+H].

Ethyl 2-(2-((4-oxo-3-(3-chlorophenyl)-2-((3-chlorophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12k). Light yellow solid (yield: 74%), m.p.: 218-219 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.17 (br s, 1H), 8.13 (s, 1H), 7.64-7.35 (m, 6H), 7.23 (dd, J = 7.97, 1.33 Hz, 1H), 7.19-6.87 (m, 5H), 4.83 (s, 2H). ESI-MS (m/z): 497.08 [M-H].

Ethyl 2-(2-((4-oxo-3-(2-chlorophenyl)-2-((2-chlorophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12l). Light yellow solid (yield: 79%), m.p.: 223-224 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.15 (br s, 1H), 8.16 (s, 1H), 7.78-7.55 (m, 4H), 7.52 (d, J = 8.03 Hz, 1H), 7.46-7.31 (m, 3H), 7.19 (t, J = 7.60 Hz, 1H), 7.12-7.01 (m, 3H), 4.85 (s, 2H). ESI-MS (m/z): 501.33 [M+H].

Ethyl 2-(2-((4-oxo-3-(4-bromophenyl)-2-((4-bromophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12m). Light yellow solid (yield: 82%), m.p.: 214-215 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.14 (br s, 1H), 8.11 (s, 1H), 7.79-7.74 (m, 2H), 7.57-7.38 (m, 7H), 7.15-6.91 (m, 3H), 7.10 (d, J = 7.99 Hz, 1H), 7.04 (d, J = 8.73 Hz, 1H), 6.96-6.94 (m, 1H), 4.84 (s, 2H). ESI-MS (m/z): 586.99 [M-H].

Ethyl 2-(2-((4-oxo-3-(3-bromophenyl)-2-((3-bromophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12n). Light yellow solid (yield: 70%), m.p.: 224-225 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.14 (br s, 1H), 8.13 (s, 1H), 7.90-7.50 (m, 5H), 7.45-7.33 (m, 2H), 7.26-6.97 (m, 5H), 4.86 (s, 2H). ESI-MS (m/z): 589.21 [M+H].

Ethyl 2-(2-((4-oxo-3-(2-bromophenyl)-2-((2-bromophenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12o). Light yellow solid (yield: 76%), m.p.:

202-203 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.12 (br s, 1H), 8.16 (s, 1H), 7.92-7.54 (m, 4H), 7.52-7.34 (m, 4H), 7.14-6.89 (m, 4H), 4.83 (s, 2H). ESI-MS (m/z): 587.06 [M-H].

Ethyl 2-(2-((4-oxo-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12p). Light yellow solid (yield: 89%), m.p.: 211-212 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.24 (br s, 1H), 8.07 (s, 1H), 7.44 (d, J = 8.88 Hz, 2H), 7.39 (d, J = 7.61 Hz, 2H), 7.13-7.00 (m, 4H), 6.94 (d, J = 8.91 Hz, 2H), 6.91 (d, J = 8.91 Hz, 2H), 4.81 (s, 2H), 3.82 (s, 3H), 3.75 (s, 3H). ESI-MS (m/z): 491.21[M+H].

Ethyl 2-(2-((4-oxo-3-(3-methoxyphenyl)-2-((3-methoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12q). Light yellow solid (yield: 84%), m.p.: 197-198 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.18 (br s, 1H), 8.09(s, 1H), 7.50-7.23 (m, 4H), 7.18-6.98 (m, 5H), 6.73 (dd, J = 8.30, 2.23 Hz, 1H), 6.57-6.49 (m, 2H), 4.82 (s, 2H), 3.80 (s, 3H), 3.74 (s, 3H). ESI-MS (m/z): 491.21 [M+H].

Ethyl 2-(2-((4-oxo-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12r). Light yellow solid (yield: 95%), m.p.: 195-196 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.18 (br s, 1H), 8.07 (s, 1H), 7.41 (dd, J = 6.85, 2.03 Hz, 2H), 7.39 (d, J = 7.71 Hz, 2H), 7.12-6.99 (m, 4H), 6.92 (d, J = 9.19 Hz, 2H), 6.88 (d, J = 9.19 Hz, 2H), 4.81 (s, 2H), 4.09 (dd, J = 13.79, 6.82 Hz, 2H), 4.00 (dd, J = 13.94, 6.97 Hz, 2H), 1.39-1.30 (m, 6H). ESI-MS (m/z): 519.60 [M+H].

Ethyl 2-(2-((4-oxo-3-(3-ethoxyphenyl)-2-((3-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12s). Light yellow solid (yield: 78%), m.p.: 187-188 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.13 (br s, 1H), 8.09 (s, 1H), 7.48-7.22 (m, 4H), 7.18-6.99 (m, 5H), 6.71 (dd, J = 8.23, 2.57 Hz, 1H), 6.55-6.48 (m, 2H), 4.84 (s, 2H), 4.07 (dd, J = 13.90, 6.89 Hz, 2H), 4.00 (dd, J = 14.04, 7.02 Hz, 2H), 1.37-1.29 (m, 6H). ESI-MS (m/z): 519.55 [M+H].

Ethyl 2-(2-((4-oxo-3-(2-ethoxyphenyl)-2-((2-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (12t). Light yellow solid (yield: 89%), m.p.: 200-201 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.14 (br s, 1H), 8.07 (s, 1H), 7.47-

7.36 (m, 4H), 7.23 (d, *J* = 8.5 Hz, 1H), 7.11-7.01 (m, 5H), 6.93 (d, *J* = 0.6 Hz, 1H), 6.82 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.84 (s, 2H), 4.12 (dd, *J* = 13.8, 6.9 Hz, 2H), 3.96 (dd, *J* = 13.8, 6.9 Hz, 2H), 1.35-1.21 (m, 6H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.31, 165.74, 156.92, 154.73, 150.40, 149.98, 137.65, 132.17, 131.14, 130.66, 128.59, 126.18, 125.11, 124.36, 122.59, 121.93, 121.83, 121.48, 121.12, 114.56, 114.25, 113.11, 65.34, 64.50, 64.31, 15.09. ESI-MS (m/z): 517.15 [M-H].

2-(4-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)phenoxy)acetic acid (23b). Light yellow solid (yield: 89%), m.p.: 290-291 ºC. ^{1}H-NMR (600 MHz, DMSO-d_6) δ: 13.08 (br s, 1H), 7.77 (s, 1H), 7.56-7.48 (m, 7H), 7.40-7.38 (m, 2H), 7.17 (t, *J* = 7.37 Hz, 1H), 7.05 (d, *J* = 6 Hz, 2H), 6.97 (d, *J* = 6 Hz, 2H), 4.74 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.20, 166.19, 159.62, 151.04, 148.47, 135.55, 132.20, 130.84, 129.91, 129.50, 129.14, 129.02, 126.78, 125.19, 121.28, 118.92, 115.86, 64.98. ESI-MS (m/z): 431.46 [M+H].

2,2'-((4-((4-oxo-3-phenyl-2-(phenylimino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23c). Light yellow solid (yield: 61%), m.p.: 250-251 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 12.99 (br s, 2H), 7.74 (s, 1H), 7.62-7.45 (m, 5H), 7.39 (t, *J* = 7.72 Hz, 2H), 7.24 (d, *J* = 1.70 Hz, 1H), 7.17 (t, *J* = 7.48 Hz, 1H), 7.09 (dd, *J* = 8.55, 1.71 Hz, 1H), 7.03 (d, *J* = 8.55 Hz, 1H), 6.98 (d, *J* = 7.40 Hz, 2H), 4.76 (s, 2H), 4.72 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.39, 170.21, 166.12, 150.95, 149.50, 148.30, 147.79, 135.56, 130.93, 129.89, 129.50, 129.15, 129.03, 127.05, 125.22, 123.37, 121.32, 119.40, 117.08, 114.45, 65.64, 65.42. ESI-MS (m/z): 505.36 [M+H].

2-(3-((4-oxo-3-(*p*-tolyl)-2-(*p*-tolylimino)thiazolidin-5-ylidene)methyl)phenolxy)acetic acid (23e). Light yellow solid (yield: 85%), m.p.: 211-213 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.01 (br s, 1H), 7.76 (s, 1H), 7.47-7.30 (m, 5H), 7.23-7.10 (m, 4H), 7.00 (dd, *J* = 8.34, 2.18 Hz, 1H), 6.86 (d, *J* = 8.14 Hz, 2H), 4.71 (s, 2H), 2.38 (s, 3H), 2.30 (s, 3H). ESI-MS (m/z): 459.36 [M+H].

2-(4-((4-oxo-3-(*p*-tolyl)-2-(*p*-tolylimino)thiazolidin-5-ylidene)methyl)phenolxy)acetic acid (23f). Light yellow solid (yield: 92%), m.p.: 289-290 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.06 (br s, 1H), 7.75 (s, 1H), 7.52 (d,

J = 8.27 Hz, 2H), 7.39 (d, *J* = 8.08 Hz, 2H), 7.34 (d, *J* = 8.27 Hz, 2H), 7.19 (d, *J* = 7.90 Hz, 2H), 7.05 (d, *J* = 8.46 Hz, 2H), 6.86 (d, *J* = 7.71 Hz, 2H), 4.74 (s, 2H), 2.38 (s, 3H), 2.30 (s, 3H). ESI-MS (m/z): 459.53 [M+H].

2,2'-((4-((4-oxo-3-(*p*-tolyl)-2-(*p*-tolylimino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23g). Light yellow solid (yield: 87%), m.p.: 217-218 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 12.98-12.97 (m, 2H), 7.71 (s, 1H), 7.39 (d, *J* = 8.11 Hz, 2H), 7.34 (d, *J* = 8.62 Hz, 2H), 7.24 (d, *J* = 1.78 Hz, 1H), 7.18 (d, *J* = 8.09 Hz, 2H), 7.11-7.00 (m, 2H), 6.86 (d, *J* = 8.25 Hz, 2H), 4.76 (s, 2H), 4.72 (s, 2H), 2.38 (s, 3H), 2.30 (s, 3H). ESI-MS (m/z): 531.02 [M-H].

2-(3-((4-oxo-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenolxy)acetic acid (23i). Light yellow solid (yield: 75%), m.p.: 254-255 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.04 (br s, 1H), 7.75 (s, 1H), 7.46-7.38 (m, 3H), 7.18-7.12 (m, 2H), 7.07 (dd, *J* = 6.78, 2.31 Hz, 2H), 7.00 (dd, *J* = 8.10, 2.31 Hz, 1H), 6.96-6.87 (m, 4H), 4.71 (s, 2H), 4.10 (dd, *J* = 13.90, 6.83 Hz, 2H), 4.02 (dd, *J* = 13.90, 6.83 Hz, 2H), 1.36 (t, *J* = 6.95 Hz, 3H), 1.33 (t, *J* = 7.05 Hz, 3H). ESI-MS (m/z): 517.19 [M-H].

2-(4-((4-oxo-3-(4-ethoxyphenyl)-2-((4-ethoxyphenyl)imino)thiazolidin-5-ylidene)methyl)phenolxy)acetic acid (23j). Light yellow solid (yield: 93%), m.p.: 256-257 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.12 (br s, 1H), 7.74 (s, 1H), 7.53 (dd, *J* = 7.07, 1.85 Hz, 2H), 7.41 (dd, *J* = 6.71, 2.13 Hz, 2H), 7.09-7.02 (m, 4H), 6.87-6.96 (m, 4H), 4.73 (s, 2H), 4.09 (dd, *J* = 13.87, 6.87 Hz, 2H), 4.02 (dd, *J* = 14.00, 7.00 Hz, 2H), 1.31-1.39 (m, 6H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.43, 166.14, 158.96, 158.61, 156.26, 150.58, 141.26, 135.27, 130.84, 130.28, 130.27, 127.88, 122.46, 122.39, 122.33, 116.91, 116.23, 115.54, 115.12, 65.00, 63.84, 63.60, 15.19, 15.09. ESI-MS (m/z): 517.06 [M-H].

2,2'-((4-((4-oxo-3-(3,4-dimethylphenyl)-2-((3,4-dimethylphenyl)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23m). Light yellow solid (yield: 91%), m.p.: 159-160 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.07 (br s, 1H), 7.70 (s, 1H), 7.33-7.17 (m, 4H), 7.16-6.98 (m, 3H),7.67 (s, 1H), 6.70-6.68 (m, 1H), 4.75-4.71 (m, 4H), 2.28 (s, 6H), 2.20 (s, 6H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ:

170.41, 170.23, 166.20, 150.45, 147.73, 146.08, 137.79, 137.57, 137.49, 133.21, 132.98, 130.75, 130.60, 130.40, 129.55, 127.14, 126.21, 123.30, 122.43, 119.61, 118.33, 117.09, 114.39, 65.72, 19.87, 19.79, 19.56, 19.30. ESI-MS (m/z): 561.31 [M+H].

2,2'-((4-((4-oxo-3-(2,5-dimethylphenyl)-2-((2,5-dimethylphenyl)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23o). Light yellow solid (yield: 78%), m.p.: 256-257 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.03 (br s, 2H), 7.74 (s, 1H), 7.32 (d, J = 7.72 Hz, 1H), 7.28-7.20 (m, 3H), 7.14-6.98 (m, 3H), 6.88 (d, J = 7.52 Hz, 1H), 6.68 (s, 1H), 4.75 (s, 2H), 4.72 (s, 2H), 2.34 (s, 3H), 2.26 (s, 3H), 2.17 (s, 3H), 1.99 (s, 3H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ: 170.37, 170.19, 165.86, 149.69, 149.51, 147.78, 146.85, 136.80, 136.44, 134.64, 133.19, 131.09, 130.99, 130.95, 130.48, 129.77, 127.02, 126.08, 125.90, 123.26, 120.62, 119.46, 117.25, 114.47, 65.60, 65.40, 21.04, 20.83, 17.35, 17.13. ESI-MS (m/z): 561.34 [M+H].

2,2'-((4-((4-oxo-3-(4-fluoropheny)-2-((4-fluoropheny)imino)thiazolidin-5-ylidene)methyl)-1,2-phenylene)bis(oxy))diacetic acid (23q). Light yellow solid (yield: 69%), m.p.: 175-176 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 12.95 (br s, 2H), 7.75 (s, 1H), 7.65-7.36 (m, 5H), 7.26-7.18 (m, 2H), 7.14-6.98 (m, 4H), 4.77 (s, 2H), 4.73 (s, 2H). ESI-MS (m/z): 541.36 [M+H].

2,2'-((4-((4-oxo-3-(4-fluoropheny)-2-((4-fluoropheny)imino)thiazolidin-5-ylidene)methyl)-1,3-phenylene)bis(oxy))diacetic acid (23r). Light yellow solid (yield: 77%), m.p.: 237-238 ºC. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 13.10 (br s, 2H), 8.05 (s, 1H), 7.66-7.58 (m, 2H), 7.39 (t, J = 8.94 Hz, 2H), 7.32 (d, J = 8.69 Hz, 1H), 7.21 (t, J = 8.69 Hz, 2H), 7.04-6.97 (m, 2H), 6.70-6.62 (m, 2H), 4.86 (s, 2H), 4.73 (s, 2H). ESI-MS (m/z): 541.42 [M+H].

Virtual Screening

The crystal structure of Sap2 in complex with A-70450 (PDB ID: 1EAG) was obtained from Protein Database Bank (http://www.rcsb.org/). All the water molecules were removed and the remaining protein structures were optimized using the Biopolymer module (SYBYL-X 2.0, Tripos, Inc.). Hydrogen atoms were added and

the combined complex structure was submitted for protein preparation and energy minimization calculation. The ligand was then removed and the binding site was defined as whole residues within a 12 Å radius subset encompassing the A-70450.

GOLD 5.0[1] was used to screen the SPECS database consisting of approximately 287000 compounds. Twenty genetic algorithm (GA) runs were performed for each molecule. For each GA run, 100000 operations were applied on a set of five islands with a population size of 100. The selection pressure, which is the ratio between the probability of the most fit member selected as a parent to the probability of an average member selected as a parent, was set at 1:1. The annealing parameters of van der Waals and hydrogen bonding were set at 4.0 and 2.5 Å to allow a few bad bumps and poor hydrogen bonds at the beginning of a GA run. The "early-termination" option was turned off to allow the continued docking even though the first three docking solutions were very similar, with the RMSD values less than 1.5 Å. The docked compounds were ranked by GoldScore implemented in GOLD.

Biological Assays

SAP2 Inhibitory Activity Assay. The fluorimetric SAP2 enzyme activity was measured by Bioteck Synergy2 spectrophotometer using a microplate reader (λ_{ex} = 340/30 nm, λ_{em} = 485/20 nm) and 96-well microplates (Corning, 3650). The peptidic FRET pair-labeled substrate Dabcyl-Arg-Lys-Pro-Ala-Leu-Phe-┆-Phe-Arg-Leu-Glu (EDANS)-Arg-OH was purchased from GL Biochem (Shanghai) Ltd. SAP2 was expressed and purified by ZoonBio Biotechnology Ltd (Nanjing, China). A 50 mM sodium citrate buffer (pH = 4.5) containing 50 mM NaCl was used for dilution. Test compounds were dissolved in DMSO and were tested at a final concentration 100 μM ~ 0.01 μM (10 μM ~ 0.001 nM for pepstatin A). The reaction mixture contained 185 μL buffer, 5 μL enzyme solution (a linear fluorescence increase of 100 units/min), 5 μL substrate solution (18.75 μM in DMSO), and 5 μL test compounds solution (in DMSO) or DMSO alone as a negative control in a final volume of 200 μL. Reactions were carried out at 30 ºC. IC_{50} values were obtained by co-incubating enzyme and

inhibitors for 30 min prior to the addition of substrate. The curve fitting was performed by log (inhibitor) *vs* response-varible slop (GraphPad Prism software).

***In vitro* antifungal activity assay.** *In vitro* antifungal activity was measured by the serial dilution method in 96-well microtest plates. The determination of MIC values was performed according to the recommendations of National Committee for Clinical Laboratory Standards (NCCLS) with RPMI 1640 (Sigma) buffered with 0.165M MOPS (Sigma) as the test medium. The MIC_{80} value is defined as the lowest concentration of test compound that results in a culture with turbidity less than or equal to 80% inhibition relative to the growth of the control. Test compounds were dissolved in DMSO serially diluted in growth medium. *C. albicans* was incubated at 35°C and growth MIC_{80} was determined at 24 h.

Nematode *C. elegans*-*Candida*-killing assay. *C. albicans* strain SC5314 was inoculated in 2 mL of YPD and grown at 30 ºC for 24 h; 10-cm tissue culture plates (BDFalcon, http://www.bdbiosciences.com) were filled with 100 µL of the culture containing solid BHI media (Difco) with kanamycin (45 µg/mL), ampicillin (100 µg/mL), and streptomycin (100 µg/mL). The plates were incubated at 30 ºC for another 24 h. Synchronized adult *C. elegans glp-4; sek-1* nematodes grown at 25 °C were collected and then washed with sterile M9 buffer. To the center of the *C. albicans* lawns, 400 to 500 washed worms were added. The plates were incubated at 25 °C for 4 h. Worms were washed four times with sterile M9 and then 15-mL conical tube was carefully added. Each well of a six-well tissue culture plate (Corning Inc.) containing 2 mL of liquid medium (80% M9, 20% BHI, 45 µg/mL kanamycin) were pipetted with thirty worms. Test compounds of various concentrations were added into the medium. Then the plates were incubated at 25 ºC overnight and examined at 24-h intervals for survival. Worms were considered dead and removed when they did not respond to being touched by a platinum wire. **FLC** at 32 µg/mL and pure phosphate-buffered saline (PBS) were used for a comparison. Animals survival curves was examined by using the Kaplan-Meier method and differences were performed by

using the log-rank test (Graphpad prism 5.0). A p- value of < 0.05 was considered to be statistically significant.

***In vivo* antifungal efficacy in *C. albicans* infected mice model.** *Candida albicans* SC5314 or fluconazole-resistant clinical isolate 103 was grown in YPD (yeast peptone dextrose) at 30 ºC. Cells were harvested, washed and resuspended in sterile saline and adjusted to 5×10^6 CFU/mL at Logarithmic-phase. ICR female mice (18-22 g; Shanghai SLAC Laboratory Animals, Shanghai, China) were used to establish mouse model of the *Candida albicans* infection. All mice were inoculated by injection of the *C. albicans* suspension into the tail vein (1×10^6 CFU/mouse). Test compounds were administered by intraperitoneal injection at dose of 2 or 5 mg/kg, and **FLC** at 0.5 mg/kg and sterile saline for a comparison. Daily monitoring and examinations were carried out to record the death rate. The survival time was observed. Mice survival curves were examined by using the Kaplan-Meier method and differences were also performed by using the log-rank test (Graphpad prism 5.0). A p- value of < 0.05 was considered statistically significant.

Human aspartic proteases inhibitory activity assays.

The assays were conducted by Huawei pharmaceutical Co. Ltd., China. The test compounds were provided in 100% DMSO. A series of dilutions of the compounds were prepared with 10% DMSO in assay buffer. The final concentration of DMSO is 1% in all the reactions.

Cathepsin and Renin activity assays. The enzymatic reactions were conducted at room temperature for 30 minutes in a 50 μL mixture containing 50 mM Tris-HCl (pH 7.4), 100 mM NaCl, 10 mM $MgCl_2$, a test compound, substrate (Z-Arg-Arg-amino-4-methylcoumarin, 10 μM for cathepsin B; Suc-Arg-Pro-Phe-His-Leu-Leu-Val-Tyr-AMC, 7.5 μM for renin) and enzyme (cathepsin B, 15 ng/well; renin, 8 ng/well). The assays were performed in triplicates at each concentration. Fluorescence intensity was

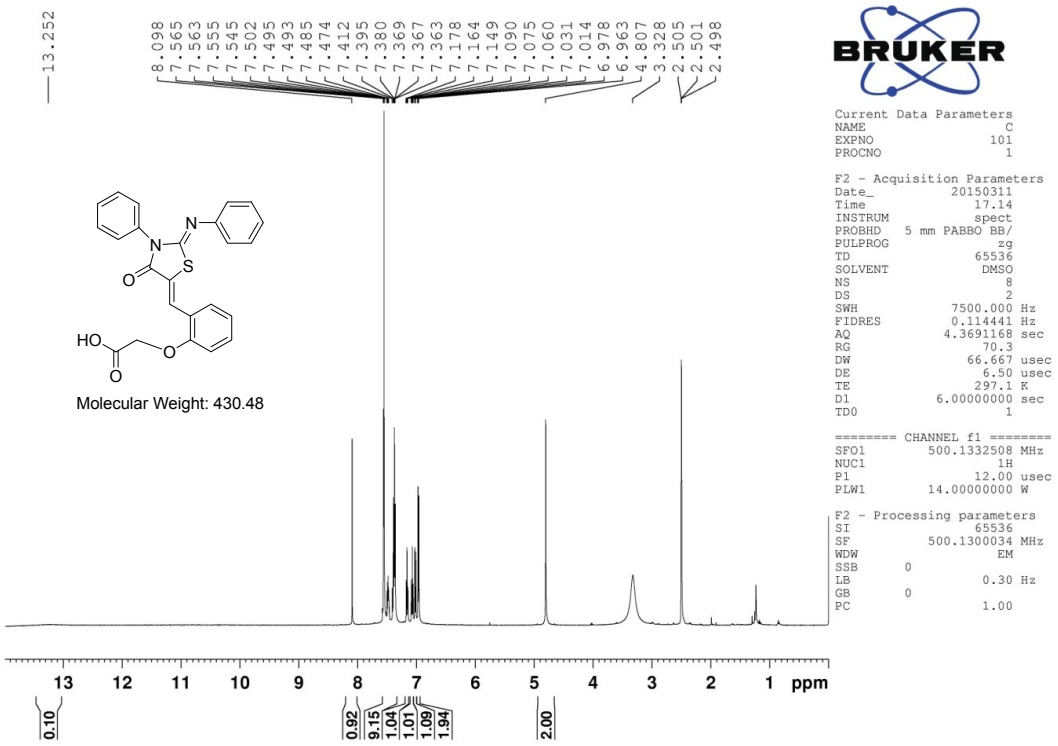
measured at an excitation of 350 nm and an emission of 460 nm using a Tecan Infinite M1000 microplate reader. The IC_{50} values were calculated using nonlinear regression with normalized dose−response fit using Prism GraphPad software.

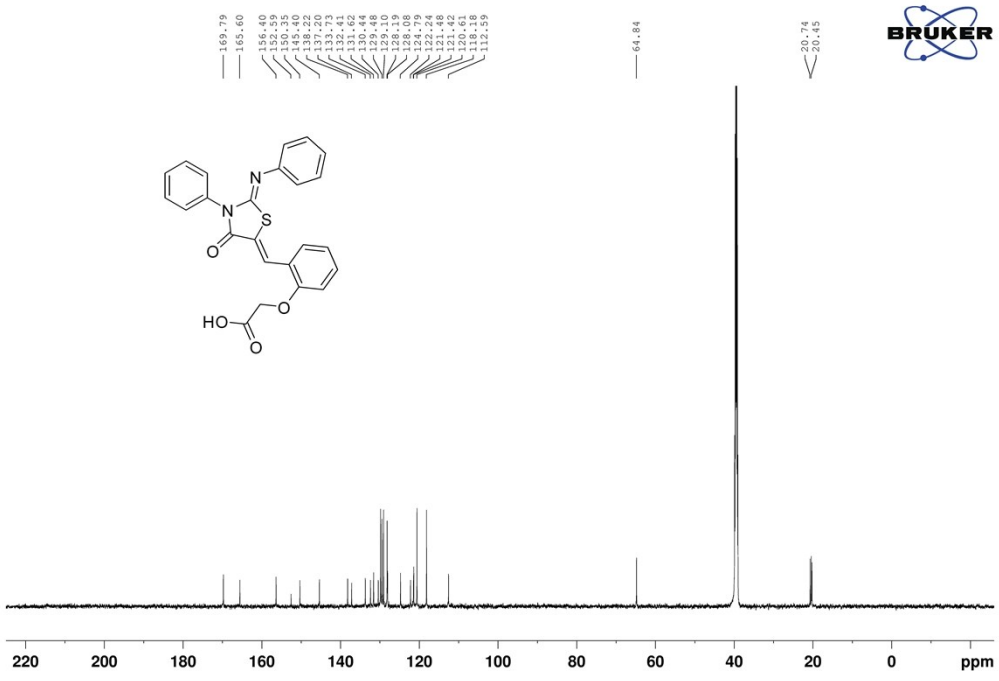
Pepsin activity assays. The enzymatic reactions were conducted in triplicates at 37 ºC for 30 minutes. Human pepsin (0.063 nM) was pre-incubated with test compounds diluted in 1 × pepsin assay buffer (50 mM sodium acetate pH 2.0, 0.025% Brij-35) for 30 minutes at 37 °C. The enzyme substrate (Mca-Gly-Lys-Pro-Ile-Leu-Phe-Phe-Arg-Leu-Lys(Dnp)-D-Arg-NH_2, 2.5 μM) was added and the plate was incubated at 37 °C for 30 minutes in a final volume of 50 μL. Fluorescence intensity was measured at an excitation of 328 nm and an emission of 393 nm using a Tecan Infinite M1000 microplate reader. The IC_{50} values were calculated using nonlinear regression with normalized dose−response fit using Prism GraphPad software.

Spectral data

Copies of NMR and HRMS spectra of representative compounds.

12a





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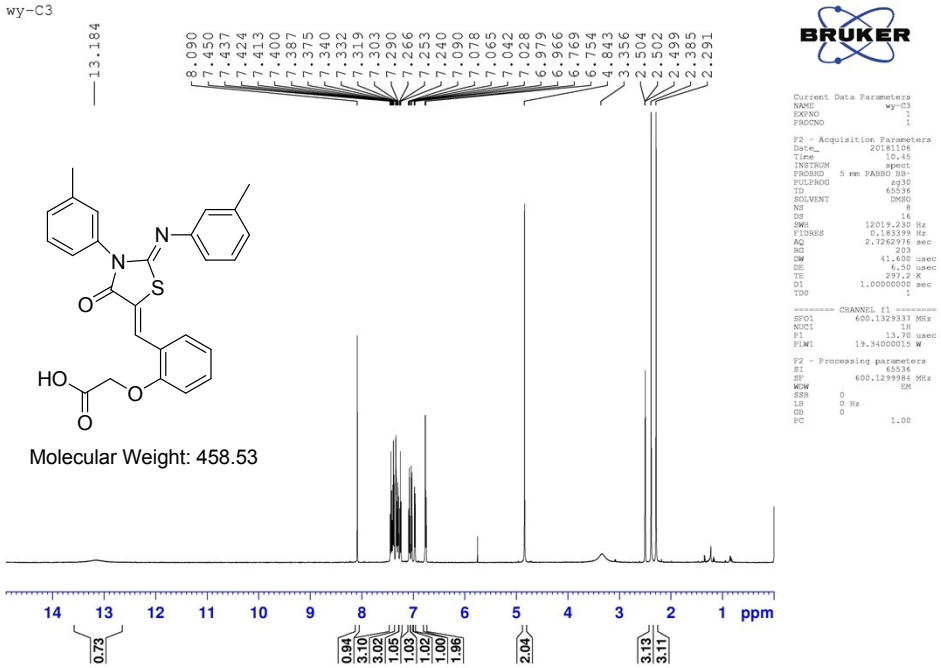
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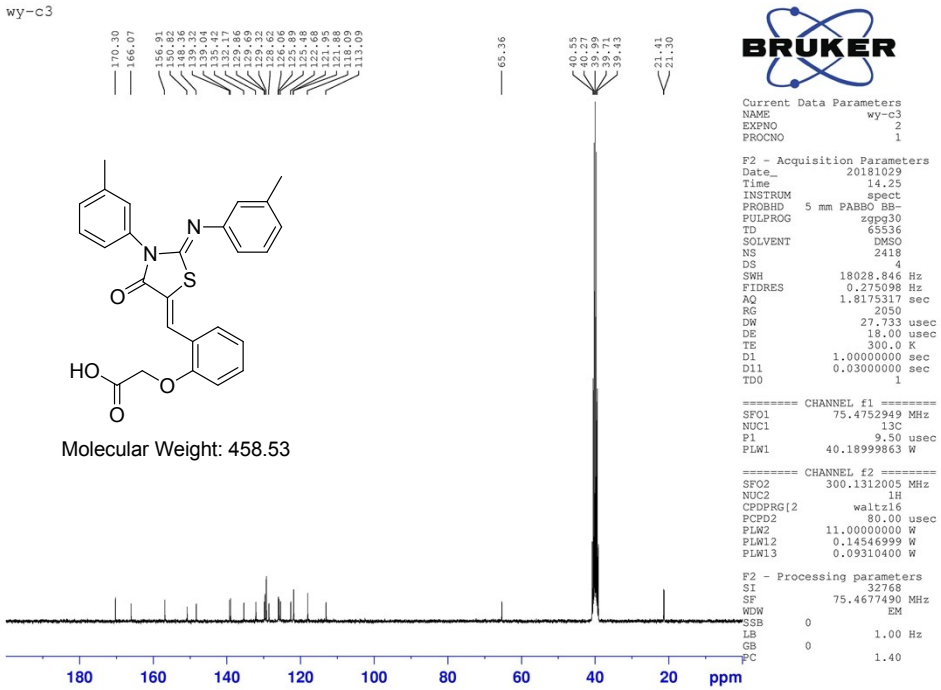
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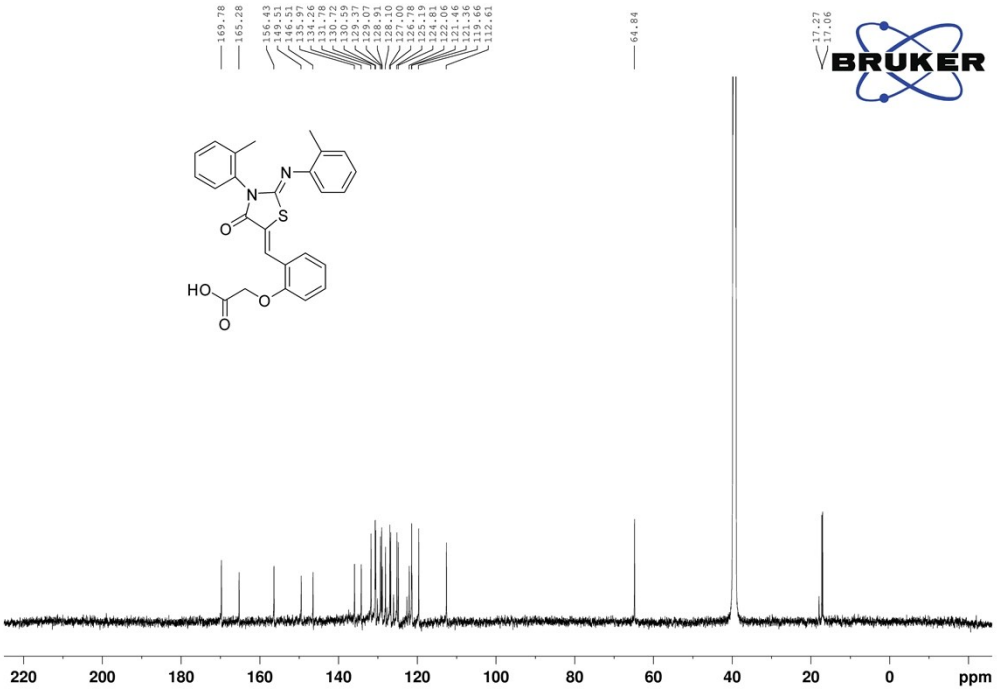
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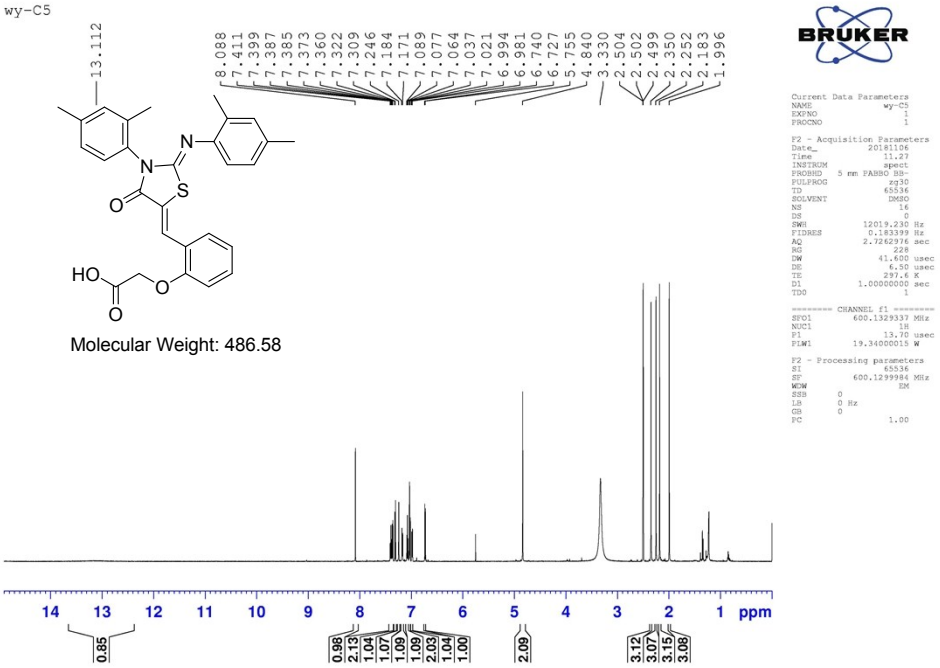
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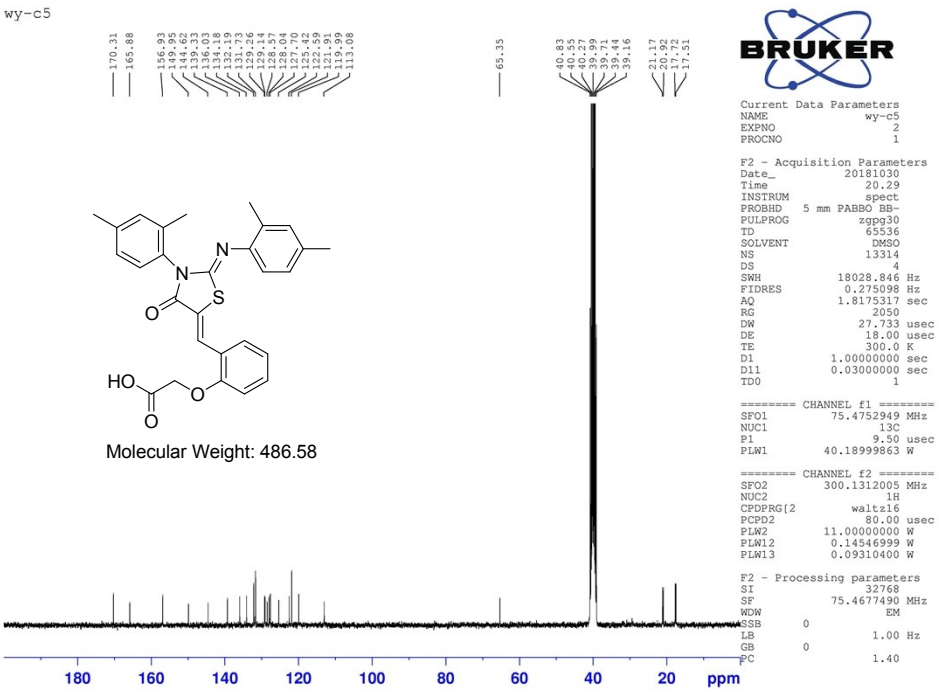
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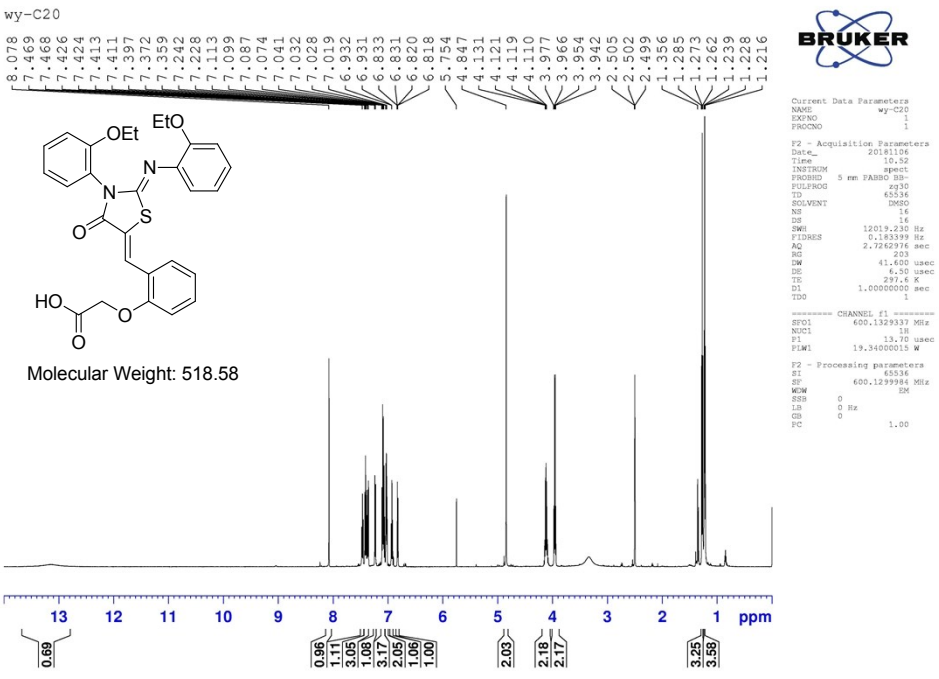
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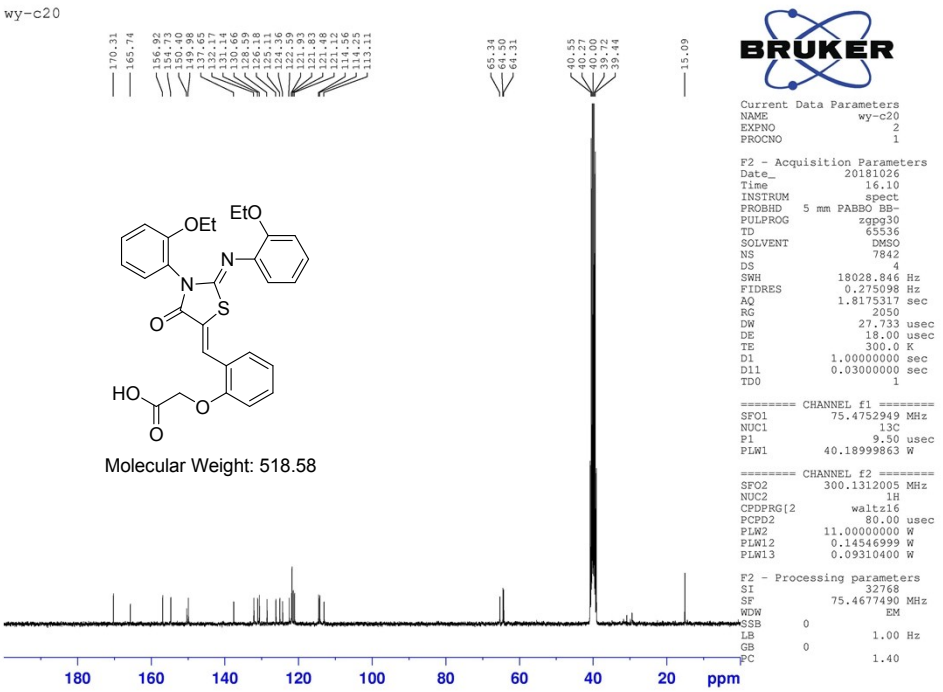
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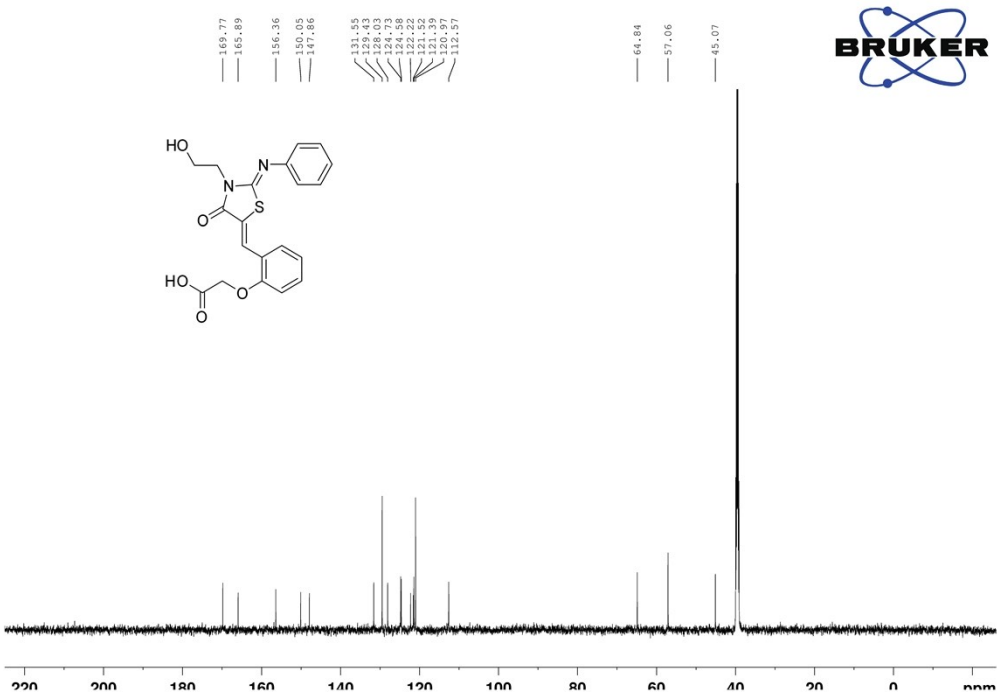
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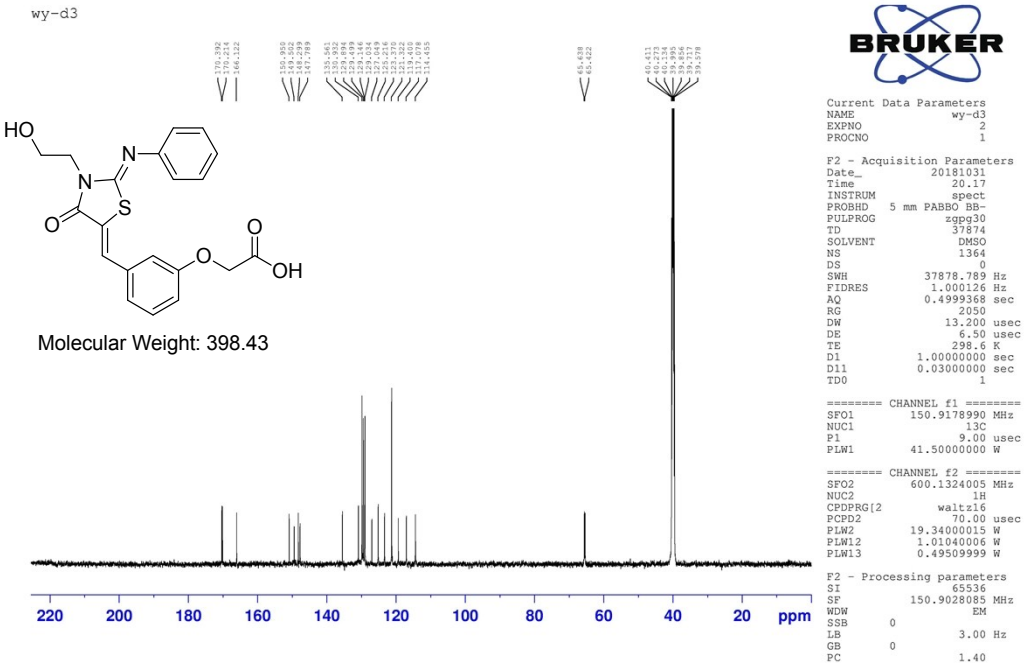


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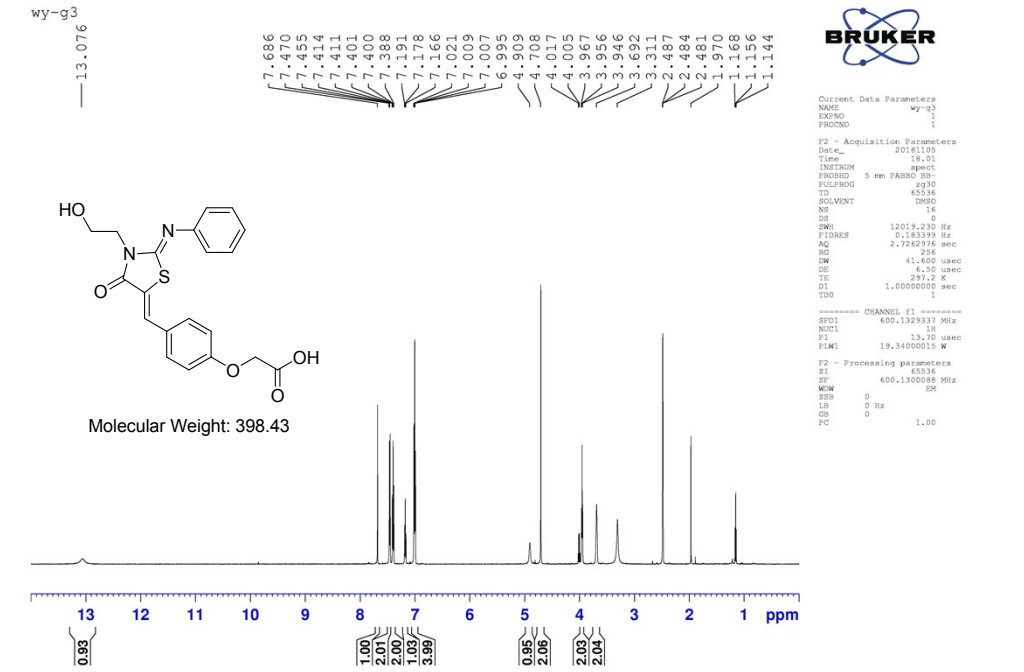


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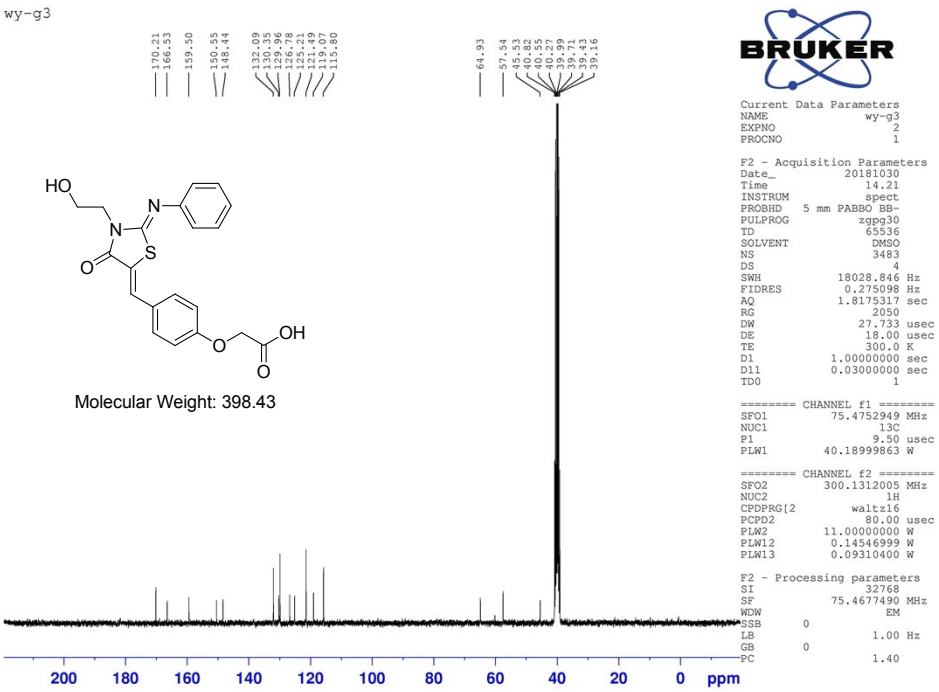
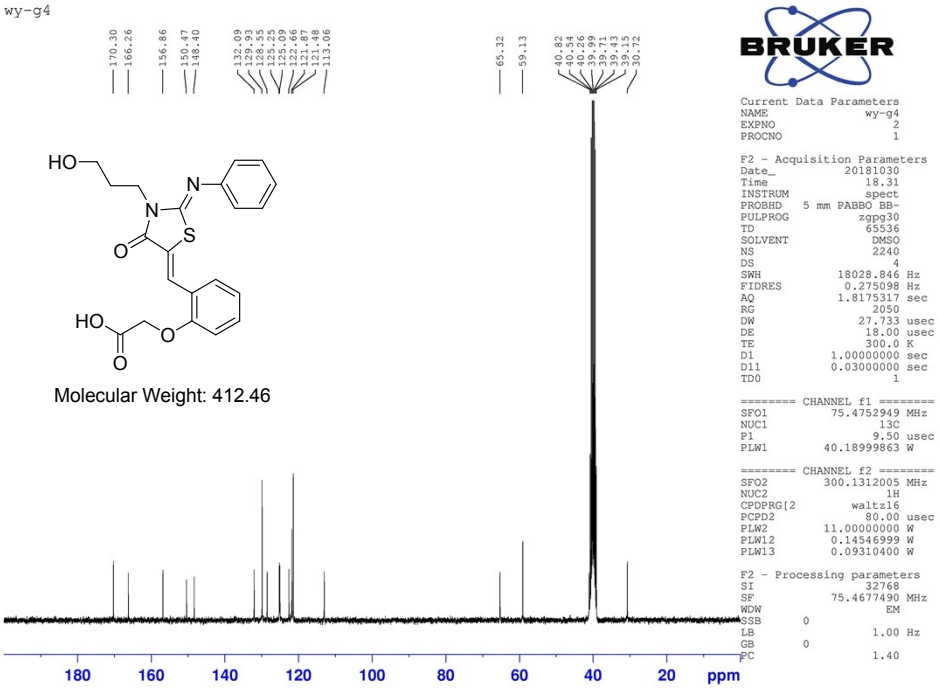
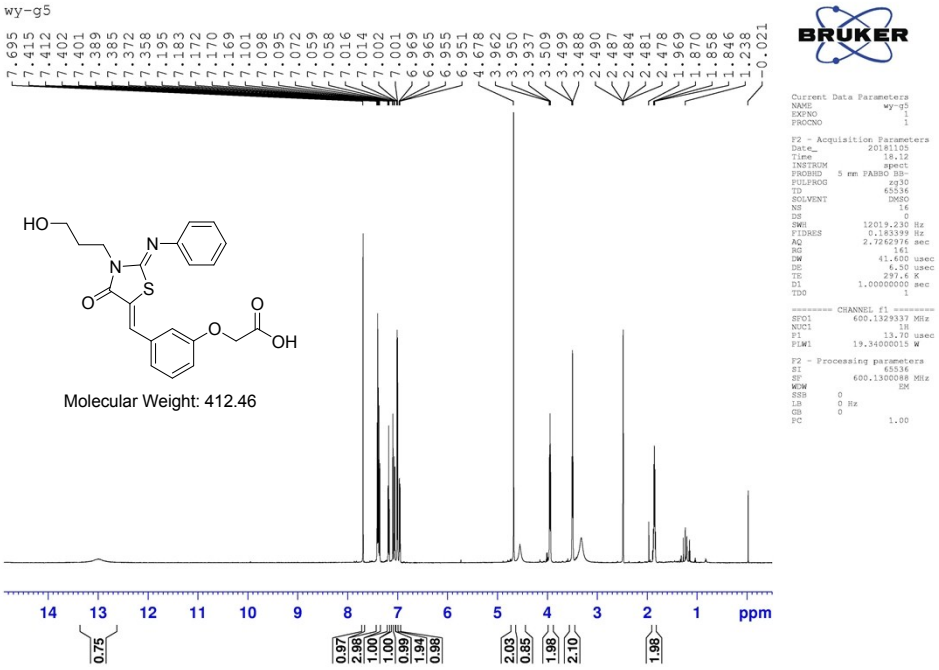
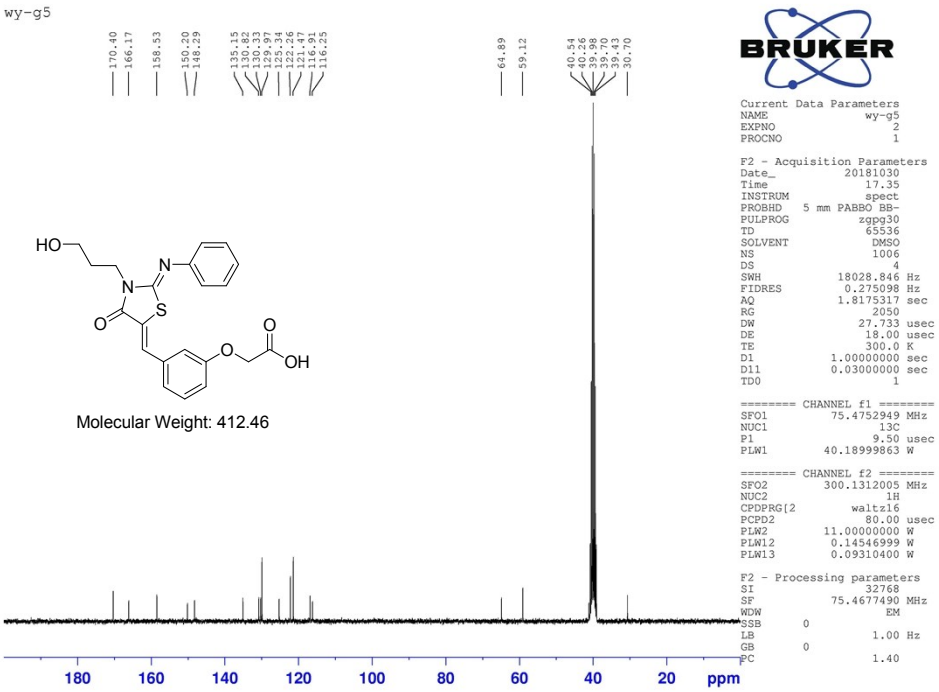

wy-g3
170.21
166.53
159.50
150.55
148.44
132.09
130.55
129.96
126.78
125.21
121.49
121.07
115.80
64.93
57.54
45.53
40.82
40.55
40.27
39.99
39.71
39.43
39.16
HO
N
N
S
O
O
OH
O
Molecular Weight: 398.43
BRUKER
Current Data Parameters
NAME wy-g3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181030
Time 14.21
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 3483
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 2050
DW 27.733 usec
DE 18.00 usec
TE 300.0 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 9.50 usec
PLW1 40.18999863 W
======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 11.00000000 W
PLW12 0.14546999 W
PLW13 0.09310400 W
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm

18d

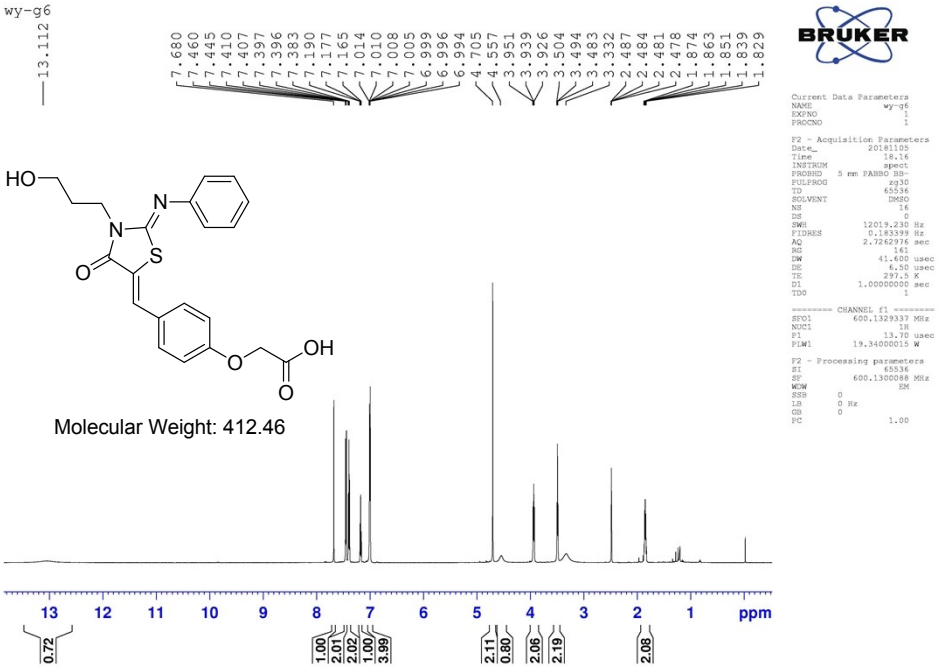

wy-g4
170.30
166.26
156.86
150.47
148.40
132.09
129.93
128.55
125.25
122.66
121.87
121.48
113.06
65.32
59.13
40.82
40.54
40.26
39.99
39.71
39.43
39.15
30.72
HO
N
N
S
O
HO
O
O
Molecular Weight: 412.46
BRUKER
Current Data Parameters
NAME wy-g4
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181030
Time 18.31
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 2240
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 2050
DW 27.733 usec
DE 18.00 usec
TE 300.0 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 9.50 usec
PLW1 40.18999863 W
======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 11.00000000 W
PLW12 0.14546999 W
PLW13 0.09310400 W
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180 160 140 120 100 80 60 40 20 ppm

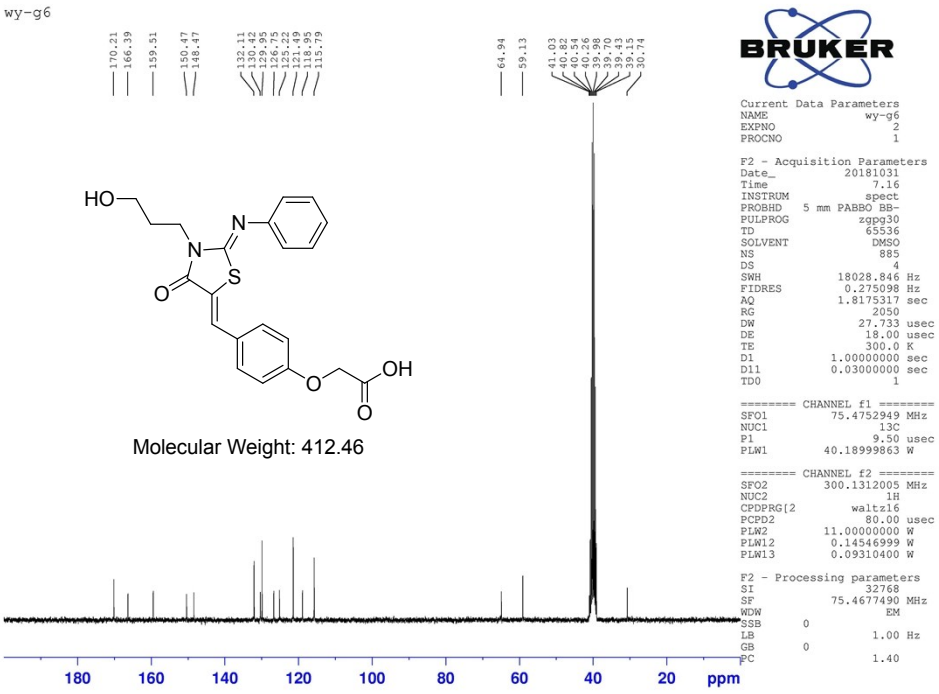
18e


wy-g5
7.695 7.415 7.412 7.402 7.401 7.389 7.385 7.372 7.358 7.195 7.183 7.172 7.170 7.169 7.101 7.098 7.095 7.072 7.059 7.058 7.016 7.014 7.002 7.001 6.969 6.965 6.955 6.951 4.678 3.962 3.950 3.937 3.509 3.499 3.488 2.490 2.487 2.484 2.481 2.478 1.969 1.870 1.858 1.846 1.238 0.021
HO
N
N
S
O
O
O
OH
Molecular Weight: 412.46
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.75 2.98 1.00 1.00 0.99 1.94 0.98 2.03 0.85 1.98 2.10 1.98
BRUKER
Current Data Parameters
NAME wy-g5
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181105
Time 18.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 0
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 161
DW 41.600 usec
DE 6.50 usec
TE 297.6 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1329337 MHz
NUC1 1H
P1 13.70 usec
PLW1 19.34000015 W
F2 - Processing parameters
SI 65536
SF 600.1300088 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00

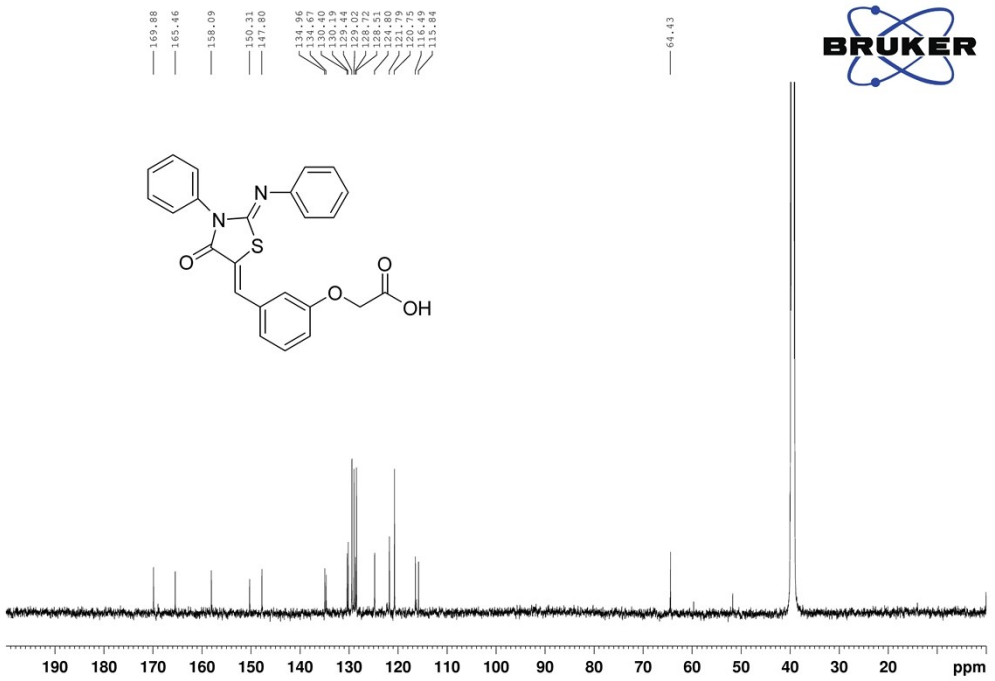

wy-g5
170.40 166.17 158.53 150.20 148.29 135.15 130.82 130.33 128.37 125.34 122.26 121.47 116.91 116.25 64.89 59.12 40.54 40.26 39.98 39.70 39.43 30.70
HO
N
N
S
O
O
O
OH
Molecular Weight: 412.46
180 160 140 120 100 80 60 40 20 ppm
BRUKER
Current Data Parameters
NAME wy-g5
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181030
Time 17.35
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1006
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 2050
DW 27.733 usec
DE 18.00 usec
TE 300.0 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 9.50 usec
PLW1 40.18999863 W
======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 11.00000000 W
PLW12 0.14546999 W
PLW13 0.09310400 W
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

18f

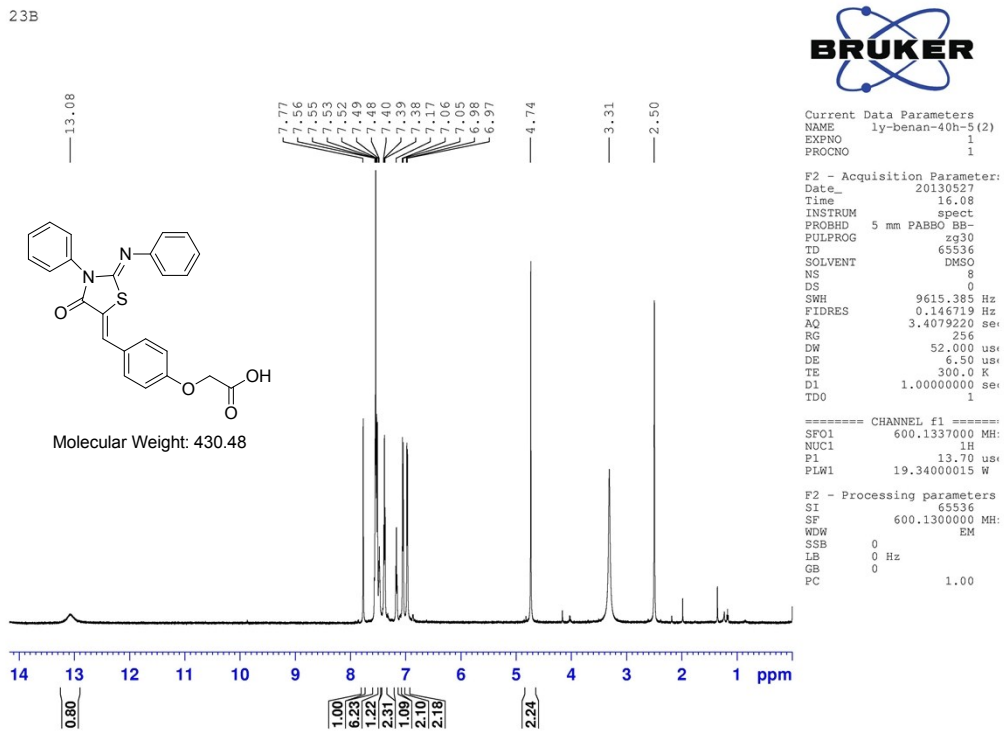

wy-g6
13.112
7.680
7.460
7.445
7.410
7.407
7.397
7.396
7.383
7.190
7.177
7.165
7.014
7.010
7.008
7.005
6.999
6.996
6.994
4.705
4.557
3.951
3.939
3.926
3.504
3.494
3.483
3.332
2.487
2.484
2.481
2.478
1.874
1.863
1.851
1.839
1.829
HO
N
N
S
O
O
OH
O
Molecular Weight: 412.46
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.72
1.00
2.01
2.02
1.00
3.99
2.11
0.80
2.06
2.19
2.08
BRUKER
Current Data Parameters
NAME wy-g6
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181105
Time 18.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 0
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 161
DW 41.600 usec
DE 6.50 usec
TE 297.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1329337 MHz
NUC1 1H
P1 13.70 usec
PLW1 19.34000015 W
F2 - Processing parameters
SI 65536
SF 600.1300088 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00

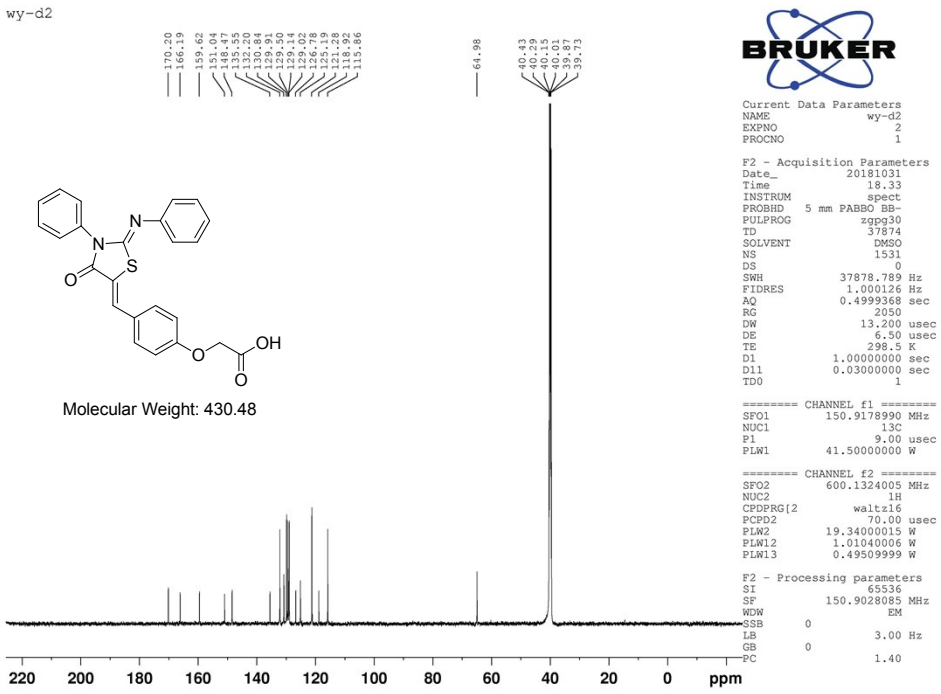

wy-g6
170.21
166.39
159.51
150.47
148.47
132.11
130.12
129.95
126.75
125.22
118.49
115.95
115.79
64.94
59.13
41.03
40.82
40.61
40.40
40.19
39.98
39.77
39.56
39.35
39.14
30.74
HO
N
N
S
O
O
OH
O
Molecular Weight: 412.46
180
160
140
120
100
80
60
40
20
ppm
BRUKER
Current Data Parameters
NAME wy-g6
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181031
Time 7.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 885
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 2050
DW 27.733 usec
DE 18.00 usec
TE 300.0 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 9.50 usec
PLW1 40.18999863 W
======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 11.00000000 W
PLW12 0.14546999 W
PLW13 0.09310400 W
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

23a

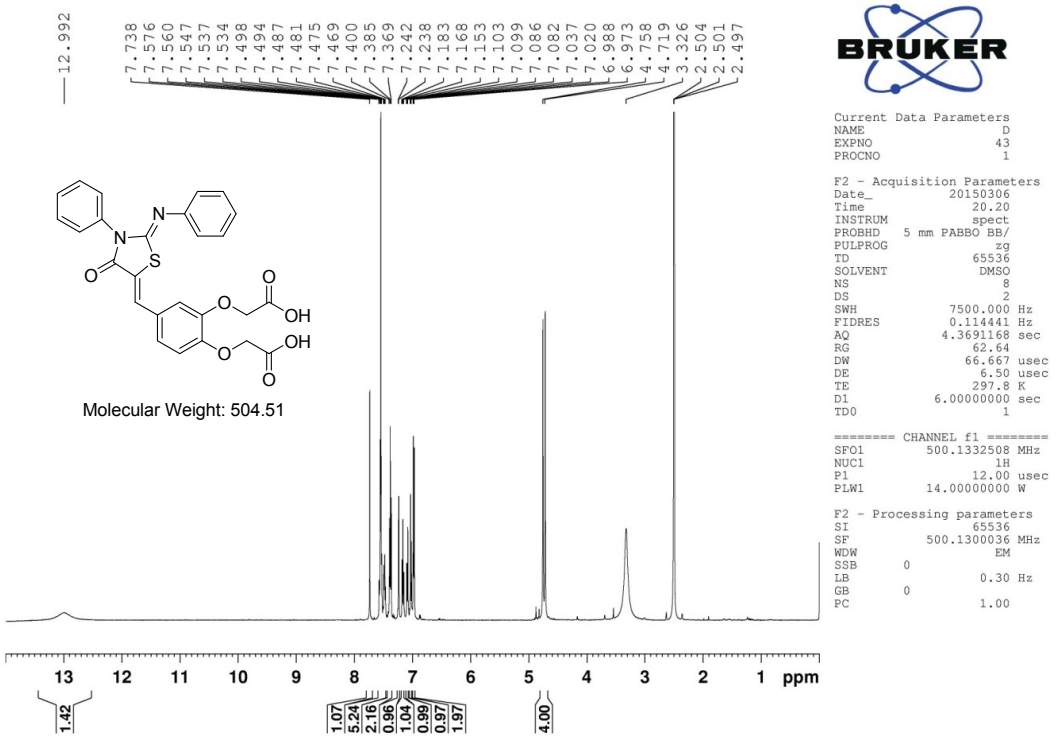

169.88
165.46
158.09
150.31
147.80
134.96
134.67
130.40
130.19
129.44
129.02
128.72
128.51
124.80
121.79
120.75
116.49
115.84
64.43
BRUKER
N
N
S
O
O
O
OH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

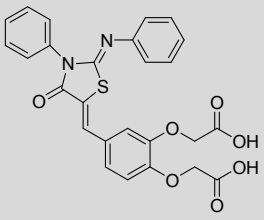
23b


23B
13.08
7.77
7.56
7.55
7.53
7.52
7.49
7.48
7.40
7.39
7.38
7.17
7.06
7.05
6.98
6.97
4.74
3.31
2.50
BRUKER
N
N
S
O
O
O
OH
Molecular Weight: 430.48
Current Data Parameters
NAME ly-benan-40h-5(2)
EXPNO 1
PROCNO 1
F2 - Acquisition Parameter
Date_ 20130527
Time 16.08
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 9615.385 Hz
FIDRES 0.146719 Hz
AQ 3.4079220 se
RG 256
DW 52.000 us
DE 6.50 us
TE 300.0 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
SFO1 600.1337000 MH
NUC1 1H
P1 13.70 us
PLW1 19.34000015 W
F2 - Processing parameters
SI 65536
SF 600.1300000 MH
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.80
1.00
6.23
1.22
2.31
1.09
2.10
2.18
2.24


wy-d2
170.20
166.19
159.62
151.04
148.47
135.55
132.20
130.84
129.31
129.50
129.14
129.02
126.78
125.19
121.28
118.92
115.86
64.98
40.43
40.29
40.15
40.01
39.87
39.73
Molecular Weight: 430.48
BRUKER
Current Data Parameters
NAME wy-d2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181031
Time 18.33
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 37874
SOLVENT DMSO
NS 1531
DS 0
SWH 37878.789 Hz
FIDRES 1.000126 Hz
AQ 0.4999368 sec
RG 2050
DW 13.200 usec
DE 6.50 usec
TE 298.5 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9178990 MHz
NUC1 13C
P1 9.00 usec
PLW1 41.50000000 W
======== CHANNEL f2 ========
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 19.34000015 W
PLW12 1.01040006 W
PLW13 0.49509999 W
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
220 200 180 160 140 120 100 80 60 40 20 0 ppm

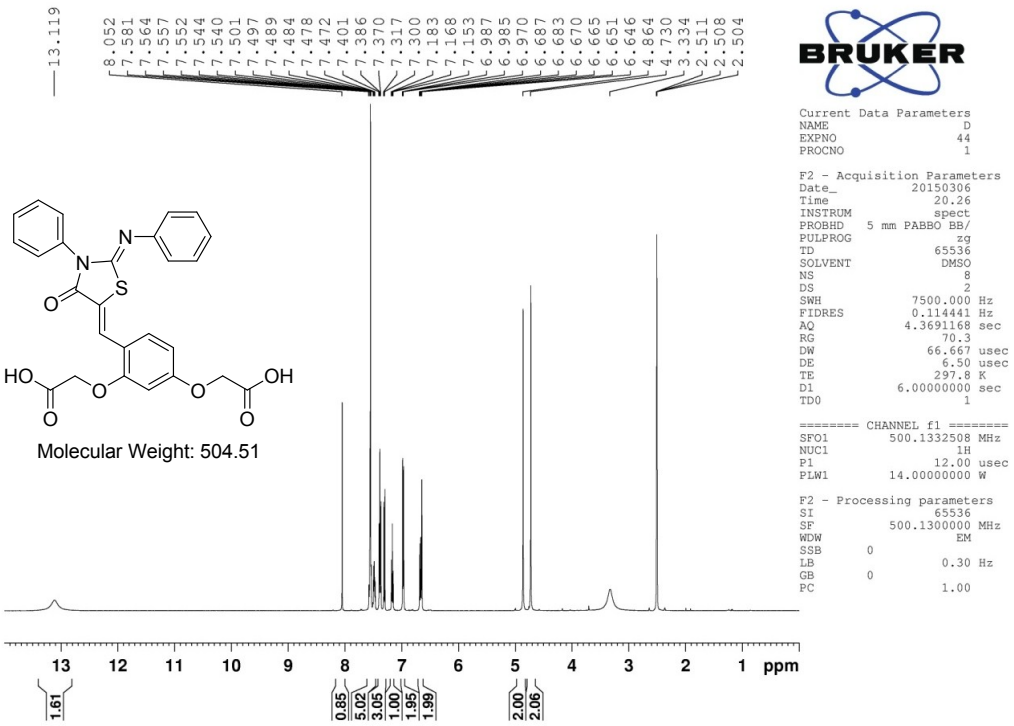
23c

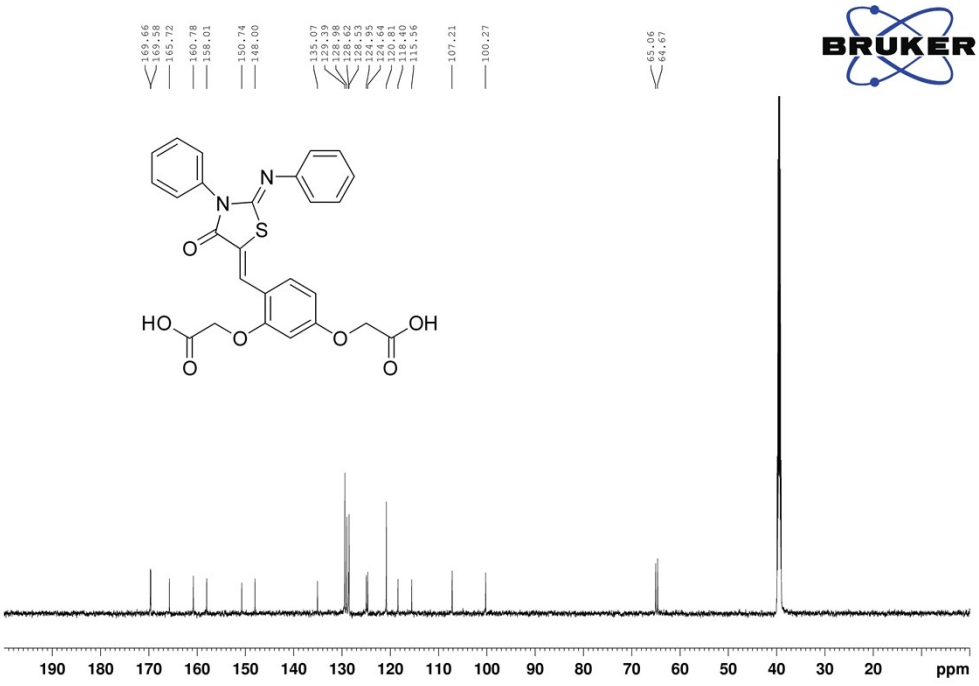

12.992
7.738
7.576
7.560
7.547
7.537
7.534
7.498
7.494
7.487
7.481
7.475
7.469
7.400
7.385
7.369
7.242
7.238
7.183
7.168
7.153
7.103
7.099
7.086
7.082
7.037
7.020
6.988
6.973
4.758
4.719
3.326
2.504
2.501
2.497
Molecular Weight: 504.51
BRUKER
Current Data Parameters
NAME D
EXPNO 43
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150306
Time 20.20
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 7500.000 Hz
FIDRES 0.114441 Hz
AQ 4.3691168 sec
RG 62.64
DW 66.667 usec
DE 6.50 usec
TE 297.8 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1332508 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300036 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.42
1.07
5.24
2.16
0.96
1.04
0.99
0.97
1.97
4.00



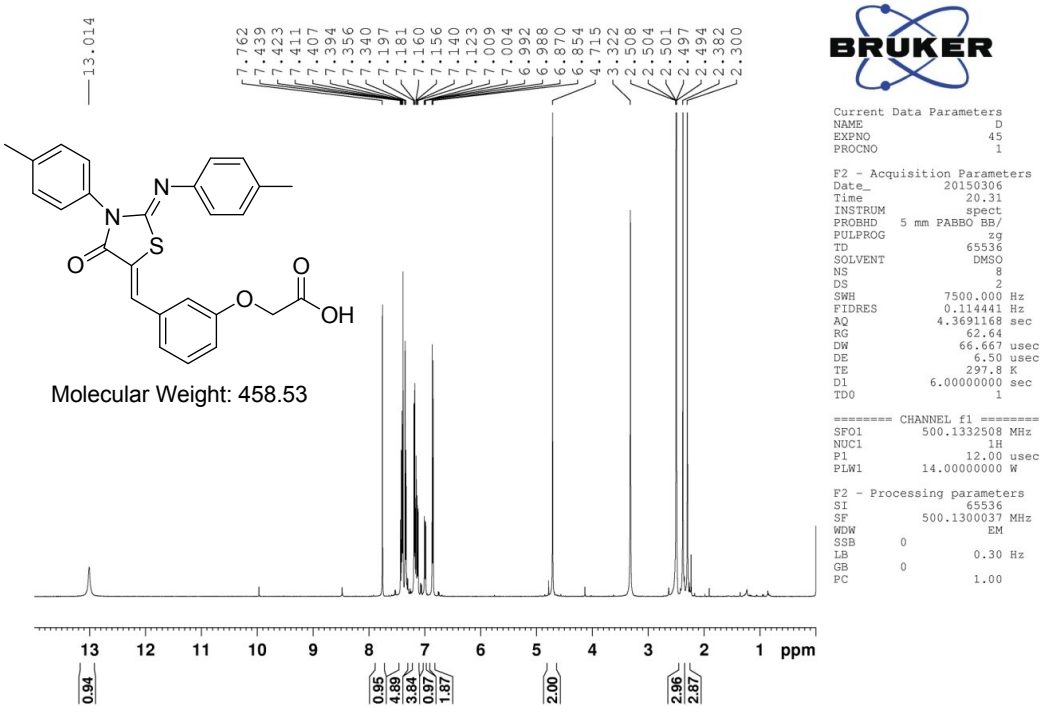
Molecular Weight: 504.51

23d



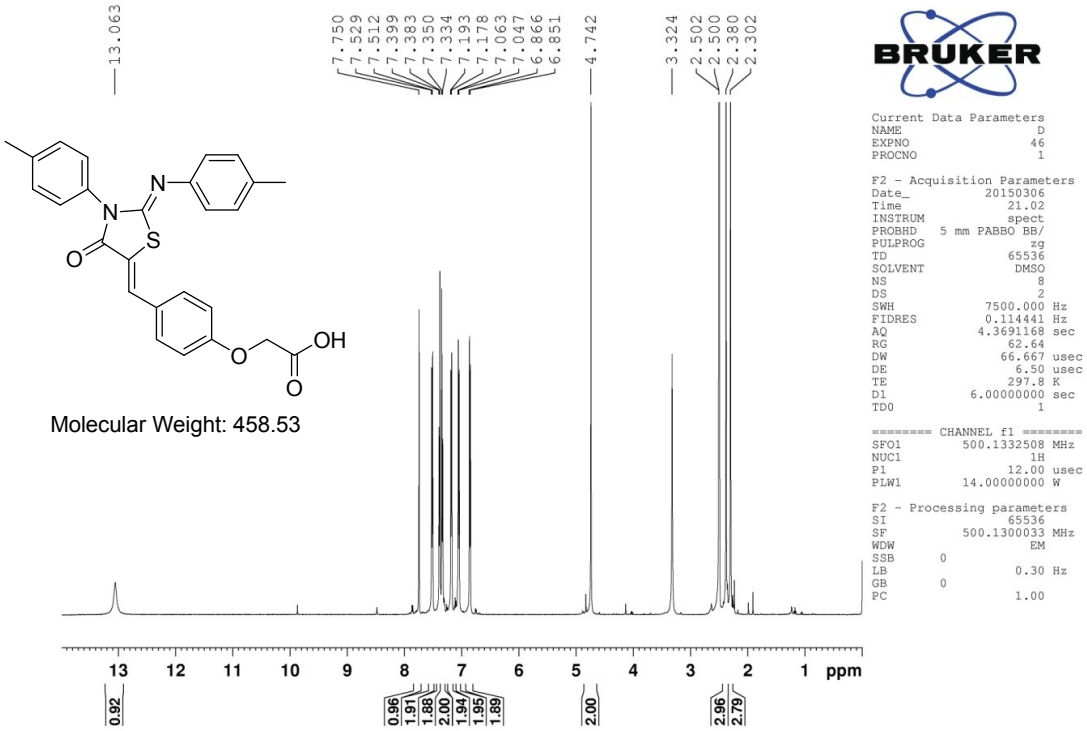


23e

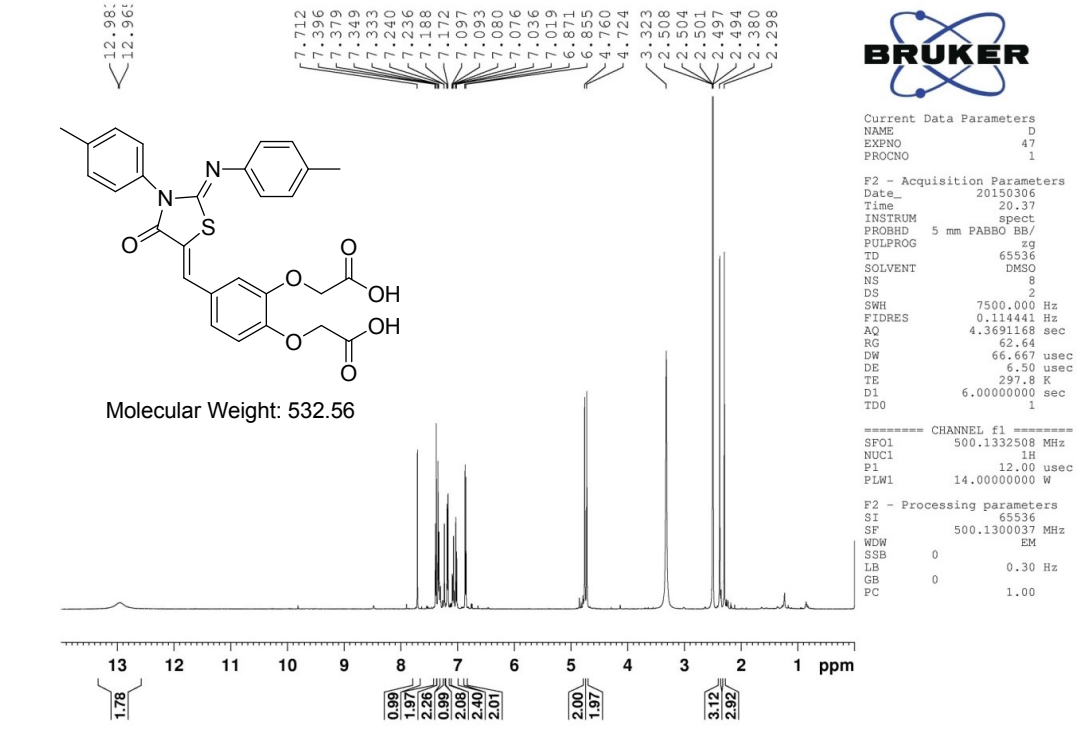



```
Current Data Parameters
NAME                  D
EXPNO                45
PROCNO                1

F2 - Acquisition Parameters
Date_          20150306
Time              20.31
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG              zg
TD                65536
SOLVENT             DMSO
NS                    8
DS                    2
SWH            7500.000 Hz
FIDRES            0.114441 Hz
AQ             4.3691168 sec
RG                62.64
DW               66.667 usec
DE                6.50 usec
TE                297.8 K
D1             6.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1          500.1332508 MHz
NUC1                  1H
P1                12.00 usec
PLW1          14.00000000 W

F2 - Processing parameters
SI                65536
SF            500.1300037 MHz
WDW                  EM
SSB                   0
LB                0.30 Hz
GB                    0
PC                1.00
```

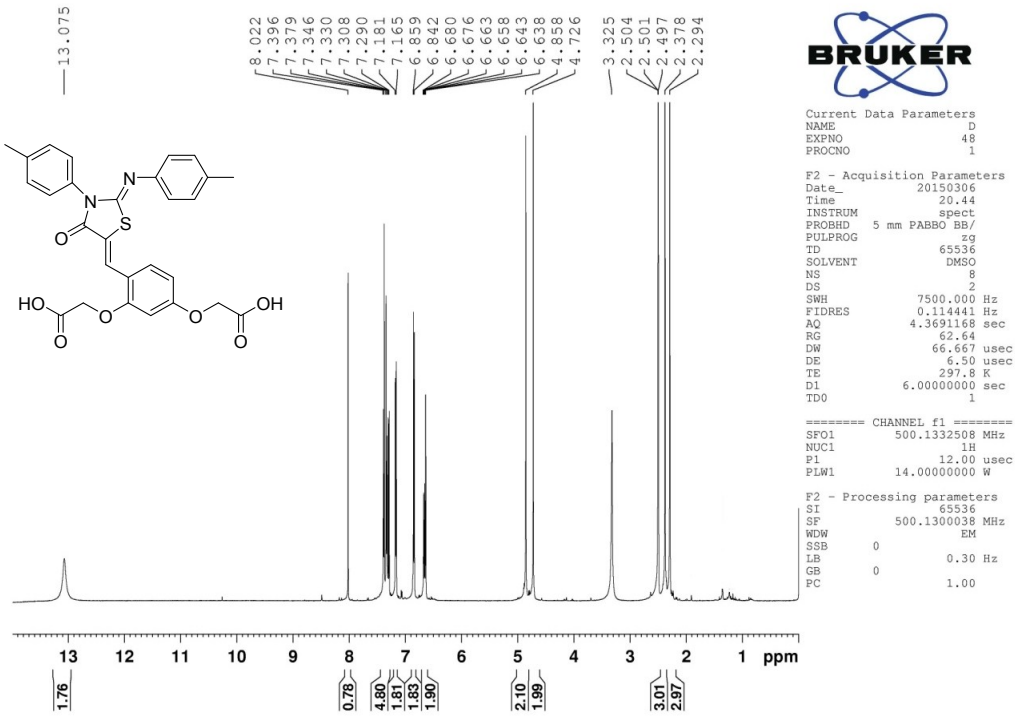
23f


13.063
7.750
7.529
7.512
7.399
7.383
7.350
7.334
7.193
7.178
7.063
7.047
6.866
6.851
4.742
3.324
2.502
2.500
2.380
2.302
OH
Molecular Weight: 458.53
BRUKER
Current Data Parameters
NAME D
EXPNO 46
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150306
Time 21.02
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 7500.000 Hz
FIDRES 0.114441 Hz
AQ 4.3691168 sec
RG 62.64
DW 66.667 usec
DE 6.50 usec
TE 297.8 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1332508 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.92
0.96 1.91 1.88 2.00 1.94 1.95 1.89
2.00
2.96 2.79

23g


12.98
12.96
7.712
7.396
7.379
7.349
7.333
7.240
7.236
7.188
7.172
7.097
7.093
7.080
7.076
7.036
7.019
6.871
6.855
4.760
4.724
3.323
2.508
2.504
2.501
2.497
2.494
2.380
2.298
OH
OH
Molecular Weight: 532.56
BRUKER
Current Data Parameters
NAME D
EXPNO 47
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150306
Time 20.37
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 7500.000 Hz
FIDRES 0.114441 Hz
AQ 4.3691168 sec
RG 62.64
DW 66.667 usec
DE 6.50 usec
TE 297.8 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1332508 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300037 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.78
0.99 1.97 2.26 0.99 2.08 2.40 2.01
2.00 1.97
3.12 2.92

23h

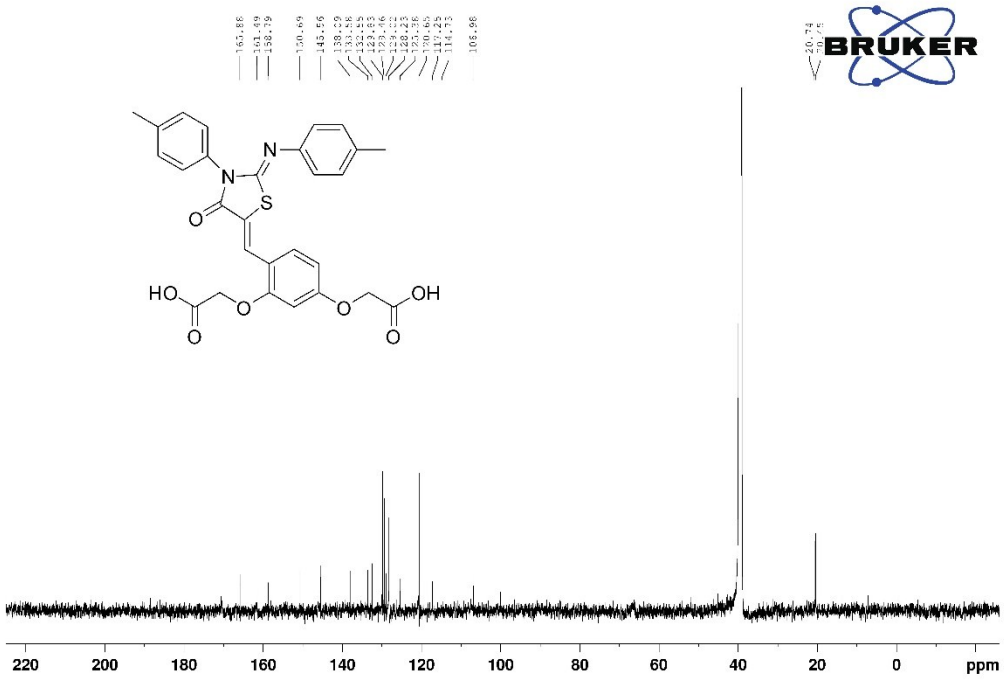


Current Data Parameters
NAME D
EXPNO 48
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150306
Time 20.44
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 7500.000 Hz
FIDRES 0.114441 Hz
AQ 4.3691168 sec
RG 62.64
DW 66.667 usec
DE 6.50 usec
TE 297.8 K
D1 6.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 500.1332508 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W

F2 - Processing parameters
SI 65536
SF 500.1300038 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



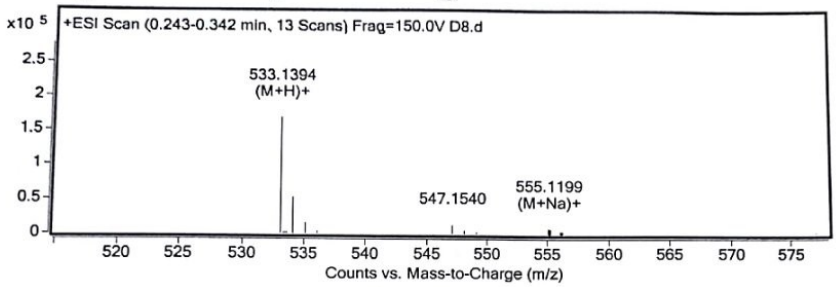
Qualitative Analysis Report

Data Filename	D8.d	**Sample Name**	
Sample Type	Sample	**Position**	P1-C1
Instrument Name	Instrument 1	**User Name**	
Acq Method	TEST-POS-WL.m	**Acquired Time**	12/22/2017 11:07:02 AM
IRM Calibration Status	Success	**DA Method**	E.m
Comment			

Sample Group **Info.**

User Spectra

Fragmentor Voltage 150 **Collision Energy** 0 **Ionization Mode** ESI



Peak List

m/z	z	Abund	Formula	Ion
121.0509	1	121445.4		
122.0536	1	7527.8		
130.1589	1	73861.5		
150.1042		8479.4		
338.3418	1	16208.6		
533.1394	1	167716.7	C28 H25 N2 O7 S	(M+H)+
534.1417	1	52480.1	C28 H25 N2 O7 S	(M+H)+
535.1409	1	16091.5	C28 H25 N2 O7 S	(M+H)+
547.154	1	12061.1		
922.0096	1	41004.5		

Formula Calculator Element Limits

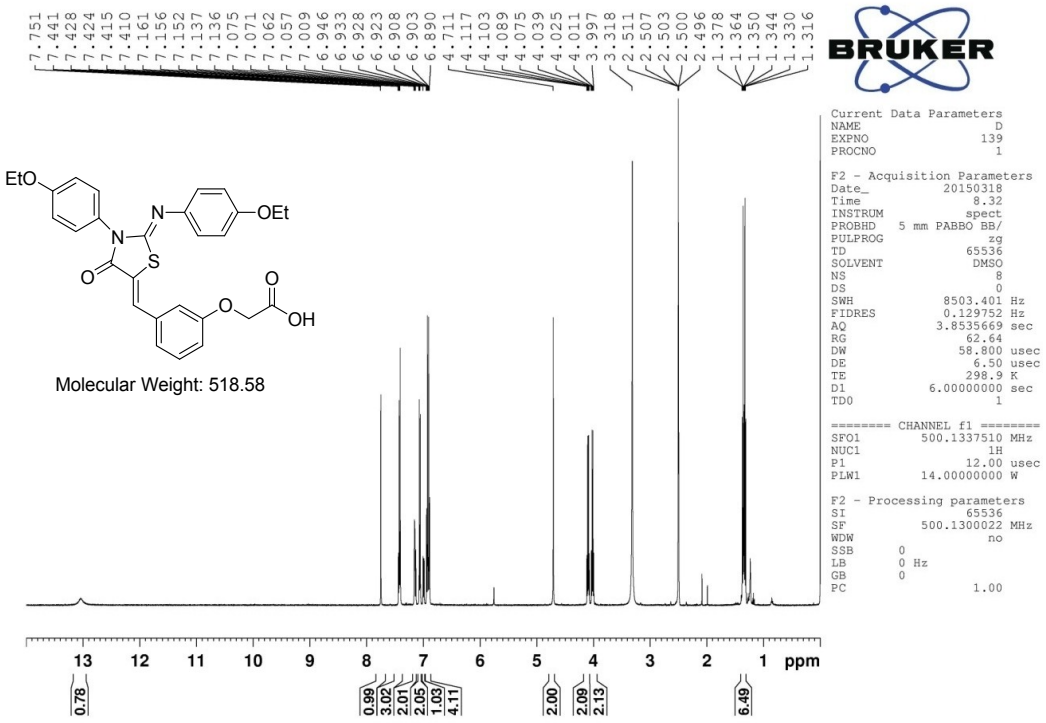
Element	Min	Max
C	0	100
H	0	100
O	7	7
N	2	2
S	1	1

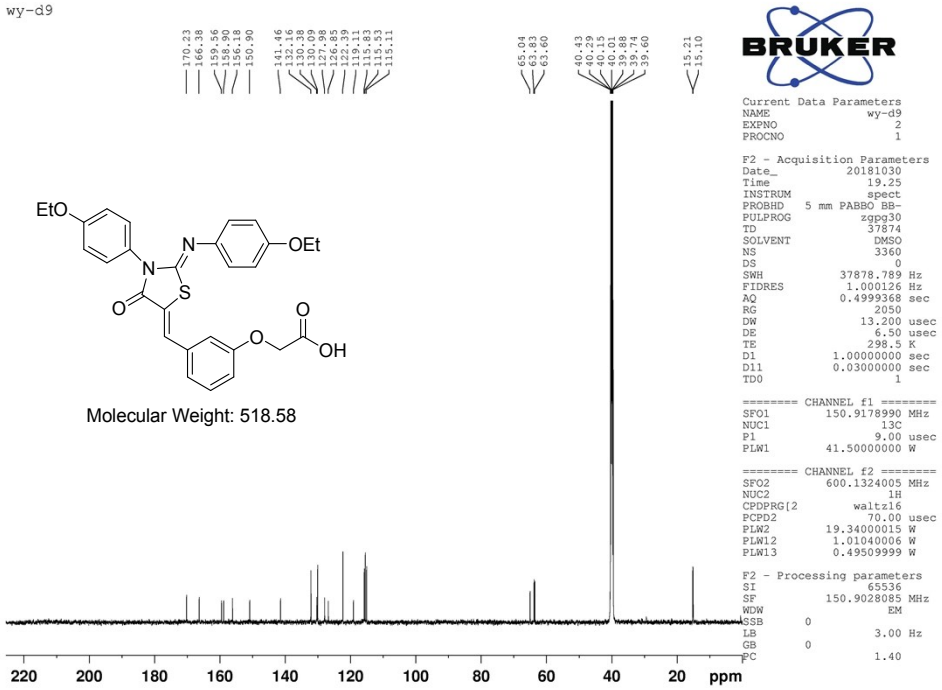
Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C28 H24 N2 O7 S	TRUE	532.1321	532.1304	-3.18	C28 H25 N2 O7 S	93.82
C28 H24 N2 O7 S	TRUE	532.1307	532.1304	-0.53	C28 H24 N2 Na O7 S	98.31

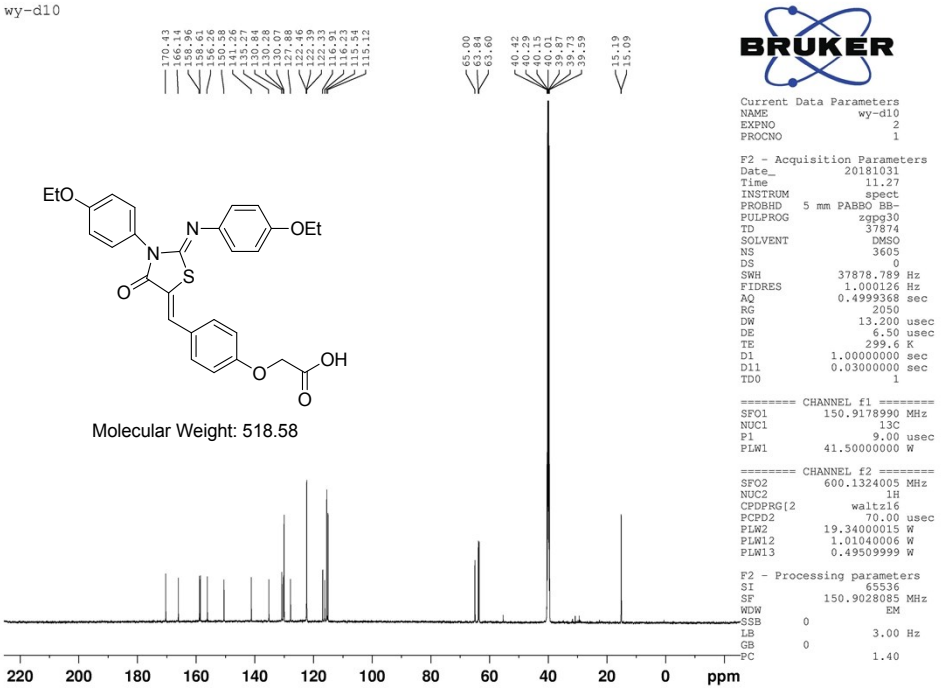
--- End Of Report ---

23i

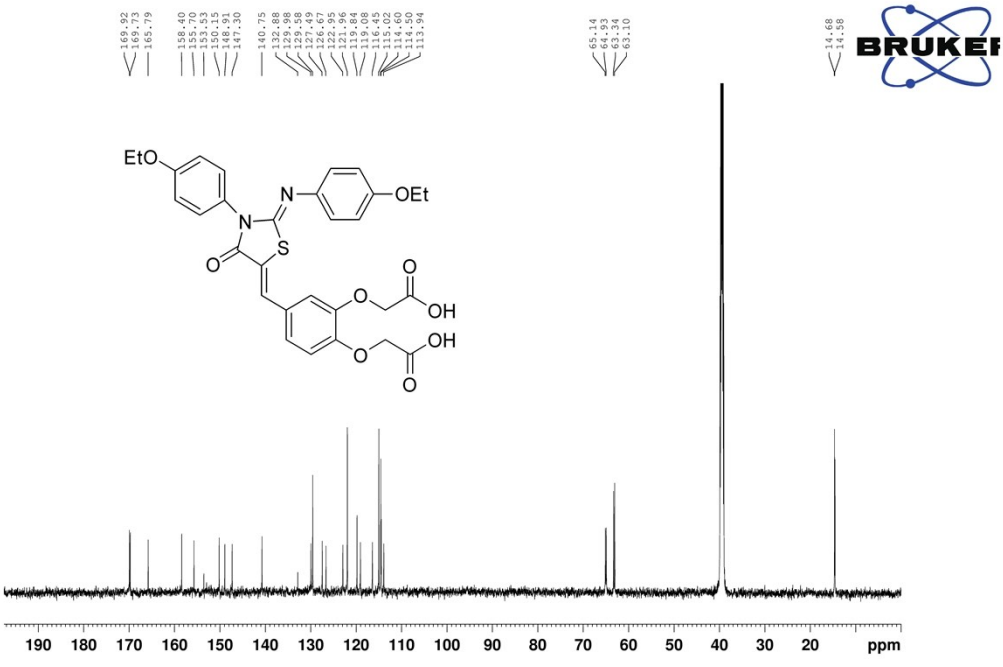

7.751 7.441 7.428 7.424 7.415 7.410 7.161 7.156 7.152 7.137 7.136 7.075 7.071 7.062 7.057 7.009 6.946 6.933 6.928 6.923 6.908 6.903 6.890 4.711 4.117 4.103 4.089 4.075 4.039 4.025 4.011 3.997 3.318 2.511 2.507 2.503 2.500 2.496 1.378 1.364 1.350 1.344 1.330 1.316
BRUKER
Current Data Parameters
NAME D
EXPNO 139
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150318
Time 8.32
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 8503.401 Hz
FIDRES 0.129752 Hz
AQ 3.8535669 sec
RG 62.64
DW 58.800 usec
DE 6.50 usec
TE 298.9 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1337510 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300022 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
EtO
N
OEt
N
S
O
O
O
OH
Molecular Weight: 518.58
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.78 0.99 3.02 2.01 2.05 1.03 4.11 2.00 2.09 2.13 6.49


wy-d9
170.23 166.38 158.96 158.90 156.18 150.90 141.46 132.16 130.38 130.09 127.98 126.85 122.39 119.11 118.83 115.53 115.11 65.04 63.83 63.60 40.43 40.29 40.15 40.01 39.88 39.74 39.60 15.21 15.10
BRUKER
Current Data Parameters
NAME wy-d9
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181030
Time 19.25
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 37874
SOLVENT DMSO
NS 3360
DS 0
SWH 37878.789 Hz
FIDRES 1.000126 Hz
AQ 0.4999368 sec
RG 2050
DW 13.200 usec
DE 6.50 usec
TE 298.5 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9178990 MHz
NUC1 13C
P1 9.00 usec
PLW1 41.50000000 W
======== CHANNEL f2 ========
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 19.34000015 W
PLW12 1.01040006 W
PLW13 0.49509999 W
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
EtO
N
OEt
N
S
O
O
O
OH
Molecular Weight: 518.58
220 200 180 160 140 120 100 80 60 40 20 ppm

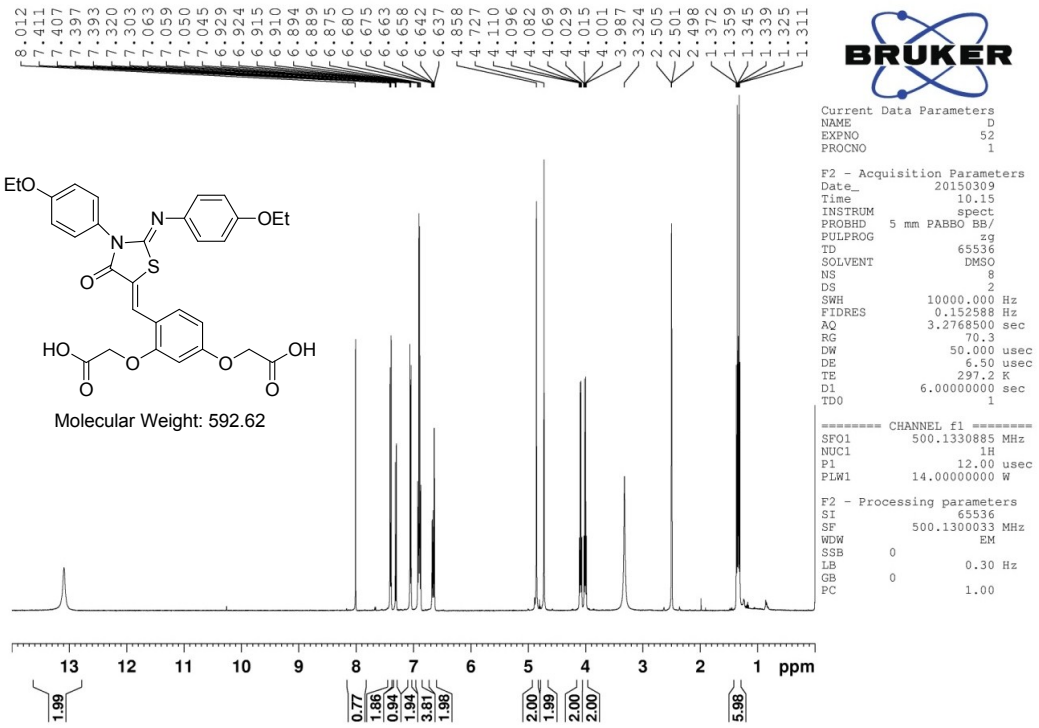
23j

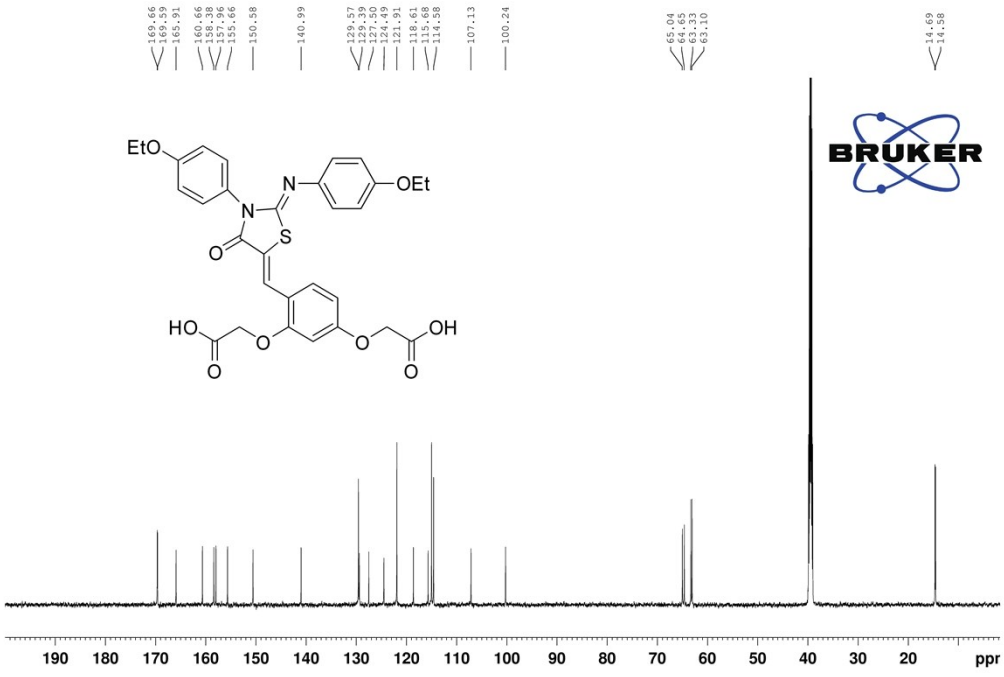

wy-d10
170.43
166.14
158.96
156.61
154.26
150.58
141.26
135.27
130.84
130.38
130.07
127.88
122.46
122.39
122.33
116.91
116.23
115.54
115.12
65.00
63.88
63.60
40.42
40.29
40.15
40.01
39.87
39.73
39.59
15.19
15.09
EtO
N
OEt
N
S
O
O
OH
O
Molecular Weight: 518.58
220
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
Current Data Parameters
NAME wy-d10
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181031
Time 11.27
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 37874
SOLVENT DMSO
NS 3605
DS 0
SWH 37878.789 Hz
FIDRES 1.000126 Hz
AQ 0.4999368 sec
RG 2050
DW 13.200 usec
DE 6.50 usec
TE 299.6 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9178990 MHz
NUC1 13C
P1 9.00 usec
PLW1 41.50000000 W
======== CHANNEL f2 ========
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 19.34000015 W
PLW12 1.01040006 W
PLW13 0.49509999 W
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

23k

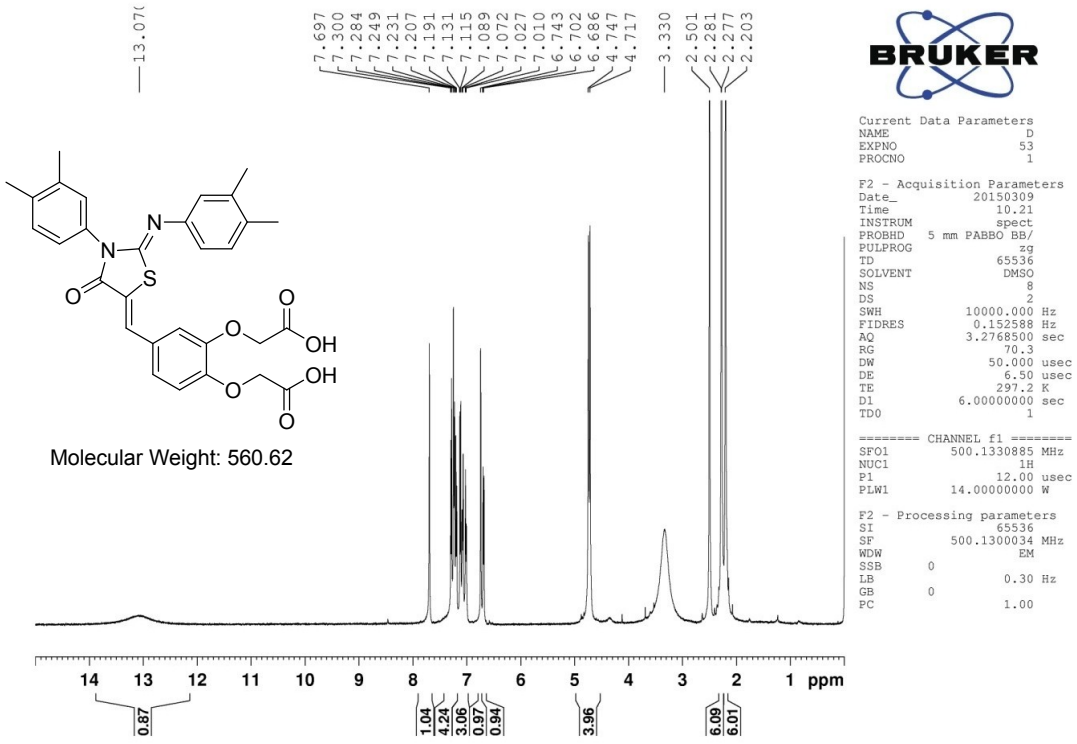

169.92
169.73
165.79
158.40
155.70
153.53
150.15
148.91
147.30
140.75
132.88
129.98
129.58
127.49
126.67
122.95
121.96
119.84
119.08
116.45
115.02
114.60
114.50
113.94
65.14
64.83
63.34
63.10
14.68
14.58
EtO
N
OEt
N
S
O
O
OH
O
OH
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
BRUKER

23l


8.012
7.411
7.407
7.397
7.393
7.320
7.303
7.063
7.059
7.050
7.045
6.929
6.924
6.915
6.910
6.894
6.889
6.875
6.680
6.675
6.663
6.658
6.642
6.637
4.858
4.727
4.110
4.096
4.082
4.069
4.029
4.015
4.001
3.987
3.324
2.505
2.501
2.498
1.372
1.359
1.345
1.339
1.325
1.311
EtO
N
OEt
N
S
O
HO
O
O
OH
O
O
Molecular Weight: 592.62
BRUKER
Current Data Parameters
NAME D
EXPNO 52
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time 10.15
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.2 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.99
0.77
1.86
0.94
1.94
3.81
1.98
2.00
1.99
2.00
2.00
5.98


169.66
169.59
165.91
160.66
158.38
157.96
155.66
150.58
140.99
129.57
129.39
127.50
124.49
121.91
118.61
115.68
114.58
107.13
100.24
65.04
64.65
63.33
63.10
14.69
14.58
EtO
N
OEt
N
S
O
HO
O
O
OH
O
O
BRUKER
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

23m

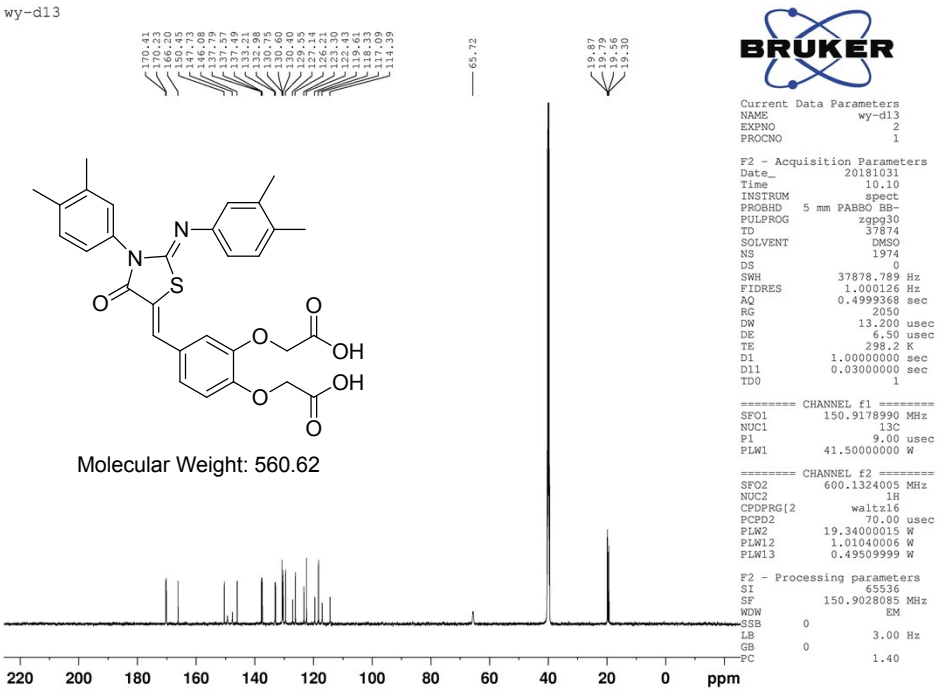


Current Data Parameters
NAME D
EXPNO 53
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150309
Time 10.21
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.2 K
D1 6.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W

F2 - Processing parameters
SI 65536
SF 500.1300034 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Current Data Parameters
NAME wy-d13
EXPNO 2
PROCNO 1

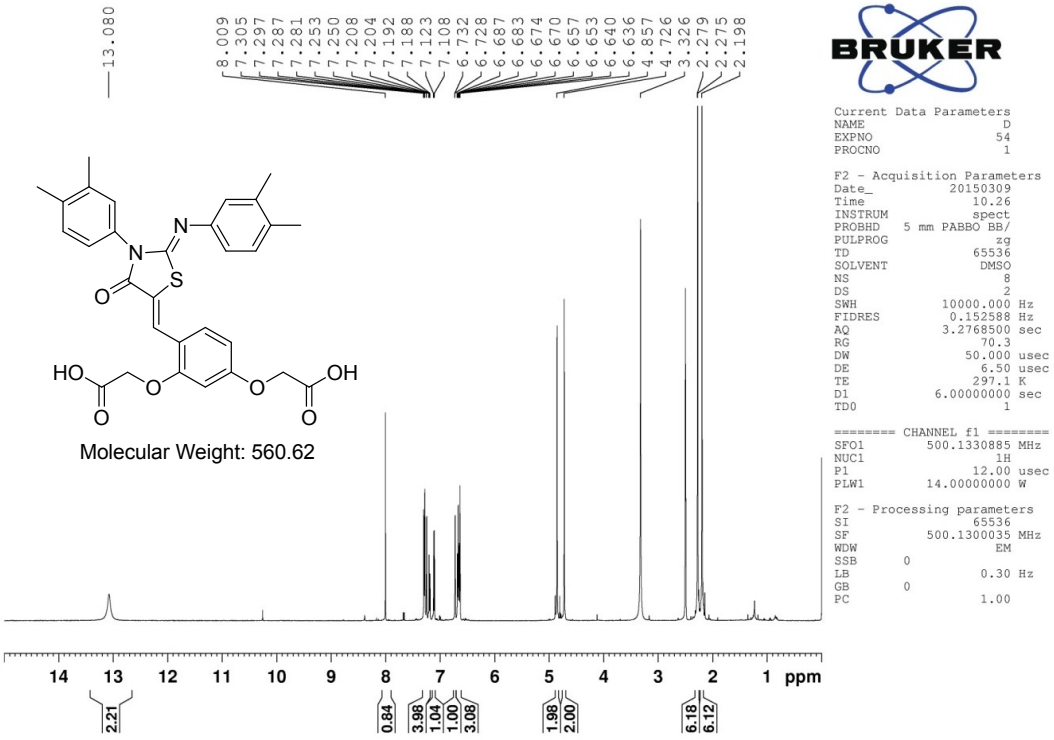
F2 - Acquisition Parameters
Date_ 20181031
Time 10.10
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 37874
SOLVENT DMSO
NS 1974
DS 0
SWH 37878.789 Hz
FIDRES 1.000126 Hz
AQ 0.4999368 sec
RG 2050
DW 13.200 usec
DE 6.50 usec
TE 298.2 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1

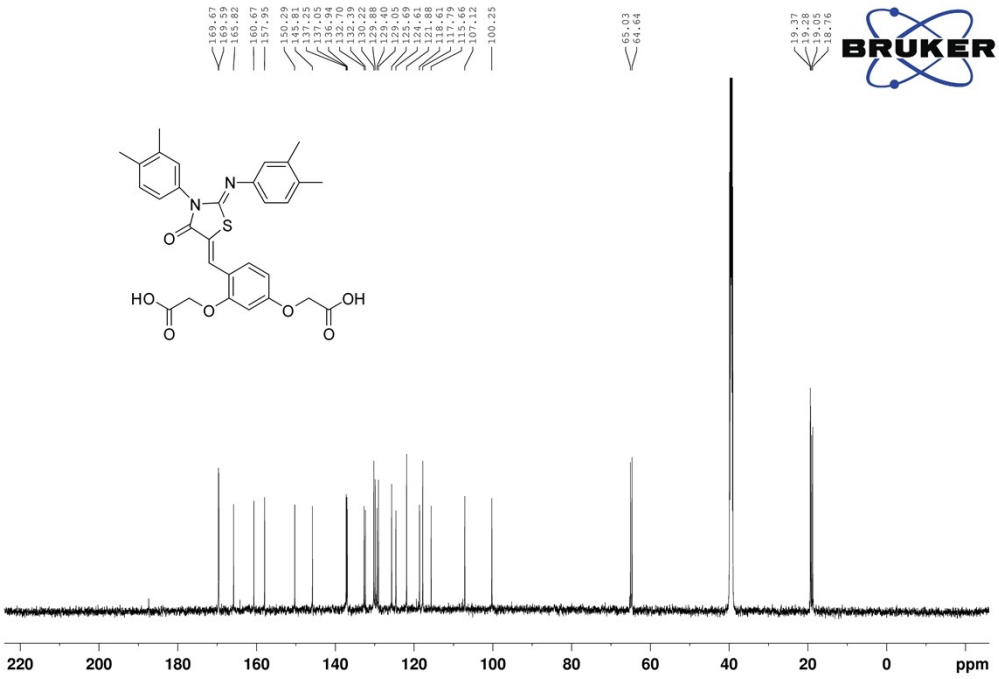
======== CHANNEL f1 ========
SFO1 150.9178990 MHz
NUC1 13C
P1 9.00 usec
PLW1 41.50000000 W

======== CHANNEL f2 ========
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 19.34000015 W
PLW12 1.01040006 W
PLW13 0.49509999 W

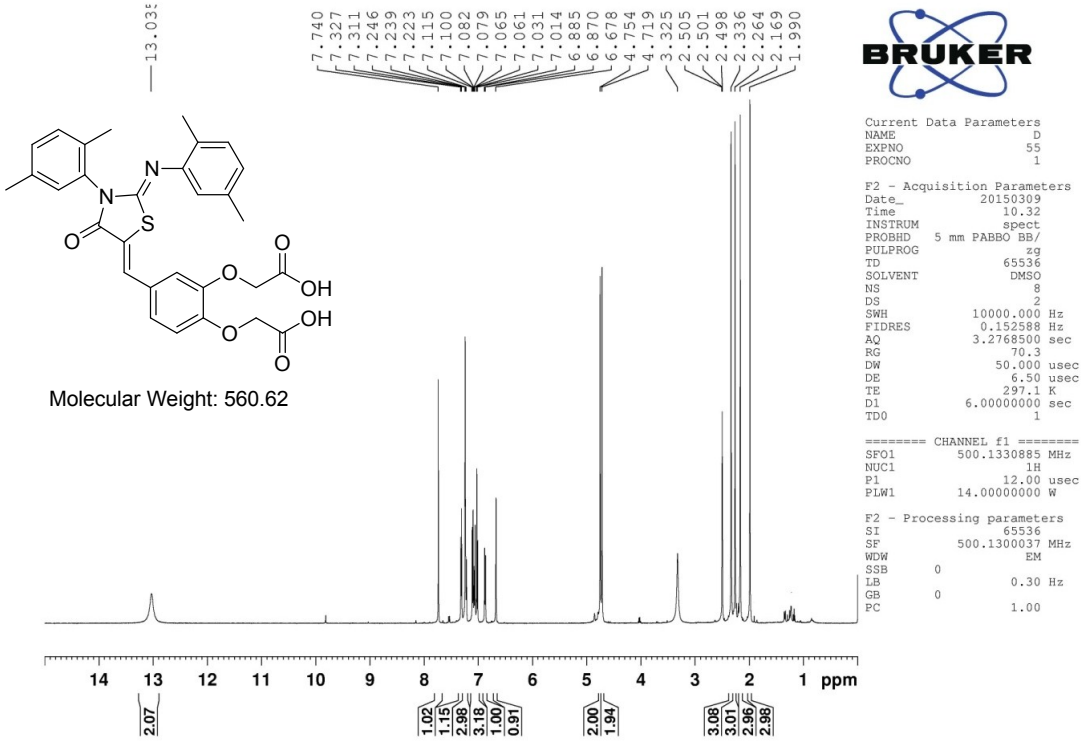
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

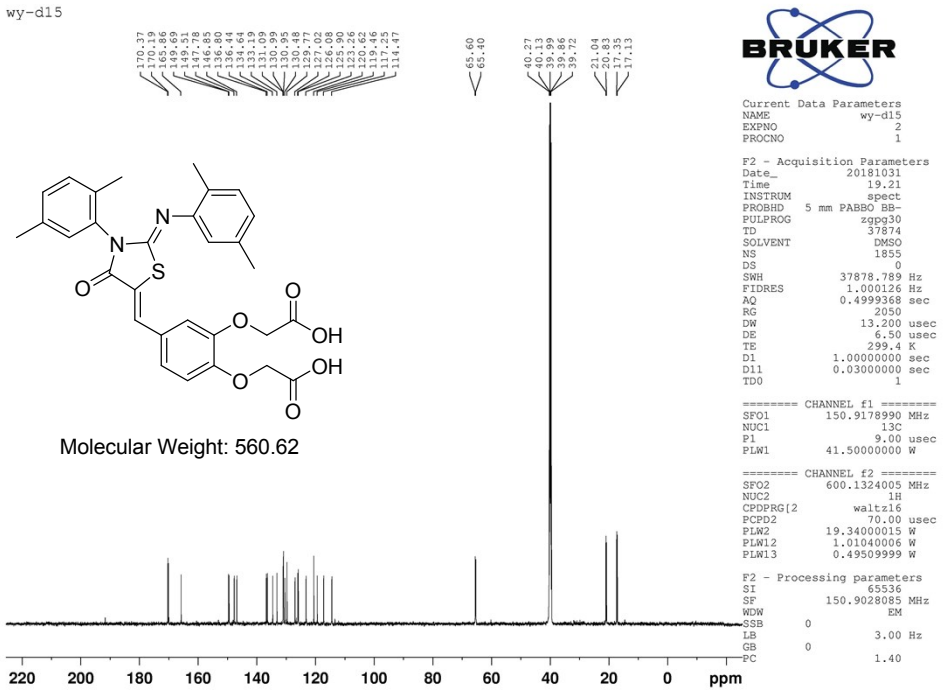
23n


13.080
8.009
7.305
7.297
7.287
7.281
7.253
7.250
7.208
7.204
7.192
7.188
7.123
7.108
6.732
6.728
6.687
6.683
6.674
6.670
6.657
6.653
6.640
6.636
4.857
4.726
3.326
2.279
2.275
2.198
HO
OH
Molecular Weight: 560.62
BRUKER
Current Data Parameters
NAME D
EXPNO 54
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time 10.26
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.1 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300035 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
2.21
0.84
3.98
1.04
1.00
3.08
1.98
2.00
6.18
6.12

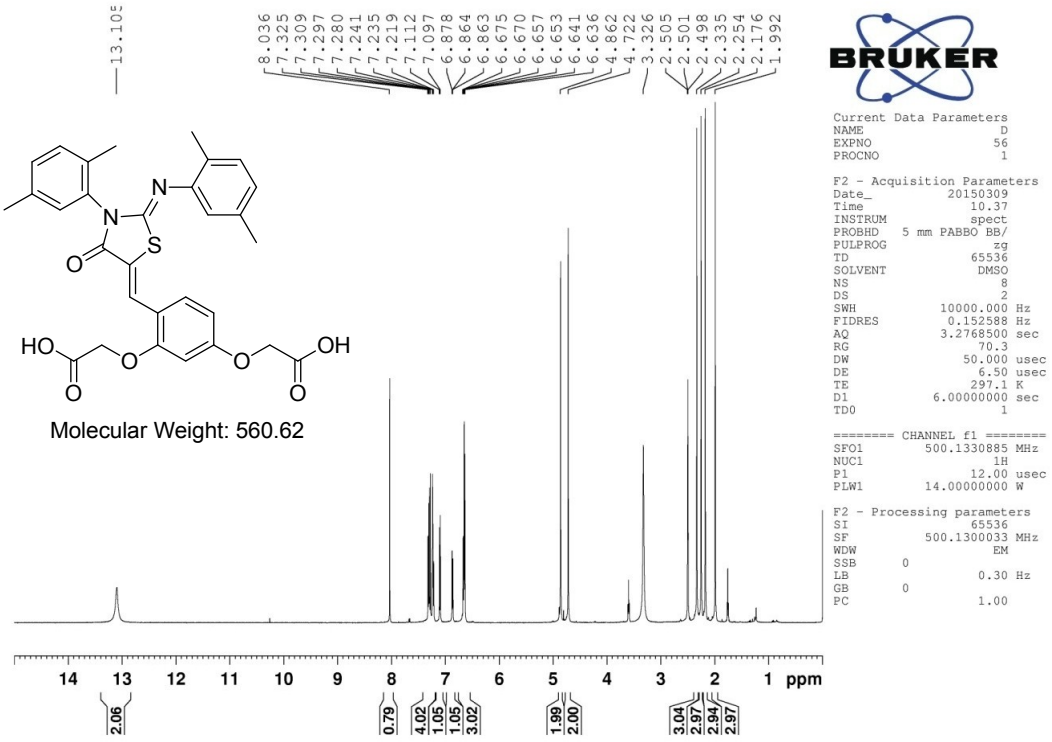

169.67
169.39
160.32
160.67
157.55
150.29
145.81
137.25
137.05
136.94
132.70
132.39
130.22
129.88
129.40
129.05
123.69
122.61
121.88
118.61
117.79
115.66
107.12
100.25
65.03
64.64
19.37
19.28
19.05
18.76
BRUKER
HO
OH
220 200 180 160 140 120 100 80 60 40 20 0 ppm

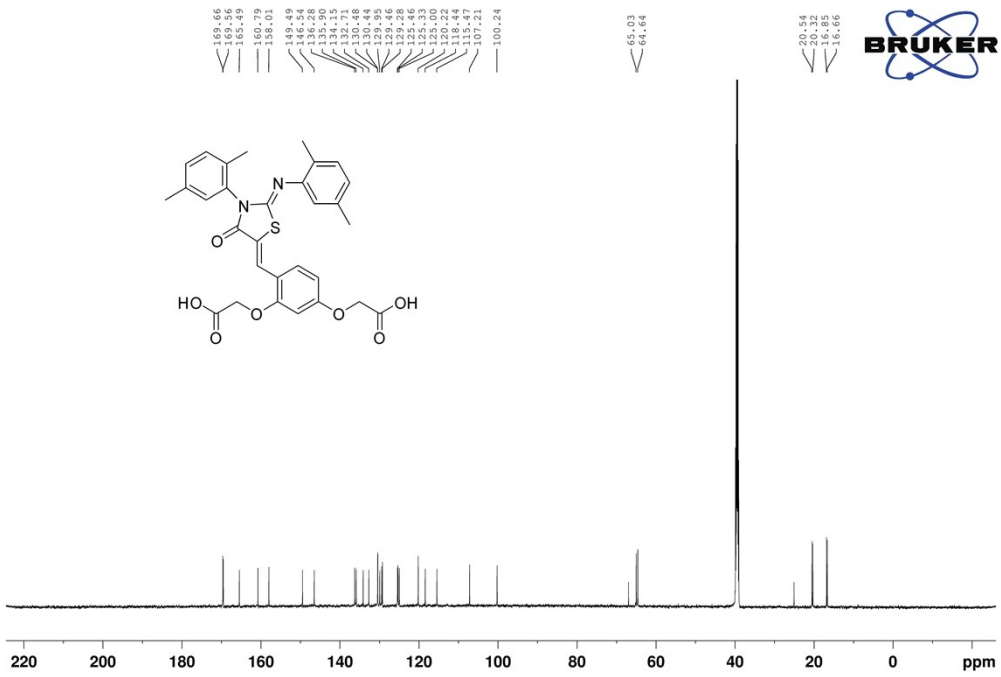
23o


13.035
7.740
7.327
7.311
7.246
7.239
7.223
7.115
7.100
7.082
7.079
7.065
7.061
7.031
7.014
6.885
6.870
6.678
4.754
4.719
3.325
2.505
2.501
2.498
2.336
2.264
2.169
1.990
Molecular Weight: 560.62
Current Data Parameters
NAME D
EXPNO 55
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time 10.32
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.1 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300037 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
2.07
1.02 1.15 2.98 3.18 1.00 0.91
2.00 1.94
3.06 3.01 2.96 2.98

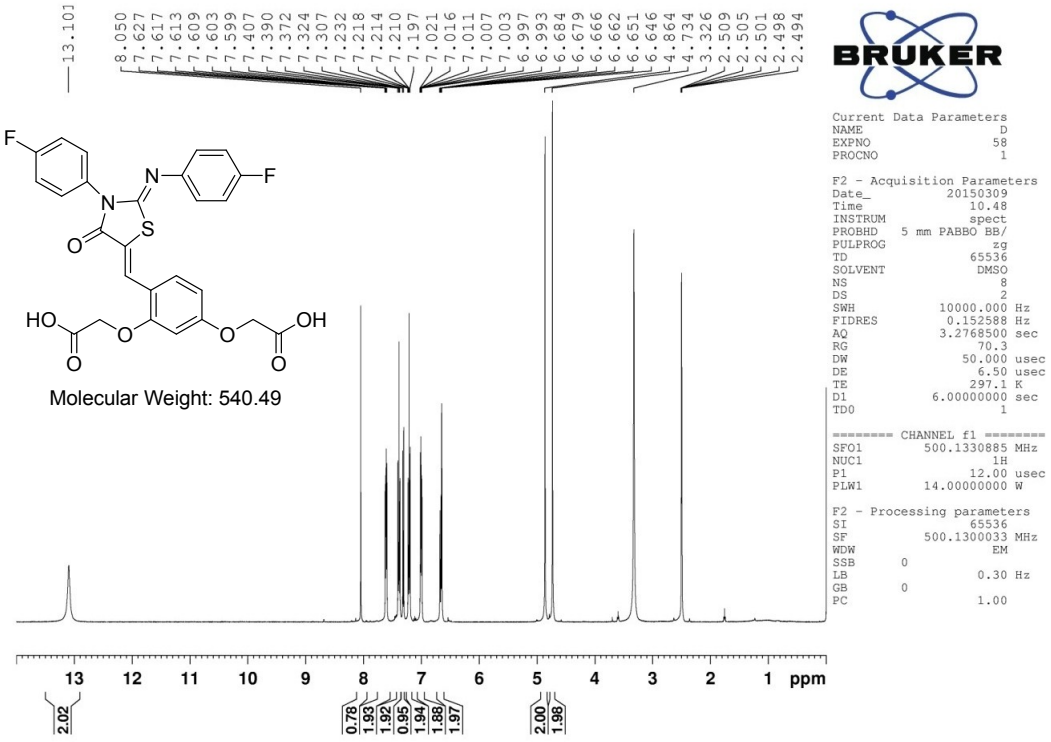

wy-d15
170.37
170.19
165.86
149.69
148.91
147.78
146.85
136.80
136.44
134.44
133.19
131.09
130.99
130.48
130.45
129.77
127.02
126.08
125.80
123.26
120.62
119.46
117.25
114.47
65.60
65.40
40.27
40.13
39.99
39.86
39.72
21.04
20.83
17.35
17.13
Molecular Weight: 560.62
Current Data Parameters
NAME wy-d15
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20181031
Time 19.21
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 37874
SOLVENT DMSO
NS 1855
DS 0
SWH 37878.789 Hz
FIDRES 1.000126 Hz
AQ 0.4999368 sec
RG 2050
DW 13.200 usec
DE 6.50 usec
TE 299.4 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9178990 MHz
NUC1 13C
P1 9.00 usec
PLW1 41.50000000 W
======== CHANNEL f2 ========
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 19.34000015 W
PLW12 1.01040006 W
PLW13 0.49509999 W
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
220 200 180 160 140 120 100 80 60 40 20 0 ppm

23p

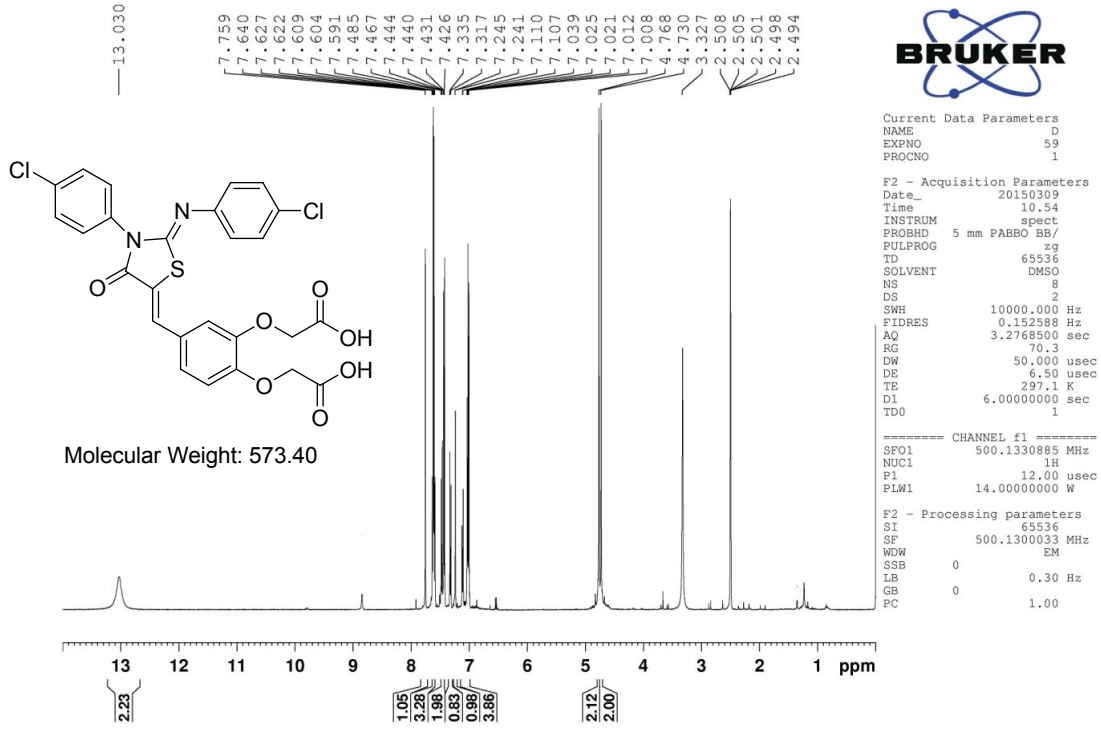

Molecular Weight: 560.62
Current Data Parameters
NAME D
EXPNO 56
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time 10.37
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.1 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm

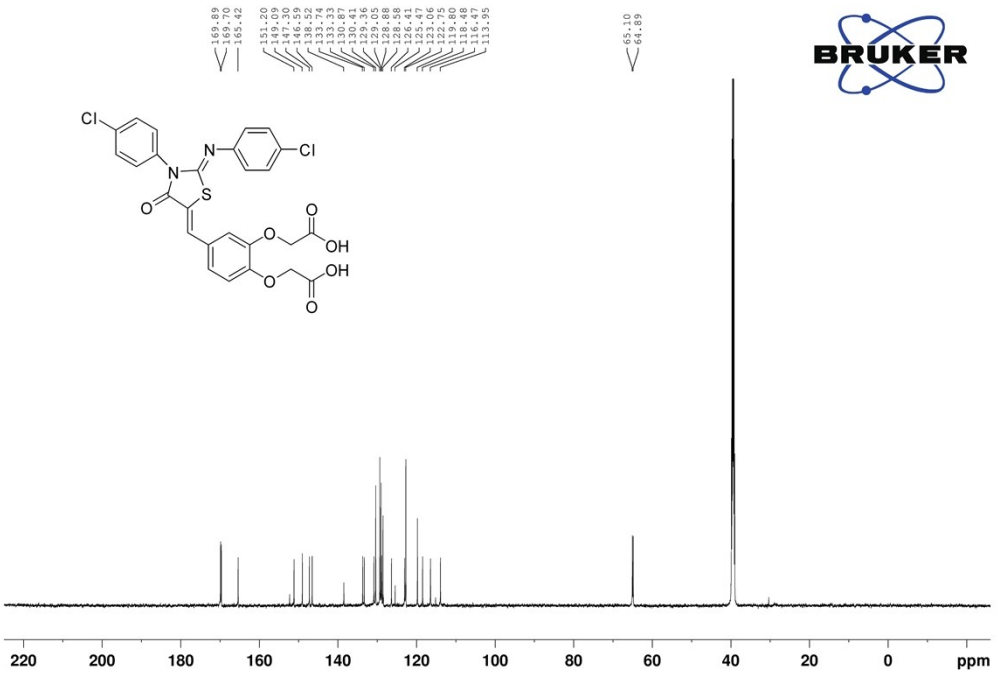

ppm

23r

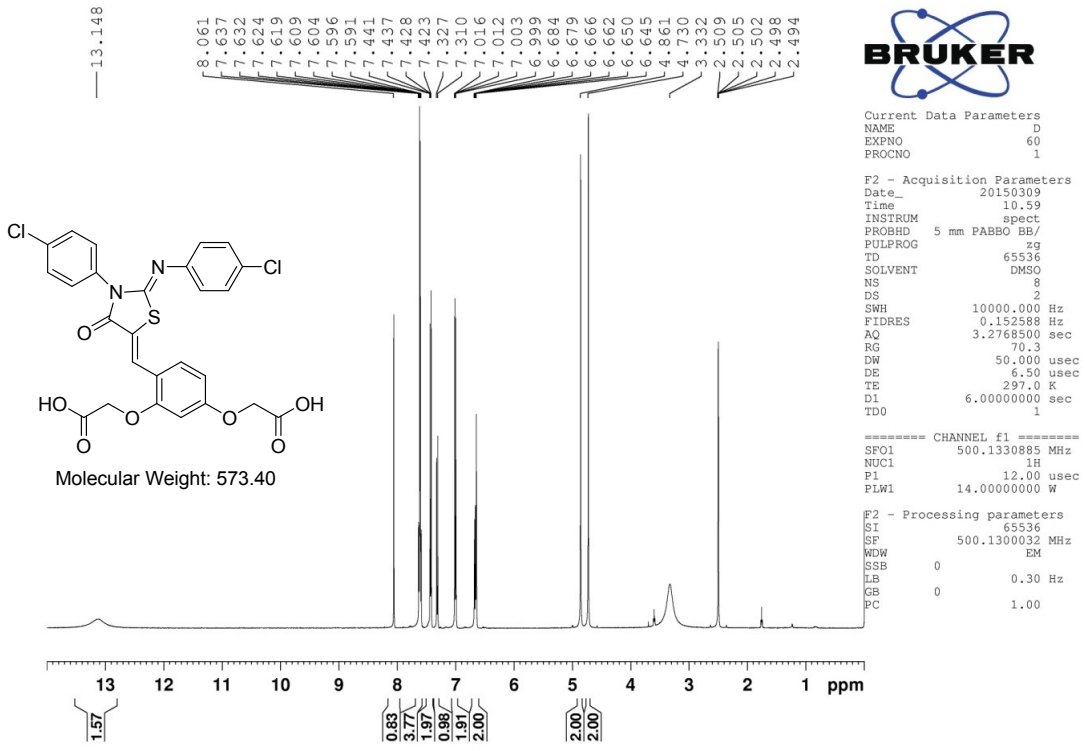

13.101
8.050
7.627
7.617
7.613
7.609
7.603
7.599
7.407
7.390
7.372
7.324
7.307
7.232
7.218
7.214
7.210
7.197
7.021
7.016
7.011
7.007
7.003
6.997
6.993
6.684
6.679
6.666
6.662
6.651
6.646
4.864
4.734
3.326
2.509
2.505
2.501
2.498
2.494
F
N
F
N
S
O
HO
O
O
O
OH
O
O
Molecular Weight: 540.49
BRUKER
Current Data Parameters
NAME D
EXPNO 58
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time 10.48
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.1 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
2.02
0.78 1.93 1.92 0.95 1.94 1.88 1.97
2.00 1.98

23s


13.030
7.759
7.640
7.627
7.622
7.609
7.604
7.591
7.485
7.467
7.444
7.440
7.431
7.426
7.335
7.317
7.245
7.241
7.110
7.107
7.039
7.025
7.021
7.012
7.008
4.768
4.730
3.327
2.508
2.505
2.501
2.498
2.494
Cl
N
Cl
N
S
O
O
O
OH
O
OH
O
Molecular Weight: 573.40
BRUKER
Current Data Parameters
NAME D
EXPNO 59
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time 10.54
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.1 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
2.23
1.05 3.28 1.98 0.83 0.98 3.86
2.12 2.00



23t

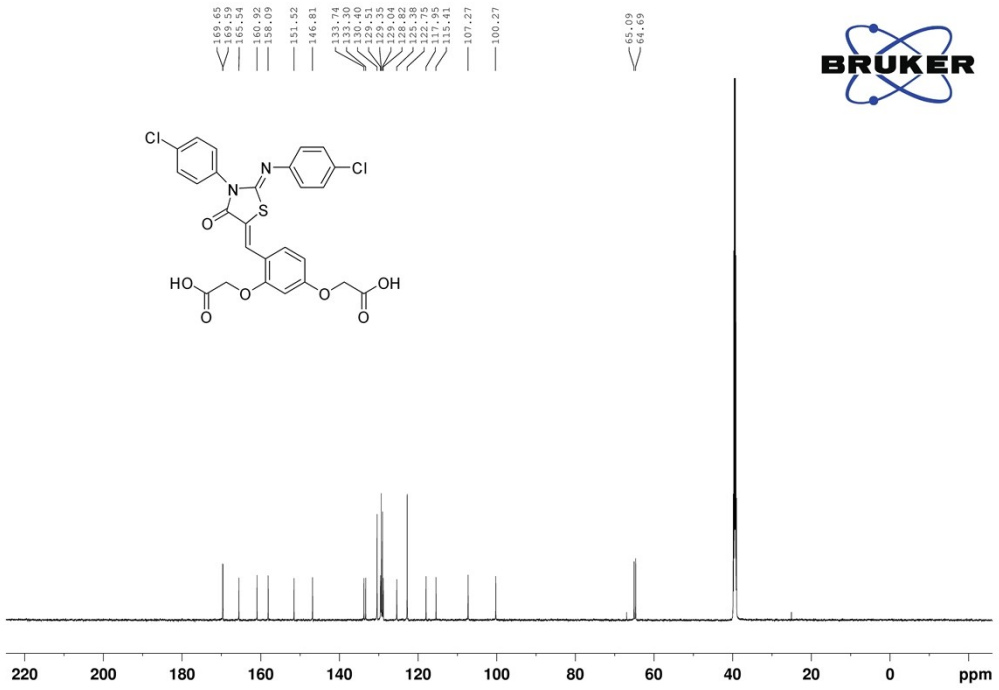


Current Data Parameters
NAME D
EXPNO 60
PROCNO 1

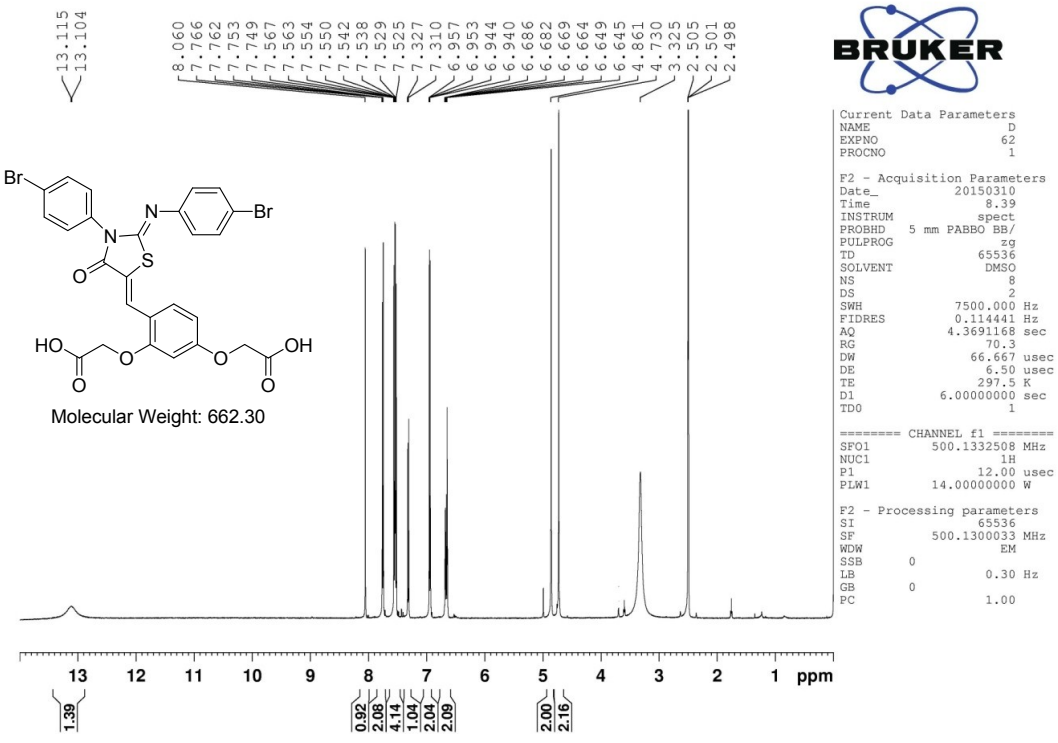
F2 - Acquisition Parameters
Date_ 20150309
Time 10.59
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 70.3
DW 50.000 usec
DE 6.50 usec
TE 297.0 K
D1 6.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 500.1330885 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W

F2 - Processing parameters
SI 65536
SF 500.1300032 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

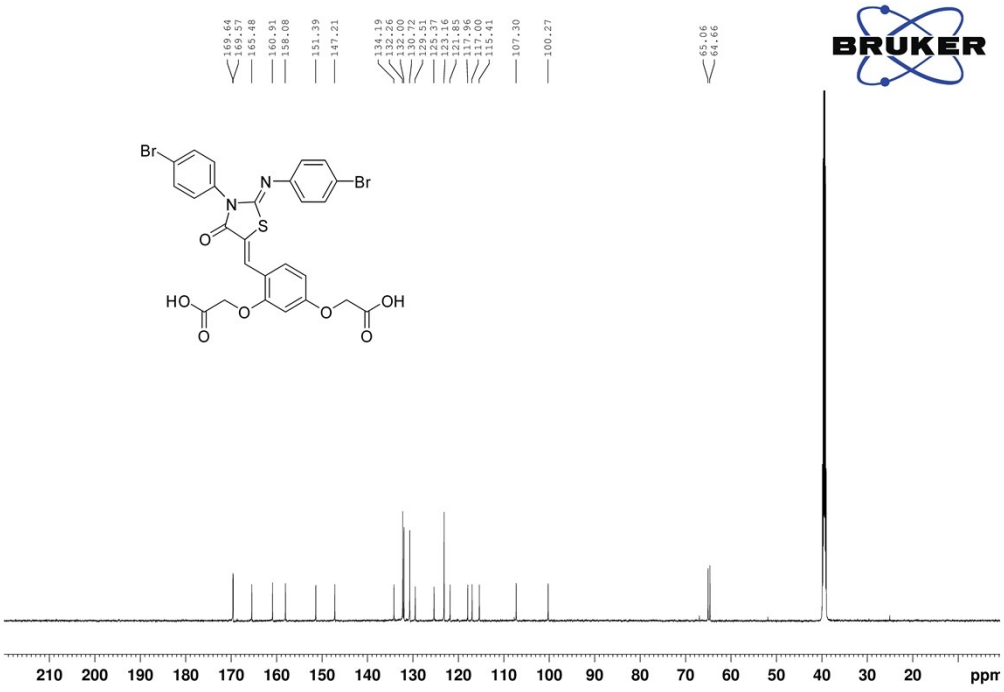


23v

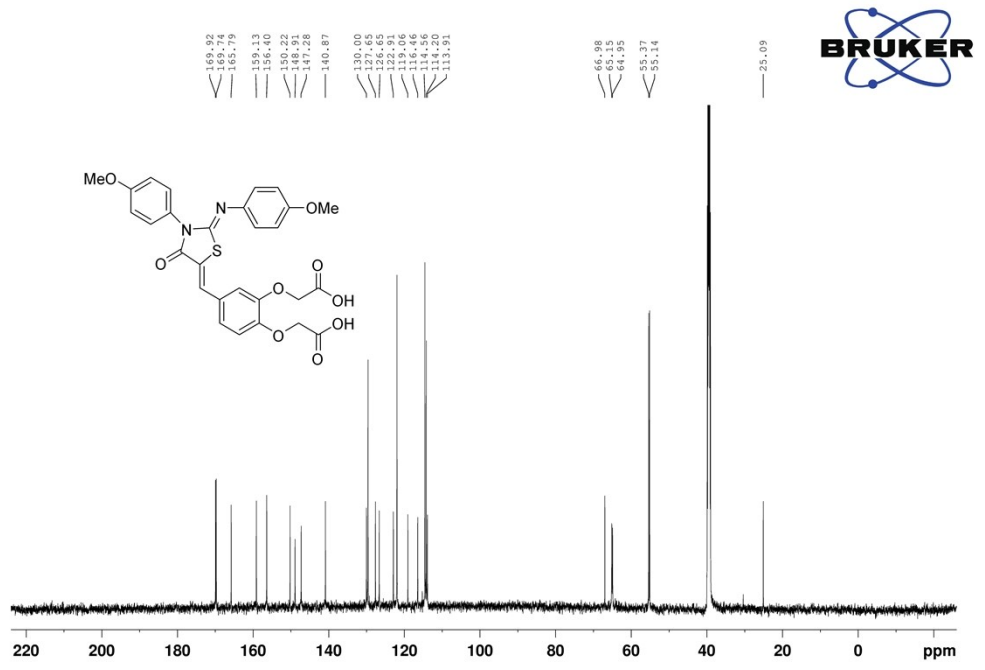


BRUKER

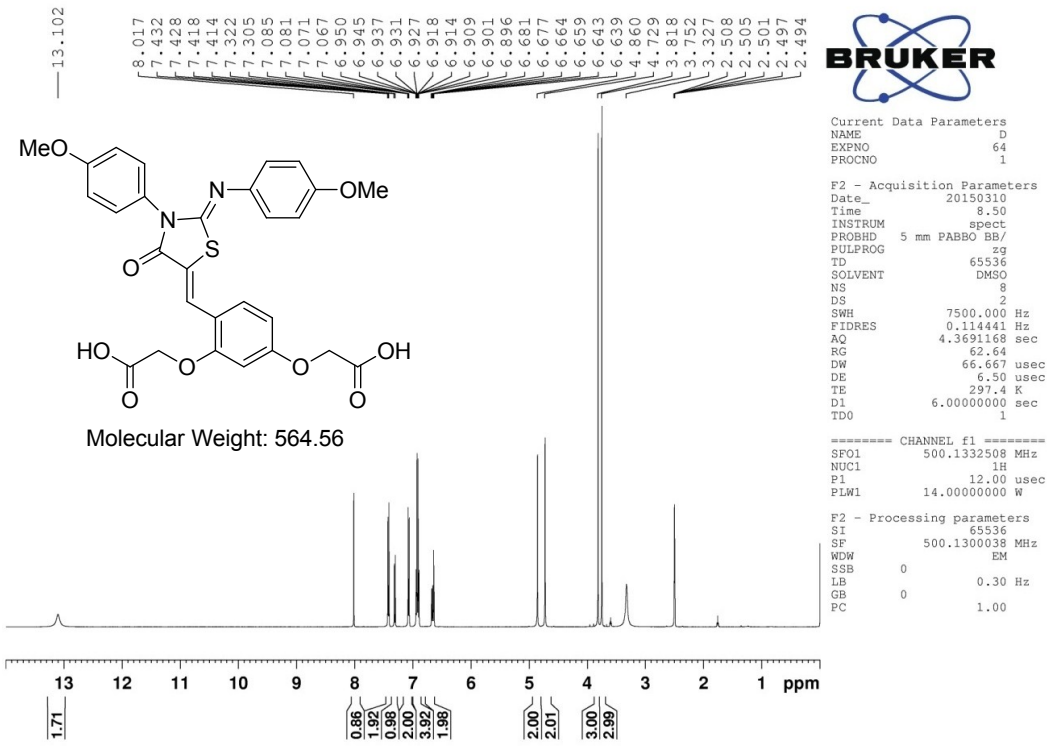
```
Current Data Parameters
NAME                  D
EXPNO                62
PROCNO                1

F2 - Acquisition Parameters
Date_          20150310
Time               8.39
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG              zg
TD                65536
SOLVENT            DMSO
NS                    8
DS                    2
SWH           7500.000 Hz
FIDRES          0.114441 Hz
AQ            4.3691168 sec
RG                 70.3
DW               66.667 usec
DE                6.50 usec
TE               297.5 K
D1            6.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         500.1332508 MHz
NUC1                 1H
P1                12.00 usec
PLW1        14.00000000 W

F2 - Processing parameters
SI                65536
SP           500.1300033 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

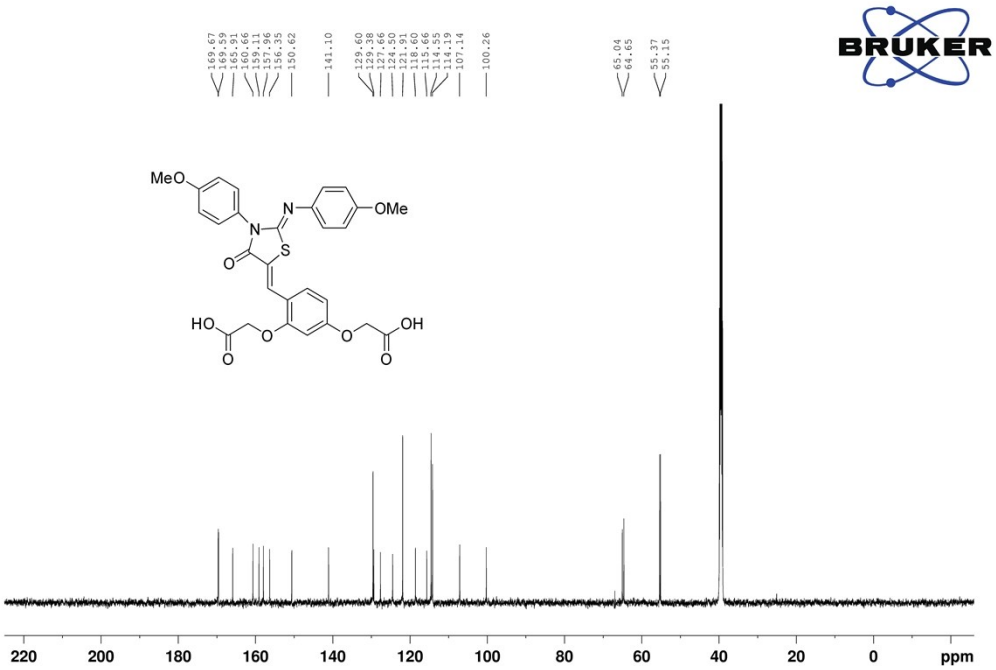

169.64
165.48
160.91
158.08
151.39
147.21
134.19
132.26
132.00
130.72
129.31
128.37
123.16
121.85
117.96
117.00
115.41
107.30
100.27
65.06
64.66
Br
N
Br
O
S
HO
O
O
O
OH
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

23w


169.92
169.74
165.79
159.13
156.40
150.22
148.91
147.28
140.87
130.00
127.65
126.65
122.91
119.06
116.46
114.56
114.20
113.91
66.98
65.35
64.95
55.37
55.14
25.09
MeO
N
OMe
O
S
O
O
OH
O
OH
220 200 180 160 140 120 100 80 60 40 20 0
ppm

23x


13.102
8.017
7.432
7.428
7.418
7.414
7.322
7.305
7.085
7.081
7.071
7.067
6.950
6.945
6.937
6.931
6.927
6.918
6.914
6.909
6.901
6.896
6.681
6.677
6.664
6.659
6.643
6.639
4.860
4.729
3.818
3.752
3.327
2.508
2.505
2.501
2.497
2.494
MeO
N
OMe
N
S
O
HO
O
O
O
OH
O
O
Molecular Weight: 564.56
BRUKER
Current Data Parameters
NAME D
EXPNO 64
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150310
Time 8.50
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 7500.000 Hz
FIDRES 0.114441 Hz
AQ 4.3691168 sec
RG 62.64
DW 66.667 usec
DE 6.50 usec
TE 297.4 K
D1 6.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1332508 MHz
NUC1 1H
P1 12.00 usec
PLW1 14.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300038 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.71
0.86
1.92
0.98
2.00
3.92
1.98
2.00
2.01
3.00
2.99


169.67
168.59
165.91
160.66
159.11
157.96
156.35
150.62
141.10
129.60
129.38
127.66
124.50
121.91
118.60
115.66
114.55
114.19
107.14
100.26
65.04
64.65
55.37
55.15
MeO
N
OMe
N
S
O
HO
O
O
O
OH
O
O
BRUKER
220 200 180 160 140 120 100 80 60 40 20 0 ppm

Reference

1. G. Jones, P. Willett, R. C. Glen, A. R. Leach and R. Taylor, *J. Mol. Biol.*, 1997, **267**, 727.