Electronic Supplementary Material (ESI) for Green Chemistry.

Water excellent solvent for the synthesis of bifunctionalized cyclopentenones

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Experimental section

All chemicals and solvents were purchased from common commercial sources and were used as received without any further purification. All reactions were monitored by TLC on silica Merck 60 F_{254} pre-coated aluminum plates Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Brüker spectrometer at 300 MHz. Chemical shifts are reported in δ units (ppm) with TMS as reference (δ 0.00). All coupling constants (J) are reported in Hertz. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Brüker at 75 MHz. Chemical shifts are reported in δ units (ppm) relative to $CDCl_3$ (δ 77.0). MW-assisted reactions were performed on a Synthos 3000 instrument from Anton Paar, equipped with a 4×24MG5 Rotor and an IR probe used for external temperature control.

LC-MS analysis were carried using an Agilent 6540 UHD Accurate Mass Q-TOF LC–MS (Agilent, Santa Clara, CA) fitted with a electrospray ionisation source (Dual AJS ESI) operating in positive ion mode. Chromatographic separation was achieved using a C18 RP analytical column (Poroshell 120, SB-C18, 50 × 2.1 mm, 2.7 µm) at 30°C with a elution gradient from 5% to 95% of B over 13 min, A being H_2O (0.1% FA) and B CH_3CN (0.1% FA). Flow rate was 0.4 ml/min.

General MW-assisted protocol for synthesis of *trans*- 4,5 diaminocyclopent-2-enones (1a-10a).

To a water solution (3 mL) of furfural (1 mmol) in a 3 mL glass vial, the amine (2.2 mmol) was added. The mixture was reacted for 5 min in a Synthos 3000 microwave instrument, fixed on the temperature value of 60 °C (IR Limit). The reaction was monitored by TLC and GC/MS analysis. Diethyl ether was added after the completion of reaction and the products were isolated after evaporation of the solvent to yield compounds **1a-10a** in 80-93 % yields.

***trans*-4,5-dimorpholinocyclopent-2-en-1-one (1a):** Spectral data were in accordance with the literature.[9a]

***trans*-4,5-bis(phenylamino)cyclopent-2-en-1-one (2a):** Spectral data were in accordance with the literature. [9a]

***trans*-4,5-bis(methyl(phenyl)amino)cyclopent-2-en-1-one** (**3a**): Spectral data were in accordance with the literature. [9a] HRMS (ESI) for ($[C_{19}H_{20}N_2O] + H)^+$ 293.1654, found 293.1644 $[M+H]^+$.

***trans*-4,5-di(pyrrolidin-1-yl)cyclopent-2-en-1-one (4a):** Spectral data were in accordance with the literature.[8f] HRMS (ESI) for ($[C_{13}H_{20}N_2O] + H)^+$ 221.1654, found 221.1649 $[M+H]^+$, 243.1452 $[M+Na]^+$.

***trans*-4,5-di(piperidin-1-yl)cyclopent-2-en-1-one (5a):** Spectral data were in accordance with the literature. [9a]

***trans*-4,5-bis(dibenzylamino)cyclopent-2-en-1-one (6a):** Spectral data were in accordance with the literature. [9a] HRMS (ESI) for ($[C_{33}H_{32}N_2O] + H)^+$ 473.2593, found 473.2583, $[M+H]^+$, 495.2543, $[M+Na]^+$.

***trans*-4,5-di(isoindolin-2-yl)cyclopent-2-en-1-one (7a):** Spectral data were in accordance with the literature. [9a]

***trans*-4,5-bis(3,4-dihydroquinolin-1(2H)-yl)cyclopent-2-en-1-one (8a):** Spectral data were in accordance with the literature.[9a]

***trans*-4,5-bis(diisobutylamino)cyclopent-2-enone (9a):** Spectral data were in accordance with the literature.[11]

***trans*-4,5-bis(diallylamino)cyclopent-2-enone (10a):** Spectral data were in accordance with the literature.[9a]

General protocol for the synthesis of 2,4 diaminocyclopent-2-enones (1b-3b) and (1c-1j).

To a water solution (3 mL) of furfural (1 mmol) in a 3 mL glass vial, the amine (2.2 mmol) was added. The mixture was reacted for 5 min in a Synthos 3000 microwave instrument, fixed on the temperature value of 60 °C (IR Limit).

In order to obtain the 2,4 bisubstituted cyclopentenones **1b-3b** the reaction mixture, after MW irradiation, was kept at room temperature for further 4 hour. After completion, diethyl ether was added (3 × 2 mL) and the organic phase was dried over Na_2SO_4 and filtered. The products were isolated after evaporation of the diethyl ether to afford compounds **1b-3b** in 85-91 % yields.

Instead, for the synthesis of compounds **1c-1j**, after MW irradiation, the addition of various nucleophiles (1 mmol) was necessary. Also in this case the mixture was maintained at room temperature for further 4 hours. The reaction was monitored by TLC and GC/MS analysis. After completion, water was removed under reduced pressure and the resulting crude product was purified by flash chromatography (CH_2Cl_2/MeOH 9.5:0.5). The products **1c-1j** were obtained in 79-89 % yields.

2,4-dimorpholinocyclopent-2-enone (1b): ^{1}H NMR (300 MHz, $CDCl_3$) 6.24 (d, *J* = 2.9 Hz, 1H, COC=C*H*), 3.78 (t, *J* = 4.7 Hz, 4H, morpholine), 3.73 (t, *J* = 4.7 Hz, 4H, morpholine), 3.73-3.72 (m, 1H, $COCH_2CHN$), 3.15-3.14 (m, 4H, morpholine), 2.54-2.52 (m, 4H, morpholine), 2.49-2.48 (m, 1H, $COCH_2$), 2.46-2.45 (m, 1H, $COCH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) 38.1, 48.1, 50.0, 60.3, 66.6, 67.1, 129.5, 151.7, 202.0.

2,4-bis(phenylamino)cyclopent-2-enone (2b): Spectral data were in accordance with the literature.[10a]

2,4-bis(methyl(phenyl)amino)cyclopent-2-enone (3b): Spectral data were in accordance with the literature.[10a]

4-(ethylthio)-2-morpholinocyclopent-2-enone (1c): Spectral data were in accordance with the literature. [10a] HRMS (ESI) for $([C_{11}H_{17}NO_2S] + H)^+$ 228.1058, found 228.1048 $[M+H]^+$.

4-(cyclohexylthio)-2-morpholinocyclopent-2-enone (1e): Spectral data were in accordance with the literature. [10a] HRMS (ESI) for $([C_{15}H_{23}NO_2S] + H)^+$ 282.1528, found 282.1523 $[M+H]^+$.

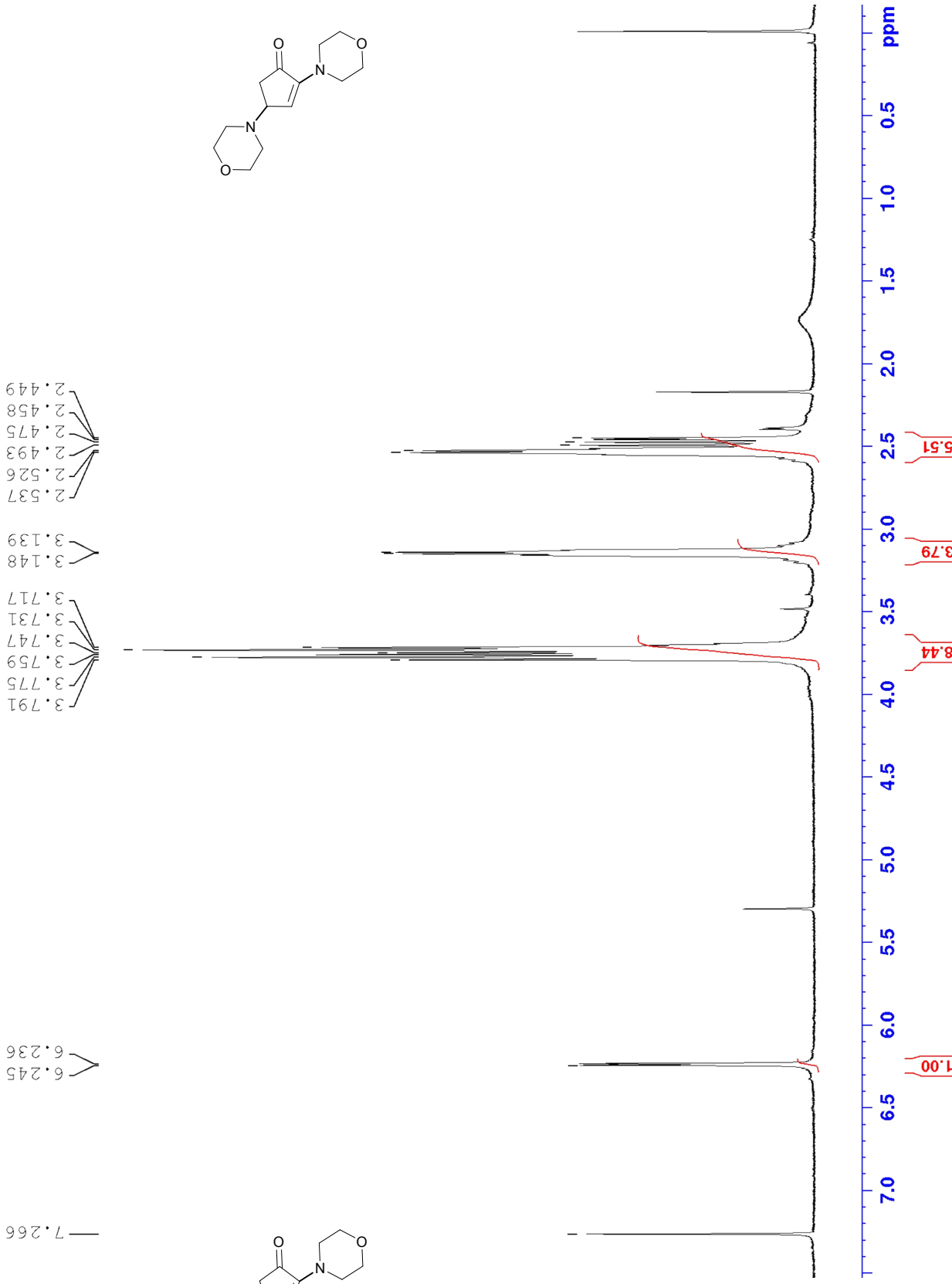
4-(phenylthio)-2-morpholinocyclopent-2-enone (1f): Spectral data were in accordance with the literature. [10a] HRMS (ESI) for $([C_{15}H_{17}NO_2S] + H)^+$ 276.1058, found 276.1050 $[M+H]^+$.

4-(benzylthio)-2-morpholinocyclopent-2-enone (1g): Spectral data were in accordance with the literature.[10a] HRMS (ESI) for $([C_{16}H_{19}NO_2S] + H)^+$ 290.1215, found 290.1212$[M+H]^+$.

4- (methyl-L-cysteinate)-2-morpholino cyclopent-2-enone (1j): ^{1}H NMR (300 MHz, $CDCl_3$) 6.23 (d, *J* = 3.0 Hz, 1H, COC=C*H*), 4.02 (dt, *J* = 9.3 Hz, *J* = 5.5 Hz, 1H, $COCHNH_2$), 3.75-3.64 (m, 4H, morpholine), 3.45-3.41 (m, 1H, SC*H*), 3.03 (s, 3H, CH_3), 2.79 (t, 2H, *J* = 9.3 Hz, $COCH_2$), 2.61-2.53 (m, 4H, morpholine), 2.49-2.46 (m, 1H, SCH_2), 2.45-2.39 (m, 1H, SCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) 37.9, 43.9, 44.2, 48.0, 49.0, 49.9, 66.9, 110.0, 152.9, 174.8, 201.8. HRMS (ESI) for $([C_{13}H_{20}N_2O_4S] + H)^+$ 301.1222, found 301.1214 $[M+H]^+$.

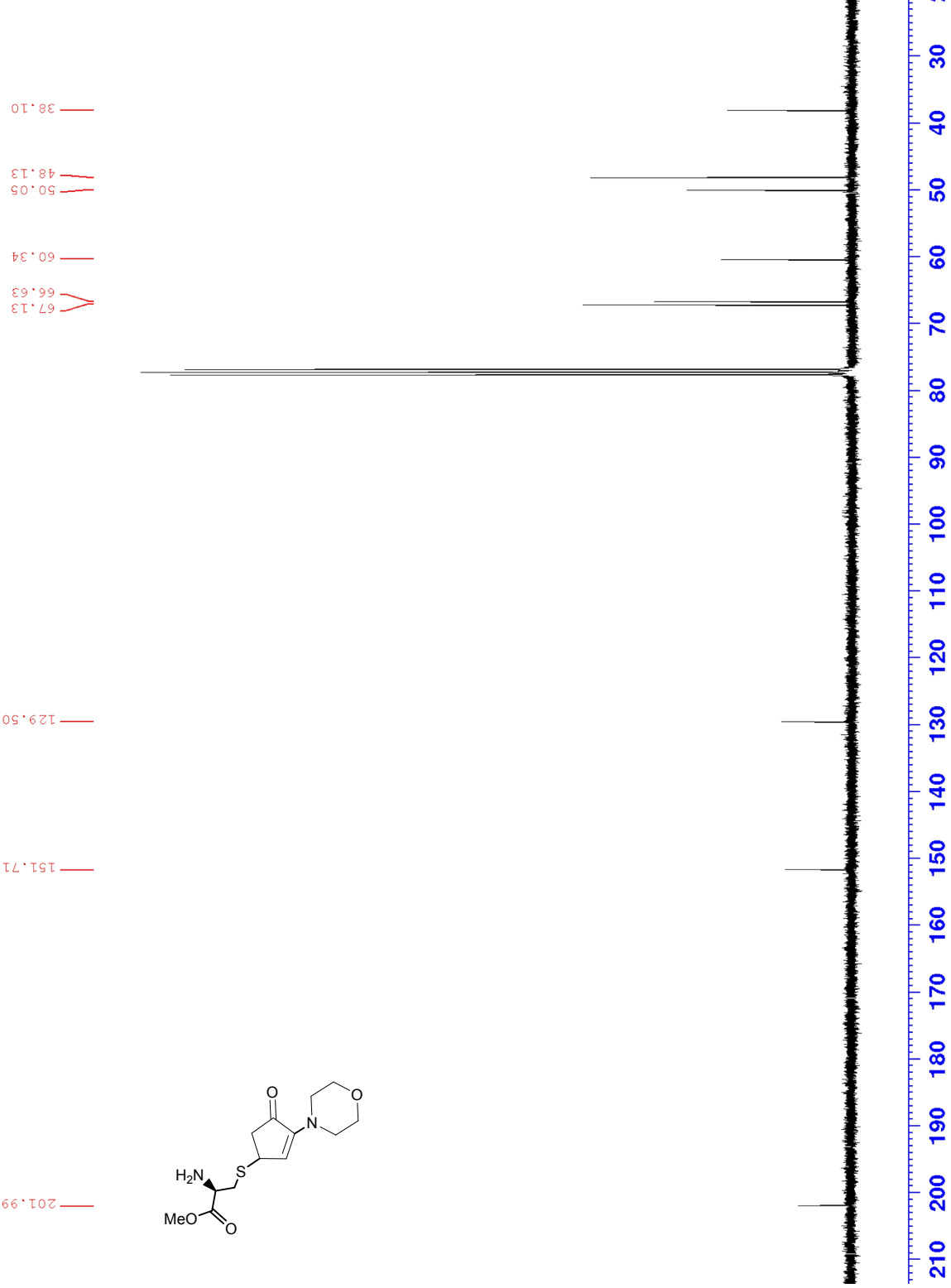
^{1}H-NMR

Compound 1b



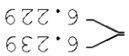
^{13}C-NMR

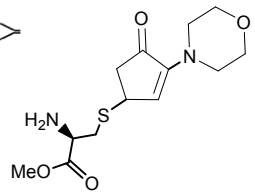
Compound 1b

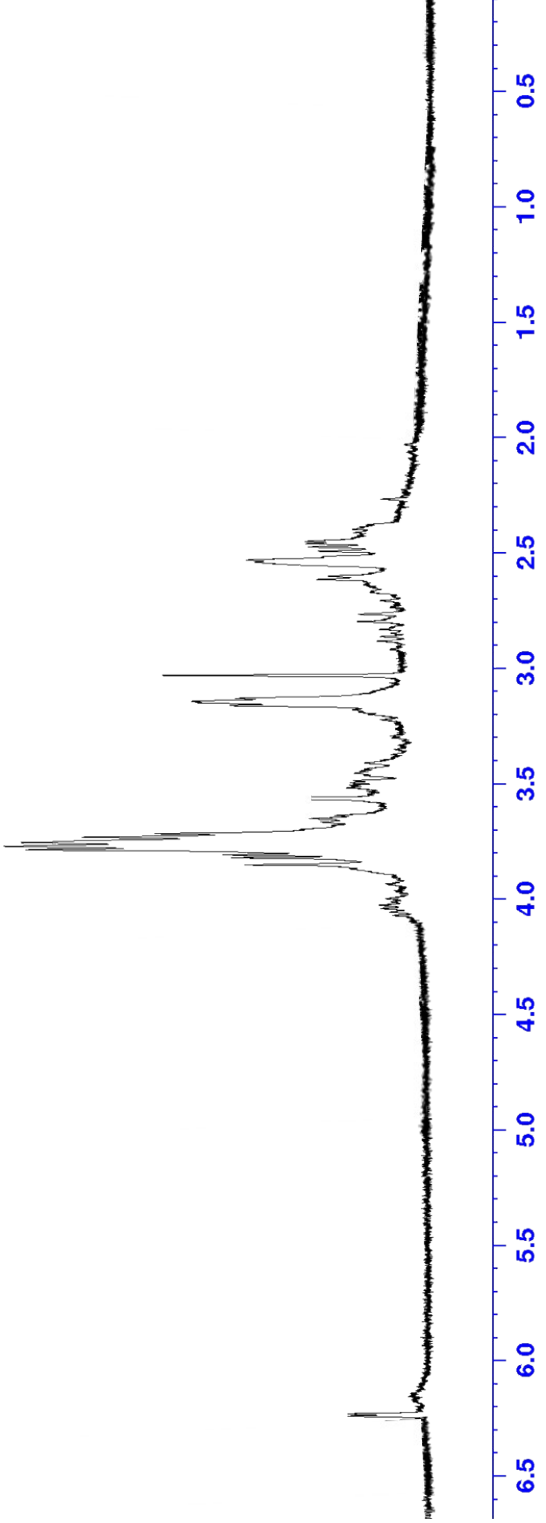


^{1}H-NMR

Compound 1j

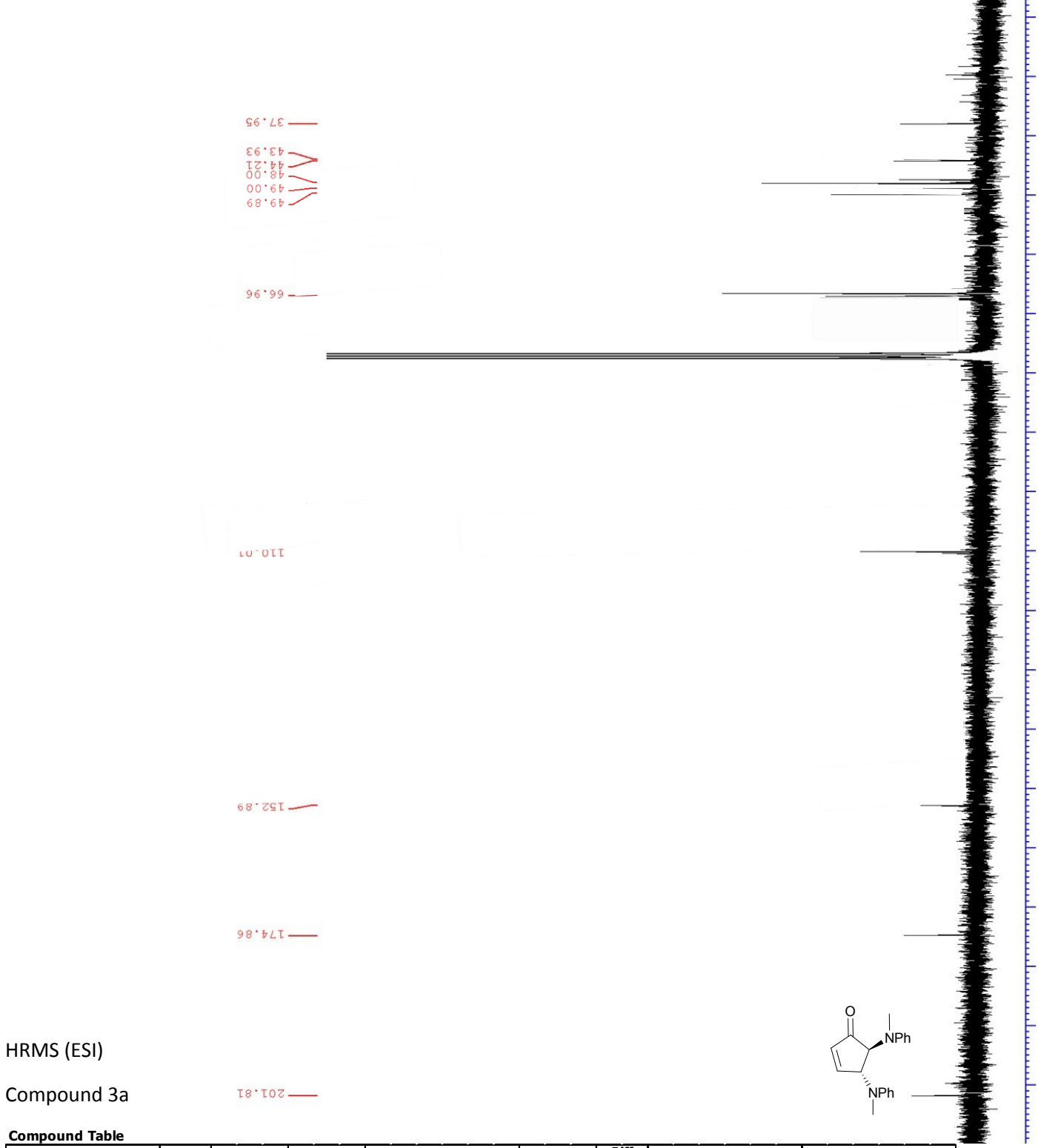






^{13}C-NMR

Compound 1j



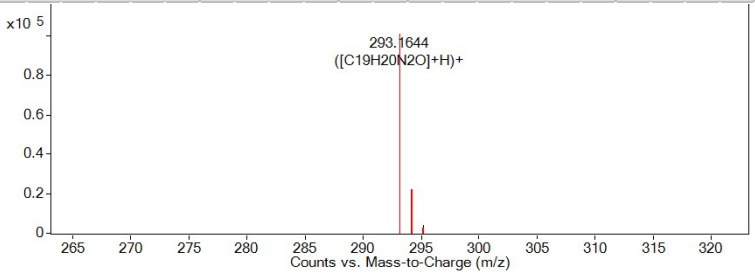
HRMS (ESI)

Compound 3a

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C19 H20 N2 O	5,959	292,1574	101081	C19 H20 N2 O	292,1576	-0,64	C19 H20 N2 O	C19 H20 N2 O

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C19 H20 N2 O	293,1644	5,959	Find By Formula	292,1574



MS Spectrum Peak List

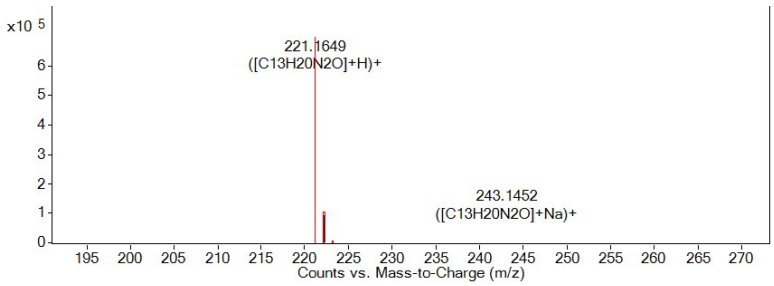
m/z	z	Abund	Formula	Ion
293,1644	1	101081,47	C19H20N2O	(M+H)+
294,1696	1	20728,57	C19H20N2O	(M+H)+
295,1686	1	4045,16	C19H20N2O	(M+H)+

Compound 4a

Compound Table

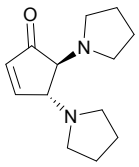
Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C13 H20 N2 O	1,928	220,1576	699293	C13 H20 N2 O	220,1576	0,14	C13 H20 N2 O	C13 H20 N2 O

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C13 H20 N2 O	221,1649	1,928	Find By Formula	220,1576

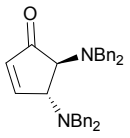


MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
221,1649	1	699293,06	C13H20N2O	(M+H)+
222,1679	1	92918,73	C13H20N2O	(M+H)+
223,1702	1	7771,66	C13H20N2O	(M+H)+
224,1697	1	658,89	C13H20N2O	(M+H)+
243,1452	1	1133,93	C13H20N2O	(M+Na)+
244,1474	1	230,81	C13H20N2O	(M+Na)+



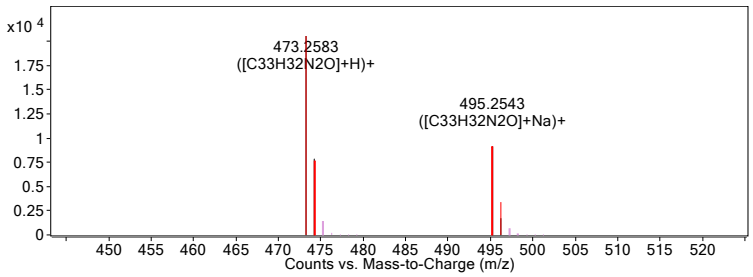
Compound 6a



Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C33 H32 N2 O	8,975	472,2554	20559	C33 H32 N2 O	472,2515	8,29	C33 H32 N2 O	C33 H32 N2 O

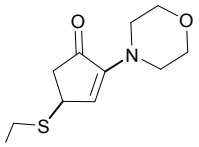
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C33 H32 N2 O	473,2583	8,975	Find By Formula	472,2554



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
473,2583	1	20558,72	C33H32N2O	(M+H)+
474,263	1	7872,94	C33H32N2O	(M+H)+
495,2543	1	9128,57	C33H32N2O	(M+Na)+
496,2627	1	1655,41	C33H32N2O	(M+Na)+

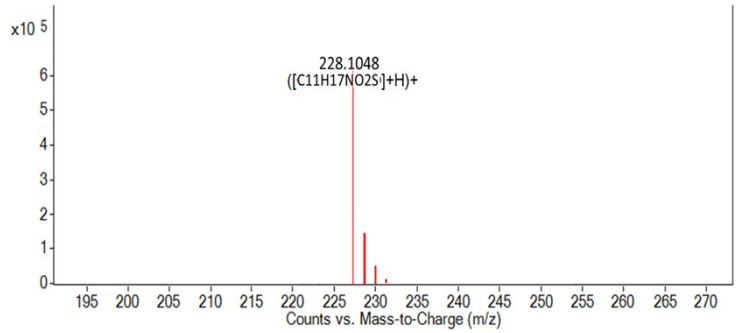
Compound 1c



Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C11 H17NO2S	3,969	227,0978	669183	C11 H17NO2S	227,098	-1,21	C11 H17NO2S	C11 H17NO2S

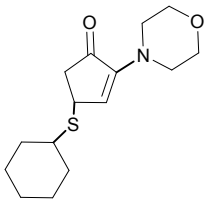
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C11 H17NO2S	228,1048	4,938	Find By Formula	227,0978



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
228,1048	1	669183,06	C15 H23NO2S	(M+H)+
229,1148	1	90819,63	C15 H23NO2S	(M+H)+
230,109	1	7817,65	C15 H23NO2S	(M+H)+
231,11	1	684,93	C15 H23NO2S	(M+H)+

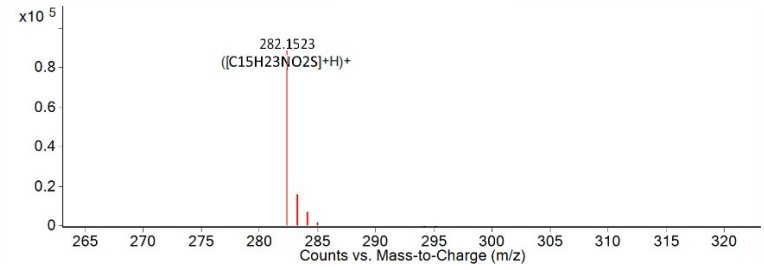
Compound 1e



Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C15 H23NO2S	4,938	281,1449	10020	C15 H23NO2S	281,1449	-1,04	C15 H23NO2S	C15 H23NO2S

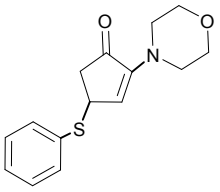
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C15 H23NO2S	282,1523	4,938	Find By Formula	281,1449



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
282,1523	1	10020,61	C15 H23NO2S	(M+H)+
283,1553	1	1584,74	C15 H23NO2S	(M+H)+
284,1576	1	843,94	C15 H23NO2S	(M+H)+
285,1697	1	149,4	C15 H23NO2S	(M+H)+

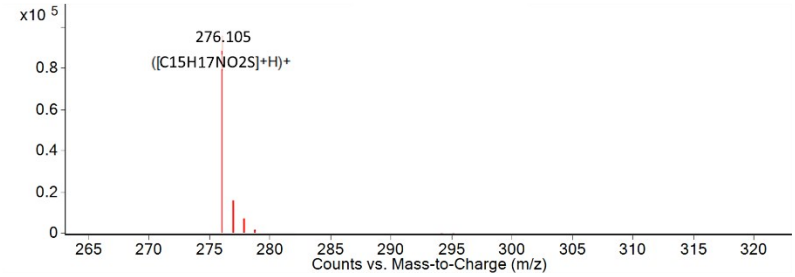
Compound 1f



Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C15 H17NO2S	6,558	275,0977	99110	C15 H17NO2S	275,098	1,04	C15 H17NO2S	C15 H17NO2S

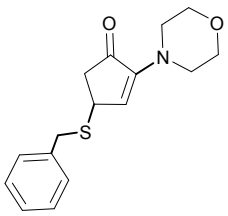
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C15 H17NO2S	276,105	6,558	Find By Formula	275,0977



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
276,105	1	99110,05	C15 H17NO2S	(M+H)+
277,112	1	18004,74	C15 H17NO2S	(M+H)+
278,104	1	7043,45	C15 H17NO2S	(M+H)+
279,09	1	1049,4	C15 H17NO2S	(M+H)+

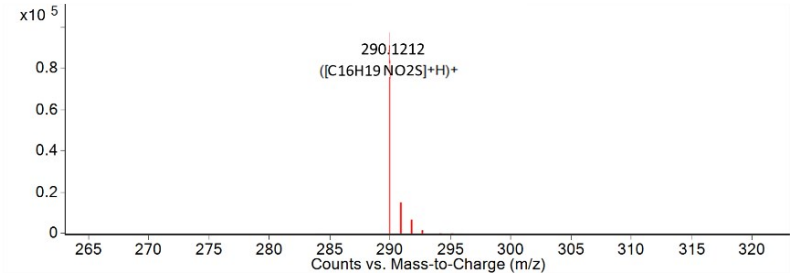
Compound 1g



Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C16H19NO2S	6,706	289,1131	98910	C16H19NO2S	289,1136	1,35	C16H19NO2S	C16H19NO2S

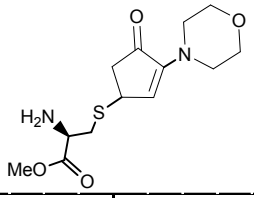
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1:C16H19NO2S	290,1212	6,706	Find By Formula	289,1131



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
290,1212	1	98910,05	C16H19NO2S	(M+H)+
291,1218	1	17825,25	C16H19NO2S	(M+H)+
292,1209	1	6943,81	C16H19NO2S	(M+H)+
293,1183	1	988,98	C16H19NO2S	(M+H)+

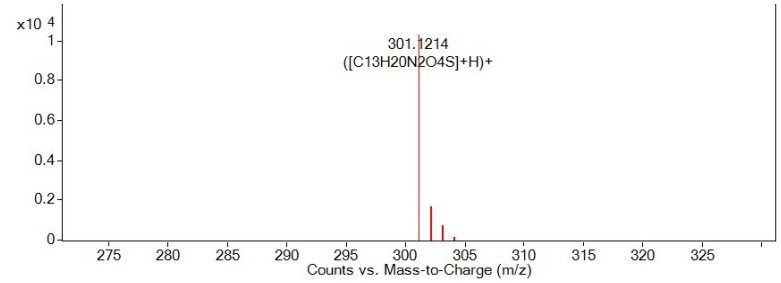
Compound 1j



Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C13 H20 N2 O4 S	2,403	300,1141	10311	C13 H20 N2 O4 S	300,1144	-1,04	C13 H20 N2 O4 S	C13 H20 N2 O4 S

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C13 H20 N2 O4 S	301,1214	2,403	Find By Formula	300,1141



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
301,1214	1	10310,61	C13H20N2O4S	(M+H)+
302,1242	1	1674,74	C13H20N2O4S	(M+H)+
303,1194	1	733,96	C13H20N2O4S	(M+H)+
304,1182	1	149,4	C13H20N2O4S	(M+H)+