

Synthesis of Benzoxazinones Sulphur analogs and their Application as Bioherbicides. 1,4-Benzothiazinones and 1,4-Benzoxathianones for Weed Control.

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Table S1. NMR data of compound **1**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	119.9
2	3.44 (s, 2H)	29.9
3	-	166.4
4	-	136.3
5	6.91 (dd, $J=7.9, 1.3$ Hz, 1H)	117.4
6	7.18 (ddd, $J=7.8, 7.5, 1.5$ Hz, 1H)	127.2
7	7.02 (ddd, $J=7.7, 7.7, 1.3$ Hz, 1H)	123.9
8	7.32 (dd, $J=7.8, 1.4$ Hz, 1H)	127.7
N	9.13 (br s, 1H)	-

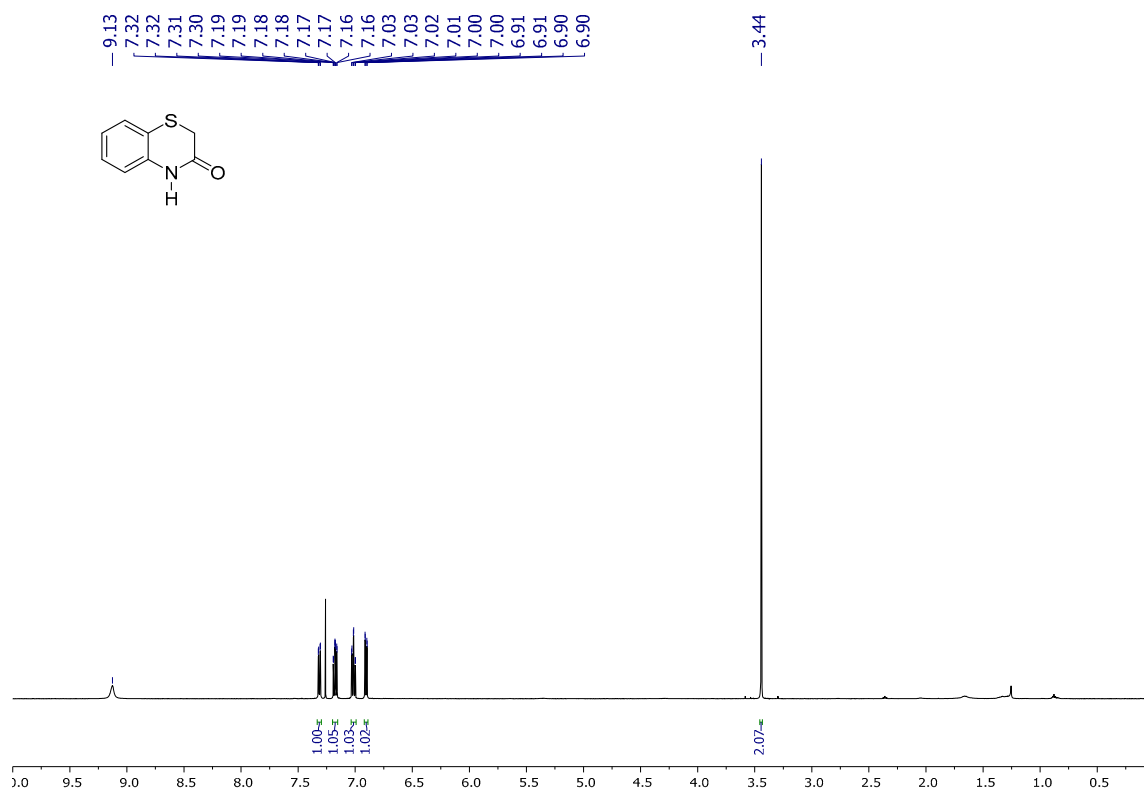


Figure S1. ^1H -NMR spectra of compound **1**

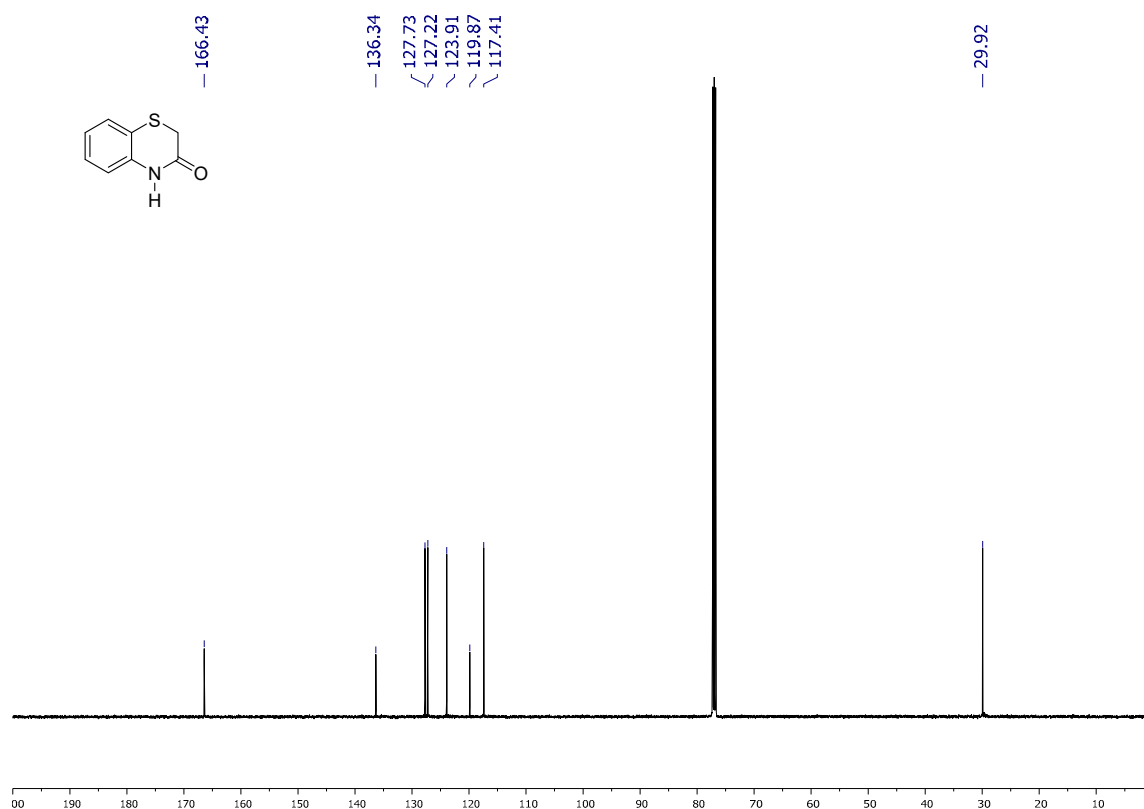
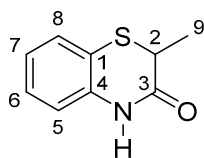


Figure S2. ¹³C-NMR spectra of compound **1**

Table S2. NMR data of compound **2**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	119.5
2	3.56 (q, $J=7.1$ Hz, 1H)	37.0
3	-	168.6
4	-	136.0
5	6.87 (dd, $J=7.9, 1.1$ Hz, 1H)	116.8
6	7.2 (ddd, $J=7.6, 7.6, 1.3$ Hz, 1H)	127.1
7	7.18 (ddd, $J=7.8, 7.5, 1.4$ Hz, 1H)	123.8
8	7.31 (dd, $J=7.8, 1.4$ Hz, 1H)	128.1
N	8.53 (br s, 1H)	-
9	1.50 (d, $J=7.1$ Hz, 3H)	15.4

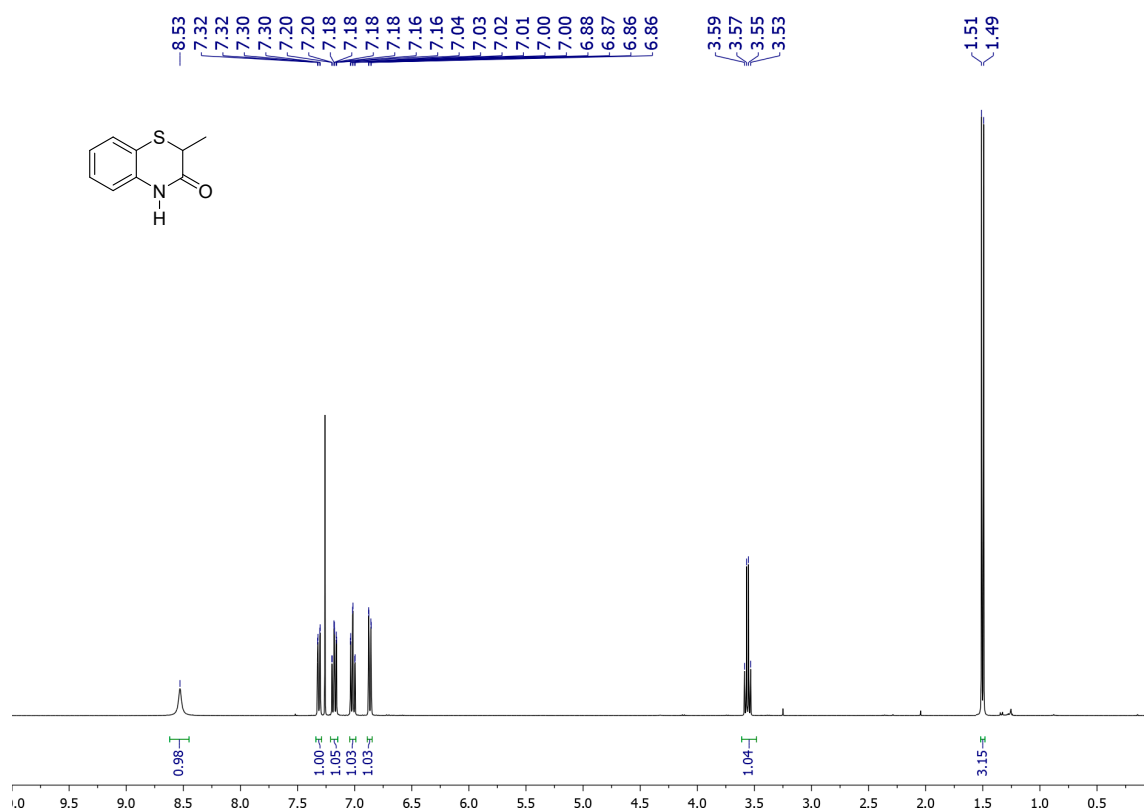


Figure S3. ^1H -NMR spectra of compound **2**

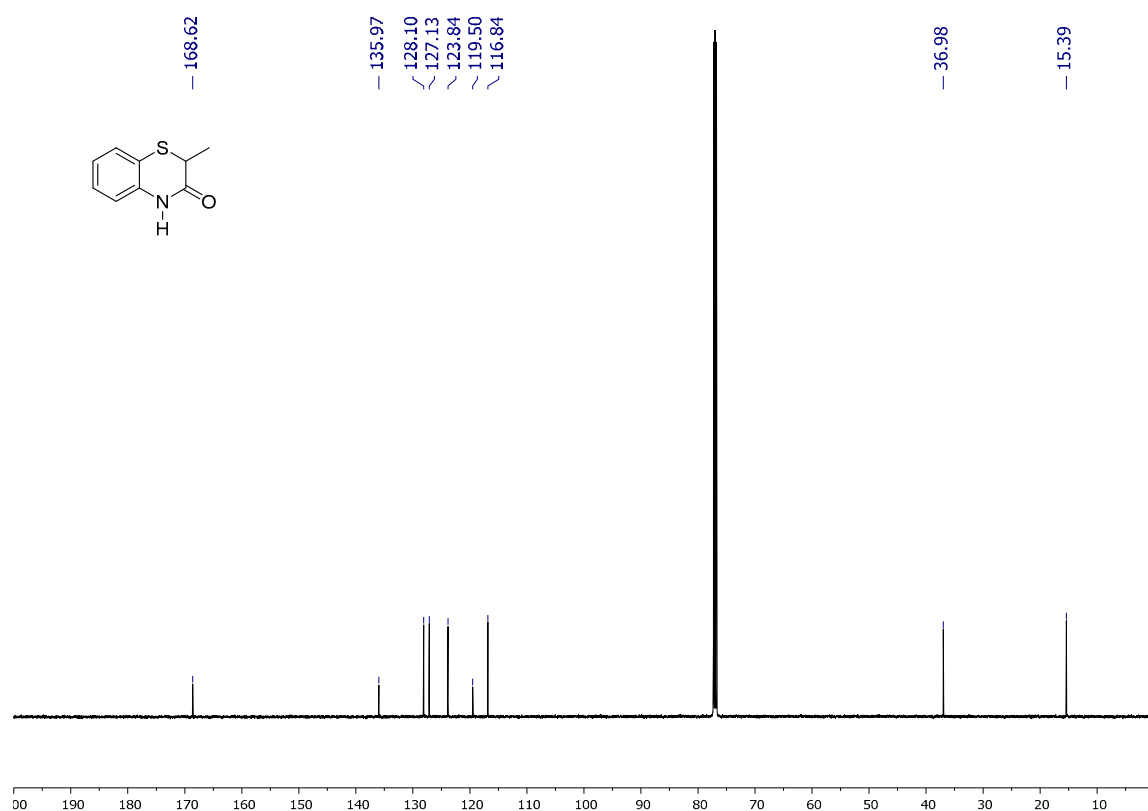
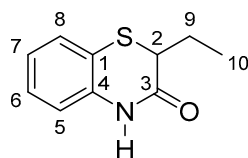


Figure S4. ^{13}C -NMR spectra of compound **2**

Table S3. NMR data of compound **3**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	118.5
2	3.32 (dd, $J=8.9, 5.9$ Hz, 1H)	44.4
3	-	168.6
4	-	136.0
5	6.85 (br d, $J=7.9$ Hz, 1H)	116.9
6	7.17 (ddd, $J=7.6, 7.6, 1.4$ Hz, 1H)	128.2
7	7.01 (ddd, $J=7.6, 7.6, 1.2$ Hz, 1H)	123.8
8	7.32 (dd, $J=7.7, 1.2$ Hz, 1H)	127.0
N	8.53 (br s, 1H)	-
9	1.95 (dq, $J=14.8, 6.0, 7.4$ Hz, 1H) 1.65 (dq, $J=14.8, 7.4, 8.8$ Hz, 1H)	23.3
10	1.07 (dd, $J=7.4, 7.4$ Hz, 1H)	11.4

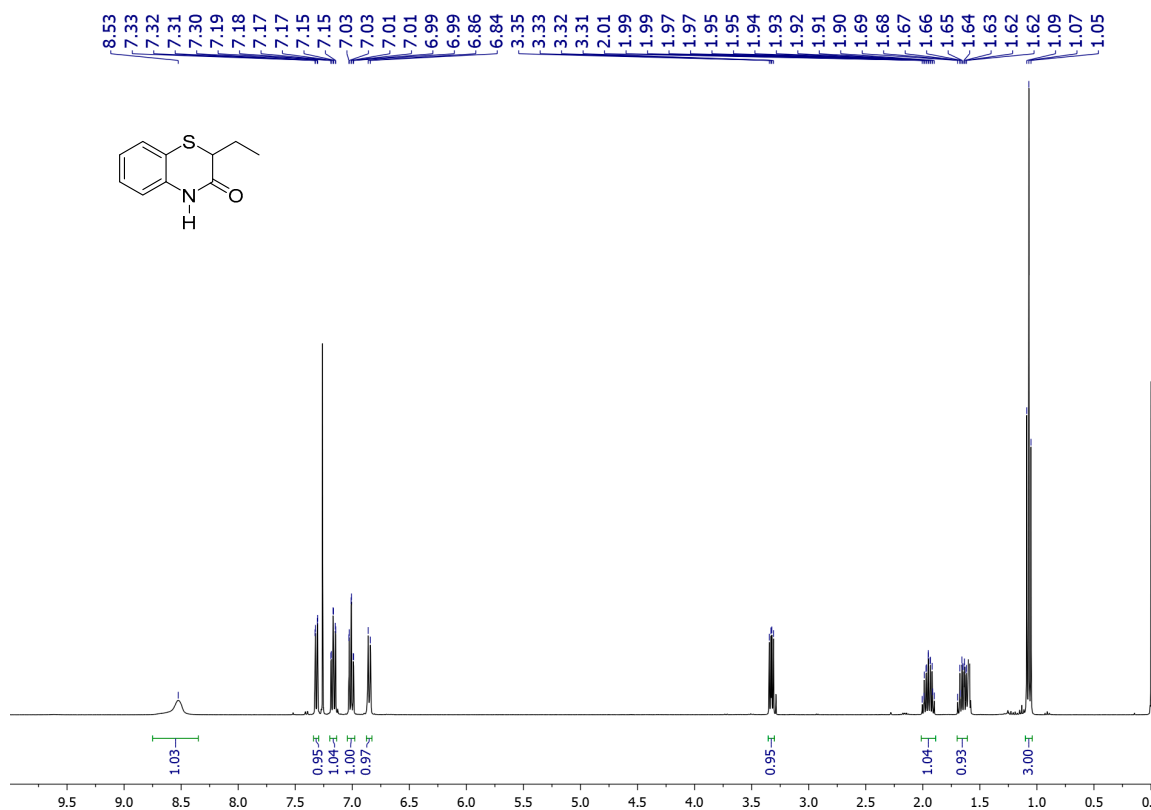


Figure S5. ^1H -NMR spectra of compound **3**

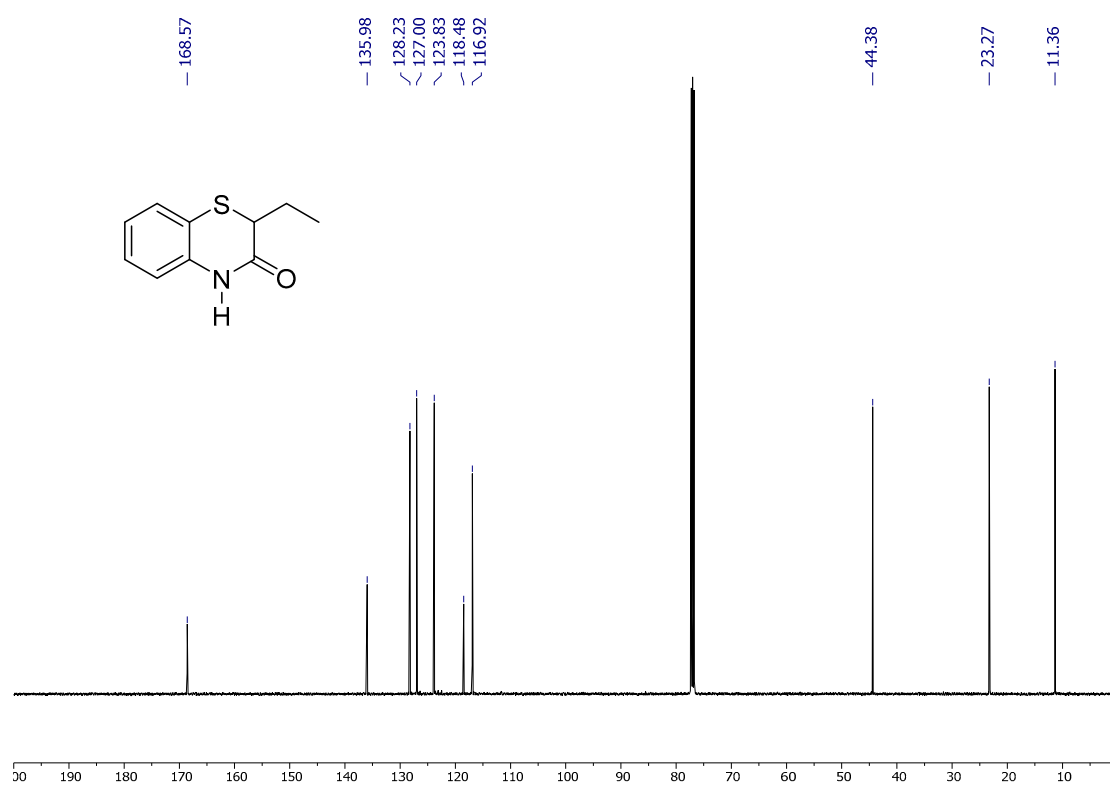
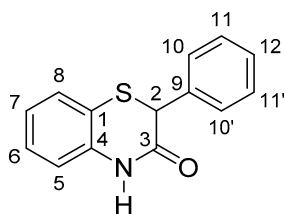


Figure S6. ^{13}C -NMR spectra of compound **3**

Table S4. NMR data of compound **4**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	119.5
2	4.70 (s, 1H)	46.3
3	-	166.2
4	-	134.7 ^a
5	6.83 (d, $J=7.9$ Hz, 1H)	116.8
6	7.17 (ddd, $J=7.5, 7.5, 1.4$ Hz, 1H)	127.3
7	7.01 (ddd, $J=7.5, 7.5, 1.2$ Hz, 1H)	124.1
8	7.27-7.34 (m, 1H)	127.94
N	8.17 (br s, 1H)	-
9	-	135.9 ^a
10, 10'	7.38 (br ddd, $J=8.3, 1.8, 0.6$, 2H)	127.95
11, 11'	7.27-7.34 (m, 2H)	128.7
12	7.27-7.34 (m, 1H)	128.3

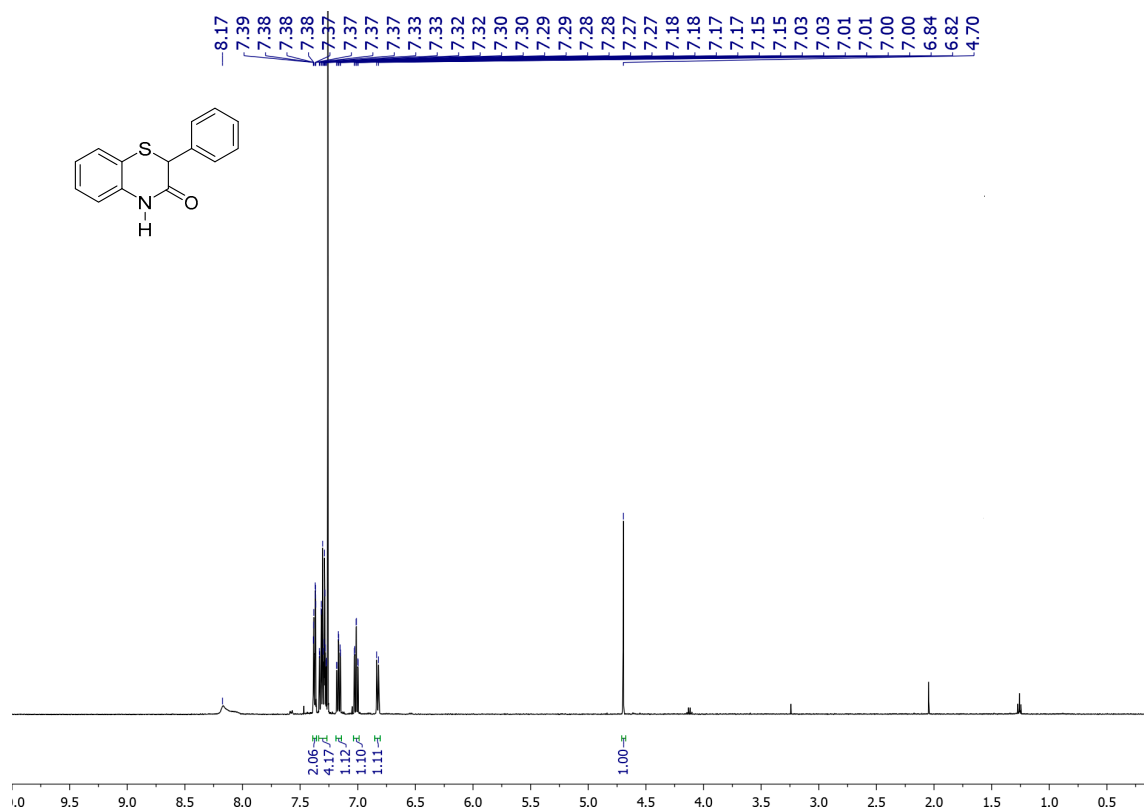


Figure S7. ^1H -NMR spectra of compound **4**

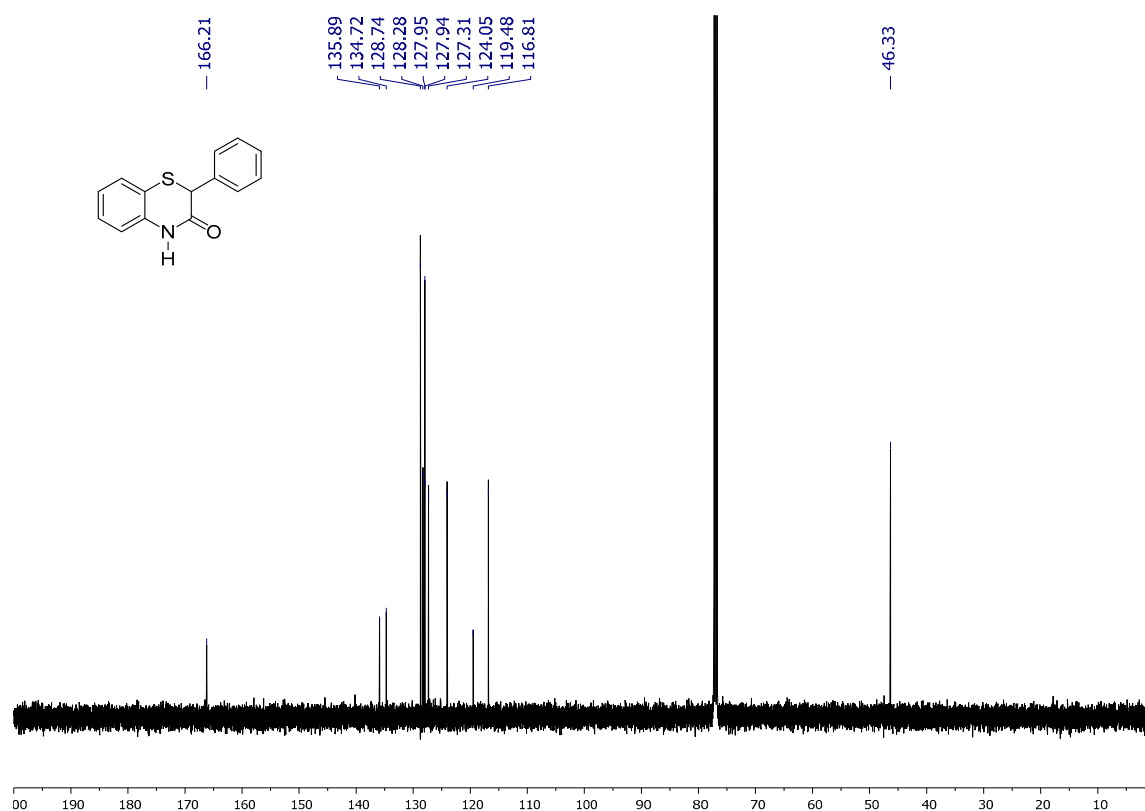
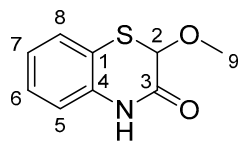


Figure S8. ^{13}C -NMR spectra of compound 4

Table S5. NMR data of compound **5**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	116.2
2	4.94 (d, $J=1.1$ Hz, 1H)	79.7
3	-	161.5
4	-	135.3
5	6.93 (br dd, $J=8.0, 1.2$ Hz, 1H)	117.3
6	7.22 (ddd, $J=8.0, 7.6, 1.4$ Hz, 1H)	127.4
7	7.06 (ddd, $J=7.6, 7.6, 1.2$ Hz, 1H)	124.2
8	7.35 (dd, $J=7.8, 1.4$ Hz, 1H)	128.8
N	8.51 (br s, 1H)	-
9	3.43 (br s, 3H)	56.1

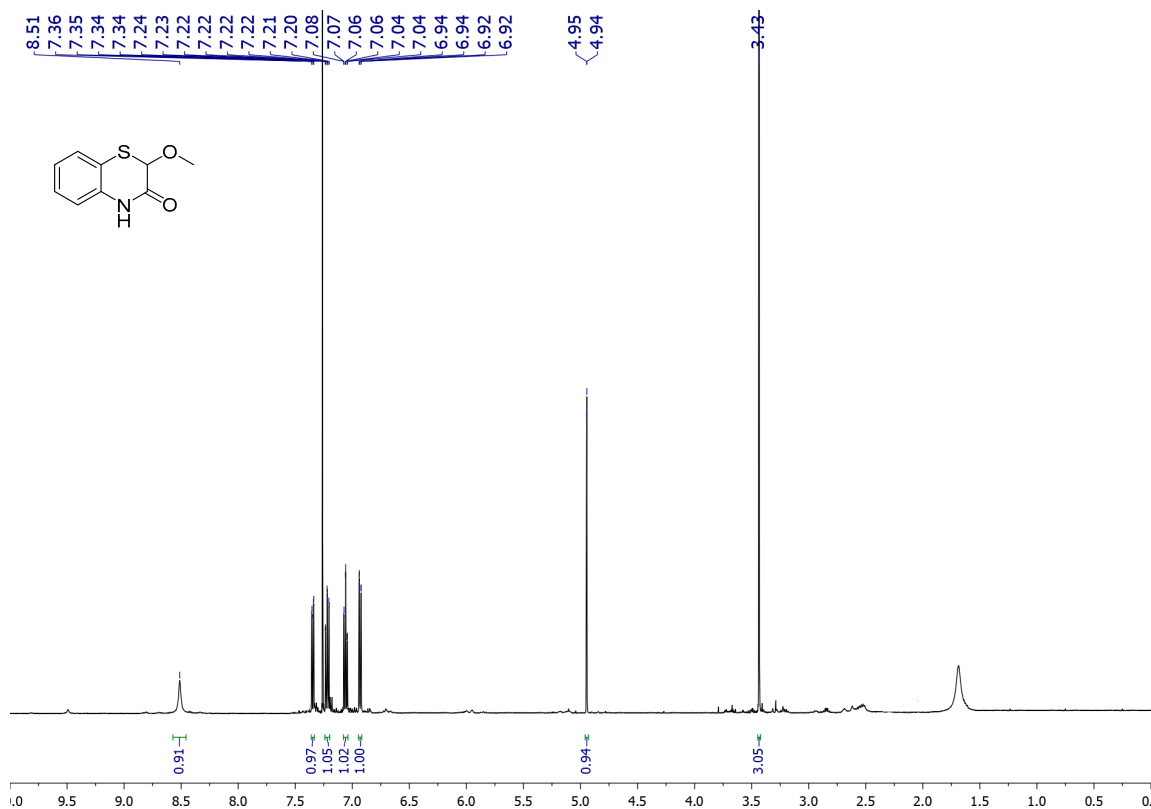


Figure S9. ^1H -NMR spectra of compound **5**

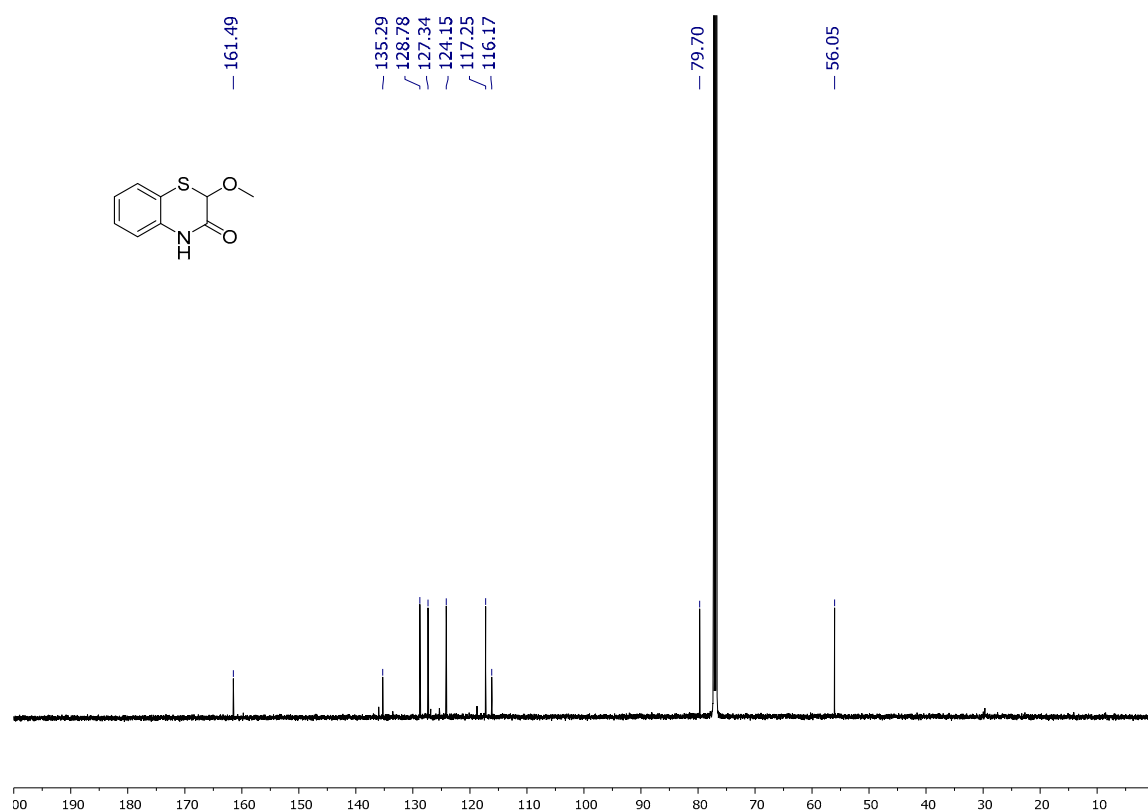
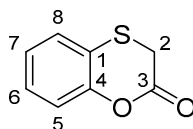


Figure S10. ^{13}C -NMR spectra of compound 5

Table S6. NMR data of compound **6**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	117.6
2	3.52 (s, 2H)	38.8
3	-	176.1
4	-	157.5
5	6.99 (dd, $J=8.1, 1.3$ Hz, 1H)	115.8
6	7.29 (ddd, $J=8.1, 7.5, 1.7$ Hz, 1H)	132.1
7	6.88 (ddd, $J=7.5, 7.5, 1.4$ Hz, 1H)	121.1
8	7.51 (dd, $J=7.7, 1.7$ Hz, 1H)	136.5

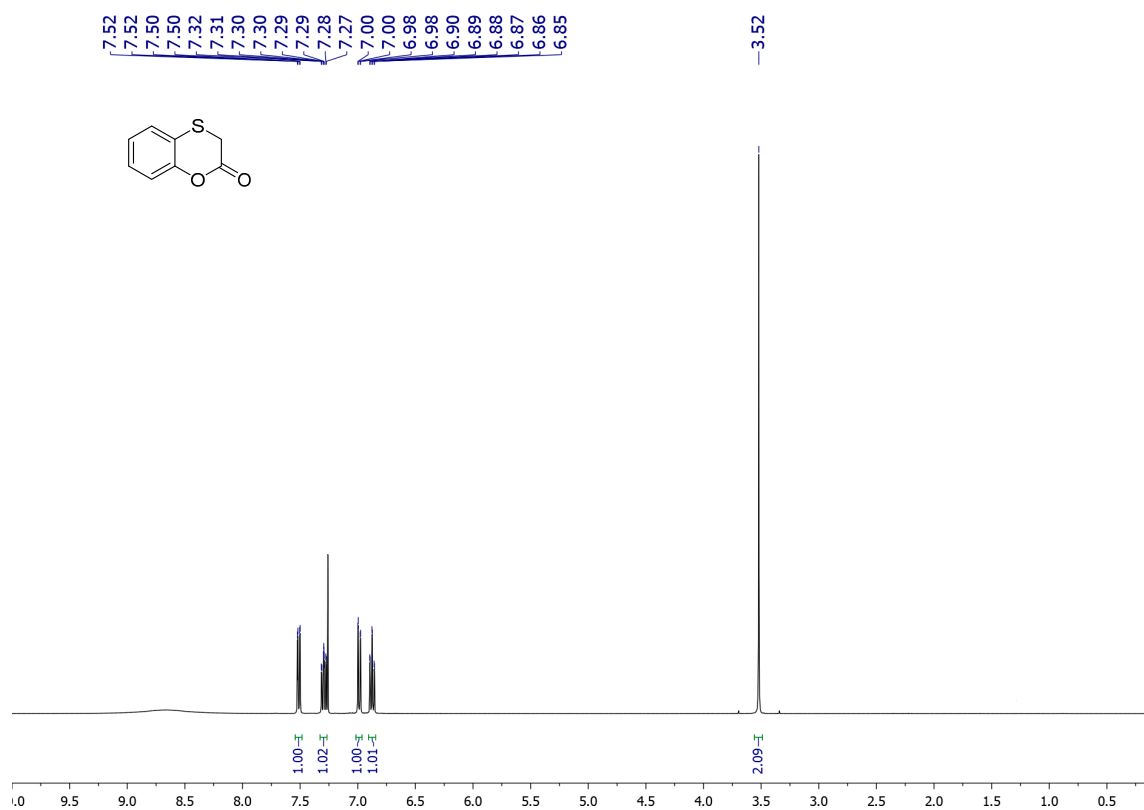


Figure S11. ^1H -NMR spectra of compound **6**

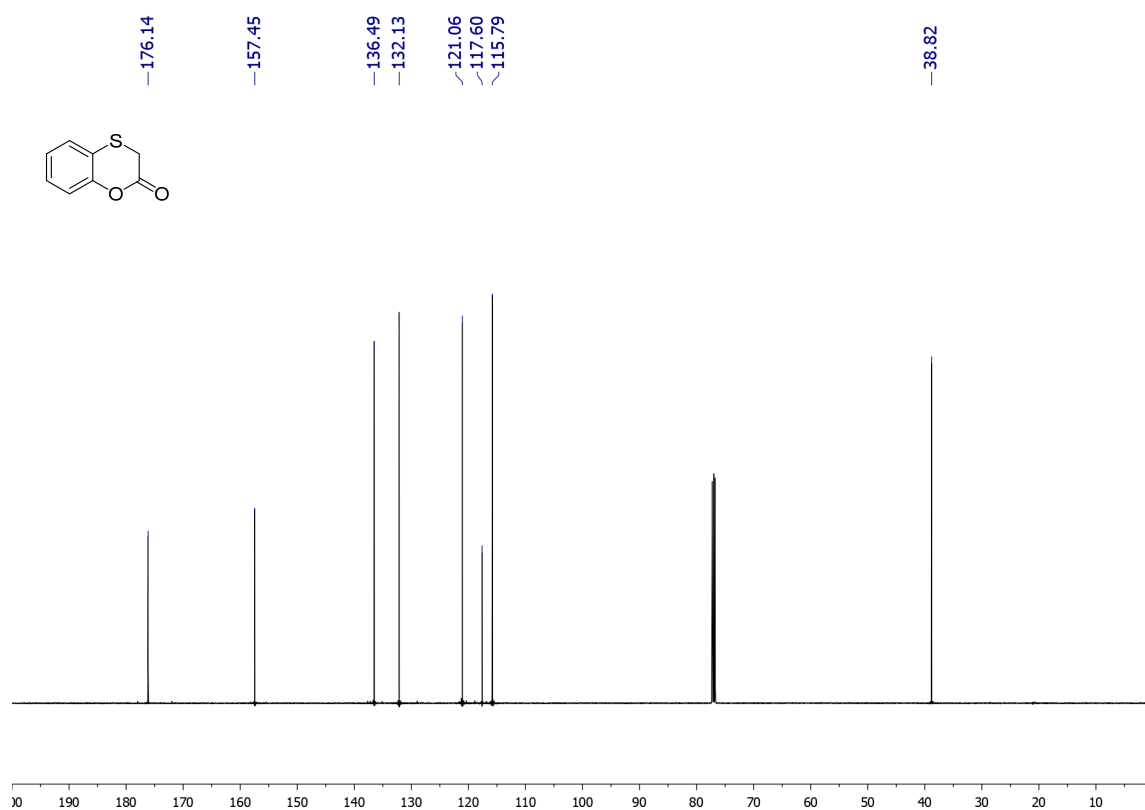
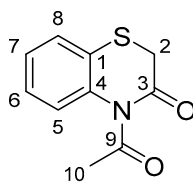


Figure S12. ^{13}C -NMR spectra of compound **6**

Table S7. NMR data of compound **1a**. ^1H -NMR (400 MHz, CDCl_3), ^{13}C NMR (125 MHz, CDCl_3).



Atom	^1H (ppm)	^{13}C (ppm)
1	-	127.9
2	3.45 (s, 2H)	36.0
3	-	169.4
4	-	135.8
5	7.46 (ddd, $J=7.8, 1.5, 0.3$, 1H)	126.1
6	7.16 (ddd, $J=7.8, 7.4, 1.4$ Hz, 1H)	126.7
7	7.26 (ddd, $J=8.2, 7.4, 1.6$ Hz, 1H)	125.8
8	7.33 (ddd, $J=8.2, 1.4, 0.3$ Hz, 1H)	129.0
9	-	173.1
10	2.70 (s, 3H)	28.3

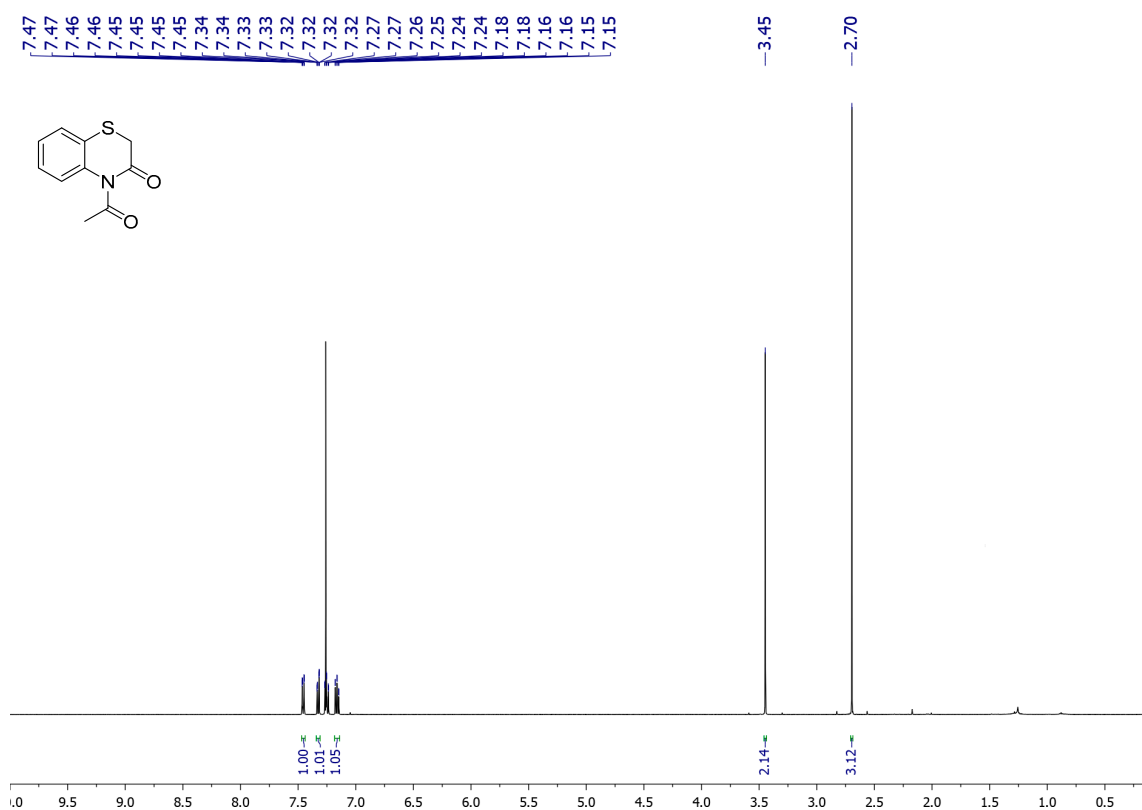


Figure S13. ^1H -NMR spectra of compound **1a**

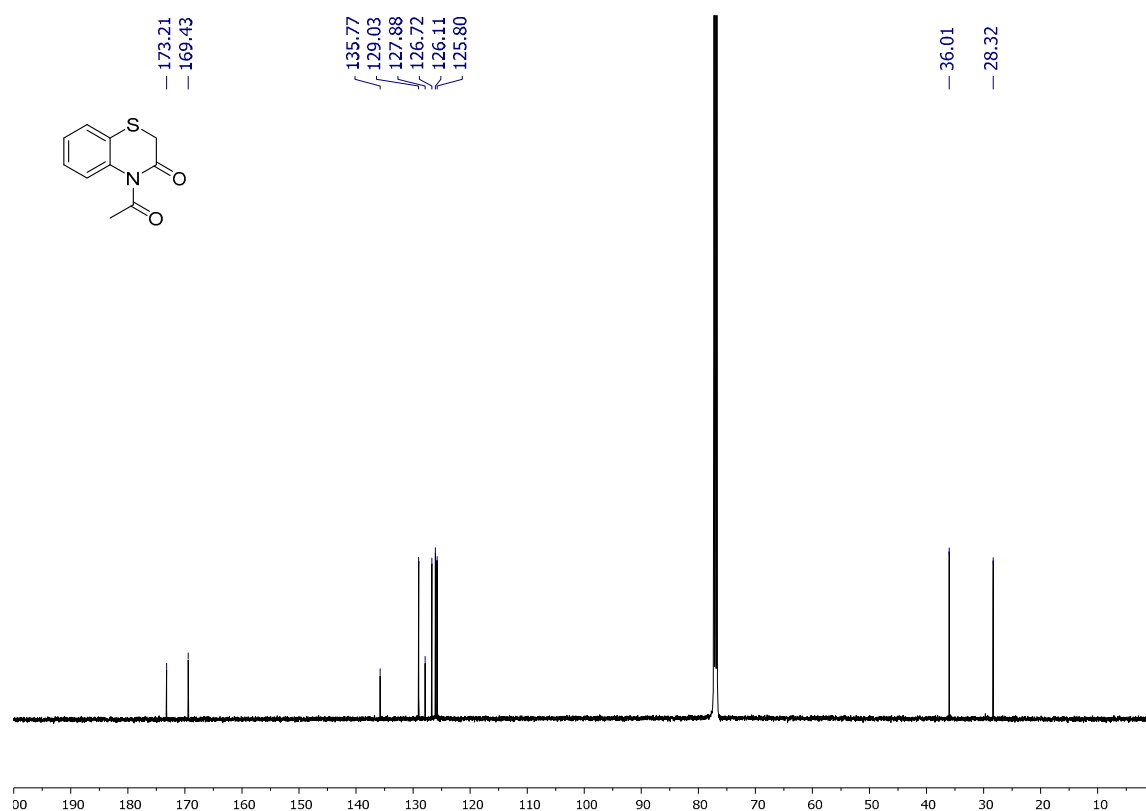
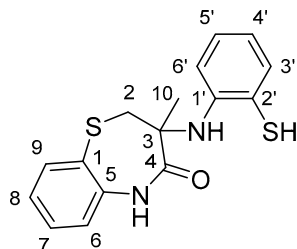


Figure S14. ^{13}C -NMR spectra of compound **1a**

Table S8. NMR data of compound 3-((2-mercaptophenyl)amino)-3-methyl-2,3-dihydrobenzo[b][1,4]thiazepin-4(5H)-one. ¹H-NMR (400 MHz, CDCl₃), ¹³C NMR (125 MHz, CDCl₃). Calculated: 316.0704 amu [C₁₆H₁₆N₂OS₂]. Found: 315.0721 [M-H]⁺



Atom	¹ H (ppm)	¹³ C (ppm)
1	-	118.0
2	3.12 (d, <i>J</i> =16.8 Hz, 1H) 2.99 (d, <i>J</i> =16.8, 1H)	48.2
3	-	56.6
4	-	165.5
5	-	127.2
6	7.01 (dd, <i>J</i> =7.6, 1.6 Hz, 1H)	119.5
7	7.07 (ddd, <i>J</i> = 7.6, 7.6, 1.5, 1H)	127.8
8	7.12 (ddd, <i>J</i> =7.7, 7.7, 1.6 Hz, 1H)	126.4
9	7.14 (dd, <i>J</i> =7.8, 1.4 Hz, 1H)	126.9
10	1.40 (s, 3H)	26.7
1'	-	140.4
2'	-	115.0
3'	6.71 (dd, <i>J</i> =8.0, 1.1, 1H)	118.2
4'	6.81 (ddd, <i>J</i> =7.8, 7.2, 1.3, 1H)	120.2
5'	7.04 (ddd, <i>J</i> = 7.8, 7.2, 1.4, 1H)	127.4
6'	7.32 (dd, <i>J</i> =7.8, 1.6 Hz, 1H)	129.1

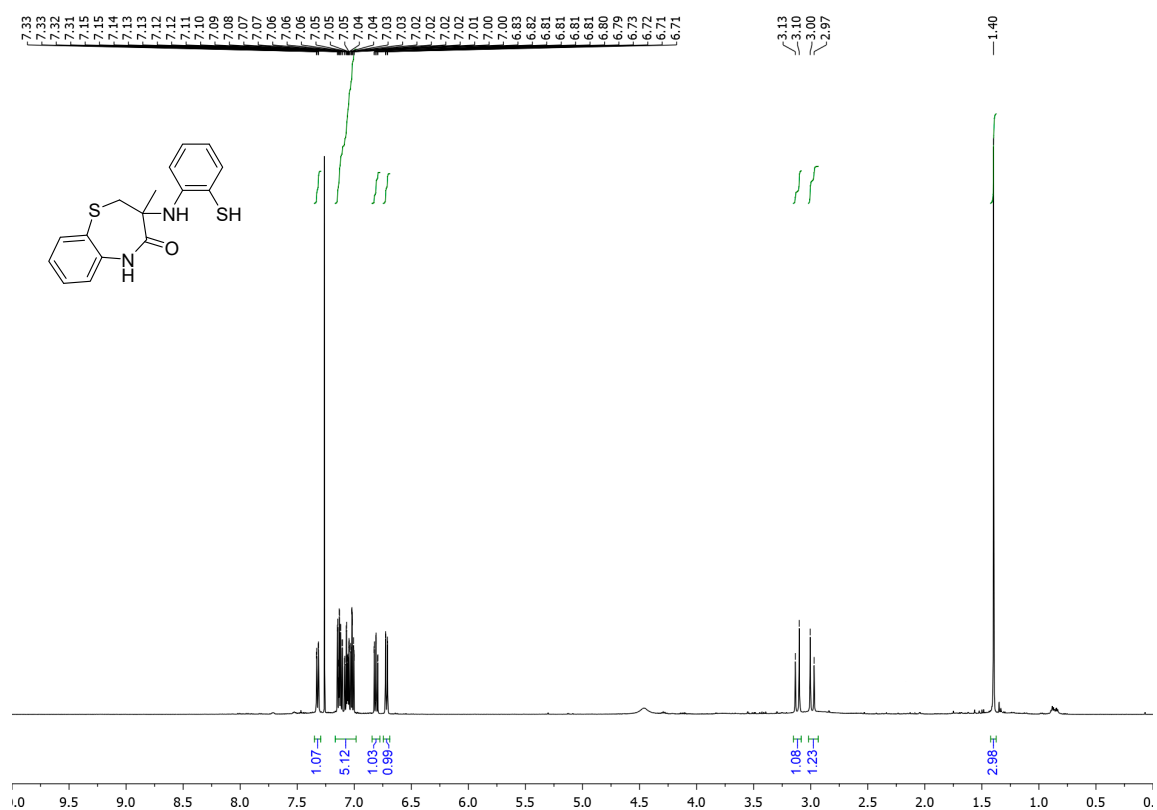


Figure S15. ¹H-NMR spectra of 3-((2-mercaptophenyl)amino)-3-methyl-2,3-dihydrobenzo[b][1,4]thiazepin-4(5H)-one

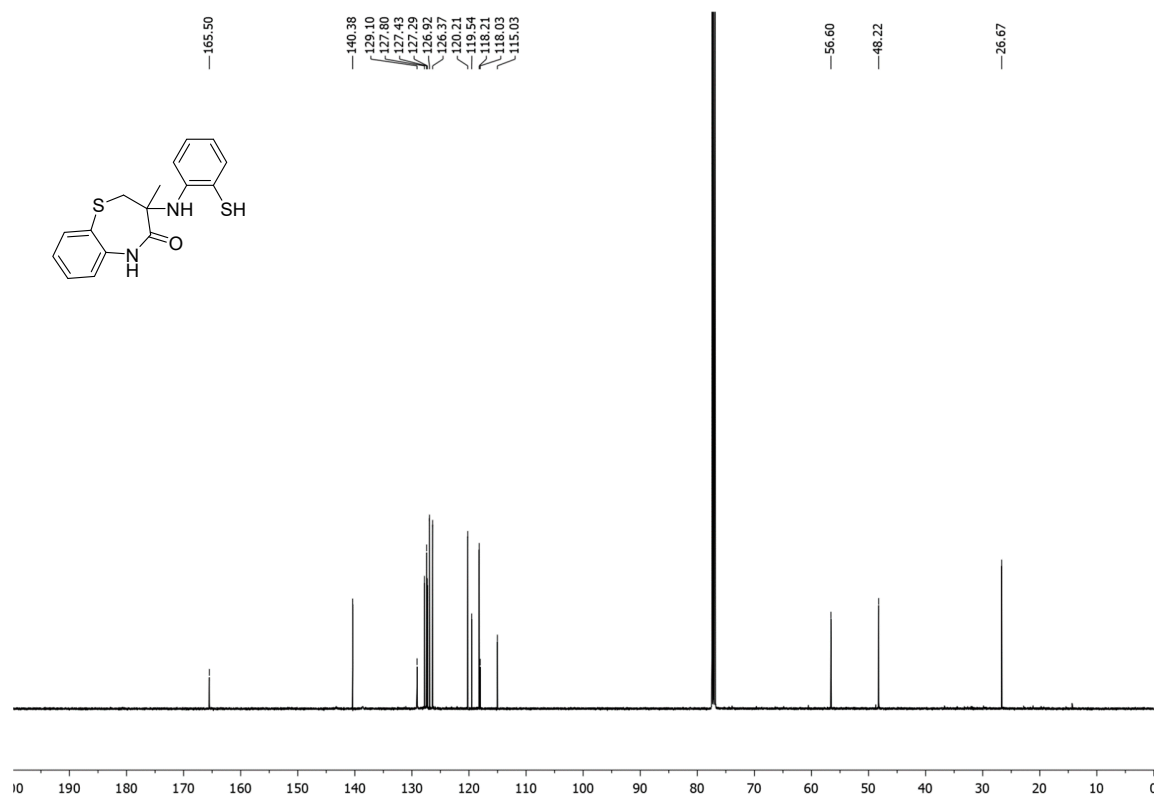


Figure S16. ¹³C-NMR spectra of 3-((2-mercaptophenyl)amino)-3-methyl-2,3-dihydrobenzo[b][1,4]thiazepin-4(5H)-one

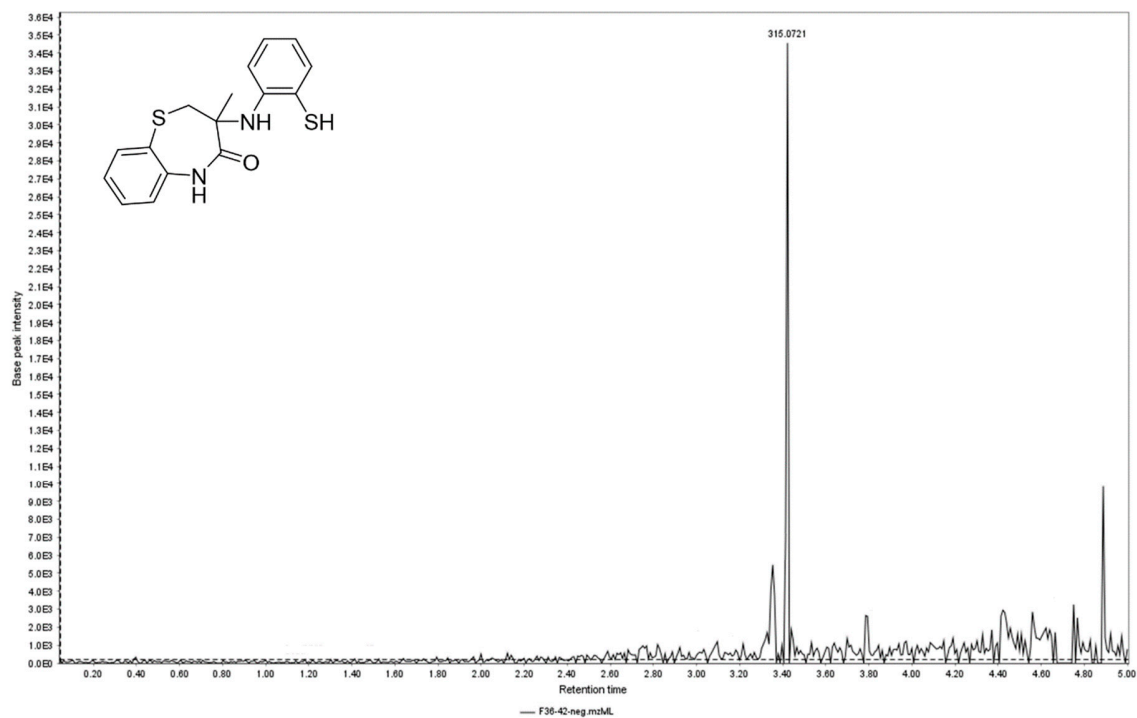


Figure S17. LC-MS data of 3-((2-mercaptophenyl)amino)-3-methyl-2,3-dihydrobenzo[b][1,4]thiazepin-4(5H)-one

Table S9. Wheat coleoptile bioassay data for 1,4-benzothiazinones and 1,4-benzoxathianones. Negative values represent inhibition of the elongation vs. control.

	1	2	3	4	1a	5	6	D-DIBOA	D-HBOA	Pendimethalin	StompAqua®	Logran®
<i>1·10⁻³ M</i>	-68±9	-97±10	-100±9	-19±9	-64±10	-49±8	9±8	-65±9	-45±10	-53±9	-41±7	-93±4
<i>3·10⁻⁴ M</i>	-32±9	-51±9	-75±9	-16±9	-34±9	-33±9	6±7	-14±7	-6±10	-52±9	-32±6	-91±3
<i>1·10⁻⁴ M</i>	-16±8	-20±9	-16±8	-12±10	-9±8	-12±7	-15±9	-18±5	-6±9	-50±8	-33±7	-88±7
<i>3·10⁻⁵ M</i>	-14±9	-20±8	-17±8	2±9	-13±7	-17±5	-17±9	-18±6	7±9	-37±7	-32±5	-35±7
<i>1·10⁻⁵ M</i>	-9±8	-5±9	-1±9	15±6	-6±9	-7±10	-17±9	6±10	-3±7	-21±10	-28±7	-6±4

Table S10. Mulliken charges distribution per atom

	D-DIBOA	D-HBOA	1
Position	Mulliken Charge		
1	0.212	0.213	-0.326
S/O-Ether	-0.324	-0.328	0.205
2	-0.338	-0.338	-0.707
3	0.209	0.149	0.186
O-Carbonyl	-0.369	-0.335	-0.340
N	-0.131	-0.414	-0.410
4	0.300	0.305	0.526
5	-0.343	-0.363	-0.372
6	-0.221	-0.222	-0.215
7	-0.221	-0.225	-0.246
8	-0.331	-0.335	-0.260
O-hydroxamic acid	-0.424		

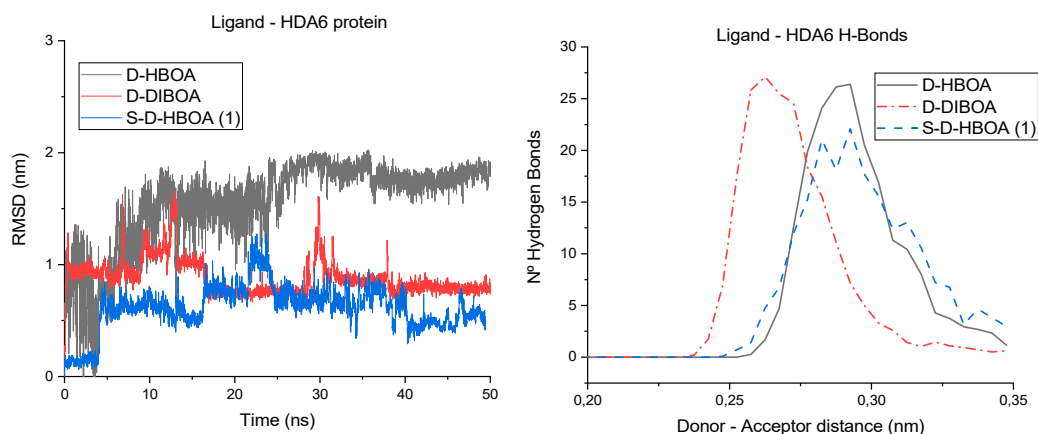


Figure S18. (Left) Root mean square deviation of the ligands D-HBOA, D-DIBOA and **1**, respect to HDA6 protein all along the MD *in silico* simulation. (Right) Distribution and number of hydrogen bonds between the ligand and HDA6 protein during the simulation.

D-DIBOA – HDA6

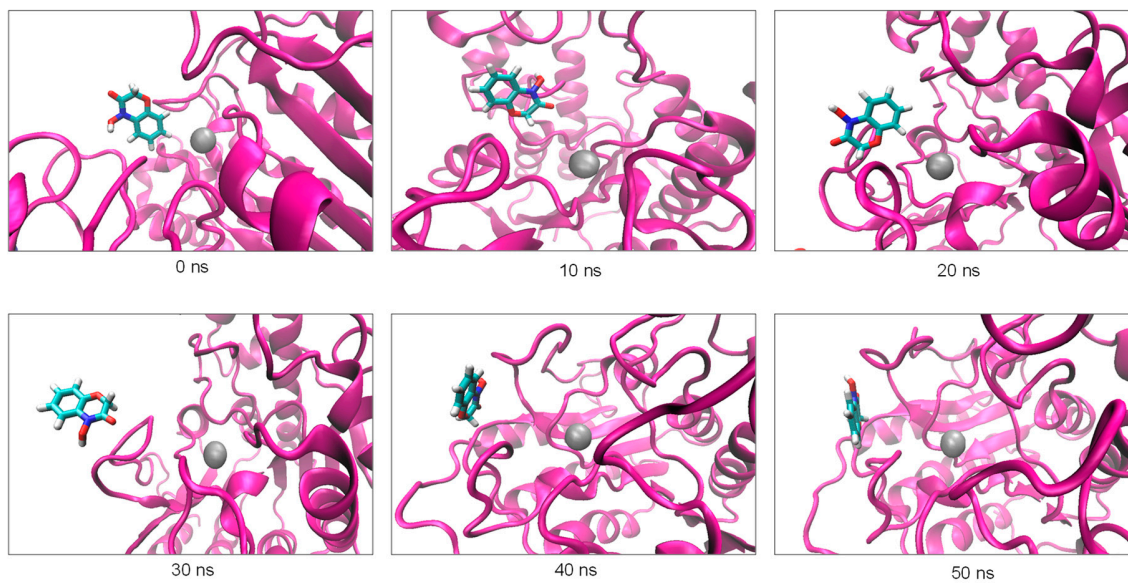


Figure S19. Snapshots of the molecular dynamic *in silico* simulation among HDA6 protein, D-DIBOA and zinc cofactor.

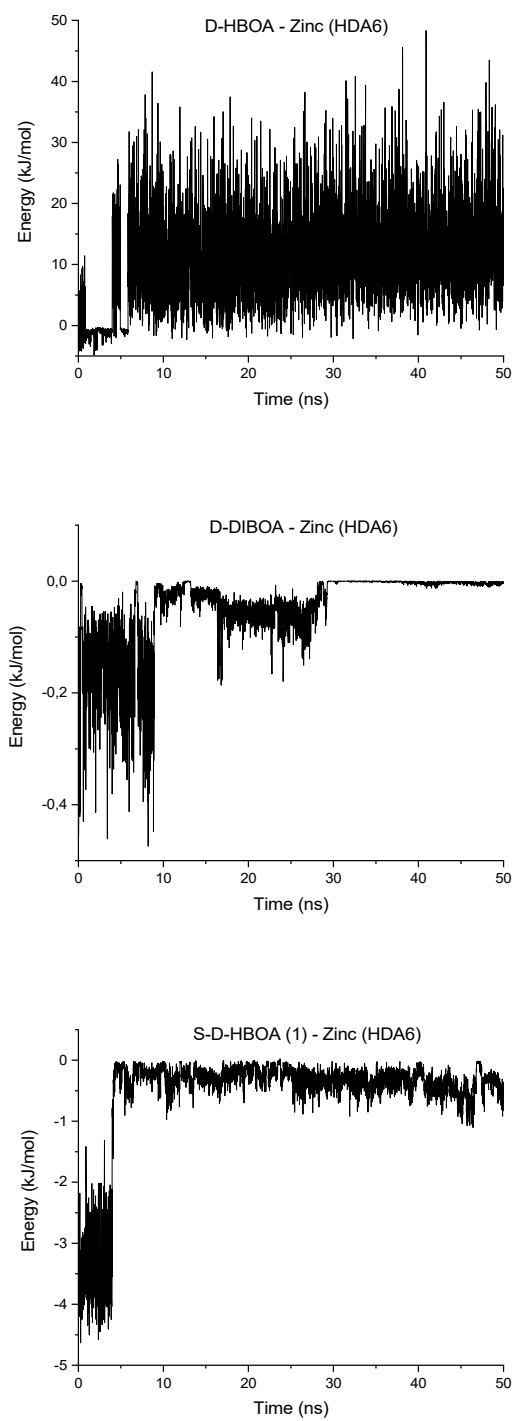


Figure S20. Energy values between the ligands and zinc cofactor along the simulated molecular dynamic.

D-HBOA – HDA6

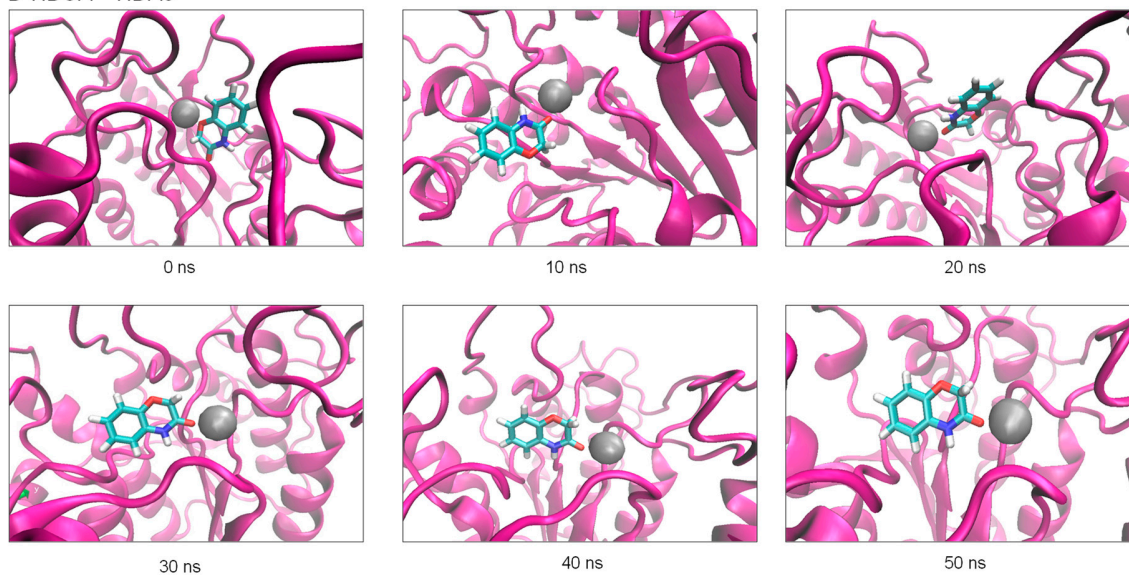


Figure S21. Snapshots of the molecular dynamic *in silico* simulation among HDA6 protein, D-HBOA and zinc cofactor.

Table S11. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Echinochloa crus-galli* germination. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Echinochloa crus-galli</i> Germination							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	2	-2	-55**	-8	-14	-5	-7	-81**
300 μ M	-12	19	-2	2	14	-5	-12	-81**
100 μ M	2	2	-7	-2	14	14	7	-81**
30 μ M	0	21	-2	-2	13	5	-2	-26*
10 μ M	7	14	16	-11	-8	-2	2	-14

Table S12. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Echinochloa crus-galli* root development. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Echinochloa crus-galli</i> Roots							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-29**	-81**	-89**	-35**	-21	-86**	-68**	-94**
300 μ M	17	-31*	-66**	-7	-26	-71**	-37**	-90**
100 μ M	11	-5	-4	-2	-3	-15	1	-82**
30 μ M	10	11	2	14	-2	-4	9	-80**
10 μ M	19	5	1	-7	-14	-1	9	-80**

Table S13. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Echinochloa crus-galli* shoots development. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Echinochloa crus-galli</i> Shoots							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-21*	-48**	-79**	-18	10	-55**	-47**	-92**
300 μ M	7	-20*	-38**	-3	5	-46**	-11	-90**
100 μ M	12	17	6	-16*	-14	-5	15	-89**
30 μ M	5	9	-2	8	-2	-14	9	-87**
10 μ M	15	20	11	11	2	7	8	-88**

Table S14. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Lolium rigidum* germination. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Lolium rigidum</i> Germination							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-19	-68**	-66**	-1	-12*	-34**	-39**	-86**
300 μ M	-10	5	-17	-32	-12	-12	-2	-86**
100 μ M	0	3	-5	15	15*	8	8	-86**
30 μ M	-7	-3	5	4	-7	3	-5	-86**
10 μ M	12*	7	10	8	2	-3	-3	-86**

Table S15. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Lolium rigidum* root formation. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Lolium rigidum</i> Roots							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-68**	-73**	-76**	-52**	-56**	-79**	-75**	-89**
300 μ M	-38**	-28*	-43**	-35*	-16	-43**	-44**	-89**
100 μ M	-23*	-15	-29*	-30	-34	-34**	-32**	-86**
30 μ M	-18	-16	-11	-30*	-26*	-20	-20*	-87**
10 μ M	-14	-10	-16	-13	-7	-6	-22	-87**

Table S16. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Lolium rigidum* shoot formation. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Lolium rigidum</i> Shoots							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-37**	-35	-72**	-24*	-14	-51**	-54**	-94**
300 μ M	-5	3	-9	3	10	-21**	-6	-91**
100 μ M	-4	3	2	-3	10	-3	-2	-91**
30 μ M	-9	3	-1	3	8	16*	10	-91**
10 μ M	-2	2	0	5	20*	8	12	-91**

Table S17. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Portulaca oleracea* germination. * Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Portulaca oleracea</i> Germination							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	0	-14	-20*	-21*	-11	-17	-24*	-13
300 μ M	-8	-8	-12	-4	-4	-7	0	-11
100 μ M	-8	1	3	-9	-9	3	5	-5
30 μ M	-9	-5	-3	-7	4	-11	-1	-5
10 μ M	-18	-1	-9	-11	4	-1	-8	-17

Table S18. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Portulaca oleracea* roots development. *Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Portulaca oleracea</i> Roots							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-59**	-74**	-83**	-81**	-56**	-90**	-84**	-89**
300 μ M	-19**	-21**	-39**	-53**	-6	-82**	-83**	-87**
100 μ M	-13*	-2	-11*	-26**	-4	-66**	-61**	-87**
30 μ M	-5	-2	-5	-6	-5	-46**	-47**	-85**
10 μ M	-5	-3	-12	-9*	-14	-15*	-14	-83**

Table S19. Data of the phytotoxicity study of S-D-HBOAs and benzoxazinones against *Portulaca oleracea* shoots development. *Indicates significant difference in the two-sided Welch's test at $p < 0.05$. ** Indicates significant difference in the two-sided Welch's test at $p < 0.01$.

	<i>Portulaca oleracea</i> Shoots							
	1	2	3	1a	5	D-DIBOA	D-HBOA	Pendimethalin
1000 μ M	-57**	-76**	-81**	-64**	-25**	-73**	-68**	-77**
300 μ M	-23**	-28**	-37**	-32**	-22**	-51**	-50**	-78**
100 μ M	-6	-12**	-29**	-4	-11*	-28**	-25**	-79**
30 μ M	-3	-2	-26**	5	-8	-13**	-11*	-78**
10 μ M	5	0	-19*	-1	-4	-6	0	-77**