

Supporting information

Acetohydroxamic Acids Salts: Mild, Simple and Effective Degradation Reagents to Counter Novichok Nerve Agents

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1 Chemicals

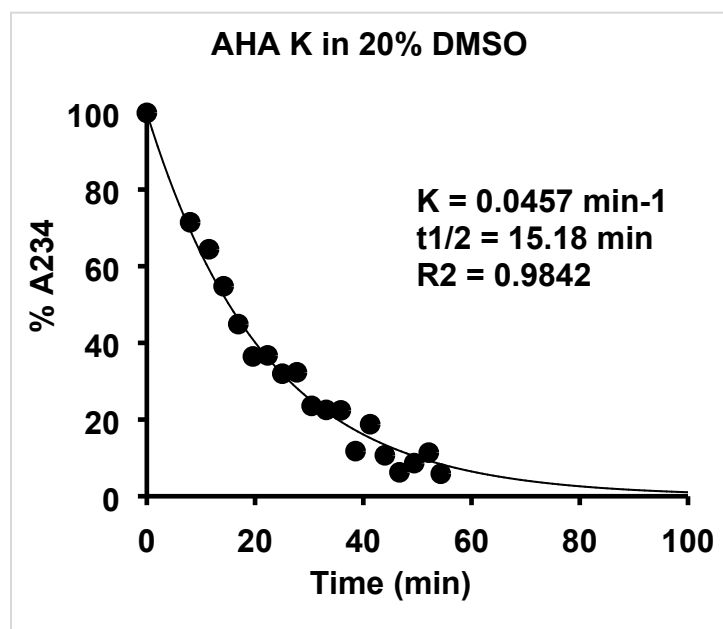
The following active pharmaceutical ingredients, reagents and solvents (HPLC grade): Acetohydroxamic Acid (AHA), Salicylhydroxamic acid (SHA), Caprylhydroxamic acid (CHA), Bufexamac (BUF), diethylamine (DEA), ethanolamine (Olamine), pyrrolidinoethanol (Epolamine), piperazine, Dimethyl sulfoxide (DMSO), propylene glycol (PG), polyethylene glycol monoethyl ether (mPEG), sodium hydroxide and potassium hydroxide were purchased from commercial suppliers and used without further purification. Deionized water was obtained from a laboratory water purification system.

N-(1-(diethylamino)ethylidene)-P-methylphosphonamidic fluoride (A230), methyl (E)-(1-(diethylamino)ethylidene)phosphoramidofluoridate (A232), ethyl (E)-(1-(diethylamino)ethylidene)phosphoramidofluoridate (A234) Was synthesized in house (>95% purity).

2 Abbreviations

AChE	acetyl choline esterase
AHA	Acetohydroxamic acid
BUF	Bufexamac
CHA	Caprylhydroxamic acid
CWAs	chemical warfare agents
DEA	Diethylamine
DMSO	Dimethylsulfoxide
epolamine	N-(2-hydroxyethyl)pyrrolidine
Eq.	Equivalent
FDA	U.S. Food and Drug Administration
MOFs	Metal–organic frameworks
mPEG	Poly(ethylene glycol) monomethyl ether
N.R	No Reaction
NMR	Nuclear Magnetic Resonance
Olamine	Ethanolamine
OPCW	Organisation for the Prohibition of Chemical Weapons
OPs	organophosphorus compounds
PG	Propylene glycol
RSDL	Reactive Skin Decontamination Lotion
SHA	Salicylhydroxamic acid
$t_{1/2}$	Half-life time

3 Kinetic Analysis and NMR spectra



Time (min)	% A234
0.0	100.00
8.0	71.46
11.5	64.42
14.2	54.77
16.9	44.90
19.6	36.46
22.3	36.74
25.0	31.97
27.7	32.33
30.5	23.57
33.2	22.52
35.9	22.40
38.6	11.77
41.3	18.79
44.0	10.68
46.7	6.24
49.4	8.64
52.1	11.37
54.3	5.88

Figure S1. Decomposition kinetic profile of A234 by AHA K in H₂O/DMSO 4:1.

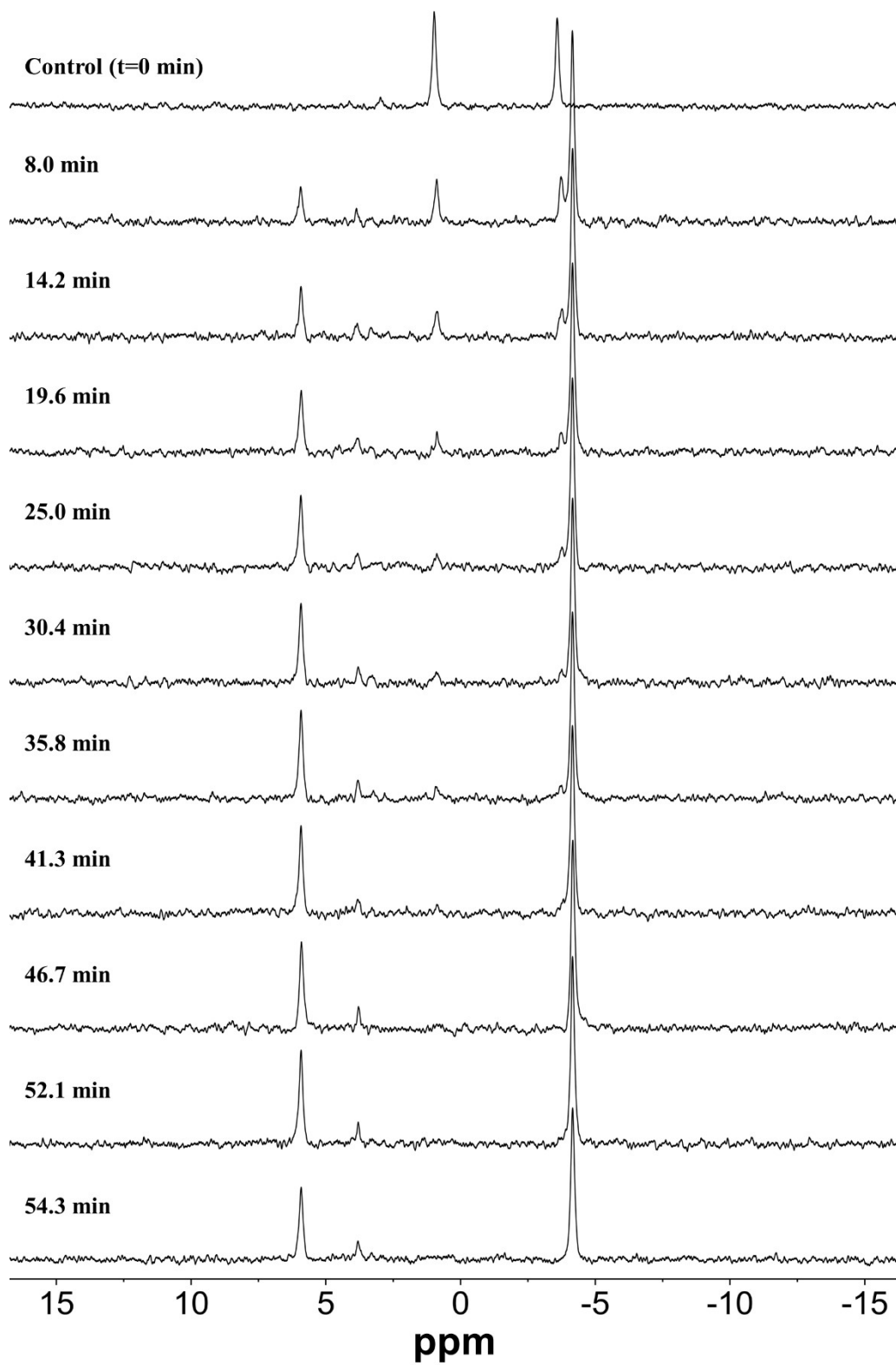
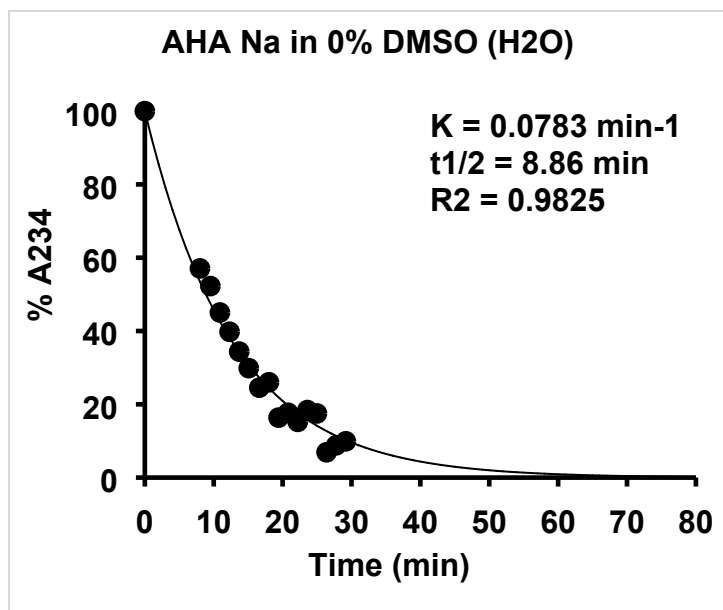


Figure S2. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA K in $\text{H}_2\text{O}/\text{DMSO}$ 4:1.



Time (min)	% A234
0.0	100.00
8.0	57.08
9.5	52.26
10.9	45.05
12.3	39.79
13.7	34.38
15.1	29.87
16.6	24.54
18.0	26.01
19.4	16.36
20.8	17.68
22.2	15.21
23.6	18.43
25.0	17.50
26.4	6.91
27.8	8.81
29.2	9.90

Figure S3. Decomposition kinetic profile of A234 by AHA Na in H₂O.

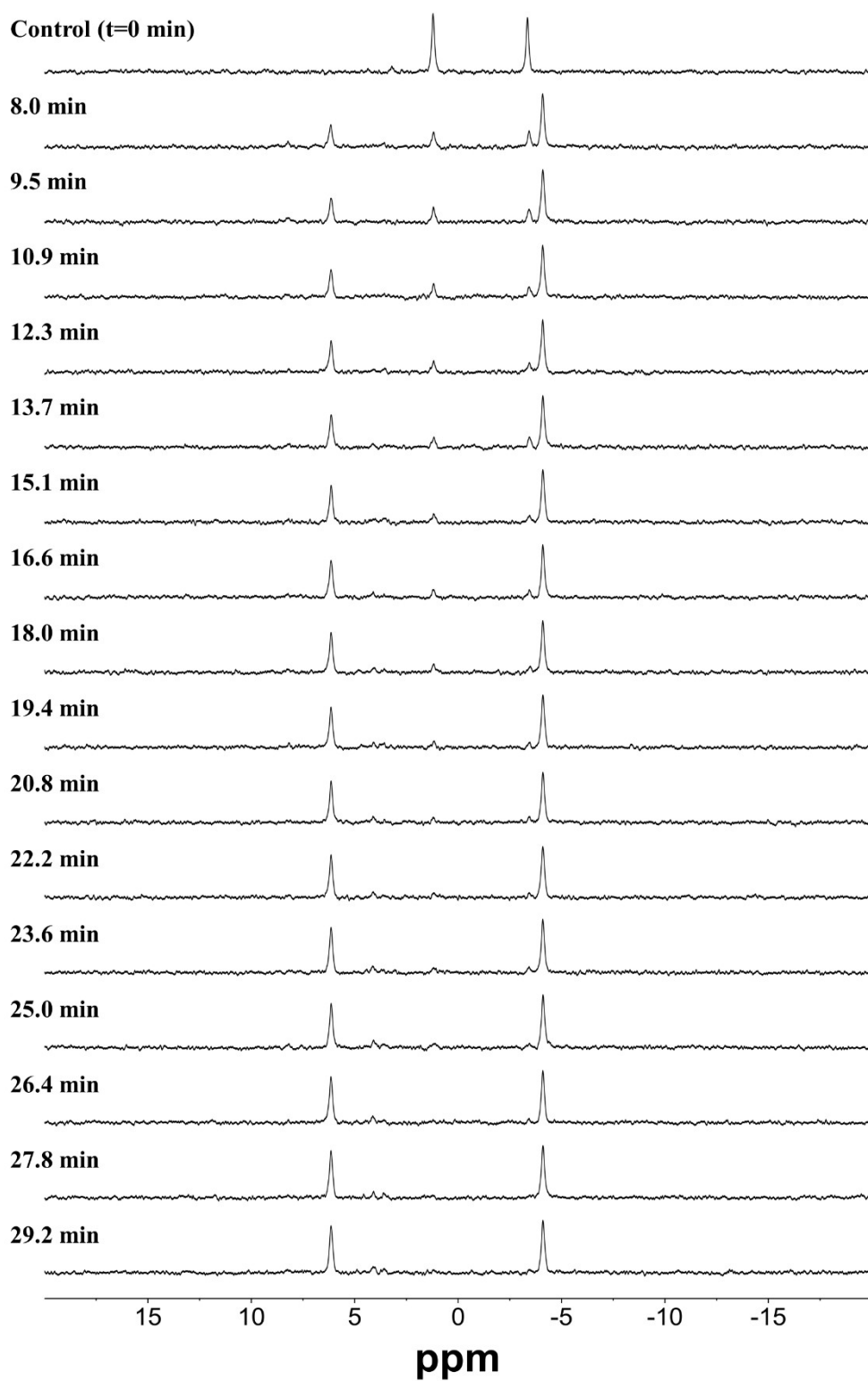
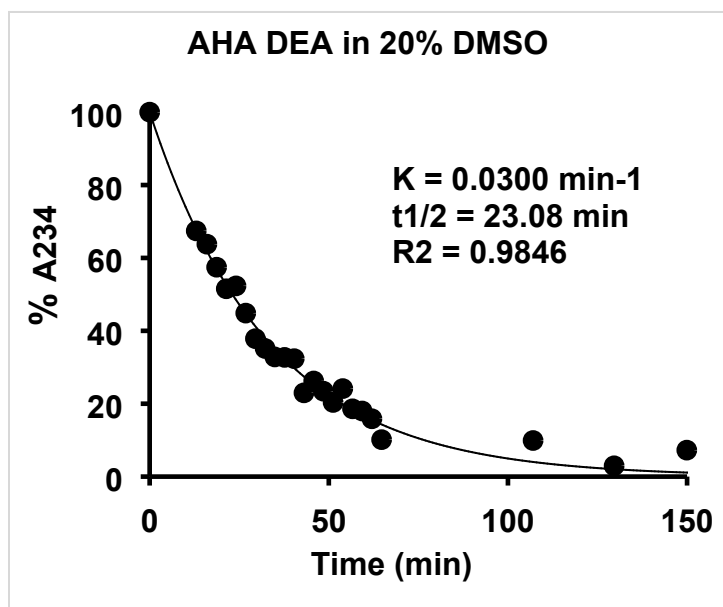


Figure S4. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA Na in H_2O .



Time (min)	% A234
0.0	100.00
13.0	67.42
16.0	63.78
18.7	57.45
21.4	51.54
24.1	52.33
26.8	44.86
29.5	37.85
32.2	35.15
34.9	32.83
37.7	32.72
40.4	32.36
43.1	22.98
45.8	26.24
48.5	23.44
51.2	20.35
53.9	24.15
56.6	18.60
59.3	18.00
62.0	15.87
64.7	10.14
107.0	9.91
129.6	2.97
149.9	7.26

Figure S5. Decomposition kinetic profile of A234 by AHA DEA in H₂O/DMSO 4:1.

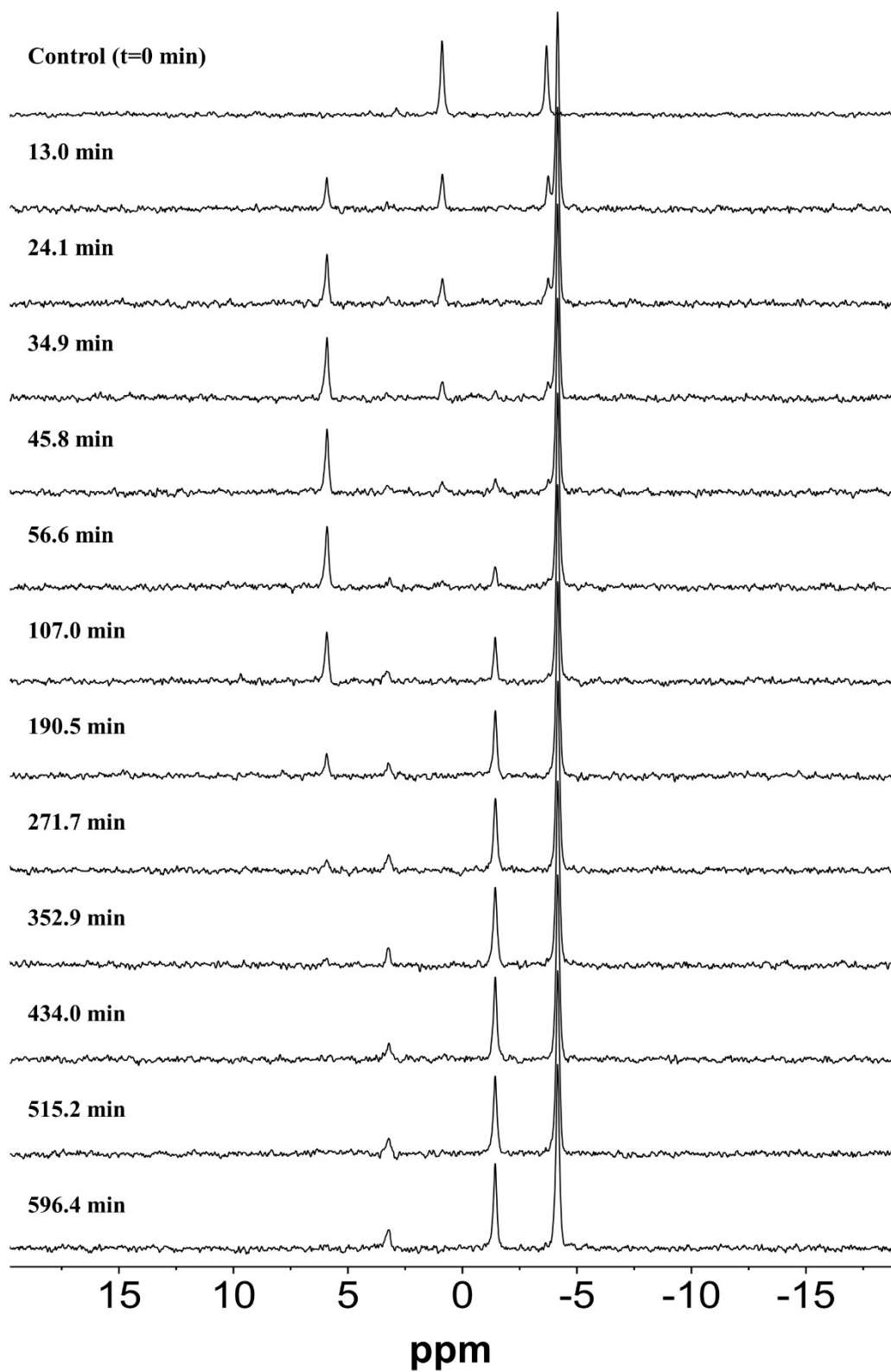
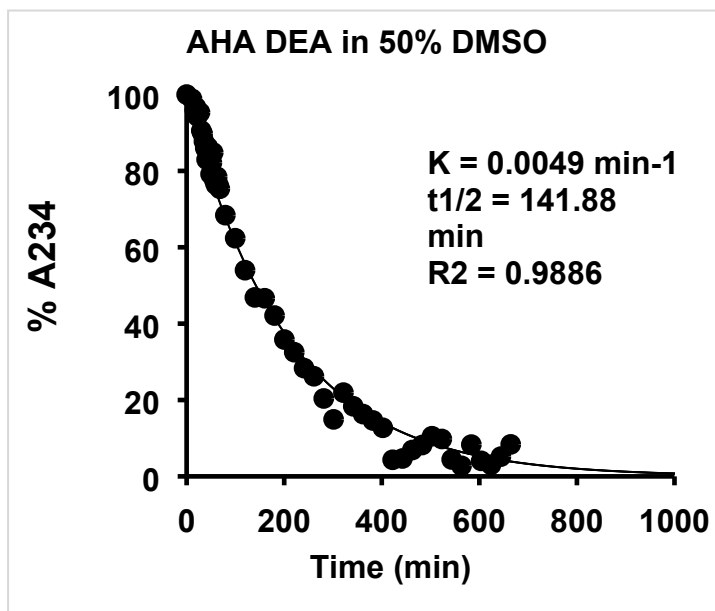


Figure S6. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA DEA in $\text{H}_2\text{O}/\text{DMSO}$ 4:1.



Time (min)	% A234	Time (min)	% A234
0.0	100.00	160.1	46.65
11.0	98.88	180.2	42.12
16.5	96.02	200.4	35.84
19.3	96.68	220.6	32.52
22.0	94.32	240.7	28.36
24.7	95.01	260.9	26.22
27.4	95.32	281.1	20.41
30.1	90.56	301.2	14.93
32.8	89.77	321.4	21.94
35.5	87.72	341.6	18.36
38.2	85.97	361.8	16.31
40.9	82.98	381.9	14.64
43.6	86.23	402.1	12.72
46.3	83.99	422.3	4.34
49.1	79.17	442.4	4.69
51.8	82.11	462.6	6.90
54.5	84.81	482.8	8.21
57.2	77.42	502.9	10.52
59.9	76.40	523.1	9.79
62.6	78.45	543.3	4.43
65.3	76.31	563.4	2.76
68.0	75.34	583.6	8.32
79.4	68.41	603.8	4.07
99.6	62.38	624.0	3.04
119.7	54.00	644.1	5.18
139.9	46.87	664.3	8.38

Figure S7. Decomposition kinetic profile of A234 by AHA DEA in H₂O/DMSO 1:1.

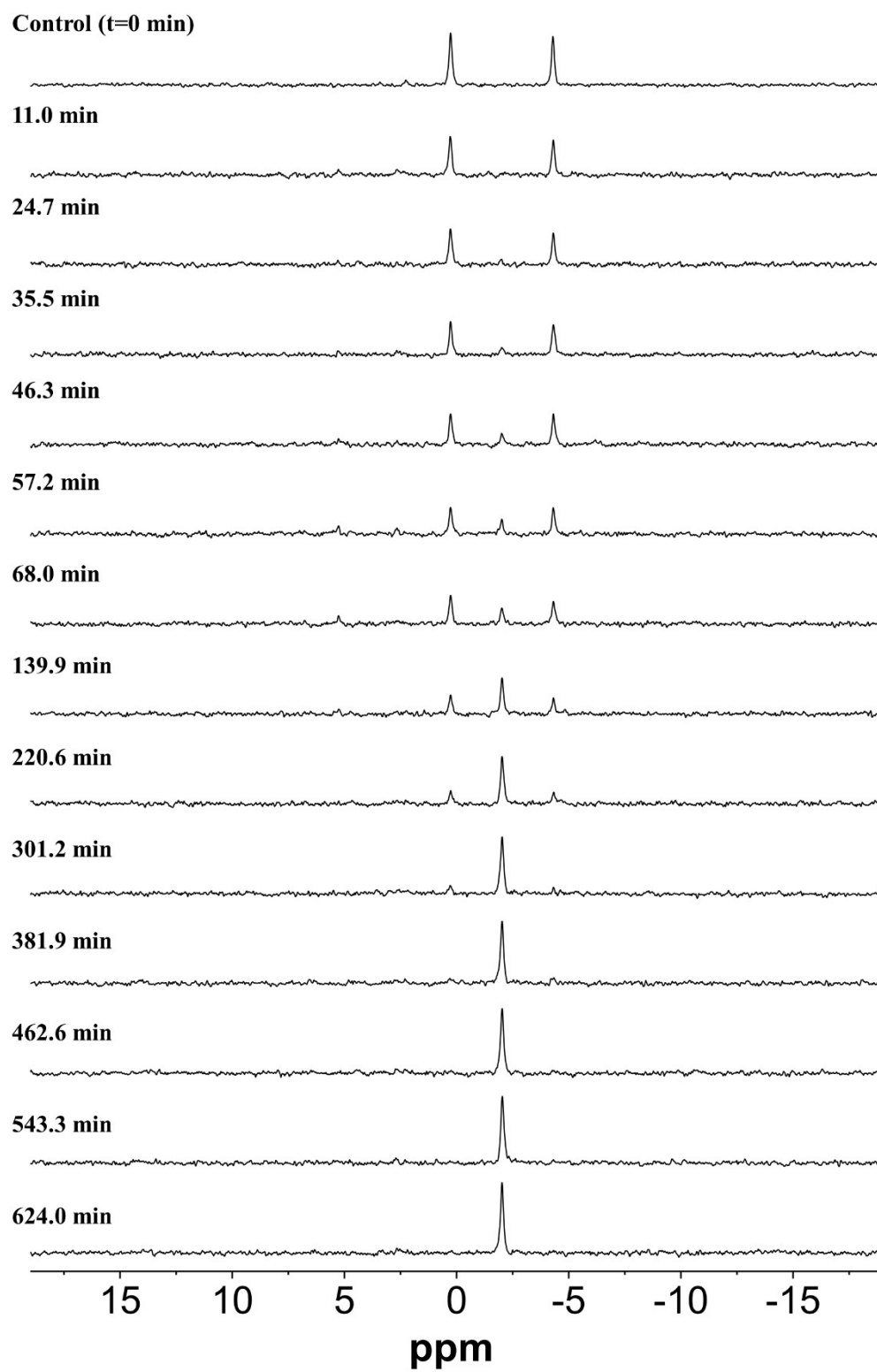
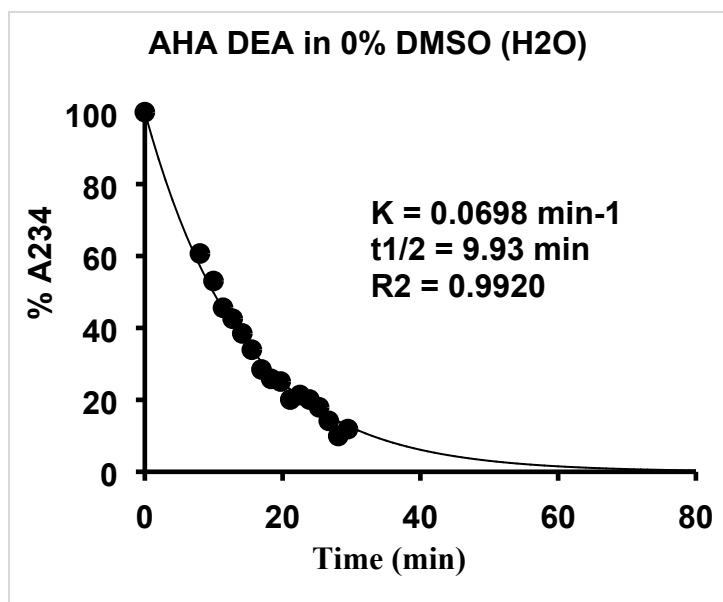


Figure S8. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA DEA in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A234
0.0	100.00
8.0	60.70
10.0	53.05
11.4	45.60
12.8	42.56
14.2	38.47
15.5	33.95
16.9	28.45
18.3	25.84
19.7	25.10
21.1	20.08
22.5	21.36
23.9	20.10
25.3	17.94
26.7	14.17
28.1	9.96
29.5	11.88

Figure S9. Decomposition kinetic profile of A234 by AHA DEA in H₂O.

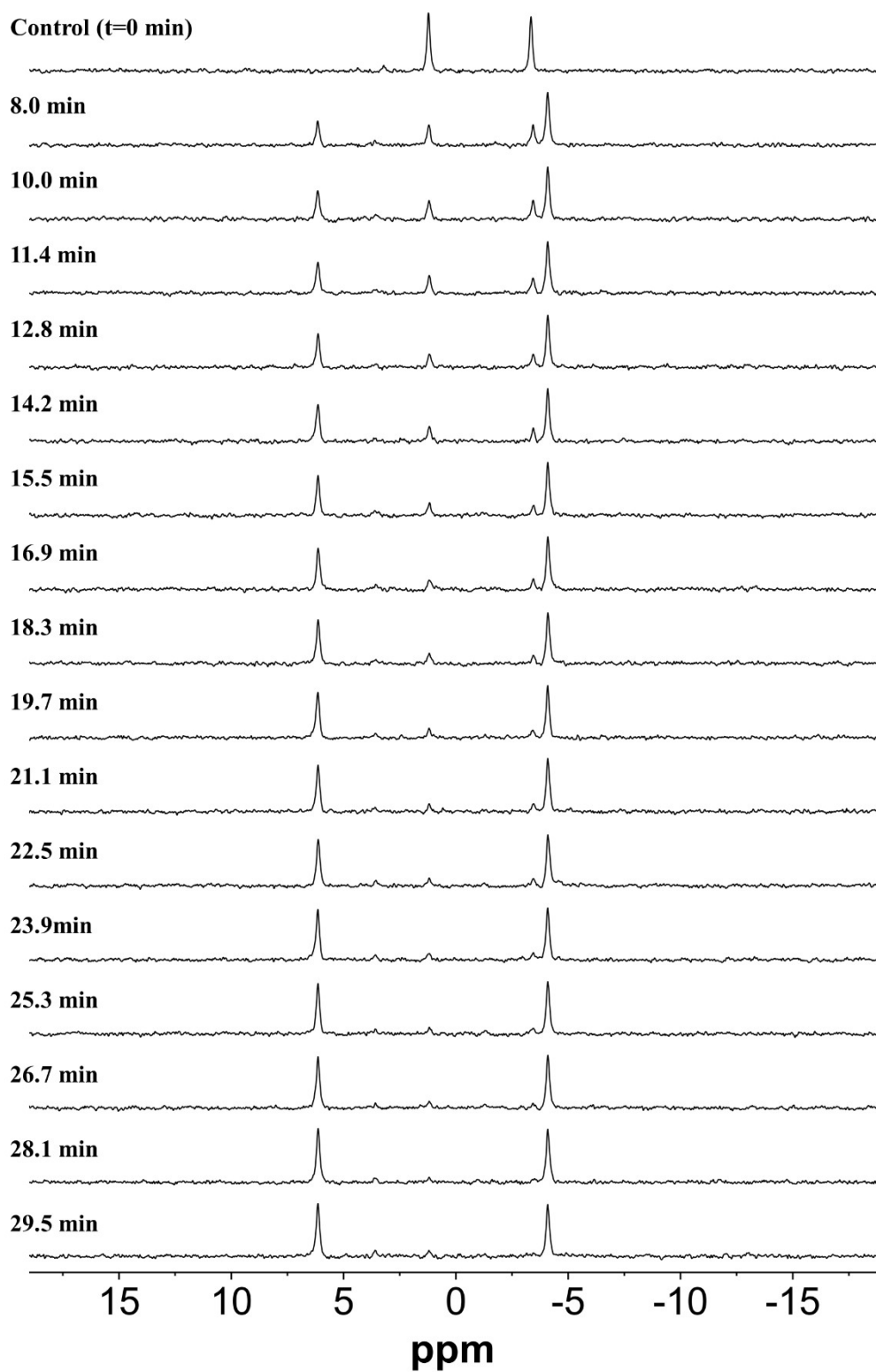
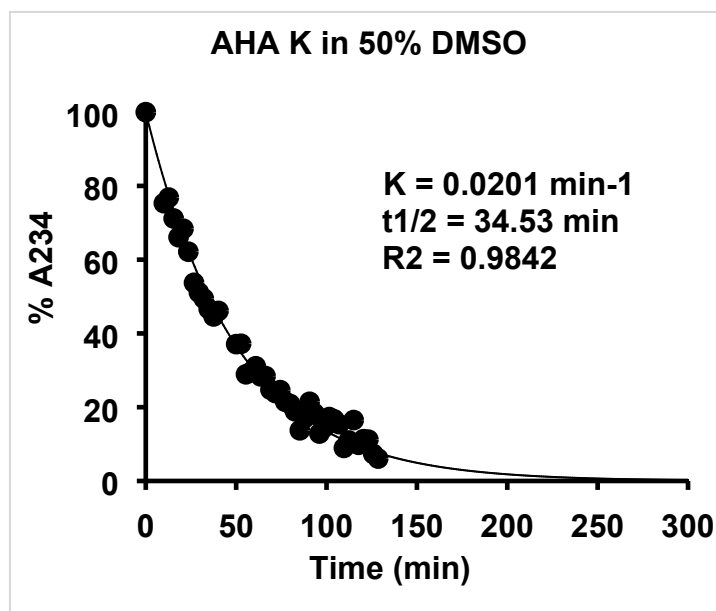


Figure S10. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA DEA in H_2O .



Time (min)	% A234	Time (min)	% A234
0.0	100.00	74.4	24.63
10.0	75.31	77.1	21.49
12.7	76.83	79.8	20.88
15.4	71.17	82.5	18.89
18.1	66.09	85.2	13.74
20.9	68.37	88.0	17.06
23.6	62.16	90.7	21.47
26.7	53.73	93.4	18.31
29.4	51.09	96.1	12.86
32.1	49.44	98.8	14.54
34.8	46.64	101.5	17.32
37.5	44.61	104.2	16.70
40.2	46.11	106.9	15.41
50.0	37.10	109.6	8.97
52.7	37.19	112.3	10.97
55.4	28.92	115.0	16.51
58.2	29.53	117.7	9.81
60.9	31.10	120.5	11.32
63.6	28.36	123.2	11.21
66.3	28.44	125.867	7.32
69.0	24.74	128.567	6.07
71.7	23.85		

Figure S11. Decomposition kinetic profile of A234 by AHA K in H₂O/DMSO 1:1.

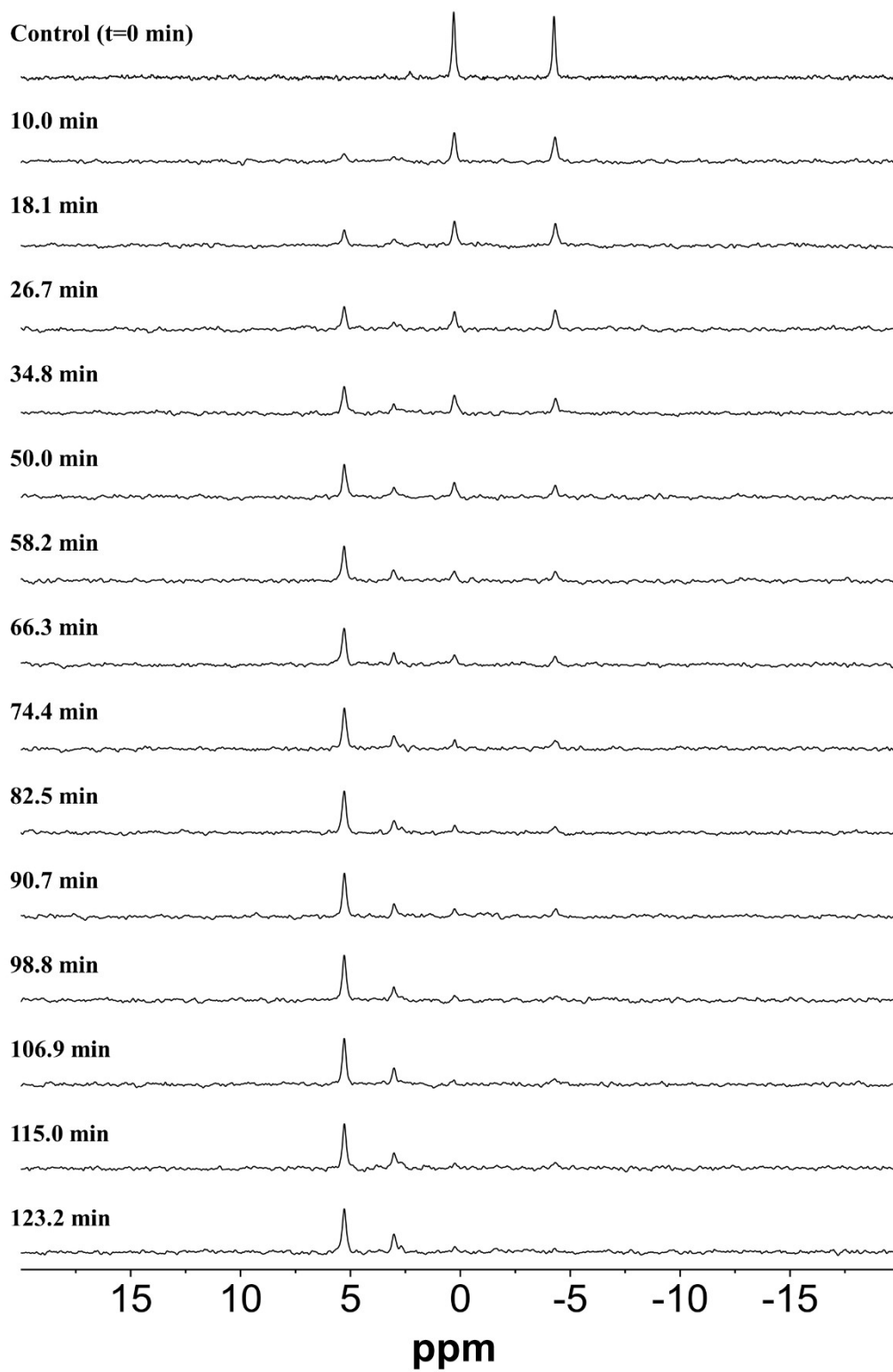
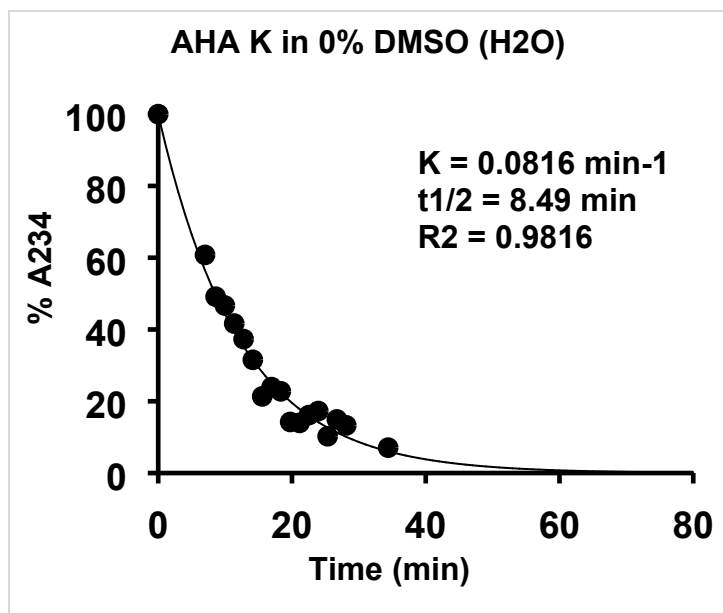


Figure S12. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA K in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A234
0.0	100.00
7.0	60.77
8.6	49.15
10.0	46.67
11.4	41.66
12.8	37.33
14.2	31.55
15.6	21.35
17.0	23.95
18.3	22.76
19.7	14.23
21.1	13.97
22.5	16.14
23.9	17.28
25.3	10.25
26.7	14.94
28.1	13.28
34.4	7.07

Figure S13. Decomposition kinetic profile of A234 by AHA K in H₂O.

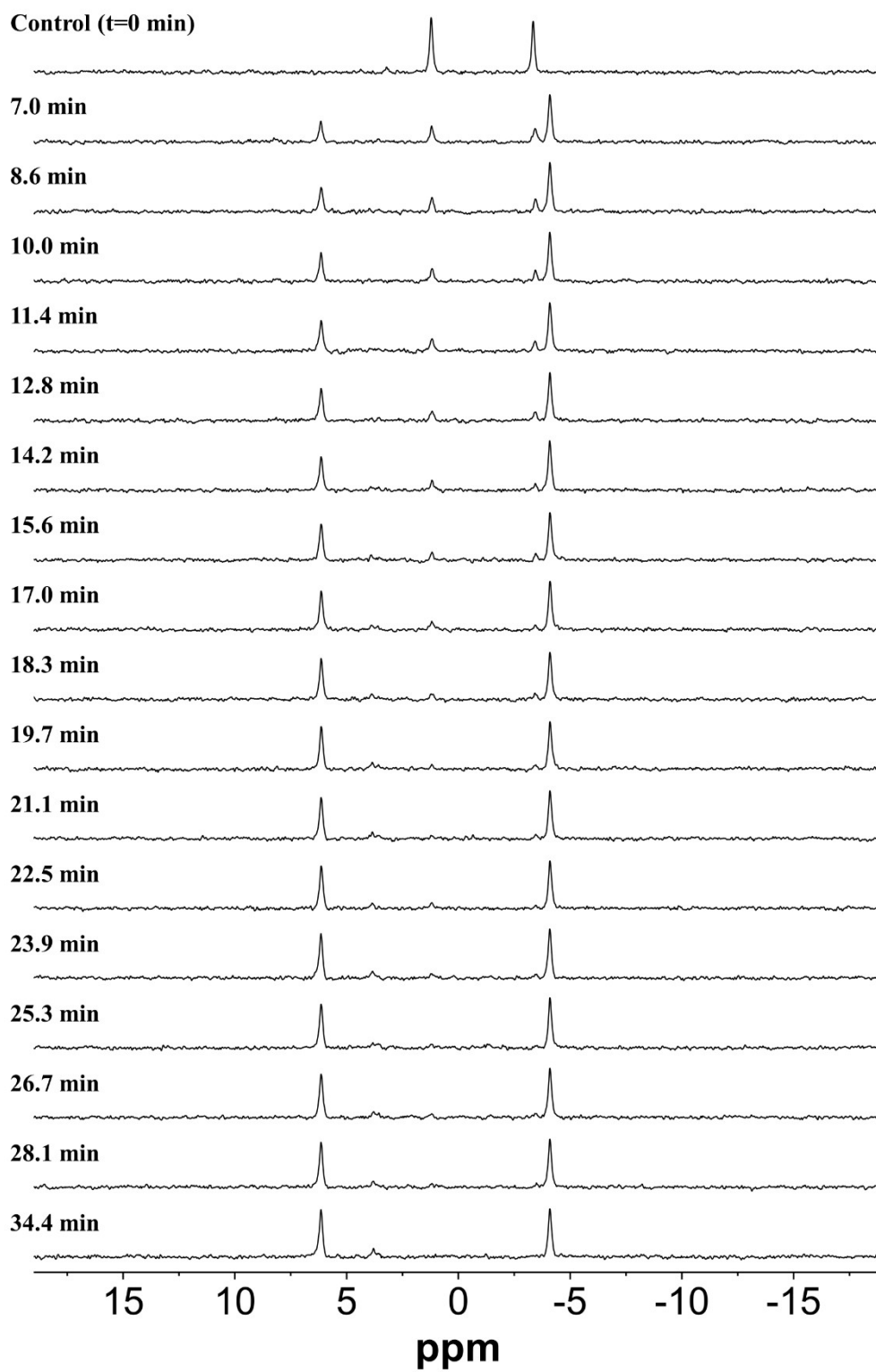
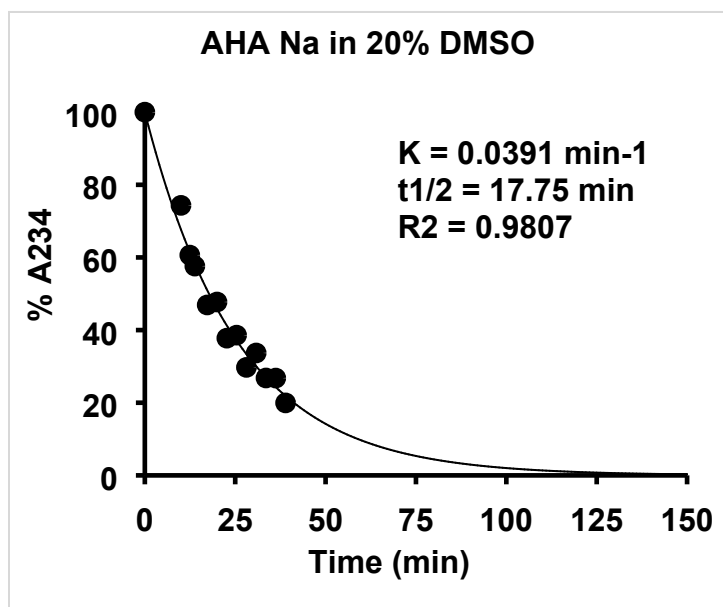


Figure S14. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA K in H_2O .



Time (min)	% A234
0.0	100.00
10.0	74.34
12.4	60.65
13.8	57.62
17.3	46.92
20.0	47.73
22.7	37.78
25.4	38.61
28.1	29.73
30.8	33.70
33.5	26.82
36.2	26.79
38.9	19.95

Figure S15. Decomposition kinetic profile of A234 by AHA Na in H₂O/DMSO 4:1.

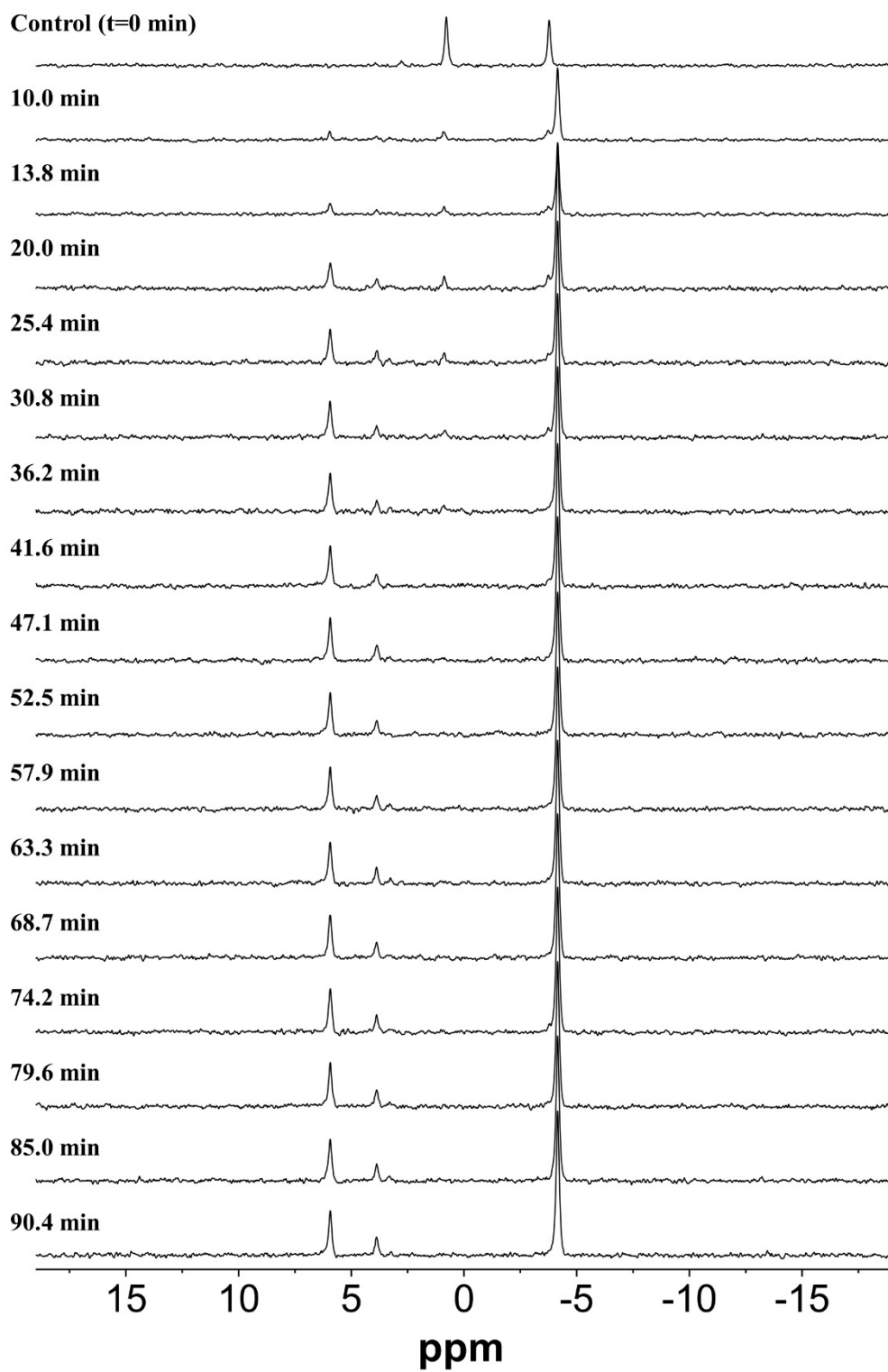
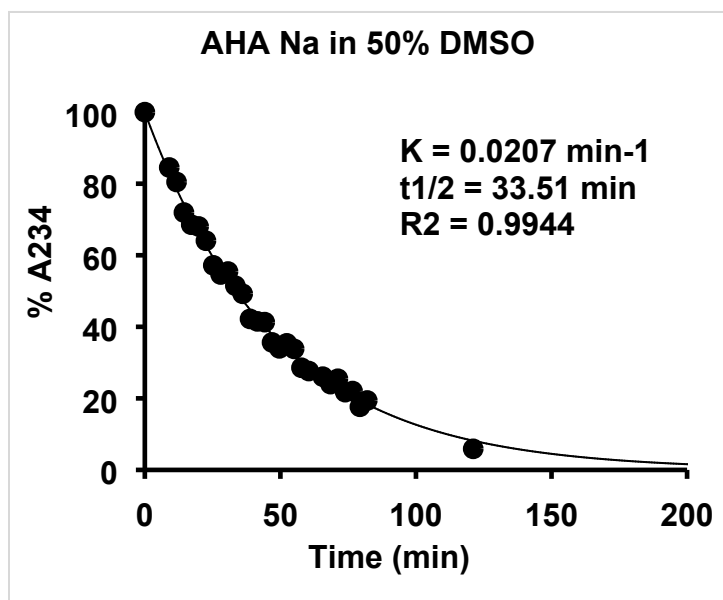


Figure S16. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA Na in $\text{H}_2\text{O}/\text{DMSO}$ 4:1.



Time (min)	% A234
0.0	100.00
9.0	84.53
11.7	80.48
14.4	71.94
17.1	68.55
19.8	68.05
22.5	64.06
25.3	57.18
28.0	54.62
30.7	55.45
33.4	51.49
36.1	49.23
38.8	42.21
41.5	41.52
44.2	41.30
46.9	35.64
49.6	33.98
52.4	35.38
55.1	33.83
57.8	28.56
60.5	27.63
65.6	26.07
68.5	23.98
71.2	25.48
73.9	21.73
76.6	22.04
79.3	17.65
82.0	19.41
121.1	5.89

Figure S17. Decomposition kinetic profile of A234 by AHA Na in H₂O/DMSO 1:1.

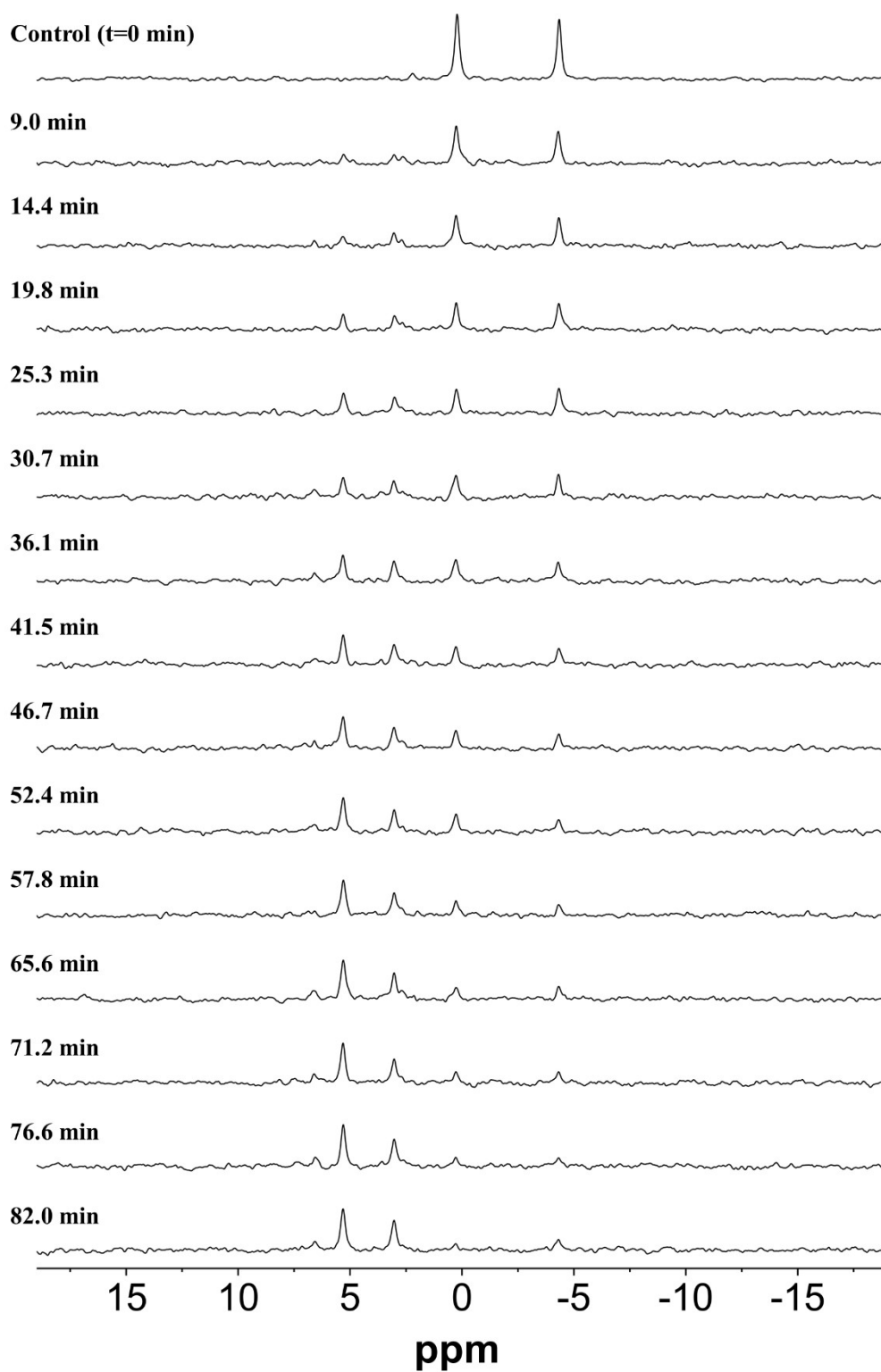
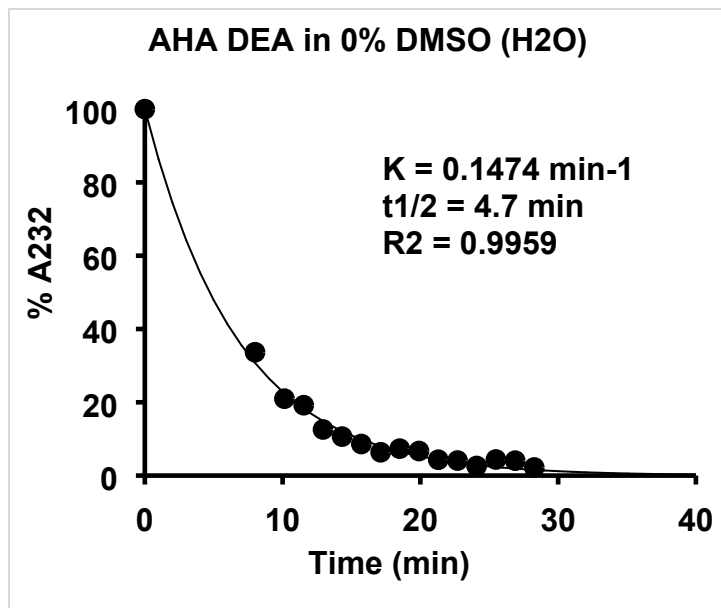


Figure S18. Stacked ^{31}P NMR spectra presenting the decomposition of A234 by AHA Na in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
8.0	33.66
10.1	20.98
11.5	19.21
12.9	12.58
14.3	10.64
15.7	8.62
17.1	6.36
18.5	7.35
19.9	6.71
21.3	4.33
22.7	4.10
24.1	2.62
25.5	4.39
26.9	4.07
28.3	2.21

Figure S19. Decomposition kinetic profile of A232 by AHA DEA in H₂O.

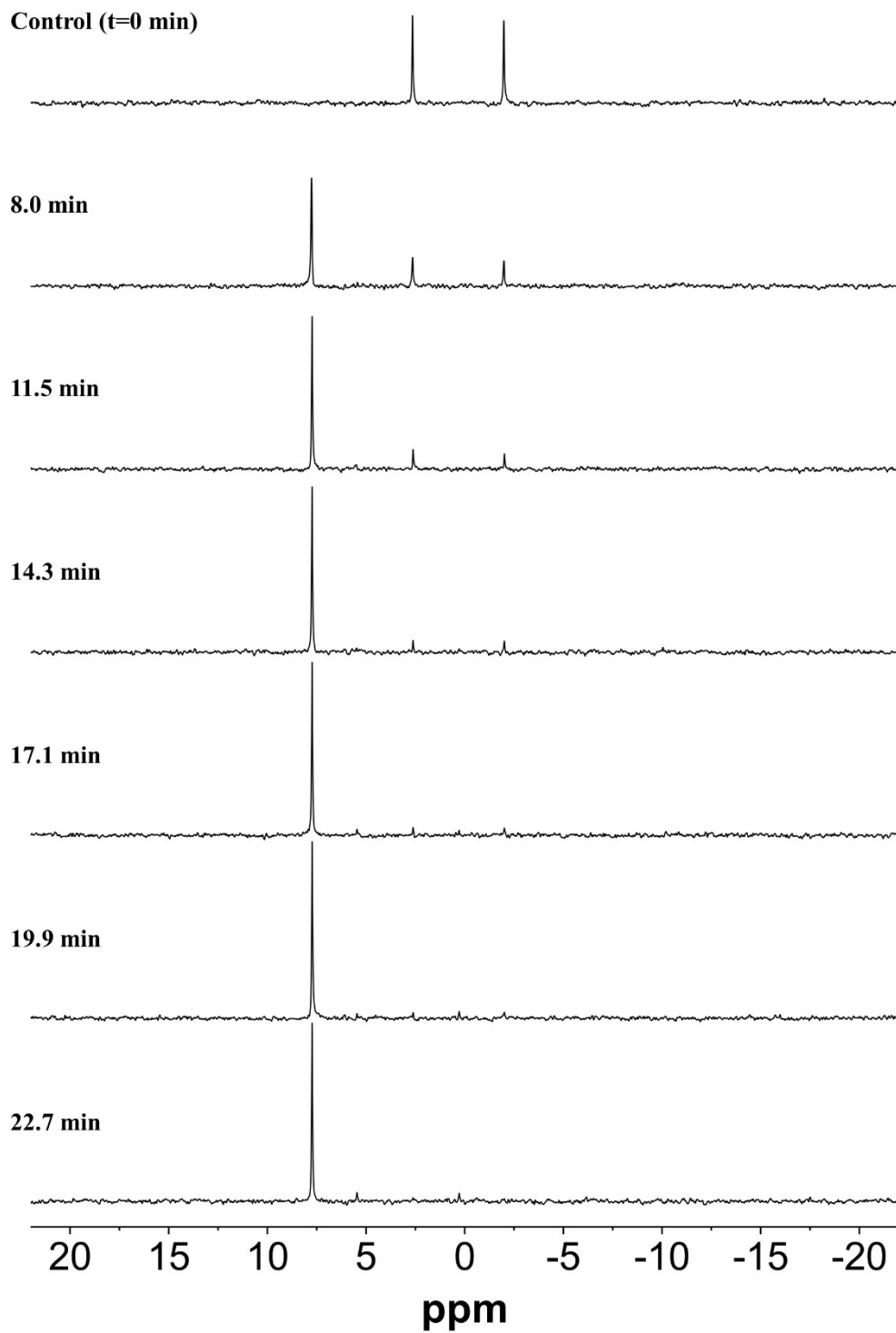
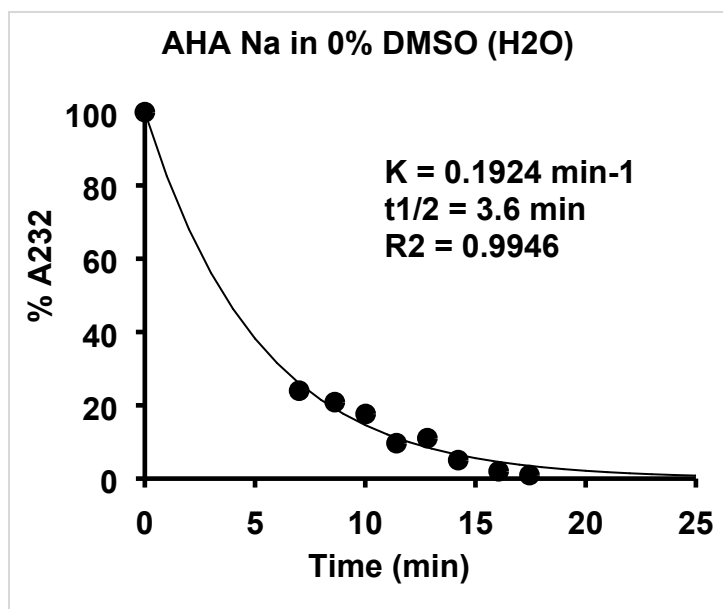


Figure S20. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA DEA in H_2O .



Time (min)	% A232
0.0	100.00
7.0	23.99
8.6	20.87
10.0	17.64
11.4	9.67
12.8	11.03
14.2	5.05
16.1	2.00
17.5	0.96

Figure S21. Decomposition kinetic profile of A232 by AHA Na in H₂O.

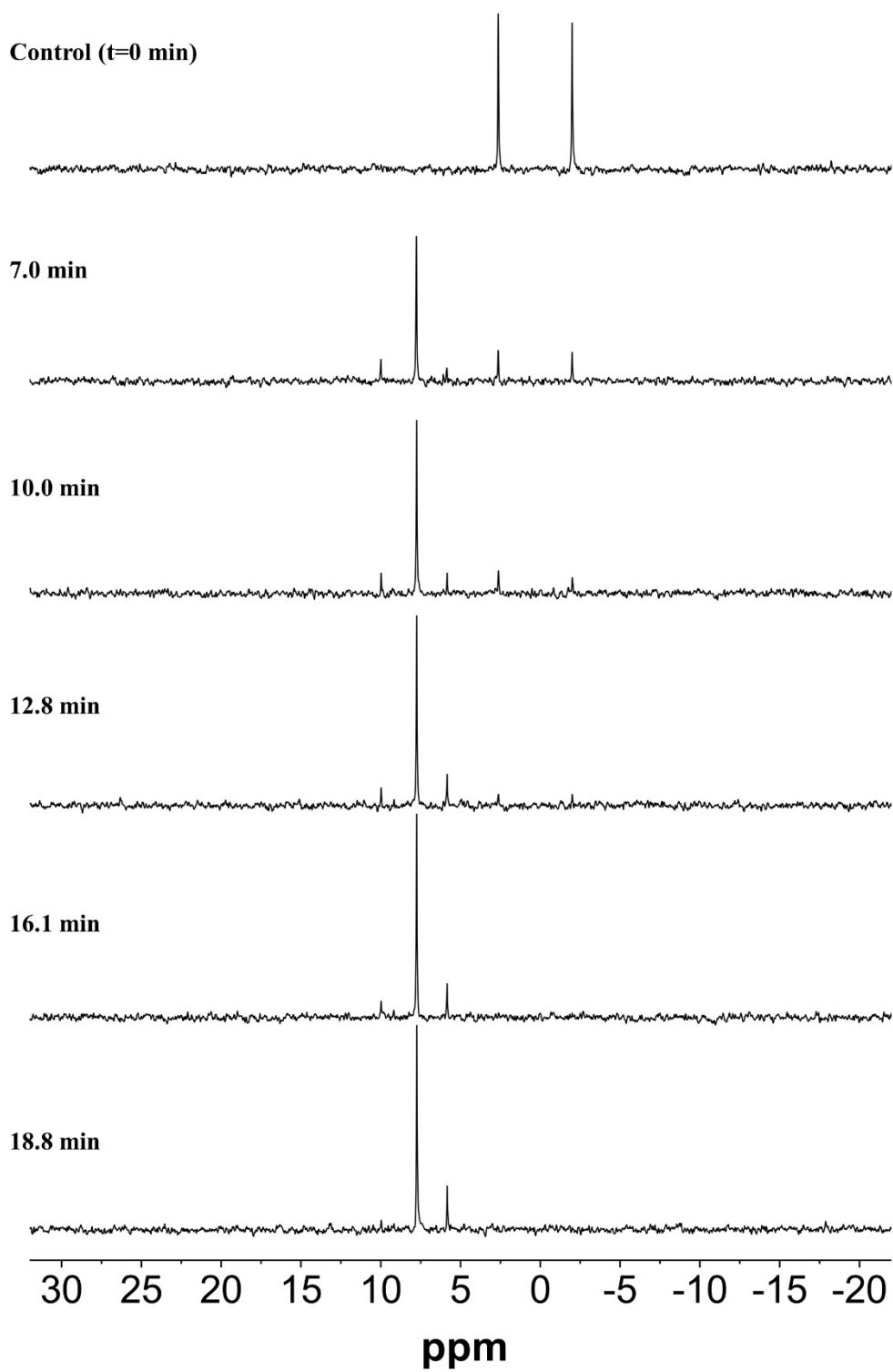
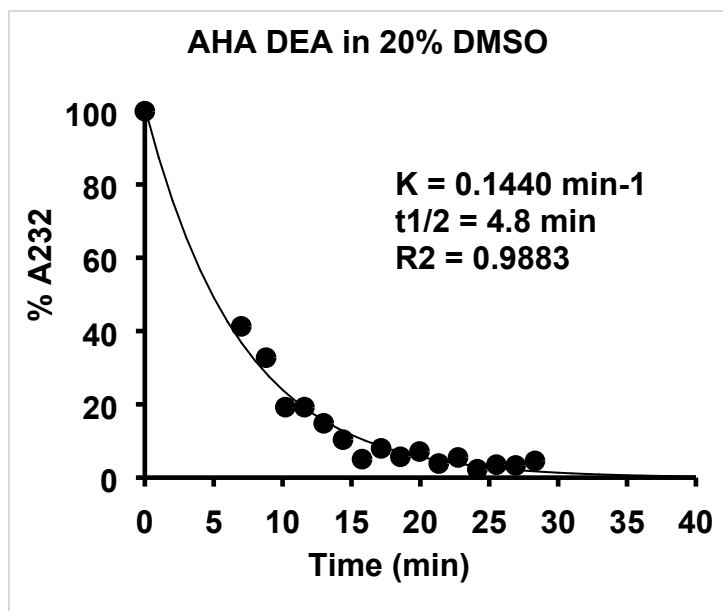


Figure S22. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Na in H_2O .



Time (min)	% A232
0.0	100.00
7.0	41.28
8.8	32.74
10.2	19.24
11.6	19.24
13.0	14.83
14.4	10.36
15.8	5.05
17.2	7.98
18.6	5.69
19.9	7.13
21.3	3.85
22.7	5.51
24.1	2.29
25.5	3.53
26.9	3.32
28.3	4.56

Figure S23. Decomposition kinetic profile of A232 by AHA DEA in H₂O/DMSO 4:1.

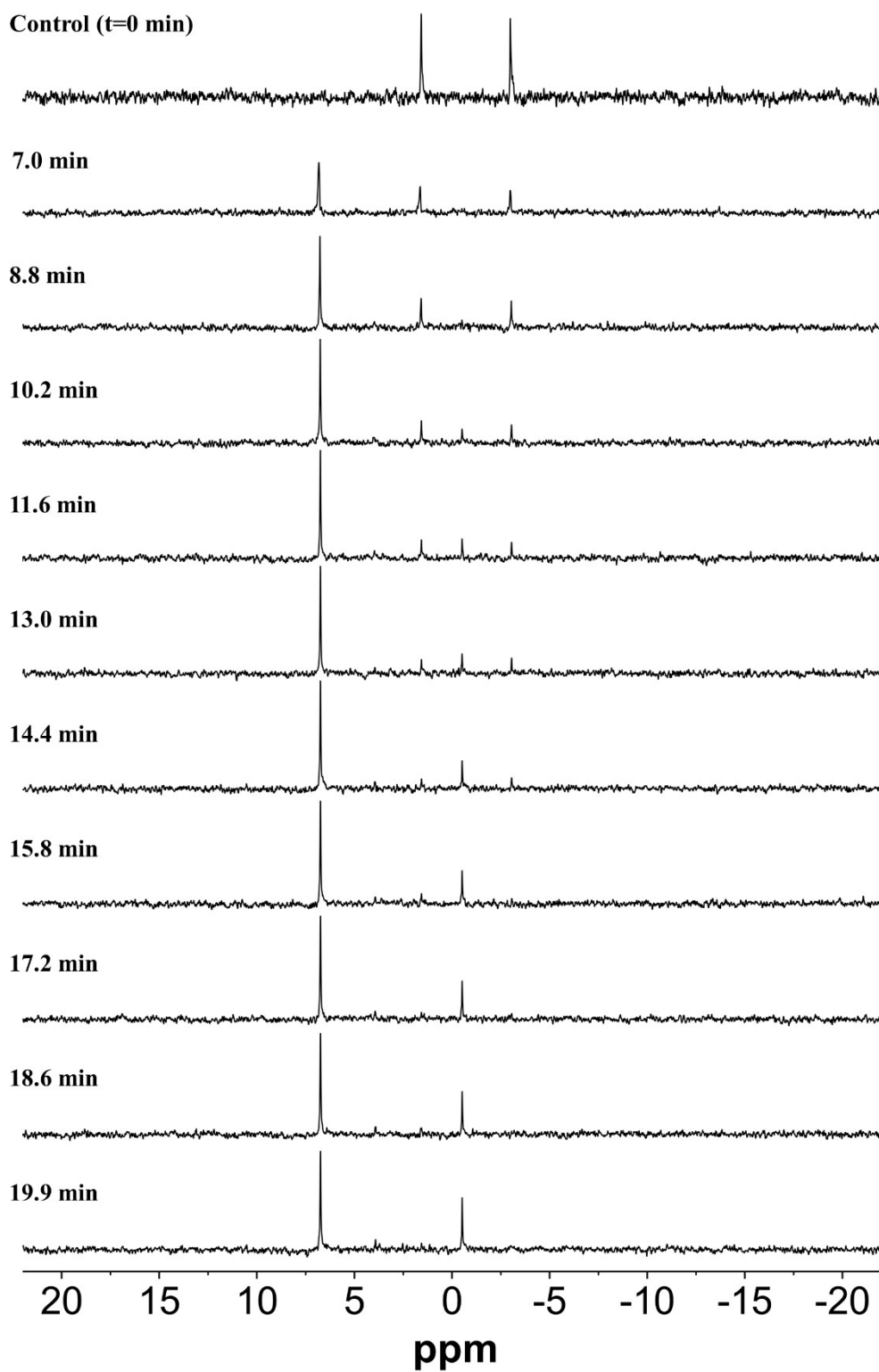
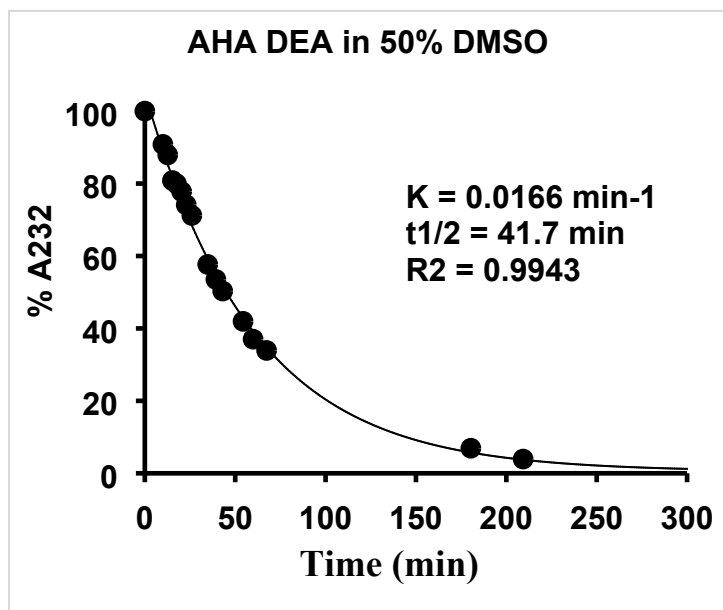


Figure S24. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA DEA in $\text{H}_2\text{O}/\text{DMSO}$ 4:1.



Time (min)	% A232
0.0	100.00
10.0	90.82
12.7	87.91
15.3	80.83
17.5	79.97
20.4	77.78
22.9	74.12
26.0	71.19
34.8	57.66
39.3	53.52
43.1	50.31
54.3	41.95
59.9	37.04
67.4	33.92
180.4	6.92
209.3	3.93

Figure S25. Decomposition kinetic profile of A232 by AHA DEA in H₂O/DMSO 1:1.

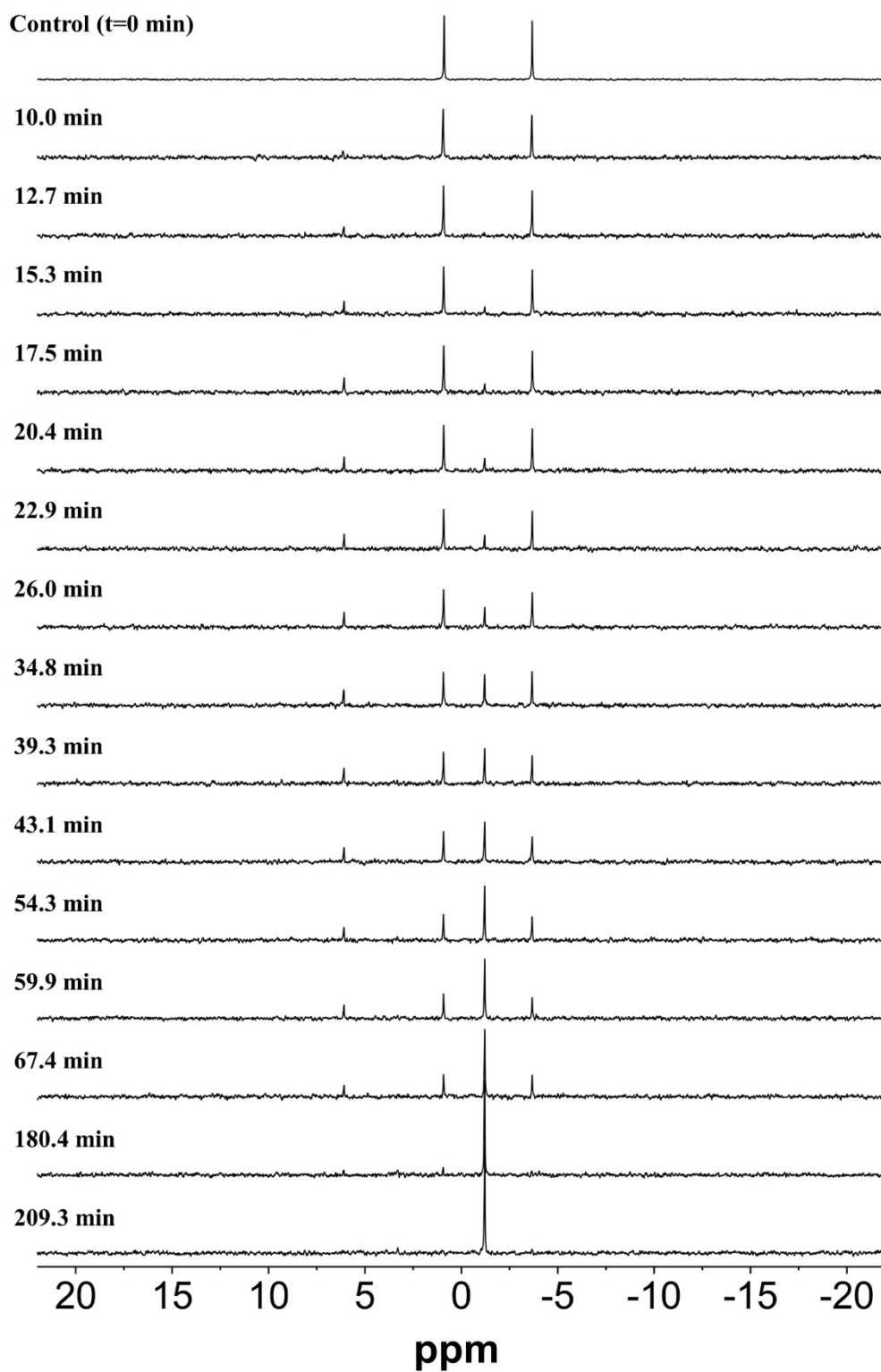
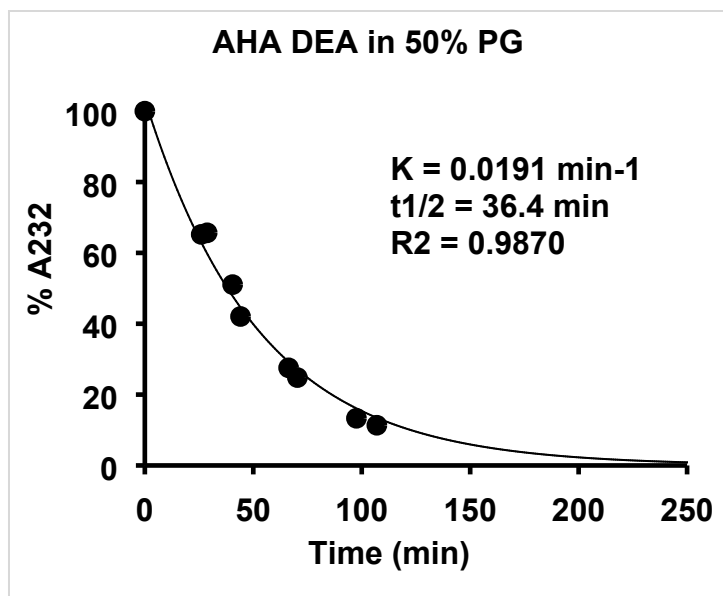


Figure S26. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA DEA in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
26.0	65.22
28.7	65.67
40.5	51.05
44.1	42.05
66.3	27.56
70.3	24.81
97.6	13.32
107.0	11.35

Figure S27. Decomposition kinetic profile of A232 by AHA DEA in H₂O/PG 1:1.

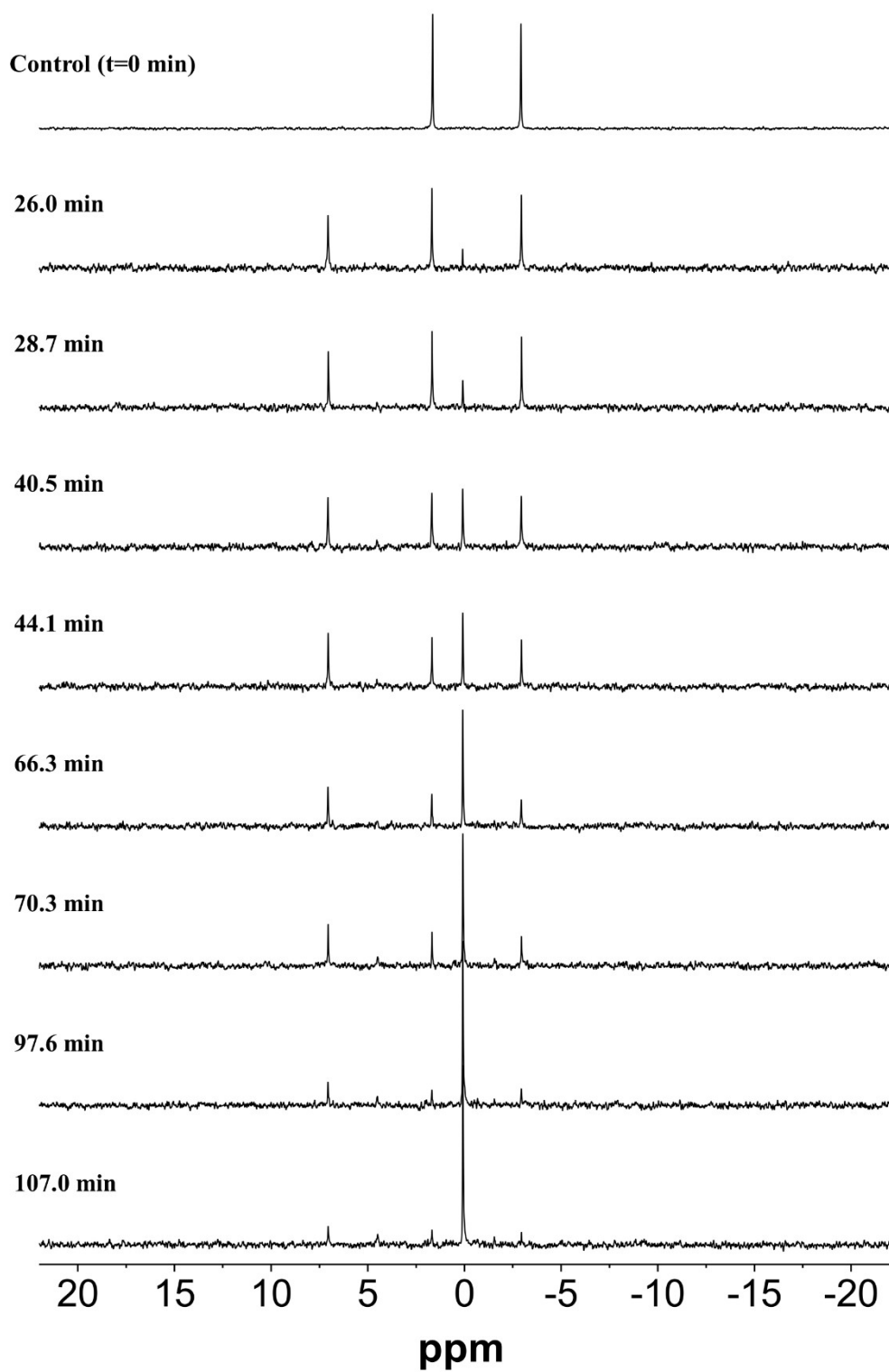
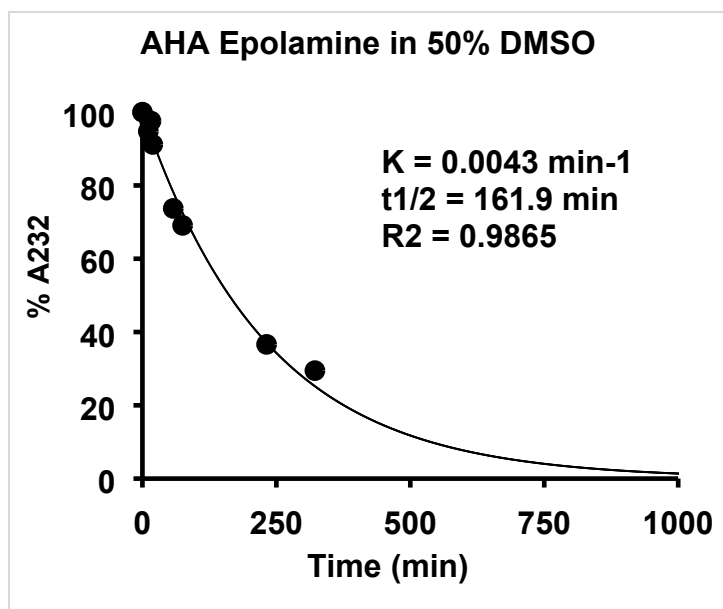


Figure S28. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA DEA in $\text{H}_2\text{O}/\text{PG}$ 1:1.



Time (min)	% A232
0.0	100.00
11.0	94.78
13.7	97.46
16.0	97.57
19.3	91.18
57.6	73.73
75.0	69.10
231.7	36.63
322.0	29.47

Figure S29. Decomposition kinetic profile of A232 by AHA Epolamine in H₂O/DMSO 1:1.

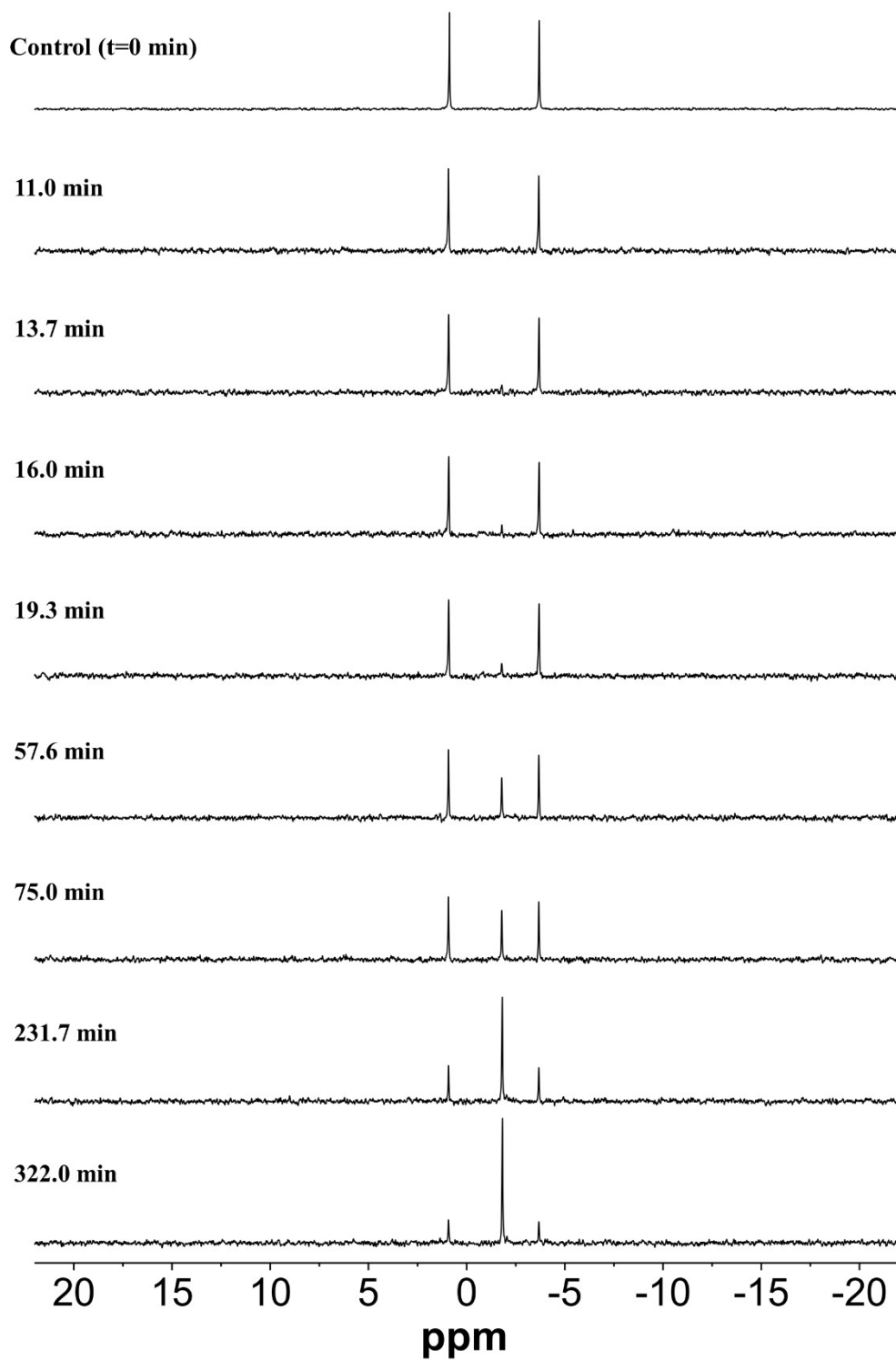
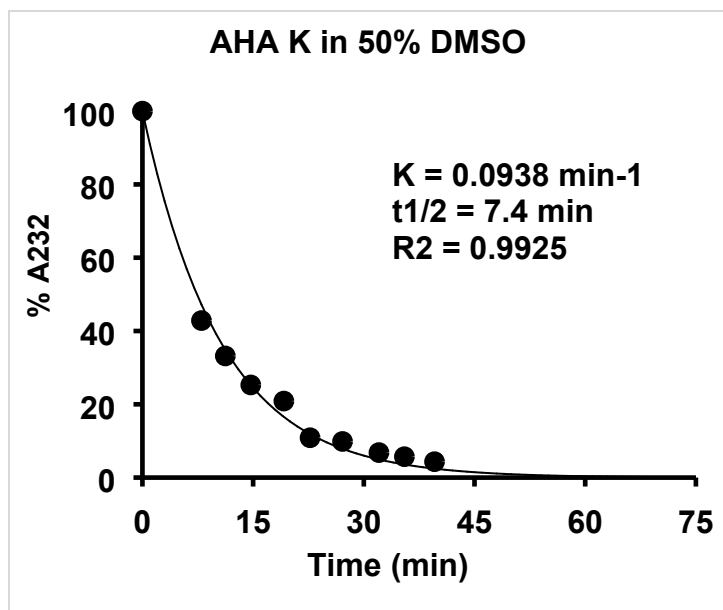


Figure S30. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Epolamine in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
8.0	42.85
11.2	33.19
14.7	25.28
19.2	20.88
22.7	10.87
27.1	9.86
32.1	6.82
35.5	5.70
39.6	4.34

Figure S31. Decomposition kinetic profile of A232 by AHA K in H₂O/DMSO 1:1.

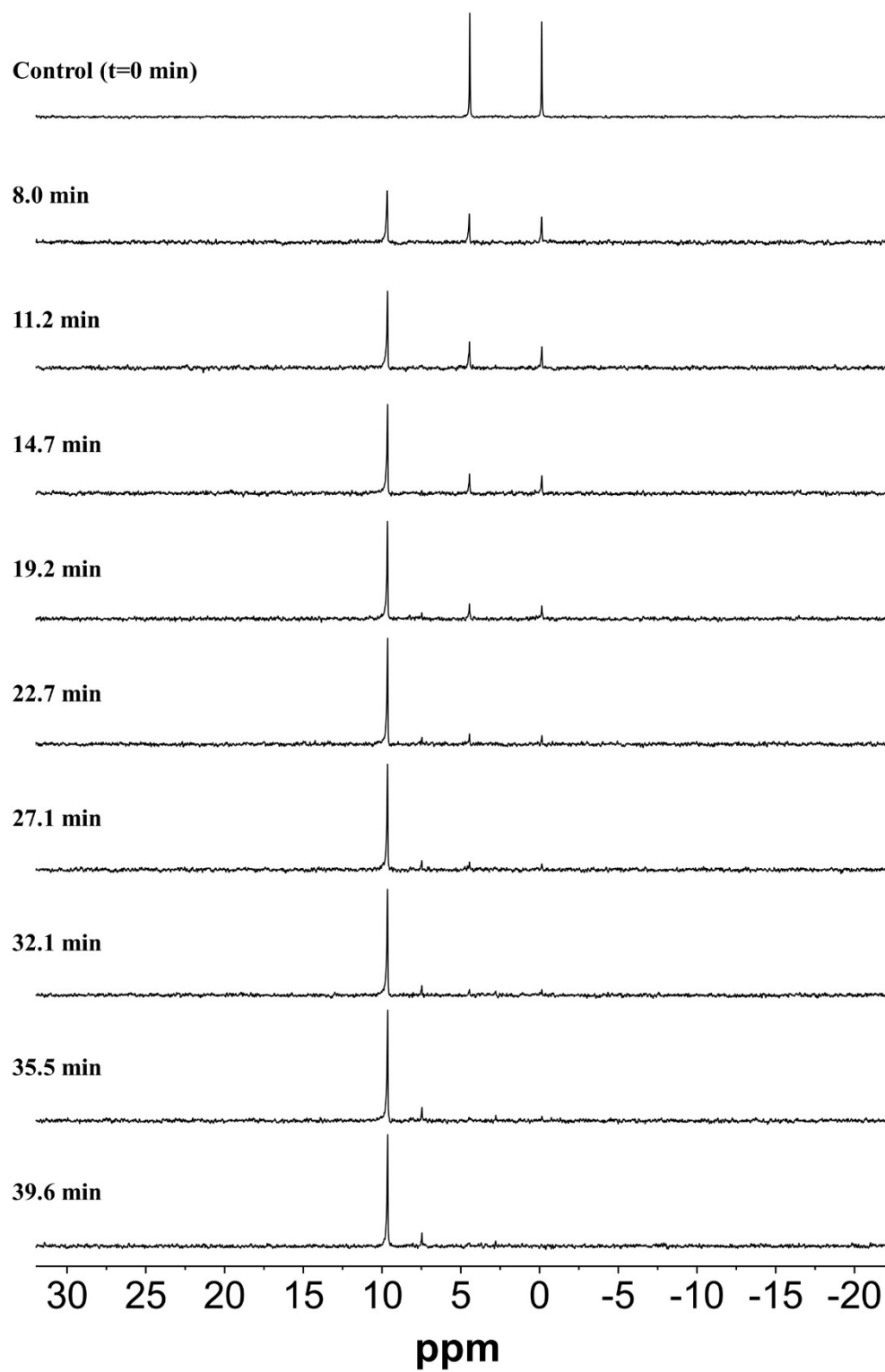
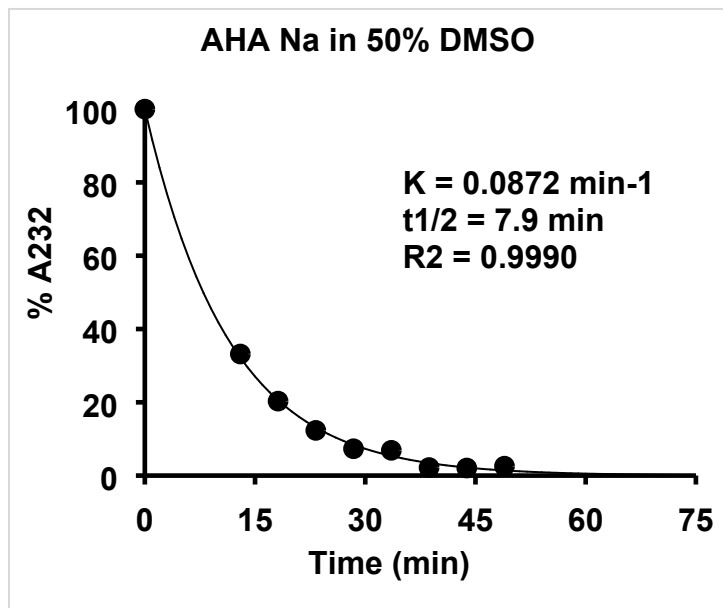


Figure S32. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA K in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
13.0	33.17
18.1	20.32
23.3	12.33
28.4	7.33
33.6	6.89
38.7	2.20
43.8	2.07
49.0	2.57

Figure S33. Decomposition kinetic profile of A232 by AHA Na in H₂O/DMSO 1:1.

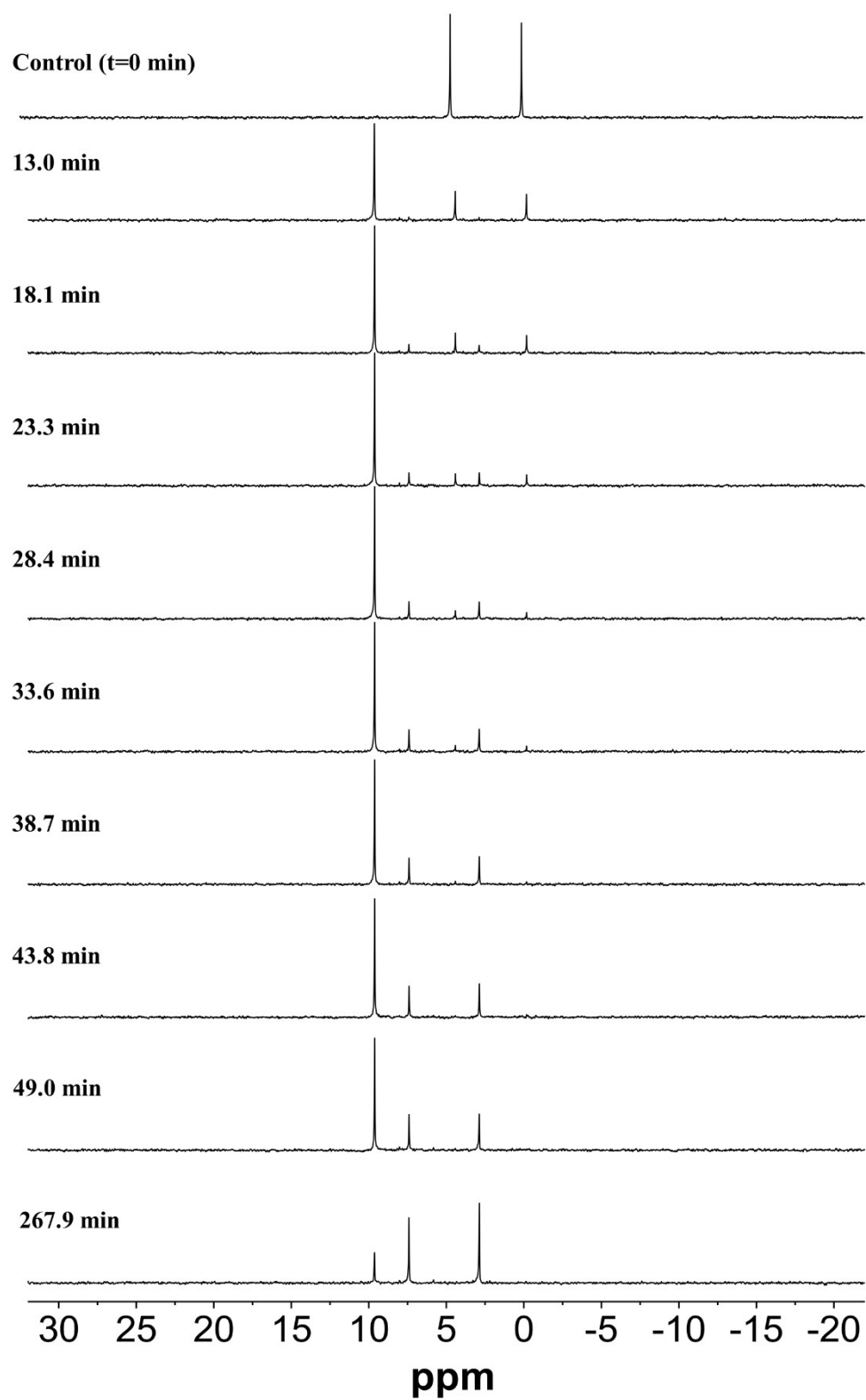
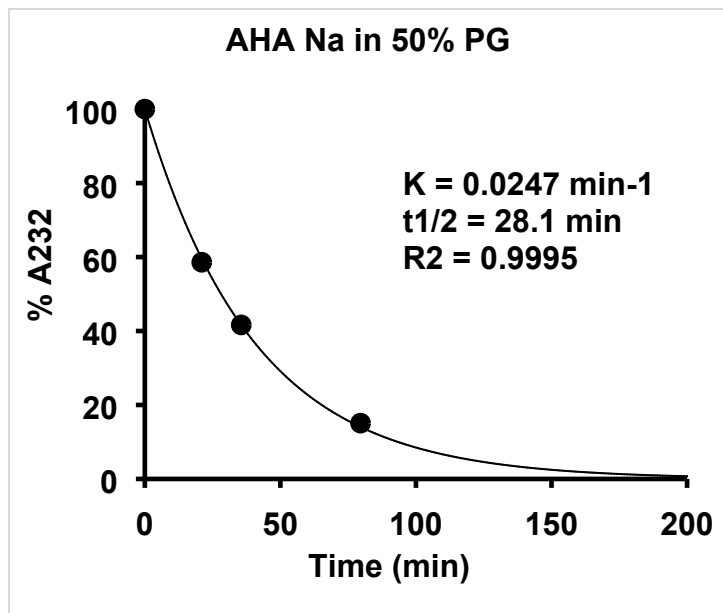


Figure S34. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Na in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
21.0	58.59
35.6	41.65
79.6	15.09

Figure S35. Decomposition kinetic profile of A232 by AHA Na in H₂O/PG 1:1.

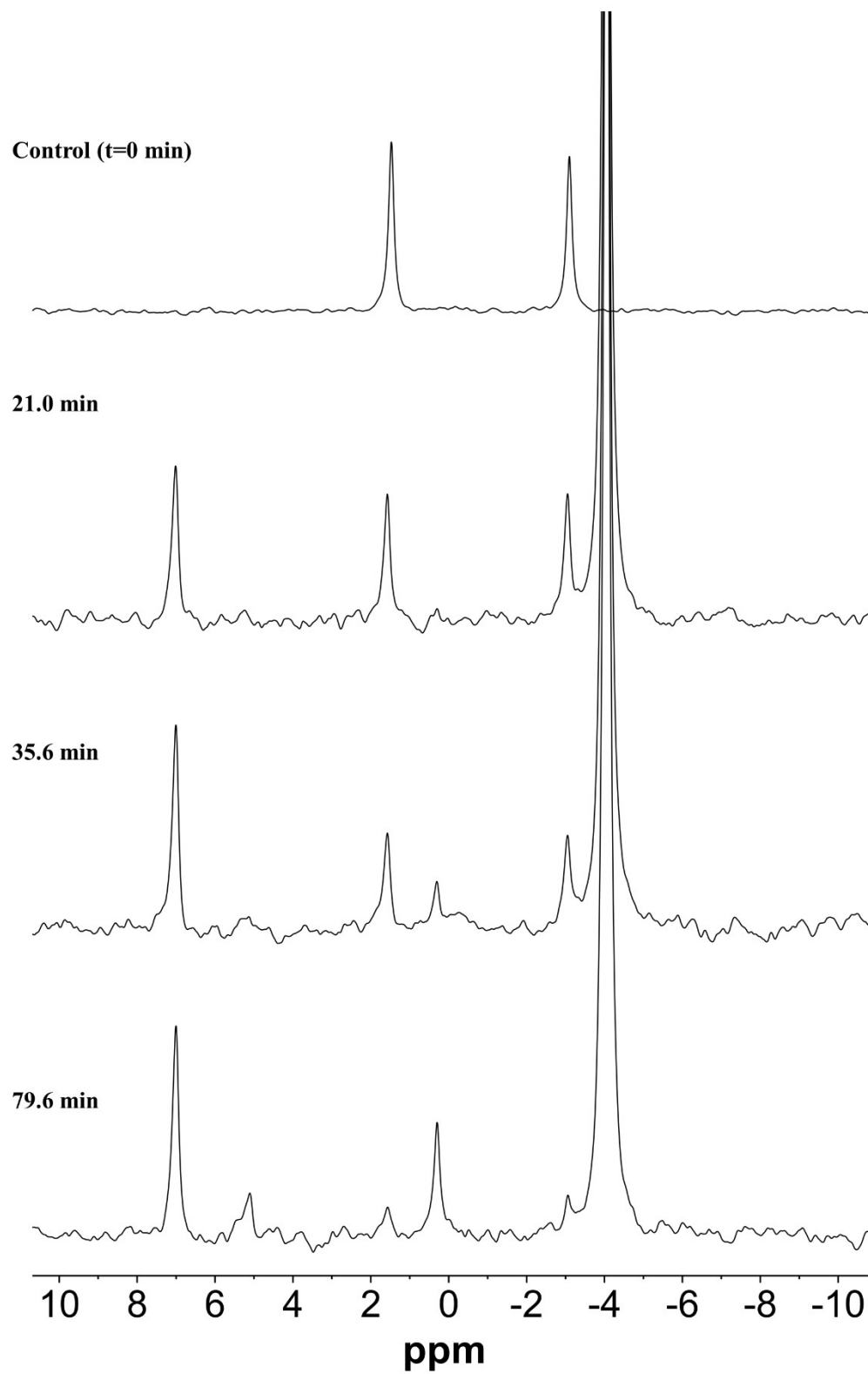
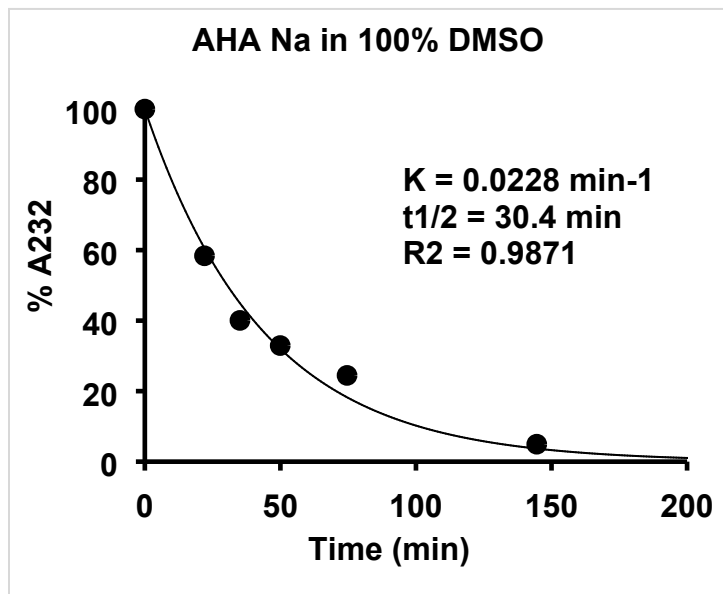


Figure S36. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Na in $\text{H}_2\text{O}/\text{PG}$ 1:1.



Time (min)	% A232
0.0	100.00
22.0	58.40
35.1	40.06
49.9	32.93
74.6	24.46
144.6	4.95

Figure S37. Decomposition kinetic profile of A232 by AHA Na in DMSO.

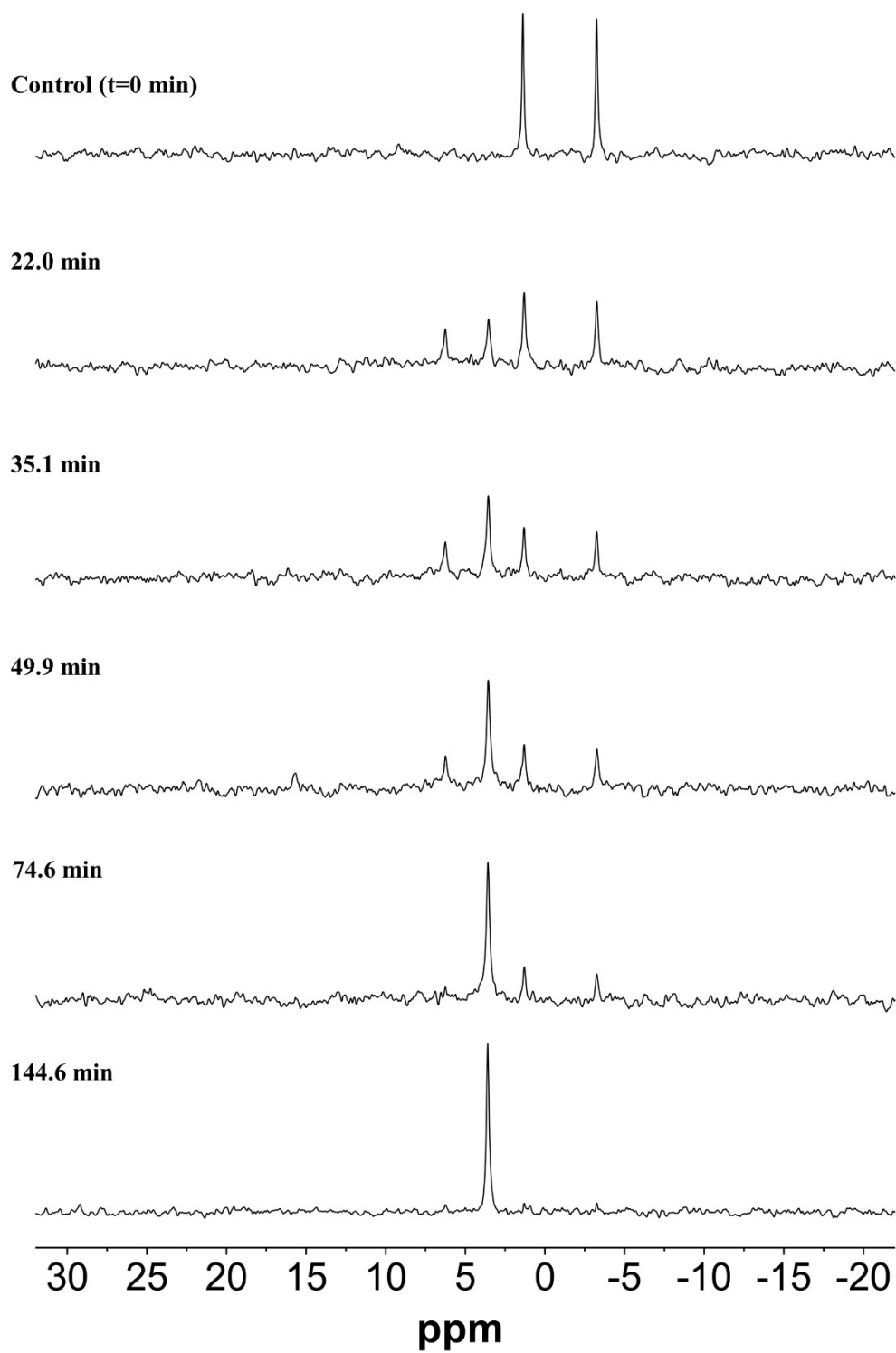
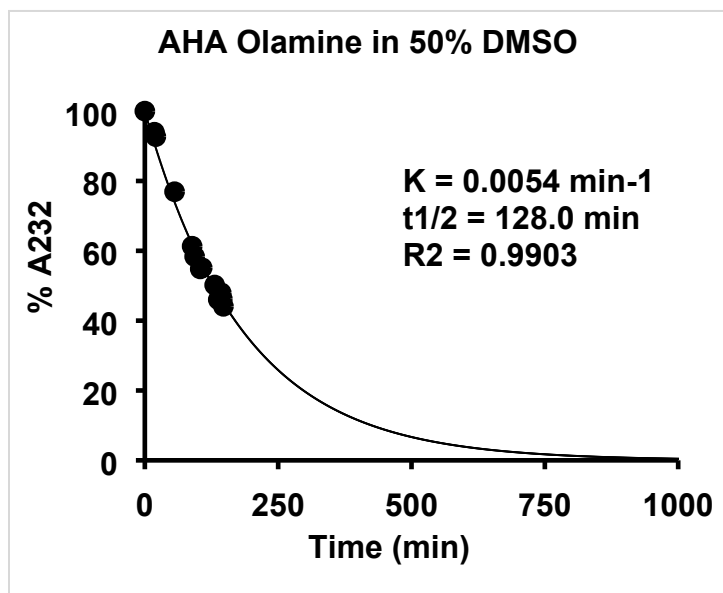


Figure S38. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Na in DMSO.



Time (min)	% A232
0.0	100.00
18.0	93.96
20.6	92.70
55.7	76.92
88.7	61.31
93.4	58.37
103.9	54.82
107.5	55.14
130.9	50.20
137.7	46.03
143.2	47.98
145.3	46.23
147.3	44.10

Figure S39. Decomposition kinetic profile of A232 by AHA Olamine in H₂O/DMSO 1:1.

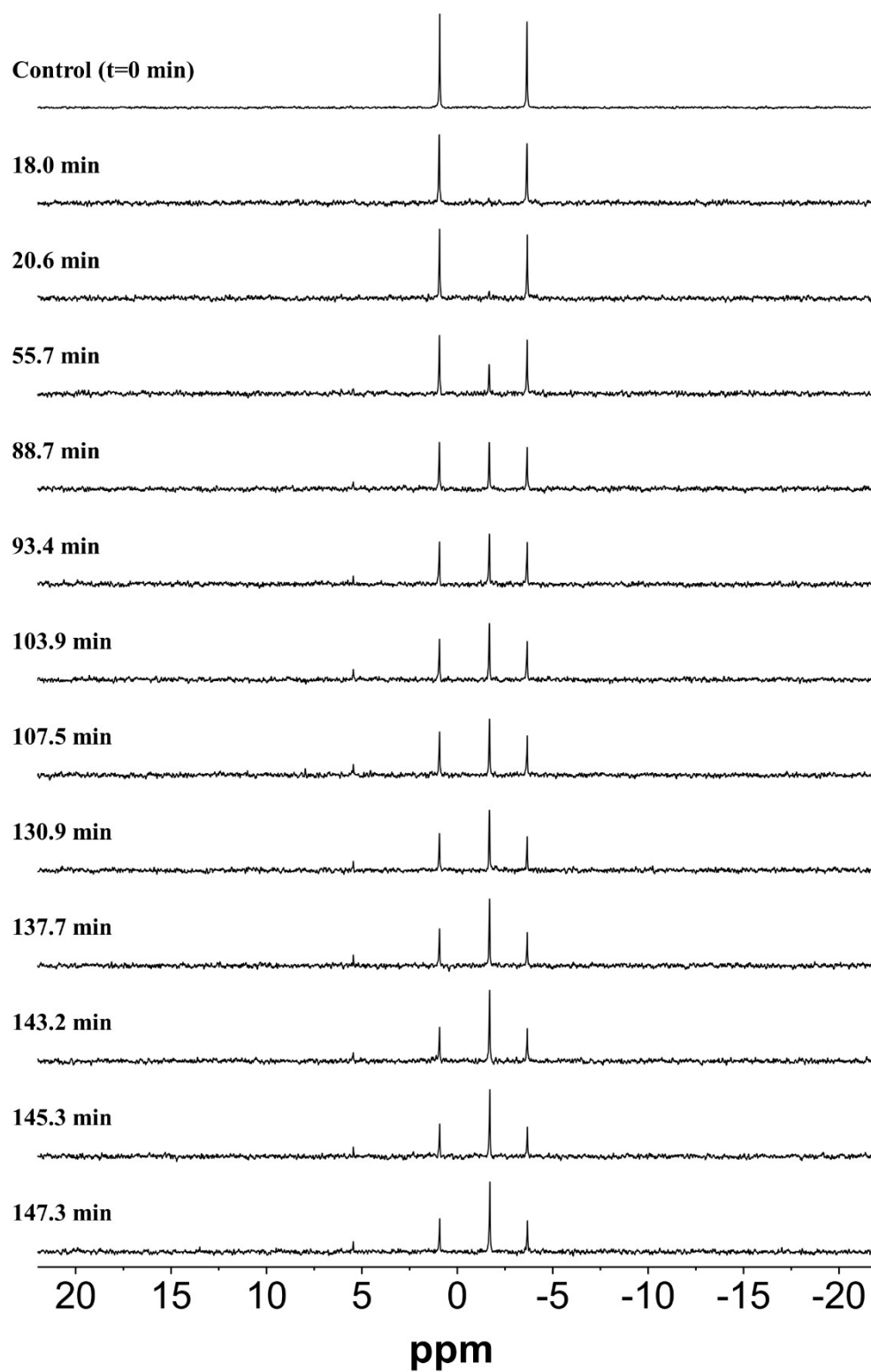
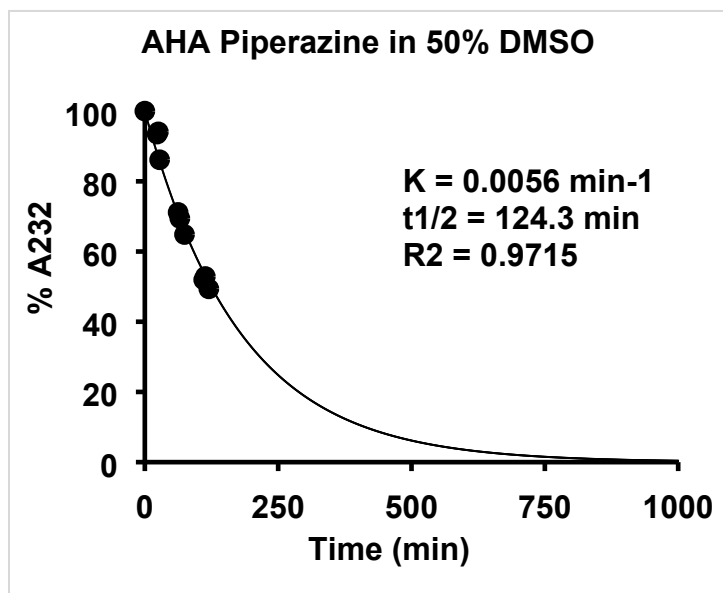


Figure S40. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Olamine in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
23.0	93.46
25.3	94.09
27.8	86.14
62.4	71.14
65.7	69.45
74.4	64.84
110.4	51.95
113.4	52.89
120.0	49.37

Figure S41. Decomposition kinetic profile of A232 by AHA Piperazine in H₂O/DMSO 1:1.

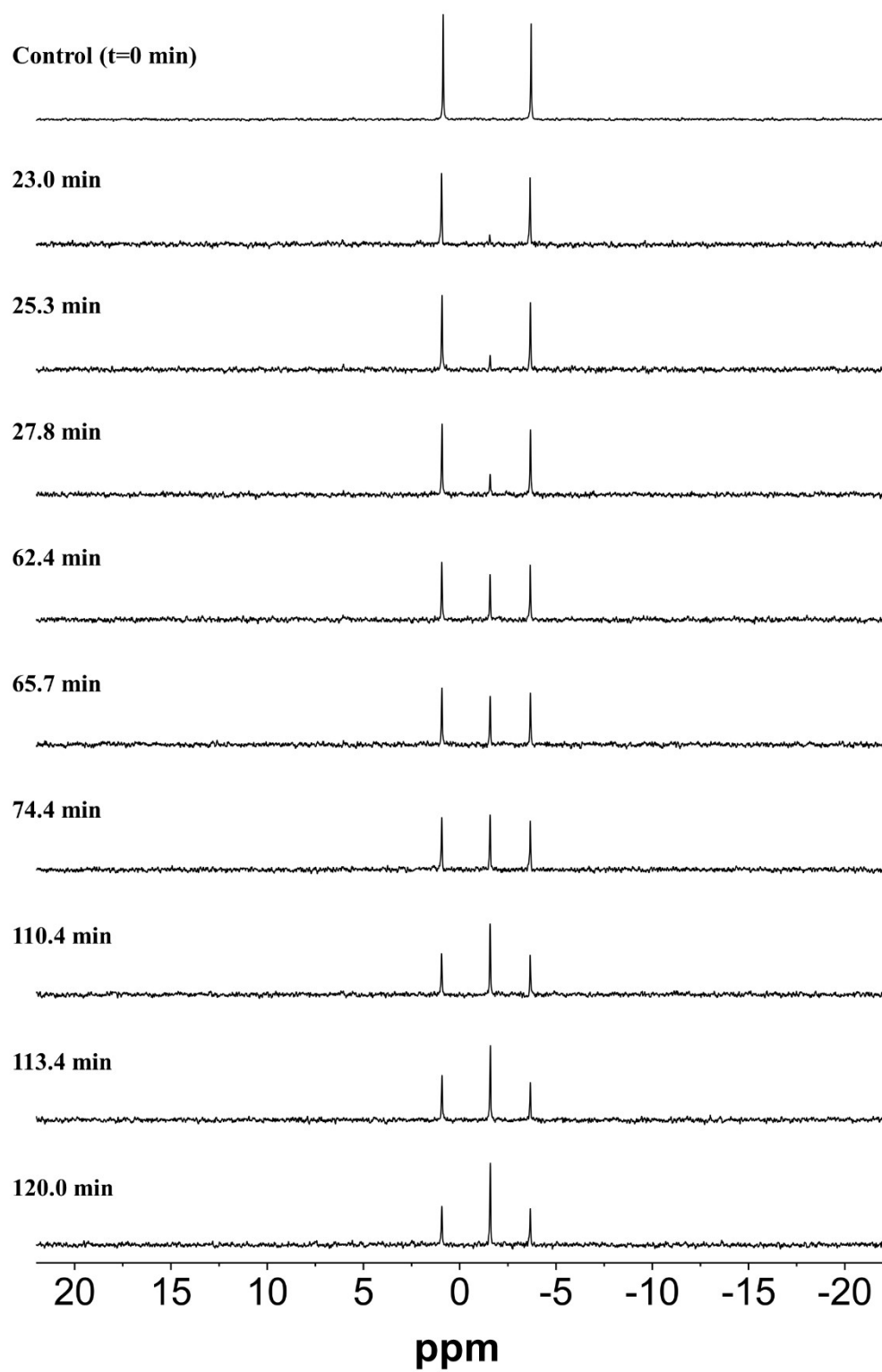
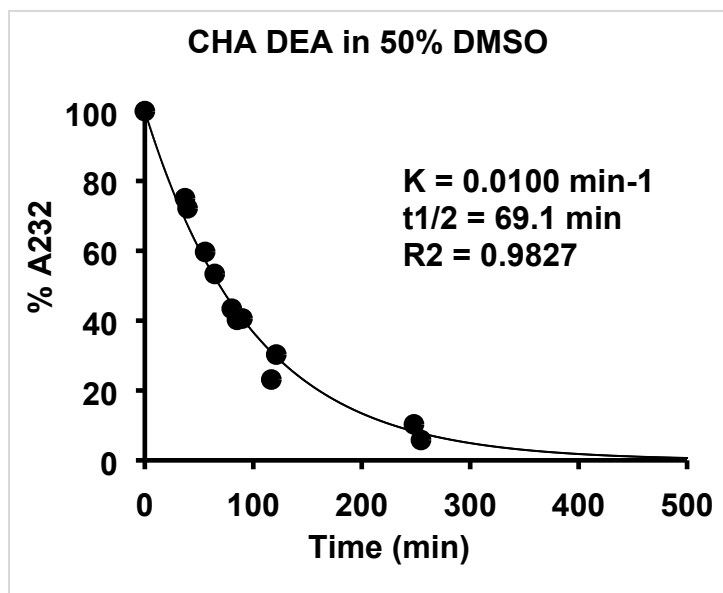


Figure S42. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by AHA Piperazine in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
37.0	75.06
39.4	72.18
55.6	59.68
64.4	53.38
80.2	43.41
85.0	40.24
90.0	40.62
116.6	23.14
121.2	30.29
248.2	10.30
254.6	5.83

Figure S43. Decomposition kinetic profile of A232 by CHA DEA in H₂O/DMSO 1:1.

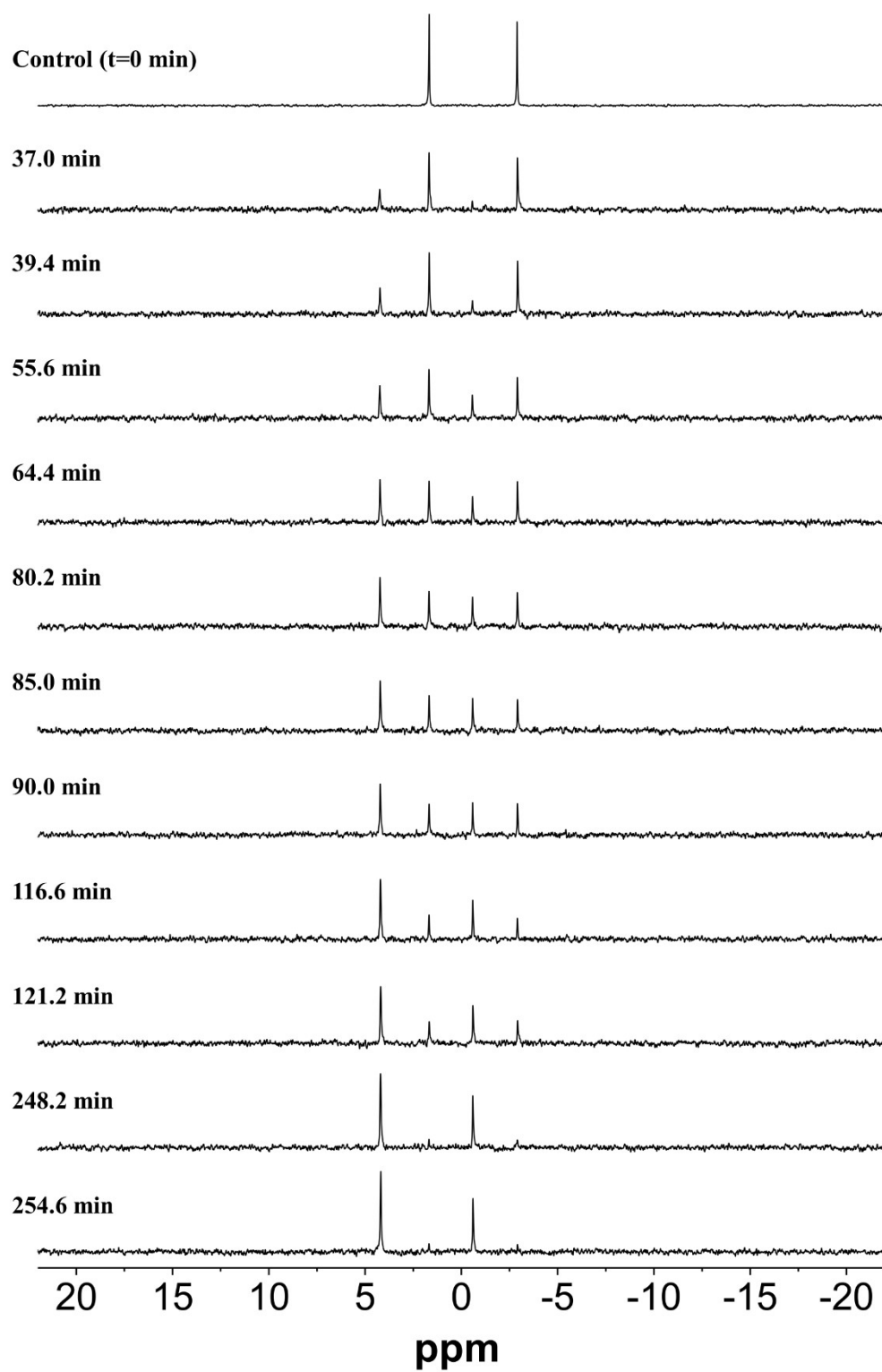
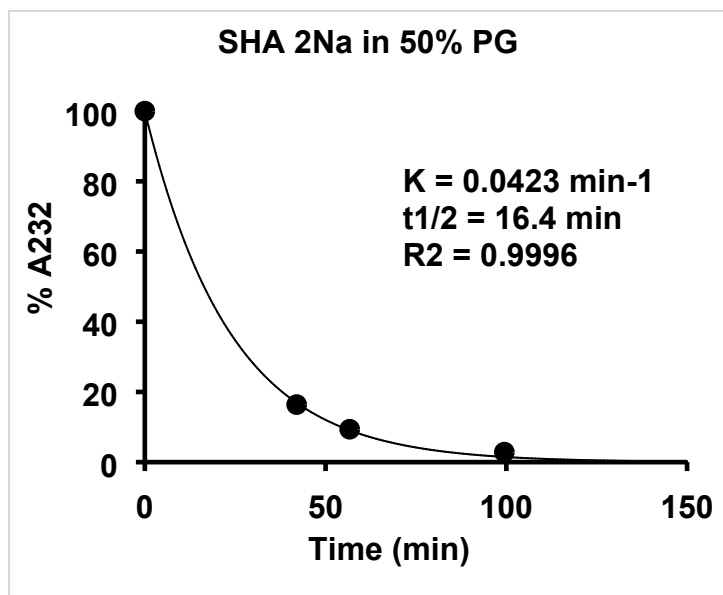


Figure S44. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by CHA DEA in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.



Time (min)	% A232
0.0	100.00
42.0	16.40
56.7	9.37
99.5	2.85

Figure S45. Decomposition kinetic profile of A232 by SHA 2Na in H₂O/PG 1:1.

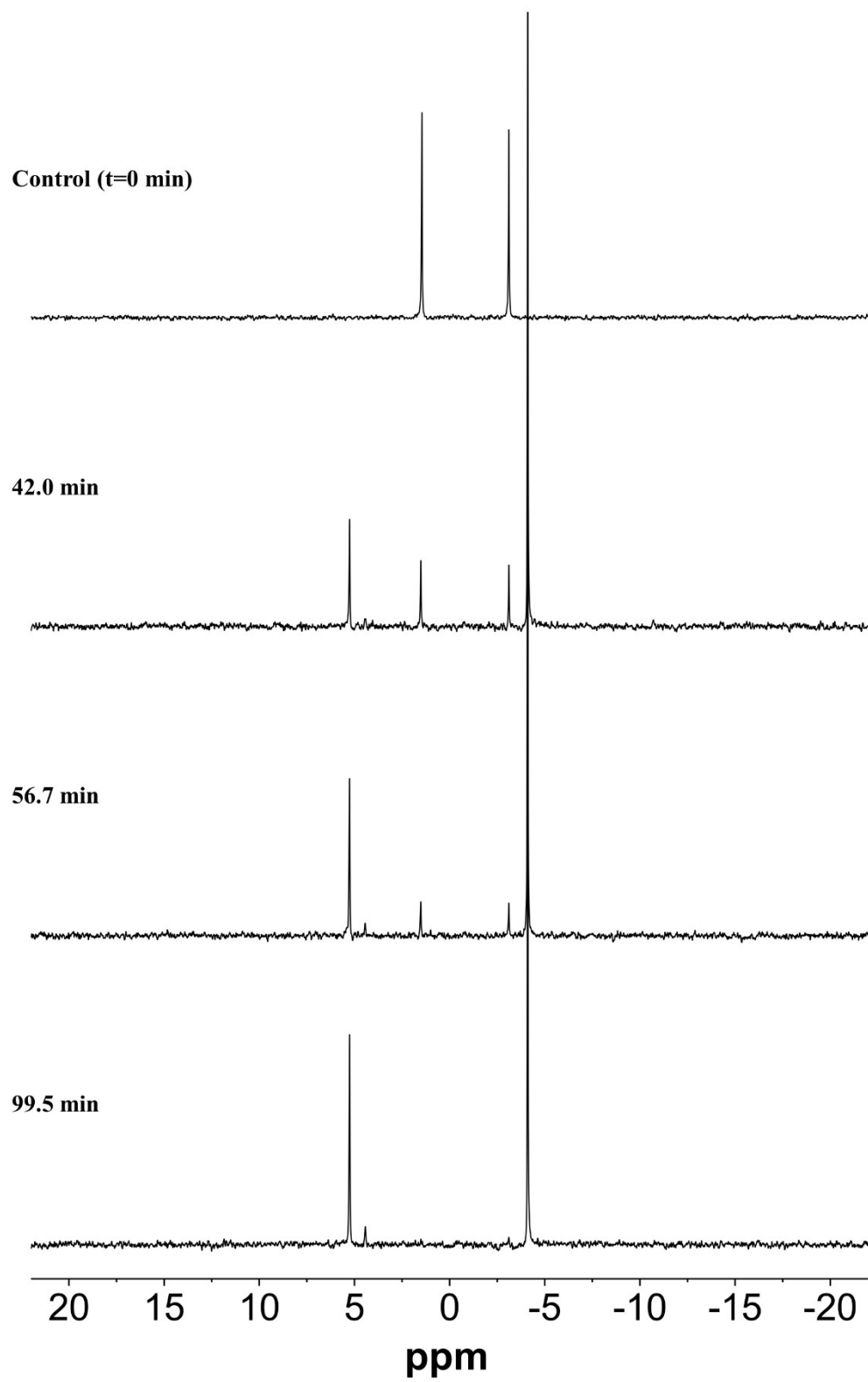
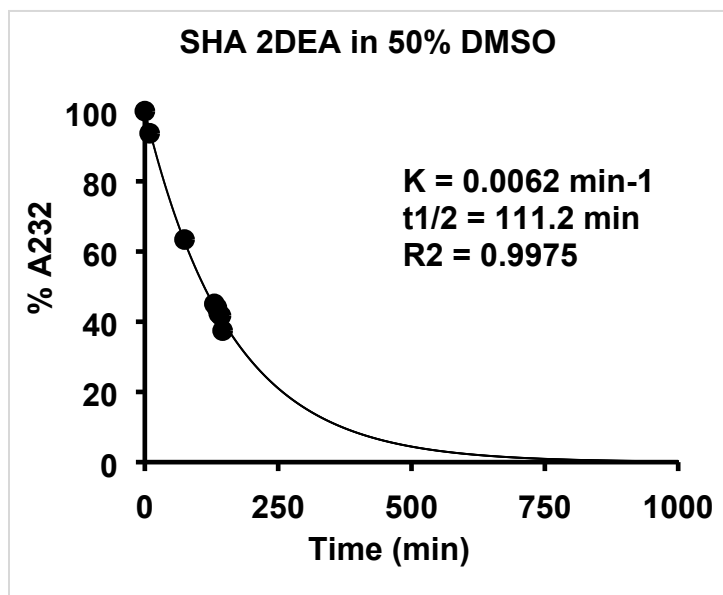


Figure S46. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by SHA 2Na in $\text{H}_2\text{O}/\text{PG}$ 1:1.



Time (min)	% A232
0.0	100.00
9.0	93.69
74.4	63.41
130.4	45.09
135.0	44.08
138.6	42.34
142.7	41.70
145.8	37.47

Figure S47. Decomposition kinetic profile of A232 by SHA 2DEA in H₂O/DMSO 1:1.

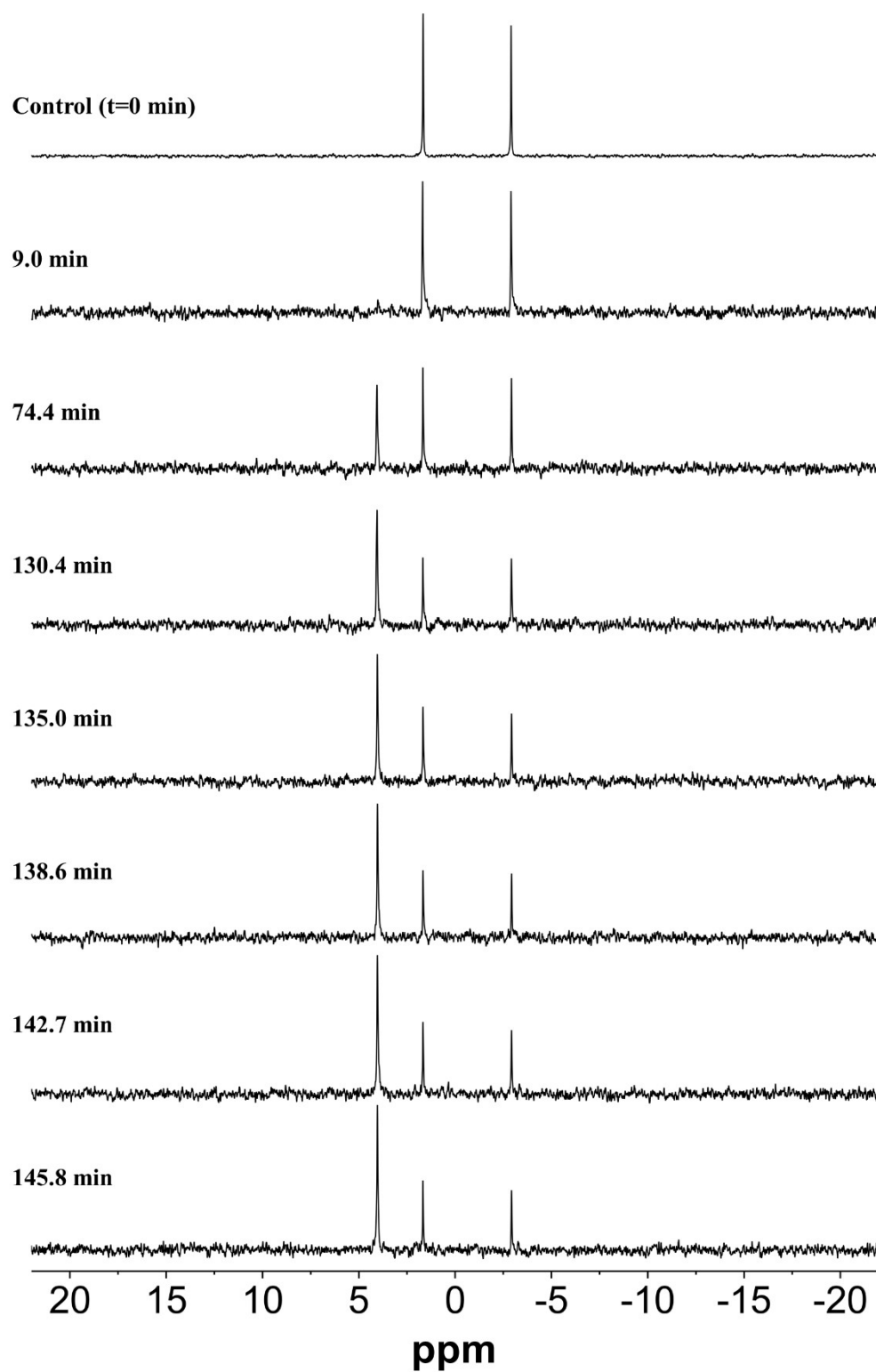


Figure S48. Stacked ^{31}P NMR spectra presenting the decomposition of A232 by SHA 2DEA in $\text{H}_2\text{O}/\text{DMSO}$ 1:1.