Supplementary Information

Discovery of potent and selective butyrylcholinesterase inhibitors through the use of pharmacophore-based screening

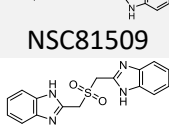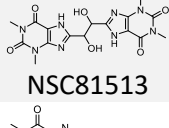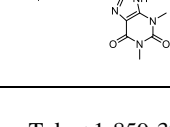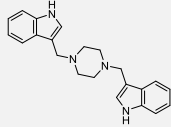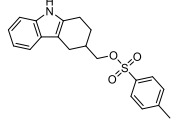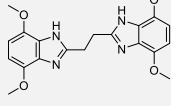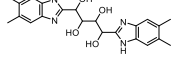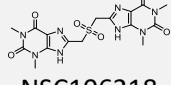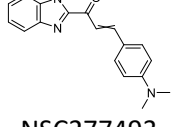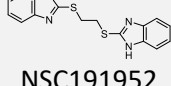Alexander Williams[a], Shuo Zhou[a], Chang-Guo Zhan[a,*]
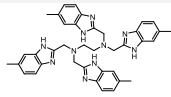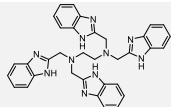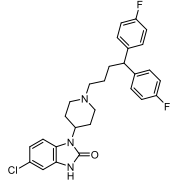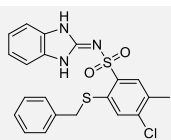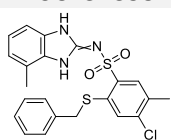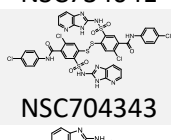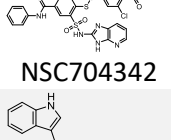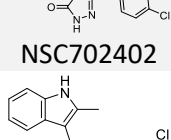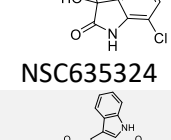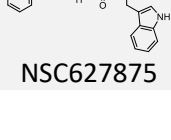
[a] Department of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, 789 S. Limestone, Lexington, KY 40536, United States
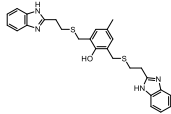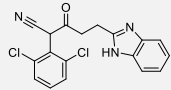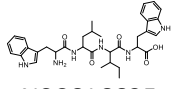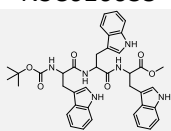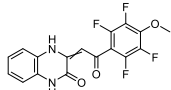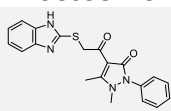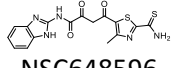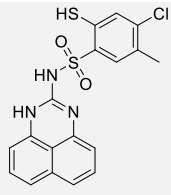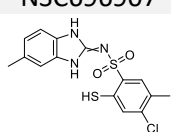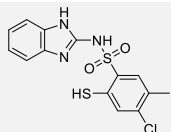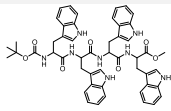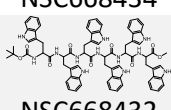
Table S1: NCI compound results including SMINA scores, difference between scores, and BChE single point results.

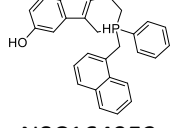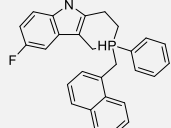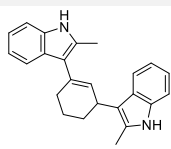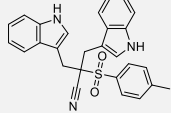| Compound #	Molecule	minimized Affinity AChE Cal/mol	minimized Affinity BCHE Cal/mol	Difference in scores	BChE Inhibition % 5µM
1	NSC23586	-7.2	-8.7	1.5	25.3
2	NSC23583	-7.2	-8.8	1.7	15.4
3	NSC14406	-7.9	-9.0	1.2	19.1
4	NSC14404	-7.7	-10.2	2.5	17.9
5	NSC81509	-7.9	-9.6	1.7	25.6
6	NSC106206	-7.1	-9.7	2.6	62.0
7	NSC81513	-8.1	-10.1	2.0	25.0
8		-6.7	-9.8	3.1	26.5

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	NSC62594				
9	NSC42258	-7.7	-9.4	1.7	76.5
10	NSC135823	-8.9	-9.5	0.6	73.1
11	NSC128762	-7.5	-8.8	1.3	16.7
12	NSC114753	-8.7	-9.2	0.5	4.0
13	NSC106218	-8.2	-9.3	1.1	8.0
14	NSC277493	-7.2	-8.7	1.5	43.2
15	NSC191952	-7.0	-9.3	2.3	81.2
16	NSC164952	-9.8	-11.0	1.1	99.7
17	NSC164949	-9.4	-10.9	1.5	97.5
18	NSC136692	-9.8	-11.2	1.4	75.0
19		-7.9	-11.5	3.6	48.5

	NSC353730				
20	 NSC348884	-9.1	-11.9	2.8	41.7
21	 NSC344032	-8.9	-11.7	2.8	92.0
22	 NSC335305	-7.8	-9.2	1.4	43.2
23	 NSC731399	-8.7	-10.3	1.6	65.7
24	 NSC734041	-7.6	-8.8	1.2	55.6
25	 NSC704343	-7.5	-10.2	2.7	-30.9
26	 NSC704342	-7.7	-9.2	1.5	9.9
27	 NSC702402	-7.9	-10.1	2.1	20.7
28	 NSC635324	-6.4	-9.6	3.3	47.5
29	 NSC627875	-8.1	-9.1	1.0	92.9

|					
30	 NSC620023	-7.7	-9.7	2.0	101.2
31	 NSC618680	-7.3	-8.8	1.5	32.7
32	 NSC616635	-7.9	-10.6	2.7	38.9
33	 NSC668429	-7.6	-9.4	1.8	79.9
34	 NSC658713	-7.6	-10.5	3.0	-11.4
35	 NSC650830	-7.2	-9.4	2.2	62.7
36	 NSC648596	-6.8	-9.0	2.2	43.5
37	 NSC696907	-8.6	-9.0	0.4	50.3
38	 NSC681175	-7.1	-9.4	2.2	50.9
39	 NSC681174	-7.1	-9.3	2.2	48.5
40	 NSC668434	-7.3	-10.3	2.9	51.2
41	 NSC668432	-6.6	-10.3	3.6	46.0

NMR Spectra of top compounds for structure confirmation and purity analysis
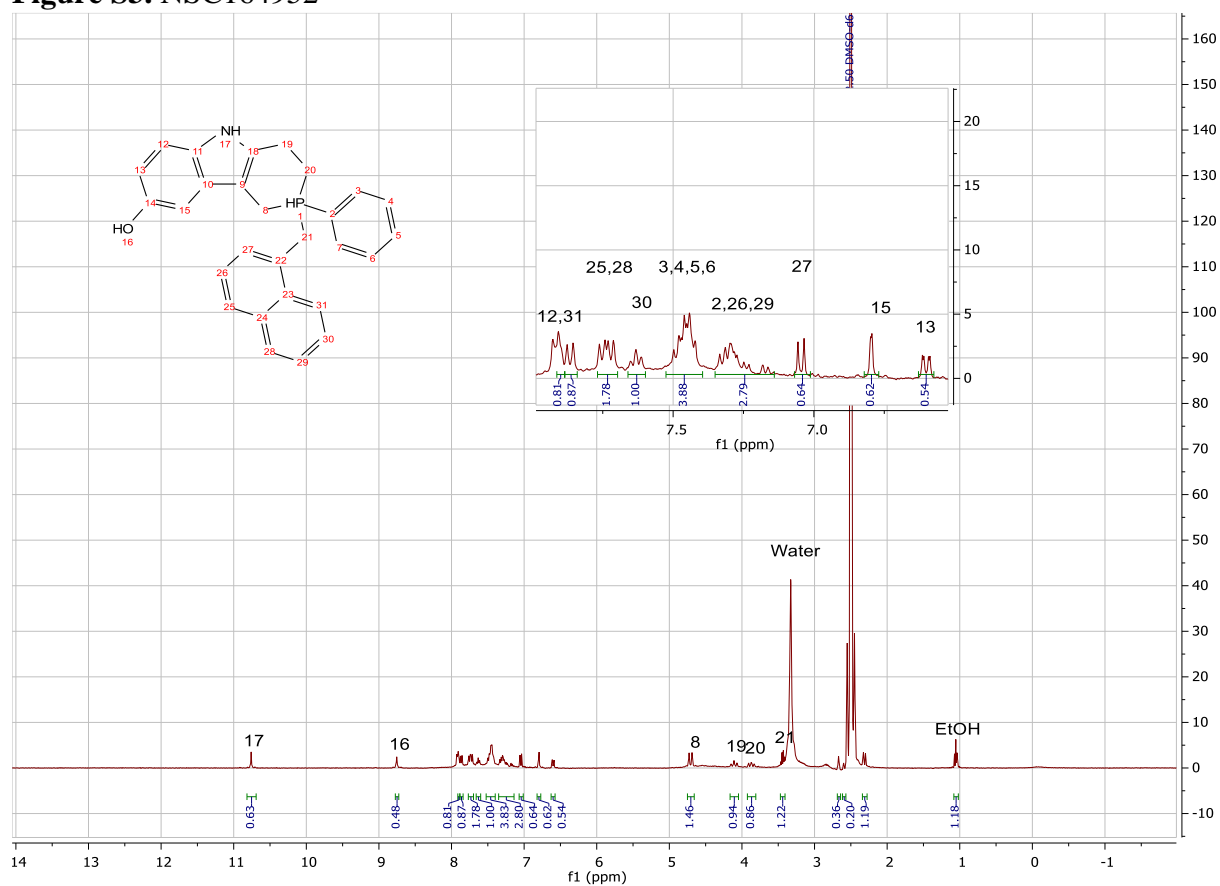
Figure S1. NSC164949
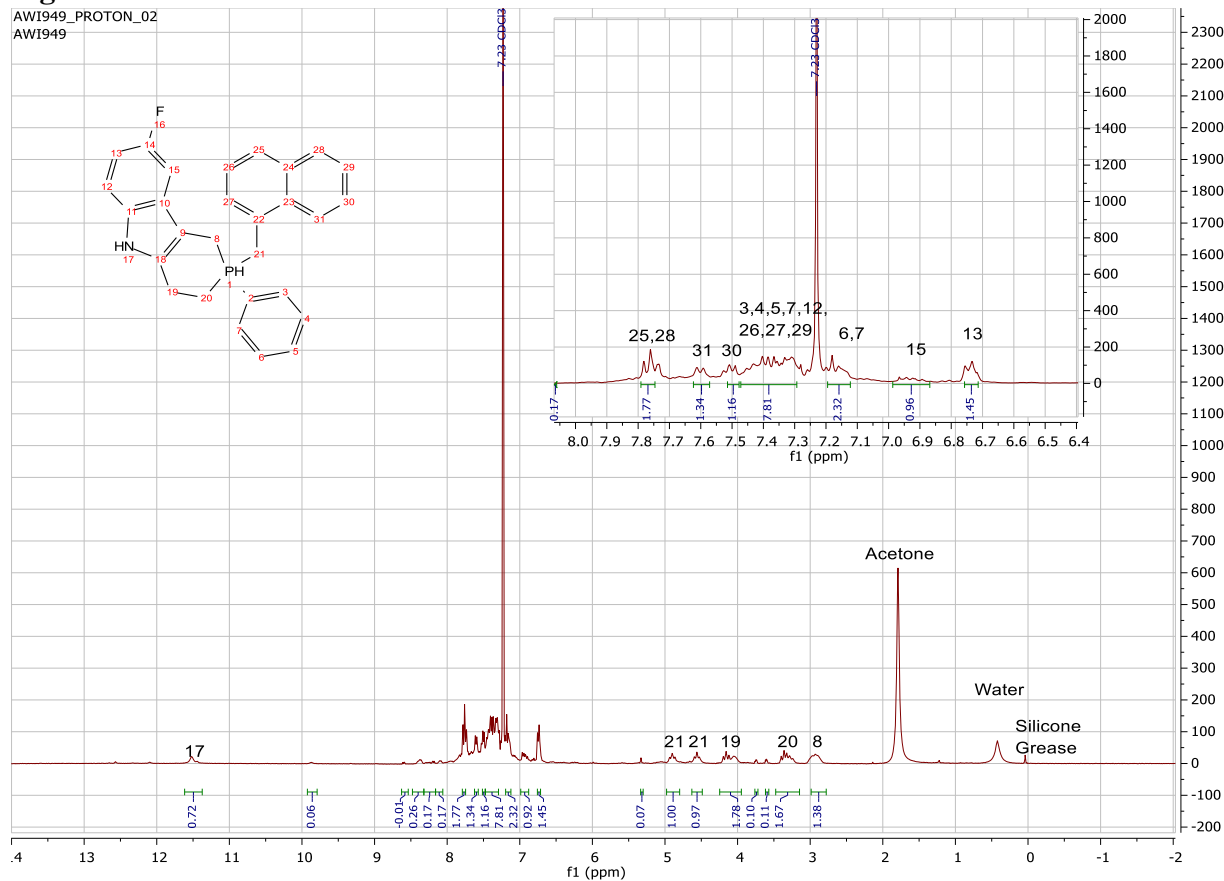
$$\frac{24.25 \; Integral \; Compound}{25.26 \; Integral \; Total} = 96\% \; Purity$$

Figure S2. NSC620023
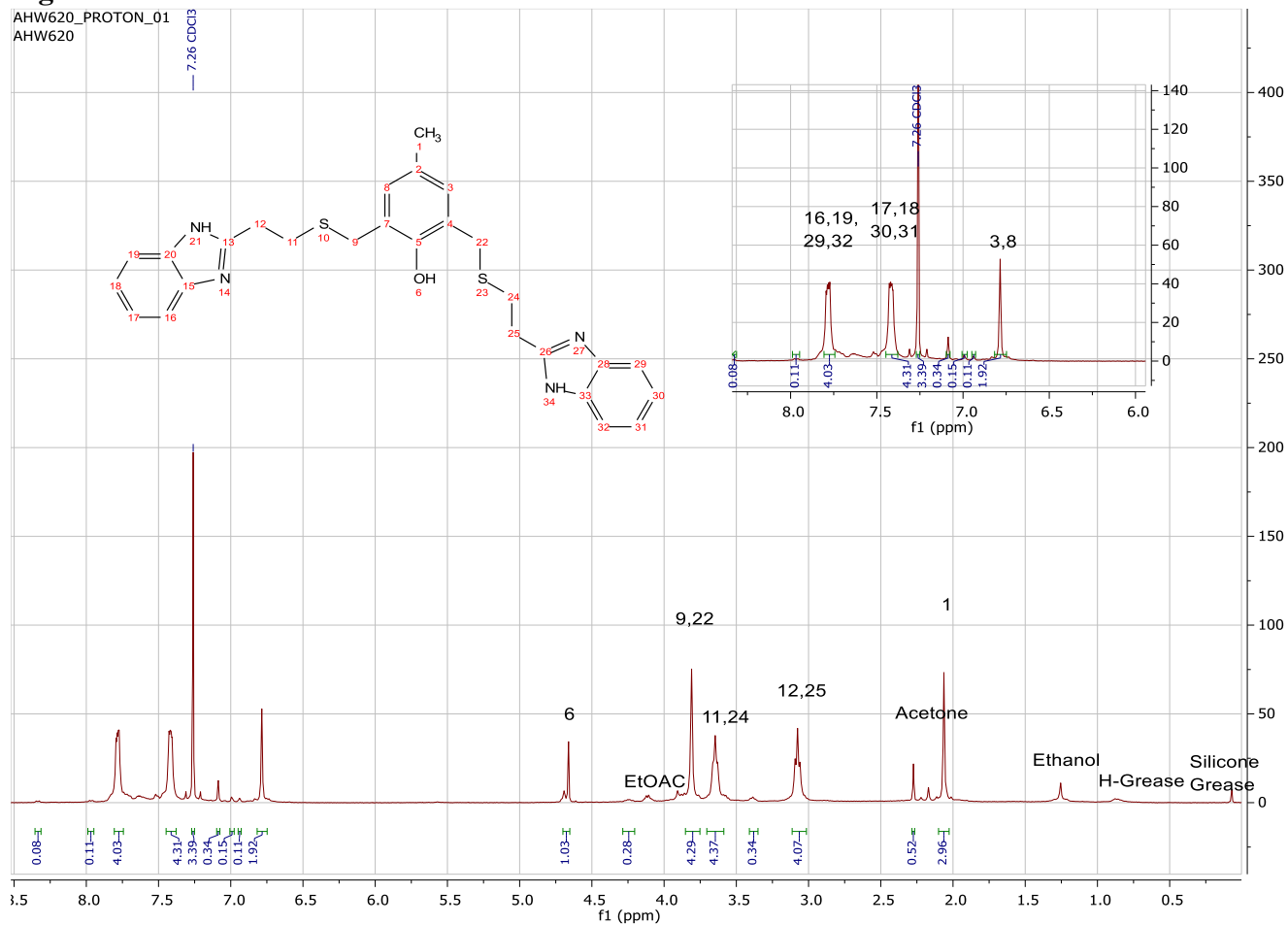
$$\frac{29.34 \ Integral \ Compound}{31.27 \ Integral \ Total} = 94\% \ Purity$$

Figure S3. NSC164952

$$\frac{19.19 \; Integral \; Compound}{21.27 \; Integral \; Total} = 90\% \; Purity$$