Supporting Information: Polyhydroxamicalkanoate as a Bioinspired Acetylcholinesterase-Based Catalyst for Acetylthiocholine Hydrolysis and Organophosphorus Dephosphorylation: Experimental Studies and Theoretical Insights

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This Supporting Information contains the general experimental procedures. Also, we show the models of polyhydroxamicalkanoate (PHA), which can be represented by a simple active site composed by one hydroxamic acid and one carboxylic acid moieties in addition to three neighboring acrylamide groups on each side. Considering the possible rotations of the active site and the relative positions of the acrylamide groups, we built a set of 15 configurations, as shown in Figure S1. We observed the highest relative total energy structure (PHA.XV) presents a cavity, as considered for nanoreactors models.¹ The relative total energy follows the same trend for HSE06 calculations, as shown in the Tables S1 and S2, without any significant structural variation. The atoms in the Table S2 are identified in the Figure S2.

With the aim to analyse the electronic configuration, we plotted, in Figure S3, the highest occupied (HOMO) and lowest unoccupied molecular orbital (LUMO) for acetylthiocholine, paraoxonethyl, and the lowest-energy PHA model. Finally, we show de configurations after PBE optimizations, in Figures S4 and S5, for ATCh/PHA, and Figures S6 and S7, for paraoxon-ethyl/PHA. Also, we compare the semi-local exchange-correlation PBE and hybrid HSE06 functionals for structural parameters of acetylthiocholine and paraoxon-ethyl, where it is possible to observe a small change in the energetic order of paraoxon-ethyl/PHA interaction, while the structures do not present significant changes (Figure S8).

A General Procedures

Polyacrylamide ($M_w = 1500 \text{ g mol}^{-1}$) was purchased from Scientific Polymer and hydroxylamine chloridrate from Merck. Acetylthiocholine chloride and paraoxon-ethyl were obtained from Sigma-Aldrich. All reagents were used as received without further purification. The Britton-Robinson bu*ff*ers, pH 7.0 and 8.0, were prepared from an equal mixture of 0.1 M acetic acid, 0.1 M boric acid and 0.1 M phosphoric acid. The pH value was adjusted using a 1.0 M NaOH solution. Borax bu*ff*er solution 0.1 M (pH 8.0 to 10.0) was prepared with anhydrous sodium tetraborate. The pH value was adjusted using a 1.0 M NaOH solution or 1.0 M HCl solution. Deionized water was purified by an ultra-pure water system (Milli-Q, Millipore).

Measurements of ultraviolet-visible (UV-Vis) spectroscopy were performed at a wavelength of 412 nm in quartz cuvettes on a double-beam spectrophotometer (JASCO V-630). The temperature was kept at 25 °C by an ETCR-762 (JASCO) water thermosttated cell holder with stirrer.

Chronoamperometric measurements were performed on a model PGSTAT302 Autolabs electrochemical system (Eco Chemie, Netherlands) controlled by the GPES software (version 4.9 -Eco Chemie, Netherlands). Screen printed electrodes made with carbon ink for the working and counter electrodes, and silver/silver chloride ink as the reference eletrode were modified with the polyhydroxamicalkanoate to generate the biomimetic electrochemical sensor.

PHA model	PBE		HSE06	HSE06		
	$\Delta E_{tot} ({\rm meV})$	φ (°)	$\Delta E_{tot} ({\rm meV})$	φ (°)		
PHA.XV	1403	17.9	1429	17.2		
PHA.XIV	1150	35.4	1202	36.0		
PHA.XIII	913	123.8	940	124.9		
PHA.XII	881	72.5	909	73.8		
PHA.X	710	71.5	718	72.6		
PHA.I	0	115.5	0	115.0		

Table S1: The relative total energy (ΔE_{tot}) and the dihedral angle (ϕ) considering PBE and HSE06 for the PHA models used in the interacting study.

References

(1) Mello, R. S.; Orth, E. S.; Loh, W.; Fiedler, H. D.; Nome, F. Polymers Containing Hydroxamate Groups: Nanoreactors for Hydrolysis of Phosphoryl Esters. *Langmuir* 2011, 27, 15112–15119.



Figure S1: The initial models for polyhydroxamicalkanoate (PHA), the functionalyzed polyacrylamide. The relative total energy (ΔE_{tot}) and the dihedral angle (ϕ) are shown for each structure.



Figure S2: The identified atoms in the Table S2 are related with the acetylthiocholine and paraoxonethyl structures.

ATCh										
d_{av}			ABC							
	PBE (Å)	HSE06 (Å)	$\Delta(\%)$		PBE (°)	HSE06 (°)	$\Delta(\%)$			
$N-C_1$	1.51	1.49	-1.3	C_3SC_4	100.2	100.6	0.4			
$C_1 - H$	1.10	1.09	-0.9	$C_1 N C_1$	109.0	109.0	0			
$N-C_2$	1.53	1.51	-1.3	$C_1 N C_2$	111.6	111.6	0			
$C_2 - H$	1.10	1.09	-0.9	SC_4O	122.2	122.0	-0.2			
$\overline{C_2} - \overline{C_3}$	1.53	1.52	-0.7	OC_4C_5	125.0	124.7	-0.2			
C ₃ -H	1.10	1.09	-0.9							
$C_3 - S$	1.82	1.81	-0.5							
$S-C_4$	1.81	1.78	-1.7							
C_4-O	1.22	1.20	-1.6							
$C_4 - C_5$	1.50	1.50	0							
$C_5 - H$	1.10	1.09	-0.9							
Paraoxon-ethyl										
d_{av}				ABC						
	PBE (Å)	HSE06 (Å)	$\Delta(\%)$		PBE (°)	HSE06 (°)	$\Delta(\%)$			
$N-O_1$	1.24	1.21	-2.4	$O_1 NO_1$	124.7	124.7	0			
$N-C_1$	1.48	1.46	-1.4	$O_1 NC_1$	117.7	117.7	0			
$C_1 - C_2$	1.40	1.39	-0.7	C_1C_2H	119.4	119.5	0.1			
$C_2 - H$	1.09	1.08	-0.9	C_2C_3H	121.2	121.2	0			
$\overline{C_2} - \overline{C_3}$	1.39	1.38	-0.7	C_4O_2P	125.8	126.7	0.7			
$C_3 - H$	1.09	1.08	-0.9	$O_2 PO_3$	116.4	116.0	-0.3			
$C_3 - C_4$	1.40	1.39	-0.7	O_2PO_4	100.4	101.0	0.6			
$C_4 - O_2$	1.38	1.37	-0.7	$O_4 PO_4$	103.5	104.0	0.5			
$O_2 - P$	1.63	1.60	-1.8	PO_4C_5	119.9	121.1	1.0			
$P - O_3$	1.48	1.46	-1.4	$O_4C_5C_6$	110.9	110.9	0			
$P-O_4$	1.59	1.57	-1.3							
$O_4 - C_5$	1.47	1.44	-2.0							
<u> </u>										
$C_5 - H$	1.10	1.09	-0.9							
$C_5 - H$ $C_5 - C_6$	1.10 1.52	1.09 1.51	$-0.9 \\ -0.7$							

Table S2: The bond lengths (d_{av}) and angles (\widehat{ABC}) of acetylthiocholine (ATCh) and paraoxonethyl considering PBE and HSE06. The variation for HSE06 to PBE is calculated as follow: $\frac{x^{HSE06}-x^{PBE}}{x^{PBE}} \times 100\%$.



Figure S3: The highest occupied molecular orbital (HOMO) and the lowest energy unoccupied molecular orbital (LUMO) of acetylthiocholine, paraoxon-ethyl, and the lowest energy configuration of the polyhydroxamicalkanoate model (PHA.I).



Figure S4: The highest energy conformations for ATCh/PHA. The relative total energy (ΔE_{tot} , in meV) is shown in the bottom of each structure.



Figure S5: The lowest energy conformations for ATCh/PHA. The relative total energy (ΔE_{tot} , in meV) is shown in the bottom of each structure.





Figure S6: The highest energy conformations for paraoxon-ethyl/PHA. The relative total energy (ΔE_{tot} , in meV) is shown in the bottom of each structure.



Figure S7: The lowest energy conformations for paraoxon-ethyl/PHA. The relative total energy (ΔE_{tot} , in meV) is shown in the bottom of each structure.



Figure S8: The exchange-correlation functionals PBE and HSE06 are compared for the lowest energy ATCh/PHA, and the different cases of paraoxon-ethyl/PHA.