This might suggest that fatty acid binding to BSA protects disulfides at Cys34 from reaction with displaced ligand. In our experiments, the apparent reaction of Cys34-blocked fatty acid free BSA with displaced thiolate leads to no further binding of $AuPEt_3$ groups. Thus, drug-induced release of Cys from BSA does not simply regenerate Cys34. It is intriguing that a perturbation at Cys34 appears to be sensed by His3, one of the ligands in the N-terminal Cu(II) site. Such a communication could easily be "wired" by two intervening helices.[16] The new His peaks (u and v) could be those of His9 and His18, which are both within these helices. Albumin is known to possess binding sites for a variety of hydrophobic molecules,[1] and this may account for the broadening (beyond detection) of the resonances for the sugar ring protons of SATg in spectra of solutions containing auranofin and BSA.

The mechanisms of the reactions leading to the formation of either Cys-Cys or Cys-STg are curious, as is the transfer of the hydrophobic SATg ligand from mercaptalbumin to blocked albumin. This work provides a basis for investigations of the involvement of albumin in the promotion of metal-ligand substitution reactions via both metal and ligand recognition processes, thiol-disulfide interchanges, and thiol-disulfide transport and delivery.

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Supplementary Material Available: The complementary spectra to Figure 1 covering the region -0.5 to 2.2 ppm showing triethylphosphine resonances and high-field-shifted albumin peaks (1 page). Ordering information is given on any current masthead page.

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Molecular Recognition and Catalysis. Acceleration of Phosphodiester Cleavage by a Simple Hydrogen-Bonding Receptor

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The design of artificial catalysts for phosphodiester cleavage (Scheme I) is an important goal that has implications for the controlled hydrolysis of DNA and RNA.[1] Of the many strategies investigated,[2-5] none approaches the efficiency of phosphodiesterase enzymes such as staphylococcal nuclease (SN), which hydrolyzes DNA 10^{16}-fold faster than the background reaction.[6] The active site of this remarkable enzyme contains two key arginines at positions 35 and 87.[7] Site directed mutagenesis studies[6,8] have established that only Arg35 binds to the monoanionic substrate whereas both residues stabilize the dianionic, trigonal-bipyramidal intermediate (Scheme I) with Arg87 playing the additional role of general acid and protonating the leaving group.

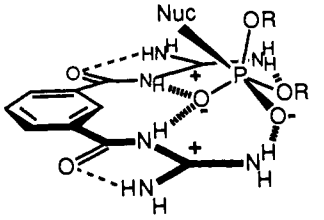


Figure 1. Possible mode of interaction between **1** and trigonal-bipyramidal intermediate in Scheme I.[13]

Scheme I

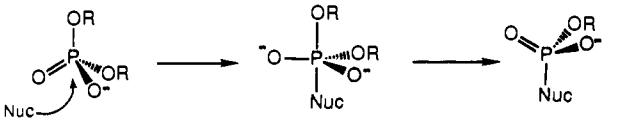
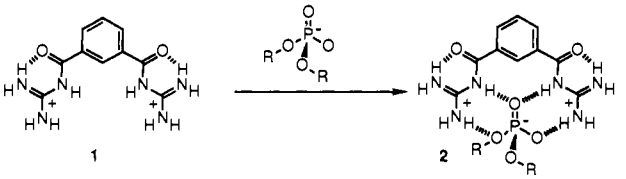


Table I.[a] Rate Constants for Phosphodiester Cleavage Reactions

receptor (concn, mM)	$k_{obsd} \times 10^5$ s^{-1}	k_{obsd}/k_{uncat}
Intramolecular Reaction of **3**[b]		
none	0.038	1
1 (30)	26.5	700
1 (20)	24.5	645
1 (10)	17	450
1 (5)	11	290
5 (10)	0.094	2.5
Intermolecular Thiolysis of **4**[c] with Ethyl Mercaptoacetate		
none	0.042	1
1 (5)	1.5	36

[a] In CH_3CN, [diester] = 1×10^{-4} M, [lutidine] = 1.25×10^{-2} M, at 25 °C. All k_{obsd} values are the average of at least three runs which differed by less than 5%. [b] Barium salt.[16] [c] Pyridinium salt.

In this paper we report the acceleration of both inter- and intramolecular phosphodiester cleavage by a synthetic receptor based on the active site of SN. Bis(acylguanidinium) **1** is formed in a single synthetic step from dimethyl isophthalate and guanidinium hydrochloride and forms strong complexes of type **2** with phosphodiesters in CH_3CN ($K_a \sim 5 \times 10^4$ M^{-1}).[9] Earlier work



from this group on barbiturate recognition[10] and on the accelerated aminolysis of phosphorodiamidates[11] indicated that the isophthaloyl spacer in **1** was well-suited to position the two guanidiniums to

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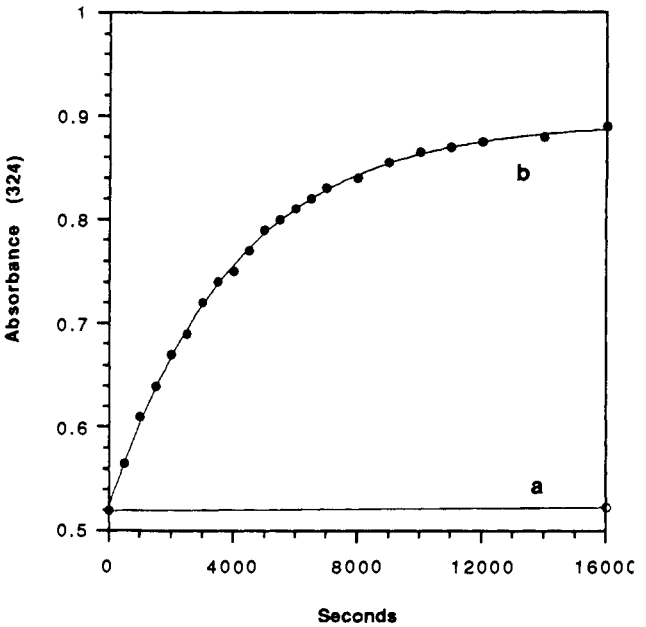
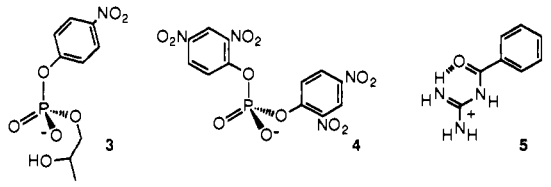


Figure 2. Release of 4-nitrophenol in the reaction of **3** and (a) no receptor and (b) **1** [30 mM].

stabilize the trigonal-bipyramidal intermediate via four hydrogen bonds with concomitant charge neutralization, as in Figure 1. Furthermore, the reduced pK_a of acylguanidinium (~8) compared to guanidinium (~14)[12] should facilitate proton transfer from the receptor to the leaving group and so promote the second step in Scheme I.[14]

The intramolecular phosphoryl transfer reactions of **3**[15] were followed through at least 3 half-lives by observing spectrophotometrically at 324 nm the release of 4-nitrophenol. The receptors were used as their bis(tetraphenylborate) (mono- in the case of **5**) salts and the diesters **3** and **4** as their barium[16] and pyridinium salts, respectively. All kinetic runs were carried out in CH_3CN with an initial concentration of diester of 1×10^{-4} M; the receptor (see Table I) and lutidine (1.25×10^{-2} M), as a general base, were present in excess. The phosphoryl-transfer reactions followed pseudo-first-order kinetics, and their rate constants[17] and conditions are collected in Table I.



The rate of release of 4-nitrophenol in the intramolecular reaction of **3** is greatly increased (Figure 2) in the presence of **1**. Comparison of the first-order rate constant with that of the uncatalyzed reaction (k_{obsd}/k_{uncat}) gives a rate acceleration of 700-fold.[18] The reaction follows Michaelis-Menten kinetics, showing saturation behavior as the concentration of receptor increases (Table I). An Eadie-Hofstee plot (R = 0.988) gave values for $k_{cat} = 3.8 \times 10^{-4}$ s^{-1} and $K_m = 1.2 \times 10^{-2}$ M. This corresponds to a maximum rate acceleration for the receptor (k_{cat}/k_{uncat}) of 10^3 and a k_{cat}/K_m of 3.2×10^{-2} M^{-1} s^{-1}. The high value of K_m (K_a = 85 M^{-1}) in these experiments, compared to the value for **2** in CH_3CN, presumably reflects the increased polarity of the medium which contains excess lutidine (1.25×10^{-2} M),[11] and this is supported by complexation studies under similar conditions. The binding arrangement provided by *two* guanidiniums in **1** is crucial for this large rate enhancement. An analogue **5** (10 mM), containing only *one* guanidinium, caused a 2.5-fold acceleration in the reaction of **3** whereas receptor **1**, at half the concentration (5 mM), increased the rate of the reaction by almost 300-fold.[19] Similar, although less dramatic, effects are seen with the bimolecular reaction between phosphodiester **4**[21] and ethyl mercaptoacetate (1.25×10^{-2} M), as added nucleophile.[22] Addition of receptor **1** (at 5 mM) caused a 36-fold increase in the rate of the intermolecular thiolysis reaction.

In summary, we have shown that substantial rate enhancements in phosphodiester cleavage reactions can be achieved by a very simple receptor containing both hydrogen bonding and electrostatic complementarity to the trigonal-bipyramidal intermediate. We are currently investigating further the mechanism of this process as well as incorporating additional functionality into the receptor to increase the catalytic activity.

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Registry No. 1, 137695-71-7; [**3**]$_2$Ba, 4286-25-3; [**4**](pyridinium salt), 76215-45-7; [**5**](BPh$_4$), 137945-61-0; SN, 9013-53-0; ethyl mercaptoacetate, 623-51-8.

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(22) The reaction was followed by observing the release of 2,4-dinitrophenol at 340 nm, and the k_{obsd} was calculated using the method of initial rates.

Rearrangement of Pentacoordinated Carbonium Ions over Zeolite Y

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Zeolites are acidic aluminosilicates widely used for cracking of high-boiling oils into gasoline and LPG.[1] Although carbenium ions are believed to be the intermediates in the cracking process, their initial formation from alkanes over the zeolite surface is still a matter of controversy.[2] Recently, there appeared reports which

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