tallized upon standing at room temperature.

TLC R_f 0.11 (50% E/H); IR (CH_2Cl_2) 3599 (m), 3422 (m) cm^{-1}; ^1H NMR (both isomers) ($CDCl_3$) δ 5.50 (m, 2), 4.15 (m, 1), 3.90 (m, 4), 3.50 (m, 1), 2.15 (m, 4), 1.90 (m, 4), 1.26 (brs, 24), 0.88 (t, 6); ^{13}C NMR ($CDCl_3$) δ 100.9, 98.3, 72.9, 71.4, 62.3, 66.8, 53.0, 49.8, 36.4, 35.9, 31.8, 29.6, 29.2, 28.4, 25.8, 25.7, 25.3, 22.6, 14.0; MS (70 eV), *m/e* (relative intensity) 230 (37.5) (M^+); mp 43-44 °C. Anal. Calcd for $C_{13}H_{26}O_2$: C, 67.85; H, 11.30. Found: C, 67.63; H, 11.48.

[1(*R*,*S*),5(*R*,*S*)]-6(*R*,*S*)-*n*-Octyl-1-2,7-dioxabicyclo[3.2.0]hept-3-ene (2). Nonyl aldehyde (2.0 g, 14 mmol) and furan (2.5 equiv) were mixed in a quartz tube and photolyzed as described above. After $9^1/_2$ h, excess furan was evaporated to give 2.9 g (13.8 mmol, 98.6%) of crude photoadduct without any remaining starting material. Flash chromatography (20% ether/hexanes, 1% Et_3N) afforded 2.63 g (12.5 mmol, 90%) of the photoadduct as a pale yellow oil.

TLC R_f 0.84 (50% E/H); IR (CH_2Cl_2) 1604 (m), 1466 (m), 1457 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.60 (m, 1), 6.26 (brd, 1, J = 5.06 Hz), 5.29 (t, 1, 2.90 Hz), 4.51 (m, 1), 3.4 (m, 1), 1.76 (m, 2), 1.26 (bs, 12), 0.88 (t, 3, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 147.9, 107.8, 104.0, 92.3, 48.8, 37.0, 31.7, 29.3, 29.2, 29.0, 24.3, 22.5, 13.9; MS (70 eV), *m/e* (relative intensity) 210 (35) (M^+), 114 (30), 97 (100).

[1(*R*,*S*),5(*R*,*S*)]-6(*R*,*S*)-*n*-Octyl-2,7-dioxabicyclo[3.2.0]heptane (3). The photoadduct **2** (2.25 g, 10.71 mmol) was dissolved in 50 mL of EtOAc (0.2 M solution), and 200 mg (ca. 20% w/w) of 5% Rh/Al_2O_3 was added to the mixture. After 1 h of hydrogenation at 1 atm, the catalyst was filtered, and the solvent was removed to afford after flash chromatography (15% ether/hexanes, 1% Et_3N) 2.21 g (10.42 mmol, 97%) of the desired oxetane as a colorless oil.

TLC R_f 0.73 (50% E/H); IR ($CHCl_3$) 1100 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.85 (d, 1 , J = 3.88 Hz), 4.25 (m, 2), 4.05 (m, 1), 3.01 (m, 1), 1.83 (m, 4), 1.30 (brs, 12), 0.88 (t, 3, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 105.7, 81.6, 67.3, 46.0, 36.8, 31.6, 29.3, 29.2, 29.0, 28.6, 24.3, 22.4, 13.8; MS (70 eV), *m/e* (relative intensity) 212 (24) (M^+), 99 (40).

[1(*R*,*S*),5(*R*,*S*)]-3[(*R*,*S*)(*S*,*R*)],8(*R*,*S*)-Dimethoxy-6(*R*,*S*)-*n*-octyl-2,7-dioxabicyclo[3.3.0]octane (6). The aldehyde **5** (14.40 g, 48 mmol) was dissolved in 250 mL (0.2 M) of methanol. The mixture turned blue after 50 min of ozonolysis at -78 °C, after which nitrogen gas was bubbled into the solution to remove excess ozone. Dimethyl sulfide (20 mL, excess) was added at -50 °C and solution was warmed to room temperature after 5 min. After 3 h of stirring anhydrous K_2CO_3 (5 g) was added to the mixture until the solution became milky white. TLC analysis indicated complete epimerization after 36 h (66% ether/hexane, R_f(starting material) = 0.47, R_f(product) = 0.26). The reaction mixture was cooled to 0 °C and dropwise addition of a saturated solution of hydrogen chloride in methanol continued until evolution of CO_2 gas ceased, and the solution became acidic (pH 1). After 30 min of stirring at room temperature, the reaction mixture was quenched by slow addition of saturated sodium bicarbonate solution. Insoluble salts were filtered and methanol was removed under vacuum. After extraction with ether the organic layers were dried over $MgSO_4$, and the solvent was removed by rotary evaporation. Flash chromatography of the red oil (10% ether/hexanes) gave 4.23 g (15 mmol) of the bis(methoxy lactols) **6** in 31% yield.

TLC R_f 0.73 (33% H/E); IR (CH_2Cl_2); ^1H NMR (major isomer only) ($CDCl_3$) δ 5.08 (dd, 1, J = 4.9 Hz, 1.6 Hz), 4.91 (s, 1), 4.49 (d, 1, J = 6.6 Hz), 3.81 (m, 1), 3.33 (s, 3), 3.31 (s, 3), 2.72 (m, 1), 2.1 (ddd, 1, J = 10.3, 8.7, 1.6 Hz), 1.9 (m, 1), 1.3 (brs, 12), 0.88 (t, 3, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 108.9, 106.7, 88.7, 87.9, 87.8, 54.7, 46.3, 46.2, 39.3, 38.4, 38.2, 37.7, 31.8, 29.5, 29.2, 26.3, 22.6, 14.0; MS (70 eV), *m/e* (relative intensity) 173 (100), 113 (44). Anal. Calcd for $C_{16}H_{30}O_4$: C, 67.16; H, 10.48. Found: C, 66.98; H, 10.56.

[1(*R*,*S*)]-6(*R*,*S*)-*n*-Octyl-2,7-dioxabicyclo[3.3.0]oct-3,8-dione) (7). The bis(methoxy lactols) **6** (3.95 g, 13.8 mmol) were dissolved in 100 mL of CH_2Cl_2. MCPBA (55.2 mmol, 12.4 g, 4 equiv) and $BF_3{\cdot}Et_2O$ (1.38 mmol, 170 μL, 0.1 equiv) were added, and stirring was continued for 6 h. NMR analysis of an aliquot indicated oxidation of only the methoxy lactol of the less substituted ring had occurred. The bis(butyrolactone) was formed after an additional equivalent of MCPBA (3.1 g) and 2.5 equiv (4.4 mL) of $BF_3{\cdot}Et_2O$ were added. After stirring for 10 h, the white precipitate was filtered, and the filtrate was treated with saturated sodium bicarbonate solution. The solution was extracted with ether (3 × 100 mL), and the combined ether extracts were washed with brine and dried ($MgSO_4$). Removal of solvent and flash chromatography (10% ether/hexanes) of the residue afforded 2.79 g (11.0 mmol, 80%) of the desired bis(butyrolactone), which exhibited spectroscopic data[5b,d] identical with that previously reported for this compound.

TLC R_f 0.23 (33% H/E); IR (CH_2Cl_2) 1797 (s), 1788 (s), 1733 (m), 1729 (m), 1725 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.98 (d, 1, J = 7.6 Hz), 4.32 (m, 1), 3.05 (m, 1), 2.98 (dd, 1, J = 17.3, 9.3 Hz), 2.52 (dd, 1, J = 17.5, 3.30 Hz), 1.75 (m, 2), 1.25 (brs, 12), 0.88 (t, 3, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 174.1, 170.2, 85.0, 77.0, 39.7, 35.1, 32.5, 31.5, 29.0, 28.9, 28.8, 24.6, 22.3, 13.7; MS (70 eV), *m/e* (relative intensity) 254 (0.4) (M^+), 141 (11.6). Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.17; H, 8.66. Found: C, 65.95; H, 8.77.

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The Effect of Hydrophobic-Lipophilic Interactions on Chemical Reactivity. 4. A Case of 17-Membered-Ring "Neighboring-Group" Participation: Compelling Evidence for Self-Coiling

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Abstract: Hydrolytic rate constants of ω-substituted *p*-nitrophenyl esters of hexadecanoic acids (**16-Y**, Y = Br, SCH_3, OH, and SH) were measured in 50:50 (v/v) Me_2SO-H_2O. The relative rate constants k_{rel} with **16-H** as the reference are 2, 8, 16, and 124 s^{-1}, respectively. For **16-SH** at the initial substrate concentration of about 2×10^{-5} M, a rate-enhancing factor of at least 6 was brought about by a 17-membered-ring "neighboring-group" participation involving the ω-sulfhydryl end group. The above evaluation was based on, and alternative explanations were excluded by, additional experiments on effects of adding four thiols of increasing chain lengths as nucleophiles, rate dependence on the initial substrate concentrations, comparison of hydrolytic rates of **16-Y** with the short-chain reference **8-H**, and the effects of adding amylose. Thus the present study rigorously demonstrates that long-chain molecules can be forced to fold and then interact intramolecularly by hydrophobic forces. It also serves as compelling evidence for the phenomenon of self-coiling.

If enzymes can fold and coil in a myriad of ways to do their jobs, long-chain molecules might be made to duplicate part of such a feat in test tubes. Knowing that these long-chain molecules will aggregate and coil-up in some hydrophilic or lipophobic, thus

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Table I. Hydrolytic Rate Constants k (10^{-3} s^{-1}) of **16-Y** in 50:50 Me_2SO–H_2O at 35 °C

substrate[a]	k	k_{rel}
16-H	0.32	1
16-Br	0.59	2
16-SCH$_3$	2.46	8
16-OH	5.01	16
16-SH	39.6[b]	124
8-H	6.68	20

[a] The substrate concentration is 1.80×10^{-5} M. [b] The experimental uncertainty is ±10%, and all other k values are accurate to within ±5%.

"aggregating", solvents,[1-5] we elected to realize this goal by making use of this special solvent effect on long-chain substrates. Besides, if we can force one end of such a molecule to be engaged in "neighboring-group" participation with the other end, we can also consider any anchimeric assistance achieved as a compelling piece of evidence for the phenomenon of self-coiling.[5]

Like a host of other reactions, the hydrolysis of esters can be intramolecularly assisted by nucleophilic neighboring groups, and the magnitude of this anchimeric effect strongly depends on the ring size of the cyclic transition state or intermediate involved.[6,7] Ordinarily, neighboring group participation can involve only 3- to 7-membered-ring transition states or intermediates; involvement of larger rings is made more difficult by the increasingly prohibitive entropy terms,[7] e.g., formation of a 17-membered-ring lactone is disfavored by 22 entropy units in comparison with that of a 5-ring lactone.[8] However, aggregation and self-coiling as consequences of hydrophobic–lipophilic interactions are entropy-favored processes,[9] thus we may let such interactions in a hydrophilic or aggregating medium pay the expenses for a path leading to very-large-ring participations.

As substrates for our study, four *p*-nitrophenyl esters of hexadecanoic acids substituted at the ω-position by Y were synthesized, i.e., *p*-$O_2NC_6H_4OOC(CH_2)_{15}Y$ or **16-Y**, with Y = Br, OH, SCH_3, and SH. Their hydrolytic behaviors at initial substrate concentrations of about 2×10^{-5} M were carefully investigated and compared with those of two model compounds (**16-H** and the octanoate **8-H**) in aggregating (50:50 v/v Me_2SO–H_2O) and nonaggregating mediums in the absence and presence of added thiols or amylose. Results of this study indicate that our goal has been achieved.

Experimental Section

Substrates: The *p*-nitrophenyl esters of hexadecanoic acids with ω-substituents (**16-Y**) were prepared from cyclopentanone and 10-undecenoic acid in seven steps. Details of this synthesis will be reported elsewhere.[10] These esters were identified by ^1H NMR and elemental analysis, and their melting points are as follows: **16-Br**, 38–39 °C; **16-SCH$_3$**, 55.5–56 °C; **16-OH**, 65.5–66.5 °C; **16-SH**, 46.5–48 °C; and **16-H**, 63–64 °C; the thermometer used was not calibrated.

Solvent. Me_2SO and water were purified as previously described,[11] and dioxane and glyme were purified by standard procedures. Kinetic experiments were performed in an equal volume of Me_2SO, or dioxane, or glyme and 0.02 M aqueous carbonate buffer solution. The pH value of the buffer was 9.65, and that of the final mixture of Me_2SO–buffer was 12.65, dioxane–buffer 11.51, and glyme–buffer 11.39. Amylose was treated by previously described procedures,[11] and the average molecular weight as measured by viscosity method was 5.6×10^4, corresponding to a degree of polymerization of 340.

Table II. Hydrolytic Rate Constants k (10^{-3} s^{-1})[a] of **16-Y** in Nonaggregating Media (50:50 Solvent–H_2O) at 35 °C

solvent	16-H	16-Br	16-OH	16-SH	8-H
dioxane–H_2O	12.8	13.4	13.3	6.70[b]	13.1
glyme–H_2O	20.7	20.5	21.4	13.8[b]	21.7

[a] The substrate concentration is 1.80×10^{-5} M. [b] The uncertainty is ±10%, but ±5% for all others.

Kinetics. Kinetic measurements were made by using a Perkin-Elmer 559 spectrophotometer with a constant-temperature bath connected to a cell holder. An 1.0-cm cell was filled with 3.00 mL of the solvent mixture and thermally equilibrated for 10 min, and 30 μL of an ethanolic solution of the substrate was injected into the cell with a microsyringe. The increase in the 410-nm absorbance of *p*-nitrophenolate at 35 °C was then traced as a function of time, pseudo-first-order rate constants were obtained in the usual manner. The kinetic data for the amylose-catalyzed hydrolysis were treated as previously described.[11a]

Results and Discussion

The hydrolytic rate constants of **16-Y** measured in 50:50 (v/v) mixtures of Me_2SO and aqueous carbonate buffer solution are listed and compared with those of **16-H** and **8-H** in Table I, in which the relative rate constants k_{rel} are based on **16-H** as the reference. The k_{rel} of **16-SH** stands out conspicuously as 124, even larger than that of **8-H**, the shorter octanoate reference which does not aggregate in this medium. Although the data strongly suggest anchimeric assistance involving very-large-ring neighboring-group participation by ω-Y groups, especially by the ω-SH (or ω-S^-) in the hydrolysis of the **16-SH** ester, the conclusive demonstration of the existence of this phenomenon is not a simple matter, since other conceivable physical or chemical paths might also accelerate or retard the hydrolysis of **16-SH**. In order to evaluate just how much out of this rate-enhancing factor of 124 was actually brought about by the formation of 17-membered-ring intermediates, all other rate-enhancing and rate-retarding possibilities had to be either assessed or eliminated.

Obviously, the first factor which can affect the k_{rel} values is the difference in the degrees of aggregation and self-coiling of the substrates. Previous work[5] has already established that **16-H** forms aggregates in the 50:50 Me_2SO–H_2O medium, thus larger k_{rel} values for other **16-Y** species could be consequences of smaller degrees of aggregation and self-coiling. Before we attempt to assess the relative importance of this factor for our target species **16-SH**, a general look at all the k_{rel} values may be in order.

In separate pieces of work we have demonstrated that the k_8/k_{16} ratios for octanoates and hexadecanoates are good indicators of the relative degrees of aggregation which can be correlated with Rekker's hydrophobic fragmental constants of the ten organic components of ten aquiorgano solvents, and the observed rate constants of twelve substituted-phenol esters of hexadecanoic acid can be correlated with Rekker's constants of these substituents.[13-15] On the basis of these observations, therefore, for the present **16-Y** series, we expect a more hydrophobic Y-substituent to produce a larger degree of aggregation and hence a smaller k_{rel} value, and if this factor *alone* were taken into account, the expected k_{rel} order would be OH > SH > H > SCH_3 > Br. This certainly is not the case, and the actual order of SH > OH > SCH_3 > Br > H looks more like a nucleophilicity order.[12] In short, the degree of aggregation does not appear to be the only factor which can affect the k_{rel} values of our **16-Y** esters.

But we still have to ask the following: what is the maximally possible value of the rate-augmentation factor induced by the

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Table III. Concentration Dependence of Hydrolytic Rates of **16-Y** in 50:50 Me_2SO–H_2O, k (10^{-3} s^{-1}),[a] 35 °C

	concentration (10^{-5} M)						
substrate	0.36	0.60	0.90	1.20	1.80	2.40	3.00
16-H	1.09	0.69	0.49	0.41	0.32	0.28	0.21
16-OH	5.81	5.59	5.30	4.98	5.01	4.88	4.71
16-SH	40.1	40.2	39.6	39.8	39.6	40.6	38.9

[a] The experimental uncertainty is within ±5% for **16-H** and **16-OH** and ±10% for **16-SH**.

Table IV. Hydrolytic Rate Constants k (10^{-3} s^{-1})[a] of Three Substrates in the Presence of Various Amounts of *n*-BuSH

	concentration of *n*-BuSH (10^{-3} M)						
substrate[b]	0.137	0.274	0.411	0.548	0.821	1.100	1.37
16-H	0.55	1.19	1.38	1.81	2.62	3.34	4.21
8-H	10.6	16.9	21.9	25.7	34.0	42.7	52.5
16-SH	15.2	12.6	13.3	13.9	14.2	15.2	15.9

[a] 50:50 Me_2SO–H_2O, 35 °C, and experimental uncertainties are ±10% for **16-SH** and ±5% for others. [b] Substrate concentration, 1.80×10^{-5} M.

difference in degrees of aggregation and self-coiling? Data set out in Tables I and II combined with our knowledge that hexadecanoic esters do not aggregate in 50:50 (v/v) dioxane–H_2O and glyme–H_2O mixtures,[14] and that **16-H** does but **8-H** does not aggregate in 50:50 Me_2SO–H_2O, can give us a clear answer. Table II convincingly demonstrates that hexadecanoates and the octanoate hydrolyze with equal ease in good or nonaggregating medium, i.e., when none of them aggregates or coils-up. Whence, the k_{rel} of **8-H** in Table I is this maximum value, i.e., 20. But this value is about 6 times smaller than the k_{rel} of **16-SH**.

At this juncture we would first like to know the relative degrees of aggregation of **16-SH** in comparison with **16-H**. Previous authors have already established that rate dependence on initial substrate concentration is one of the best evidences for the phenomenon of intermolecular aggregation, but not for self-coiling.[1,3,5] Thus such a rate vs. concentration study was made and the results are presented in Table III. It shows that for **16-H** there is a great concentration dependence, for **16-OH** a small one, and for **16-SH** none. Apparently, substantial ionization of the sulfhydryls has effectively prevented aggregation of **16-SH**, at least at relatively low concentrations. This is not surprising since on the basis of four lines of evidence it has been shown that carboxylate groups can completely inhibit this intermolecular process of aggregation.[5] In a sense this state of affairs is fortunate because we can thus conclude the following: If there were no rate-reducing self-coiling for **16-SH**, then the rate-enhancing factor caused by the difference in degrees of aggregation should be 20, out of a total of 124. In other words, there had to be a rate-enhancing factor of 124/20 or about 6 for which only the sulfhydryl groups were responsible. Furthermore, if there *were* rate-reducing self-coiling for the **16-SH** molecules in their un-ionized form, or if there were still some degree of aggregation which somehow evaded the detection by the above-mentioned method of rate dependence on initial substrate concentration, the last-mentioned factor had to be greater than 6. Since the rates of conformational changes, of ionization and reprotonation, are many orders of magnitude greater than the rate for 2 molecules of our substrate to meet by diffusion at a concentration of about 2×10^{-5} M, it is entirely possible for **16-SH** to be constantly engaged in coiling-up processes without aggregation.

In fact, we have already ascertained that even in a less-aggregating medium (60:40 Me_2SO–H_2O) self-coiling will reduce the rate of **16-H** by a factor of 2.4.[5,16] Also, it has to be noted that only a portion of some favorably positioned coiled-up conformers could have their SH groups undergo the consecutive processes of deprotonation and nucleophilic attack on the carbonyl carbon and thus facilitate the hydrolysis, whereas all other coiled-up conformers would have their hydrolysis slowed up. Therefore, we can safely infer that the rate-increasing factor effected by the sulfhydryl groups was greater, perhaps by several times, than 6.

How did the sulfhydryl groups speed up the hydrolysis? Four possibilities can be conceived: (1) random intermolecular nucleophilic attack by the catalytic sulfhydryl group, most likely in its ionized form, on the carbonyl carbon of another **16-SH** molecule; (2) similar but nonrandom catalytic interaction between two **16-SH** molecules parallelly lined up by hydrophobic–lipophilic forces; (3) random intramolecular attack by the (ionized) ω-sulfhydryl leading to the formation of the 17-membered-ring tetrahedral intermediate; and (4) a similar but nonrandom 17-ring path greatly facilitated by a largely increased coiled-up population which was a consequence of hydrophobic interactions between a **16-SH** molecule and its surrounding solvent species.

Ordinarily, in less-demanding circumstances the intermolecular paths 1 and 2 above can be easily negated by the observed rate law for the hydrolysis which was first order with respect to **16-SH** concentration.[17] With a desire to establish our case with rigor and scrupulosity, however, we probed for and finally succeeded in listing the following additional lines of evidence.

First, data of Table II have already invalidated path 1, for there is no reason to expect that random attacks could be much less effective (by two orders of magnitude) in good or nonaggregating solvents. Similarly, by the same token possibility 3 can be disposed of.

Secondly, the effects of adding various amounts of *n*-BuSH on the hydrolytic rates of **16-H**, **8-H**, and **16-SH** were studied (Table IV). The added nucleophile accelerates the rates of **16-H** and **8-H** but retards somewhat that of **16-SH**. Path 1 is thus once more discredited. Incidentally, the slight retardation effected by *n*-BuSH as well as the other *n*-alkyl mercaptans discussed below (Tables IV and V) might be a reflection of the perturbation or interference of path 4 by the formation of very-short-lived H bonds between ionized and unionized (or even unionized and unionized) sulfhydryl bearing species.[18] With the increasing concentration of the mercaptans, however, this inhibitory effect would be overpowered by the rate-enhancing catalytic effect of the sulfide nucleophiles.

A third set of experiments further rendered unacceptable possibility 2, which was shown to be inconsistent with the observed

(16) The corresponding factor in the more aggregating 50:50 Me_2SO–H_2O medium could not be assessed because there is no plateau region in the rate vs. concentration plot.

(17) A referee has kindly and correctly pointed out that if rate-enhancing micelles with a critical micelle concentration (cmc) below the lowest concentration used were the cause of the observed effect, the rate could also be first order. However, the possibility that the **16-SH** molecules were involved in micelle formation under the experimental conditions used in this work, i.e., the range of initial substrate concentration of 3.6×10^{-6} to 3.0×10^{-5} M, was extremely remote. This statement is based on the following: (1) The cmc of anionic surfactants with hydrocarbon chains is in a range $\geq 10^{-4}$ M (e.g., see: Fendler, J. H.; Fenfler, E. J. "Catalysis in Micellar and Macromolecular Systems"). The "cmc" (*if* there were such a value) of the un-ionized **16-SH** would be expected to be much larger (cf. ref 20). (2) Previously we have demonstrated by four lines of evidence (ref 5) that an ionized group, the carboxylate, can completely inhibit the intermolecular aggregation of a similarly constructed 16-carbon substrate in the same medium. (3) As discussed in the text, data in Table III indicate that there is also no detectable tendency for the substantially ionized **16-SH** to aggregate in the concentration range (up to 3×10^{-5} M) studied.

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Table V. Rate Constants k (10^{-3} s^{-1})[a] of Hydrolysis of **16-H** and **16-SH** in the Presence of Thiols, 50:50 Me_2SO–H_2O, 35 °C

	concentration of n-$C_6H_{13}SH$ (10^{-3} M)						
substrate[b]	0.14	0.28	0.41	0.56	0.82	1.20	1.60
16-H	1.35	2.06	2.87	3.56	5.61	7.60	8.70
16-SH	29.8	23.5	18.1	14.6	14.9	15.2	16.4
	concentration of n-$C_8H_{17}SH$ (10^{-3} M)						
substrate[b]	0.14	0.28	0.41	0.56	0.82	1.20	1.60
16-H	3.04	5.78	9.45	12.6	18.4	26.3	35.0
16-SH	28.7	20.4	14.7	13.9	15.3	18.5	21.8
	concentration of n-$C_{12}H_{25}SH$ (10^{-3} M)						
substrate[b]	0.03	0.06	0.12	0.18	0.30	0.36	
16-H	12.5	15.8	19.3	27.8	50.2		
16-SH	31.2	28.0	18.5	17.7	23.9	27.7	

[a] The experimental uncertainty is ±15% in the presence of n-$C_{12}H_{25}SH$ and ±5% for the other thols. [b] Substrate concentration, 1.80×10^{-5} M.

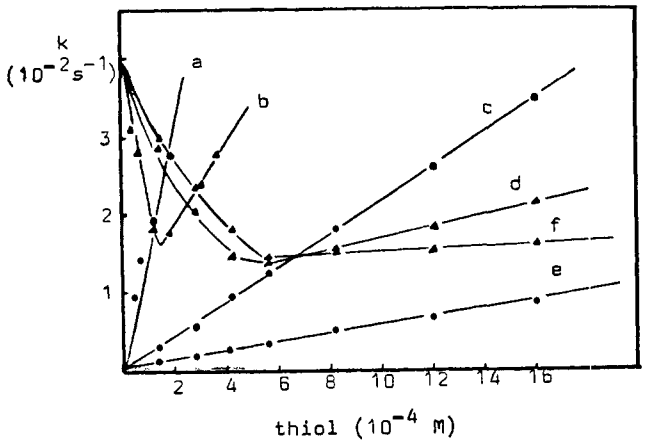

Figure 1. Chain-length effects on thiol-affected hydrolytic rates of **16-H** and **16-SH** in 50:50 Me_2SO–H_2O at 35 °C: (a) **16-H** catalyzed by n-$C_{12}H_{25}SH$, (b) **16-SH** by n-$C_{12}H_{25}SH$, (c) **16-H** by n-$C_8H_{17}SH$, (d) **16-SH** by n-$C_8H_{17}SH$, (e) **16-H** by n-$C_6H_{13}SH$, and (f) **16-SH** by n-$C_6H_{13}SH$.

kinetics. The effects of adding varying amounts of mercaptans with increasing chain lengths, i.e., n-$C_6H_{13}SH$, n-$C_8H_{17}SH$, and n-$C_{12}H_{25}SH$,[19] on the hydrolytic rates of **16-H** and **16-SH** were systematically evaluated, as shown in Table V and Figure 1. The rates of the former are accelerated with increasing concentrations of the thiols, and the catalytic effectiveness grows with the chain length. This is not surprising since such proximity effects have been observed and discussed by previous workers.[20,21] The rate of **16-SH**, however, is reduced at n-$C_{12}H_{25}SH$ concentrations up to 4×10^{-4} M. Thus at the very low substrate concentration used in the present work (1.80×10^{-5} M), any contribution from path 2 can be disregarded.

With the first three possibilities all eliminated, therefore, the 4th is proven to be the only path which enhanced the rate of **16-SH** at least 6 times that of **16-H** in the initial substrate-concentration range below 3×10^{-5} M.

Yet we were not satisfied, and the issue was finally and decisively settled by making use of a flexible host, namely amylose.

(19) Insolubility of n-$C_{16}H_{33}SH$ precluded its use.
(20) Knowles, J. R.; Parsons, C. A. *J. Chem. Soc., Chem. Commun.* **1976**, 755.
(21) Oakenfull, D.; Fenwick, D. E. *Aust. J. Chem.* **1974**, *27*, 2149.

Table VI. Kinetic Parameters of the Hydrolysis of **16-Y** Catalyzed by Amylose in 50:50 Me_2SO–H_2O at 35 °C

substrate[a]	10^3k_{un}, s^{-1}	10^3k_c,[b] s^{-1}	K_d,[b] mM	k_c/k_{un}
16-H	0.32	44.0	0.0063	138
16-Br	0.59	44.0	0.0049	75
16-SCH_3	2.46	47.6	0.0045	19
16-OH	5.01	43.2	0.0033	7.8
16-SH	39.6	20.0	0.0019	0.5

[a] Substrate concentration, 1.80×10^{-5} M. [b] Experimental uncertainty, ±15%.

Very recently it has been demonstrated that amylose can wrap-up long-chain substrates as single pieces in their straightened-up conformations and thus completely inhibit neighboring group participation involving 5-, 6- and 7-membered-ring intermediates.[22] Therefore, it will handle all the **16-Y** molecules likewise. Our results tabulated in Table VI indicate the following: First, the K_d values for all the **16-Y**'s lie in a similar range. Secondly, the k_c for **16-SH** is 2×10^{-2} s^{-1}, close to those of all the other **16-Y**'s around 4×10^{-2} s^{-1}.[23] Thirdly, the k_c/k_{un} values of 0.5 for **16-SH** imply that the 17-ring participation is even more effective than the catalytic effect provided by the host-molecule amylose. And finally, the decreasing order of catalytic efficiency for **16-Y**'s, k_c/k_{un}, is H > Br > SCH_3 > OH > SH, exactly the opposite of the order listed in Table I.

Conclusion

By judicious choice of a solvent system, long-chain molecules can be forced to fold and interact intramolecularly by hydrophobic forces. While previously presented evidence for self-coiling is indirect,[5] the present work may serve as a most convincing proof for this phenomenon. Hopefully, some synthetic organic chemists may sometime apply this trick advantageously in their exciting endeavors.

Registry No. 16-H, 1492-30-4; **16-Br**, 92269-99-3; **16-SCH_3**, 92270-00-3; **16-OH**, 92270-01-4; **16-SH**, 92284-09-8; **8-H**, 1956-10-1; n-BuSH, 109-79-5; n-$C_6H_{13}SH$, 111-31-9; n-$C_8H_{17}SH$, 111-88-6; n-$C_{12}H_{25}SH$, 112-55-0; amylose, 9005-82-7.

(22) (a) Hui, Y. Z.; Cheng, X.-E.; Jiang, X.-K.; Gu, J.-H.; Shen, Y.-D., submitted for publication. (b) Hui, Y.-Z.; Wang, S.-J.; Jiang, X.-K. *J. Am. Chem. Soc.* **1982**, *104*, 347.
(23) At present, we would rather venture not to speculate on the underlying subtle cause(s) of the fact that the k_c of **16-SH** was slightly smaller under these circumstances.