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The effect of hydrophobic–lipophilic interactions on chemical reactivity. 10. The competition between the aggregation of long-chain esters and the formation of inclusion complexes of these esters with amylose

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Abstract. The hydrolytic pseudo-first-order rate constants (k_{ad}) of *p*-nitrophenyl esters of dodecanoic acid (C12) and hexadecanoic acid (C16) at different initial substrate concentrations ($[S]_t$) in the six aquiorgano binary mixtures of different compositions (ϕ) were measured. These rate constants (k_{ad}) were compared with the corresponding rate constants obtained in the absence of sodium carboxymethylamylose (Na-CMA) (k_{un}) in order to study the competition between the formation of inclusion complexes of these esters with Na-CMA and the aggregation of these long-chain substrates. Values of $\Delta CAgC$ and k_{ad}/k_{un} were compiled and their significance discussed on the basis of a postulated two-path mechanism. Our results suggest that in addition to path A which involves encapsulation by Na-CMA of the monomeric C12 or C16 only, there is a second path (path B). Path B describes a process in which Na-CMA breaks up aggregates of all sizes into smaller ones as well as monomeric species which can be wrapped-up by Na-CMA simultaneously or subsequently.

Keywords. Hydrophobic–lipophilic interactions; aggregation of long-chain esters; inclusion complexes; chemical reactivity.

1. Introduction

In aquiorgano or aqueous solutions in the presence of amylose or its derivative, sodium carboxymethylamylose (Na-CMA), the hydrophobic-lipophilic force acts on long-chain ester substrate molecules (S) as if with ambivalent intentions. On the one hand, it strives to loop them into hairpins, or better still, push them together and make them form aggregates (Menger and Portony 1968; Blyth and Knowles. 1971; Guthrie 1973; Murakami *et al* 1977; Jiang *et al* 1984, 1985; Menger and Venkataram 1986). On the other hand, it contrives to keep them single and straightened-up in the helical cavities of amylose or Na-CMA (Hui *et al* 1981; Cheng *et al* 1985; Jiang *et al* 1984). Thus the same force appears to lead to two competing processes. It also leads us to ask two questions. (1) Can the second process, the formation of inclusion complexes, compete or coexist with the first (aggregation)? (2) If it can, then how?

Our previous work has already demonstrated that in $\phi = 0{\cdot}50$ or 50 : 50 (v/v) Me_2SO–H_2O solutions, phenyl and para-substituted phenyl esters of hexadecanoates at concentrations ranging from 1×10^{-5} M to 5×10^{-5} M can form host-guest complexes with amylose (Hui *et al* 1982, 1984; Jiang *et al* 1984, 1985) while they are already involved in the reversible process of aggregation (k_{agg}) and de-aggregation (k_{deag}) (Jiang *et al* 1984). The same is true with dodecanoates and octanoates

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(Huang 1985). Therefore, in the sense that coexistence signifies the ability to compete, the first question has already been affirmatively answered, with the stipulation that such things happen either only in the aqueous solution or in certain aquiorgano mixtures within a narrow range of ϕ values (volume fractions of the organic cosolvent).

Scheme I

$$\text{Path A: } S_n \underset{k_{agg}}{\overset{k_{deag}}{\rightleftharpoons}} nS \underset{k_{dewrp}}{\overset{+\text{Am},\, k_{wrp}}{\rightleftharpoons}} \text{Am}\cdot S,$$

$$\text{Path B: } S_n + \text{Am} \xrightarrow{k_{brk}} S_{n-q} + (q-x)S + x\ \text{Am}\cdot S,$$

$$x \leq q;\ q < n.$$

We may now attempt to address the second problem, i.e., how does the second process compete with the first? Scheme I depicts two possibilities. (1) Path A: Amylose (Am) or Na-CMA (Am) can only wrap up monomeric S molecules (k_{wrp}) to form inclusion complexes Am·S, whereas the monomeric species S are continuously formed from de-aggregation (k_{deag}) of the aggregates S_n (the subscript n stands for the degree of aggregation) which function as reservoirs of S. (2) Path B: Am somehow can perturb or break up S_n (k_{brk}) partially or wholly and encapsulate one or more "liberated" S molecules simultaneously or subsequently. A notable feature of this path is that it might lead to increased concentration of the monomeric species ([S]).

At the first glance, it appears extremely difficult to prove or disprove the reality of path B. For instance, although chemical intuition suggests that the weakly organized S_n can hardly withstand or completely survive a head-on collision with the giant Am molecule, one can always argue that the above-mentioned previous observations on hexadecanoates, dodecanoates and octanoates can be easily rationalized by path A alone, because k_{deag} should be very much larger than k_{wrp}, thus plenty of monomeric S are always constantly available from de-aggregation of S_n.

In fact, we took the last statement as a possible key which might help us solve this intriguing problem. In conformity with that statement we speculated that operation of two open paths (A + B) could more effectively increase the total amount of the monomeric species (S + Am·S) than the operation of only path A could. Thus finding a way to measure the change in the concentration of the monomeric species upon addition of Am might shed light on our problem.

Fortunately we already have in our hands a tool which may prove to be useful for our purpose. The previous paper of this series (Part 9, Jiang *et al* 1987a) has discussed the significance and method of measuring the critical aggregate concentration, or CAgC (see also Guthrie 1973; Murakami *et al* 1977; Menger and Venkataram 1986; Jiang *et al* 1984), of these long-chain esters. The CAgC value can be obtained from a hydrolytic rate constant (k) versus initial substrate concentration ($[S]_i$) plot and is a measure of the highest possible concentration of the monomeric species in a particular aggregating medium, as exemplified by the

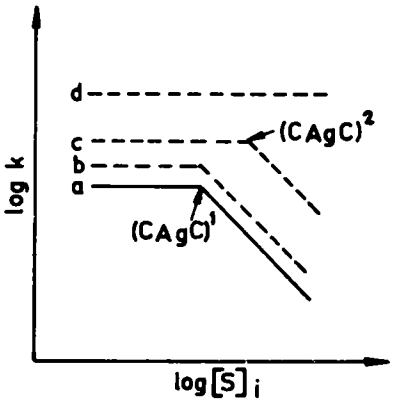

Figure 1. Log k vs. $[S]_i$ plots for an aggregating medium. Effects of adding Am on the hydrolytic behavior of an ester S (cf. text).

$(CAgC)^1$ of curve (a) in figure 1. Indeed, on the basis of previously discussed propositions, even before experimentation one could make up or sketch out a scenario for possible events (pertinent to the viability of path B) that might occur after adding Am to a solution of an ester S in an aggregating medium (dashed lines in figures 1 and 2). In figure 1, the solid line (a) represents the hydrolytic behavior of a long-chain ester S in a particular aggregating medium in the absence of Am; its CAgC is designated as $(CAgC)^1$. If Am is added, the CAgC is designated as $(CAgC)^2$. Dashed-line (b) represents an event with $(CAgC)^2 = (CAgC)^1$, i.e., $\Delta CAgC = (CAgC)^2 - (CAgC)^1 = 0$, whereas line (c) depicts a case with $\Delta CAgC > 0$. Line (d) can be regarded as purely fictitious right at the beginning; it says that aggregates are completely annihilated by Am. Figure 2 shows the same plots in a highly aggregating medium, i.e., $(CAgC)^1$ cannot be found within the range of substrate concentration ($[S] \geq 2 \times 10^{-6}$ M) capable of being measured by the spectrometer. Lines a, b, and c bear the same meaning as their counterparts in figure 1.

The present work is therefore an effort at realizing or invalidating these expectations by studying dozens of these log k vs. $[S]_i$ plots derived from a large number of observed hydrolytic rate constants, designated as k_{un} for those measured in the absence of Am, and k_{ad}, in the presence of Am. The symbol (m) pertains to the monomeric state, and (ag), the aggregated state. Thus k_{ad} (m)/k_{un} (m) represents the ratio of the rate constants in the presence of Am to that of the monomeric species in the absence of Am at a particular initial substrate concentration $[S]_i$. The significance of such ratios as well as the $\Delta CAgC$ values will be discussed after the experimental results are presented.

Six aqueous binaries of various compositions (ϕ) were used in this investigation, viz., MeOH–H_2O, EtOH–H_2O, *n*-PrOH–H_2O, *t*-BuOH–H_2O, dioxane (DX)–H_2O, and Me_2SO–H_2O. NaCMA (Am) of five different degrees of substitution (D.S.) were used, namely, D.S. = 0·00 (i.e. amylose), 0·12, 0·18, 0·24, and 0·29. The esters used as substrates (S) were the *p*-nitrophenyl esters of dodecanoic acid (C12) and hexadecanoic acid (C16). N-Dodecanyl-3-acetoxypyridinium iodide, designated as 1, was also used as a substrate.

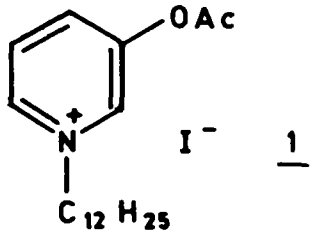

Chart 1

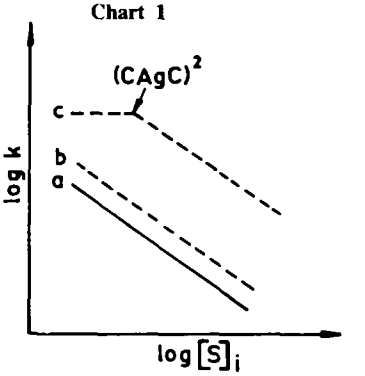

Figure 2. Log k vs. $[S]_i$ plots for an highly aggregating medium. Effects of adding **Am** on the hydrolytic behavior of an ester **S** (cf. text).

2. Experimental

Substrates: Para-nitrophenyl dodecanoate (C12) and hexadecanoate (C16) and N-dodecanyl-3-acetoxypyridinium iodide (1) were prepared by methods reported previously (Jiang *et al* 1984; Hui *et al* 1983).

Amylose and sodium carboxymethylamylose: The amylose used was purified by the procedure previously described (Hui *et al* 1983). Sodium carboxymethyl amylose (Na-CMA), with different degrees of substitution by the $-CH_2CO_2Na$ group, was prepared by reactions of amylose with various amounts of chloroacetic acid and sodium hydroxide in 40:60 ethanol-water mixtures (Huang 1985). The degree of substitution for Na-CMA (abbreviated as DS) is defined as the number of carboxymethyl groups contained in each anhydroglucose unit.

Kinetics: The kinetic measurements of k_{ad} were carried out under identical conditions as described in part 9, except that buffer solutions containing 2×10^{-4} M of pre-dissolved amylose or Na-CMA were used. Rate constants measured in the absence of Na-CMA were reported in the previous paper. The experimental uncertainties for k_{ad} are around 5–10%.

3. Results

The hydrolytic pseudo-first-order rate constants (k_{ad}) of C12 and C16 at different initial substrate concentrations ($[S]_i$) in the presence of 2×10^{-4} M Na-CMA in six aquiorgano binary mixtures of different compositions (ϕ) are listed in tables 1 and

Table 1. Hydrolytic pseudo-first-order rate constants (k_{ad}, 10^{-3} s^{-1}) of C12 at different initial concentrations ($[S]_i$) in the presence of 2×10^{-4} M Na-CMA (DS = 0·12) in six aquiorgano mixtures of various compositions (ϕ).

Organic cosolvent	ϕ	$[S]_i$, 10^{-5} M								
		0·2	0·4	0·6	0·8	1·0	2·0	4·0	6·0	10·0
MeoH	0·20	123	122	113		60·8	25·0	11·4		3·8
	0·25	153	151	153	123	93	39·2	14·6		5·4
	0·30	163	162	162		160	85	40·0		13·2
EtOH	0·20	116	117	91		52·5	27·0	12·0		4·2
	0·25	103	100	103		86	39·4	21·9		7·9
	0·30	74·2	74·7			74·7	66·7	32·1		10·4
n-PrOH	0·15	59·3	60·0	54·4		38·4	19·8	8·5		3·3
	0·175	34·3	35·0			34·8	26·3	11·7		4·7
	0·20	22·7	22·7			22·5	22·6	22·5	21·3	12·8
t-BuOH	0·15	35·6	39·1	34·0		20·3	12·0	7·1	5·2	3·9
	0·175	25·7	25·7	25·3		24·7	15·6	9·9	6·2	4·7
	0·20	13·8	13·7			13·8	13·8	12·8	11·3	7·1
	0·10[a]	21·3	13·3	8·4		4·9	2·7	1·4		
	0·15[a]	21·7	17·2	11·8		7·5	3·7			
	0·175[a]	13·0	13·2	13·1		12·4	7·1	3·6		1·6
	0·20[a]	9·8	9·8			9·9	9·6	8·8		4·0
	0·25[a]	6·0	6·2	6·2		6·1		6·3		6·0
Dioxane	0·15	113	112	90		53·3	27·0	12·5		4·8
	0·30	51·7	52·0	52·2		52·5	51·1	26·3		12·7
Me_2SO	0·15	117	116			53·3	28·0	13·3		6·0
	0·30	183	183			185	85	44·2		15·8
	0·0[a]	21·2	10·3	7·2		4·5	2·3			

[a] In the presence of 2×10^{-4} M Na-CMA with DS = 0·24.

Table 2. Hydrolytic pseudo-first-order rate constants (k_{ad}, 10^{-3} s^{-1}) of C16 at different initial concentrations ($[S]_i$) in the presence of 2×10^{-4} M Na-CMA in three aquiorgano mixtures of various compositions (ϕ).

Organic cosolvent	ϕ	D S of NaCMA	$[S]_i$, 10^{-5} M							
			0·2	0·4	0·6	1·0	2·0	4·0	6·0	10·0
t-BuOH	0·15		17·0	8·9	6·9	4·3	2·2	1·2		
	0·20	0·12	10·5	10·4	9·6	7·7	4·0	2·4		
	0·25		6·9			6·8	6·6	6·8	5·9	4·1
Dioxane	0·20	0·12	26·3	15·9	10·7	6·7	3·5	1·74		0·72
	0·40	0·12	21·3	21·3	21·0	19·0	11·5	5·9		2·5
Me_2SO	0·20	0·12	15·1	7·5	4·53	2·7	1·44			
	0·40	0·0	57·3	57·2	52·5	32·9	20·0	11·6		6·1
	0·40	0·12	72·0	45·8	30·1	20·9	10·4	5·2		2·6
	0·40	0·29	26·4	13·2	9·3	6·3	3·13	1·60		0·65
	0·50	0·0	79	78	78	79	53·3	29·3		12·1
	0·50	0·12	119	79	57·3	37·5	17·9	8·17		3·93

2, respectively. Corresponding rate constants measured in the absence of Na-CMA (k_{un}) have been reported in the previous paper of this issue. The logarithms of all these k (k_{ad} or k_{un}) have been plotted against log $[S]_i$ to yield many figures, only one of which is given as an example (figure 3), since for each aquiorgano binary system a similar figure can be drawn. Figure 3 shows that the possible effects of adding Na-CMA as postulated in the inroductory remarks (cf. figures 1 and 2) have been borne out by experimental data. The $(CAgC)^2$ values, as defined in the introduction, are derived from the 239 rate constants (k_{ad}) tabulated in tables 1 and 2. The $(CAgC)^1$ values are obtained from k_{un} data presented in part 9. Both of them, as well as their differences, $\Delta CAgC$ $[(CAgC)^2 - (CAgC)^1]$, are presented in table 3. For C16, owing to much higher degrees of aggregation, only a few $\Delta CAgC$ values can be obtained under our experimental conditions. Since the CAgC values for substrate 1 cannot be precisely measured and the $\Delta CAgC$ of 1 appear to be roughly nil, they are not tabulated.

4. Discussion

In §1, we have already briefly proposed a second possible mode of competition between inclusion-complex formation and aggregation, as depicted symbolically by path B in the scheme. Since the aggregation number n is not an exact number but represents a certain condition-dependent distribution of numbers, the quotation-marked rate or equilibrium constants are merely conceptual abstractions. Although nothing quantitative can be deduced from such a scheme, it nevertheless may be qualitatively meaningful. To be more exact or specific, we presume that the existence of path A as the first mode of competition is a self-evident fact which requires no further discussion; but path B as a speculation needs some elaboration. We visualize that the perpetually moving and tumbling giant polymers Am (amylose or Na-CMA) are in constant collisions with aggregates (S_n) of all sizes.

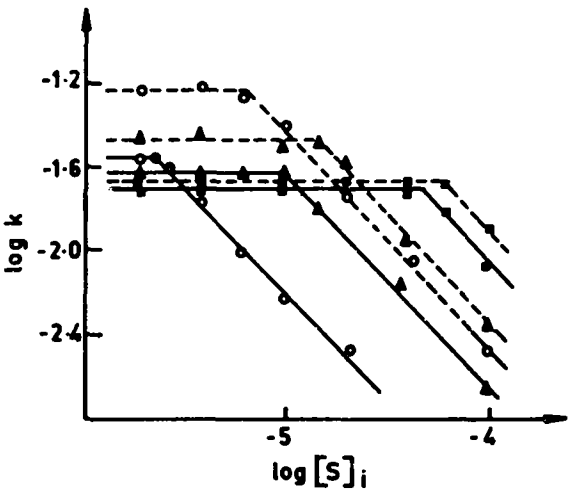

Figure 3. Log k vs. log $[S]_i$ plots for **C12** in *n*-PrOH–H_2O mixtures of different ϕ. ○: ϕ = 0·15; ▲: ϕ = 0·175; ■: ϕ = 0·20; solid lines are for k_{un}; dashed lines are for k_{ad}.

Table 3. $(CAgC)^1$, $(CAgC)^2$ and ΔCAgC values (10^{-5} M) for C12 and C16 in various aquiorgano mixtures.[a]

Organic cosolvent	ϕ	C12			C16		
		$(CAgC)^1$	$(CAgC)^2$	ΔCAgC	$(CAgC)^1$	$(CAgC)^2$	ΔCAgC
MeOH	0·20	0·20	0·58	0·38~0·58			
	0·25	0·30	0·66	0·36			
	0·30	0·60	1·23	0·57			
EtOH	0·20	0·2	0·51	0·31~0·51			
	0·25	0·48	0·91	0·43			
	0·30	1·26	1·82	0·56			
n-PrOH	0·15	0·28	0·65	0·37			
	0·175	1·0	1·51	0·51			
	0·20	5·0	6·17	1·17			
tBuOH	0·15	0·26	0·32	0·12			
	0·175	1·0	0·98	−0·02			
	0·20	4·2	4·0	−0·2	0·60	0·72	0·12
Dioxane	0·15	0·2	0·48	0·28~0·48			
	0·30	1·8	2·29	0·49			
	0·40				0·83	1·1	0·27
Me_2SO	0·15	0·2	0·46	0·26~0·46			
	0·30	0·2	1·0	0·8~1·0			
	0·50				0·2	0·28	0·08~0·28
	0·50				0·2	1·38[b]	1·18~1·38

[a] The $(CAgC)^1$ values were reported in part 9. The $(CAgC)^2$ values are derived from the k_{ad} values measured in the presence of 2×10^{-4} M of Na-CMA (DS = 0·12) which are listed in tables 1 and 2.

[b] Derived from k_{ad} values measured in the presence of 2×10^{-4} M of amylose (i.e. DS = 0)

Some of the "head-on" or forceful collisions may break an aggregate into one or more smaller aggregates (S_{n-q}) as well as one or more (q) monomeric species out of which one or more (x) monomers may be captured immediately or later on by Am as "guests" in Am·S. We further imagine that at initial substrate concentrations ($[S]_i$) fairly or very close to $(CAgC)^1$ small aggregates S_n may be easily broken into very small aggregates (S_{n-q}) plus some monomers or even completely into monomers (S), but at concentrations much higher than $(CAgC)^1$, although S_{n-q} species may still retain respectful sizes, some monomers or very small aggregates are bound to be simultaneously formed nevertheless. In other words, we believe path B is the most effective way to increase the concentration of the monomeric species (S + Am·S). To put it more bluntly, with Occam's razor in mind we suggest: any experimental observation of a positive ΔCAgC value under certain circumstances would make the existence of path B most likely.

A quick glance at table 3 may please those who agree with or can tolerate our speculations because most of the ΔCAgC listed are positive. Thus path B appears to be viable and realistic indeed. Naturally, things are much more complicated than has been said, and a closer scrutiny of the data (cf. tables 3 and 5) will further reveal other noteworthy and intriguing points.

Table 4. Hydrolytic pseudo-first-order rate constants, k_{ob} (10^{-3} S^{-1}), for 1 in pure water.

DS	Na-CMA conc. (10^{-4} M)	[S]$_i$, 10^{-5} M						
		1·0	2·0	4·0	8·0	10·0	20·0	40·0
	0	0·82	0·80	0·83	0·80	0·79	0·60	0·45
0·12	2·0	13·6	13·6	13·6	13·6	13·5	13·0	11·3
0·12	4·0	13·7	13·8	13·7	13·7	13·1	12·0	
0·18	2·0	9·65	9·61	9·6	9·5	8·61	7·18	

4.1 *The ΔCAgC values*

Table 3 reveals two outstanding facts: (1) Out of the twenty ΔCAgC (10^{-5} M) values, sixteen are positive and greater than about 0·15, the remaining four (−0·2 to 0·12) all belong to the *t*-BuOH system. (2) All the above mentioned sixteen ΔCAgC follow the same rule, they increase with increasing ϕ values for each of the five systems (MeOH, EtOH, *n*-PrOH, dioxane, Me_2SO). Let us address the second observation first.

Positive ΔCAgC values signify that in a particular system $(CAgC)^2$ values increase more rapidly than $(CAgC)^1$ when more of the organic component is added to that aqueous binary, whereas for negative ΔCAgC the reverse should be true. Since both inclusion-complex formation (k_{wrp}) and aggregation (k_{agg}) are driven by hydrophobic-lipophilic forces (both ΔG_{wrp} and ΔG_{agg} are negative), or in other words, increasing the lipophilicity of the medium should disfavor both of these two competing processes, i.e., increasing ϕ should favor both k_{dewrp} and k_{deag} (both ΔG_{dewrp} and ΔG_{deag} are positive) (Hui *et al* 1982; Jiang *et al* 1984, 1987), it does not seem immediately clear why we should have such a range of ΔCAgC, from values as high as +1·3 (Me_2SO, C16) to as low as −0·2. Perhaps the following considerations are pertinent to this problem.

These two processes are both similar and dissimilar. They are similar in the sense that they are both consequences of hydrophobic interactions, but dissimilar because they may conform to different types of energetics. For instance, aggregation is favored by ΔS (Reichardt 1979) but encapsulation of uncharged esters by Am are disfavored by ΔS and favored by ΔH (Jiang *et al* 1985; Bender and Komiyama 1978; Murakami *et al* 1975), whereas complex formation of charged S species with Am is favored by both ΔS and ΔH (Hui *et al* 1981). In fact, our very recent work on both fluorocarbon and hydrocarbon substrates show that, in comparison with complex formation with cyclodextrins, encapsulation by Am may require additional help from lipophilic forces (Jiang *et al* 1987b). This state of affairs may be looked upon as a natural consequence of the fact that the structures and properties of the guest (S) and host (Am) are completely different, thus the general and specific solvent effects of the organic cosolvents on S and Am must be different (cf. part 9). These solvent effects surely depend on the nature of the organic cosolvent. Therefore, for each aquiorgano solvent system, the rate of free energy change (ΔG) with increasing ϕ should be different for these two competing processes, i.e., $d\Delta G_{deag}/d\phi$ and $d\Delta G_{dewrp}/d\phi$ are different, and naturally, the ΔCAgC values will vary accordingly.

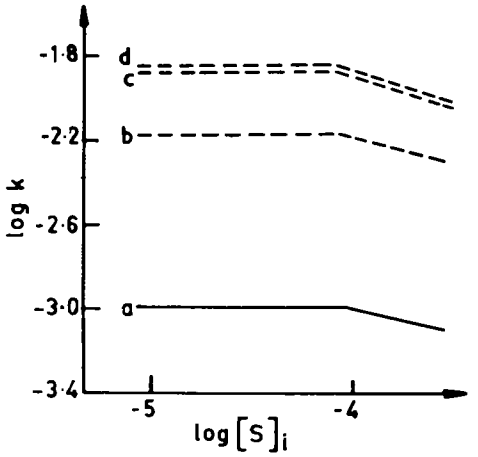

Figure 4. Log k_{ob} vs. log [S]$_i$ plots for 1 in pure water: a: in the absence of Na-CMA; b: in the presence of 2×10^{-4} M Na-CMA (DS = 0·18); c: in the presence of 2×10^{-4} M Na-CMA (DS = 0·12); d: in the presence of 4×10^{-4} M Na-CMA (DS = 0·12).

The sixteen positive ΔCAgC values for the five solvent systems (vide supra) suggest that in these media $d\Delta G_{dcag}/d\phi$ is larger than $d\Delta G_{dcwrp}/d\phi$, i.e., upon adding more organic cosolvent, the substrate S loses its ability to aggregate faster than the host Am loses its ability to wrap up S. The lone exception thus far found is *t*-BuOH, the most lipophilic of all the six organics. It is hardly surprising if one remembers that it has acted just like that in a study involving ten aquiorgano systems (Jiang *et al* 1984). However, there is an additional message from the present work, it says: the properties of *t*-BuOH molecules are exceptionally well-adapted to solvate (thus stretch out) the Am molecules.

Finally, we want to present a particularly noteworthy piece of observation which has direct bearing on the credibility of path B. The preceding work (part 9) has established that among six cosolvents Me_2SO is least capable of increasing $(CAgC)^1$, yet the present work (cf. table 3) indicates that Me_2SO is the most capable of increasing ΔCAgC! In order to rationalize this interesting combination of facts, one would have to postulate then that k_{wrp} (or the hydrophobic-lipophilic interactions between Am and S) would be favored by increasing ϕ if path A alone were operating. This sounds unreasonable, thus we cast another vote of confidence for path B.

The behavior of the pyridinium compound 1 deserves some comments. Being positively charged and thus more hydrophilic, it barely shows some tendency to aggregate. This is not unexpected since it has been known that 16–CO_2^- is the maverick among six 16–Y substrates (when Y = H, NO_2, Cl, CH_3, OCH_3, aggregation observed, Jiang *et al* 1984). Nevertheless, it is noteworthy that the approximate CAgC of 1 is still much smaller than the CMC values of charged surfactants. Thus 1 may be a member of those compounds whose behavior lies in-between neutral compounds which form aggregates and charged compounds which form micelles. We believe CAgC values are normally several orders of magnitude smaller than CMC values. This difference might be used to differentiate between the two types of molecular assemblies.

4.2 *The k_{ad}/k_{un} ratios*

The ratios of the rate constants measured in the presence and absence of Am, listed as k_{ad}/k_{un} values in table 5, also deserve our attention. Previous work has established that our observed k_{ad} are catalyzed-hydrolysis rate constants of monomeric substrate species inside the helical cavities of Am. (Hui *et al* 1982, 1983; Jiang *et al* 1985; Huang 1985). Thus higher k_{ad}/k_{un} values signify both higher catalytic efficiencies and higher association constants ($K_a = 1/K_d$) of the inclusion complexes. Data compiled in table 5 reveal two interesting aspects. First, the k_{ad} (m)/k_{un} (m) values obtained from the monomeric region for all six solvents are almost always smaller than the average k_{ad} (ag)/k_{un} (ag) values obtained from the aggregate region. This fact is certainly in harmony with the proposition that path B is in operation. Secondly, all these ratios decrease with increasing ϕ. Clearly, this is

Table 5. The k_{ad} (m)/k_{un} (m) and average k_{ad}(ag)/k_{un} (ag) values for the hydrolysis of C12 and C16 in various binary mixtures.

Organic cosolvent	ϕ	Na-CMA[a] DS	for C12		for C16	
			k_{ad} (m) / k_{un} (m)	k_{ad} (ag) / k_{un} (ag)	k_{ad} (m) / k_{un} (m)	k_{ad} (ag) / k_{un} (ag)
	0·0	0·24		15·4		
MeOH	0·20	0·12		5·8		
	0·25	0·12	1·1	3·3		
	0·30	0·12	1·0	2·0		
EtOH	0·20	0·12		11·5		
	0·25	0·12	2·9	6·8		
	0·3	0·12	1·8	2·6		
	0·3	0·18	1·5	1·7		
n-PrOH	0·15	0·12	2·1	4·5		
	0·175	0·12	1·4	1·8		
	0·20	0·12	1·0	1·2		
t-BuOH	0·15	0·12	3·4	5·6		18·5
	0·175	0·12	2·1	2·5		
	0·20	0·12	1·3	1·8	1·1	1·7
	0·25	0·12			0·95	0·93
	0·10	0·24		10·5		
	0·15	0·24	1·6	2·0		
	0·175	0·24	1·0	1·0		
	0·20	0·24	1·0	0·9		
Dioxane	0·15	0·12		23·5		
	0·20	0·12				34·0
	0·30	0·12	2·2	3·2		
	0·40	0·12			1·3	1·8
Me_2SO	0·15	0·12		45·5		
	0·30	0·12		25·6		
	0·40	0·12				55
	0·50	0·12				15·5
	0·40	0·29				17·5
	0·40	0·00				90

[a] The concentration of Na-CMA was 2×10^{-4} M.

a reflection of the fact that the association constants or the tendency (or driving force) of the inclusion-complex formation are unfavorably affected by larger amounts of the organic cosolvent.

Notably, among the organic cosolvents studied, Me_2SO possesses the least ability to de-aggregate (lowest CAgC values, cf. part 9), yet it is one of the most capable to increase ΔCAgC and it also gives the highest k_{ad} (ag)/k_{un} (ag) ratios. Thus Me_2SO can provide the widest range of composition (ϕ) for the study of the two competing processes, and the previous use of Me_2SO–H_2O as the medium was a fortunate choice which led, among other results, to the first successful application of Rekker's hydrophobicity-lipophilicity constants to the correlation analysis with rate constants (Fan and Jiang 1985; Huang 1985).

5. Conclusion

Hydrophobic-lipophilic interactions, together with Nature's other forces, lead to the creation of the most complicated and wonderful things, such as vesicles, cells and life. Aggregation and self-coiling may be one of the simplest ways in which hydrophobic-lipophilic forces manifest themselves since even micelle formations usually involve interactions among electrically charged species. The host-guest interactions of the flexible linear polymers amylose and Na-CMA with straight-chain substrates are also expressions of hydrophobicity-lipophilicity, except that here lipophilic interactions between the host and guest may also contribute to this process which in a sense mimics the induced-fit of enzymes. By now it can be said affirmatively that these two processes can coexist or effectively compete with each other. Furthermore, our data suggest that there are more than one pathways for them to compete (cf. scheme I), and that the big Am molecules can smash the larger aggregates into smaller pieces as well as monomeric ones. The role of the organic cosolvent, including their varying solvation effects on S, S_n, Am, and Am·S, is both important and interesting. Although all of them disfavor both aggregation and inclusion-complex formation, their abilities to do so differ. In fact, trying to understand more about the pertinent intrinsic properties of these and other organic solvents remains a challenge. Such understanding may very well lead to practical applications. Like the CMC in micelle chemistry, the CAgC may prove to be a useful tool in the study of aggregation and inclusion-complex formation in the future. All in all, however, we are just beginning to understand a little, and only in a simplistic and qualitative way, about these intriguing, complicated and often puzzling phenomena, and we believe other interested workers will develop some new weaponry for further and much improved studies of these phenomena.

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