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The effect of hydrophobic-lipophilic interactions on chemical reactivity. 9. Putting the spotlight on lipophilic forces in solvent-effect studies

XI-KUI JIANG*, XING-YA LI* and BANG-ZHOU HUANG
The Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai, China

Abstract. The hydrolytic rate constants of the *p*-nitrophenyl esters of acetic, octanoic, dodecanoic and hexadecanoic acids in six aquiorgano binary mixtures of graded compositions at various initial substrate concentrations were measured and discussed in terms of the hydrophobic-lipophilic interactions between the substrate molecules and the organic cosolvents which were MeOH, Me_2SO, 1, 4-dioxane, 1,2-dimethoxyethane, *n*-propanol and *t*-butanol. The accelerating or retarding effects of the organic cosolvents on the rate constants of hydrolysis were found to be directly related to the lipophilicities of the solvents which were changed either by changing the content (ϕ) or the nature of the organic cosolvent. The classification or ordering of the six solvents on the basis of their solvent effects were found to conform to the lipophilicity order derived from Rekker's Σf values. The results support the proposition that lipophilic interactions can play an important role in solvent effects of aqueous binaries.

Keywords. Hydrophobic-lipophilic interactions; chemical reactivity; solvent-effect studies; hydrolysis rate constant; lipophilicity order.

1. Introduction

Solvent effects of aquiorgano binary mixtures on the hydrolytic behavior of carboxylic derivatives have interested or intrigued many physical and organic chemists, and much elegant work has been done on this subject (e.g. Elsemongy *et al* 1981, Guthrie 1973, Murakami *et al* 1977, Oakenfull 1973, Oakenfull and Fenwick 1974, Singh *et al* 1981, Holterman and Engberts 1983, Jiang *et al* 1984, 1985, Fan *et al* 1985). These effects can be very complicated and even capricious sometimes, thus in addition to the more usual notions, the concept of hydrophobic interactions has to be invoked to rationalize or interpret the results (e.g. Engberts 1982, Oakenfull and Fenwick 1974, 1977, 1979, Jiang *et al* 1984, 1987). The present work on solvent effects is an attempt to reveal contributions from hydrophobic-lipophilic interactions (hereafter abbreviated to lipophilic interactions† clearly and

*To whom all correspondence should be addressed

† Hydrophobic-lipophilic interactions are time and again simply referred to as hydrophobic interactions because (1) the lipophilic component (van der Waals interactions between the hydrocarbon portions of molecules) of hydrophobic-lipophilic interactions are often not considered to be so important (see, e.g., Ben-Naim 1980, Franks 1975, Oakenfull and Fenwick 1977, Shapiro and Ohki 1974, Tanford 1980), and (2) it is exceedingly difficult to experimentally assess the relative importance of these two forces. The present authors are among those who believe that under certain circumstances the contributions from lipophilic forces should not be overlooked (see, e.g., Diederich *et al* 1986, Jiang *et al* 1987). In order to call our readers' attention to lipophilicity in the present work, we choose to use the word "lipophilic" as the shortened form of the term "hydrophobic-lipophilic" without any intention of overemphasizing the importance of lipophilicity or playing down the importance of effects derived from changes in water structure (hydrophobicity).

in a relatively simple manner, without implying that other forces are of less importance.

Suppose we divide the solvation effects of the organic component in an aquiorgano solvent into two parts: (1) its solvation effects on the reagent, i.e., in our case, its effects on the nucleophile OH^-, and on the cation Na^+; (2) solvation effects on the organic substrate. The latter sometimes might again be composed of two parts: (a) a general effect involving heteroselective solvation (Reichardt 1979) brought about by lipophilic forces; (b) a specific solvation with lipophilic interactions as one of the contributing forces (vide infra). Then, by (1) comparing the hydrolytic behavior of ester substrates with different chain lengths under otherwise identical conditions and (2) using organic components of different lipophilicities (Rekker 1977; Jiang *et al* 1984; Menger and Venkataram 1986) for aquiorgano solvents with different compositions, it might be possible to demonstrate convincingly the significance of lipophilic interactions between the organic substrate and solvent molecules without disregarding other important solvent properties such as dielectric constant or other polarity parameters, pH, and hydrogen-bonding ability etc.

However, there is another basic and important phenomenon which should be taken into account carefully before we can proceed with the aforementioned approach, namely, the aggregation of long-chain substrates in aggregating solvents. Aggregation and self-coiling have been found to profoundly affect hydrolytic behavior and other properties of organic molecules (e.g. Menger and Portnoy 1968, Blyth and Knowles 1971, Guthrie 1973, Murakami *et al* 1977, Jiang *et al* 1984, 1985, Menger and Venkataram 1986, Shobha and Balasubramanian 1986.) Therefore, for long chain substrates in aggregating media, only the rate constants of their "monomeric" forms can be compared with those of their shorter counterparts. Fortunately, it is usually possible to determine fairly precisely the "critical aggregate concentration", or CAgC (vide infra; see also figure 1), from log k vs. initial [substrate] plots, thus rate constants of the "monomeric" forms can be obtained when they are measured in the concentration range below CAgC.

On the basis of the above mentioned considerations, we reckoned that a systematic collection and a full analysis of all the rate data obtained from different solvent systems with graded compositions might reveal contributions from lipophilicity in solvent effects. We believe this goal has been achieved.

The *p*-nitrophenyl esters of acetic, octanoic, dodecanoic, and hexadecanoic acids, hereafter abbreviated as C2, C8, C12 and C16 were used as substrates in this study. Six organic components were used for the aqueous binaries, namely, MeOH, *n*-PrOH, *t*-BuOH, 1,4-dioxane, 1,2-dimethoxyethane (DME), and Me_2SO. Composition of the binary mixtures are expressed by ϕ, the volume fraction of the organic component of the aqueous-organic solvent, e.g., for a 60:40 (v/v) organic:H_2O mixture, $\phi = 0{\cdot}60$.

2. Experimental

p-Nitrophenyl carboxylates with various chain lengths were prepared by methods described previously (Jiang *et al* 1984).

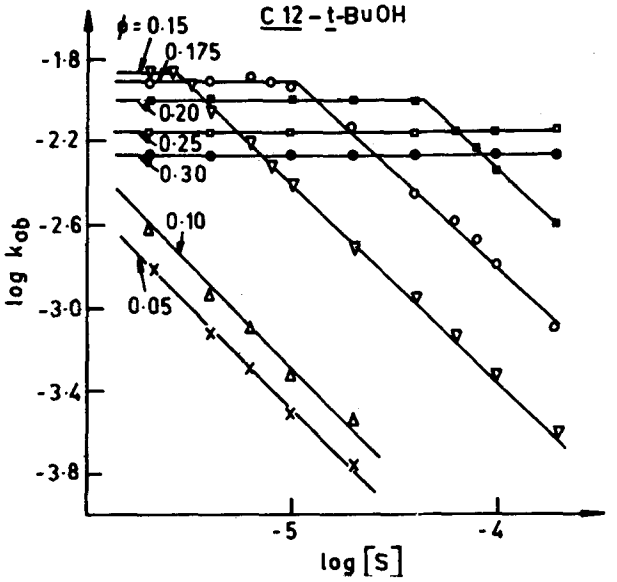


Figure 1. Hydrolysis of **C12** in various proportioned *t*BuOH-H_2O mixtures at different initial [*S*]. Plot of log k_{ob} vs log [*S*] at different ϕ's indicated by numbers.

Water was deionized and all organic solvents were purified by the usual methods as described elsewhere (Perrin 1980).

Aqueous 0·01 M $NaHCO_3$-NaOH solution containing 2% NaCl with pH = 11·70 was used as the buffer solution which was mixed with the organic solvent in various proportions. The pH values of the binary solvent mixtures are listed in table 1. The volume fractions of the organic solvents in the binary mixtures are expressed as ϕ values as mentioned in the introductory remarks.

2·1 *Kinetics*

Kinetic measurements at 35°C were performed on a Perkin-Elmer 559 spectrophotometer equipped with a thermostatted cell holder. The wavelength used for

Table 1. pH values of the binary solvent mixtures at 25°C; for ϕ = 0·00, pH = 11·70

	ϕ = 0·05	0·01	0·15	0·175	0·20	0·25	0·30	0·40		ΔpH[a]
MeOH	11·70	11·71	11·72		11·73	11·73	11·74			0·04
n-PrOH	11·77	11·85	11·92	11·96	11·98	12·03	12·07			0·37
t-BuOH	11·74	11·83	11·92	12·12	12·02	12·08	12·13			0·43
Dioxane	11·82	11·94	12·06		12·18	12·30	12·42	12·62	12·84	0·72
DME	11·77	11·89	11·99		12·12	12·25	12·37			0·67
Me_2SO	11·76	11·88	12·06		12·24	12·42	12·61	12·99	13·32	0·91

[a]ΔpH is the difference of the pH at ϕ = 0·30 and the pH at ϕ = 0·0 i.e., 11·7.

monitoring the formation of the *p*-nitrophenol was 410 nm. All the rate constants are accurate to within ±5–8% except in cases when the substrate molecules are aggregating. In these cases the kinetics deviate from first-order, hence the pseudo-first order rate constants were obtained from the linear portion of the curves for the initial stage of the reaction (Murakami *et al* 1974; Jiang *et al* 1984), and the experimental uncertainties are around ±10%.

3. Results

A total of four hundred and eighty-six pseudo-first-order rate constants (k_{ob}) of the hydrolysis of C2, C8, C12 and C16 in six aquiorgano binary mixtures of graded compositions (ϕ) at various initial substrate concentrations ([S]) are listed in tables 2, 3, 4 and 5, respectively.

4. Discussion

For solvent effect studies, the direct comparision of hydrolytic rate constants of a short-chain ester with those of a long-chain ester will become hardly meaningful if the latter type of substrate begins to aggregate. Previous results have indicated that the hydrolysis of long-chain esters in aggregating solvents is an exceedingly complicated process, and the relative importance of the various paths leading to the product P from substrate S depicted in scheme I, i.e., k_m, k_{agg}, k_{coil}, may change greatly under different conditions. (Jiang *et al* 1984, 1985; Fan and Jiang 1985).

Table 2. Rate constants, k_{ob} (10^{-2} s^{-1}), of the hydrolysis of C2 in various aquiorgano solvents at different initial [S] (10^{-5}M) and ϕ values.

Organic cosolvent	ϕ	Initial [S], 10^{-5} M			Organic cosolvent	ϕ	Initial [S], 10^{-5} M		
		0·2	2·0	20			0·2	2·0	20
n-PrOH	0·00	8·71	8·62	8·62	DME	0·05	8·65	8·63	8·65
	0·05	8·36	8·27	8·36		0·10	8·75	8·68	8·71
	0·10	8·18	8·27	8·18		0·15	8·89	8·95	8·90
	0·15	8·18	8·07	8·07		0·20	9·05	9·13	8·99
	0·20	7·42	7·31	7·42		0·25	9·35	9·29	9·15
	0·25	6·32	6·30	6·27		0·30	9·60	9·48	9·25
	0·30	5·67	5·60	5·70					
					Dioxane	0·05	0·96	9·51	9·51
t-BuOH	0·05	8·33	8·33	8·33		0·10	10·4	10·3	10·3
	0·10	7·50	7·70	7·60		0·15	11·0	11·0	11·2
	0·15	6·90	6·93	6·87		0·20	12·0	12·1	12·0
	0·20	5·43	5·47	5·40		0·25	12·8	13·0	12·8
	0·25	4·60	4·69	4·53		0·30	13·2	13·2	13·2
	0·30	3·53	3·63	3·51					
					Me_2SO	0·15	14·3	14·5	
						0·25	19·0	19·5	

Table 3. Rate constants of the hydrolysis of C8, k_{ob} (10^{-3} s^{-1}) at 35°C.

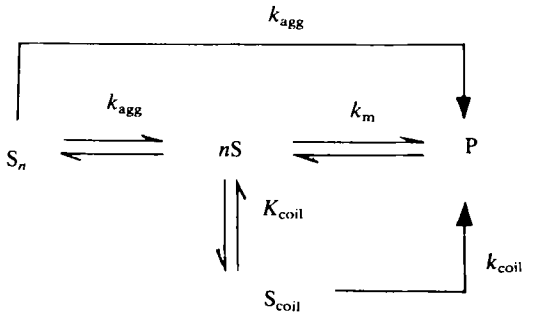
Organic cosolvent	Initial [S], 10^{-5} M														
	ϕ	0·2	0·4	0·6	0·8	1·0	1·2	1·5	2·0	2·5	4·0	6·0	8·0	10·0	20·0
MeOH	0·00	48·5	50·4			49·1			29·0		13·3			5·2	
	0·05	88·9	88·9			89·3			63·3		34·1			12·0	
	0·10	133	133			136			120		94·7			31·7	
	0·20	183	183			185			181		173			91·1	
n-PrOH	0·05	44·9				44·0	43·7		35·0		18·0			6·8	
	0·10	39·1							39·3	38·7	27·3	17·8		10·9	
	0·15	30·7				30·0					31·0	30·5	30·5	26·1	
	0·20	20·8							21·0						21·3
	0·25	18·0				18·3									17·9
	0·30	16·0							16·0						15·7
t-BuOH	0·05	42·3		41·3		41·3	40·7	38·3	28·3		14·9			5·4	
	0·10	34·6				34·5		34·5	33·3		18·0			6·9	3·6
	0·15	23·7				24·3			24·0		23·3	21·1		13·3	7·1
	0·20	13·1							13·1						12·8
	0·25	8·6							8·7						8·7
	0·30	6·6							6·5						6·7
DME	0·05		43·0			43·0			31·1		16·0			6·1	
	0·10		40·0						40·3		22·0			8·6	
	0·15		37·4						37·3		35·5	21·0		13·0	
	0·20		34·3								34·0	31·7		16·1	
	0·25		33·3						32·9			32·7	32·7	31·3	
	0·30		32·7						33·0				32·0	32·7	
Dioxane	0·05		51·3		50·2	50·4			45·6		22·7			8·5	
	0·10		51·8			51·1			50·7		47·1			17·6	
	0·15		51·6			51·6			51·0		50·7	48·0		30·3	
	0·20		51·0			51·0					51·0	49·8		47·6	29·3
	0·25		50·9						50·7				50·7	49·0	41·0
	0·30		51·8											50·2	45·7
Me_2SO	0·15		59·6			60·4			59·6		43·1	26·7		15·7	
	0·30		72·0			71·1			70·2		70·2	67·6		42·7	
	0·45		87·1			88·0					85·3			86·2	

Table 4. Rate constants of the hydrolysis of C12, k_{ob} (10^{-3} s^{-1}) at 35°C.

Organic component of solvent	Initial [S], 10^{-5} M													
	ϕ	0·2	0·3	0·35	0·40	0·6	0·8	1·0	2·0	4·0	6·0	8·0	10·0	20·0
MeOH	0·20	75·0			37·0			10·4	4·37	2·0			1·0	
	0·25	137	137	116	70·8	52·0		28·7	11·7	5·0			1·87	
	0·30	165				167	153	79·2	43·3	20·2				
n-PrOH	0·05	2·6			1·11			0·49	0·25					
	0·10	6·8			3·10			1·20	0·58	0·31				
	0·15	28·4	26·1		20·2	12·7		7·7	4·1	2·1			0·90	
	0·175	25·0			25·0	24·7		23·7	13·3	6·80			2·62	
	0·20	22·4						22·0	21·7	21·7	17·8		10·7	6·1
	0·25	18·3							18·0		18·2		18·0	17·8
	0·30	15·6							15·5					15·3
t-BuOH	0·05	1·5			0·75	0·51		0·31	0·21					
	0·10	2·4			1·15	0·80		0·46	0·28	0·16				
	0·15	13·4	12·1		8·9	6·1	4·6	3·8	1·90	1·10				
	0·175	12·5			12·5	12·5	12·3	11·6	7·3	3·6	2·7		1·6	0·8
	0·20	10·3			10·3			10·3	10·3	9·8	7·1	6·0	4·6	2·3
	0·25	7·1							7·0					7·0
	0·30	5·5							5·5					5·7
DME	0·15	9·2			4·5			1·7	0·75					
	0·20	20·2			9·8			3·17	1·47					
	0·25	30·6			22·7			8·13	3·60					
	0·30	30·5			30·4			24·0	11·0	4·92			2·0	
Dioxane	0·10	5·3			2·5	1·6		0·95	0·49					
	0·15	12·0			6·0			2·27	1·00					
	0·175	19·0			10·2	6·0		3·73	1·7	0·93				
	0·20	24·2			14·4	9·4		5·00	2·9					
	0·25	24·8			25·2	24·9	21·8	16·8	7·5	4·0			1·58	
	0·30	23·3			24·0	24·2		23·1	21·1	10·8			3·93	
Me_2SO	0·15	5·07			2·60	1·78		1·10	0·60					
	0·30	28·0			15·3	11·3		7·0	3·42	1·67			0·54	

Table 5. Rate constants of the hydrolysis of C16, k_{ob} (10^{-3} s^{-1}).

Organic cosolvent	Initial [S], 10^{-5} M								
	ϕ	0·2	0·4	0·6	0·8	1·0	2·0	4·0	6·0	10·0
t-BuOH	0·15	0·97	0·55	0·34		0·23	0·19			
	0·175	5·5	2·9	2·1		1·25	0·83	0·475		
	0·20	9·6	9·6	8·3		6·0	3·0	1·48		0·64
	0·25	7·3				7·3	7·3	7·2	6·6	4·4
	0·30	5·4	5·5					5·5		5·5
n-PrOH	0·15	5·8	2·7			0·92	0·68	0·35		0·34
	0·20	21·3	21·9	21·9	19·7	14·3	7·3	3·6		1·4
	0·25	18·7					18·7		18·9	13·7
	0·30		15·3				15·5			
DME	0·30	5·2	2·4			0·89				
Dioxane	0·20	0·94	0·51			0·20	0·14			
	0·30	7·5	3·40			1·30	0·62	0·29		0·18
	0·40	16·2	15·9			14·2	6·4	3·4		1·25
Me_2SO	0·20	0·18	0·10			0·08	0·07			
	0·40	1·46	0·76			0·38	0·22	0·16		
	0·50	9·8	5·4			2·21	1·15	0·64		0·27



Scheme I

Fortunately, we can usually get around such complications by measuring the rate constants of the "monomeric" forms from log k vs. initial [S] plots as exemplified by the curves in figure 1. If the solvent is not too strongly aggregating, then there will be a plateau region in which k_{ob} is independent of the initial [S], this k_{ob} is generally accepted as the rate constant of the monomeric ester (Guthrie 1973; Murakami *et al* 1977; Jiang *et al* 1984; Menger and Venkataram 1986). Another important feature of these curves is the break-points after which the k_{ob} values decrease with increasing [S]. In analogy to the CMC of micelle chemistry we can designate them as the critical aggregate concentrations, or CAgC, and a discussion of our CAgC values tabulated in tables 6 and 7 will be presented later. Incidentally, the k_{ob} values of C2 are always independent of [S] (table 2).

Table 6. CAgC values for C8 in various aquiorgano mixtures.

Organic cosolvent	CAgC (10^{-5} M)						
	ϕ = 0·0	0·05	0·10	0·15	0·20	0·25	0·30
n-PrOH	1·0	1·6	2·9	8·3	>10		
t-BuOH		1·5	2·2	5·5	>10		
Dioxane		1·7	3·6	6·2	>10	>10	
DME		1·4	2·0	3·6	7·2	>10	
Me_2SO				2·8			5·9
MeOH		1·3	2·6		5·3		

Table 7. CAgC values for C12 in various aquiorgano mixtures.

Organic cosolvent	CAgC (10^{-5} M)						
	ϕ = 0·00	0·10	0·15	0·175	0·20	0·25	0·30
n-PrOH	<0·2	<0·2	0·28	1·0	5·0	>10	
t-BuOH		<0·2	0·26	1·0	4·2	>10	
Dioxane					<0·2	0·63	1·8
DME					<0·2	0·26	0·74
Me_2SO							<0·2
MeOH					<0·2	0·30	0·66

For each subsrate and solvent a figure with curves corresponding to different ϕ's can be obtained, as exemplified by figure 1. Whenever there is a break-point in these curves, a CAgC value can be determined, and with these CAgC values (tables 6, 7) one can judge which k_{ob} can be used as rate constants for monomeric substrates.

Although a number of factors will influence the magnitude of the k_{ob}, e.g., pH, H-bonding, or other solvent polarity properties, these will tend to remain relatively unchanged when different esters are compared in the same medium. This has allowed us to show the contributions of lipophilic forces, i.e., lipophilic solvation of the esters by the organic solvent molecules, by the following approach.

For each substrate a figure consisting of log k vs. ϕ curves corresponding to different solvent systems is drawn, i.e., figure 2 for C2, figure 3 for C8 and figure 4 for C12, (the curves for Me_2SO and DME are missing because C12 aggregates at these ϕ values; for the same reason, the MeOH, Me_2SO, DME, dioxane curves cannot be constructed for C16), then (1) the different curves for different solvents in the same figure, and (2) the different trends of these curves in different figures for short and long substrates, are compared and analysed.

Several interesting and significant observations will stand out by following the aforementioned approach (for somewhat related observations, see Elsemongy *et al* 1981, Singh *et al* 1981, Yang and Fagley 1981, Engberts 1982): (1) There are three types of solvents, Me_2SO and MeOH increase the rates with increasing ϕ, *n*-PrOH and *t*-BuOH decrease the rates with increasing ϕ, dioxane and DME are in

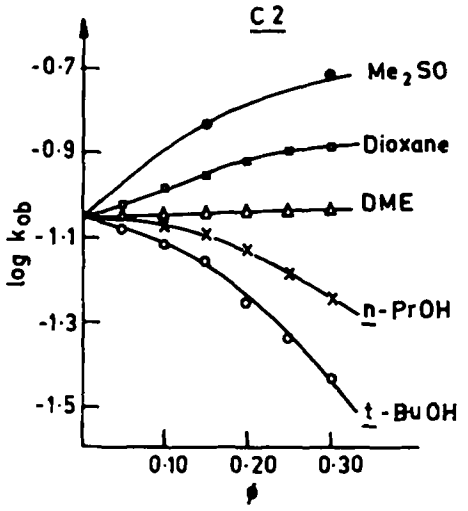


Figure 2. Log k_{ob} vs ϕ plots for **C2** in different aquiorgano solvents.

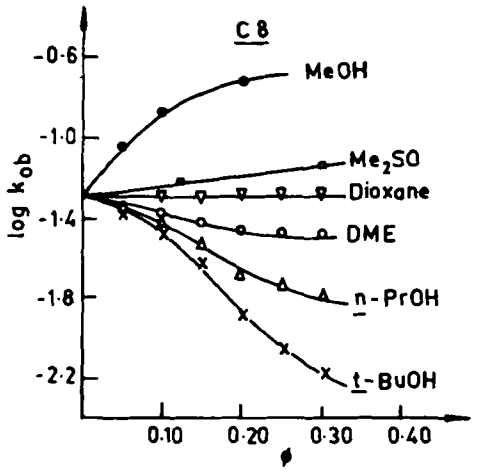


Figure 3. Log k_{ob} vs ϕ plots for monomeric **C8** in different aquiorgano solvents.

between. With increasing ϕ, dioxane increases the rates of C2 but has little effect on those of C8, whereas DME has little effect on the rates of C2 but decreases the rates of C8 to some extent. (2) A comparison of the trends or "slopes" of all the curves for C8 and C12 (figures 3 and 4) with those for C2 (figure 2) will show a very intriguing feature: all the curves for C2 seem to have been "pushed down" by some "force" when they reappear in figures 3 and 4. Why?

On the basis of our propositions previously stated, we rationalize our results in terms of the following reasonings or speculations (designated later as points 1, 2 etc.).

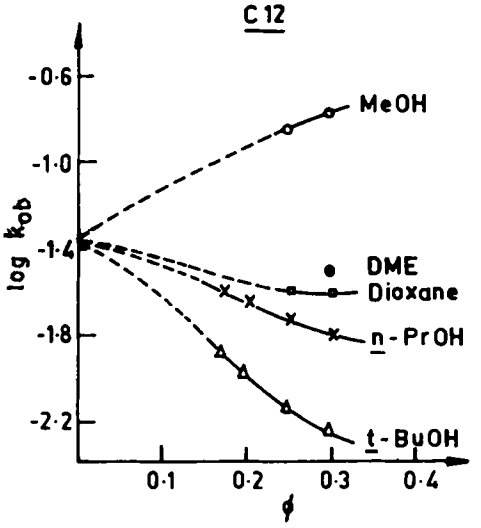
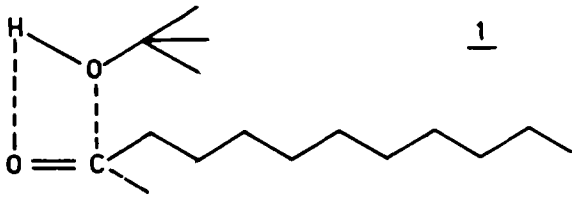


Figure 4. Log k_{ob} vs ϕ plots for monomeric **C12** in different aquiorgano solvents.

1. Solvation of ^{-}OH through H-bonding by the solvent molecules is in the order: protic > aprotic; and for the protic solvents: H_2O > MeOH > *i*-PrOH, *t*-BuOH. Since the solvating abilities of water and the cosolvents should also be related to the acceptor numbers AN (Gutmann 1978; Reichardt 1979), which are 54·8 for H_2O, 41·3 for MeOH, 37·1 for EtOH and 33·5 for *i*-PrOH. Thus the factor of desolvation of OH^- upon adding more organic cosolvent alone will tend to increase the rates in varying degrees for all organic cosolvents, and more so for the aprotic ones. (AN values: Me_2SO 20·4, dioxane 10·8, DME 10·2). The fact, however, is that only some of them accelerate the rates. And, in our judgement, the most important conclusion that can be deduced from this fact is: the conspicuous retarding (instead of accelerating) effects of adding more *n*-PrOH and *t*-BuOH are necessarily consequences of the operation of another opposing force.
2. The opposing force most likely originates from lipophilic interactions between organic cosolvent molecules and the esters, including C2 which also possesses a phenyl group. These interactions will lead to the well-known phenomenon of heteroselective solvation (Reichardt 1979) of substrate molecules by organic cosolvent molecules and thus retarded rates.
3. The magnitude of the above mentioned lipophilic heteroselective solvation effect on C8 should be larger than that of C2. Thus a crucial test of the credibility of our proposition (point 2) is whether this expectation has been borne out by fact. The fact is: everyone of the five curves in figure 2 is "pushed down" in figure 3, it could hardly be a consequence of fortuity.
4. Another possibility exists, especially when *n*-PrOH and *t*-BuOH are the cosolvents, namely, specific solvation involving "complexes" such as 1, which can also be looked upon as encounter pairs with longer lives than those involving smaller molecules. In these complexes H-bonding and polar interactions together will tend to hold the polar parts of the ester and cosolvent molecules together,



1

whereas lipophilic interactions will try to pull the hydrocarbon moieties together. Certainly, larger organic fragments of either partner of the complex will tend to increase the magnitude of this specific solvation effect (cf. MH values which reflect the lipophilicity of the alkyl groups, Menger, 1986).

5. The desolvation and increased activity of the ^{-}OH brought about by the addition of organic cosolvents is reflected in the increased pH values which can be arbitrarily measured by ΔpH values defined as the difference of pH at $\phi = 0{\cdot}30$ and pH at $\phi = 0{\cdot}00$. The tabulated ΔpH values make the last column of table 1 the most noteworthy column. Evidently the trend of these ΔpH values are in complete harmony with discussions presented in point 1. Of course, the higher cation solvation ability of Me_2SO (Parker 1969) may also contribute to the exceptionally high ΔpH value for Me_2SO.

6. The somewhat peculiar behavior of MeOH is manifested by both its exceptional ability to accelerate the hydrolytic rate (figures 3 and 4) and its unusually low ΔpH value. This is very likely a consequence of the fact that the pKa of MeOH is 15·7–16, very close to the pKa value of H_2O, i.e., 15·7 (Lowry 1982) (the pKa's of other alcohols have been reported to be >17). Thus a second and possibly more reactive nucleophile, $^{-}OCH_3$, may also be participating in the "hydrolysis" of the substrates.

7. Finally we have yet another piece of clear evidence for the existence of lipophilic interactions in solvent effects from the perspective of the applicability of Rekker's f constants (Rekker 1977; Rekker and de Kort 1979). Very recently, first examples of successful correlations of f constants with the deaggregating abilities of ten organic cosolvents (Jiang *et al* 1984) and hydrolytic rate constants of twelve substituted phenyl esters of *n*-hexadecanoates have been reported (Fan and Jiang 1985). The individual curves corresponding to the different cosolvents in figures 2, 3 and 4 all show the same ordering of their effects on the hydrolytic rates, viz., (on account of the facts already discussed in point 6, MeOH is excluded from this ordering).

t-BuOH,	*n*-PrOH,	DME,	dioxane,	Me_2SO
(0·37)	(0·34)	(−0·15)	(−0.42)	(−1·35)

Evidently this ordering is exactly the same as the ordering according to Rekker's Σf values shown in paranthesis. Thus lipophilic forces are doubtlessly involved in these solvent effects.

In support of the above arguments are the trends of the CAgc values shown in tables 6 and 7. The CAgC is a direct physical indicator of the deaggregating ability of an organic cosolvent, i.e., a larger value reflects a higher ability. Table 6 shows that at $\phi = 0{\cdot}20$ for *n*-PrOH and *t*-BuOH, the CAgC already can no longer be found in the range of substrate concentrations studied (i.e., no break-point appears

for the "plateau" line in this concentration range) the corresponding value for dioxane and DME is somewhere between 0·25 and 0·30, whereas in the ϕ = 0·30 Me_2SO-H_2O system, C8 still aggregates easily. Therefore the order of deaggregating abilities derived from CAgC data again looks familiar, i.e., *n*-PrOH, *t*-BuOH > dioxane, DME > Me_2SO. From these observations we are tempted to conclude: The dynamic processes of lipophilic heteroselective solvation of monomeric organic substrates and deaggregation of the substrate aggregates by organic cosolvent molecules are in essence or in nature one and the same thing, although they may be looked upon as two processes. The actors under our spotlight are all interacting with lipophilic (as well as other important) forces.

It has been shown previously that in a particular medium, the k_{ob} of a nonaggregating shorter substrate divided by the k_{ob} of the monomeric form of an aggregating longer substrate gives a measure of the rate retarding effect of self-coiling of the longer substrate (Jiang *et al* 1984). The present work provides some additional data in terms of the k_8/k_{16} or k_8/k_{12} ratios listed in table 8. Evidently, there is practically no rate retardation brought about by self-coiling in *n*-PrOH, *t*-BuOH, and DME and a very small effect in dioxane. This ratio is not available for the Me_2SO system since aggregation occurs in the whole range of composition studied and no CAgC values can be obtained.

5. Conclusion

In the past it has not been easy to reveal the contributions to the total solvent effect from lipophilic interactions between organic cosolvent and substrate molecules in a relatively simple and straight forward manner, either because the substrates used were relatively small or because complicating factors such as aggregation made a direct comparison of long-chain substrates with short ones impossible. The present work makes this comparison possible by first finding out the CAgC values of the long-chain esters under specific conditions, then comparing the rate constants of the monomeric forms of octanoates, dodecanoates, hexadecanoates with those of

Table 8. The rate ratios k_8/k_{12} and k_8/k_{16} in various aquiorgano mixtures.

Organic cosolvent	ϕ	k_8/k_{12}	k_8/k_{16}
n-PrOH	0·20	1·0	1·0
	0·25	1·0	1·0
	0·30	1·0	1·0
t-BuOH	0·20	1·1	1·2
	0·25	1·1	1·0
	0·30	1·1	1·0
DME	0·25	1·1	
	0·30	1·1	
Dioxane	0·25	2·0	
	0·30	2·1	

the acetates. When such comparisons were made in six aquiorgano solvents the lipophilicity of which could be changed by either the nature or the content of the organic componant, it became clear that lipophilic interactions were playing an important role in solvent effects of aqueous binaries.

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