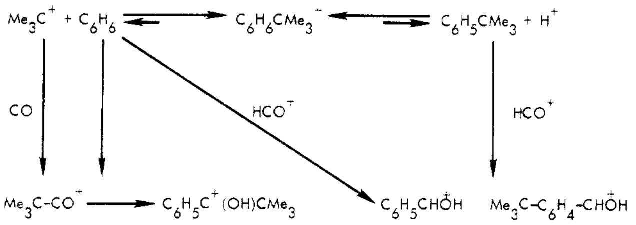
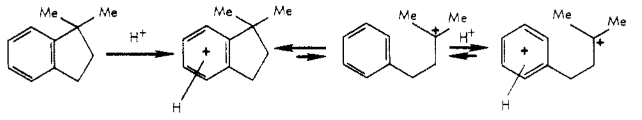
Scheme I



3 4

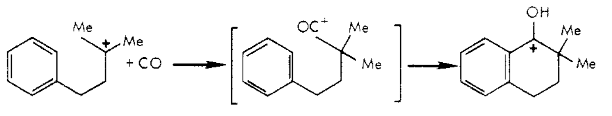
is understandable, since the starting **4** is too hindered sterically to undergo the Gattermann–Koch reaction.[3] It is noteworthy that according to literature reports **2a** reacts with pivaloyl chloride and $AlCl_3$ to form exclusively **5** and its positional isomers, while benzene under the same conditions forms **6**,[8] together with **2a**[8a] and a rearrangement product, 3-methyl-3-phenyl-2-butanone.[8b]

The CO insertion is also favored in a bicyclic system like 1,1-dimethylindane (**7**). Dealkylation of protonated **7** should generate a phenyl-substituted tertiary alkyl cation (**8**), which in a very strong acid can be protonated in the aromatic ring (**9**).



7 **7-H$^+$** **8** **9**

In the absence of the second proton addition, the equilibrium between **7-H$^+$** and **8** should favor the former. Indeed, in agreement with this expectation based on the behavior of phenylalkanes (**2**),[4] the ^{13}C NMR spectrum of **7** in HF–SbF_5 exhibited a signal for the carbocationic center at δ 332, which was not observed in the spectrum of the solution of **7** in HF–TaF_5 (**7-H$^+$**).[9] Nevertheless, treatment of the latter solution with CO at −20 °C resulted in the trapping of **8** by CO, followed by cycliacylation to the protonated form of 2,2-dimethyltetralone (**10**).



8 **10-H$^+$**

The analysis of the quenched reaction product indicated that ring enlargement to **10** is favored over the Gattermann-Koch formylation of **7** by a ratio of 85:15. Since 1,1-dimethylindane (**7**) and its homologues are formed in various alkylation reactions,[10] the ring enlargement by CO insertion can be of preparative interest.

Experimental Section

Carbonylation of *p*-Di-*tert*-butylbenzene (5). A Hastelloy-C autoclave was charged with a mixture of **5** (4.76 g, 25 mmol) benzene (40 mL) and anhydrous $AlCl_3$ (3.4 g, 25 mmol), pressurized with CO to 1.25 MPa and stirred for 3 h at room temperature. The autoclave was once refilled with CO after 1 h. The total pressure drop was 1.1 MPa (35 mmol CO). The autoclave was vented and then opened, and the reaction mixture was poured onto 100 mL of ice–water. The organic layer was separated, and the aqueous solution was extracted twice with 50-mL portions of benzene. The combined organic layer was dried overnight (Na_2SO_4). Solvent evaporation gave 4.7 g of a liquid (86% yield) identified as **6**[8] by H NMR: δ 0.68 (s, 18 H), 6.53 (AA′BB′, $J_{AA'} = J_{BB'} = 9$, $J_{AB} = 20$ Hz, 4 H). Its purity was at least 95% (by GLC); only traces of the dealkylation product **2a** were observed.

Carbonylation of 1,1-Dimethylindan (7). A solution of **7** (1 g, 6.6 mmol) in Freon-11 (3.0 mL) was added slowly to TaF_5 (5.5 g, 20 mmol) and HF (12 mL, 600 mmol) in a Teflon-lined Hastelloy-C autoclave, with cooling and magnetic stirring. The autoclave was filled with CO (2.65 MPa at −25 °C) and stirred at −25 to −20 °C.[11] The reaction, as monitored by the pressure drop, was completed in 1.5 h. The autoclave was opened after 2 h, and the reaction mixture was quenched in ice. Extraction with pentane, drying (Na_2SO_4 + NaF), and solvent evaporation gave a liquid (1.06 g, 90%); GLC analysis (5% Carbowax 20M, 3 m × 3 mm o.d., 130 °C, and 5% SP2250, 3 m × 3 mm o.d., 140 °C) showed two partially overlapping peaks as 98–99% of the mixture. The minor product was an aldehyde and represented 15% of the mixture, as calculated by the integration of the CH═O peak (δ 9.95) in the ^1H NMR spectrum. Oxidation with Jones reagent (8 N CrO_3 in 8 N H_2SO_4) in acetone at room temperature followed by $NaCO_3H$ extraction removed the aldehyde from the product (NMR, GLC). Ketone **10** had a ^1H NMR (in $CDCl_3$) spectrum in agreement with that in literature:[12] δ 1.18 (s, 6 H), 1.90 (t, $J = 6$ Hz, 2 H), 2.77 (t, $J = 6$ Hz, 2 H), 7.05–7.50 (m, 3 H), 7.93–8.17 (m, 1 H); mass spectrum,[13] m/e (relative intensity) 175 (13) 174 (M^+, 74), 159 (43), 145 (5.8), 132 (10), 131 (50), 129 (5.2), 128 (7.0), 119 (23), 118 (100), 116 (13), 115 (10), 103 (6.0), 91 (22), 90 (70), 89 (21), 77 (11), 65 (6.3), 64 (7.1), 63 (8.8), 59 (8.8), 51 (12), 41 (9.9), 39 (15).

Acknowledgment. Dr. C. S. Hsu is thanked for the GLC/MS experiments and Mrs. L. Craine, Mr. W. H. Dougherty, and Mr. W. Hoff, for experimental assistance.

Registry No. 5, 1012-72-2; **6**, 22583-66-0; **7**, 4912-92-9; **10**, 2977-45-9; CO, 630-08-0.

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(11) Reaction at room temperature gave a less pure product.

(12) Burdon, M. G.; Moffatt, J. G. *J. Am. Chem. Soc.* **1966**, *88*, 5855. Our NMR spectra were run at 60 MHz on a Varian A-60 instrument.

(13) GLC/MS experiments were done on a Du Pont 21-491 instrument. The relative intensities are given in parentheses. Only the peaks with an intensity higher than 5% of the base peak are listed.

Micellar Inhibition of the Neutral Hydrolysis of 3-Substituted 1-Benzoyl-1,2,4-triazoles. Microenvironmental Effects at the Surface of Sodium Dodecylsulfate and Cetyltrimethylammonium Bromide Micelles

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Rate enhancement or inhibition of unimolecular reactions in the presence of micelles can generally be interpreted in terms of substrate–micelle binding constants and microenvironmental effects operating at the micellar reaction site(s).[1,2] However, a detailed molecular picture

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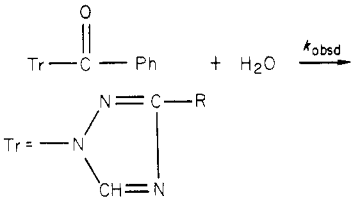
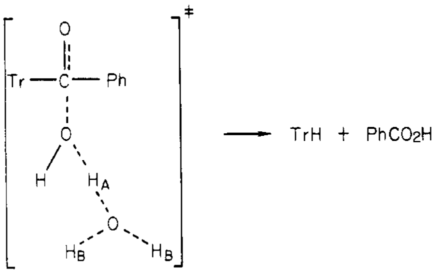
of the micellar rate effect hinges on the model chosen for the description of the molecular structure of the micelle. In this respect there is considerable controversy. For example, Menger has contrasted the classical oil droplet model[3] with his porous cluster model[4] that assumes the presence of water-filled grooves allowing extensive water penetration beyond the surface of the micelle. Still more recent models include those of Flory[5] and of Fromherz.[6]

In the present study we exploit the water-catalyzed hydrolysis of the 1-benzoyl-1,2,4-triazoles[7] **1-3** in the presence of anionic (NaDodSO$_4$) and cationic (CTAB) micelles as a possible kinetic probe for the reaction sites of substrates of varying hydrophobicity within the micellar aggregates.

The hydrolysis of **1-3** is pH independent between at least pH 3 and 5 and involves water-catalyzed nucleophilic attack of water at the amide carbonyl group. Proton inventory studies[7] revealed that three protons (H_A, H_B's) contribute to the solvent deuterium isotope effect (k_{H_2O}/k_{D_2O} = ca. 2.5-3.5). Recently, a transition state containing more than two water molecules has also been proposed.[8] Mixed aqueous solvent effects have been analyzed in detail, in particular the influence of hydrophobic interactions.[9]



1, R = Me
2, R = H
3, R = Ph



Results and Discussion

Table I. Neutral Hydrolysis of 3-Substituted 1-Benzoyl-1,2,4-triazoles in the Presence of Micelles of NaDodSO$_4$ and CTAB at 25 °C[a]

amphiphile	concn, M	$10^4 k_{obsd}$, s^{-1} 1	 2	 3
		9.23	20.9	12.4
NaDodSO$_4$	0.02	7.21	13.6	1.98
NaDodSO$_4$	0.03	5.53	10.8	1.42
NaDodSO$_4$	0.04	4.77	9.14	1.23
NaDodSO$_4$	0.06	3.54	6.73	0.86
NaDodSO$_4$	0.08	2.89	5.87	0.86
NaDodSO$_4$	0.10	2.55	5.03	0.76
NaDodSO$_4$	0.12	2.47	4.47	0.72
CTAB	0.002	8.75	19.6	4.21
CTAB	0.004	8.36		2.75
CTAB	0.005		18.6	2.41
CTAB	0.006	7.81	18.0	2.04
CTAB	0.007	7.43	17.3	
CTAB	0.009	7.21	16.7	1.87
CTAB	0.011		16.3	1.74
CTAB	0.013	6.65	15.7	1.58
CTAB	0.015	6.47		1.53
CTAB	0.017	6.15		
CTAB	0.019	6.07		
CTAB	0.034		11.3	
CTAB	0.052		9.48	
CTAB	0.101		6.69	
CTAB	0.212		4.26	

[a] All solutions contain 10^{-3} M HCl.

Table II. Association Constants and Micellar Rate Constants for the Micelle-Inhibited Neutral Hydrolysis of 1-3 at 25 °C

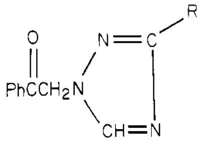
compd	amphiphile	K, M^{-1}	$10^4 k_m$, s^{-1}	k_w/k_m
1	NaDodSO$_4$	2.3×10^3	0.61	15
2	NaDodSO$_4$	3.2×10^3	1.68	12.5
3	NaDodSO$_4$	3.6×10^4	0.54	23
2	CTAB	2.1×10^{3a}	2.22	9.5
3	CTAB	1.4×10^{5b}	1.25	9.9

[a] For **4**, $K = 2.2 \times 10^3$ M^{-1}. [b] For **5**, $K = 2.1 \times 10^5$ M^{-1}.

Pseudo-first-order rate constants (k_{obsd}) for the water-catalyzed hydrolysis of **1-3** in the presence of varying concentrations of sodium dodecylsulfate (NaDodSO$_4$) and cetyltrimethylammonium bromide (CTAB) at 25 °C are listed in Table I. Reaction rates are retarded upon incorporation of **1-3** into the anionic as well as into the cationic micelles. Clearly the charge type of the micelle is not a dominant factor in determining the kinetic micellar effect. The S-shaped curves of k_{obsd} vs. detergent concentration were graphically analyzed in terms of the enzyme model for micellar catalysis,[2] employing eq 1.

$$(k_w - k_{obsd})^{-1} = (k_w - k_m)^{-1} + (k_w - k_m)^{-1}(KC)^{-1} \quad (1)$$

Herein, k_w is the pseudo-first-order rate constant for hydrolysis in water, k_m is the micellar rate constant, K is the substrate-micelle association constant divided by the aggregation number of the micelle, and C is the total detergent concentration minus the critical micelle concentration (cmc). The derived values of K and k_m are shown in Table II.[10] In order to ratify the K values derived from the kinetic analysis, we determined association constants independently for binding of the stable model substrates **4** and **5** to CTAB by ultrafiltration, using a Thomapore tubular membrane[11] (Table II). The similarity of the K



4, R = H
5, R = Ph

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(10) The variation of k_{obsd} for hydrolysis of **1** in CTAB was not large enough to provide fully reliable values for K and k_m. However the overall behavior of **1** is quite similar to that of **2**.

Table III. Neutral Hydrolysis of 1-3 in Dioxane-Water Mixtures at 25 °C

% dioxane (w/w)	n_{H_2O}	ϵ	$10^4 k_{obsd}$, s^{-1}		
			1	2	3
0.00	1.000	78.6	9.23	20.9	12.4
10	0.978	69.8	5.42	12.6	7.74
20	0.951	60.8	3.58	8.22	4.89
30	0.919	51.9	1.98	4.07	2.52
40	0.880	43.0	0.88	2.77	1.37
50	0.830	34.3	0.51	1.35	0.64
52.5	0.816	32.0	0.42	1.18	0.52

values obtained for **2** and **4** and for **3** and **5** lends support to the applicability of the enzyme model. The data in Table II indicate that inhibition of the hydrolysis is somewhat stronger by $NaDodSO_4$ than by CTAB. The association constants are quite high, in particular for **3**, the most hydrophobic substrate. As expected,[1a] the K values are rather similar for the anionic and cationic micelle.

Several factors can be invoked to rationalize the rate inhibition, the two most plausible being the reduced micropolarity and the decreased water concentration at the reaction sites in $NaDodSO_4$ and CTAB micelles.[12] Considering the first factor, it has been estimated that the effective dielectric constant is ca. 32 near the binding site of several fluorescent pH indicators at the surface of both $NaDodSO_4$ and CTAB micelles.[13] This smaller value with respect to that of water (ϵ = 78) most likely reflects the proximity of the hydrocarbon chain and/or stems from a dielectric saturation effect.[14] Since the rates of neutral hydrolysis of 1-acyl-1,2,4-triazoles clearly respond to changes in solvent polarity,[9] k_{obsd} values were determined in the typically nonaqueous solvent[15] 1,4-dioxane–water as a function of the dielectric constant (ϵ). The results, summarized in Table III, show that at ϵ = 32 the k_{obsd} values are close to the k_m values listed in Table II, the best correspondence being observed for hydrolysis of **1**-**3** in micellar $NaDodSO_4$. These findings suggest that the micellar rate effects can be accounted for without implying that the hydrolysis occurs in a relatively dry region of the micelle. Recently, in an independent study, Menger came to essentially the same conclusion based on kinetic data for the neutral hydrolysis of bis(4-nitrophenyl) carbonate in the presence of micelles of two cationic detergents.[16]

Of course, it is questionable how far any solvent system may faithfully mimic the average of the many reaction sites available at a micellar surface. But our results make it clear that the kinetic data as expressed in k_w/k_m for **1**-**3** are fully reconcilable with the reduced micropolarity at the micellar reaction sites. It is worth noting that this conclusion applies equally well for substrates of widely different hydrophobicities (**1** vs. **3**) and binding constants K. Thus, binding sites within the micelle which possess the specific structural features necessary for strong hydrophobic interactions are immersed in highly aqueous environments. This indicates that the micelles have a rugged surface, consistent with the micellar models proposed recently.[4-6,17]

Experimental Section

Materials. The 1-benzoyl-1,2,4-triazoles **2**-**5** were kindly supplied by Dr. W. Karzijn.[7,9b] $NaDodSO_4$ and CTAB were purified by standard methods.[1a] 1,4-Dioxane was purified by the method of Eigenberger[18] and finally passed through a column of alumina. The water used in the kinetic measurements was deionized and distilled twice. All solutions were acidified with dilute HCl to a pH value of ~4.0 in order to prevent catalysis by OH^- ions.

1-Benzoyl-3-methyl-1,2,4-triazole (1) was prepared from 3-methyl-1,2,4-triazole[19] according to a general method:[20] mp 56.8–57.1 °C (from ether–hexane); ^1H NMR (Varian A-60, $CDCl_3$) δ 2.40 (s, 3 H), 8.73 (s, 1 H), 7.27–8.33 (m, 5 H); IR (Nujol) 1726 cm^{-1} (CO); UV (MeCN) λ_{max} 250.5 nm. Anal. Calcd for $C_{10}H_9N_3O$: C, 64.23; H, 4.55; N, 22.47. Found: C, 63.88; H, 4.79; N, 22.34.

Kinetic Measurements. The reactions were followed in 1-cm quartz cuvettes which were placed in a thermostated cell holder of a Cary 210 spectrophotometer. Under vigorous stirring, ca. 5 μL of a solution of **1**-**3** in acetonitrile was added to ca. 2.5 mL of the aqueous surfactant solution. The reactions were followed at the wavelength of maximum absorption of the substrates for about 3 half-lives. Good first-order kinetics were observed, and k_{obsd} values were reproducible to within 1.5%.

Binding Constants. The binding constants of **4** and **5** with CTAB were obtained with a Thomapore millipore filter. The circulation rate was 300 mL h^{-1} and the filtrate was collected at a rate of 9 mL h^{-1}. The analysis of the data was essentially similar to that used in the procedure with an artificial kidney.[21] The solute concentrations were determined by UV spectroscopy and the CTAB concentrations by titration with sodium tetraphenylborate.[22]

Registry No. 1, 79745-99-6; 2, 60718-51-6; 3, 79746-00-2; 4, 58905-26-3; 5, 79746-01-3; SDS, 151-21-3; CTAB, 57-09-0.

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[12] One of the referees has pointed out that reduced water nucleophilicity could also be invoked as one of the factors determining the rate reduction. Although our results provide no evidence against this possibility, we note that previous studies have shown that water activity and probably also water nucleophilicity at the micellar surface do not deviate significantly from that in bulk water. See, for example: (a) Bunton, C. A.; Huang, S. K. *J. Org. Chem.* **1972**, *37*, 1790. (b) De Albrizzio, J. P.; Cordes, E. H. *J. Coll. Interface Sci.* **1979**, *68*, 292.

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[17] See also: (a) Menger, F. M.; Bonicamp, J. M. *J. Am. Chem. Soc.* **1981**, *103*, 2140. (b) Russell, J. C.; Whitten, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 3219.

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Acid Hydrolysis of Carboxylic Esters in a Two-Phase System in the Presence of Catalytic Amounts of Quaternary Onium Salts. Mild and Selective Cleavage of *tert*-Butyl Esters

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Carboxylic acids are often protected by conversion into the corresponding *tert*-butyl esters,[1] which are highly stable under neutral and basic conditions and are indeed hydrolyzed under acidic conditions. The latter reaction is usually carried on at reflux in toluene in the presence of *p*-toluenesulfonic acid,[2] at room temperature in di-

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