g (15 mmol) of **5**, dissolved in 8 mL of dry THF, were added dropwise with stirring over 10 min. The solution was maintained at −80 °C for 30 min and then allowed to warm to 0 °C over a 90-min period. Then 8 mL (24 mmol) of 3 M NaOH solution was introduced. While the resulting alkaline mixture was maintained at 0–5 °C, 9 mL (100 mmol) of 30% H_2O_2 solution was carefully added (severe foaming occurred). The green solution which remained was stirred at 25 °C for 1 h before 100 mL of a saturated solution of K_2CO_3 was added. Extraction with ether (100 mL) was followed by washing with H_2O and brine. Drying and evaporation of solvent produced 2.84 g of cloudy, viscous oil which was chromatographed on 80 g of silica gel ($CHCl_3$ eluting solvent). Evaporation of solvent from appropriate fractions gave 1.41 g (70%) of a pale-yellow, clear oil: UV (pentane) 260 nm (ε 810); IR[18] (thin film) 3450 (broad), 3030, 2980, 1595, 1090 cm^{-1}; NMR, see Table I. Distillation afforded an analytical sample. Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88; O, 11.75. Found: C, 79.60; H, 9.09; O, 11.31.

Acknowledgment. We wish to thank the Dreyfus Foundation for partial support of this work and for providing summer research stipends to D.K.M. and D.J.T.

Registry No.—**1**, 121-46-0; **2b**, 1624-13-1; **2c**, 2957-68-8; **3**, 5240-87-9; **4a**, 69631-83-0; **4b**, 69631-84-1; **5**, 69124-20-5; **5**·DNP, 69124-21-6; **6**, 69631-85-2.

References and Notes

(1) Presented at the 11th Great Lakes Regional Meeting of the American Chemical Society, Stevens Point, Wis., June 1977.
(2) Willcott, M. R.; Davis, R. E.; Holder, R. W. *J. Org. Chem.* **1975**, *40*, 1952–1957.
(3) Gore, W. E.; Armitage, I. M. *J. Org. Chem.* **1976**, *41*, 1926–1930.
(4) Masamune, S.; Kim, C. U.; Wilson, K. E.; Spessard, G. O.; Georghiou, P.; Bates, G. S. *J. Am. Chem. Soc.* **1975**, *97*, 3512–3513. Masamune, S.; Yamamoto, H.; Kamata, S.; Fukugawa, A. *ibid.*, 3513–3515.
(5) Wilson, K. E., Ph.D. Dissertation, University of Alberta, 1972.
(6) See ref 2 and the references cited therein.
(7) Cannell, L. G. *Tetrahedron Lett.* **1966**, 5967–5972.
(8) Bird, C. W.; Cookson, R. C.; Hudec, J. *Chem. Ind. (London)* **1960**, 20–21. Bird, C. W.; Colinese, D. L.; Cookson, R. C.; Hudec, J.; Williams, R. O. *Tetrahedron Lett.* **1961**, 373–375.
(9) Arnold, D. R.; Trecker, D. J.; Whipple, E. B. *J. Am. Chem. Soc.* **1965**, *87*, 2596–2602.
(10) Mango, F. *Adv. Catal.* **1969**, *20*, 291–325.
(11) Gilliland, W. L.; Blanchard, A. A. *Inorg. Synth.* **1946**, *2*, 234–237.
(12) (a) Kono, H.; Hooz, J. *Org. Synth.* **1973**, *53*, 77–86. (b) Zweifel, G.; Brown, H. C. *Org. React.* **1963**, *13*, 1–54.
(13) (a) Wiberg, K. B.; Lowry, B. R.; Colby, T. H. *J. Am. Chem. Soc.* **1961**, *83*, 3998–4006. (b) Bly, R. K.; Bly, R. S. *J. Org. Chem.* **1963**, *28*, 3165–3172.
(14) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159–7161.
(15) Willcott, M. R.; Lenkinski, R. E.; Davis, R. E. *J. Am. Chem. Soc.* **1972**, *94*, 1742–1744.
(16) The hydroxyl protons were not included in the LIS calculations because of contact shift contributions.
(17) Lord, R. C.; Walker, R. W. *J. Am. Chem. Soc.* **1954**, *76*, 2518–2525. Schleyer, P. v. R. *ibid.* **1958**, *80*, 1700–1704.
(18) The IR spectrum of **6** was substantially different from that of **4a** in the fingerprint region.

Micellar Catalysis in the Oximation Reaction of Aliphatic and Cyclanic Ketones. Hydrophobic Interactions

A. Finiels and P. Geneste*

Laboratoire de Chimie Organique Physique Appliquée, Ecole Nationale Supérieure de Chimie de Montpellier, 34075 Montpellier Cédex France

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Micellar catalysis has been the object of numerous studies[1-5] which have explained this phenomenon in terms of the free energy of the reaction. The increase in the reaction rate is due to a decrease in the value of $\Delta G^{\ddagger}$ because of a variation in the enthalpy and the entropy of activation caused by hydrophobic interactions.[6] This has been postulated for several reactions including the hydrolyses of esters[7,8] and Schiff bases[9] and solvolysis reactions.[10]

In contrast, micellar catalysis of additions of nucleophiles to carbonyl groups has received little attention. We have previously studied[11] the oximation of cyclohexanone and 4-*tert*-butylcyclohexanone under identical conditions in the presence of sodium lauryl sulfate and found that the catalytic effect is greater for the more hydrophobic 4-*tert*-butylcyclohexanone.

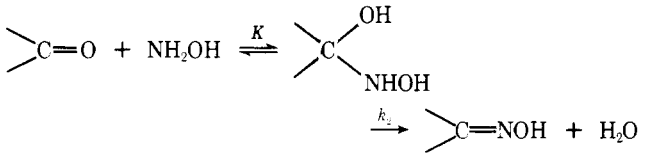
It might be reasonably supposed that the amphipathic substrate is solubilized in the interior of the micelle. This more intimate association of the substrate and the micelle allows a better stabilization of the transition state by the negative charges on the micelle and gives a greater catalysis.

We wished to examine this hypothesis by a study of several other ketones differing in the length and the nature of their hydrocarbon chain.

Experimental Section

The reaction which was examined is the oximation of ketones which occurs in two steps (addition of hydroxylamine and dehydration of the carbinolamine), either of which may be rate determining depending on whether the reaction is run in a acidic or basic medium. The catalytic effects of surfactants in acid were not significant,[11] probably because of the slight change of structure between the transition state and the initial ketone.[12,13]

In basic solution, the effects were much more pronounced than in acid solution. The reaction kinetics were followed spectrophotometrically by monitoring the appearance of the product oxime at 220 nm.



Under conditions where the kinetics are pseudo-first-order, the experimentally observed rate constant, k_{exptl},[11] is given by the expression

$$k_{exptl} = Kk_2 \frac{[NH_2OH][H^+]}{1 + [NH_2OH]K} \quad (1)$$

Inversion of this equation gives the following relationship

$$\frac{1}{k_{exptl}} = \frac{1}{k_2K[H^+]} \cdot \frac{1}{[NH_2OH]} + \frac{1}{k_2[H^+]} \quad (2)$$

In principle, utilization of this linear relationship allows the extraction of both k_2 (the second-order rate constant for dehydration of the carbinolamine) and K (the pH-independent equilibrium constant for the ketone–carbinolamine interconversion) by varying the concentration of hydroxylamine. In practice, we were only able to separate these kinetic constants for acetone and 2-butanone, as we were limited to nonsaturating concentrations of hydroxylamine by its solubility.

We define k^0 as the experimental rate constant in aqueous solution and k^{ψ} as the experimental rate constant in the presence of micelles. Each rate constant is the mean of at least three runs and we estimate the precision to be ±3%.

The ketones were commercial products purified by recrystallization or spinning band distillation. The concentration varied between 10^{-4} and 10^{-3} M and that of hydroxylamine hydrochloride was generally about 0.2 M. This large excess is necessary in order for the reaction to proceed to completion and for pseudo-first-order kinetics to be observed.[13] The ionic strength was maintained constant at 0.5 M by the addition of NaCl and kinetic measurements were made at T = 30 ± 0.1 °C at pH 8.5 (borax buffer). This pH value was chosen so as to obtain convenient reaction rates with the ketones we used.

The experimental curves, showing the variation of the rate constant with pH for cycloheptanone with hydroxylamine in the presence of surfactant, are given in Figure 1. It can be readily seen that sodium lauryl sulfate (NaLS) catalyzes the reaction in both neutral and basic solutions. Consequently, we chose to study this anionic surfactant.

The commercial product is recrystallized according to the method of Duynstee and Grunwald.[14] The concentration of surfactant in the reaction medium was 0.1 M, substantially larger than the critical micelle concentration (8.1×10^{-3}M),[1] and on the plateau of saturation for all of the compounds. We also demonstrated that the surfactant

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Table I. Catalytic Effects for Aliphatic Ketones, Cycloalkanones, and Substituted Cyclohexanones

ketones	k^{Ψ}/k^{0}	ketones	k^{Ψ}/k^{0}
$CH_3C(O)CH_3$	1.3	cyclobutanone	1.4
$CH_3C(O)CH_2CH_3$	1.8	cyclopentanone	2.1
$CH_3C(O)(CH_2)_2CH_3$	2.4	cyclohexanone	4.0
$CH_3C(O)(CH_2)_3CH_3$	3.2	cycloheptanone	3.3
$CH_3C(O)CH_2)_4CH_3$	3.9	cyclooctanone	4.6
$CH_3C(O)(CH_2)_5CH_3$	4.4	cyclononanone	5.7
$CH_3C(O)(CH_2)_8CH_3$	5.0		
$CH_3C(O)CH_2C(CH_3)_2OH$	1.0	cyclohexanone	4
		4-methylcyclohexanone	7.7
		4-ethylcyclohexanone	9.5
		4-*tert*-butylcyclohexanone	10
		4-*tert*-amylcyclohexanone	12.6

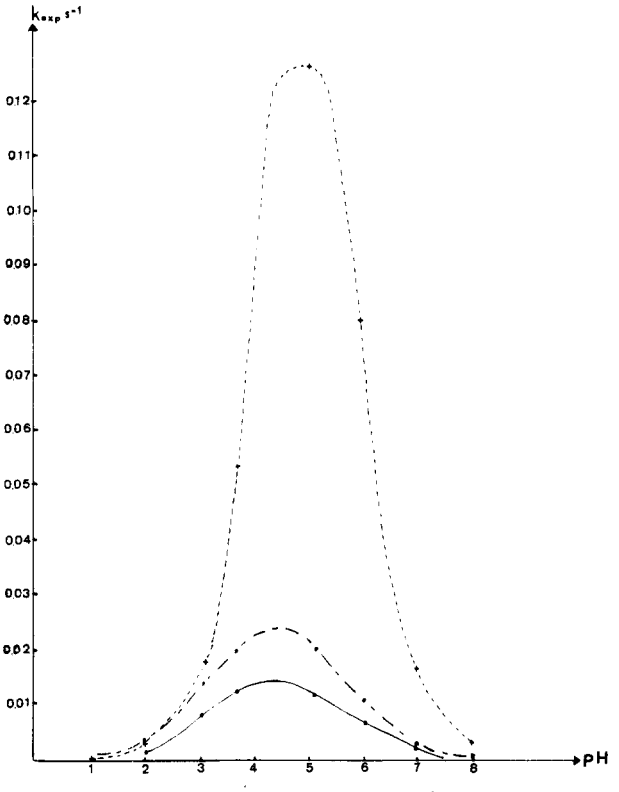

Figure 1. Effect of pH on the pseudo-first-order rate constant for the reaction of cycloheptanone with hydroxylamine in water at an ionic strength maintained at 0.17 M by NaCl, T = 40 °C. The buffers used are HCl for pH 1, 2, and 3.1, formate buffer for pH 3.7, acetate buffer for pH 5.1, phosphate buffer for pH 6 and 7, and tris(hydroxymethyl)aminomethane buffer for pH 8: (- - -) with 0.05 M NaLS; (—) with 0.05 M CTAB; and (· - - - - ·) without surfactant.

is stable under the conditions which were used.

In the same neutral or/and basic conditions cationic surfactants (as cetyltrimethylammonium bromide or CTAB) have practically no effect,[11] which would be expected from a consideration of the reaction mechanism in which a product-like transition state with a partial positive charge is formed.[15]

Results and Discussion

Aliphatic Ketones. Methyl ketones of the form $CH_3(CH_2)_nC(O)CH_3$ ($0 \leq n \leq 5$ and $n = 8$) were employed and the results in the presence of NaLS are reported in Table I. A comparison of the catalytic effects for the various ketones shows that the effect increases as the hydrocarbon chain is lengthened. A plot of log (k^{Ψ}/k^{0}) as a function of the number $(n + 1)$ of carbon atoms gives a straight line from $n = 0$ to 4 and afterwards a plateau with log (k^{Ψ}/k^{0}) independent of n. The slope of the line at $n < 4$ gives the increment in energy per methylene group due to hydrophobic interactions (about −160 cal/mol) for relatively short alkyl chains (Figure 2).

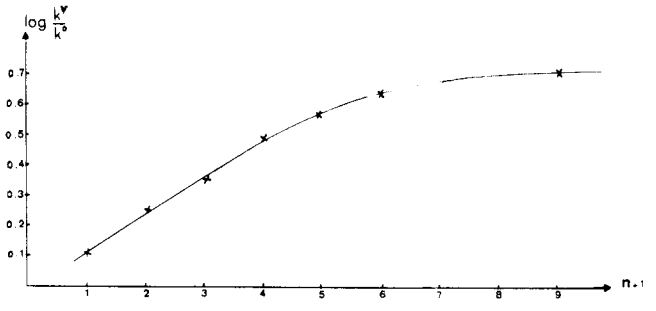

Figure 2. log k^{Ψ}/k^{0} vs. $(n + 1)$ for aliphatic ketones.

This value, however, is characteristic of the experimental constant which is a composite rate constant.

Using the effects on k_2 obtained with acetone and 2-butanone, we find an effect of approximately −500 cal ± 100 per methylene, a value comparable to those in the literature. For example, in the acylation of aryl oxime, Berezin et al. found a decrease in the free energy of 430 cal/methylene[16] and Gitler and Ochoa-Solano found a value of −630 cal/methylene in the hydrolysis of *p*-nitrophenyl esters.[7] These values are characteristic of hydrophobic interactions and probably represent the free energy necessary to transfer a methylene group for the aqueous phase to the micelle.

It can be seen that, among all of the aliphatic ketones which were examined, 4-hydroxy-4-methyl-2-pentanone showed no effect. This molecule has two hydrophilic groups which reduce its hydrophobic character, not allowing it to penetrate sufficiently into the interior of the micelle.

Cycloalkanones. The catalytic effect of NaLS increases with the ring size (Table I). A plot of log (k^{Ψ}/k^{0}) as a function of ring size presents a linear correlation. The slope of the line gives a free energy change per methylene group of −160 cal/mol, identical with that obtained for the straight chain ketones. This result could be due to a folding back of the chain in the case of the aliphatic ketones.[17]

Substituted Cyclohexanones. The results have been collected in Table I. The most surprising fact is that the catalytic effect changes from 4 to 7.7 on replacing a hydrogen by a methyl group, in the 4 position.

In addition, contrary to the other series, a linear correlation does not exist between the catalytic effect and the number of carbons of the substituent. The reason for this phenomenon is probably the presence of branched substituents.

The study, by depolarized Rayleigh diffusion, of the interactions between the hydrocarbon chains of surfactants and organic substrates shows a similar behavior:[18] nonsubstituted straight chains have high affinities which increase with the length of the chain; and branching or the presence of a benzene ring, on the contrary, has a negative influence. In our case, branching appears to have little influence on the hydrophobicity of the compound. Thus, 4-ethylcyclohexanone and 4-

tert-butylcyclohexanone show almost the same catalytic effect.

In addition, if we consider only the straight chain carbons as a first approximation, a *tert*-butyl group corresponds to two carbon atoms and a *tert*-amyl group to three carbon atoms. Using this approximation, we find, on plotting log (k^{Ψ}/k^{0}) as a function of the number of "apparent" carbon atoms in the substituent, that a similar energetic increment per methylene is found as in the series of aliphatic ketones.

The results which we have obtained confirm the initial hypothesis that hydrophobic substances are solubilized in the interior of the micelle, with the hydrophobic chain or the ring oriented between the detergent carbon chains, so that the functional group is located near the surface.

The study of aromatic ketones should permit us to verify this last point: the work of Fendler et al.[19] has shown that aromatic molecules such as acetophenone are bound in the Stern layer of various surfactants. We should thus find only a small catalytic effect with benzaldehyde and acetophenone. The results are in agreement with this prediction $k^{\Psi}/k^{0} = 1.4$ for benzaldehyde and 1.5 for acetophenone.

In contrast, acetylcyclohexane gives rise to a much larger catalytic effect (3.7-fold) included between those for 2-hexanone and 2-heptanone, implying a behavior similar in the interior of the micelle.

A plausible explanation for our results is that the hydrophobic interactions of these ketones serve to orient the ketone in the micelle such that the carbonyl group is in a favorable orientation for transition state stabilization of the incipient positive charge by the negative charges on the micelle. For the ketones with carbon chains of $n > 4$, additional carbons may give rise to greater hydrophobic bonding with the micelle but apparently have no effect on the orientation of the ketone. Thus, the additional hydrophobic interactions stabilize both the initial state and the transition state equally and no further rate increase is observed.

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Registry No.—CH_3COCH_3, 67-64-1; $CH_3COCH_2CH_3$, 78-93-3; $CH_3CO(CH_2)_2CH_3$, 107-87-9; $CH_3CO(CH_2)_3CH_3$, 591-78-6; $CH_3CO(CH_2)_4CH_3$, 110-43-0; $CH_3CO(CH_2)_5CH_3$, 111-13-7; $CH_3CO(CH_2)_8CH_3$, 112-12-9; $CH_3COCH_2C(OH)(CH_3)_2$, 123-42-2; cyclobutanone, 1191-95-3; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; cyclooctanone, 502-49-8; cyclononanone, 3350-30-9; 4-methylcyclohexanone, 589-92-4; 4-ethylcyclohexanone, 5441-51-0; 4-*tert*-butylcyclohexanone, 98-53-3; 4-*tert*-amylcyclohexanone, 16587-71-6.

References and Notes

(1) E. H. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.* **8**, 271 (1970); E. H. Fendler and J. H. Fendler, "Catalysis in Micellar and Macromolecular Systems", Academic Press, New York, 1975.
(2) E. H. Cordes and R. B. Dunlap, *Acc. Chem. Res.*, **2**, 329 (1969).
(3) E. H. Cordes, "Reaction Kinetics in Micelles", Plenum Press, New York, 1973.
(4) I. V. Berezin, K. Martinek, and A. K. Yatsimirskii, *Usp. Khim*, **42**, 1729 (1973).
(5) C. A. Bunton, *Prog. Solid State Chem.*, **8**, 239 (1973).
(6) W. P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw-Hill, New York, 1969, Chapter 8.
(7) C. Gitler and A. Ochoa-Solano, *J. Am. Chem. Soc.*, **90**, 5004 (1968).
(8) L. R. Romsted and E. H. Cordes, *J. Am. Chem. Soc.*, **90**, 4404 (1968).
(9) M. T. A. Behme and E. H. Cordes, *J. Am. Chem. Soc.*, **87**, 260 (1965).
(10) M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *J. Am. Chem. Soc.*, **87**, 266 (1965).
(11) P. Geneste, R. Durand, A. Finiels, and B. Schlick, *Tetrahedron Lett.*, 431 (1976).
(12) G. Lamaty, A. Natat, A. Petitjean, and J. P. Roque, *Recl. Trav. Chim. Pays-Bas*, **95**, 93 (1976).
(13) G. Lamaty, A. Natat, A. Petitjean, J. P. Roque, P. Geneste, and B. Schlick, *Recl. Trav. Chim. Pays-Bas*, **95**, 54 (1976).
(14) E. F. Duynstee and E. Grunwald, *J. Am. Chem. Soc.*, **81**, 4540 (1959).
(15) A. Finiels and P. Geneste, *Bull. Soc. Chim. Fr.*, in press.
(16) A. K. Yatsimirski, K. Martinek, and I. V. Berezin, *Tetrahedron*, **27**, 2855 (1971).
(17) P. Geneste, G. Lamaty, and B. Vidal, *Bull. Soc. Chim. Fr.*, **6**, 2027 (1969).
(18) P. Bothorel, unpublished results.
(19) J. H. Fendler, E. H. Fendler, G. A. Infante, Pong-Su-Shih, and L. K. Patterson, *J. Am. Chem. Soc.*, **97**, 89 (1975).

Cyclopropane Formation as Evidence for a 3-Halo 1,4-Zwitterion

H. K. Hall, Jr.,* A. Buyle Padias, A. Deutschman, Jr., and I. J. Westerman

Department of Chemistry, University of Arizona, Tucson, Arizona 85721

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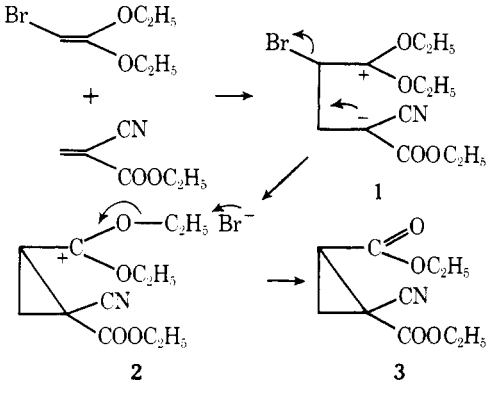
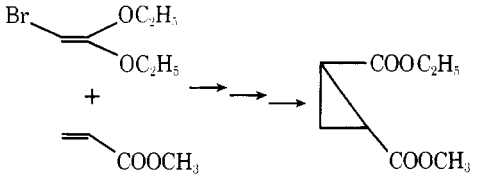
Recent investigations of the synthesis of cyclobutane derivatives by reaction of electron-rich olefins with electron-poor olefins have focused on 1,4-zwitterions as the key intermediates in these reactions.[1] As additional evidence for them, we now report that 1,4-zwitterions carrying a 3-halo substituent form cyclopropanes.

1,1-Diethoxy-2-bromoethylene reacts with ethyl α-cyanoacrylate at 0 °C during 1 h to form diethyl 1-cyano-1,2-cyclopropanedicarboxylate (**3**). The initially formed 1,4-



zwitterion **1** undergoes intramolecular displacement of bromide ion to form the dialkoxycarbenium ion **2**, which in turn undergoes dealkylation to form cyclopropane **3** and ethyl bromide.

Methyl acrylate reacts similarly with 1,1-diethoxy-2-bromoethylene to form ethyl methyl 1,2-cyclopropanedicarboxylate:



Methyl acrylate was much less reactive than methyl α-cyanoacrylate. At room temperature no reaction occurs when methyl acrylate and 1,1-diethoxy-2-bromoethylene are mixed in a 1/1 mol ratio. After heating the two compounds at 90 °C for 24 h in the presence of an inhibitor, only a trace of cyclopropane is detected by gas chromatography. The two compounds were heated without solvent in the presence of an inhibitor at 110 °C for 20 h to yield ethyl methyl 1,2-cyclopropanedicarboxylate in 50% yield. Under the same conditions, acrylonitrile gave a complex mixture of products.

In the absence of a 3-bromo substituent, analogous 1,4-zwitterions undergo ring closure to cyclobutane derivatives.[2,3] It is interesting that the 3-bromo substituent competes ef-

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