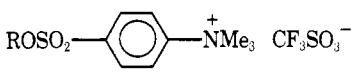
Surfactants as Electrophilic Substrates. Micellar and Self-Phase Transfer Reactions of Surfactant Sulfonates

Sir:

Most functional cationic surfactants bear (potentially) nucleophilic moieties,[1] such as hydroxyl,[1a] sulfhydryl,[2] imidazolyl,[3] or hydroxamic acid,[1] and, in micellar form, readily mediate the basic cleavage of activated esters.[1-3] Far less is known about cationic surfactants as electrophilic *substrates*. Several groups have investigated the decomposition of alkyldiazonium ions in aqueous alkylammonium ion micelles.[4] The micellar hydrolysis of "amsylates" (I)[5] and the use of "betylates" (e.g., II)[6] as intermediates in the conversion of alcohols



I

$$n\text{-}C_{16}H_{33}OSO_2CH_2CH_2\overset{+}{N}Me_3\ \ FSO_3^-$$

II

to S_N2 products have also been reported. In these cases,[4-6] the cationic center of the surfactant substrate forms part of the leaving group, so that reaction does not lead to products of further interest qua surfactants.

We now communicate initial studies of surfactant sulfonates (III) in which the cationic center is an integral part of the substrate's *alkyl* residue, making possible simple syntheses of new functional surfactants (IV) by S_N2 displacements; cf. Scheme I. Further, we describe the kinetic properties of III relative to suitable model systems, anion exchange reactions of IV, and synthesis of a thiocholine surfactant from IVe.

Surfactant IIIa[7] (mp 106–108 °C) was prepared in 89% yield by reaction of $n\text{-}C_{16}H_{33}N^+(CH_3)_2CH_2CH_2OH\ Cl^-$ [8] with methanesulfonyl chloride and pyridine in CH_2Cl_2. Similarly prepared from the corresponding hydroxy compounds were choline mesylate (V)[7,9] and *n*-cetyl mesylate[7] (mp 49–50 °C). Comparative reactivities of 16-OMs, V, and cetyl mesylate were determined in S_N2 displacement reactions with thiophenoxide ion at pH 9.0. Thiophenol is fully ionized at this pH,[10,11] and reaction kinetics were followed by monitoring the disappearance of thiophenoxide absorbance at 273 nm (λ_{max} of $C_6H_5S^-$ in micellar 16-OMs).[11-13] Pseudo-first-order rate constants were determined for reactions of 5.0×10^{-5} M thiophenoxide with various concentrations of 16-OMsCl (5.0×10^{-4} to 1.0×10^{-2} M),[14] V (1.0×10^{-4} to 2.5×10^{-3} M), and cetyl mesylate (1.0 to 5.0×10^{-4} M, solubilized with 10^{-2} M CTACl). A portion of the kinetic data appears in Table I.[15]

The effective invariance of k_ψ for the reaction of thiophenoxide with 16-OMsCl over surfactant concentrations ranging from 5.0×10^{-4} to 1.0×10^{-2} M indicates that all thiophenoxide ions have been bound by 16-OMs micelles even at low micellar concentrations.[12] Extremely strong binding of thiophenoxide to CTA micelles has been noted previously.[11] Comparison of 16-OMs and V (at 10^{-2} M, Table I) reveals a kinetic advantage of 43 for the micellar mesylate, but most, if not all, of this catalysis is probably due to the binding of thiophenoxide[11] by the cationic 16-OMs micelles, and the consequent conversion of a bimolecular reaction (cf. V + $C_6H_5S^-$) to a quasiunimolecular reaction.[16] Indeed, at comparable concentrations, the reaction of thiophenoxide with micellar 16-OMs is only marginally faster than its reaction with cetyl mesylate/CTACl. It is known that electron-withdrawing substituents on the substrate accelerate S_N2 reactions with strong nucleophiles,[17] but comparable activation apparently accrues either upon solubilizing an alkyl mesylate in a quaternary ammonium ion micelle or by covalently binding the mesylate to the micelle's surfactant "monomers". This observation may have strategic importance for synthetic planning.

Table I. Reactions of Mesylates and Thiophenoxide Ion[a]

substrate	concn, M	k_ψ, s^{-1}	k_{rel}	
16-OMs	5.0×10^{-4}	1.51×10^{-3}		2.97
16-OMs	1.0×10^{-2}	1.62×10^{-3} [b]	43.0	
V	1.0×10^{-2}	3.74×10^{-5}	1.00	
cetyl-OMs[c]	5.0×10^{-4} [d]	5.08×10^{-4}		1.00

[a] In 0.01 M borate buffer, pH 9.0, 25 °C. [b] 1.75×10^{-3} s^{-1} at pH 10.0. [c] Solubilized with 10^{-2} M CTACl. [d] Limited solubility precluded the use of higher concentrations.

Micellar 16-OMsCl was not highly reactive toward nucleophiles other than thiophenoxide, and so the corresponding trifluoromethane sulfonate, 15-OTf,OTf (IIIb),[18] was prepared by reacting 2 equiv of trifluoromethanesulfonic anhydride with 1 equiv each of $n\text{-}C_{16}H_{33}N^+(CH_3)_2CH_2CH_2OH\ Br^-$ and pyridine (25 °C, 30 min) in CH_2Cl_2 solution. 16-OTf,OTf could not be isolated free of pyridinium salts, but its quantitative formation was readily ascertained in situ by NMR.[19]

Although insoluble in water, quaternary ammonium triflates are readily soluble in various organic solvents.[20] Accordingly, CH_2Cl_2 solutions of 16-OTf,OTf were briefly stirred under two-phase conditions with (saturated) aqueous solutions of alkali metal bromide, acetate, azide or (1.35 N) thioacetate salts. Simple workup[21] afforded 75–81% yields of 16-Br,[7] 16-OAc,[7] 16-N_3,[7] and 16-SAc,[7] all as the triflate salts; cf. Scheme I.

The new surfactants were soluble in organic solvents but not in water at 25 °C. However, ion exchange of 16-Br,OTf, 16-N_3,OTf, or 16-SAc,OTf with Dowex 1-X8 in the halide form (25–50 mesh beads, water, 85–90 °C, 10 min), followed by filtration and lyophilization, afforded 90% isolated yields of the corresponding water-soluble surfactant bromide or chloride salts.[22]

Counterion control of the new surfactants' solubility properties is clearly of synthetic interest. Moreover, the effect of ion exchange is reversible; addition of CF_3SO_3H[20] to aqueous

Scheme I

$$n\text{-}C_{16}H_{33}N^+(CH_3)_2CH_2CH_2OSO_2R\ X^- + M^+Y^- \longrightarrow n\text{-}C_{16}H_{33}N^+(CH_3)_2CH_2CH_2Y\ RSO_3^-$$

IIIa (16-OMs), R = CH_3; X = Cl — $NaSC_6H_5$ → IVa (16-SC_6H_5), Y = SC_6H_5

IIIb (16-OTf), R = CF_3; X = CF_3SO_3 —
- NaBr → IVb (16-Br), Y = Br
- KOAc → IVc (16-OAc), Y = OAc
- NaN_3 → IVd (16-N_3), Y = N_3
- NaSAc → IVe (16-SAc), Y = SAc

$$(CH_3)_3N^+CH_2CH_2OSO_2CH_3\ Cl^-$$

V

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solutions of the surfactant halides precipitated the surfactant triflates. The cycle of reactions depicted in eq 1 has been carried out with high efficiency.[24]

$$\text{16-OTf,OTf} \xrightarrow[CH_2Cl_2/H_2O]{NaBr} \text{16-Br,OTf} \xrightarrow[H_2O]{\text{Dowex 1-X8}} \text{16-Br,Br} \xrightarrow[H_2O]{TfOH} \text{16-Br,OTf} \quad (1)$$

In an important application, 16-SAcCl, prepared by ion exchange of 16-SAc,OTf (Scheme I), was deprotected with aqueous HCl; lyophilization then afforded thiocholine surfactant VI. The kinetic properties of this highly reactive micellar reagent are under intensive study.[25]

$$n\text{-}C_{16}H_{33}N^+(CH_3)_2CH_2CH_2SH\ Cl^-$$

VI

The water-insolubility of 16-OTf,OTf[26] precluded precise kinetic comparison with 16-OMsCl, but approximate relative reactivities were determined at 25 °C under two-phase, saturated aqueous $NaBr/CH_2Cl_2$ conditions. Whereas 2.8×10^{-2} M 16-OTf,OTf was completely converted to 16-Br,OTf in 300 s, both 2.4×10^{-2} M 16-OMsCl and 10^{-2} M cetyl triflate failed to react after 3600 s. Addition of 10^{-3} M CTABr (as a phase transfer catalyst) to the cetyl triflate/NaBr system produced complete reaction after 750 s. Not only is 16-OTf seen to be considerably more reactive than 16-OMs,[18] but extrapolation of the cetyl triflate results strongly implies that 16-OTf is capable of *self-phase transfer catalysis*.[27,28]

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(7) Structurally consistent IR and NMR spectra, and a satisfactory elemental analysis were obtained.
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(12) The critical micelle concentration (cmc) of 16-OMs is 3.0×10^{-4} M in 0.01 M borate, pH 9.0, 25 °C (surface tension method).
(13) Control experiments in micellar cetyltrimethylammonium (CTA) bromide showed that oxidative dimerization of thiophenoxide did not significantly compete with S_N2 displacement under our experimental conditions. Additionally, 16-OMsCl was titrimetrically stable to aqueous NaOH at pH 9.0 or 10.0 over the duration of the 16-OMs/thiophenoxide reactions.
(14) The reaction product of 16-OMs and thiophenoxide was shown to be 16-SC_6H_5 (IVa, Scheme I) by UV studies under kinetic conditions. We followed the disappearance of $C_6H_5S^-$ (273 nm) and the simultaneous formation of 16-SC_6H_5 (260 nm). Authentic 16-SC_6H_5[7] was prepared (as the $CH_3SO_3^-$ salt) by reacting 16-OMsCl with ethanolic $NaSC_6H_5$ (25 °C, 1 h), followed by acidification (HCl), precipitation (ether), and removal of 16-SC_6H_5Cl (water).
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(21) The CH_2Cl_2 phase was dried and solvent was evaporated. The residue was washed with ether and recrystallized several times from CH_2Cl_2/ether.
(22) The surfactant halides were characterized by NMR, IR, and elemental analysis. In particular, surfactant triflates (and NaOTf) show strong sulfonate and C–F stretching absorptions at ~1260, 1160, and 1035 cm^{-1} (in Nujol).[23] These bands were absent in the IR spectra of the ion-exchanged, halide surfactants.
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(24) 16-Br,Br was independently prepared from n-$C_{16}H_{33}N(CH_3)_2$ and 1,2-dibromoethane: R. A. Moss and C. W. Kabis, unpublished work. This sample[7] was identical (IR, NMR) with the material prepared by ion exchange (eq 1).
(25) R. A. Moss, G. O. Bizzigotti, T. J. Lukas, and W. J. Sanders, submitted for publication. At pH 7.96, the cleavage of p-nitrophenyl acetate by 0.02 M micellar VI is characterized by $k_\psi = 9.71\ s^{-1}$, corresponding to a second-order rate constant of 485 L/mol s. Under comparable conditions, micellar VI is 34 600 times more reactive than CTACl as a micellar esterolysis reagent and is currently the most reactive self-contained functional micellar esterolysis reagent yet reported.
(26) 16-OTf,OTf could not be subjected to halide ion exchange without concommitant S_N2 reaction.
(27) Related phenomena were encountered by King et al. in their study of betylates II.[6]
(28) The limited solubility of 16-OTf,OTf in water, coupled with its high reactivity, suggests that its self-phase transfer reactions may occur very near the aqueous/organic interface; cf. M. Makosza, *Pure Appl. Chem.*, **43**, 439 (1975).

Robert A. Moss,* Winfred J. Sanders
Wright and Rieman Laboratories, Department of Chemistry
Rutgers, The State University of New Jersey
New Brunswick, New Jersey 08903

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Oxygenation of Cyclic Dienes to Endoperoxides

Sir:

Addition of ground-state triplet oxygen to conjugated dienes is spin forbidden. However, Barton and co-workers[1,2] reported that ammoniumyl radicals and certain Lewis acids are effective in catalyzing specific 1,4 addition of triplet oxygen to various 1,3-dienes. In their proposed mechanism, the novel concept[1] invoked is the function of the "catalyst" which, in the assembly with the diene and oxygen, overcomes the spin barrier impeding the cycloaddition. Our interest in specific oxygenation[3] of olefins led us to investigate this reaction in detail. We now report our findings that (1) the assembly of oxygen, diene, and "catalyst" is not central to the oxygenation; (2) the "catalyst" functions as a radical initiator; and (3) the "catalytic" oxygenation can best be described by a cation-radical chain mechanism.

We initiated our investigation using ergosteryl acetate (**1**) as the diene and tris(p-bromophenyl)ammoniumyl tetrafluoroborate (**2**) as the "catalyst", which were chosen on the basis of Barton's original work[1] and our intended magnetic resonance studies. Cation radical **2** dissolved in CH_2Cl_2 at −70 °C and then frozen at −120 °C in the ESR cavity exhibited a broad singlet with $\langle g \rangle = 2.009$.[4] When 1 or more equiv of solid **1** were added to this solution with temperature maintained at −70 °C and then frozen in the ESR cavity as above, a broad unresolved signal with $\langle g \rangle = 2.004$ resulted. A gradual shift of ESR signals, along with color changes from blue to red, was observed at intermediate stages of mixing. The resulting $\langle g \rangle$

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