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Cleavable surfactants

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Cleavable surfactants†

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†Dedicated to Professor Donald J. Cram on the occasion of his 75th birthday.

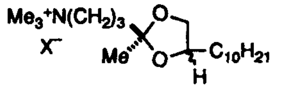
(Received May 27, 1994)

A brief review of cleavable surfactants, synthesized and characterized by the author and his co-workers, is presented. Two types of cleavable surfactants have been reported; each contains a labile functional group. Both single and double-chain *first generation* cleavable surfactants are cleaved to give nonsurfactant fragments: a water-insoluble organic compound and a water-soluble ionic compound. Single-chain *second generation* cleavable surfactants are cleaved to give another surfactant and a water-soluble organic compound; double-chain *second generation* surfactants are cleaved to give two single-chain surfactants. Cleavable surfactants allow the elimination of problems associated with the presence of aggregated surfactants after their beneficial use.

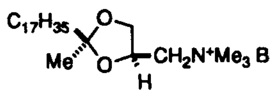
Surfactants are useful in a broad spectrum of applications as diverse as oil recovery,[1] drug delivery,[2] and organic synthesis.[3] But sometimes the presence of an aggregated surfactant during manipulations after its beneficial use can lead to complications like the formation of persistent emulsions. Cleavable (destructible) surfactants, which contain a labile functional group, present the potential for elimination of at least some of these problems. Two types of cleavable surfactants have been reported. In single and double-chain *first generation* cleavable surfactants the labile functional group separates the major lipophilic and hydrophilic portions. Cleavage at the functional group converts the surfactant into two nonsurfactant products: an ionic, water-soluble compound and a neutral, water-insoluble compound. Single-chain *second generation* cleavable surfactants are cleaved to give another surfactant and a water-soluble, neutral compound; double-chain analogues are cleaved to give two single-chain surfactants. With both single and double-chain systems, the daughter surfactants generally have *higher* critical aggregation concentrations than the parent surfactants. This article presents a brief review of our work on cleavable surfactants; notable contributions to this area by others[4] have not been included.

We have prepared first generation cleavable surfactants with three different types of labile linkages: ketal groups, silicon-oxygen bonds, and β-aryloxy sulfones. Cationic surfactants with ketal groups include single-chain **1**[5] and **2**,[6] double-chain **3**[7,8] and **4**,[9] and related surfactants.[3a,8,10] Compounds **5**[9] comprise our ketal-based anionic and zwitterionic double-chain cleavable surfactants.

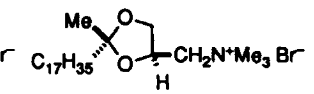
Reflecting the stability-lability characteristics of the ketal group itself, each ketal-based cleavable surfactant is stable under neutral and basic conditions but undergoes acid-catalyzed hydrolysis to give keto and *vic*-diol fragments as illustrated with **1** (eq 1). However, the reactivity of a given cleavable surfactant depends on its specific nature. For example, anionic surfactant **5a** is more



1, $X^- = Cl^-; Br^-; MeSO_3^-$



2a



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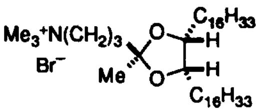
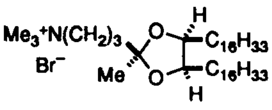


3a



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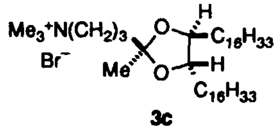
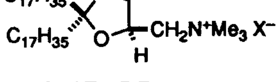
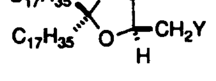


3c

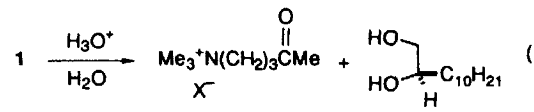


4a, $X^- = Br^-$
b, $X^- = MeSO_3^-$



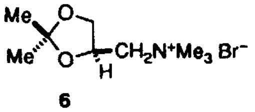
5a, $Y = O(CH_2)_3SO_3^-\ Na^+$
b, $Y = N^+Me_2(CH_2)_3SO_3^-$

reactive than cationic **4**.[9] This reactivity difference is ascribed to two related factors associated with the likely protonation of the dioxolane ring during acid-catalyzed hydrolysis.[11] On an intramolecular basis, the cationic substituent of **4** electrostatically hinders, whereas the anionic substituent of **5a** facilitates protonation. On an aggregate basis, electrostatic depletion and accumulation of H_3O^+ exist at the bilayer-water interfaces of vesicular **4** and **5a**, respectively, relative to the bulk aqueous phase.[12]


(1)

Surfactants **1** were used in the formulation of microemulsions composed of **1**, 1-butanol, hexane, and aqueous 0.01 M $NaHCO_3$,[13] which can serve as solvents for homogeneous reactions of water-insoluble organic substrates with water-soluble inorganic reagents on a synthetic scale.

Cleavable surfactants present the opportunity for study of the dependence of functional group reactivity on aggregate morphology and surfactant stereochemistry. The hydrolytic reactivities of micellar **2** and vesicular **4a** were uniformly less than that of nonaggregating **6** due to microenvironmental effects in the aggregate-water interfaces involving electrostatic depletion of H_3O^+ and a lower polarity relative to the bulk aqueous phase.[6] The reactivity of the ketal group had no appreciable dependence on aggregate morphology since the hydrolysis rates for micellar **2** and vesicular **4a** were comparable. The **2a**:**2b** reactivity ratio changed on going from homogeneous to mixed micelles, suggesting that there are varying surfactant-surfactant interactions in the different micelles.


6

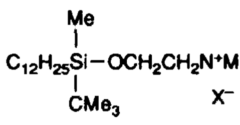
The monolayer characteristics of diastereomers **2a** and **2b** are interesting. Surfactants **2a**, **2b**, and their 1:3 and 3:1 mixtures gave identical surface pressure-area isotherms at 25 °C on a pH 7.5 buffer subphase.[6a] In contrast the 1:1 mixture gave a slightly more expanded monolayer film, indicating a dependence of packing on stereochemistry as the film is compressed.

The study of surfactants **3a-c** centered around the expression of their diastereomeric nature in vesicular and monolayer form.[7] Their vesicles were characterized by dynamic laser light scattering to give sizes, by differential scanning calorimetry to give bilayer phase transition temperatures,[14] and by [^{14}C]sucrose entrapment and release studies to give bilayer membrane permeabilities. Clear differences among **3a-c** were found in the latter two studies. The phase transition temperature order for both sonicated and vortexed vesicles was **3a** > **3c** > **3b**, and for sonicated vesicles the permeability order was **3b** > **3c** > **3a**. The three surfactants also displayed different monolayer characteristics. The degrees of expansion in the surface pressure-area isotherms, the monolayer stability limits, and the propensities of the films to spread from their crystals followed the same order: **3b** > **3c** > **3a**. The combined results suggested that in both vesicular and monolayer form **3a** has the tightest, and **3b** the loosest surfactant packing. The differences in packing were interpreted in terms of various orientations of **3a-c** at the aggregate-water and air-water interfaces.

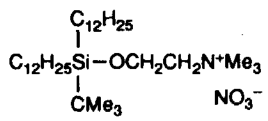
Cleavable surfactants **3** and **5a** have also been used as vesicular hosts in studies of amphiphilic ketone epimerizations[8] and alkyl phenyl ether monohalogenations,[15] respectively. The results obtained with **5a** in the latter study represent an impressive example of the isolation of neutral organic compounds from cleavable surfactant-based vesicular solutions. The isolation of products and unreacted starting materials was straightforward and quantitative. For example, 0.024 mg of nonyl phenyl ether was isolated quantitatively from 1.00 mL of a 0.020 M solution of vesicular **5a**.

Cleavable surfactants based on the silicon-oxygen bond are cationic single-chain **7**[16] and double-chain **8**.[10] Both micellar **7** and vesicular **8** are cleaved at the silicon-oxygen bond by aqueous acid and base as illustrated with **7** (eq 2). Surfactant **7a** was also cleaved with F^- in water or chloroform-tetrahydrofuran (eq 3).

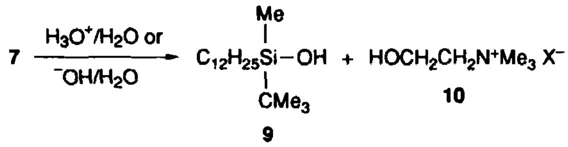
Surfactant **7a** had about the same catalytic activity as hexadecyltrimethylammonium bromide (HTABr) in an oxidation reaction under micellar-emulsion conditions.[16a] Persistent emulsions complicated the extractive

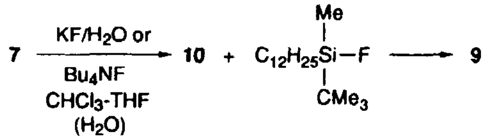

$C_{12}H_{25}Si(Me)(CMe_3)-OCH_2CH_2N^+Me_3\ X^-$

7a, $X^- = NO_3^-$
b, $X^- = Cl^-$


$C_{12}H_{25}Si(C_{12}H_{25})(CMe_3)-OCH_2CH_2N^+Me_3\ NO_3^-$

8


(2)


(3)

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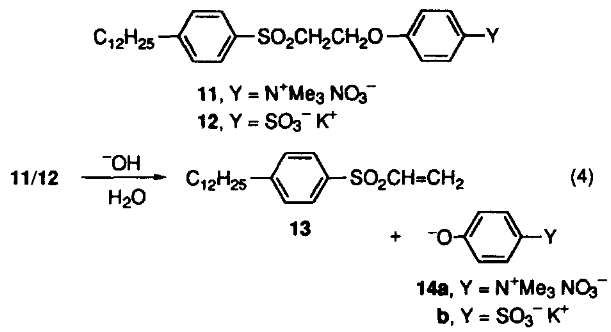
workup of reaction mixtures containing HTABr, but not of those containing **7a**.

Cleavable surfactants based on β-aryloxy sulfones are single-chain cationic **11** and anionic **12**.[17] These surfactants undergo E1cB elimination to yield vinyl sulfone **13** and phenoxide ion **14** (eq 4). Both **11** and **12** are stable for extended periods in acidic media up to 75°C. Surfactant **11** decomposed slowly in water alone and completely within 10 min in aqueous 0.1 M $NaHCO_3$. On the other hand, **12** was stable in water and even in 0.01 M K_2CO_3. It decomposed in 0.1 M K_2CO_3 and 0.01 M KOH. The difference in labilities derives from two factors. The first involves the fact that **14a** is a better leaving group than **14b**, and the second electrostatic effects on interfacial $[H_3O^+]$ analogous to those noted above.

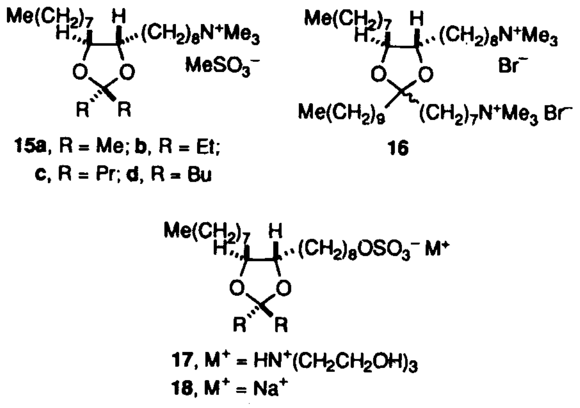


11, Y = $N^+Me_3\ NO_3^-$
12, Y = $SO_3^-\ K^+$

14a, Y = $N^+Me_3\ NO_3^-$
b, Y = $SO_3^-\ K^+$

To date we have prepared second generation cleavable surfactants only with ketal linking groups. Cationic single and double-chain systems are **15**[18,19] and **16**,[20] respectively, and anionic single-chain systems are **17** and **18**.[19] The single-chain surfactants form micelles and are cleaved to give threo *vic*-diol-substituted single-chain surfactants and low molecular weight ketones as illustrated with **17** (eq 5). The double-chain system **16**, which contains two head groups, also forms micelles and is cleaved to give two single-chain surfactants: *vic*-diol-substituted **19** and keto-substituted **20** (eq 6). The critical micelle concentrations of **19** and **20** are about three times that of **16**. Since it is possible to convert micellar **16** into nonaggregated **19** and **20**, micellar **16** could be used as a storage and release devise. A water-insoluble compound could be solubilized in micellar **16** and then desolubilized as desired by hydrolysis of **16**. This release process would not be complicated by the formation of a water-insoluble compound derived from **16**, as would be the case with first generation cleavable surfactants.

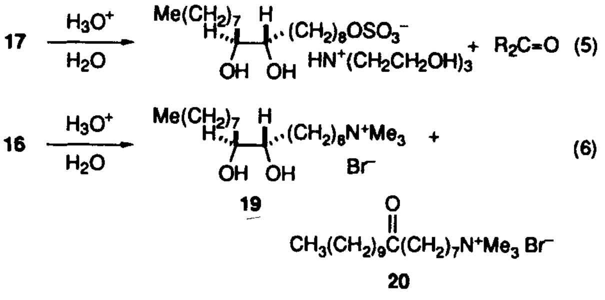
Overall, we have prepared and characterized a number of single and double-chain first and second generation cleavable surfactants with a wide range of stability-lability characteristics. They can facilitate the use of micellar, vesicular, and microemulsion media as solvents for homogeneous reactions of water-insoluble organic substrates with water-soluble reagents. Aggregates of second generation cleavable surfactants are potential entrapment and release devices. Stereoisomeric cleavable surfactants provide an opportunity for investigation of the dependence of aggregate and monolayer character on surfactant stereochemistry.



15a, R = Me; **b**, R = Et; **c**, R = Pr; **d**, R = Bu

16

17, $M^+ = HN^+(CH_2CH_2OH)_3$
18, $M^+ = Na^+$



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