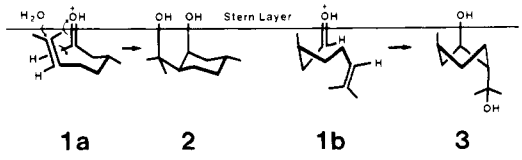
Scheme II



To explain the changes in product ratio and increase in rate induced by the micelle, it is suggested that the reaction is occurring near the interface, where the high proton activity associated with the Stern layer promotes the acid-catalyzed cyclization[19] more effectively. On the basis of current views for the structure of SDS micelles[1,2] and "interfacial models" proposed[11] for photochemical micellar reactions, the folded conformations **1a** and **1b** may orient themselves in the micelle with the protonated carbonyls outward as shown in Scheme II. This arrangement favors the cyclization of **1a** but imposes an additional energy barrier to the reactivity of **1b**, both in the form of a more hydrophobic solvent (micellar core) for the incipient C-8 carbocation and additional energy needed to expose the carbocation to water. The overall result is then the enhanced formation of **2** over **3**, in accord with the Curtin–Hammet principle[20] which relates the product composition only to the relative energies of the respective transition states of the reactant conformations (**1a**, **1b**).

On the basis of these results the opportunity exists for expanding the scope of this reaction to the general area of cationic polyene cyclizations,[6,7] where relatively poor yields and a plurality of products are often encountered. The micelle may allow some of these systems to cyclize under mild aqueous conditions at concentrations far above the compounds solubility in water.

Experimental Section

Analyses by GLC were performed on a Varian 3700 (FID) equipped with a 12 ft × $^1/_8$ in. i.d. glass column configured for on-column injection and packed with 5% Triton X-305 on Chromosorb W. H.P. 80–100 mesh. The oven temperature was programmed from 70 to 170 °C at 5 °C/min with 10 min initial hold. A flow rate of ≃35 mL/min of helium was employed. Compounds were purified by collection in glass capillaries or $^1/_8$ in. glass tubing from an F&M 810 GC equipped with a TC detector, $^1/_4$ in. glass column, packed and generally operated as above. IR spectra were determined on a PE-281 as solutions in CCl_4; MS were determined on a HP-5875 GC/MS. NMR spectra were determined on a Varian T-60-A as solutions in $DCCl_3$ using Me_4Si as an internal standard. Sodium dodecyl sulfate was obtained from Aldrich Chemical Company and recrystallized twice from ethanol or from Bio-Rad Laboratories and used directly. The SDS purity was checked by a control reaction, followed by extraction and GLC, and also by a cmc determination using conductivity. The citronellal [$[\alpha]^{23}_D$ = +13.1° (*c* 0.1 g/mL, ethanol), 96% by GLC] was a gift from SCM Organic Chemicals and was used as received.

Cyclization of Citronellal in Acetate Buffer. A pH 5.49, 0.04 M acetate buffer was prepared (0.0038 M acetic acid and 0.0362 M sodium acetate). SDS (1.1 g, 3.8 mmol) was added to buffer, final volume of 100 mL, to yield a 0.038 M solution of pH 5.52. Aliquots (90 mL) of buffer and SDS/buffer were each placed in 100-mL flasks and deaerated with argon. Citronellal (0.0126 g, 0.082 mmol) (average C_0 calculated from rate expression) was added by repeatable syringe using underwater injection. Each sample was prepared in duplicate, stirred briefly until it appeared homogeneous, deaerated again with argon, sonicated for 15 min, and placed in a bath at 20 °C. The reactions were sampled periodically (Table I) and methyl octanoate in ether added as an internal standard. They were extracted with ether (1 × 50 mL, 3 × 30 mL) and washed successively with saturated $NaHCO_3$ (1 × 15 mL), water (1 × 15 mL), and saturated NaCl (1 × 15 mL). Extracts were concentrated to ≃3 mL in a Kuderna–Danish evaporative still and analyzed by GLC using the internal standard and response factors determined from pure standards. It is necessary to inject a concentrated solution of diols **2** and **3** at the start of a series of runs to avoid adsorption in the GLC and obtain a linear response for the concentration range of interest. Alcohols **2** and **3** were separated and collected by preparative GLC and identified by comparison of NMR[14] and IR[12] data to published values. The isopulegols **4** and **5** were identified by GLC peak enrichment and MS comparison to authentic compounds. Cyclizations of citronellal in citrate/phosphate buffers were generally carried out as above.

Cyclization of Citronellal in Dilute Sulfuric Acid. Aqueous H_2SO_4 (1.1 mL, 0.92% w/w) was added to a 0.038 M solution of SDS (2.2 g, 7.6 mmol in 200 mL of H_2O) to yield a solution of pH 3.4. Citronellal (see Table IV) was added to 90-mL aliquots of this solution after deaereation with argon, and the reaction was generally carried out as above except sonication was not used and the reaction was run at room temperature (≃22 °C).

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Registry No. (+)-**1**, 2385-77-5; (+)-**2**, 92471-23-3; (−)-**3**, 91739-72-9; sodium dodecyl sulfate, 151-21-3.

Supplementary Material Available: Figure 1, a first-order plot of the log citronellal concentration vs. time in acetate buffer with and without SDS (1 page). Ordering information is given on any current masthead page.

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Electrochemical Synthesis of 4,4,4-Trifluorobutanal

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Electrolysis of solutions containing trifluoroacetate ions and an organic cosolute with a terminal double bond often entails addition of the initially formed trifluoromethyl radicals to the double bond to give the intermediate species $CF_3CH_2\dot{C}HX$.[1-4] Because these radicals can be converted to stable compounds by any of several different reactions, the product is usually a mixture of mono- or bis-trifluoromethylated derivatives, and it is often not practical to isolate satisfactory amounts of a particular material in a pure state. When this difficulty can be overcome, the simplicity of the electrochemical process makes it an attractive synthetic method, as illustrated by the recently described procedures for the preparation of 4,4,4-trifluoro-2-butanone[5] and 12,12,12-trifluorododecanoic acid.[6] The work reported here resulted from an ongoing search for useful applications of this approach. It was found that

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4,4,4-trifluorobutanal (1) can be conveniently prepared by anodic trifluoromethylation of 2-propen-1-ol (allyl alcohol).

Solutions of trifluoroacetic acid, the alcohol, and a small amount of base were electrolyzed in a number of solvents. NMR spectra were used to obtain a preliminary indication of the nature of the product mixture and of the number of faradays required to maximize the product concentrations. Both the yield and product distribution were found to be markedly solvent dependent. In anhydrous methanol, the ^{19}F spectrum was dominated by a pair of overlapping triplets provisionally assigned to the dimethyl acetal of 1 and the corresponding hemiacetal, since the proton spectrum showed that little or no aldehyde was present. Apparently the radical, $CF_3CH_2\dot{C}HCH_2OH$, presumably formed at the anode, is very readily oxidized to $CF_3CH_2{}^+CHCH_2OH$. This ion can lose a proton to give the enol of 1 and then 1 itself, which is converted to the acetal with trifluoroacetic acid serving as the catalyst. Smaller peaks in the ^{19}F spectrum probably correspond to minor amounts of the expected byproducts, including $CF_3CH{=}CHCH_2OH$, $CF_3CH_2CH_2CH_2OH$, $CF_3CH_2CH(CF_3)CH_2OH$, and oligomeric products, but none of these was isolated.

Pouring the electrolyzed solution into water caused partial hydrolysis of the acetal. After isolation of the insoluble oil and extraction of the aqueous layer with dichloromethane, the ^1H and ^{19}F NMR spectra suggested that roughly equal amounts of aldehyde, acetal, and hemiacetal were present. These were separated from the less volatile byproducts by a preliminary distillation and further hydrolyzed by distilling with dilute aqueous sulfuric acid. Because the first distillate still contained considerable amounts of unhydrolyzed or partially hydrolyzed acetal, it was subjected to a second similar hydrolysis step and finally dried and distilled to give nearly pure 1. The method is much simpler than any of the several multistep procedures used to obtain this aldehyde previously.[7,8] If subjected to routine procedures for oxidation or reduction, the product provides good yields of 4,4,4-trifluorobutanoic acid or 4,4,4-trifluorobutanol.

Experimental Section

Commercial trifluoroacetic acid, allyl alcohol, and sodium acetate were used as received. Methanol was refluxed over magnesium methoxide and distilled. Almost equally good results were obtained with untreated anhydrous methanol, but deliberate addition of increasing amounts of water as a cosolvent progressively lowered the yields. The electrolysis cell[5] was charged with 20.4 mL (300 mmol) of allyl alcohol, 30 mL (389 mmol) of the acid, and 1.6 g (20 mmol) of sodium acetate in 200 mL of methanol. The reaction was carried out by using a nearly constant current of 0.6 A until 0.48 faradays had been consumed. The mixture was then poured into 700 mL of water, the dense oil layer separated, and the aqueous layer extracted with several portions of dichloromethane. The combined nonaqueous solutions from four identical runs were distilled to recover the solvent and further distilled at 70 torr with the receiver cooled in dry ice until about 70–75 g of material, including some residual dichloromethane, had been collected and the temperature at the top of the short Vigreux column had reached 55 °C. The distillate was then subjected twice to the following three-step treatment: (1) Ten grams of 98% sulfuric acid in 350 mL of water were added and the resulting two-phase mixture was distilled until the temperature at the top of the column reached 100 °C and about 90 mL had been collected. Much of this material consisted of an azeotrope boiling at 79–81 °C. (2) The distillate was poured into 300 mL of water, the oil layer isolated, and the water layer extracted with several portions of dichloromethane. (3) The combined nonaqueous layers were distilled to remove the solvent. After the first treatment, the residue contained 1 and a significant amount of unhydrolyzed acetal or hemiacetal; after the second, hydrolysis was complete, and further distillation gave 37.8 g (300 mmol, 25% based on allyl alcohol) of colorless oil boiling between 91 and 96 °C (lit.[7] bp 94–96 °C). The ^1H and ^{19}F NMR spectra of a 12% solution in $CDCl_3$ (1% Me_3Si) showed only trace impurity peaks, indicating that the material was nearly pure 1: ^{19}F NMR (t, J = 10.55 Hz), 11.75 ppm downfield from external trifluoroacetic acid; ^1H NMR δ 9.78 (br s, 1 H), 2.17–2.87 (complex m, 4 H).

Registry No. 1, 406-87-1; CF_3CO_2H, 76-05-1; $CH_2{=}CHCH_2OH$, 107-18-6; $CF_3(CH_2)_2CH(OMe)_2$, 92670-97-8; $CF_3(CH_2)_2CH(OH)OMe$, 92670-98-9.

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Mechanism for the Reaction of *trans*-2-Phenylcyclopropylamine with Nitrous Acid

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trans-2-Phenylcyclopropylamine (2-PCPA) is an antidepressant drug which inactivates the enzyme monoamine oxidase (MAO); the mechanism of this enzyme inactivation and the structure of the enzyme adduct were reported recently.[2] Part of the structure proof for the enzyme adduct involved the conversion of 2-PCPA to cinnamaldehyde using sodium nitrite in HCl followed by chromic acid oxidation; the first of these reactions gives a mixture of cinnamyl chloride and cinnamyl alcohol.[2] Cyclopropylamine is known to give allyl alcohol upon treatment with aqueous sodium nitrite,[3] and Corey and Atkinson[4] showed that the C_2–C_3 bond is cleaved in the reaction. This is not a surprising result since the C_1–C_2 bond of cyclopropylamine is not polarized and the Woodward–Hoffmann rules[5] predict that for a concerted process, it is the C_2–C_3 bond of a substituted cyclopropane that should break. Kirmse and Schütte[6] investigated the diazotization and subsequent ring opening of *N*-nitroso-*N*-(2-phenylcyclopropyl)urea and suggested, however, that, in this case, the reaction is not concerted. Hausser and Uchic[7] found that the rate of solvolysis of *trans*-2-phenylcyclopropyl chloride was 4×10^4 times faster than that of cyclopropyl chloride and concluded that the increased rate was the result of phenyl stabilization of the positive charge in the transition state. Because of the increased polarization of the C_1–C_2 bond in 2-phenylcyclopropylamine relative to cyclopropylamine and the suggestion[6] that ring opening of (2-phenylcyclopropyl)diazonium ion is not concerted, we wanted to determine if there is a difference in 2-phenylcyclopropylamine from

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