45 °C for 0.5 h. Sodium hydride (0.25 mmol) (10 mg of 60% NaH dispersed in mineral oil washed with petroleum ether) was added to the solution. After cessation of gas evolution 0.5 mL of 5% DCl was added. TLC on silica gel (9% MeOH in $CH_2Cl_2$, UV visualization) showed only the ring-contracted product **3** had formed; this was confirmed by proton NMR on the reaction mixture.

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**Registry No.** 1, 92397-66-5; 2, 92397-67-6; 3, 92397-68-7; 4, 92397-69-8; 5, 92397-70-1.

## Acid-Catalyzed Cyclization of Terpenoids in a Micellar System. Selectivity and Rate Enhancement in the Cyclization of Citronellal

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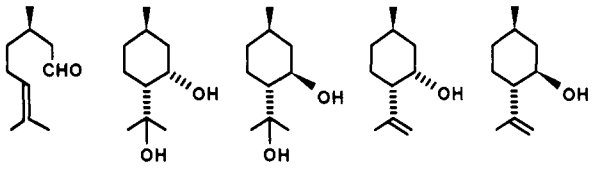
The subjects of micellar structure[1] and induced selectivity[2,3] in micelle-catalyzed reactions have been recently reviewed. Applications of micellar catalysis to synthetic organic chemistry have been discussed,[2,4,5] and it was noted[4] that the examples were quite limited.

Despite the theoretical and practical importance for terpenoid and related syntheses of the stereocontrolled, cationic cyclization of functionalized mono- and polyenes such as epoxy olefins,[6] ene allylic alcohols,[7] ene acetals,[7] and ene aldehydes,[8] reports on the effect of micelles on these reactions cannot, to the best of our knowledge, be found in the literature. In fact, micellar effects in nonphotochemical cyclizations appear to be relatively rare[4,9] and those involving carbon–carbon bond formation rarer still.[10] Several examples of induced regioselectivity in micellar photocyclizations, especially photodimerizations, have appeared and have been recently reviewed.[2,11]

In this paper we report our observations concerning the effect of a sodium dodecyl sulfate (SDS) micelle on the stereochemical course of the acid-catalyzed cyclization of the monoterpene (+)-citronellal (1), as evidenced by a large change in the ratio of the two major products. A modest rate increase for the SDS-catalyzed cyclization was also observed.

### Results and Discussion

The cyclization of (+)-citronellal (1) in aqueous sulfuric acid (5–9%) at room temperature yields[12-14] a 2:1 mixture of *cis*- and *trans*-*p*-menthane-3,8-diols **2** and **3** as the major products, plus a small amount of the corresponding isopulegols **4** and **5**.




**1** **2** **3** **4** **5**

The product data in Table I refer to a cyclization reaction performed with and without SDS in a $4 \times 10^{-2}$ M acetate buffer, pH 5.5 at 20 °C, followed over a period of 4 days. An initial citronellal concentration of $\simeq 9.2 \times 10^{-4}$ M, which is slightly below its solubility limit in water, was employed. The product distribution of the control reaction (no SDS) compares well to the prior results of Zimmerman.[12] Upon addition of SDS, however, the product ratio of diols **2**:**3** increased from 2:1 to 5:1 and the reaction proceeded at a faster rate (Table I). The SDS was used at a concentration of 0.038 M, well above its critical micelle concentration (cmc) in water of 0.008 M, and its presence caused a small increase in product yield (Table I).

The decrease in citronellal followed first-order kinetics with a $k_{abs}$ of $2.99 \times 10^4$ L/mol h in the presence of SDS vs. $6.04 \times 10^3$ in buffer alone—a rate acceleration of about fivefold. The rate data are summarized in Table II. Comparison of our $k_{abs}$ values in aqueous buffers with published data for citronellal in aqueous unbuffered HCl shows a considerable difference.[15,16]

To determine if there was a buffer effect on either product ratios or rates, the experiment was repeated in $3.1 \times 10^{-2}$ M citrate/phosphate buffer, pH 5.4, and the product ratios were the same (Table III). There was a small decrease (7%) in $k_{abs}$ for the citrate/phosphate control relative to acetate buffer, and a larger decrease (18%) in the $k_{abs}$ with SDS (Table II). For a reaction of this type, probably first order in hydrogen ion, a 0.1 unit error in pH measurement causes a 1.25 factor change in $k_{abs}$. It is thus doubtful that these small recorded differences correspond to any specific buffer effect.

Experiments were carried out at lower pH's in the citrate/phosphate buffer and also dilute sulfuric acid. Sufficient analyses for rate measurements were not made due to the faster rate and the slow workup procedure. Clearly, however, the SDS effect on rates increases relative to pH 5.5 (Table IV). In a $7 \times 10^{-2}$ M citrate/phosphate buffer at pH 4.1, only 6.3% of the citronellal remains with SDS after 1 h, against 57% in the control. In aqueous

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**Table I. Effect of SDS on the Cyclization of Citronellal in Acetate Buffer (pH 5.5): Product Data**

| | concn of product,[a] $10^{-5}$ M | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | diol 2 | | diol 3 | | ratio of 2:3 | | isopulegols 4 + 5 | | % recovery[b] | |
| time, h | buffer | SDS/buffer | buffer | SDS/buffer | buffer | SDS/buffer | buffer | SDS/buffer | buffer | SDS/buffer |
| 0.25 | 0.23 | 1.13 | 0.07 | | 3.43 | | 0.43 | 0.68 | 106 | 103 |
| 2.5 | | 9.92 | | 1.94 | | 5.11 | | 2.05 | | 96 |
| 5.5 | | 24.48 | | 4.93 | | 4.97 | | 3.71 | | 97 |
| 7 | 3.93 | 28.98 | 1.25 | 5.93 | 3.14 | 4.89 | 1.13 | 4.14 | 90 | 96 |
| 26 | 13.71 | 62.24 | 6.21 | 13.15 | 2.21 | 4.73 | 2.97 | 7.98 | 83 | 102 |
| 48.5 | 24.25 | | 10.71 | | 2.26 | | 4.29 | | 79 | |
| 53 | | 63.47 | | 13.22 | | 4.80 | | 7.99 | | 95 |
| 76 | 38.41 | | 17.85 | | 2.15 | | 6.20 | | 90 | |
| 96.75 | 39.79 | | 18.80 | | 2.12 | | 6.54 | | 85 | |

[a] Average of two determinations for each variable. [b] Employing methyl octanoate as an internal standard and correcting for response; unreacted citronellal included.

**Table II. Effect of SDS on Citronellal Cyclization in Acetate Buffer (pH 5.5) and Citrate/Phosphate Buffer (pH 5.4): Rate Data at 20 °C**

| | acetate buffer | | SDS/acetate buffer | | | |
|---|---|---|---|---|---|---|
| kinetic parameters | reaction 1 | reaction 2 | reaction 1 | reaction 2 | citrate/phosphate buffer[a] | SDS/citrate/phosphate buffer[a] |
| $k_{obsd}$ ($h^{-1}$) | 1.98 ($10^{-2}$) | 1.93 ($10^{-2}$) | 9.16 ($10^{-2}$) | 9.13 ($10^{-2}$) | 2.23 ($10^{-2}$) | 9.77 ($10^{-2}$) |
| $t_{1/2}$ (h) | 35.02 | 35.93 | 7.57 | 7.59 | 31.1 | 7.09 |
| pH | 5.49 | 5.49 | 5.52 | 5.51 | 5.40 | 5.40 |
| $k_{abs}$[b] | 6.12 ($10^3$) | 5.96 ($10^3$) | 3.03 ($10^4$) | 2.95 ($10^4$) | 5.60 ($10^3$) | 2.45 ($10^4$) |
| $C_0$ (calcd molar concn) | 9.2 ($10^{-4}$) | 9.2 ($10^{-4}$) | 9.0 ($10^{-4}$) | 9.3 ($10^{-4}$) | 9.2 ($10^{-4}$) | 8.9 ($10^{-4}$) |
| coeff of determn | 0.995 | 0.998 | 0.999 | 0.999 | 0.999 | 0.999 |

[a] Average of two experiments. [b] $k_{abs} = k_{obsd}$ ($h^{-1}$)/[$H^+$] (mol/L) = L $mol^{-1}$ $h^{-1}$.

**Table III. Product Ratios of Diols 2 and 3 for All Experimental Conditions**

| | | av $C_0$, | ratio of 2:3 | |
|---|---|---|---|---|
| reaction media | pH | $10^{-4}$ M | no SDS | with SDS |
| acetate buffer ($4.0 \times 10^{-2}$ M) | 5.5 | 9.2 | 2.19 | 4.89 |
| citrate/phosphate buffer ($3.1 \times 10^{-2}$ M) | 5.4 | 9.1 | 1.88 | 4.59 |
| citrate/phosphate buffer ($7.0 \times 10^{-2}$ M) | 4.1 | 7.2 | 1.99 | 4.49 |
| water/$H_2SO_4$ | 3.4 | 7.2 | | 5.15 |
| water/$H_2SO_4$ | 3.4 | 331.0 | | 4.66 |

$H_2SO_4$ at pH 3.4 with SDS, no citronellal remained after 3 h. A 45-fold more concentrated citronellal ($3.3 \times 10^{-2}$ M) solution in SDS, acidified with $H_2SO_4$, was also totally reacted after 3 h and the same approximate product ratio was maintained (Table III). Thus, the use of SDS in these systems seems to have considerable synthetic utility to produce certain products selectively and at a faster rate.

As summarized in Table III, we have found the product ratios for diols **2**:**3** to be independent of citronellal concentration, buffer, pH, acid, and ionic strength, i.e., the ratios are solely dependent on the presence of SDS under the conditions studied.

In order to explain the enhanced formation of **2** over **3** induced by the SDS micelle, one must first consider the stereochemical course of this reaction as it proceeds in aqueous acids. Naves and Ochsner[13] have shown that the cyclization of (+)-**1** yields (+)-**2** and (−)-**3**, which they proved differed in configuration only at carbon-3 as both yielded the same (−)-8-hydroxymenthone upon oxidation with chromic acid. The absolute configurations (+)-**2** and (−)-**3** were further secured[14] by the direct chemical conversion of (−)-**3** to (−)-menthol acetate, whose absolute configuration was known from X-ray analysis of (−)-menthol.[17] These results show that the diastereomeric diols (+)-**2** and (−)-**3** have the same absolute configuration

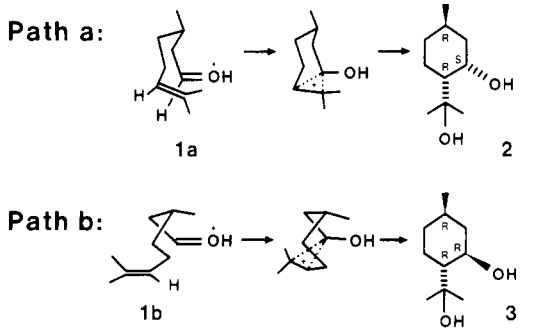
**Table IV. Citronellal Remaining at Lower pH after Cyclization at 20 °C ($C_0 = 7.2 \times 10^{-4}$ M)**

| | | 1 h | | 23 h | |
|---|---|---|---|---|---|
| reaction conditions | pH | % | concn (M) | % | concn (M) |
| citrate/phosphate/buffer | 4.1 | 57.0 | 4.1 ($10^{-4}$) | 0.5 | 3.8 ($10^{-6}$) |
| SDS/citrate/phosphate buffer | 4.1 | 6.3 | 4.4 ($10^{-5}$) | 0.9 | 6.2 ($10^{-6}$) |

| | | 3 h | | 24 h | |
|---|---|---|---|---|---|
| reaction conditions[a] | pH | % | concn (M) | % | concn (M) |
| SDS/$H_2O$/$H_2SO_4$ | 3.4 | 0.6 | 4.4 ($10^{-6}$) | 0.7 | 4.8 ($10^{-6}$) |
| SDS/$H_2O$/$H_2SO_4$[b] | 3.4 | 0.1 | 3.0 ($10^{-5}$) | 0.04 | 1.3 ($10^{-5}$) |

[a] $H_2SO_4$ reactions run at room temperature (≃22 °C). [b] Initial citronellal concentration: $C_0 = 3.3 \times 10^{-2}$ M.

**Scheme I**




(*R*) at carbon-4, a result in agreement with the finding of Arigoni[18] for the solvolytic cyclization of (−)-(3*R*)-linalyl *p*-nitrobenzoate to (+)-(4*R*)-α-terpineol.

The formation of (+)-**2** and (−)-**3** in solution can be rationalized as shown in Scheme I. The observed preference for path a over b is understood under the assumption[12] of a lower energy for the transition state of path a, resulting from the stabilizing effect of the oxygen upon the tertiary carbocation.

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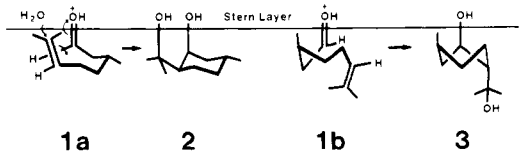
**Scheme II**




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).

**Acknowledgment.** We thank Professors F. M. Menger and C. G. Trowbridge of Emory University, Atlanta, Ga, for helpful discussions and Dr. Terence Radford and Mr. Ernest Thomas Jr. of these laboratories for GC/MS interpretation and determinations.

**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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