genolysis of **11b** (purified by chromatography on silica gel, Et_2O–hexanes–Et_3N 80:20:1) according to the procedure described above: ^1H NMR (D_2O) δ 1.70 (3 H, d, CCH_3), 3.00 (2 H, m, NCH_2), 3.40 (6 H, s, OCH_3), 4.65 (2 H, m, ArCH, $CH(OMe)_2$), 6.90 (3 H, m, arom); mass spectrum, *m/e* 241.1319 (7, M^+; calcd *m/e* 241.1315), 209 (5), 137 (100), 75 (49).

2-[*N*-(2,3-Dihydroxybenzyl)-*N*-methylamino]acetaldehyde Dimethyl Acetal Hydrochloride (12c). ^1H NMR (D_2O) δ 2.86 (3 H, s, NCH_3), 3.24 (2 H, d, NCH_2), 3.48 (6 H, s, OCH_3), 4.25 (2 H, s, $ArCH_2$), 4.75 (1 H, t, $CH(OMe)_2$), 6.85 (3 H, m, arom); mass spectrum, *m/e* 241.1321 (14, M^+; calcd *m/e* 241.1315), 210 (4), 209 (3), 166 (75), 123 (100), 75 (72).

2-[*N*-[1-(2,3-Dihydroxyphenyl)ethyl]-*N*-methylamino]-acetaldehyde Dimethyl Acetal Hydrochloride (12d). ^1H NMR (D_2O) δ 1.67 (3 H, d, CCH_3), 2.8 (3 H, br s, NCH_3), 3.20 (2 H, m, NCH_2), 3.42 (6 H, s, OCH_3), 4.75 (2 H, m, ArCH and $CH(OMe)_2$), 6.85 (3 H, m, arom); mass spectrum, *m/e* 255.1470 (5, M^+; calcd *m/e* 255.1471), 180 (13), 137 (100), 75 (63).

1,2,3,4-Tetrahydro-4,7,8-isoquinolinetriol Hydrochloride (13a). Acetal **12a** was treated with 6 M HCl for 5.5 h. The product (25 mg, 90% yield) precipitated from solution as off-white crystals which were collected by filtration and dried in vacuo over NaOH: mp 168–172 °C dec, lit.[7] 172 °C dec.[2]

***cis*- and *trans*-1,2,3,4-Tetrahydro-1-methyl-4,7,8-isoquinolinetriol Hydrochloride (13b).** Acetal **12b** was treated with 6 M HCl for 6 h. HPLC indicated the formation of *cis*- and *trans*-**13b**[2] in a 1:4 ratio. The precipitated product (60% yield, 97% trans by HPLC) was collected and dried as before. The supernatant contained an additional 25% yield of *cis*- and *trans*-**13b** (1:6): mp 193–196 °C dec.[2]

1,2,3,4-Tetrahydro-2-methyl-4,7,8-isoquinolinetriol Hydrochloride (13c). Acetal **12c** was treated with 6 M HCl for 4 h. The precipitate (66% yield) was collected and dried as before: mp 168–172 °C dec.[2]

***cis*- and *trans*-1,2,3,4-Tetrahydro-1,2-dimethyl-4,7,8-isoquinolinetriol Hydrochloride (13d).** Acetal **12d** was treated with 6 M HCl for 11 h to afford *cis*- and *trans*-**13d** (45% yield, 1:2). The product could be isolated by cautious neutralization with sodium carbonate followed by trituration with ethanol to remove sodium chloride as previously described.[2]

Acknowledgment. We gratefully acknowledge support of this investigation by the U. S. Public Health Service, Grant 1 R03 AA05472, and Biomedical Research Support Grant 5 S07 RR07067.

Registry No. **2**, 41462-20-8; **3b**, 41462-27-5; **3d**, 92366-88-6; **4b**, 92366-89-7; **4d**, 92366-90-0; *cis*-**5b**, 85507-48-8; *trans*-**5b**, 85507-49-9; *cis*-**5d**, 92469-54-0; *trans*-**5d**, 92469-55-1; **6**, 92366-91-1; **10**, 92366-92-2; **11a**, 92366-93-3; **11b**, 92366-94-4; **11c**, 92366-95-5; **11d**, 92366-96-6; **12a**, 92366-97-7; **12b**, 92366-98-8; **12c**, 92366-99-9; **12d**, 92367-00-5; **13a**, 85507-50-2; *cis*-**13b**, 85507-51-3; *trans*-**13b**, 85507-52-4; **13c**, 82334-25-6; *cis*-**13d**, 92469-56-2; *trans*-**13d**, 92469-57-3; 1,2-bis(methoxymethoxy)benzene, 3688-89-9; 2-aminoacetaldehyde dimethyl acetal, 22483-09-6; **9**, 5779-91-9.

Observation of an Aziridine Intermediate in a Displacement Reaction on Tetrahydro-5-(tosyloxy)-2(1*H*)-pyrimidinone

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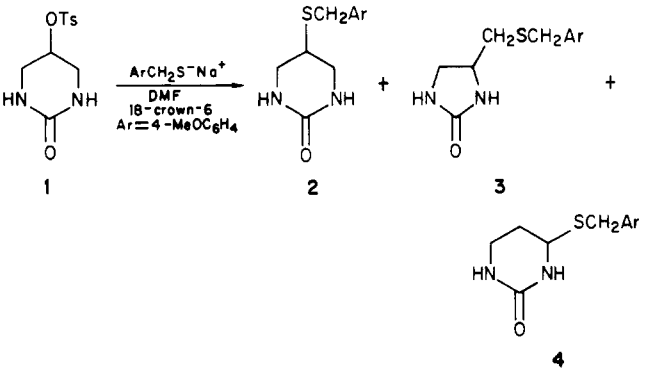
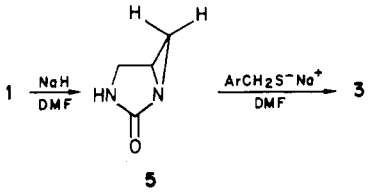
Three displacement products were isolated from the reaction of tetrahydro-5-(tosyloxy)-2(1*H*)-pyrimidinone (**1**) with sodium 4-methoxy-α-toluenethiolate. The product mix, as ascertained by TLC, was dependent on the relative proportions of sodium hydride and 4-methoxy-α-toluenethiol. Mass spectral and elemental analyses suggested that the products were isomeric. Structural assignments were made on the basis of NMR spectra (see Table I). The expected product **2** was identified principally by its ^{13}C NMR spectrum which was consistent with a symmetrical tetrahydro-2(1*H*)-pyrimidinone structure analogous to the starting tosylate. Assignment of the structures of **3** and **4** to the other two products was based on comparison of their NMR spectra with those of **2**. In particular, the



ring-contracted product **3** had ^{13}C NMR resonances indicative of methylene and methine groups attached to nitrogen and a methylene group attached to sulfur; the downfield shift of the carbonyl resonance paralleled the effects seen with cyclic ketones and anhydrides when ring size was reduced from six to five members.[1] The proton NMR spectrum of **4** included a multiplet at δ 1.97 ascribed to a methylene group bearing no heteroatom and a triplet at δ 4.48 consistent with a methine group bearing two heteroatoms and coupled to the methylene group at δ 1.97 (confirmed by double irradiation). The ^{13}C NMR spectrum of **4** affirmed the presence of these types of substituted carbon atoms.

The formation of **3** could be explained by the intermediacy of aziridine **5** which could arise from intramolecular displacement of the tosylate by the anion formed from reaction of excess sodium hydride with the ureylene function. Nucleophilic attack on **5** would be expected to



occur at the methylene group of the aziridine ring to give **3**.[2] In support of this, treatment of tosylate **1** with sodium hydride produced a compound which had lost the tosylate group and had NMR spectral properties consistent with the aziridine structure **5** (see Table II). The two protons of the aziridine ring methylene group were nonequivalent, but no geminal coupling was observed (very small couplings of <1 Hz have been reported for geminal protons in aziridines[3,4]). The upfield resonance (δ 1.99) was assigned to the endo proton on the basis of the expectation that it would be shielded by the carbonyl group and have the smaller coupling to the methine group.[3,4] Reaction of

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(2) A similar process has been reported for 6-isopropyl-3-oxa-1-azabicyclo[3.1.0]hexan-2-one. Marchand, J.; Rocchioccioli, F.; Pais, M.; Jarreau, F.-X. *Bull. Soc. Chim. Fr.* **1972**, 4699.
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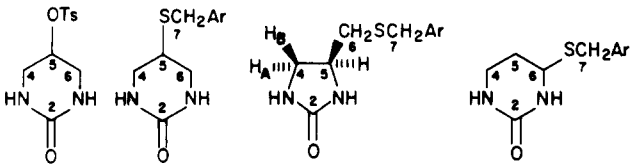
0022-3263/84/1949-4555$01.50/0

Table I. ^1H and ^{13}C NMR Data

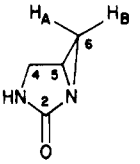


1 2 3 4

nucleus	position	δ (multiplicity, J) 1	2	3	4
^1H	4A	3.14 (br d, ~14)[a]	2.8–3.5 (m)[b]	3.51 (dd, 8.5, 8.7)[b]	3.05–3.65 (m)[c]
	4B	3.42 (br d, ~14)		3.12 (dd, 5.1, 8.5)	
	5	4.83 (m)	2.8–3.5 (m)	~3.8 (obsc)	1.7–2.35 (m)
	6A	3.14 (br d, ~14)	2.8–3.5 (m)	2.53 (d, 6.2)	4.48 (dd, ~4, ~4)
	6B	3.42 (br d, ~14)			
	7		3.70 (s)	3.66 (s)	3.74 (s)
^{13}C	2	154.8[a]	155.4 (s)[a]	163.0 (s)[a]	155.0 (s)[a]
	4	43.6	44.8 (t)	45.1 (t)	36.4 (t)
	5	71.1	36.2 (d)	51.5 (d)	26.9 (t)
	6	43.6	44.8 (t)	34.9 (t) or 36.1 (t)	55.3 (d)
	7		33.8 (t)	34.9 (t) or 36.1 (t)	33.2 (t)

[a] Me_2SO-d_6. [b] $CDCl_3$ + CD_3OD. [c] $CDCl_3$.

Table II. ^1H and ^{13}C NMR[a] Data for 5



nucleus	position	δ (multiplicity, J)
^{13}C	2	171.6 (s)
	4	42.2 (t)
	5	35.3 (d)
	6	34.4 (dd)
^1H	4	3.68 (d, 3.7)
	5	2.96 (m)
	6A	1.99 (d, 3.7)
	6B	2.41 (d, 4.8)

[a] $CDCl_3$.

5 with 4-methoxy-α-toluenethiolate gave only the ring-contracted product 3.

Experimental Section

Melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Proton and ^{13}C magnetic resonance spectra were recorded on JEOL FX-90-Q, Varian FT-80A, and Perkin-Elmer R-32 (90 MHz) spectrometers; Me_4Si was internal reference for the proton spectra while Me_2SO was used for the ^{13}C spectra. Chemical ionization mass spectra were recorded on a Finnegan 3300 spectrometer with methane as reagent gas. Infrared spectra were obtained on a Perkin-Elmer 229B spectrophotometer. Chromatography was done at medium pressure by using Baker silica gel for flash chromatography (40-μm average particle size). DMF and pyridine were dried over Linde 3A molecular sieves.

Tetrahydro-5-(tosyloxy)-2(1*H*)-pyrimidinone (1). A solution of 52 g (0.44 mol) of tetrahydro-5-hydroxy-2(1*H*)-pyrimidinone[5] and 123 g (0.64 mol) of tosyl chloride in 1 L of dry pyridine was stirred at room temperature for 48 h. The pyridine was evaporated in vacuo, and the residue was stirred with absolute ethanol to produce a white solid. The solid was washed with water and then absolute ethanol to give 60 g (50%) of 1. Crystallization from methanol gave colorless crystals: mp 187–9 °C; IR (KBr) 1670 cm^{-1}; NMR, see Table I. Anal. Calcd for $C_{11}H_{14}N_2O_4S$: C, 48.88; H, 5.22; N, 10.36. Found: C, 48.77; H, 5.11; N, 10.23.

4-[[[(4-Methoxyphenyl)methyl]thio]methyl]-2-imidazolidinone (3). To a solution of 13.5 g (87.6 mmol) of 4-methoxy-α-toluenethiol in 200 mL of dry DMF under nitrogen atmosphere were added 4.25 g (106 mmol) of a 60% dispersion of NaH in mineral oil. The reaction was heated in an oil bath at 80 °C for 20 min with stirring. To this solution were added 2.6 g (10 mmol) of 18-crown-6. The solution was cooled to room temperature, and 20 g (74 mmol) of 1 were added with cooling to maintain the reaction at room temperature. After being stirred for 1.5 h, the reaction was heated at 50 °C for 15 min to assure completion. After being cooled, the reaction was neutralized with dilute AcOH, and the DMF was evaporated in vacuo. The residue was stirred with Et_2O to obtain a white solid which was purified by chromatography on silica gel eluting with 0–3% MeOH in CH_2Cl_2 to give 15.5 g (83%) of 3 as a solid: mp 125–7 °C (colorless crystals from CH_2Cl_2); mass spectrum, m/z 253 ($M + H^+$); IR (CH_2Cl_2) 1715 cm^{-1}; NMR, see Table I. Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.14; H, 6.39; N, 11.10. Found: C, 57.25; H, 6.61; N, 10.93.

Tetrahydro-5- and -4-[[(4-methoxyphenyl)methyl]thio]-2(1*H*)-pyrimidinones (2 and 4). Both compounds were produced by the same reaction. The procedure was the same as that for the preparation of 3 except a 0.5 to 1 equiv excess of thiol over NaH was used and care was taken to make sure all the NaH had reacted before the tosylate was added. Workup and chromatography were also the same; 2 eluted slightly before 4. 2 (27–33%): mp 170–2 °C (colorless crystals from EtOAc); mass spectrum, m/z 253 ($M + H^+$); IR (CH_2Cl_2) 1675 cm^{-1}; NMR, see Table I. Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.14; H, 6.39; N, 11.10. Found: C, 57.11; H, 6.31; N, 11.24. 4 (40–50%): mp 173–4 °C (colorless crystals from CH_2Cl_2 plus MeOH); mass spectrum, m/z 253 ($M + H^+$); IR (CH_2Cl_2) 1678 cm^{-1}; NMR, see Table I. Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.14; H, 6.39; N, 11.10. Found: C, 57.46; H, 6.39; N, 11.06.

1,3-Diaza[3.1.0]bicyclohexan-2-one (5). To a solution of 1.35 g (5.0 mmol) of 1 (dried with P_2O_5) in 150 mL dry CH_2Cl_2 was added 0.3 g (5.7 mmol) of a 60% dispersion of NaH in mineral oil. The reaction mixture was heated at reflux until gas evolution ceased. The reaction solution was decanted from a sticky residue, filtered, and evaporated to give a solid which was extracted twice with dry Et_2O. Concentration of the Et_2O solution gave 110 mg (22%) of 5 as a colorless crystalline solid: mp 79–81 °C; IR (CH_2Cl_2) 1732 cm^{-1}; NMR, see Table II. Anal. Calcd for $C_4H_6N_2O$: C, 48.97; H, 6.16; N, 28.55. Found: C, 48.68; H, 6.09; N, 28.55.

Reaction of 5 with Sodium 4-Methoxy-α-toluenethiolate. A solution of 49 mg (0.5 mmol) of 5 and 77 mg (0.5 mmol) of 4-methoxy-α-toluenethiol in 1.0 mL of $CDCl_3$ was monitored by proton NMR. No reaction occurred at room temperature or at

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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.

Acknowledgment. We thank E. Reich for elemental analyses, M. Mentzer for mass spectral data, and D. Staiger and G. Zuber for some of the NMR data. We acknowlede the encouragement of Dr. G. Dunn.

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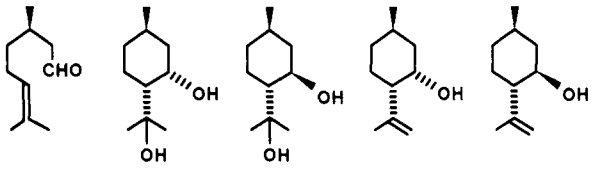
The subjects of micellar structure[1] and induced selectivity[2,3] in micelle-catalyzed reactions have been recently reviewed. Applications of micellar catalysis to synthetic organic chemistry have been discussed,[2,4,5] and it was noted[4] that the examples were quite limited.

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 4×10^{-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 2.99×10^4 L/mol h in the presence of SDS vs. 6.04×10^3 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 3.1×10^{-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 7×10^{-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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