(70 eV), *m/e* (relative intensity) 159.0 (12.6), 158.0 (molecular ion, 96.4), 129.0 (19.3), 115.0 (23.0), 92.0 (100).

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Registry No. **1**, 704-02-9; **2**, 2958-72-7; (*Z*)-**3**, 101418-76-2; (*E*)-**3**, 101418-83-1; **4**, 101418-77-3; **4** (mesylate), 101418-82-0; **5**, 101470-91-1; **6**, 101418-78-4; **7**, 101418-79-5; **8**, 101418-80-8; **9**, 101418-81-9; ethyl (diethoxyphosphinyl)acetate, 867-13-0.

Selective Functionalization. 9. The Chlorination of Phenol and Some Phenyl Ethers by Functionalized Surfactants

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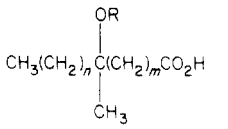
The possiblity that the regioselectivity of organic reactions might be modified advantageously in a micellar environment has been investigated for many systems including aromatic substitution[1-7] and addition to alkenes.[8-10] In our previous studies,[5] we showed that the regioselectivity of the chlorination of phenol was modified in a micellar environment so that ortho chlorination was enhanced. This result was consistent with the time average orientation of phenol in the micellar environment in which the ortho protons occupy the most polar environment as shown by NMR studies.[11] Jaeger and his colleagues showed in a related study that chlorination of pentyl phenyl ether at the para position was promoted in micellar solution,[3] and they have recently extended their study to arylalkyl ethers with longer alkyl chains[6] but without improvement in control of regioselectivity. We also showed that a tertiary alcohol located at C-3 of a stearate molecule (**1a**) in a micellar environment could promote highly regioselective chlorination of phenol in the ortho position.[5] In this paper we report the extension of these experiments to the C-6 functionalized stearate **2a** and to the chlorination of anisole and pentylphenyl ether.

The new C-6 functionalized stearate was prepared by a Grignard reaction on the corresponding ketone which was



	n	*m*		R		R
1	14	1	a	H	b	Me
2	11	4	a	H	b	Me
3	5	10	a	H	b	Me

obtained by the method of Robinson.[12] Phenol was chlorinated in aqueous acetonitrile (9:1 v/v) by using *tert*-butyl hypochlorite as the source of the chlorine. Experiments were carried out in the absence of surfactants and in the presence of sodium dodecylsulfate (SDS) alone and in combination with the stearate derivatives **2a,b**. The total concentration of surfactant was maintained well above the cmc at 300 mM, and the substrate was present in a twofold excess over the chlorinating agent, *tert*-butyl hypochlorite. For those reactions in which a stearate was included, *tert*-butyl hypochlorite was added first followed by the substrate 1 min later. Under these conditions, polychlorination was totally absent, and yields were 40–60% based upon chlorinating agent used, greater than in our previous studies. Products were analyzed by GLC using the excess substrate as an internal standard.

Under the above reaction conditions, the chlorination of phenol alone yielded approximately equal proportions of 2- and 4-chlorophenols (Table I, entry 1). The micellar environment imposed an average orienting effect upon phenol so that the proportion of ortho chlorination was raised (entry 2). A further and substantial enhancement to the selectivity of the reaction was obtained by including the 6-functionalized stearate **2a** in the micellar solution. As the concentration of **2a** was increased, so the selectivity of the reaction rose (entries 3–6) to a maximum of 94% 2-chlorophenol. If the methyl ether of **2a**, **2b**, was used in its place, the chlorination showed the selectivity of an unfunctionalized micelle only. The results follow a similar pattern to those in our previous study using the stearates **1a** and **3a**[5] in which ortho chlorination was promoted by both functionalized surfactants.

The ethers were chlorinated under similar conditions and were introduced into the reaction dissolved in a small volume of acetonitrile to give a homogeneous solution. With anisole as substrate, it was anticipated that the micellar environment would promote ortho chlorination because our NMR studies[11] had shown that the time average orientation of anisole in micellar solution places the ortho protons in the most polar environment as with phenol. The results show a substantial enhancement of ortho chlorination as expected (entries 7 and 8) and parallel those obtained previously for phenol.[5] In contrast, with pentyl phenyl ether as substrate, the opposite time average orientation had been observed,[11] and accordingly, enhanced para chlorination would be expected. Once again, the results confirmed the expectation (entries 12 and 13) and showed a similar pattern of behavior to that described by Jaeger's group.[3] Our intention to investigate the course of chlorination mediated by the functionalized stearic acids **1–3** was that the tertiary hypochlorites produced by exchange with *tert*-butyl hypochlorite would be localized in a specific micellar environment close to the head groups (**1**) or within the hydrophobic region (**3**) or in an intermediate region (**2**). This localization of the reagent might then lead to pronounced changes in regioselectivity of chlorination if the less substrates were solublized in an organized manner by the micelle but

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Table I. Chlorination of Phenol and Its Ethers (30 mM) in Aqueous Acetonitrile (9:1 v/v) by *t*-BuOCl (15 mM)

substrate	entry	[SDS], mM	stearate	[stearate], mM	normalized, % 2-Cl	4-Cl
phenol	1				48	52
	2	300			58	42
	3	290	**2a**	10	86	14
	4	285	**2a**	16	88	12
	5	280	**2a**	20	89	11
	6	270	**2a**	30	94	6
anisole	7				49	51
	8	300			73	27
	9	270	**1a**	30	72	28
	10	270	**2a**	30	77	23
	11	270	**3a**	30	77	23
pentyl phenyl ether	12				31	69
	13	300			21	79
	14	270	**1a**	30	18	82
	15	270	**2a**	30	20	80
	16	270	**3a**	30	17	83

differently from phenol. However chlorination of both anisole and pentyl phenyl ether was not influenced significantly by the inclusion of the functionalized surfactants in the micelle (entries 9–11, 14–16) under conditions that caused a substantial change in the regioselectivity of phenol chlorination (entries 3–6).

Our results confirm that the average orientation of a molecule in a micellar environment has an influence upon the course of chlorination. However there is little encouragement to believe that a micellar environment has sufficient organization to control substitution reactions of nonpolar aromatic molecules in general. Recent work by Menger[13] and Whitten[14] with hydrocarbon substrates in micellar solution emphasized the disorder of micelles and the relatively high polarity of solubilization sites even of hydrocarbons. It is therefore not surprising that molecules with polar substituents such as aromatic ethers do not show highly selective reactions. Selectivity, in principle, can arise from the effects of localized reagents in specific reaction sites or from a change in the relative rates of reaction between free and micellar bound substrates at the ortho and para position. In our earlier work,[11] we investigated the partition of anisole and phenol between SDS micelles and bulk solvent (1:9 CD_3CN/D_2O) by NMR spectroscopy. We found that approximately 9% of phenol and 6% of anisole (30 mM total concentration) were free of micellar SDS (300 mM total concentration) and that the cmc of SDS under these conditions was 25 mM. Since for both anisole and phenol chlorination occurred almost equally at the ortho and para positions in free solution, the observed selectivity could be accounted for by an especially high rate of ortho chlorination alone in micellar solution. This explanation is consistent with results for anisole because functionalization of the surfactant has no significant effect upon selectivity. The partition of phenol into the micelle is not greatly different from that of anisole under the reacting conditions. Hence the enhanced selectivity in the chlorination of phenol is probably due to an additional factor. The use of methyl ethers of the functionalized surfactants abolished the additional selectivity in phenol chlorination. The exceptionally high selectivity observed in chlorination of phenol may therefore be due to a combination of the average orientation imposed by the micelle and hydrogen bonding between the phenolic hydroxyl group and the reaction site. This mechanism has been proposed to account for high ortho regioselectivity in the biomimetic nitration of phenol.[15]

Experimental Section

6-Oxostearic acid was prepared by the method of Robinson.[12]

6-Hydroxy-6-methylstearic acid (2a) was prepared as described previously[5] for the analogues **1a** and **3a** in 98% yield. The product was a wax. Found: C, 72.6; H, 12.2. $C_{19}H_{38}O_3$ requires C, 72.5; H, 12.1% Mass spectrum, *m/z* observed (calculated): $M^+ - CH_3$, 299.2600 (299.2586); $M^+ - OH$, 297.2792 (297.2793); $M^+ - (H_2O, CH_3)$, 281.2480 (281.2480). NMR δ_H ($CDCl_3$, 90 MHz): 3.95 (2 H, br, exchangeable with D_2O, OH), 2.30 (2 H, t, CH_2CO_2H), 1.75–1.1 (31 H, br m, CH_2, CCH_3), 0.90 (3 H, t, CH_3CH_2). IR ν_{max} (liquid film, cm^{-1}): 3350 (br, OH)–2350 (CO_2H), 1710 (CO_2H). The corresponding sodium salt was prepared from the acid by titration and had ν_{max} 3350 (br, OH, no CO_2H) and 1560 (CO_2) cm^{-1}. The methyl ether **2b** was prepared from the acid as described previously[5] and was also a wax. Mass spectrum *m/z* observed (calculated): $M^+ - CH_3$, 314.2780 (314.2776); $M^+ - CH_3O$, 297.2784 (297.2793). NMR δ_H ($CDCl_3$): 3.16 (3 H, s, OCH_3), 2.37 (2 H, t, CH_2CO_2H), 1.8–1.05 (33 H, br, CH_2CCH_3), 0.87 (3 H, t, CH_3CH_2).

Pentyl phenyl ether and pentyl chlorophenyl ethers were prepared by the Williamson method and were purified by distillation under reduced pressure. Boiling points (°C, (pressure)) [ref 3 bp]: pentyl phenyl ether, 50 (0.3 mm) [94–96, (23 mm)]; 2-chlorophenyl pentyl ether, 80 (0.45 mm) [78–80 (0.1 mm)]; 4-chlorophenyl pentyl ether, 113–115 (0.5 mm) [113–115 (0.5 mm)]; 2,4-dichlorophenyl pentyl ether, 82 (0.05 mm) [118–120 (0.1 mm)], 2,6-dichlorophenyl pentyl ether, 60 (0.1 mm); 2,4,6-trichlorophenyl pentyl ether 78 (0.1 mm). All materials used were homogenous by GLC. Anisole and phenol and their chlorination products were commerical samples purified by redistillation or recrystallization to be homogenous by GLC. Sodium dodecylsulfate sulfate was BDH ultra pure grade and was characterized through the courtesy of Dr. R. W. Richards (Strathclyde).

GLC Analyses. Phenol and anisole and their chlorination products were determined by GLC analysis on 10% FFAP on Chromosorb G at 170 and 140 °C, respectively. At a flow rate of 20 mL min^{-1} the retention times (min) were as follows: phenol, 3.9; 2-chlorophenol, 2.7; 4-chlorophenol, 10.6; 2,4,6-trichlorophenol, 7.4; anisole, 2.0; 4-chloroanisole, 6.8; 2-chloroanisole, 7.8. Pentyl phenyl ether and its chlorination products were analyzed on 5% Apiezon L on Chromosorb W at 170 °C. At a flow rate of 20 mL min^{-1} the retention times were as follows: phenyl ether, 2.1; pentyl 2-chlorophenyl ether, 5.1; pentyl 4-chlorophenyl ether, 5.8; pentyl 2,4-dichlorophenyl ether, 11.8; pentyl 2,6-dichlorophenyl ether, 6.4; pentyl 2,4,6-trichlorophenyl ether, 8.8.

Chlorination Experiments. Phenol was chlorinated as described previously[5] but with the time allowed for hypochlorite exchange reduced from 5 to 1 min. Chlorination of anisole and phenol was carried out by adding a solution of the ether in acetonitrile (0.1 mL) to the aqueous solution of SDS and the appropriate chlorinating agent (0.9 mL) at the required concentrations to give the concentrations reported in Table I. Anisole

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and its chlorination products were analyzed by direct sampling of the reaction mixtures on to the GLC column. Penyl phenyl ether and its chlorination products were separated from the surfactants which interfered with the GLC analysis by adding to the reaction mixture pentane (10 mL) followed by 33% w/v aqueous calcium chloride solution. The solution was mixed vigorously and the pentane layer separated and concentrated under a stream of nitrogen. The extraction procedure and the GLC analyses were all calibrated with authentic samples.

Registry No. **1a**, 88099-78-9; **2a**, 101375-82-0; **2a**·Na, 101375-85-3; **2b**, 101375-83-1; **3a**, 88099-77-8; phenol, 108-95-2; anisole, 100-66-3; pentyl phenyl ether, 2050-04-6; 2-chlorophenol, 95-57-8; 4-chlorophenol, 106-48-9; 2-chloroanisole, 766-51-8; 4-chloroanisole, 623-12-1; pentyl 2-chlorophenyl ether, 51241-39-5; pentyl 4-chlorophenyl ether, 51241-40-8; pentyl 2,4-dichlorophenyl ether, 63076-61-9; pentyl 2,6-dichlorophenyl ether, 95249-04-0; pentyl 2,4,6-trichlorophenyl ether, 101375-84-2; 2,4,6-trichlorophenol, 88-06-2.

Energies of the Stilbenes and Stilbene Dibromides

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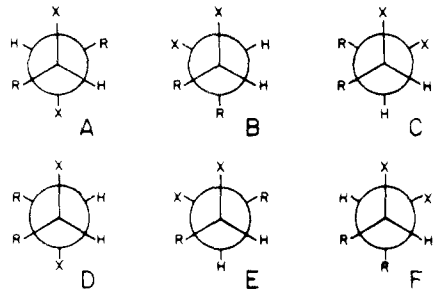
The enthalpy difference of the stilbenes is of the interest in connection with the much-studied[1,2] mechanism of photochemical interconversion of the two stereoisomers; it also has a bearing (see below) on the mechanism of bromine elimination from the corresponding dibromides.[3] Interpretation of the latter reaction also depends crucially on a knowledge of the conformational equilibria in the two dibromides (vide infra). This note deals with these two problems.

The standard free-energy difference $\Delta G°$ of the stilbenes has been determined in a hydrocarbon solvent at 27 °C, by equilibration, to amount to 3.7 ± 0.1 kcal/mol (15.5 ± 0.4 kJ/mol),[4] the trans isomer being the more stable one. Through determination of the dependence of the equilibrium composition on temperature, $\Delta H°$ (in toluene) was estimated to be 2.3 ± 0.3 kcal/mol (9.6 ± 1.3 kJ/mol); however, because of the one-sideness of the equilibrium and the corresponding small changes of $\Delta G°$ over a relatively large range (−30 to +90 °C) of temperature, the accuracy of this value is subject to question. Unfortunately a rather discrepant value of 5.7 ± 0.2 kcal/mol (23.9 ± 0.8 kJ/mol) was found from differences in heat of hydrogenation,[5] a method which, at first sight, would seem to be more accurate, since it is more direct and the number whose difference is taken are not large. A priori, however, it is not clear which of the two values is closer to the true one.

The heats of the combustion of the stilbenes were determined[6] a number of years ago and are 7401.1 ± 0.7 kJ/mol (1768.0 ± 0.2 kcal/mol) for the cis isomer and 7361.1 ± 0.5 kJ/mol (1758.5 ± 0.1 kcal/mol) for the trans isomer. Since *trans*-stilbene was burned as a solid and *cis*-stilbene as a liquid, these values are not directly comparable and could not, at the time, be used to compute the heat of isomerization. However, since then the increments needed to convert these data to the gas phase have been reported: the heat of vaporization of the cis isomer is 15.8 ± 0.3 kcal/mol (66.1 ± 1.3 kJ/mol),[7] and the heat of sublimation of the trans isomer is 95.4 ± 3.0 kJ/mol (22.8 ± 0.7 kcal/mol).[8] With these additional data one can compute the heats of combustion of the stilbenes in the vapor phase to be 7467.2 ± 1.5 kJ/mol (1783.8 ± 0.4 kcal/mol) for the cis isomer and 7456.5 ± 3.0 kJ/mol (1781.3 ± 0.7 kcal/mol) for the trans isomer. The difference, 10.7 ± 3.4 kJ/mol (2.5 ± 0.8 kcal/mol), represents the heat of isomerization, in good agreement with the value obtained from the temperature dependence of equilibrium and in disagreement with the hydrogenation value. The lower value ($\Delta H°$ = 2.3 ± 0.3 kcal/mol, 9.6 ± 1.3 kJ/mol) may therefore be accepted as the correct one.

Scheme I



The mechanism of elimination of the stilbene dibromides with iodide ion to give stilbenes, iodine, and bromide has been studied by Miller and co-workers.[3,9,10] The experimental facts are as follows: (1) The reaction is quite stereospecific[11] in most solvents (methanol being an exception),[9,10] the meso dibromide giving only *trans*-stilbene and the *dl* dibromide giving 88–96% *cis*-stilbene, suggesting that the elimination is largely anti. From this it might be assumed that the major course of the *dl* dibromide elimination with iodide proceeds by the same mechanism as the elimination from the meso dibromide, whatever that mechanism may be.[10] (2) The meso dibromide reacts 323 times as fast as the *dl* one in DMF at 36 °C,[3] implying a difference in activation energy of 3.5 kcal/mol (14.8 kJ/mol). (3) The equilibrium constant for the meso and *dl* dibromides in benzene is 3.0 at 80 °C, implying a $\Delta G°$ of 0.77 kcal/mol (3.2 kJ/mol) favoring the meso isomer.[12] (4) *trans*-Stilbene is more stable (vide supra) than *cis*-stilbene by $\Delta G°$ = 3.7 kcal/mol (15.5 kJ/mol) at 27 °C (hydrocarbon solvent).

From these data it was concluded[10] that, since the energy differences between the starting materials were small but those between the products much larger, the large difference in activation energy—which was nearly the same as the difference in product free energy—suggested that the transition state in this reaction was product-like. However, this conclusion must be accepted with some caution, as will be explained in the sequel.

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