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STEREOCHEMICAL MICELLAR KINETIC DIFFERENTIATION: FACTS OR ARTIFACTS?

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The study of micelle catalyzed organic reactions[1,2] and, in particular, micellar stereochemical processes,[3] due to the analogy postulated between enzymes and micelles,[4] has become an area of increasing interest. The recent observation of Bunton *et al.*[5] that (*R*)- and (*S*)-*p*-nitrophenyl O-methylmandelates (I) are saponified in borate buffers in the presence of cetyltrimethyl ammonium bromide (CTABr) at identical rates while the (*R*/*S*) mixture is saponified at a rate greater than either the (*R*)- or (*S*)-enantiomer is thus of extreme importance in its implications on the nature of micellar catalysis.

Possible chiral substrate-micelle interactions are summarized in the Table. Enantiomeric substrates must interact and/or react with achiral micelles in enantiomeric modes, *i.e.*, at kinetically identical rates. The interaction and/or reaction of enantiomeric substrates with chiral micelles or of diastereomeric substrates with either achiral or chiral micelles must occur in diastereomeric modes, *i.e.*, at kinetically non-identical rates.[6]

TABLE

Chiral Substrate-Micelle Interactions

Substrates/Micelle	Achiral	Chiral
enantiomers	enantiomeric	diastereomeric
diastereomers	diastereomeric	diastereomeric

The observations of Bunton *et al.*[5] are readily explicable within this framework: since (*R*)- and (*S*)-I react at identical rates in the CTABr system they obey the enantiomeric substrate-achiral micelle relationship, indicating no possible micellar chirality on the reaction time scale. The non-identical rates for racemic and optically pure ((*R*) or (*S*)) I are encompassed only by the diastereomeric substrate-achiral micelle relationship, *i.e.*, aggregation of substrate molecules (*RR* or *SS* *vrs.* *RS*) on a finite kinetic time scale. Such lengthy interactions are heretofore unprecedented, although on the nmr time scale they have been observed.[7]

Reinvestigation of the saponification of (*R/S*)- and (*R*)-I in sodium tetraborate decahydrate buffer (0.01 molar) and CTABr (0.5-8.0 x 10^{-3} molar) or CTACl (1.0-8.0 x 10^{-3} molar) indicates that the rates of saponification of both the racemic and optically pure esters proceed, within experimental error, at identical rates (k_ψ^{max} 1.4 x 10^{-1} sec^{-1} at 3 x 10^{-3} molar CTABr at one month and 1.1 x 10^{-1} sec^{-1} at 4 x 10^{-3} molar CTACl at two months (*vide infra*)).[8] At other concentrations of micelle similar results are obtained ((CTABr) x 10^3 molar, k_ψ x 10^2 (*R* ester) sec^{-1}, k_ψ x 10^2 (RS ester) sec^{-1}; at one month: 1.0, 11.1 ± 0.3, 10.9 ± 0.4; 4.0, 11.4 ± 0.2, 11.8 ± 0.8; at ten months: 0.5, 2.0 ± 0.1, 2.1 ± 0.1; 4.0, 5.3 ± 0.4, 5.0 ± 0.5). (Errors of the orders of magnitude reported herein correspond to errors in the determination of $t_{1/2}$ of less than one second or errors in the determination of A_t of *ca.* 0.001 absorbancy unit.) Thus, the previous claim for stereochemical differentiation and the suggestion[5] that chiral substrate interactions must be considered in this case is not substantiated.

A possible explanation for the previously reported[5] stereochemical differentiation was discovered during the course of this work: the individual values of k_ψ at fixed micelle concentrations are dependent on the age of the micelle-buffer solution. Thus, k_ψ at 1 x 10^{-3} molar CTABr is 10.9 ± 0.4 x 10^{-2} sec^{-1} after one month and 2.0 ± 0.1 x 10^{-2} sec^{-1} after ten months. The corresponding values at 4 x 10^{-3} molar CTABr are 11.4 ± 0.2 x 10^{-2} sec^{-1} and 5.31 ± 0.42 x 10^{-2} sec^{-1} at 1 and 10 months, respectively. Corresponding runs on freshly recrystallized active and racemic esters were all performed within a matter of days in the present work.

We are currently investigating the nature of this time dependency in micelle catalyzed (CTABr and CTACl) saponification reactions; preliminary indications are that neither carbon dioxide uptake nor microbial degradation of micelle solutions is responsible for the observed time dependency.

FOOTNOTES AND REFERENCES

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8. Reactions performed on a Gilford Model 2400S thermostatted at 25.00 ± 0.05° at 400 nm (p-$NO_2C_6H_4O^-$ appearance). Final substrate concentration 1.4 x 10^{-5} molar in 0.5 vol % purified p-dioxane. (R/S)-I, mp 48-49°,

lit:[5] 46-48°; (R)-I, mp 54-55°, $[\alpha]_D^{25}$ -111.7 ± 1.6° (c 1.5, 95% ethanol), lit:[5] 49-50°; CTABr, mp 239-241° dec., lit:[9] 227-235° dec., CTACl, mp 232-233° dec., lit:[10] 240°. Each kinetic run performed a minimum of three times, correlation coefficients for individual runs 0.99 or greater.

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