scribed as a half-chair conformation with C-11 and C-12 being 0.24 and 0.47 Å on opposite sides of the best plane (average deviation 0.06 Å) through the other four atoms. The C-11═O-32 carbonyl group points to the β side of the molecule. There are considerable distortions from planarity about the conjugated 1,4-diketone portion of the molecule with torsion angles as great as 32.4°. The dispositions of the C-3═O-15 and C-14═O-40 carbonyl groups are such that they do not bisect the bonds to the geminal disubstituents on the adjacent carbon atoms.

Barbatusin seems to be related biosynthetically to the ferruginol class of diterpenes[4] as well as to a number of quinonoid diterpenes isolated from various sources,[3,5] in particular from *Labiatae* species,[6] with the rare feature of containing a methylcyclopropyl ring at the C-13 atom.[7] In view of the reactivity of the cyclopropane molecule, barbatusin may represent an interesting and unusual intermediate in the biosynthesis of some naturally occurring quinonoid diterpenes.[8,9]

Acknowledgment. Two of us (A. H.-J. Wang and I. C. Paul) thank the National Institutes of Health for support through Grant No. GM-19336. One of us (R. Zelnik) is grateful to the Conselho Nacional de Pesquisas for Research Grant No. 10.468/68 and thanks Dr. Daniel Watts for helpful discussions.

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(8) P. Rüedi and C. H. Eugster, *Helv. Chim. Acta*, **55**, 1994 (1972).

(9) The final values for the atomic coordinates, thermal parameters, and observed and calculated structure factors will appear following these pages in the microfilm edition of this volume of this journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JACS-73-598.

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Dramatic Rate Enhancement of the Aquation of the Tris(oxalato)chromate(III) Anion by Surfactant Solubilized Water in Benzene

Sir:

Racemization, aquation, and ligand-exchange reactions of tris(oxalato)chromate(III) anion, $Cr(C_2O_4)_3{}^{3-}$, have been discussed in terms of a "one-ended dissociation"[1-3] (Scheme I). The subsequent fate of the octahedral site on the metal ion vacated by such a dissociation, however, has not been unequivocally established. One school favors a rate determining step which involves the synchronous Cr–O bond breaking and nucleophilic attack by water (path A)[2,3] while there are arguments in support of an alternative mechanism in which the octahedral site remains vacant during the Cr–O bond breaking (path B).[1,4] Kinetic investigations of the dependence of the aquation rate on water concentration would provide sufficient evidence to allow a distinction between these alternative pathways. Since the uncatalyzed rate of aquation for the $Cr(C_2O_4)_3{}^{3-}$ is extremely slow (there is only 9.4% conversion to *cis*-$Cr(C_2O_4)_3(H_2O)_2{}^-$ in 522 hr at 47 °[1c]), such an investigation is not feasible. To overcome this problem we have localized $Cr(C_2O_4)_3{}^{3-}$ and water in the hydrophilic cavity of surfactant aggregates dissolved in benzene. In this system we not only find rate enhancements of the "neutral" rate by factors up to 5×10^6 with respect to that in water but can precisely control the concentrations of both water and $Cr(C_2O_4)_3{}^{3-}$.

Aquation of $Cr(C_2O_4)_3{}^{3-}$ has been investigated in water solubilized by surfactant aggregates of octylammonium tetradecanoate (OAT), dodecylammonium propionate (DAP), and hexadecyltrimethylammonium butyrate (CTABu) in benzene.[6] Typical rate profiles of pseudo-first-order rate constants, k_ψ, against surfactant concentration are shown in Figure 1.[9] The rate constant for aquation of $Cr(C_2O_4)_3{}^{3-}$ to *cis*-$Cr(C_2O_4)_2$-

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(1) (a) C. A. Bunton, J. H. Carter, D. R. Llewellyn, C. J. O'Connor, A. L. Odell, and S. Y. Yih, *J. Chem. Soc.*, 4615 (1964); (b) C. A. Bunton, J. H. Carter, D. R. Llewellyn, A. L. Odell, and S. Y. Yih, *ibid.*, 4622 (1964); (c) D. R. Llewellyn, C. J. O'Connor, A. L. Odell, and R. W. Olliff, *ibid.*, 4627 (1964).

(2) R. E. Hamm, *J. Amer. Chem. Soc.*, **75**, 609 (1953).

(3) K. Krishnamurty and G. M. Harris, *J. Phys. Chem.*, **64**, 346 (1960).

(4) Indirect support for path B came from the inertness[5] of the coordinated water of the *cis*-diaquobisoxalatochromate(III) anion, $Cr(C_2O_4)_2(H_2O)_2{}^-$. The one-ended dissociation of $Cr(C_2O_4)_3{}^{3-}$ must be reversible in order to allow the other end to dissociate. If the vacant octahedral site were aquated, this water would necessarily be labile, contrary to the behavior of $Cr(C_2O_4)_2(H_2O)_2{}^-$.

(5) J. Aggett, I. Mawston, A. L. Odell, and B. E. Smith, *J. Chem. Soc. A*, 1413 (1968).

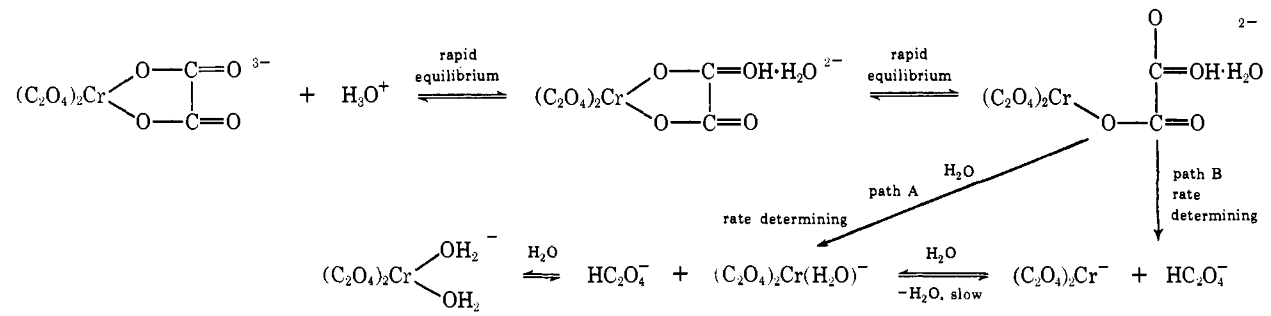
(6) Formation of OAT, DAP, and CTABu aggregates, containing three to seven monomers, has been demonstrated in benzene by ^1H nmr investigations. Changes in the appropriate proton magnetic resonance frequencies as functions of surfactant concentration established that the polar carboxyl and ammonium groups are located at the interior of the aggregates while the hydrophobic hydrocarbon chains are in contact with the nonpolar benzene. In keeping with current terminology[7] we have called these aggregates "reversed" or "inverted" micelles. The concentration at which aggregation occurs, *i.e.*, the critical micelle concentration or cmc, for OAT, DAP, and CTABu in benzene has been determined to be $(1.9\text{–}2.2) \times 10^{-2}$, $(3\text{–}7) \times 10^{-3}$, and 1.4×10^{-3} *M*, respectively.[8]

(7) S. I. Ahmad and S. Friberg, *J. Amer. Chem. Soc.*, **94**, 5196 (1972); S. Friberg and S. I. Ahmad, *J. Phys. Chem.*, **75**, 2001 (1971).

(8) E. J. Fendler, J. H. Fendler, R. T. Medary, and V. A. Woods, *Chem. Commun.*, 1497 (1971); J. H. Fendler, E. J. Fendler, R. T. Medary, and V. A. Woods, *J. Amer. Chem. Soc.*, **94**, 7288 (1972); E. J. Fendler, S, A. Chang, J. H. Fendler, R. T. Medary, O. A. El Seoud, and V. A. Woods in "Reaction Kinetics in Micelles and Membranes," E. H. Cordes, Ed., Plenum Press, New York, N. Y., 1972; J. H. Fendler, E. J. Fendler, R. T. Medary, and O. A. El Seoud, *J. Chem. Soc., Faraday Trans. 1*, in press.

(9) Rate measurements were carried out by following the decrease in absorbance at 416 nm spectrophotometrically. Reactions were initiated by injecting known volumes (5–20 μl) of aqueous solutions of $K_3[Cr(C_2O_4)_3] \cdot 3H_2O$ to thermostated surfactant solutions (5 ml) in carefully dried benzene. Good first-order plots were obtained in all cases up to 90% reaction. The product of the reaction was identified as $Cr(C_2O_4)_2(H_2O)_2{}^-$ from its known spectrum.[2] k_ψ was independent of substrate concentration in the range $(1\text{–}20) \times 10^{-4}$ *M*.

Scheme I



$(H_2O)_2^-$ in the presence of 1.1×10^{-1} *M* water solubilized in 7.58×10^{-2} *M* OAT in benzene at 24.5° ($k_\psi = 8.1 \times 10^{-3}$ sec^{-1}) is a factor of 5×10^6 greater than that in aqueous solution at the same temperature[10] ($k_\psi = 1.5 \times 10^{-9}$ sec^{-1} estimated from the available data at 47°[1c] using the Arrhenius parameters for the acid-catalyzed rate[1b]). The magnitude of the rate in the micelle solubilized water is even greater than that obtained in 3.5 *M* $HClO_4$[1b] (for purposes of comparison, the rate profile for the acid-catalyzed aquation is also included in Figure 1). Increasing concentration of surfactant at a given water concentration causes an exponential decrease in the rate (Figure 1). In DAP, plots of log k_ψ *vs.* log [DAP] are linear with negative slopes but the values approach zero with increasing water concentration.[11]

The concentrations of DAP used are at least 100-fold greater than the cmc[6] and hence if all the micellar aggregates were saturated with water, one would observe k_ψ to be independent of surfactant concentration. Analogous behavior has been observed in micellar catalyses in aqueous solutions.[12] The concentrations of OAT used are, however, less than ten times greater than the cmc,[6] and thus the observed catalysis might be in the region where one would expect sigmoidal dependence of the rate on the surfactant concentration in a water saturated micellar system. Consequently the results in OAT cannot be interpreted analogously to those in DAP.

At constant surfactant concentration (in the range of surfactant concentration where the surfactant concentration–rate profile is nearly linear) the rate constants for the aquation of $Cr(C_2O_4)_3^{3-}$ exhibit a linear dependence on the concentration of water (insert in Figure 1). This result is only compatible with the synchronous breaking of the Cr–O bond and the nucleophilic attack of water. Thus, in an environment where water is solubilized by surfactant aggregates, mechanism A prevails.[13]

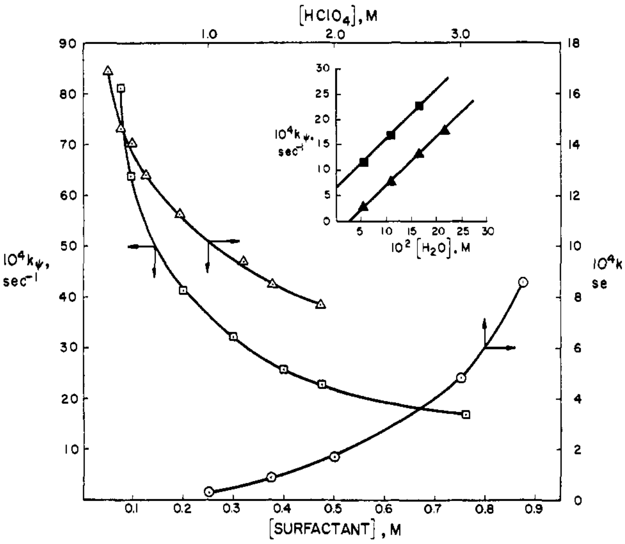


Figure 1. Rate constants of aquation of $Cr(C_2O_4)_3{}^{3-}$ to *cis*-$Cr(C_2O_4)_3(H_2O)_2{}^-$ by surfactant solubilized water (1.1×10^{-1} *M*) in benzene at 24.5°: (⊡) OAT, (△) DAP, and (⊙) data from ref 1b for aquation in aqueous $HClO_4$ at 25°. Insert: rate constants for aquation as a function of water concentration (■, 0.759 *M* OAT; ▲, 0.473 *M* DAP).

The observed rate enhancement for aquation is clearly not simply the result of favorable partitioning of the substrate between the nonpolar benzene and polar surfactant interior since the rate of aquation of $Cr(C_2O_4)_3^{3-}$ is considerably greater in the present media than that in water (by a factor at least 5×10^6; *vide supra*) and that in benzene.[14] Since the aquation is acid catalyzed, the rate being dependent on $-H_0$,[1b] the dramatic rate enhancement reported here is most likely the consequence of hydrogen bonding between the oxygen atoms of the substrate and the ammonium ion of the surfactants thereby facilitating proton transfer and increasing the concentration of the one-ended dissociated species in the preequilibria steps. The apparent proton donating ability of OAT and DAP is of the same magnitude as that of concentrated aqueous solutions of mineral acids. The lack of aquation in water solubilized by CTABu in benzene,[14] a surfactant in which proton donation from the trimethylammonium ion is of course unfeasible, substantiates this interpretation. It is also probable that the effective activity of water is greatly increased in the hydrophilic center of the surfactant aggregate[15] thereby contributing to the overall rate enhancement *via* acceleration of the rate-determining step. The reason for the apparent self-inhibition by the surfactant at constant water concentration, but increasing surfactant concentration (*i.e.*, in-

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[10] The limiting factor in the observed rate enhancement is the solubilization of water by the surfactant in benzene. At lower concentrations of surfactant the water is not solubilized and therefore we cannot measure the rate at concentrations ≤ cmc, where the rate enhancement may be even greater.

[11] Values of d log k_ψ/d log [DAP] are −0.61, −0.34, and −0.25 for water concentrations of 5.5, 11, and 16.5 $\times 10^{-2}$ *M*, respectively.

[12] E. H. Cordes and R. B. Dunlap, *Accounts Chem. Res.*, 2, 329 (1969); E. J. Fendler and J. H. Fendler, *Advan. Phys. Org. Chem.*, **8**, 271 (1970); T. C. Bruice in "The Enzymes," Vol. 2, 3rd ed, Academic Press, New York N. Y., 1970, p 217; H. Morawetz, *Advan. Catal.* 20, 341 (1969).

[13] This environment, of course, may differ appreciably from that of bulk water.

[14] A saturated solution of $K_3[Cr(C_2O_4)_3] \cdot 3H_2O$ in DMSO (5 μl) added to 5.0 ml of 0.091 *M* CTABu in benzene or to 5.0 ml of pure benzene produced no change in the visible spectrum at 39.8° for 6 hr.

[15] F. M. Fowkes in "Solvent Properties of Surfactant Solutions," K. Shinoda, Ed., Marcel Dekker, New York, N. Y., 1967, p 67.

creasing concentration of surfactant aggregates) is that once the micelles are saturated with water additional surfactant simply results in a decrease in the effective water concentration per micelle and consequently a decrease in the rate-determining step *via* path A (Scheme I).

We are currently investigating the physical properties of water localized in the hydrophilic cavity of surfactant aggregates in nonpolar solvents as well as catalysis of mechanistically diverse reactions in these media.

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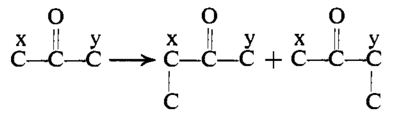
A Method for the Regiospecific Synthesis of Mannich Bases. Reaction of Enol Borinates with Dimethyl(methylene)ammonium Iodide

Sir:

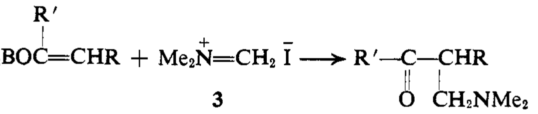
Several valuable indirect solutions have been developed (among others, enamines,[1] trimethylsilyl enol ethers,[2,3]) to thwart the serious synthetic restrictions which accompany attempts at site-specific α-alkylation of ketones (eq 1). In general, this methodology requires the initial conversion of a parent unsymmetrical ketone to a suitable derivative, and also requires the specific formation of one of two possible enol(ate)s. As a result, unless the influence of certain determinate factors prevails (steric, thermodynamic, etc.), isomeric mixtures of derivatives (and products) may also be encountered.[3]



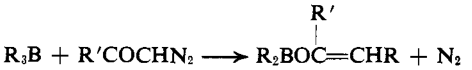
$$\overset{x}{\mathrm{C}}-\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\overset{y}{\mathrm{C}} \longrightarrow \underset{\mathrm{C}}{\overset{x}{\mathrm{C}}}-\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\overset{y}{\mathrm{C}} + \overset{x}{\mathrm{C}}-\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\underset{\mathrm{C}}{\overset{y}{\mathrm{C}}} \qquad (1)$$

1 2

An alternative approach which we wish to describe, and document for the preparation of certain Mannich bases, involves *the initial and unequivocal preassembly of the necessary (masked carbonyl) carbon skeleton, such that subsequent unidirectional α-substitution is ensured.* The "Mannich reagent," dimethyl(methylene)ammonium iodide[4] (**3**), reacts with enol borinates to provide excellent yields of β-dimethylamino ketones (eq 2), and, under the mild experimental conditions employed, in no case was there evidence for formation of the positional isomer (*e.g.*, **1** ⇄ **2**). The necessary enol borinates need not be isolated—THF solutions of these intermediates are easily and unambiguously obtained by the reaction of trialkylboranes with α-diazo ketones[5,6] (eq 3). This simple one-flask method thus efficiently permits the regiospecific construction of certain Mannich bases, uncomplicated by problems associated with the Mannich condensation.[7]

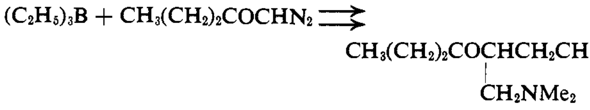


$$\mathrm{R_2BO\overset{R'}{C}{=}CHR + \underset{\mathbf{3}}{Me_2\overset{+}{N}{=}CH_2}\,\bar{I} \longrightarrow R'{-}\underset{O}{\underset{\|}{C}}{-}\underset{CH_2NMe_2}{CH}R} \qquad (2)$$



$$\mathrm{R_3B + R'COCHN_2 \longrightarrow R_2BO\overset{R'}{C}{=}CHR + N_2} \qquad (3)$$

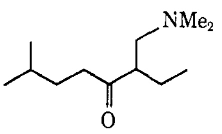
For example, sequential treatment of a THF solution of triethylborane with diazomethyl *n*-propyl ketone (in THF), followed (after nitrogen evolution ceased) by 1.15 equiv of salt **3** (in DMSO), afforded after a hydrolytic work-up a 91% yield of 3-dimethylaminomethyl-4-hexanone (methiodide, 87%, mp 110–111.5°) (eq 4).



$$\mathrm{(C_2H_5)_3B + CH_3(CH_2)_2COCHN_2 \rightrightarrows CH_3(CH_2)_2CO\underset{CH_2NMe_2}{CH}CH_2CH_3} \qquad (4)$$

Cosolvent DMSO is crucial to the success of the reaction. In its absence only inconsequential amounts (*cs.* 5–10%) of Mannich bases could be isolated. Other examples are illustrated in Table I.

By similar methodology the "isomeric set" of Mannich bases **4** and **5** were synthesized[9]—conversions



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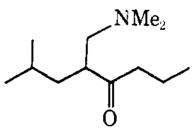

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which would (at best) be ambiguous to accomplish using the Mannich condensation.[7]

Enol borinates are also intermediates in the "conjugate additions" of organoboranes to a variety of α,β-unsaturated ketones and aldehydes.[10] We investigated this route by generating the enol borinate de-

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(1) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

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(3) An extensive discussion and review of methods appears in H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 9.

(4) J. Schreiber, H. Maag, N. Hashimoto, and A. Eschenmoser, *Angew. Chem., Int. Ed. Engl.*, 10, 330 (1971).

(5) J. Hooz and S. Linke, *J. Amer. Chem. Soc.*, **90**, 6891 (1968); J. Hooz and D. M. Gunn, *ibid.*, **91**, 6195 (1969); J. Hooz and G. F. Morrison, *Can. J. Chem.*, **48**, 868 (1970); J. Hooz and J. N. Bridson, *ibid.*, 50, 2387 (1972).

(6) For isolation of these intermediates, see D. J. Pasto and P. W. Wojtkowski, *Tetrahedron Lett.*, 215 (1970).

(7) The Mannich condensation (using unsymmetric ketones) usually gives rise to isomeric mixtures, and reports regarding the constitution of the major product have been the source of several revisions.[8] Although it usually corresponds to substitution at the most highly substituted (*i.e.*, most stable) enol, some *predictive* uncertainty nonetheless exists. The major Mannich product (63% yield) from methyl isobutyl ketone (using CH_2O and diethylamine hydrochloride), for example, is 1-diethylamino-5-methyl-3-hexanone.[8c]

(8) (a) M. Brown and W. S. Johnson, *J. Org. Chem.*, 27, 4706 (1962); (b) H. O. House and B. M. Trost, *ibid.*, **29**, 1339 (1964); (c) T. A. Spencer, D. S. Watt, and R. J. Friary, *ibid.*, **32**, 1234 (1967); (d) G. L. Buchanan, A. C. W. Curran, and R. T. Wall, *Tetrahedron*, **25**, 5503 (1969).

(9) Yields of **4** and **5** are 90 and 60%, respectively, but isolation in pure form is complicated by concurrent formation of the respective conjugated enones.

(10) A. Suzuki, A. Arase, H. Matsumoto, M. Itoh, H. C. Brown, M. M. Rogić, and M. W. Rathke, *J. Amer. Chem. Soc.*, **89**, 5708 (1967); H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **89**, 5709 (1967); H. C. Brown, G. W. Kabalka, M. W. Rathke, and M. M. Rogić, *ibid.*, 90, 4165 (1968); H. C. Brown, M. W. Rathke, G. W. Kabalka, and M. M. Rogić, *ibid.*, **90**, 4166 (1968); H. C. Brown and G. W. Kabalka, *ibid.*, **92**, 712, 714 (1970); H. C. Brown and E. Negishi, *ibid.*, **93**, 3777 (1971).