of the epoxy alcohol moiety to the metal center allows the hydroxy group to attack the epoxide in "endo-mode" rather than in "exo-mode" due to preferential polarization of the carbon–oxygen bond of C-2 position as in **14**.[22]

The next phase of our efforts involved introduction of the requisite C-2 side chain and inversion of the C-3 chiral center. Debenzylation of **7** followed by selective protection as its acetonide afforded the acetonide **15**. Upon sequential dehydration, ozonolysis, Wittig reaction,[23] and deprotection,[9d] **15** yielded the α,β-unsaturated ester **17**. According to the method developed by Yamamura and co-workers,[3,9d] the C-3 hydroxyl group of **17** was then inverted through the oxidation–reduction sequence to give the diol **18**. The diol **18** thus obtained was identical in every respect (^{1}H NMR, IR, MS, αD, mp) with the authentic sample which we have previously prepared.[9g] Since **18** has already been converted to (+)-citreoviral (**19**),[9g] a key intermediate in the synthesis of (−)-citreoviridin (**2**),[9a,c] the synthesis of **18** constitutes a formal synthesis of (−)-citreoviridin (**2**) as well as (+)-citreoviral (**19**).

Having established the method for the construction of the properly functionalized tetrahydrofuran unit, the synthesis of verrucosidin (**1**) was then investigated. Hydrolysis of the tetrahydrofuran **10** gave the triol **20** which was converted to the acetonide ester **21**[24] in the same manner as described for the preparation of **16**. Successive deprotection, inversion of the C-3 hydroxyl group, and formation of the epoxide through mesylation served to transform **21** to the epoxy ester **24**.

The epoxy ester **24** was successively subjected to reduction and oxidation to afford the aldehyde **25**. Aldol reaction of **25**[25] with the lithium enolate of the ketone **26**,[26] generated through the action of lithium hexamethyldisilazide, gave the aldol **27** as an inseparable diastereoisomeric mixture. Upon dehydration followed by desilylation, **27** yielded the enone **28** as a sole product. Reduction of **28** with LAH at −90 °C proceeded stereoselectively to give an inseparable 4:1 epimeric mixture[21] of the diol **29**. Finally, mesylation[28] of this epimeric mixture of **29** directly furnished (+)-verrucosidin (**1**) and its stereoisomer **30** in a ratio[21] of 2:3.[29] The synthetic substance, mp 90–92 °C, $[\alpha]^{26}$D +92.9° (*c* 0.42, MeOH), was identical with natural verrucosidin (**1**), mp 90–91 °C, $[\alpha]^{26}$D +92.4° (*c* 0.25, MeOH), by spectroscopic (^{1}H and ^{13}C NMR, IR, MS, UV) and chromatographic comparisons. It is worthwhile to mention that acid treatment of **30** followed by mesylation afforded a 1:3 mixture[21] of verrucosidin (**1**) and **30** giving the procedure for recycling **30**.

Acknowledgment. We are grateful to Professor Shosuke Yamamura, Keio University, for providing spectra of synthetic intermediates. We also thank Professor Thomas M. Harris, Vanderbilt University, for a generous gift of natural verrucosidin and its ^{1}H NMR spectrum.

(22) For Lewis acid mediated nucleophilic opening of epoxy alcohols, see: Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557. Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1987**, *109*, 576.

(23) Ireland, R. E.; Norbeck, D. W. *J. Org. Chem.* **1985**, *50*, 2198.

(24) The corresponding methyl ester, $[\alpha]^{18}$D +25.6° (*c* 0.72, $CHCl_3$) [lit.[3] +23.6° (*c* 1.04, $CHCl_3$)], prepared by ester exchange reaction of **21** (KOH, MeOH), exhibited spectra properties (^{1}H NMR, IR, MS) in accord with those of the authentic methyl ester prepared by Yamamura and co-workers.[3]

(25) White, C. T.; Heathcock, C. H. *J. Org. Chem.* **1981**, *46*, 191.

(26) The ketone **26** was prepared in enantiomerically pure form from 6-ethyl-4-hydroxy-3,5-dimethyl-2-pyrone[27] (15 steps, 20% overall). Details of the synthesis will be reported in due course.

(27) Osman, M. A.; Seibl, J.; Pretsch, E. *Helv. Chim. Acta* **1977**, *60*, 3007.

(28) Upon mesylation (MsCl, *n*-BuLi, THF, −78 °C), retro-aldol reaction took place to give (−)-verrucosal (74%), $[\alpha]^{27}$D −28.6° (*c* 0.30, MeOH) [lit.[2] $[\alpha]^{27}$D −23.5° (*c* 0.40, MeOH)], whose spectral properties (^{1}H NMR, IR, MS) were identical with those reported.[2]

(29) Reduction of **28** with $NaBH_4$–$CeCl_3$[30] at −30 °C in methanol proceeded with opposite stereoselectivity giving a 1:4 epimeric mixture[21] of **29** (96%) which, upon mesylation, gave **1** and **30** in a ratio[21] of 1:5 (70%). These results suggest that the epoxide formation should involve not only the S_N2 type of reaction pathway but also a solvolytic reaction pathway where the isomer **30** would be produced preferentially. On the basis of this mechanistic consideration, we assumed that the major isomer of the LAH reduction of **28** might be the anti isomer.

(30) Luche, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.

Supplementary Material Available: Optical rotations and spectral and analytical data for **4**, **5**, **7–13**, **15–18**, **21–24**, **26**, **28**, and **30** (4 pages). Ordering information is given on any current masthead page.

On the Water Content of Micelles: Infrared Spectroscopic Studies[1]

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While experimental and theoretical studies[2–7] continue to advance our understanding of micellar structure, the question of water penetration into the micellar interior remains somewhat unsettled.[8,9] Recent calculations[3] show that even though water molecules penetrate deeply into micelles, the central core is devoid of water. In this communication, direct experimental evidence is presented which confirms the recent calculations on micelles of sodium octanoate: these micelles do contain a central core devoid of water, while at the same time water penetrates at least up to position 7 of the octanoate chain.

Infrared spectroscopy is well suited to detect hydrogen bonding.[10–13] In particular, such an interaction between a carbonyl group (acceptor) and water (donor) is used here to detect the presence of water in micelles. Sodium 7-oxooctanoate (7-oxo-Na-C_8)[14] is the "probe", and the C=O stretching band of the keto group is used as the "sensor". There are many advantages in using a molecule such as sodium 7-oxooctanoate as the probe; e.g., it is a surfactant by itself;[15] its cmc (≈0.25 M) is similar to that of Na-C_8; the C=O group in keto surfactants has been shown to provide a realistic measure of the polarity of the environment of micelles[17] and lipid bilayers;[18] and it may be safely assumed that individual molecules of 7-oxo-Na-C_8 are able to adopt all conformations adopted by those of Na-C_8.

(1) Issued as NRCC publication no. 29042.

(2) Szleifer, I.; Ben-Shaul, A.; Gelbart, W. M. *J. Chem. Phys.* **1986**, *85*, 5345–5358.

(3) Watanabe, K.; Ferrario, M.; Klein, M. L. *J. Phys. Chem.* **1988**, *92*, 819–821.

(4) Menger, F. M. *Acc. Chem. Res.* **1979**, *12*, 111–117.

(5) Dill, K. A.; Koppel, D. E.; Cantor, R. S.; Dill, J. D.; Bendedouch, D.; Chen, S. H. *Nature (London)* **1984**, *309*, 42–45.

(6) Menger, F. M.; Bonicamp, J. M. *J. Am. Chem. Soc.* **1981**, *103*, 2140–2141.

(7) Menger, F. M.; Doll, D. W. *J. Am. Chem. Soc.* **1984**, *106*, 1109–1113.

(8) Villalain, J.; Gomez-Fernandez, J. C.; Prieto, M. J. E. *J. Colloid Interface Sci.* **1988**, in press.

(9) Faure, A.; Tistchenko, A. M.; Chachaty, C. *J. Phys. Chem.* **1987**, *91*, 1827–1834.

(10) Bellamy, L. J. *Advances in Infrared Group Frequencies*; Methuen and Company: London, 1968.

(11) Pimentel, G. C.; McClellan, A. L. *The Hydrogen Bond*; W. H. Freeman: San Francisco, 1960.

(12) Joesten, M. D.; Schaad, L. J. *Hydrogen Bonding*; Marcel Dekker: New York, 1974.

(13) Hallam, H. E. In *Infrared Spectroscopy and Molecular Structure*; Davies, M., Ed.; Elsevier: Amsterdam, 1963.

(14) 7-Oxooctanoic acid was prepared by alkaline (60% KOH) treatment of 2-acetylcyclohexanone and characterized by its infrared, NMR, and mass spectra.

(15) The cmc of 7-oxo-Na-C_8 (≈0.25 M) was determined from the changes in its infrared spectrum as a function of concentration:[16] Casal, H. L., to be published.

(16) Umemura, J.; Mantsch, H. H.; Cameron, D. G. *J. Colloid Interface Sci.* **1981**, *83*, 558–568.

(17) Menger, F. M.; Jerkunica, J. M.; Johnston, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 4676–4678.

(18) Menger, F. M.; Aikens, P.; Wood, M., Jr. *J. Chem. Soc., Chem. Commun.* **1988**, 180–181.

0002-7863/88/1510-5203$01.50/0 Published 1988 by the American Chemical Society

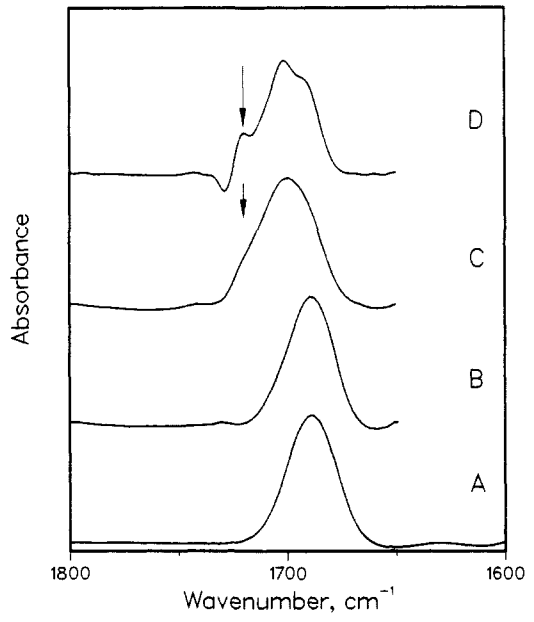

Figure 1. Infrared spectra (1800–1600 cm^{-1}) of the following: A, sodium 7-oxooctanoate (0.92 M in D_2O); B, sodium octanoate (1.56 M) and sodium 7-oxo-octanoate (0.11 M) in D_2O; C, sodium octanoate (1.60 M) and 5-nonanone (0.09 M) in D_2O; and D, result of deconvolution of the spectrum shown in C, a Lorentzian line shape of 15 cm^{-1} full width at half height was deconvoluted by using a resolution enhancement factor of 2.

Figure 1 shows infrared spectra[19,20] (1800–1600 cm^{-1}) of micelles of 7-oxo-Na-C_8 (part A) and micelles of Na-C_8 containing 7-oxo-Na-C_8 (part B). The concentration of surfactant in these samples was ca. 4 times the cmc in order to ensure that the molecules are mainly micellar. In both cases (Figure 1 (parts A and B)), there is only one band[21] at 1689 cm^{-1}, typical of the C=O group of 7-oxo-Na-C_8 bound to water.[22] These two spectra indicate that in the interior of micelles of Na-C_8 and 7-oxo-Na-C_8 there is enough water to engage in hydrogen bonding to all of the C=O groups at position 7. Of course, it could be argued that the 7-oxo-Na-C_8 molecules come out of the micelles, engage in hydrogen bonding to the solvent, and then "drag" the water molecules inside thereby modifying the micelle. If this were the case, the infrared bands of C=O groups would not provide a reliable measure of water penetration. However, spectra of ketones as guests in micelles demonstrate the utility of these carbonyl groups. In the infrared spectrum of Na-C_8 micelles mixed with 5-nonanone (Figure 1C) the bands observed are due to the C=O stretching mode of the guest ketone. After band narrowing,[23] three bands are apparent at 1720, 1701, and 1692 cm^{-1} (Figure 1D). Previous work[26] has shown that the band at 1720 cm^{-1}, marked with ↓, is due to nonbound ketone, while the bands at 1701 and 1692 cm^{-1} are due to the ketone bound to water. Thus, the spectrum of the guest ketone demonstrates the *coexistence* of at least two micellar regions; one is devoid of water while the other contains water. The relative intensities[27] of the bands due to "bound" and "free" C=O groups, I_{bound}/I_{free} is 8.0. This number gives a relative measure of water penetration, increasing as more water penetrates and binds to the C=O groups.

In the case of the guest ketone (5-nonanone) the exact location of the keto group in the micelle is not known compared to the case of 7-oxo-Na-C_8. It is safe to assume that molecules of 7-oxo-Na-C_8 occupy all the same positions that Na-C_8 molecules do; they are able to adopt the very same conformations, undergo the same amount of coiling, etc. Molecules of 5-nonanone may also adopt all the same conformations as 7-oxo-Na-C_8, but because they lack a polar carboxylate group they have one more degree of freedom: they can reside in the center of the micelle (either curled up or spanning the center). This turns out to be an advantage here; the only difference between spectra of 7-oxo-Na-C_8 as guest and 5-nonanone as guest is the appearance of "free" nonbound C=O groups. Therefore, this is a clear demonstration that the inner core or center of Na-C_8 micelles does not contain any water which can hydrogen bond to the keto group of 5-nonanone. The high value of I_{bound}/I_{free} measured from the spectra of 5-nonanone in Na-C_8 micelles shows that most of the ketone is bound and therefore the water-free micellar region must be small.

Experiments with micelles formed by molecules with longer chains such as sodium dodecanoate, SDS, and Triton X-100 yielded the same general results,[28] supporting the conclusions reached with micelles of Na-C_8. In all cases, the C=O stretching of 7-oxo-Na-C_8 showed that *all* the keto groups were hydrogen bonded, while the C=O stretching of a guest ketone (7-tridecanone for the longer surfactants) showed coexistence of at least two environments: one with and one without water. For example, I_{bound}/I_{free} for 7-tridecanone in sodium dodecanoate at 46 °C is 2.0 and I_{bound}/I_{free} = 3.0 for 7-tridecanone in SDS at 45 °C, while it is only 0.8 for 7-tridecanone in Triton X-100. The values of I_{bound}/I_{free} are dependent on the chain length and nature of the head group of the surfactant. I_{bound}/I_{free} decreases as the chain length increases implying a larger central region devoid of water. The difference in I_{bound}/I_{free} for micelles of SDS and Na-C_{12} correlates with the recently found differences in chain conformation for these two types of surfactants.[29] Infrared spectra of sodium 5-oxostearate and sodium 12-oxostearate were also recorded (0.5 M solutions in D_2O at 85 °C). In the spectrum of 5-oxo-Na-C_8 only one C=O band at 1698 cm^{-1} was observed showing that water binds to all of the C=O groups at position 5. The spectrum of 12-oxo-Na-C_{18} shows two bands at 1720 and 1700 cm^{-1} due to the C=O group at position 12. In this case not all of the C=O groups are hydrogen bonded; the parameter I_{bound}/I_{free} is ≈10. In the case of lipid bilayer membranes, studies with guest ketones[26] yield values of I_{bound}/I_{free} of the order of 0.5. Lipid bilayers are more ordered than micelles with less water penetration.[18]

Interestingly, preliminary experiments show that the guest ketones (such as 5-nonanone and 7-tridecanone used here) may be expelled *reversibly* out of the micelle by cooling to several degrees below the critical micellization temperature of the various micelles. The reversibility of this event is monitored by the appearance of a nonbound C=O band. Thus, the C=O groups hydrogen bond to water reversibly according to their environment.

These results are in accord with previous work[17] with use of ^{13}C NMR spectra of ketones and keto-surfactants to determine extent of water penetration. In that work, however, no direct evidence of two environments for the ketone was found, since in the presence of chemical exchange, the NMR spectrum yields an average signal. The time scale of the infrared spectrum[30] allows the detection of the two environments (when they give rise to

(19) Infrared spectra were recorded at 2 cm^{-1} resolution with a Digilab FTS-60 Fourier transform spectrometer equipped with a DTGS detector. In all cases, the samples were held in cells of 50 μm pathlength fitted with CaF_2 windows.

(20) All samples were prepared in D_2O, vortexed, warmed (to 40 °C), and kept for 24 h before collection of spectra.

(21) The presence of *only* one band in these two spectra was confirmed by deconvolution and derivation. In the spectrum of the 7-oxo-Na-C_8 monomer in D_2O (≈0.1 M) there is also *only* one band at 1689 cm^{-1}.

(22) The C=O stretching band of 7-oxo-Na-C_8 is at 1719 cm^{-1} when not bound to water: for example, in *n*-octane.

(23) Fourier self-deconvolution with a Lorentzian line shape of 15 cm^{-1} full width at half height and a resolution enhancement factor of 2 was used.[24,25]

(24) Moffatt, D. J.; Kauppinen, J. K.; Cameron, D. G.; Mantsch, H. H.; Jones, R. N. National Research Council of Canada, 1986; bulletin no. 18.

(25) Mantsch, H. H.; Casal, H. L.; Jones, R. N. *Adv. Spectrosc.* **1986**, *13*, 1–46.

(26) Casal, H. L. *J. Phys. Chem.*, submitted for publication.

(27) The relative integrated intensities of the different bands were determined by curve-fitting by using an iterative procedure.[24] The estimated error in I_{bound}/I_{free} is ±10%.

(28) Surfactant/guest molar ratios are always higher than 15:1.

(29) Menger, F. M.; Dulany, M. A.; Carnahan, D. W.; Lee, L. H. *J. Am. Chem. Soc.* **1987**, *109*, 6899–6900.

(30) Grevels, F. W.; Jacke, J.; Klotzbücher, W. E.; Krüger, C.; Seevogel, K.; Tsay, Y. H. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 885–887.

sufficiently different spectra). In the NMR experiment, one "average" environment for the ketone was found due to exchange of the ketone between the two media, one with water and one without. In the infrared the two environments are separable.

The results presented here give a picture of micelles which is compatible with current views.[3,4] Water penetrates *almost* everywhere into micelles; there is a region (assumed to be the central core) completely devoid of water. Probe molecules are able to move in and out of the different environments. Further work is in progress using this methodology to probe the structure of other systems.

Acknowledgment. Thanks are due to Dr. U. Köhler for his advice on the synthesis of 7-oxo-octanoic acid and to Dr. J. Villalain for a preprint of his work.[8]

The Influence of a Carboxylate Group on the Rate of O-Acylation of 2-Hydroxymethylimidazoles by a Strained Amide

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During the course of all serine protease[1] catalyzed ester and amide hydrolyses, the Ser–OH group of the catalytic triad (Asp CO_2^-–HisIm–SerOH) becomes transiently acylated. Although this suggests common hydrolytic pathways, continuing studies with serine proteases (SPases) indicate subtle substrate-dependent diversities. These include differing sites of initial acylation[2] and different numbers of protons in flight in the rate-limiting step.[3] The role of the essential Asp CO_2^- component has not been generally resolved. Two possibilities, general base enhancement of the imidazole basicity and electrostatic stabilization of imidazolium, have been favored.[1] Evidence exists that enzymes inhibited with species approximating the initial tetrahedral intermediate maintain an Asp CO_2^-–H-Im^+-His H-bond, thus supporting the electrostatic role.[4] Even so, it is possible that different substrates may recruit different levels of involvement of the various catalytic components. Nevertheless, the wide-spread occurrence of this catalytic triad suggests a considerable mechanistic advantage to the enzymes that employ it.

If such an arrangement leads to obvious acceleration, it is surprising how few studies have directly addressed the ability of a triad to facilitate O-acylation in a small molecule. A number of reports deal with the reaction of amino alcohols with esters[5] or reactive amides.[5b,1,6] A smaller number deal with the interaction of CO_2^- and imidazole during acyl transfer to H_2O[7] (which is more properly a model for the deacylation of SPases). Apparently the preliminary reports of Bender et al.[8] are the only published ones employing a model of the triad in acylation, in this case by *m*- and *p-tert*-butylphenylacetate.

We have shown that the direct O-acylation of **1c** and **d** by **2**[9] proceeds to **3** via the process shown in eq 1.[6] Herein we report an incremental study of the effect of the remote carboxylate in **1a** on the analogous process.

Shown in Figure 1 are Brønsted plots (log k_2^{max} versus imidazole pK_a^{Im})[11] for reaction of **1a–e** with **2** in H_2O, 40% and 80% v/v EtOH/H_2O. (pK_a^{Im} and k_2^{max} values are given as Supplementary Material.) Several common features are of note. (1) The log k_2 values[11] plateau above pK_a^{Im} indicating the basic form is active. (2) The reaction product in all cases is CH_2-O-acylated as judged by ^{1}H NMR, IR, and mass spectral data (see Supplementary Material). (3) With no CH_2OH group present, the k_2^{max} values

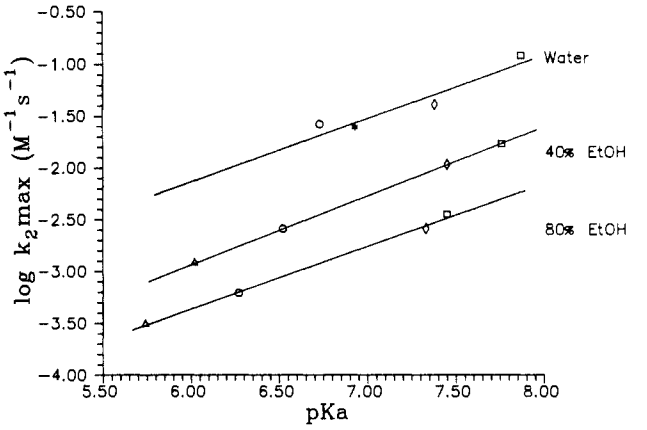

Figure 1. Brønsted plots of the maximal second-order rate constant (k_2^{max}) versus pK_a^{Im} for **1a** (◇), **1b** (△), **1c** (○), **1d** (*), and **1e** (□) with twisted amide **2** in H_2O ($\beta = 0.6 \pm 0.1$), 40% ($\beta = 0.66 \pm 0.03$) and 80% (0.60 ± 0.02) (v/v) EtOH/H_2O, $T = 25$ °C, $\mu = 0.2$ (KCl).

Table I. pK_a^{Im} Values for **1a–c,e** Determined by Potentiometric Titration at 25 °C, $\mu = 0.2$ (KCl) in H_2O, 40% and 80% (v/v) EtOH/H_2O[a]

		pK_a^{Im}	
compd	H_2O	40% EtOH/H_2O[b]	80% EtOH/H_2O[b]
1a	7.38 ± 0.05	7.45 ± 0.02	7.33 ± 0.02
1b	6.18 ± 0.02	6.02 ± 0.02	5.74 ± 0.02
1c	6.73[c]	6.52 ± 0.02	6.27 ± 0.02
1e	7.88 ± 0.03	7.76 ± 0.02	7.45 ± 0.02

[a] Averages of duplicate measurements. [b] Adjusted pK_a values according to pH = (meter reading) −0.09 (40% EtOH/H_2O) or pH = (meter reading) −0.2 (80% EtOH/H_2O): Bates, R. G.; Paabo, M.; Robinson, R. A. *J. Phys. Chem.* **1963**, *67*, 1833. [c] Eiki, T.; Kawada, S.; Matsushima, K.; Mori, M.; Tagaki, W. *Chem. Lett.* **1980**, 997.

(1) For pertinent reviews of the structural and mechanistic properties of this class of enzymes see: (a) Walsh, C. *Enzymatic Reaction Mechanisms*; W. H. Freeman: San Francisco, CA, 1979; pp 56–97. (b) Fersht, A. *Enzyme Structure and Mechanism*, 2nd ed.; W. H. Freeman: San Francisco, CA, 1985. (c) Dugas, H.; Penney, C. *Bioorganic Chemistry*; Springer Verlag: New York, 1981; pp 208–226. (d) Schowen, R. L. In *Principles of Enzyme Activity*; Liebman, J. F.; Greenberg, A. Eds.; VCH Publishers Inc. U.S.A., Vol. 9, in press.

(2) (a) Hubbard, C. D.; Shoupe, T. S. *J. Biol. Chem.* **1977**, *252*, 1633. (b) Hubbard, C. D.; Kirsch, J. F. *Biochemistry* **1972**, *11*, 2483. (c) Quinn, D. M.; Elrod, J. P.; Ardis, R.; Friesen, P.; Schowen, R. L. *J. Am. Chem. Soc.* **1980**, *102*, 5358.

(3) (a) Stein, R. L.; Strimpler, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 4387, and references therein. (b) Venkatasubban, K. S.; Schowen, R. L. *CRC Crit. Rev. Biochem.* **1984**, *17*, 1.

(4) (a) Abeles, R. H.; Liang, T. C. *Biochemistry* **1987**, *26*, 7603. (b) Bone, R.; Shenvi, A. B.; Kettner, C. A.; Agard, D. A. *Ibid.* **1987**, *26*, 7609.

(5) (a) For leading references see footnote 3 of ref 6. (b) Cram, D. J.; Lam, P. Y.-S.; Ho, S. P. *J. Am. Chem. Soc.* **1986**, *108*, 839. (c) Cram, D. J.; Katz, H. E.; Dicker, I. B. *J. Am. Chem. Soc.* **1984**, *106*, 4987.

(6) Somayaji, V.; Skorey, K. I.; Brown, R. S.; Ball, R. G. *J. Org. Chem.* **1986**, *51*, 4866.

(7) (a) Komiyama, M.; Bender, M. L. *Bioorg. Chem.* **1977**, *6*, 13. (b) Komiyama, M.; Bender, M. L.; Utaka, M.; Takeda, A. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 2634. (c) Mallick, I. M.; D'Souza, V. T.; Yamaguchi, M.; Lee, J.; Chalabi, P.; Gadwood, R. C.; Bender, M. L. *J. Am. Chem. Soc.* **1984**, *106*, 7252. (d) Rogers, G. A.; Bruice, T. C. *J. Am. Chem. Soc.* **1974**, *96*, 2473. (e) Komiyama, M.; Breaux, E. J.; Bender, M. L. *Bioorg. Chem.* **1977**, *6*, 127.

(8) (a) D'Souza, V. T.; Hanabusa, K.; O'Leary, T.; Gadwood, R. C.; Bender, M. L. *Biochem. Biophys. Res. Commun.* **1985**, *129*, 727. (b) D'Souza, V. T.; Bender, M. L. *Acc. Chem. Res.* **1987**, *20*, 146. (c) The above two (ref 8a and b) report an interesting cyclodextrin with an attached pendant imidazolyl benzoate facilitating the hydrolysis of *m*- and *p-tert*-butylbenzoate. Evaluation of the extent of cooperativity is difficult at present since full experimental details and controls are not yet reported.

(9) Somayaji, V.; Brown, R. S. *J. Org. Chem.* **1986**, *51*, 2676.

(10) All new imidazoles had satisfactory elemental and spectroscopic (IR, ^{1}H NMR, MS) analyses. The product esters from **1a–e** and **2** were characterized by ^{1}H NMR, exact mass, and IR (Supplementary Material).

(11) Second-order rate constants (k_2) for **1a–e** with **2** were evaluated from slopes of the k_{obsd} versus [**1a–e**] plots at different pH values. The maximal second-order rate constant (k_2^{max}) was calculated from $k_2 = k_2^{max}K_a^{Im}/([H^+] + K_a^{Im})$.

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