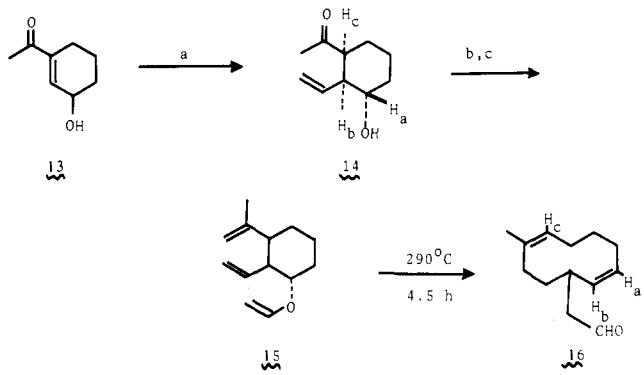
Scheme II[a]



[a] a, $(CH_2{=}CH)_2CuLi$, Me_2S, THF; b, $C_2H_5OCH{=}CH_2$, $Hg(OAc)_2$; c, $(C_6H_5)_3P{=}CH_2$, THF.

cyclodecadienes.

Hydroxyenone **13**[12] (Scheme II) provided **14**[13] (mp 70–71 °C; NMR ($CDCl_3$, 270 MHz) δ 5.90–5.74 (1 H, m), 5.19–5.07 (2 H, m), 4.10–4.00 (1 H, m, H_a), 3.01 (dt, J = 8, 4 Hz, H_c), 2.53 (dt, J = 9, 5 Hz, H_b), 2.11 (3 H, s)) upon stereoselective cuprate[14] addition and kinetic protonation of the resultant enolate. The derived triene **15** was converted to (2*Z*,7*Z*)-8-methylcyclodecadien-1-acetaldehyde (**16**) in 55% yield (Scheme II):[15] IR (neat) 2707, 1721, 748, 725 cm^{-1};[16,17] NMR ($CDCl_3$, 270 MHz) δ 9.64 (1 H, t, J = 2 Hz), 5.33 (1 H, dt, J = 4, 11 Hz, H_a), 5.05 (2 H, m, H_b, H_c), 1.69 (3 H, s). Extensive decoupling of the NMR spectrum supported the armchair[18] conformation of **16**.

Since the *Z,Z* isomer is the thermodynamically most stable of the 1,6-cyclodecadienes,[18] we are not able to rule out at this time the possibility that diradicals are involved in the formation of **16** as opposed to a concerted pathway. The stereochemical consequences of this and related Cope–Claisen rearrangements and their application to natural products synthesis are under investigation.

Acknowledgment. We express our thanks to the National Institutes of Health (CA 16432) and Hoffmann-La Roche for financial support of this work. The Bruker 270-MHz NMR instrument is supported by National Institutes of Health Research Grant No. 1-P07-PR00798 from the Division of Research Sources.

References and Notes

(1) (a) F. E. Ziegler, *Acc. Chem. Res.*, **10**, 227 (1977); (b) G. B. Bennett, *Synthesis*, 589 (1977); (c) S. J. Rhoads and N. R. Raulins, *Org. React.*, **22**, 1 (1975).
(2) The ordering of events in the reaction is implied by the order of the names. For the Claisen–Cope rearrangement, see A. F. Thomas, *J. Am. Chem. Soc.*, **91**, 3281 (1969); A. F. Thomas, *Helv. Chim. Acta*, **53**, 605 (1970); A. F. Thomas and G. Ohloff, *Ibid.*, **53**, 1145 (1970); A. F. Thomas and M. Ozianne, *J. Chem. Soc. C*, 220 (1970); B. Bowden, R. C. Cookson, and H. A. Davis, *J. Chem. Soc., Perkin Trans. 1*, 2634 (1973); R. C. Cookson and N. R. Rogers, *Ibid.*, 2741 (1973); Y. Fujita, T. Onishi, and T. Nishida, *Synthesis*, 532 (1978).
(3) Thermolyses were conducted in sealed tubes under N_2 at a maximum of 4-atm pressure employing a KNO_3-$NaNO_3$-$NaNO_2$ bath heated by two immersion heaters and controlled by a Bayley precision temperature controller Model 124. We are grateful to Professor J. A. Berson for the use of this equipment.
(4) Prepared by the method of J. L. Herrmann, G. R. Kieczykowski, and R. H. Schlessinger, *Tetrahedron Lett.*, 2433 (1973).
(5) All new compounds gave satisfactory spectral, mass spectral, and/or combustion analysis data.
(6) J. M. Conia and P. LePerchec, *Synthesis*, 1 (1975).
(7) In a similar system, a β-naphthyl group has been reported to control the stereochemistry of the rearrangement so that the new carbon–carbon bond is formed trans to the β substituent: A. Horeau, E. Lorthioy, and J. P. Guette, *C.R. Hebd. Seances Acad. Sci., Ser. C*, **269**, 558 (1969).
(8) Private communication from G. Stork, Columbia University.
(9) W. S. Johnson, L. Werthermann, W. R. Bartlett, T. J. Brocksom, T. Lee, D. J. Faulkner, and M. R. Petersen, *J. Am. Chem. Soc.*, **92**, 741 (1970).
(10) K. K. Chan, N. Cohen, J. P. DeNoble, A. C. Specian, and G. Saucy, *J. Org. Chem.*, **41**, 3497 (1976).
(11) K. Takeda and I. Horibe, *J. Chem. Soc., Perkin Trans. 1*, 870 (1975), and earlier papers in this series; T. C. Jain, C. M. Banks, and J. E. McCloskey, *Tetrahedron Lett.*, 841, (1970); K, Morikawa and Y. Hirose, *Ibid.*, 869 (1969); R. V. H. Jones and M. D. Sutherland, *Chem. Commun.*, 1229 (1968); N. H. Fischer and T. J. Mabry, *Ibid.*, 1235 (1967); A. S. Rao, A. Paul, Sadgopal, and S. C. Bhattacharyya, *Tetrahedron*, **13**, 319 (1961).
(12) E. J. Corey and D. Crouse, *J. Org. Chem.*, **33**, 298 (1968).
(13) The coupling constants at room temperature are average values. Low temperature NMR showed that there are at least two conformations of **14**. Definitive evidence for the structure of this substance was obtained by single-crystal X-ray diffraction details of which will be reported independently. We are grateful to Mr. Michael Vary for his expertise in the X-ray analysis.
(14) R. D. Clark and C. H. Heathcock, *Tetrahedron Lett.*, 1713 (1974).
(15) VPC yield. In addition to **16**, two unidentified aldehydes (9%) and olefinic products of elimination (12%) accounted for all distillable products.
(16) The absence of IR absorptions in the region of 1000–900 cm^{-1} is indicative of the lack of *E*-disubstituted and trisubstituted olefins: J. F. Traynham and W. C. Baird, Jr., *J. Org. Chem.*, **27**, 3189 (1962); J. A. Marshall and G. L. Bundy, *J. Am. Chem. Soc.*, **88**, 4291 (1966).
(17) K. Nakanishi, "Infrared Absorption Spectroscopy", Holden-Day, San Francisco, 1962, p 24.
(18) A. Almenningen, G. G. Jacobsen, and H. M. Seip, *Acta Chem. Scand.*, **23**, 1495 (1969); J. Dale, T. Ekeland, and J. Schaug, *Chem. Commun.*, 1477 (1968).
(19) National Institutes of Health Career Development Awardee, 1973–1978.

Frederick E. Ziegler,*[19] John J. Piwinski
Sterling Chemistry Laboratory, Yale University
New Haven, Connecticut 06520
Received December 1, 1978

Analysis of Monolayer Films at the Air–Water Interface by Field Desorption Mass Spectrometry

Sir:

The direct sampling of surfactant molecules in monolayer films at the air–water interface using a conventional field emitter[1] and subsequent recording of their field desorbed mass spectra are demonstrated for the first time. The technique has proven applicable to a variety of surface films whose components differ in molecular weight and molecular charge.

Renewed interest in studying chemical reactions occurring in surfactant monolayer arrays has been promoted by the development of sensitive instrumental methods allowing the detection, separation, and characterization of the small amounts of materials, $\sim 10^{-9}$–10^{-10} mol/cm^2, contained in such films. Recently, applications of the following analysis methodologies have been reported: absorption and emission spectrometry,[2,3] infrared spectrometry,[4-6] vapor phase chromatography,[7] and high performance liquid chromatography.[8,9] An important piece of characterization information previously unavailable has been the molecular weight of the surfactant reaction products.

Field desorption mass spectrometry (FD MS) has proven a relatively mild technique for obtaining molecular ions of nonvolatile substances, including salts of ionizable organic compounds as well as high molecular weight monomeric and oligomeric compounds, with little or no fragmentation.[10] Normally, a field ion emitter, prepared according to the procedure of Schulten and Beckey,[1] is immersed in a solution containing the compound to be analyzed and introduced into the FD ion source, a high field is applied, and the desorbed, positively charged ions are mass analyzed and detected. In the present work, the hydrophobic emitter is simply dipped once in and out of a monolayer covered air–water interface and analyzed using a Varian-Mat 731 mass spectrometer equipped with an electron impact/field ionization/field desorption (EI/FI/FD) source operated in the FD mode. Potentials of +8 and −4 kV were applied to the field emitter and extraction element, respectively. A summary of the results for the surfactant compounds which have been examined in this manner is given in Table I and a typical spectrum is shown in Figure 1.

An upper limit to the amount of surfactant film transferred

0002-7863/79/1501-1612$01.00/0

Table I. Summary of FD MS Results

surfactant[a]	subphase	ions obsd (mass)	comments[b]
n-octadecanol	H_2O	270	fleeting, low
n-oxtadecanal	H_2O	268	fleeting, low
n-octadecanoic acid	10^{-3} N HCl	284	moderate
n-octadecanoic acid	10^{-3} N NaOH	284, 306	306 required emitter heating
cis-9,10-*n*-octadecenoic acid	10^{-2} N H_2SO_4	282	moderate
N,N-dimethyl-*n*-octadecylamine	10^{-3} N NaOH	297	strong
N,N-dimethyl-*n*-octadecylamine	10^{-3} N HCl	297, 298	persistent, very strong
cholesterol, neat[c]	10^{-2} N HCl		no ions observed
cholesterol, mixed[d]	10^{-2} N HCl	386	moderate
vitamin K_1[e]	H_2O	450	strong
chlorophyll *b*[e]	buffer[f]	907.5	strong
$Ru^{II}(bpy)[bpy(C_{19}H_{39})_2](CN)_2$, **1**[e]	H_2O	998[g]	very strong

[a] Films were compressed to Π = 20 dyn/cm (21-23 °C) except where noted. [b] Signal strength observed (low, moderate, strong, very strong) and duration. [c] Film contains only cholesterol compressed to $\Pi \approx 1$ dyn/cm. [d] Mixed film containing 80 mol % cholesterol and 20 mol % *cis*-9,10-octadecenol compressed to $\Pi \approx 1$ dyn cm. [e] Film compressed to Π = 10 dyn/cm. [f] 10^{-3} M borate buffer, pH 8.2. [g] Ruthenium isotope pattern centered on ^{102}Ru; see Figure 1.

onto the emitter has been obtained by measuring the film area, held at constant surface pressure (Π) on the air-water interface, before and after dipping. For an initial film covered surface area of 12.0 cm^2, the maximum area decrease observed was ~0.15-0.30 cm^2, the monolayer being formed from $Ru^{II}(bpy)[bpy(C_{19}H_{39})_2](CN)_2$, **1**.[11] Since the molecular area of **1** was known to be 6.7×10^{-15} cm^2 (Π = 10 dyn/cm, 22 °C),[11] the maximum amount of material that could have been transferred is 35-75 ng. The accuracy of this number is limited by the measurement of the small (1-3%) decrease in film area and is undoubtedly too high since the two posts between which the emitter wire is suspended also are dipped into the film. Considering the field emitter wire to have a nominal diameter (including dendrite growth) of ~55 μm and length of 0.25 cm, the smooth surface area of this right cylinder is $\sim 4.4 \times 10^{-3}$ cm^2. Monolayer coverage of this surface would require only 1.1 pmol or 1.1 ng of **1**. This approximation assumes that, at the moment of deposition, the monolayer film bridges between the points of the dendridic growth and does not cover the dendrites on their long axes. Such behavior is suggested by Bikerman, who showed that the area decrease at the air-water interface for monolayer films transferred onto fine grooved or gauze surfaces was the same as that observed with highly polished surfaces.[13] In the present experiments the observed signal was 1.8×10^{-13} A·s at 15 mV. Given that the measured maximum amount of sample transferred to the emitter was ~75 ng and the estimated minimum sample actually on the active surface was ~1.1 ng, then the instrumental sensitivity[14] lies between 2.1×10^{-12} and 1.6×10^{-10} A·s/μg for compound **1**.

Attempts to perform similar sensitivity measurements using films formed solely from cholesterol were unsuccessful. It appears that the emitter simply fractured the rigid cholesterol monolayer film upon dipping with little or no material transferred to the emitter. A similar observation was made when trying to sample another known rigid film composed of cadmium stearate (subphase: 2.5×10^{-4} M $CdCl_2$, 1.0×10^{-3} M NaOH). By using a less brittle two-component film spread from a solution containing 80 mol % cholesterol and 20 mol % *cis*-9,10-octadecenol, an observed signal of $\sim 1.4 \times 10^{-12}$ A·s at an average of 30 mV was obtained for cholesterol. Following the reasoning of the above calculations based on **1**, the instrumental sensitivity for cholesterol under these conditions falls between 3.6×10^{-9} and 4.8×10^{-11} A·s/μg. Olson, Cook, and Rinehart[15] have determined the sensitivity for cholesterol by freeze loading on a near-equivalent instrument to be 5.6×10^{-11} A·s/μg. We suggest that the higher numbers observed here are due to practically exclusive deposition of sample at or near the active tips of the emitter.

The spectra obtained showed little or no fragmentation.

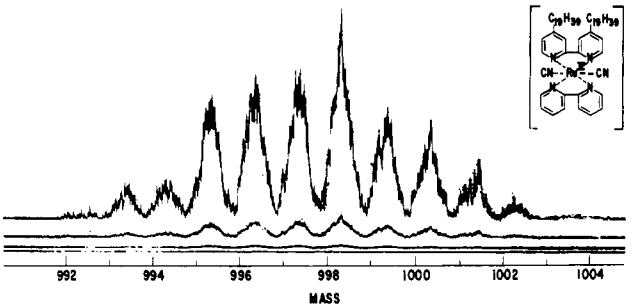


Figure 1. FD MS of a monolayer film of $Ru^{II}(bpy)[bpy(C_{19}H_{39})_2](CN)_2$, **1**, transferred from distilled water (Π = 10 dyn/cm, 21 °C).

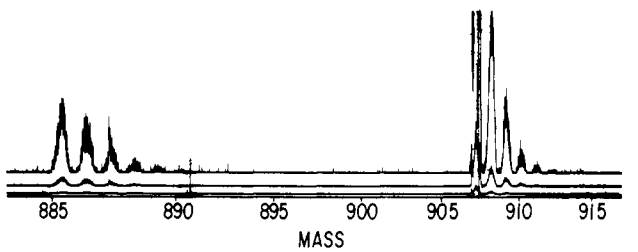


Figure 2. FD MS of a monolayer film of chlorophyll *b* sampled (Π = 10 dyn/cm) after standing 10 min on an aqueous 10^{-3} N HCl subphase ($\Pi \approx 0$ dyn/cm, 22 °C).

Compounds exhibiting appreciable volatility under the MS conditions, such as *n*-octadecanol and *n*-octadecanal, were removed from the emitter surface rapidly at room temperature and gave fleeting signals of low intensity. Such a result indicates that MS analysis of volatile, but thermally stable, surfactant compounds should be done in combination with gas chromatography.[16] When *n*-octadecanoic acid was spread on aqueous sodium hydroxide, the resulting spectrum showed the sodium carboxylate as well as the un-ionized carboxylic acid. In order to obtain an appreciable signal intensity for the salt, the emitter wire required heating (~10 mA). A very strong and persistent signal was observed for an $(M + 1)^+$ ion by sampling a film of *N,N*-dimethyl-*n*-octadecylamine spread on an acidic subphase. Similar strong intensity signals of long duration have been recently reported for volatile amines undergoing ionization in the presence of a surface bound proton source and a high field.[17]

In the conventional manner, we have analyzed surfactants in solution having molecular weights as high as 1531 at unit resolution with strong signal intensities. Although the highest mass of a material analyzed for this report is only 998 (**1**), we perceive no difficulties in sampling and analyzing surface films having monomeric or oligomeric components with masses

approaching the present limitations of the instrumentation (~3000).

Of considerable interest is the ease by which biologically important and chemically unstable surfactants, illustrated here by vitamin K_1 and chlorophyll *b*, may be sampled and analyzed. Such a characterization technique need not be limited to the monolayer model but should be extendable to sampling surfactants constrained at other interfaces modeling biological organization.

Chemical reactions may be monitored by sampling the film at various times. For instance, it is known that chlorophyll loses its magnesium atom to become metal-free pheophytin when brought into contact with aqueous acid. Figure 2 reproduces the original oscillographic tracing of an emitter sampled film of chlorophyll *b*[18] which had been spread ($\Pi \approx 0$ dyn/cm) on an aqueous 10^{-3} M HCl subphase for 10 min (22 °C). While the spectrum of chlorophyll *b* on neutral subphase showed only the molecular ion at mass 907.5 the formation of the metal-free pheophytin *b* (mass 885.5) is clearly demonstrated on aqueous acid. Owing to uncertainties in the mechanism by which ionization and subsequent field desorption take place the observed variation in signal intensity for different compounds, and lack of precision in replicate measurements, this method presently can give only a qualitative indication of the extent of reaction.

With a means to obtain a surfactant's molecular weight added to the other methods of separation and characterization, we are close to realizing as complete an experimental description of the chemistry occurring in films of monomolecular thickness as for reactions occurring in homogeneous solution.

References and Notes

(1) Schulten, H. R.; Beckey, H. D. *Org. Mass Spectrom.* **1972**, *6*, 885.
(2) Kuhn, H.; Möbius, D.; Bücher, H. "Techniques of Chemistry", Weissberger, A., Ed.; Interscience: New York, 1972; Vol I, Part IIIB.
(3) Whitten, D. G.; Hopf, F. R.; Quina, F. H.: Sprintschnik, G.; Sprintschnik, H. W. *Pure Appl. Chem.* **1977**, *49*, 379.
(4) Rosilio, C.; Ruaudel-Teixier, A. *J. Polym. Sci., Part A-1* **1975**, *13*, 2459.
(5) Letts, S. A.; Fort, T., Jr.; Lando, J. B. *J. Colloid Sci.* **1976**, *56*, 64.
(6) Enkelmann, V.; Lando, J. B. *J. Polym. Sci., Part A-1* **1977**, *15*, 1843.
(7) (a) Valenty, S. J. *Macromolecules* **1978**, *11*, 1221. (b) Richard, M. A.; Deutch, J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1978**, *100*, 6613.
(8) Gaines, G. L., Jr.; Behnken, P. E.; Valenty, S. J. *J. Am. Chem. Soc.* **1978**, *100*, 6549.
(9) Valenty, S. J. *J. Am. Chem. Soc.*, **1979**, *101*, 1.
(10) Schulten, H.-R. "Methods of Biochemical Analysis", Glick, David, Ed.; Wiley: New York, 1977; Vol. 24, pp 313–448.
(11) The preparation and characterization of **1** are found in ref 12.
(12) Valenty, S. J.: Behnken, P. E.; Gaines, G. L. Jr. *J. Am. Chem. Soc.*, submitted for publication.
(13) Bikerman, J. J. *Proc. R. Soc. London, Ser. A* **1939**, *170*, 130.
(14) Calculated as described in ref 15.
(15) Olson, K. L.; Cook, J. C.; Rinehart, K. L., Jr. *Biomed. Mass Spectrom.* **1974**, *1*, 358.
(16) Valenty, S. J., 176th National Meeting of the American Chemical Society, Miami Beach, Fla., Sept 1978; American Chemical Society: Washington, D.C.; COLL 081; *Adv. Chem. Ser.*, in press.
(17) Ligon, W. V. Jr. *Science*, in press.
(18) The application of FD MS to the analysis of porphine compounds has been described by Evans et al.[19]
(19) Evans, N; Games, D. E.; Jackson, A. H.; Matlin, S. A. *J. Chromatogr.* **1975**, *115*, 325.

Woodfin V. Ligon, Jr.,* Steven J. Valenty*
General Electric Company
Corporate Research and Development
Schenectady, New York 12301

Received November 3, 1978

Duplex Cyclodextrin

Sir:

During the past decade, the basic characteristics of enzymes such as saturation kinetics or large catalytic constants have been successfully modeled not only by the use of naturally occurring compounds[1] but also by the construction of partially[2] or completely[3] artificial molecules of appropriate shape and necessary functionalization. A remarkable strengthening of the hydrophobic binding was also achieved on increasing the area of the hydrophobic recognition site of a host molecule.[4,5] The observation that the introduction of a second (appropriate) recognition element ("double recognition" [6]) onto the host molecules mentioned above afforded a significant increase in binding gave rise to a new strategy for the modeling of more complex and sophisticated enzyme functions (Figure 1).

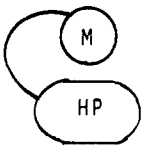


Figure 1. Double recognition:[6] M acts as a coordination binding site and/or a catalytic site.

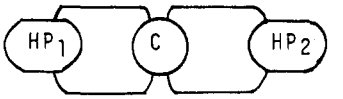


Figure 2. Triple recognition for ligase-type activity: HP_1, HP_2, hydrophobic binding sites; C, another recognition element (acid, base, metal, etc.).

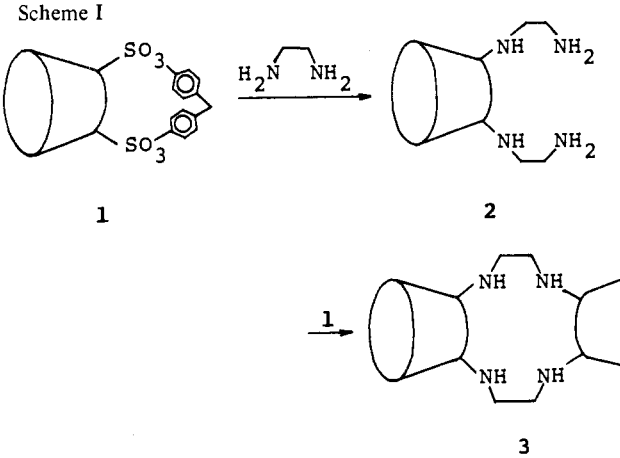
In order to construct better enzyme models, a more precise (synthetic) recognition system is required. Triple recognition, for example, should be the minimal condition necessary for modeling a ligase-type activity (to show specificity toward both S_1 and S_2 as well as toward the functional group(s) F_1 and F_2 in eq 1). In this communication, the authors report that a novel host molecule, **duplex cyclodextrin,** which has two hydrophobic binding sites (HP_1 and HP_2 in Figure 2) together with another recognition element C, does specifically bind methyl orange, a guest dye molecule having two hydrophobic recognition elements. Thus, capped β-cyclodextrin (**1**)[5a] was converted to di(ω-aminoethylamino)-β-cyclodextrin (**2**) in 80% yield on heating in a large excess of ethylenediamine at 50 °C for 3 h.

$$S_1\text{-}F_1 + F_2\text{-}S_2 \rightarrow S_1\text{-}F_{1,2}\text{-}S_2 \qquad (1)$$

The tetramine treated with a slight excess of **1** in DMF–pyridine (1:1 by volume) at 80 °C for 72 h gave **duplex β-cyclodextrin (3)** (Scheme I) in 16% yield.[7] Purification of **2** or **3** was achieved by the ion-exchange column chromatography through anion- (IR-45) and cation- (Dowex-50W) exchange resins followed by microcrystalline cellulose column chromatography.

A paper chromatogram (7% NH_4OH–EtOH–BuOH, 5:5:1) of **3** thus purified exhibited a clear single spot of R_f 0.6 (ninhydrin). The elemental analysis of **3** was satisfactory, although

Scheme I



0002-7863/79/1501-1614$01.00/0