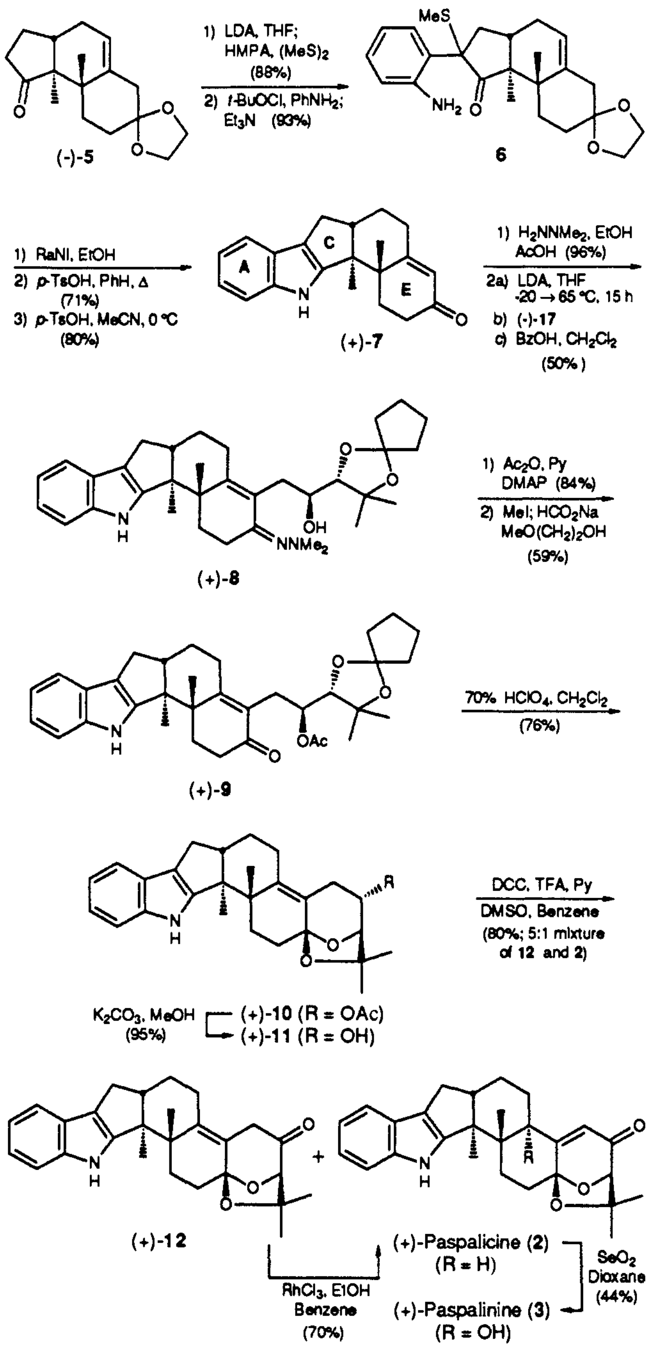
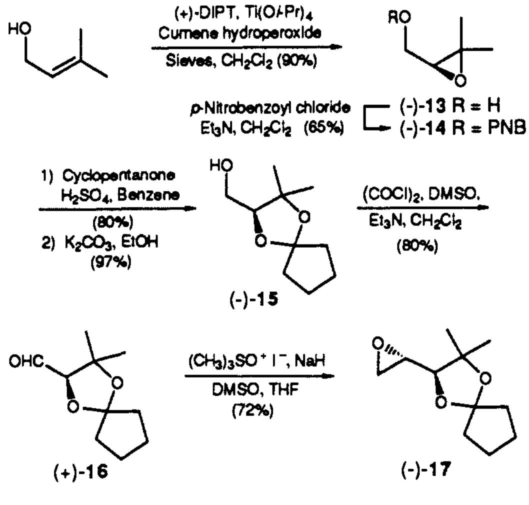
Scheme II



Scheme III



Oxidation of (+)-**2** with selenium dioxide[11] then provided (+)-paspalinine (**3**) in 44% yield, along with an as-yet-unidentified byproduct. Detailed analysis again established the identity of synthetic (+)-**3** with the natural material.[10] Given the importance of the C(4b) tertiary hydroxyl group for tremorgenic activity,[2c] the latter transformation should prove useful for elaboration of other significant structures.

In summary, the first total syntheses of (+)-paspalicine (**2**) and (+)-paspalinine (**3**) have been achieved in 22 and 23 steps, respectively, exploiting a unified strategy which earlier afforded (−)-paspaline (**1**). Progress toward construction of the remaining members of this class, as well as the design and synthesis of biologically active congeners, will be reported in due course.

Acknowledgment. Support for this investigation was provided by the National Institutes of Health (Institute of Neurological Disorders and Stroke) through Grant 18254. In addition, we thank Drs. G. Furst, P. Carroll, and Mr. J. Dykins, Directors of the University of Pennsylvania Central Spectroscopic Facilities, for aid in obtaining the high field NMR, X-ray diffraction, and high-resolution mass spectral data, respectively.

Supplementary Material Available: Spectroscopic and analytical data for (+)-**2**, (+)-**3**, (+)-**7**, (+)-**8**, (+)-**11**, (+)-**16**, and (−)-**17** (2 pages). Ordering information is given on any current masthead page.

---

(11) Furlenmeier, A.; Fürst, A.; Langemann, A.; Waldvogel, G.; Kerb, U.; Hocks, P.; Wiechert, R. *Helv. Chim. Acta* **1966**, *49*, 1591.

Solution Chemistry and Derivatives of Centered Zirconium Chloride Cluster Phases

Friedhelm Rogel and John D. Corbett*

Department of Chemistry, Iowa State University
Ames, Iowa 50011

Received July 9, 1990

The diverse chemistry of centered zirconium analogues of the traditional $(Nb,Ta)_6Cl_{12}^{n+}$ clusters that has been broadly developed via high-temperature solid-state reactions[1-8] has now been extended to a surprisingly versatile solution chemistry of some of the same clusters. Solid phases of general compositions $M^1_x[Zr_6(Z)Cl^i_{12}]Cl^a_n$ with five different interstitial atoms Z = H, Be, B, C, and Fe have been dissolved in acetonitrile and solid derivatives isolated. Fifteen products have been structurally characterized.[9] Reactants with $n < 6$ exhibit intercluster bridging by shared chlorine atoms, increasing in number with decreasing n. Therefore, excision of soluble cluster units from such solids requires that additional ligands open up these Zr–Cl^a–Zr linkages or, alternatively, displace the bridging chlorides. The inner Cl^i atoms are not disturbed. In practice, we find that the phases with $n = 3$, 4, or 6 often react with either $n - 6$ chloride anions or 6 neutral ligands L (NH_2R, PR_3) to afford new $(Zr_6Cl_{12}Z)Cl_6^{m-}$ or $Zr_6Cl_{12}Z\cdot L_6$ products.

---

(1) Ziebarth, R. P.; Corbett, J. D. *Acc. Chem. Res.* **1989**, *22*, 256.
(2) Ziebarth, R. P.; Corbett, J. D. *J. Am. Chem. Soc.* **1989**, *111*, 3272.
(3) Ziebarth, R. P.; Corbett, J. D. *J. Am. Chem. Soc.* **1987**, *109*, 4844.
(4) Zhang, J.; Corbett, J. D., unpublished research.
(5) Ziebarth, R. P.; Corbett, J. D. *J. Am. Chem. Soc.* **1988**, *110*, 1132.
(6) Ziebarth, R. P.; Corbett, J. D. *Inorg. Chem.* **1989**, *28*, 626.
(7) Zhang, J.; Ziebarth, R. P.; Corbett, J. D., to be submitted.
(8) Rogel, F.; Zhang, J.; Payne, M. W.; Corbett, J. D. *Adv. Chem. Ser.* **1990**, *226*, 369.
(9) Rogel, F. Ph.D. Dissertation, Iowa State University, 1990.

0002-7863/90/1512-8198$02.50/0 © 1990 American Chemical Society

Table I. Dimensional Data and Electron Counts for Some Centered Zirconium Chloride Clusters

	d(Zr–Z), Å	*d*(Zr–Zr), Å	*d*(Zr–L[a]), Å	CBE[b]	ref
$KZr_6Cl_{15}Fe$	2.423 (3)	3.428 (3)	2.630 (5)	18	4
$(Et_4P)_4Zr_6Cl_{18}Fe{\cdot}2CH_3CN$	2.439 (1)	3.450 (1)	2.570 (2)	18	this work, 9
$KZr_6Cl_{15}C$	2.279 (1)	3.223 (1)	2.668 (1)	14	3
$Rb_4Zr_6Cl_{18}C$	2.287 (1)[c]	3.234 (1)[c]	2.592 (2)[c]	14	4
$(Et_4N)_4Zr_6Cl_{18}C{\cdot}2CH_3CN$	2.296 (1)	3.248 (1)	2.597 (1)	14	this work
$K_3Zr_6Cl_{15}Be$	2.333 (1)	3.300 (1)	2.683 (2)	14	5
$Na_4Z4_6Cl_{16}Be$	2.333 (1)	3.299 (1)	2.667, 2.773 (3)	14	6
$Zr_6Cl_{12}Be(EtNH_2)_6{\cdot}8CH_3CN$[d]	2.328 (1)	3.292 (1)	2.435 (4)	14	this work
$Zr_6Cl_{12}Be(PEt_3)_6$[d]	2.335 (2)	3.303 (3)	2.821 (6)	14	this work
$Rb_5Zr_6Cl_{18}B$	2.317 (1)	3.277 (1)	2.679 (2)	14	2
$(Ph_4P)_4Zr_6Cl_{18}B{\cdot}(Ph_4P)_2ZrCl_6$	2.3543 (7)	3.327 (1)[c,e]	2.661 (1)	13	this work
$(Et_4N)_4Zr_6Cl_{18}Be{\cdot}2CH_3CN$	2.404 (1)	3.399 (1)	2.568 (2)	12	this work
$Li_6Zr_6Cl_{18}H$	(2.257)	3.1916 (8)	2.687 (1)	13	7
$Zr_6Cl_{12}H(EtNH_2)_6{\cdot}8CH_3CN$[d]	(2.240[c])	3.167 (1)[c]	2.415 (4)	13	this work
$Zr_6Cl_{12}(PMe_2Ph)_6$	(2.28)	3.223 (3)	2.80 (1)	?	13

[a] The group exo at zirconium vertices. [b] Cluster-based electron count. [c] Average value. [d] Studied at −10 to −60 °C. Others are room-temperature measurements. [e] Trigonally compressed (D_{3d}) cluster.

Details affecting the reactivity of diverse starting materials appear complex at this early stage.

Reactions of solid $KZr_6Cl_{15}C$,[3] $KZr_6Cl_{15}Fe$,[4] $Rb_5Zr_6Cl_{18}B$,[2] $K_3Zr_6Cl_{15}Be$,[5] and $Na_4Zr_6Cl_{16}Be$[6] with chloride have led to two types of products. First is a series of isostructural compounds with the stoichiometry $(Et_4Y^+)_4[(Zr_6Cl_{12}Z)Cl_6{}^{4-}]{\cdot}2CH_3CN$, Y = N or P, Z = C or Fe. The clusters in these products and all of the foregoing starting materials contain the optimal, closed-shell complement of 14 cluster-based electrons (CBE) for main-group[1] or 18 electrons for transition-metal interstitial elements.[10] Second, oxidation of solutions of 14-electron clusters to 13- and 12-electron examples by solvent or other means has also been observed with an overall color change from light orange to very dark red. The higher charged cluster anion $Zr_6Cl_{18}Be^{6-}$ that presumably results from solution of $K_3Zr_6Cl_{15}Be$ or $Na_4Zr_6Cl_{16}Be$ in the presence of Cl^- is slowly oxidized by solvent at −18 to 5 °C to give good yields of several examples of 12-electron clusters, $(Et_4N^+)_4[(Zr_6Cl_{12}Be)Cl_6{}^{4-}]{\cdot}2CH_3CN$, for instance, while the $Zr_6Cl_{18}B^{5-}$ anion from the rubidium salt reacts with the solvent extensively at 50 °C to yield, among other products, $(Ph_4P^+)_4[(Zr_6Cl_{12}B)Cl_6]^{4-}]^-{\cdot}(Ph_4P^+)_2ZrCl_6{}^{2-}$ with a 13-electron cluster. Cyclovoltammograms of $Rb_5Zr_6Cl_{18}B$ solutions indicate the formation of not only 14-, 13-, and 12-electron clusters, already known with different interstitials, but also a possible 15-electron cluster.

Displacement of chloride by primary amines or triethylphosphine proceeds readily and virtually quantitatively for the two reactants above and $Li_6Zr_6Cl_{18}H$[7] that have $x = n$. These yield xMCl plus the corresponding $Zr_6Cl_{12}Z{\cdot}L_6$ with Z = Be or H and L = $EtNH_2$, *i*-$PrNH_2$, or Et_3P (see Figure 1). Compounds with $x < n$ or no cations such as $Cs_3Zr_6Cl_{16}Be$ and $Zr_6Cl_{12}Mn$ are basically unreactive under the same conditions. In addition, $KZr_6Cl_{15}C$ undergoes a chloride redistribution reaction in the presence of primary or tertiary amines, Et_4NBr, and 2,2,2-crypt to yield only the above $(Zr_6Cl_{12}C)Cl_6{}^{4-}$ derivative from solution (plus insoluble microcrystalline products). Solutions of $KZr_6Cl_{15}Fe$ with neutral ligands rapidly change color from blue to brown, and in one case a good yield of only a mononuclear iron(II) chlorozirconate(IV) was isolated. Larger interstitials appear to give generally more reactive clusters, possibly because of greater accessibility of the zirconium vertices therein to attack by nucleophiles.

The effective sizes of individual interstitials Be–C are known to be quite constant among chloride clusters.[2] The dimensions of selected cluster phases, Table I, reveal that small, regular changes accompany alterations in ligands or electron count if we neglect the secondary role of alkali-metal cations. Replacement of intercluster bridging chloride by more basic terminal chloride is known to increase the opposed *d*(Zr–Z).[2,3,5] The *d*(Zr–Z) data for Fe- and C-centered clusters indicate that a ~0.015-Å increase accompanies conversion of the bridged $(Zr_6Cl_{12}Z)Cl_{6/2}$ to $(Zr_6Cl_{12}Z)Cl_6$. This combined with data for $14e^-$, Be-centered clusters as well as the hydride data alone shows that the change from $(Zr_6Cl_{12}Z)Cl_6$ to $(Zr_6Cl_{12}Z)L_6$ contracts the Zr–Z bonds by a similar 0.015 Å. The conversion of $Rb_5Zr_6Cl_{18}B$ to the 13-electron $Zr_6Cl_{18}B^{4-}$ is accompanied by a ~0.035-Å increase in *d*(Zr–B). The 12-electron Be-centered cluster continues this trend, *d*(Zr–Be) increasing by ~0.07 Å relative to $K_3Zr_6Cl_{15}Be$ or by 0.045 Å for the oxidation alone. There is no doubt that bonding electrons are being removed in these cases, presumably from the $t_{2g}{}^6$ HOMO.[1] The oxidation of these clusters to metastable 12-electron units parallels the behavior of $(Nb,Ta)_6Cl_{12}{}^{m+}$ analogues, those high-temperature $16e^-$ and $15e^-$ products also being oxidized near room temperature to 14-electron units.[11,12] The two-electron differences between the cluster configurations of group 4 and group 5 metals have been interpreted earlier.[2]

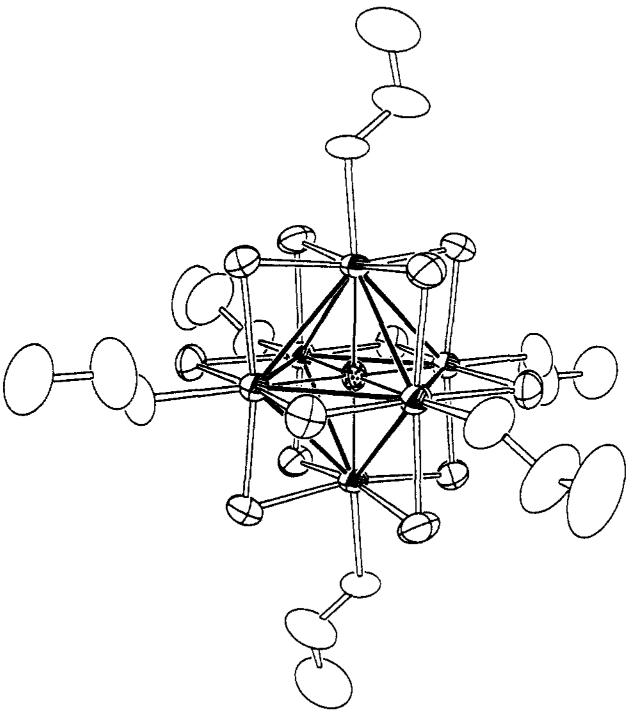


Figure 1. The cluster derivative $(Zr_6Cl_{12}Be)(EtNH_2)_6$, with solid lines emphasizing the Zr_6Be unit: Zr, shaded; Be, dotted; Cl, crossed; N and C, open ellipsoids (90% probability); hydrogen atoms have been omitted.

Finally, the 13-electron cluster $Zr_6Cl_{12}H(EtNH_2)_6$ affords an interesting comparison with $Zr_6Cl_{12}{\cdot}(PMe_2Ph)_6$, which Cotton et al.[13] obtained in low yields from $Zr_2Cl_6(PMe_2Ph)_4$ and charac-

---

[10] Hughbanks, T.; Rosenthal, G.; Corbett, J. D. *J. Am. Chem. Soc.* **1988**, *110*, 1511.

[11] McCarley, R. E.; Hughes, B. G.; Cotton, F. A.; Zimmerman, R. *Inorg. Chem.* **1965**, *4*, 1491.

[12] Fleming, P. B.; Dougherty, T. A.; McCarley, R. E. *J. Am. Chem. Soc.* **1967**, *89*, 159.

terized by X-ray diffraction. Since RNH_2 and PR_3 ligands do not seem to materially alter dimensions of Be-centered clusters (Table I), the ~0.04 Å greater radius of the $Zr_6Cl_{12}(PMe_2Ph)_6$ cluster relative to $Zr_6Cl_{12}(H)(NH_2Et)_6$ suggests that the former may be an empty 12-electron unit rather than a similar hydride. However, this distinction is lessened by the fact that the earlier structural study was done at room temperature, whereas ours was carried out at −60 °C.

Acknowledgment. This research was supported by the National Science Foundation, Solid State Chemistry, via Grants DMR-8318616 and -8902954, and was carried out in facilities of the Ames Laboratory, DOE.

Supplementary Material Available: Some synthetic details and tables of refinement data and structural parameters for and distances in $(Zr_6Cl_{12}Be)(EtNH_2)_6 \cdot 8CH_3CN$ (6 pages). Ordering information is given on any current masthead page.

---

(13) Cotton, F. A.; Kibala, P. A.; Roth, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 298.

Self-Replicating Reverse Micelles and Chemical Autopoiesis

Pascale Angelica Bachmann,† Peter Walde,†
Pier Luigi Luisi,*,† and Jacques Lang‡

Institut für Polymere, ETH-Zentrum
CH-8092 Zürich, Switzerland
Institut Charles Sadron (CRM-EAHP), CNRS
6, rue Boussingault, F-67000 Strasbourg, France

Received June 18, 1990

Whether or not and to what extent synthetic chemical structures are able to self-replicate is a fascinating and important question, as it binds chemistry with one of the most basic cell processes. A few ingenious chemical structures endowed with the property of self-replication have been proposed over the years,[1-3] some of them including nucleotides as basic units.

The analogy with cell replication would be stronger if the self-replicating structure would be closed, i.e., provided with a geometrically defined boundary. It has been proposed recently, in a theoretical paper,[4] that reverse micelles can be good models for such a closed, self-replicating structure.

A reverse micelle is basically a water droplet stabilized in organic solvent by a layer of surfactant. If the reverse micelle hosts guest molecules that by reacting with themselves yield the very surfactant that builds the micelle, we have indeed a situation in which a closed chemical structure is able to replicate itself. Acutally, as pointed out in the cited theoretical paper,[4] these are all conditions that correspond to an autopoietic system, according to the definition proposed by Maturana and Varela[5,6] and reviewed by Fleischaker.[7] Autopoiesis is actually an attempt to define the identity of the living, based on a structure defined by a boundary and by a series of interdependent reactions that build the same boundary and components, which then assemble in the structure itself. It is thus a concept that is more general than self-replication (which actually may be seen as a byproduct of autopoiesis). To the best of our knowledge, none of the self-replicating organic structures presented in the literature can be considered as autopoietic systems.[4,8] It is the aim of this paper to provide the first experimental evidence of a closed, self-replicating chemical structure, which can be seen as a simple chemical autopoietic system.

Table I. Changes of the Parameters of the Octanoic Acid Sodium Salt Reverse Micellar System in 9:1 (v/v) Isooctane/1-Octanol during the LiOH-Catalyzed Hydrolysis of Octanoic Acid Octyl Ester

	starting conditns (t = 0 h)	at half time (t = 35 h)	at equilibrium (t = 300 h)
[octanoic acid sodium salt], mM	50	59	68
[octanoic acid octyl ester],[a] mM	25	16	7
w_0	9.2	7.8	6.8
[M],[b] mM	1.91	2.60	3.03
N_M[c]	26.1	22.7	22.4
R_w,[d] Å	12.0	10.7	10.3
R_H,[e] Å	22.7	[f]	20.5

[a] As determined by FTIR. Uncertainty ±2%. [b] As determined by fluorescence quenching. Uncertainty ±8%. [c] Number of octanoate molecules per micelle, as calculated from [M]. [d] Calculated from [M]. [e] As determined by quasielastic light scattering. Uncertainty ±2.5%. [f] Not determined.

The system we used consists of 50 mM octanoic acid sodium salt as surfactant and aqueous LiOH (preferred to NaOH because of its higher water solubility), in 9:1 (v/v) isooctane/1-octanol. The alcohol (which is essential for constituting stable reverse micelles) is actually a cosurfactant, which partitions between the micelle layer and the bulk solvent. Following the method described by Bowcott and Schulman,[9] we could show that 14% of the total 1-octanol, i.e., 90 mM, is localized at the micellar interface. In this reverse micellar system we could solubilize 0.8% (v/v) of aqueous LiOH (2.86 M), which corresponds to a $w_0 = 9.2$ ($w_0 = [H_2O]/[\text{octanoic acid salt}]$) and to 23 mM LiOH (overall concentration).

We have characterized this micellar system at this w_0 by quasielastic light scattering,[10] establishing the presence of relatively monodisperse, spherical aggregates having an average radius of 22.7 ± 0.3 Å. This corresponds to a water pool radius R_w of circa 12 Å, taking 10.4 Å for the extended length of one octanoic acid molecule.[11]

The reaction we have utilized is the hydrolysis of octanoic acid octyl ester (typically 25 mM) catalyzed by LiOH. Octanoic acid octyl ester, because of the partly polar character of the ester bond, will also be present at the micellar interface (see Figure 1), although it will be preferentially localized in the bulk solvent.[12] Hydrolysis yields both the surfactant (the octanoic acid salt) and the cosurfactant (1-octanol). Since LiOH is not soluble in the organic phase, it will be localized in the water pool; and therefore the hydrolysis reaction will take place at the micellar interface, i.e., still within the domain of the micelle.[13] Since reverse micelles are highly dynamic entities, which by collision exchange very rapidly the water pool content,[14,15] at any given time, we will have

---

* To whom correspondence should be addressed.

† Institut für Polymere, ETH-Zentrum.

‡ Institut Charles Sadron (CRM-EAHP), CNRS.

(1) Von Kiedrowski, G. *Angew. Chem.* **1986**, *98*, 932-934.

(2) Zielinski, W. S.; Orgel, L. E. *Nature* **1987**, *327*, 346-347.

(3) Tjivikua, T.; Ballester, P.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1990**, *112*, 1249-1250.

(4) Luisi, P. L.; Varela, F. *Origins Life Evol. Biosphere* **1989**, *19*, 633-643.

(5) Maturana, H.; Varela, F. *Autopoiesis and Cognition*: *The Realization of the Living*; D. Reidel: Boston, 1980.

(6) Varela, F.; Maturana, H.; Uribe, R. *BioSystems* **1974**, *5*, 187-196.

(7) Fleischaker, G. R. *BioSystems* **1988**, *22*, 37-49.

(8) An inorganic autopoietic system, so-called osmotic growth, has recently been discussed in the literature: Zeleny M.; Klir, G. J.; Hufford, K. D. *Artif. Life* **1988**, 125-139.

(9) Bowcott, J. E.; Schulman, J. H. *Z. Elektrochem.* **1955**, *59*, 283-290.

(10) Quasielastic light scattering experiments were made with a Malvern 4700 PS/MW spectrometer and an argon ion laser (coherent, Innova Model 200-10, λ_0 = 488 nm).

(11) Small, D. M. *Handbook of Lipid Research*; Plenum Press: New York, 1986; Vol. 4, p 67.

(12) Note that the infrared spectrum of the ester in the carbonyl stretching region between 1800 and 1500 cm^{-1} is not affected by the reverse micelles, indicating that the ester is localized preferentially in the bulk solvent phase.

(13) This was not so, for example, in the reaction between trimethylamine and cetyl bromide, which leads to the surfactant CTAB (cetyltrimethylammonium bromide) and which was also attempted in CTAB reverse micelles; in this case, due to the unfavorable partition of the reagents, the synthetic reaction takes place mostly in the bulk solvent (Mascolo, G; Giustini M.; Luisi, P. L.; Lang, J. *J. Colloid Interface Sci.*, in press).

(14) Flechter, P. D. I.; Robinson, B. H. *Ber. Bunsen-Ges. Phys. Chem.* **1981**, *85*, 863-867.

(15) Luisi, P. L.; Giomini, M. P.; Pileni, M. P.; Robinson, B. H. *Biochim. Biophys. Acta* **1988**, *947*, 209-246.