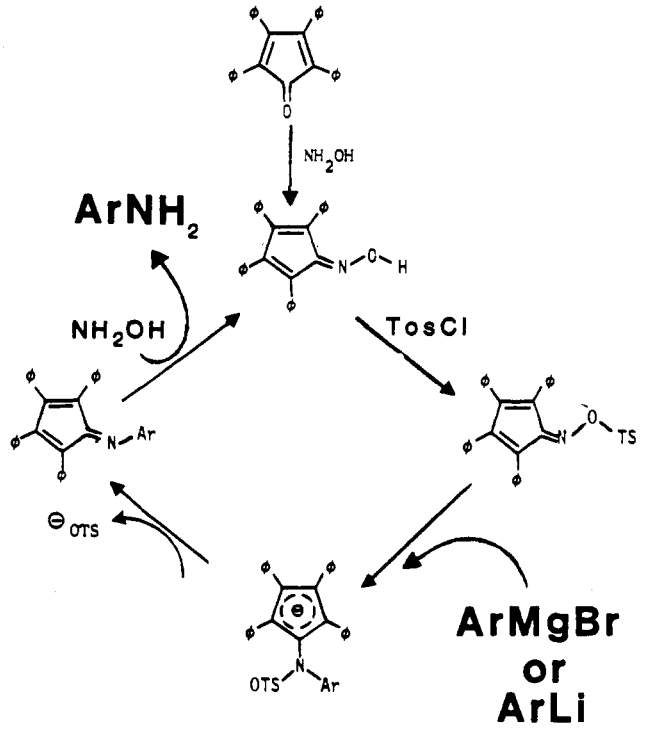


Figure 1.

commercially available; the oxime and oxime *O*-tosylate are readily obtained by successive treatment with hydroxylamine and tosyl chloride.

The reaction leading to the formation of the imine probably proceeds via nucleophilic addition to the heteroatom, creating a highly stabilized cyclopentadienyl anion. The intermediate anion then undergoes elimination of the tosylate. The only significant side reaction appears to be reduction of the imine tosylate to the unsubstituted imine (vide infra). One possible means of eliminating this problem may be substituting a different carbanion stabilizing moiety for the tetraphenylcyclopentadiene system. This type of structural change may also prove to be an effective means for tailoring a specific substrate to match a particular organometallic reagent.

The present results (Table I) demonstrate that the oxime *O*-tosylate of tetraphenylcyclopentadienone reacts with aryllithium or arylmagnesium bromide to give the corresponding imine in good to excellent yield. The final reaction involves the conversion of the imine to the oxime and arylamine and is carried out by reaction with excess hydroxylamine in aqueous pyridine (e.g., entry 8a, Table I). Significant features of this synthetic method are the good yields of aryl amines which are obtained, and the unusual mode of activating the effective aminating reagent *O*-tosylhydroxylamine by attaching an auxilliary group (tetraphenylcyclopentadienyl moiety) which then can be removed and efficiently recycled through the sequence (e.g., Figure 1; entry 8b, Table I).[19,20]

(19) Aliphatic lithium and Grignard reagents also react with the oxime *O*-tosylate of cyclopentadienone to yield the corresponding imine. Competing side reactions are the formation of the unsubstituted imine and double addition of the nucleophile on nitrogen to yield 1-(dialkylamino)-2,3,4,5-tetraphenylcyclopentadiene, 1-(alkylamino)-2,3,4,5-tetraphenylcyclopentadiene and 1-amino-2,3,4,5-tetraphenylcyclopentadiene. The reaction of *n*-BuZnBr with the oxime tosylate yields comparable amounts of the unsubstituted imine and the *n*-butylimine, but no double addition is observed. This suggests that oxime tosylates may be useful in efficient synthesis of aliphatic amines, if organometallic reagents with metals less electropositive than lithium, magnesium, or zinc are employed and if the oxime moieties are chosen to maximize stabilization of carbanion intermediates (arising from nucleophilic addition on nitrogen) in preference to radical intermediates formed by one-electron transfer. Preliminary experiments with functionalized organolithiums and organomagnesiums (e.g., *N,N*-dialkylcarboxyamide, methoxy, α-thio) indicate that optimal yields of monosubstituted imines are highly dependent on the choice of metal, and investigation of this aspect is in progress.

Acknowledgment. This work was supported in part by a grant from the donors of the Petroleum Research Fund, administered by the American Chemical Society, by the Pennwalt Corporation Grant of Research Corporation, by NSF, and by continued assistance from the University Research Committee (UCLA). M.J.T. acknoweledges a President's Undergraduate Fellowship. We thank Professor Wayne Thompson, Kenneth Kloc, and Chris Buhr, for stimulating discussions and preprints.

Registry No. *N*-Phenyl-2,3,4,5-tetraphenylcyclopentadienimine, 35160-46-4; *N*-(2-naphthyl)-2,3,4,5-tetraphenylcyclopentadienimine, 91550-18-4; *N*-(1-naphthyl)-2,3,4,5-tetraphenylcyclopentadienimine, 91550-19-5; *N*-(9-phenanthryl)-2,3,4,5-tetraphenylcyclopentadienimine, 91550-20-8; *N*-(2,3,5,6-tetramethylphenyl)-2,3,4,5-tetraphenylcyclopentadienimine, 91550-21-9; 2,3,4,5-tetraphenylcyclopentadienimine, 91550-22-0; *N*-(2-furyl)-2,3,4,5-tetraphenylcyclopentadienimine, 91550-23-1; *N*-(3-furyl)-2,3,4,5-tetraphenylcyclopentadienimine, 91550-24-2; tetraphenylcyclopentadiene oxime tosylate, 91550-25-3; phenylmagnesium bromide, 100-58-3; 2-naphthylmagnesium bromide, 21473-01-8; 1-naphthylmagnesium bromide, 703-55-9; 9-phenanthrylmagnesium bromide, 71112-64-6; 2,3,5,6-tetramethylphenylmagnesium bromide, 75724-98-0; 2-lithiofuran, 2786-02-9; 3-lithiofuran, 53101-93-2; aniline, 62-53-3; tetraphenylcyclopentadiene oxime, 91550-26-4.

Supplementary Material Available: Full experimental details for preparation of oximes and imines (2 pages). Ordering information is given on any current masthead page.

(20) It has been found that the reaction times are much shorter when an excess of organometallic reagent is used, compared to stoichiometric amounts of oxime tosylate and organometallic (10–60 min vs. overnight). For inexpensive organometallics this practice is of little consequence but the experimental conditions reported here may require modification when stoichiometric quantities are employed. Many aromatic amines are considerably more expensive than the corresponding bromides used as precursors for the organometallic reagent (e.g., 9-aminophenanthrene $108/g vs. 9-bromophenanthrene, $1/g.; Aldrich catalog, 1984–1985; see Table I, entry 4).

Design and Reactivity of Topologically Unique, Chiral Phosphonamides. Remarkable Diastereofacial Selectivity in Asymmetric Olefination and Alkylation

Stephen Hanessian,* D. Delorme, S. Beaudoin, and Y. Leblanc

Department of Chemistry, Université de Montréal Montréal Québec, Canada H3C 3V1

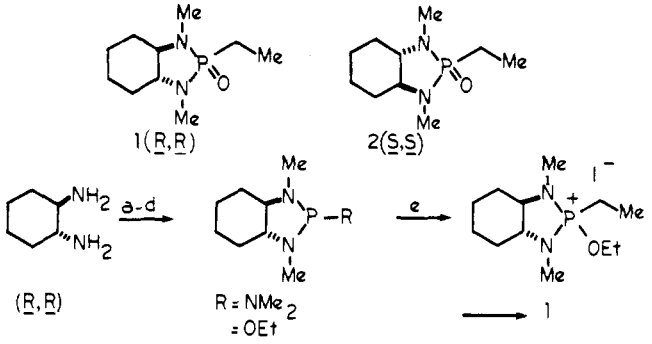
Received April 24, 1984

In spite of the phenomenal progress made in the general area of asymmetric synthesis in recent years,[1,2] comparatively little effort has been devoted to asymmetric olefination reactions and the few examples have involved substituted cycloalkanones.[3,5] In addition to the many problems that are omnipresent in Wittig-type olefinations.[6,7] controlling the stereochemistry of unsymmetrical olefins is perhaps a most sought after requirement.[8,9] In this

(1) "Asymmetric Synthesis—A Multivolume Treatise"; Morrison, J. D., Ed.; Academic Press: New York, 1984.
(2) ApSimon, J. W.; Seguin, R. P. *Tetrahedron* **1979**, *35*, 2797.
(3) Bestmann, H. J.; Lienert, J. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 763. See also: Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699.
(4) Tömösközi, I.; Janzo, G. *Chem. Ind.* **1962**, 2085. An error exists in the Table regarding the values of the optical rotations and/or the optical purities reported in this paper.
(5) Johnson, C. R.; Elliot, R. C.; Meanwell, N. A. *Tetrahedron Lett.* **1982**, *23*, 5005. See also: Johnson, C. R.; Elliott, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 7041.
(6) Bestmann, H. J. *Pure Appl. Chem.* **1980**, *52*, 771. See also: Gosney, I.; Rowley, A. G. In "Organophosphorus Reagents in Organic Synthesis"; Cadogan, J. I. G., Ed.; Academic Press, New York, 1979; p 17.
(7) See, for example: McMurry, J. E.; von Beroldinger, L. A. *Tetrahedron* **1974**, *30*, 2027. Heathcock, C. H.; Radcliffe, R. *J. Am. Chem. Soc.* **1971**, *93*, 1746. Sowerby, R. L.; Coates, R. M. *J. Am. Chem. Soc.* **1972**, *94*, 4758.
(8) See, for example: Reitz, A. B.; Mutter, M. S.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1984**, *106*, 1873. Anderson, R. J.; Henrick, C. A. *J. Am. Chem. Soc.* **1975**, *97*, 4327. Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1 and references cited therein. For some mechanistic insights, see: Vedejs, E.; Meier, G. P.; Snoble, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 2823 see also ref 6.

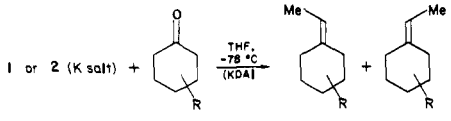
0002-7863/84/1506-5754$01.50/0

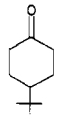
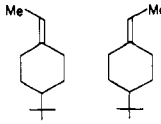
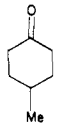
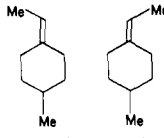
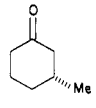
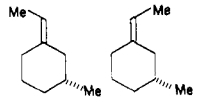
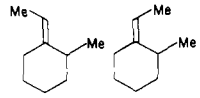
Scheme I[a]



[a] (a) $ClCO_2Et$, aqueous NaOH, benzene, 77%; (b) LAH, THF, 92%; (c) $(Me_2N)_3P$, benzene, reflux, 74%; (d) EtOH, benzene, reflux; (e) EtI, benzene, reflux, 87% (2 steps).

Table I. Asymmetric Olefination with Reagents 1 and 2

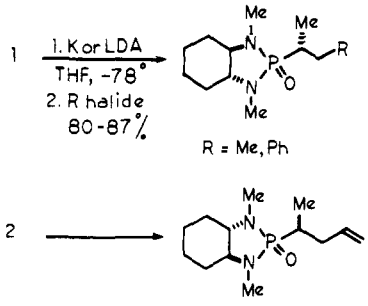


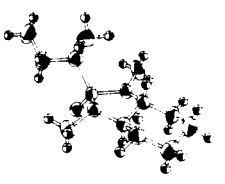
reagent	ketone	products	$[\alpha]_{Hg}$	% optical purity
1. *R,R*		 *R* 95:5 *S*	−19°	90
2. *S,S*		5:95	+18.9°	90
3. *R,R*		 *R* 85:15 *S*	−12.5°	69
4. *R,R*	 (+)-*R*	 *E,R* 93:7 *Z,R*	−52.8°	86
5. *S,S*		15:85	+12.5°	69
6. *R,R*	 rac	 *E* 72:28 *Z*	−24.3°	

regard, the formation of optically active olefins from achiral ketones would constitute a veritable challenge in reagent design.

We wish to report on the synthesis of topologically unique, enantiomeric chiral bicyclic phosphonamide reagents **1** and **2** (Scheme I) and to demonstrate their remarkable stereodifferentiating reactivity toward alkyl cyclohexanones (Table I) as well as alkyl halides. Paramount in the design of these reagents was the inherent C_2 symmetry of the parent chiral diamines[10] and the stereoelectronic consequences[11] resulting from the spatial disposition of the heteroatoms. To further challenge the validity of the design and the prospects of achieving asymmetric olefination,

Scheme II





R = Me (from 1)

we chose among several substituted cyclohexanones, achiral, axially symmetrical analogues, which, in the event of a stereodifferentiating reaction, would lead to *axially dissymmetric, optically active olefins*.[3,12-14]

The synthesis of the chiral bicyclic phosphonamide **1** (waxy crystals, $[\alpha]_D$ −91.8° (*c* 1.22, $CHCl_3$], ^{31}P NMR 47.0 ppm, M^+ 216.1372) starting from the known, optically active (*R,R*)-1,2-diaminocyclohexane[10] is shown in Scheme I. The *S,S* reagent, $[\alpha]_D$ +90.1° (*c* 2.62, $CHCl_3$], was similarly prepared from the enantiomeric diamine. Treatment of 4-*tert*-butylcyclohexanone with the anion of **1** generated with KDA, gave a 82% yield of (*R*)-(4-*tert*-butylcyclohexylidene)ethane with an optical purity of 90 ± 2%[15] (Table I, entry 1). Reaction with 4-methylcyclohexanone under the same conditions proceeded with the same sense of induction to give a mixture of *R* and *S* olefins corresponding to an optical purity of 69% in favor of the (−)-*R* isomer (Table I, entry 3). The ratios of isomers was reversed with the enantiomeric *S,S* reagent.

Treatment of (+)-3-methylcyclohexanone under the same conditions gave (*E*,3*R*)-(3-methylcyclohexylidene)ethane with high optical purity (86%) as evidenced by direct comparison with an authentic sample (Table I, entry 4). Reaction with ethylidenetriphenylphosphorane gave a 3:2 ratio of the diastereomeric *E*,3*R* and *Z*,3*R* olefins, respectively, indicating a modest inherent bias for the *E,R* isomer.[16] Interestingly, using the *S,S* reagent **2**, it was possible to reverse the ratio obtained with the enantiomeric reagent to give an 85:15 mixture of the *Z*,3*R* and *E*,3*R* isomers, respectively (70% optical purity), counteracting the inherent bias toward the *E,R* olefin in this system.[17] When *rac*-2-methylcyclohexanone was subjected to the same olefination with the *R,R* reagent, a 72:28 mixture of optically active olefins was obtained to which we assign the *E* and *Z* structures, respectively, on the basis of ^{13}C NMR and NOE studies and the results obtained above (Table I, entry 6).[5]

Although the precise reasons for the high diastereofacial selectivity in these reactions cannot be delineated at the moment, it is clear that nucleophilic attack is taking place from the more accessible face of the anion. The remarkable asymmetric olefination in the case of 4-*tert*-butylcyclohexanone can be attributed to attack from the equatorial side of the carbonyl group by the *pro-R* face of the anion. The potential reversibility of the olefination reaction via intermediate β-alkoxyphosphonamides prompted us to probe the reactivity of the phosphonamide anion derived from **1** and **2** toward alkyl halides (Scheme II). In each case a high preponderance (80%) of one diastereomer was formed

(9) Corey, E. J.; Kwiatkowski, G. T. *J. Am. Chem. Soc.* **1968**, *90*, 6816; **1966**, *88*, 5652, 5654.

(10) Galsbol, F.; Steenbol, P.; Sorensen, S. B. *Acta Chem. Scand.* **1972**, *26*, 3605. Asperger, R. G.; Lin, C. F. *Inorg. Chem.* **1965**, *4*, 1492. See also: Onuma, K.; Ito, T.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2012.

(11) Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Baldwin, J. E., Ed.; Pergamon Press: Oxford, 1983. Gorenstein, D. G.; Luxon, A. B.; Goldfield, E. M. *J. Am. Chem. Soc.* **1980**, *102*, 1757.

(12) Brewster, J. H.; Privett, J. E. *J Am. Chem. Soc.* **1966**, *88*, 1419.

(13) Duraisamy, M.; Walborsky, H. M. *J. Am. Chem. Soc.* **1983**, *105*, 3252. Walborsky, H. M.; Banks, R. B.; Banks, M. L. A.; Duraisamy, M. *Organometallics* **1982**, *1*, 667.

(14) For a recent example of transfer of chirality to an axial chiral element, see: Meyers, A. I.; Wettlaufer, D. G. *J. Am. Chem. Soc.* **1984**, *106*, 1135.

(15) Authentic (−)-(*R*)-(4-*tert*-butylcyclohexylidene)ethane, $[\alpha]_{Hg}$ −19° (*c* 1.53, $CHCl_3$) was prepared from (4-*tert*-butylcyclohexylidene)acetic acid of 98% optical purity on the basis of the procedures described by Walborsky and co-workers.[13]

(16) For an example of inherent bias in a related reaction, see: Koreeda, M.; Brown, L. *J. Org. Chem.* **1983**, *48*, 2122.

(17) Similar results were obtained using enantiomeric benzylphosphonamides related to **1** and **2** which gave optically active benzylidenealkylcyclohexanes.[3,12]

and isolated as a crystalline product as evidenced by single-crystal X-ray analysis and ^{31}P NMR.[18] Thus, as originally anticipated, from inspection of molecular models, easier access by the bulky base to the *pro-R* hydrogen in the *R,R* reagent, for example, leads to a carbanion that shows high diastereofacial bias.[19]

Reagents of the type described in this work are unique because of their inherent topology, chirality, and symmetry elements, which are *integral parts of the molecules*, and they differ from other types of phosphorus reagents where asymmetric induction in olefination has been reported.[3-5] The synthesis of optically enriched (alkylcyclohexylidene)ethanes[20] and alkylphosphonamides such as demonstrated in the present study may find applications in the synthesis of vitamins,[20] pheromones,[21] etc. as well as in the design of novel chiral catalysts.[22]

Acknowledgment. We acknowledge financial support from NSERCC, Le Ministère de l' Education du Québec in the form of fellowships to Y.L., D.D., and G. Caron (summer undergraduate research participant). We thank M. Evans for mass spectra, and Dr. Phan Viet Tan for high-resolution NMR spectra and NOE measurements. We are indebted to Prof. F. Brisse and F. Bélanger-Gariépy for the X-ray determination.

Supplementary Material Available: Analytical data, experimental procedure, and a perspective view of the product from **1**, R = Me (9 pages). Ordering information is given on any current masthead page.

(18) For R = Me, mp 96–96.5 °C: $[\alpha]_D$ −81.5° ($CHCl_3$), R = Ph, mp 95–97 °C, $[\alpha]_D$ −34.6°. The allyl derivative from the *S,S* reagent showed mp 87–89 °C, $[\alpha]_D$ +92.8°.

(19) When the anion was quenched with deuteriomethanol and the resulting deuterated phosphonamide (54% deuterium content) was treated sequentially with KDA then benzyl bromide (THF, −78 °C), the diastereomerically pure *R*-benzylated product contained only 14% deuterium, indicating a higher proportion of *pro-R* deuterio species in the deuterated phosphonamide and reflecting on the substantial "*pro-R*" bias of the anion.

(20) Batcho, A. D.; Berger, D. E.; Davoust, S. G.; Wovkulich, P. M.; Uskokovic, M. R. *Helv. Chim. Acta* **1981**, *64*, 1682.

(21) Mori, K. In "The Total Synthesis of Natural Products"; ApSimon, J. A., Ed.; Wiley-Interscience: New York, 1981, Vol. 4, p 1.

(22) See, for example: Halpern, J. *Science* (*Washington, D.C.*) **1982**, *217*, 401. Bosnich, B.; Fryzuk, M. D. *Top. Stereochem.* **1981**, *12*, 119. Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1978**, *10*, 175. Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978**, 329 and references cited therein.

Ghost Vesicles[1]

Steven L. Regen* and Jae-Sup Shin

Department of Chemistry, Marquette University
Milwaukee, Wisconsin 53233

James F. Hainfeld and Joseph S. Wall

Department of Biology
Brookhaven National Laboratory
Upton, New York 11973

Received June 11, 1984

In this communication we describe the use of surfactant vesicles as templates for the synthesis of ultrathin spherical polymer membranes. Microspheres that are produced *upon removal of the lipid bilayer* are termed "ghost vesicles".

We have previously reported the synthesis of a new class of polymerized vesicles in which a lipid bilayer is encased within concentric polymeric counterions.[2] Recently it occurred to us that by forming cross-linked analogues, it might be possible to extract the surfactant bilayer and to leave behind extremely thin

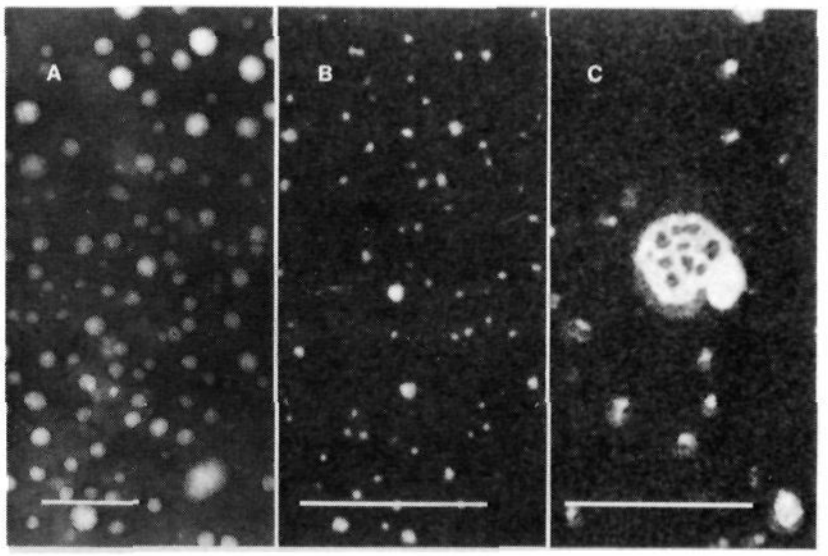


Figure 1. Electron micrographs of **3**: (A) 2% uranyl acetate stain (bar represents 3000 Å); (B) STEM (bar represents 5200 Å); (C) STEM (bar represents 2600 Å).

polymeric spheres. We further reasoned that such "ghost vesicles" would not only be unique in structure, but that they also could be of considerable practical value. They could, for example, serve as attractive packaging material for the encapsulation of metal colloids, enzymes, and other catalysts.[3] Because of their thinness, the barrier toward mass transport of reactants into and products out of the carrier should be minimal. In addition, ultrathin membranous compartments might constitute an ideal medium for separating donor and acceptor species over *short* distances, making highly efficient energy- or electron-transfer processes possible.[4] With these ideas in mind, we have begun to focus on the feasibility of preparing such polymers. In this report we now describe the synthesis and preliminary characterization of the first example of a ghost vesicle, derived from polymerized vesicles of diallylammonium dihexadecylphosphate (**1**) plus sodium dihexadecylphosphate (**2**).

Dihexadecylphosphoric acid was converted into **1** by treatment with diallylamine in ethanol/water (6/4); the resulting surfactant was recrystallized from ethyl acetate and gave the expected ^1H NMR spectrum. Dispersal of 118 mg (0.18 mmol) of **1** plus 104 mg (0.18 mmol) of **2** in 100 mL of water, via vortex mixing and sonication at 80 °C (to constant turbidity), afforded a stable vesicle dispersion. Thin-layer chromatography indicated that no lipid decomposition occurred during sonication [silica gel, 1:1 $CHCl_3/CH_3OH$, R_f(**1**) 0.75; R_f(**2**) 0.70]. Vesicle polymerization was carried out by direct UV irradiation at 254 nm (12 h) under a nitrogen atmosphere using procedures similar to those previously described.[5] Thin-layer chromatography indicated the disappearance of **1**, retention of **2**, and a product remaining at the origin. Temperature-dependent turbidity measurements (400 nm) confirmed the presence of bilayers, before and after photopolymerization; both exhibited a well-defined phase transition in the expected range of 63–66 °C.[6] The resulting dispersion was (a) treated with 20 mL of 1.0 M HCl and stirred at room temperature for 6 h, (b) dialyzed twice against 2 L of water for 24 h, and (c) freeze-dried. After the successive and dropwise addition of chloroform (10 mL) and ether (10 mL), the mixture was allowed to stand for 6 h. The vesicular ghost was then collected by filtration and dried [24 h, 25 °C (0.05 mm)], yielding 15.3 mg (62%) of **3**. Anal. Calcd for a polymer having a repeating unit consisting of $C_6H_{12}NCl \cdot {}^1/_4H_2O$: C, 52.17; H, 9.12; Cl, 25.67; N, 10.14; P, 0.00. Found: C, 52.18; H, 9.00; Cl, 25.57; N, 9.88; P, 0.05. The IR spectrum of **3** showed nearly complete disappearance of the olefinic absorption band $\nu_{C=C}$ 1635 cm^{-1}, indicating that the extent of polymerization is high.

(1) Supported by the Division of Basic Energy Sciences of the Department of Energy, Contract EG-77-S-02-4446 (Marquette), and by NIH Grant 1R01GM31975-01 (Brookhaven).

(2) Regen, S. L.; Shin, J.-S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1984**, *106*, 2446.

(3) Kurihara, K.; Fendler, J. H. *J. Am. Chem. Soc.* **1983**, *105*, 6152. Tricot, Y. M.; Fendler, J. H. *Ibid.* **1984**, *106*, 2475.

(4) Calcaterra, L. T.; Closs, G. L.; Miller, J. R. *J. Am. Chem. Soc.* **1983**, *105*, 670.

(5) Regen, S. L.; Singh, A.; Oehme, G.; Singh, M. *J. Am. Chem. Soc.* **1982**, *104*, 791.

(6) Okahata, Y.; Ando, R.; Kunitake, T. *Ber. Bunsenges, Phys. Chem.* **1981**, *85*, 789.

0002-7863/84/1506-5756$01.50/0