be broadly operative in oxidative additions and reductive eliminations that involve metalloradicals.

Selective reaction of methane with (TMP)Rh• in benzene solvent is a distinctive feature of this system in that other reported metal complexes have manifested a preference for aromatic C–H bond reactivity.[12-17] Aromatic C–h bond reactions are favored thermodynamically because the difference in M–phenyl and M–CH_3 bond energies (10–25 kcal mol^{-1})[15-19] more than compensates for the difference in C–H bond energies ($C–H_{(C_6H_6)}$ = 110 kcal mol^{-1}, $C–H_{(CH_4)}$ = 105 kcal mol^{-1}). Oxidative addition of C–H bonds to a single metal center usually occurs under thermodynamic control, which results in a preference for reactions with aromatics.[15,16] Reaction of a phenyl C–H bond with two metalloradicals requires a nonlinear Rh···C···H···Rh transition state, which places the two sterically demanding (TMP)Rh• groups in an untenable proximity. We currently believe that the absence of (TMP)Rh• reactivity with benzene is a kinetic effect arising from unfavorable steric interactions in the transition state.

The general reaction of two metalloradicals with methane and the corresponding enthalpy–bond energy relationship are given by eqs 3 and 4. Evaluation of eq 4 using $\Delta H_2°$ (−12 kcal mol^{-1})

$$2M^{\bullet} + CH_4 \rightleftharpoons M–CH_3 + M–H \quad (3)$$

$$\Delta H_2° = (H_3C–H) - [(M–CH_3) + (M–H)] \quad (4)$$

and $H_3C–H$ (105 kcal mol^{-1}) results in an estimate of 117 kcal mol^{-1} for the sum of the (TMP)Rh–H and (TMP)Rh–CH_3 bond energies.[7c] IR data suggest that the Rh–H bond energy in (TMP)Rh–H is somewhat smaller than the 62-kcal value observed for (OEP)Rh–H[1,2] (ν((OEP)Rh–H) = 2220 cm^{-1}, ν((TMP)Rh–H) = 2095 cm^{-1}). Estimating the Rh–H bond energy for (TMP)Rh–H at ~60 kcal mol^{-1} places the Rh–CH_3 bond energy at ~57 kcal mol^{-1}.

Bimolecular reductive eliminations of methane from reactions of metal hydride and methyl complexes provided early evidence that thermodynamic rather than kinetic factors were responsible for limiting the reactions of methane with transition-metal complexes.[20] More recent studies have provided examples of homogeneous metal complexes that react with alkanes by oxidative addition to a single metal center,[13-16,21-26] σ-bond metathesis of M—X units,[27-29] and addition to M=X groups.[30-33] Mechanistic studies have illustrated the importance of alkane C–H σ-bond donation in oxidative additions[34] and four-centered cyclic interactions in reactions of M—X and M=X units.[27-30] The reaction of (TMP)Rh• with methane expands the mechanistic versatility for alkane reactions by providing an example of oxidative addition of a methane C–H unit with two metalloradicals through a probable linear four-centered transition state. The reaction of (TMP)Rh• with methane is also unusual in permitting the direct observation of the reactive metal species, (TMP)Rh•, complete selectivity for reaction of CH_4 in benzene solvent, and the exclusion of undesirable intramolecular C–H bond reactions. We are currently refining and extending the kinetic and thermodynamic measurements for the methane reaction, examining the reactivity of a series of alkanes, and extending this work to iridium porphyrins.

Acknowledgment. We gratefully acknowledge helpful discussions of this work with Professor Donald H. Berry and partial financial support by the National Science Foundation through Grant CHE-87-16691.

Registry No. (TMP)Rh, 121393-39-3; CH_4, 74-82-8; (TMP)$RhCH_3$, 121471-27-0; (TMP)RhH, 124535-65-5; (TMP)Rh^-, 124535-66-6; D_2, 7782-39-0.

(11) Chao, T. H.; Espenson, J. H. *J. Am. Chem. Soc.* **1978**, *100*, 129.
(12) Castelhano, A. L.; Griller, D. *J. Am. Chem. Soc.* **1982**, *104*, 3655.
(13) Graham, W. A. G.; Ghosh, C. K. *J. Am. Chem. Soc.* **1987**, *109*, 4726.
(14) Hackett, M.; Whitesides, G. M. *J. Am. Chem. Soc.* **1988**, *110*, 1449.
(15) (a) Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* **1989**, *22*, 91. (b) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1984**, *106*, 1650.
(16) (a) Nolan, S. P.; Hoff, C. D.; Stoutland, L. J.; Newman, J. M.; Buchanan, J. M.; Bergman, R. G.; Yang, G. K.; Peters, K. S. *J. Am. Chem. Soc.* **1987**, *109*, 3143. (b) Stoutland, P. O.; Bergman, R. G.; Nolan, S. P.; Hoff, C. D. *Polyhedron* **1988**, *7*, 1429.
(17) Bulls, A. R.; Bercaw, J. E.; Manriquez, J. M.; Thompson, M. E. *Polyhedron* **1988**, *7*, 1409.
(18) Bruno, J. W.; Marks, T. J.; Morss, L. R. *J. Am. Chem. Soc.* **1983**, *105*, 6824.
(19) Dias, A. R.; Simoes, J. A. M. *Polyhedron* **1988**, *7*, 1531.
(20) (a) Nappa, M. J.; Santi, R.; Diefenbach, S. P.; Halpern, J. *J. Am. Chem. Soc.* **1982**, *104*, 619. (b) Halpern, J. *Acc. Chem. Res.* **1982**, *15*, 332. (c) Halpern, J. *Inorg. Chim. Acta* **1985**, *100*, 41.
(21) Janowicz, A. H.; Bergman, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 3929.
(22) McGhee, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 4346.
(23) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1985**, *107*, 620.
(24) Hoyano, J. K.; Graham, W. A. G. *J. Am. Chem. Soc.* **1982**, *104*, 3723.
(25) Chetcuti, P. A.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1987**, *109*, 942.
(26) (a) Berry, M.; Elmitt, K.; Green, M. L. H. *J. Chem. Soc., Dalton Trans.* **1979**, 1950. (b) Cooper, N. J.; Green, M. L. H.; Mahtab, R. *J. Chem. Soc., Dalton Trans.* **1979**, 1557.
(27) Thompson, M. E.; Baxter, S. M.; Bulls, A. R.; Burger, B. J.; Nolan, M. C.; Santarsiero, B. D.; Schaefer, W. P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 203.
(28) Fendrick, C. M.; Marks, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 425.
(29) (a) Watson, P. L. *J. Am. Chem. Soc.* **1983**, *105*, 6491. (b) Watson, P. L.; Parshall, G. W. *Acc. Chem. Res.* **1985**, *18*, 51.
(30) Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731.
(31) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729.
(32) McDade, C.; Green, J. C.; Bercaw, J. E. *Organometallics* **1982**, *1*, 1629.
(33) Cook, B. R.; Reinart, T. J.; Suslick, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 7281.
(34) (a) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7332. (b) Stoutland, P. O.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 5732.

Template-Directed Synthesis of (±)-Allosamizoline and Its 3,4-Epimers

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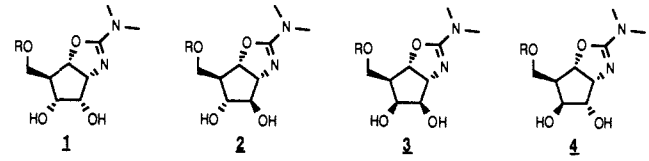
The importance of chitin as one of the main structural components of insect cuticles[1] and fungal cell walls[2] generates interest in discovering agents that may interact with its biosynthesis. A screen for chitinase inhibitors revealed the presence of a novel pseudotrisaccharide allosamidin in the mycelial extract of *Streptomyces* sp. no. 1713.[3] Its structure derives from its hydrolysis, which produces 2 equiv of D-allosamine and 1 equiv of a new aminocyclitol, named allosamizoline, whose structure was initially suggested to be the cis diol **1a**[4] and later revised to the trans diol **2a**.[5] Since the structural assignment rests on inter-



1 **2** **3** **4**

a) series R = H b) series R = CH_2Ph

†NSF Predoctoral Fellow.

(1) Kramer, K. J.; Dziadik-Turner, C.; Koga, D. *Comprehensive Insect Physiology Biochemistry and Pharmacology*; kerkut, G. A., Gilbert, L. I., Eds.; Pergamon Press, Inc.: New York, 1985; Vol. 3. Andersen, S. D. *Annu. Rev. Entomol.* **1979**, *24*, 29.
(2) Barrett-Bee, K.; Hamilton, M. *J. Gen. Microbiol.* **1984**, *130*, 1857. Bartnicki-Garcia, S. *Annu. Rev. Microbiol.* **1968**, *22*, 87.
(3) Sakuda, S.; Isogai, A.; Matsumoto, S.; Suzuki, A. *J. Antibiot.* **1987**, *40*, 296.
(4) Sakuda, S.; Isogai, A.; Matsumoto, S.; Suzuki, A.; Koseki, K. *Tetrahedron Lett.* **1986**, *27*, 2475.

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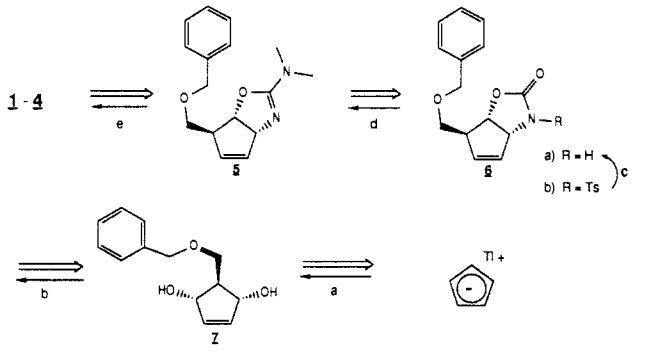
Scheme I. Retrosynthetic Analysis and Synthesis of Allosamizoline and Analogues[a]



[a](a) $PhCH_2OCH_2Cl$, ether, −20 °C, then thiourea, O_2, methylene blue, methanol, *hν*, 0 °C; 33%. (b) Two equivalents of TsNCO, THF, then $(dba)_3Pd_2{\cdot}CHCl_3$, $(i\text{-}PrO)_3P$, THF, room temperature; 93%. (c) Na, naphthalene, DME, −78 °C; 91%. (d) $CF_3SO_3CH_3$, CH_2Cl_2, then $(CH_3)_2NH$; 100%. (e) See text.

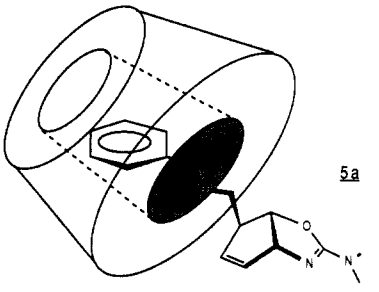
pretation of NMR data, which can be ambiguous in the case of five-membered rings, we undertook a synthesis of all four 3,4-epimers of allosamizoline, **1a**–**4a**. This densely functionalized series of cyclopentanes in which each ring carbon is substituted poses intriguing synthetic challenges which we believe can be approached by template directed reactions based upon transition metal and cyclodextrin chemistry.

Retrosynthetically, the cyclopentene **5** (see Scheme I) becomes a key intermediate since cis hydroxylation can provide diols **1** and **3** and trans hydroxylation, diols **2** and **4**. Accessibility of the oxazoline **5** from the oxazolidin-2-one **6** suggests the virtues of our Pd(0)-catalyzed oxazolidinone synthesis from vinyl epoxides or their equivalents.[6,7] Prospects for employing Pd-catalyzed asymmetric induction led us to focus on the later route wherein the meso diol **7** becomes the critical intermediate.

In a single operation, cyclopentadienylthallium[8] was alkylated in ether at −20 °C, the reaction mixture filtered through a plug of Celite with the aid of an ice-cold pentane wash, and the resultant solution concentrated at 0 °C (on a 43-mmol scale concentrated to 15 mL) and then added to a methanol solution of thiourea and methylene blue for the singlet oxygen reaction.[9,10] Chromatographic purification gave crystalline (mp 51–2 °C) diol **7**[11] (diastereomeric ratio 12:1). Assignment of the stereochemistry of the major diol as depicted rests upon the anticipated addition of singlet oxygen to the less hindered face of the monosubstituted cyclopentadiene.[8]

Oxazolidin-2-one formation also involves a single operation. The cis diol **7** is exposed to 2 equiv of *p*-tolylsulfonyl isocyanate followed by a Pd(0) catalyst, to produce the oxazolidinone **6b** (mp 105–6 °C),[11] which is easily reductively desulfonylated to the parent oxazolidinone **6a** (mp 85–6 °C).[11] An ancillary experiment preliminarily explored the possibility of an asymmetric synthesis of **6** using chiral ligands. Since phosphine ligands[12] failed to effect the formation of oxazolidinones, our excellent experience with BINAPO led us to explore this ligand.[13] Use of 3 mol % of $(dba)_3Pd_2CHCl_3$ and 6 mol % of (−)-BINAPO at ambient temperature gave a 91% yield of oxazolidinone of 59–65% ee. While this result is already quite encouraging, efforts will be directed toward further enhancements.

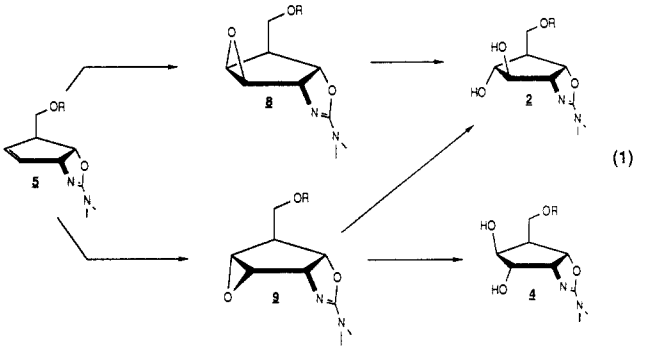
O-Alkylation and exposure of the resultant imino ether to dimethylamine completes the synthesis of the key cyclopentane[11] in a total of four stages. Initial efforts focused on the cis hydroxylation with osmium tetraoxide. Use of the standard catalytic procedure with NMO (*N*-methylmorpholine *N*-oxide) in 3:1 THF–water gives a 4.6:1 ratio of diol **3b**[11] to diol **1b**, from which the major isomer is isolated in 82% yield. The prediction that hydroxylation occurs preferentially on the convex face of the bicyclic system, as well as NOE studies on both cis diols, leads to the assignment of cis diol **3b** for the major isomer. Attempts to effect cis hydroxylation from the more hindered face by various known procedures failed. On the other hand, enhancing the steric shielding of the β face of the cyclopentene by complexing the benzyl group with β-cyclodextrin[14] (depicted schematically in **5a**)



5a

reverses the ratio of the two diols (62% yield based upon 24% recovery of starting material) to 1:2 in favor of the isomer corresponding to the originally assigned structure of allosamizoline **1b**.[11] Catalytic debenzylation (H_2, 10% Pd/C, CH_3OH, 40 psi) of both cis diols, **1b** as its trifluoroacetate salt and **3b** as its hydrochloride salt, and comparison of the pseudomonosaccharide **1a** and **3a** to an authentic sample of allosamizoline reveals that neither corresponds, confirming the reassignment. The table that appears in the supplementary material summarizes the ^1H and ^{13}C NMR data.

Formation of the trans vicinal diols **2** and **4** envisions opening of the epoxides **8** and **9** (eq 1). Steric and electronic factors conspire to favor regioselective opening of **8** to form **2**, whereas



(1)

epoxide **9** would be anticipated to form both trans diols. Epoxidation with trifluoroperacetic acid followed by catalytic hydrogenolysis did allow isolation of small amounts of the two epoxides **8** (R = H) and **9** (R = H). Molecular modeling indicates that $J_{1,5}$ and $J_{4,5}$ should be diagnostic of stereochemistry in that the dihedral angles of 140.7° and 50.7° for **8** (R = H) should give rise to couplings of about 3–5 and 1–3 Hz, respectively, whereas the dihedral angles of 97.6° and 74.5° for **9** (R = H) should give rise to couplings of about 0 Hz. Indeed, the former shows H(5) to be a tdd (J = 7.5, 3.3, 1.7 Hz) at δ 2.50 and the latter to be a triplet (J = 5.6 Hz), in excellent accord with our

(5) Sakuda, S.; Isogai, A.; Makita, T.; Matsumoto, S.; Koseki, K.; Kodama, H.; Suzuki, A. *Agric. Biol. Chem.* **1987**, *51*, 3251. Sakuda, S.; Isogai, A.; Matsumoto, S.; Suzuki, A.; Koseki, K.; Kodama, H.; Yamada, Y. *Agric. Biol. Chem.* **1988**, *52*, 1615.

(6) Trost, B. M.; Sudhakar, A. *J. Am. Chem. Soc.* **1987**, *109*, 3792; **1988**, *110*, 7933. Trost, B. M.; Hurnaus, R. *Tetrahedron Lett.*, in press.

(7) Hayashi, T.; Yamamoto, A.; Ito, Y. *Tetrahedron Lett.* **1987**, *28*, 4837; **1988**, *29*, 99.

(8) Corey, E. J.; Weinshenker, N. M.; Schaef, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675.

(9) Cf.: Kaneko, C.; Sugimoto, A.; Tanaka, S. *Synthesis* **1974**, 876.

(10) Initial use of anionic rose bengal led to some double-bond isomerization, which could be eliminated by switching to cationic methylene blue.

(11) This compound has been fully characterized spectroscopically and the elemental composition established by combustion analysis or high-resolution mass spectroscopy.

(12) See, however, ref 7.

(13) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143.

(14) For a review on cyclodextrin, see: Szejtli, J. *Cyclodextrin Technology*; Klewer Academic Publishers: Dordrecht, The Netherlands, 1988.

predictions. The former solvolyzes very cleanly and rapidly to the trans diol **2a**, which is identical spectroscopically and chromatographically with allosamizoline. The latter is remarkably robust to acid solvolysis, forming a mixture of the two trans diols upon prolonged reaction times.

Synthetically, a solution of 5.4 M trifluoroperacetic acid in trifluoroacetic acid (prepared by adding 4 equiv of trifluoroacetic anhydride to 3.3 equiv of 90% aqueous hydrogen peroxide) at 0 °C is added carefully to the cyclopentene **5** at 0 °C (**CAUTION!**) and the mixture evaporated in vacuo and then solvolyzed in 10% aqueous trifluoroacetic acid at 40 °C. Direct hydrogenolysis (10% Pd/C, 40 psig H_2, methanol, room temperature) gives a 67% overall yield of pure (±)-allosamizoline (mp 203–5 °C) and 16% of the epoxide **9** (R = H). Thus, allosamizoline is readily available in 19% overall yield in six stages. The synthesis of all four diol diastereomers not only provides unambiguous establishment of the relative stereochemistry but also provides all of the diastereomers to evaluate structure–activity relationships when incorporated into pseudosaccharides and, more generally, the ability of these cyclopentane derivatives to function as pseudoglucosamine analogues. More generally, the utility of the Pd-catalyzed protocol for vicinal hydroxyamination and the novel exploitation of cyclodextrin as a temporary diastereochemical control element is highlighted.

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Supplementary Material Available: Spectral data for **1ab**, **2ab**, **3ab**, **4ab**, **5**, **6ab**, and **7** and table of NMR comparisons of synthetic diastereomers and allosamizoline (3 pages). Ordering information is given on any current masthead page.

Cross-Linked Polystyrene Incorporating Water Pools

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Past experience with polymer chemistry[1,2] and with microemulsion systems[3] led us recently to combine the fields. As will be described, new polymeric materials were prepared by rigidifying reverse micellar systems formed by adding water and a suitable surfactant to a polymerizable monomer.

Years ago the term "water pool"[4] was coined to depict aqueous microdroplets that form in apolar solvents containing a surfactant, AOT.[5] So effective is AOT that one can readily dissolve 10–20% water in octane to give optically clear solutions. The size of the resulting water pools depends on the $[H_2O]/[AOT]$ ratio, henceforth called R. For example, hydrodynamic radii of 3.6 and 14.5 nm in octane are obtained with R values of 11 and 56, respectively.[6] We now report on (a) the preparation of systems where styrene/divinylbenzene[7] (rather than octane) comprised the apolar continuous phase and (b) the subsequent conversion of these microemulsions into solids by photopolymerization.[8,9]

Table I lists 10 polymers, the first nine of which were produced from water pools of various sizes and concentrations. Scanning

Table I. Surface Areas of Water Pool Modified Polymers

polymer	[AOT], M	$[H_2O]$, M	R ($[H_2O]/[AOT]$)	surf. area,[a] m^2/g
1	0.10	1.39	14	1.4
2	0.20	2.78	14	19.4
3	0.50	6.95	14	1.2
4	0.20	1.83	9.2	26.9
5	0.20	1.11	5.6	18.0
6	0.30	2.78	9.3	24.0
7	0.40	2.78	7.0	11.6
8	0.50	2.78	5.6	2.2
9[b]	0.20	2.78	14	33.6
10	0	0		0.9

[a] BET adsorption analysis. Particle size of the polymer: 150–250 mesh. [b] Polymer made from 100% divinylbenzene.

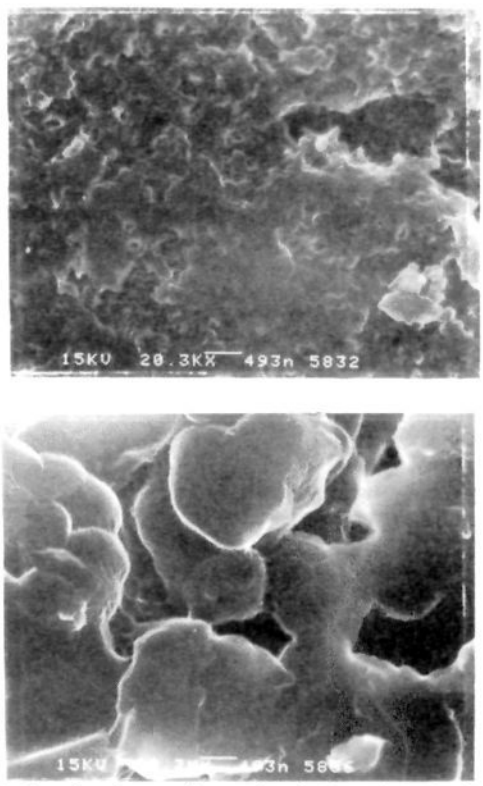

Figure 1. Scanning electron micrographs of polymer **4** (top) and polymer **8** (bottom) taken at 20 300 magnification. Scale bar is 493 nm.

(1) Menger, F. M.; Tsuno, T. *J. Am. Chem. Soc.* **1989**, *111*, 4903.
(2) Hammond, G. S.; Trapp, O. D.; Keys, R. T.; Neff, D. L. *J. Am. Chem. Soc.* **1959**, *81*, 4878.
(3) Menger, F. M.; Saito, G. *J. Am. Chem. Soc.* **1978**, *100*, 4376.
(4) Menger, F. M.; Donohue, J. A.; Williams, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 286.
(5) Aerosol O.T. 1,4-bis(2-ethylhexyl)sodium sulfosuccinate (supplied by Fisher). For a review of AOT-induced water pools, see: *Reverse Micelles*; Luisi, P. L., Straub, B. E., Eds.; Plenum: New York, 1984.
(6) Zulauf, M.; Eicke, H.-F. *J. Phys. Chem.* **1979**, *83*, 480.
(7) Aldrich (55% purified by distillation) and abbreviated DVB.
(8) Polymerizations were carried out by irradiating for 10 h in a Rayonet reactor optically clear mixtures of the following: AOT (0.10–0.50 M) and H_2O (1.4–7.0 M, 2.5–12.5 vol %) in styrene/divinylbenzene (6:4 v/v) with 2% benzoyl peroxide initiator. Reacting systems (3 mL in 10-mL test tubes) became progressively more opaque with no apparent phase separation. The resulting porous polymer rods were either used as such or else ground into a powder with the aid of a Technilab Micro-Mill. Polymer particles were (a) sieved into two sizes (150–250 mesh and >400 mesh), (b) washed with methanol and hexane to remove any monomer and AOT, and (c) dried thoroughly under vacuum. IR data and elemental analyses indicated that no detectable AOT remained.
(9) Polymerization of acrylamide in microdroplets stabilized by AOT is described by Candau et al.: Candau, F.; Zekhnini, Z.; Durand, J.-P. *J. Colloid Interface Sci.* **1986**, *114*, 398. The system is totally different from ours in that they polymerized the dispersed phase within the pools whereas we polymerized the continuous phase external to the pools.

0002-7863/90/1512-1263$02.50/0