Table II. Stereoselective Enolization of Representative Ketones with R_2BCl and Amines

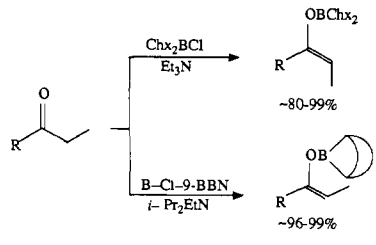
ketone	B-Cl-9-BBN[a] Z:E	Chx_2BCl[b] Z:E	yield of E isomer, % present[c]	literature[d]	ref
propiophenone	>99:1	<1:99	>99	3	2b
phenyl benzyl ketone	>99:1	15:85	85		
isopropyl ethyl ketone	65:35 (98):(2)[e]	<1:99	>99	81	2b
cyclohexyl ethyl ketone	60:40 (96):(4)[e]	<1:99	>99	86	1a
diethyl ketone	>99:1	21:79	79	31	2b

[a] Enolization carried out at 25 °C using *i*-Pr_2EtN. [b] Enolization carried out at 0 °C using Et_3N. [c] Highest conversion to (*E*)-enolate achieved with Chx_2BCl. [d] Highest conversion to (*E*)-enolate achieved for triflates. [e] *E*/*Z* ratio obtained after equilibration at 25 °C of the corresponding enol borinate. For the first two ketones, direct measurement of the *Z*/*E* ratio of enol borinates by PMR; for the other ketones, indirect measurements of *Z*/*E* ratio based upon analysis of the benzaldehyde aldol product.

surprised to find dicyclohexylboron chloride gave exclusively the (*E*)-enol borinate from propiophenone. Moreover, the syn/anti ratio of aldols obtained from these two enol borinates corresponds closely to the *Z*/*E* ratio of the enol borinates formed in the enolization stage as determined by the PMR analysis of the products. In addition, the conversion of a number of cyclic ketones to pure (*E*)-enol borinates, required by their cyclic structures, provided aldols which analyzed predominantly or exclusively for the anti aldol products: cyclopentanone, ~100%; cyclohexanone, 98%; cycloheptanone, 97%; cyclooctanone, ~100%. Previous workers in this area have also relied on this method to establish the *Z*/*E* ratio of their enol borinates.[1,2] Consequently, with the additional data now available, it appears safe to conclude that under our conditions, the *Z*/*E* ratio of the enol borinate formed in the enolization can be safely deduced from the syn to anti ratio of the aldol products for cases where the *Z*/*E* ratio cannot be measured directly.[9]

Our experimental data for the enolization of propiophenone and diethyl ketone by two different R_2B groups, Chx_2B- and 9-BBN, two different leaving groups, Cl and OTf, and two different amines, Et_3N and *i*-Pr_2EtN, are summarized in Table I. It is seen that the stereochemical outcome of the reaction varies not only with the steric requirements of R_2B and the steric requirements of the amine[1,2] but also with the nature of the leaving group, Cl or OTf.

The effect of varying the amine and the alkyl groups on boron are considerably more significant in the case of R_2BCl than in the case of R_2BOTf. It is observed that triflates lead to syn aldol ((*Z*)-enol borinate) predominantly, irrespective of the amine used or the steric requirements of the alkyl groups on the boron reagent. On the other hand, Chx_2BCl and Et_3N provide the anti aldol ((*E*)-enol borinate) preferentially. Encouraged by these results, the R_2BCl reagents were applied to several other representative ketones. The results established that the synthesis of either (*Z*)- or (*E*)-enol borinate can be achieved with high stereochemical purity (~80–99%) by proper choice of reagent and amine (Table II) (eq 5).



(5)

(9) It has been reported recently that the stereochemistry of aldol products derived from amide enolates can be influenced by dissolved ammonium salts (ref 10). In our studies, the ammonium salts separate from the reaction medium essentially quantitatively and have no observable effect on the stereochemistry of the aldol products.

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This appears to be the first successful conversion of ketones into enol borinates that are largely or entirely the *E*-isomer. This discovery, combined with the fact that the dialkylboron chlorides are readily synthesized and are very stable, makes the methodology here described a valuable procedure for applying the aldol reaction to synthesis. The preferred formation of the (*E*)-enolate over the (*Z*)-enolate is favored by the following: (a) use of R_2BCl instead of R_2BOTf; (b) use of Et_3N instead of *i*-Pr_2EtN; (c) use of Chx_2B (larger steric requirements) instead of 9-BBN (smaller steric requirements).

The R_2BOTf reagents achieve the conversion of representative ketones into pure (*Z*)-enol borinates (leading to the syn aldol). However, the R_2BCl reagents now make possible the conversion of representative ketones into either the essentially pure (*Z*)-enol borinates or the essentially pure or predominant (*E*)-enol borinates, the latter being a transformation not previously available.

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On the Control of Microenvironment Shape of Functionalized Network Polymers Prepared by Template Polymerization

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The introduction of clusters of functional groups at or near the surface of network polymers may be achieved by template polymerization.[1] The latent functional groups are covalently incorporated into the network by copolymerization of a template assembly with crosslinking monomer. Removal of the template subsequent to polymerization generates a functionalized site.

Molecular recognition has been the principle diagnostic used to evaluate maintenance of the stereochemical integrity of functional groups *after* removal of the template molecule. Crosslinked macromolecules, functionalized by the template synthesis method, have been shown to exhibit an affinity for original template molecules in batch competition rebinding studies[2-4] and when the polymeric materials are used as chromatographic supports.[5,6]

It was earlier shown that rebinding selectivity to template-functionalized polymers could be influenced by changing the initial positioning of the functional groups.[7,8]

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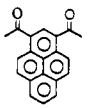
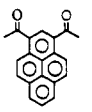
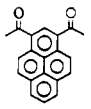
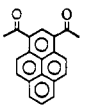
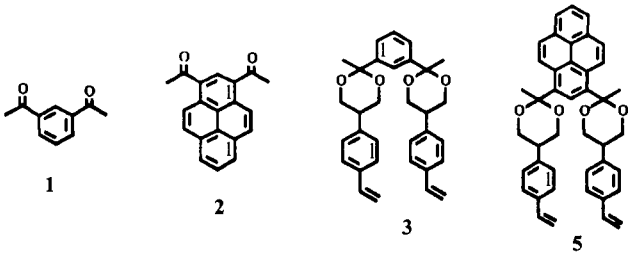
Table I. Summary of Hydrolysis and Rebinding Studies of Templated Macroporous Styrene–Diisopropenyl Copolymers

original template	hydrolysis[a] yield	rebinding template	% bound/1,3-diol unit[b]	% bound/site
	93 ± 2		82 ± 6	82 ± 6
			60 ± 4	60 ± 4
			32 ± 2	32 ± 2
	80 ± 2		51 ± 1	102 ± 2
			22 ± 2	45 ± 5
	70 ± 2		73 ± 4	146 ± 8
			78 ± 5	155 ± 11

[a] Average of at least four hydrolysis reactions involving at least three separate preparations of polymers. [b] Rebinding yields obtained from a calculation of depletion measurements and from a subsequent hydrolysis of rebound polymers.

A strategic array of functional groups is only one of several factors that are important for molecular recognition. A site with shape complimentary to that of the substrate constitutes yet an additional factor.

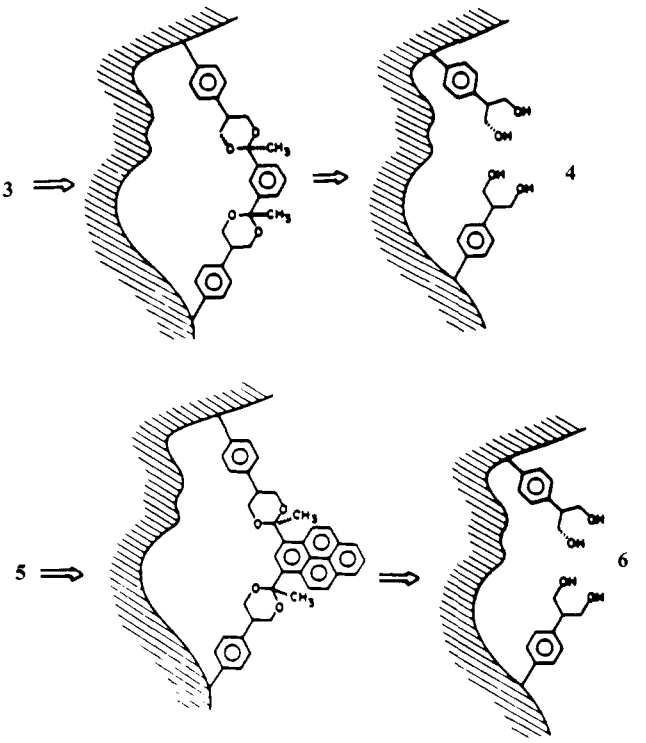
The extent to which these individual factors contribute to the selectivity exhibited by template functionalized polymers has been difficult to establish.[1a,6d] We report in the present communication evidence that the template *shapes* the microenvironment during polymerization. These sites exhibit rebinding selectivities that are sensitive to these effects, and, indeed, shape selectivity may be the most important recognition factor.



1 2 3 5

The *cis,cis*-4-vinylphenylbisketal template **3**[9,10] was copolymerized with styrene-*m*-diisopropenylbenzene (50% w/w) and acetonitrile as diluent (f_m = 0.5)[11] at a template loading of 80 μmol template/g monomer (AIBN initiator). The resulting material, a macroporous network polymer,[12,13] is processed as

Scheme I



described previously.[13a] In a typical example, four hydrolysis cycles (MeOH/10% H_2SO_4 (10:1) reflux 22 h) resulted in liberation of 82% of the theoretical yield of 1,3-diacetylbenzene and hydrolyzed polymer **4**. In saturation rebinding experiments, (3-fold excess of diketone, reflux C_6H_6, trace TSA 22 h) 1,3-diacetylbenzene was quantitatively rebound to **4** (Table I). Interestingly, when this same hydrolyzed polymer (**4**) was reketalized with 1,3-diacetylpyrene (**2**), less than half of the sites were reoccupied on the polymer (Table I).[14] In a competitive rebinding experiment employing equimolar amounts of diketones **1** and **2**, the kinetic selectivity was 70:30 in favor of 1,3-diacetylbenzene (95% coverage). The failure of 1,3-diacetylpyrene to quantitatively rebind at the bis-1,3-diol sites of polymer **4** can be attributed to a number of factors. It is not, however, a consequence of the spacing between the two carbonyls since this distance is identical in both diketones. One intriguing explanation for this selectivity arises from differences in the shape of the two diketones. Although both templates are flat, 1,3-diacetylpyrene is significantly larger than 1,3-diacetylbenzene and may not, therefore, "fit" in the site created by the latter.

In an effort to document the origin of this selectivity, the *p*-vinylphenylbisketal derivative of 1,3-diacetylpyrene (**5**) was prepared[9] and copolymerized with styrene-*m*-diisopropenylbenzene under identical conditions to that of the 1,3-diacetylbenzene template (**3**). The material was subjected to four hydrolysis cycles (70% combined yield of 1,3-diacetylpyrene). The resulting hydrolyzed polymer **6** exhibited a kinetic selectivity toward diketones **1** and **2** that was virtually identical with polymer **4** (69:31, 85% coverage). However, under saturation binding conditions, polymer **6** binds *equivalent* amounts of 1,3-DAB and 1,3-DAP to the bis-1,3-diol sites. Furthermore, each site is capable of accommodating, on average, more than 1 equiv of diketone (Table I).

Possible explanations for these differences have been sought. If templates **3** and **5** differed significantly in their mode of incorporation into the growing polymeric network, sites of quite different topology could be produced.[15] These sites could in turn

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(14) Only small (~2-fold) differences in rates of formation of monoketal and bisketals were observed in the homogeneous rates of ketalization of diketones **1** and **2** with 2-phenyl-1,3-propanediol.

(15) Preliminary studies reveal that the mode of incorporation of templates **3** and **5** into the matrix are indistinguishable.

give rise to selectivities that do not arise from template shape. Although X-ray crystal structures of **3** and **5** exhibit the s-trans and s-cis structures, respectively, solution phase NMR studies and MM2 calculations reveal a very low barrier separating two freely interconverting conformational isomers. These results suggest that the two template molecules (**3** and **5**) should be incorporated into the growing polymer network in a similar manner. The different selectivities that these materials exhibit must be attributed to other factors.

Another possibility recognizes that the rebinding step can result in formation of a bisketal (two-point rebinding) or monoketal (one-point rebinding). FT-IR studies have permitted quantitative evaluation of the residual carbonyl groups remaining after rebinding. Rebinding of **4** with 1,3-diacetylbenzene results in 30 ± 10% sites with one-point rebinding. From a related study, 1,3-diacetylpyrene is found to rebind to **6** with 35 ± 10% one-point rebinding. On the basis of these results, the two materials (**4** and **6**) do not differ with regard to the manner in which the diketone substrates rebind at each site. Furthermore, since a significant fraction of substrate molecules are initially rebound at only one carbonyl, an important component of the selectivity must arise from the *shape* of the site.

The origins of these differences can be traced to the polymerization reactions. Templates of different shape produce sites of different architecture. The application of this finding to the design of shape-selective catalysis is currently under investigation.

Acknowledgment. We are grateful to the Materials Science Division of the National Science Foundation for financial support of this work. We also thank T. K. Dougherty for several preliminary binding studies.

The Lithium–Metalloid Exchange Reaction.[1] NMR Studies of the Phenyllithium–Iodobenzene Exchange

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The metal–halogen exchange reaction, independently discovered by Wittig and Gilman,[2] continues to find many applications for the preparation of organolithium reagents. It is a complex reaction for which single electron transfer,[3] four center,[4] S_N2,[4a,b] and ate complex[1a,1b,5] mechanisms have been proposed. Previously we reported kinetic evidence for an intermediate in the degenerate exchange of iodobenzene and phenyllithium,[1a] the hypervalent 10-I-2$^-$ diphenyliodinanide species **1**. We report here evidence that **1** can be observed as a discrete solvent-separated ion pair in THF–HMPA solution and that it can function as a phenyl anion donor.

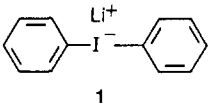

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Figure 1 presents ^{13}C NMR spectra of THF solutions containing phenyllithium (0.04 M) and HMPA (0–0.4 M) at −105 °C. In THF, PhLi exists as an equilibrium mixture of monomer and dimer which exchange slowly on the NMR time scale at temperatures below −90 °C (Figure 1A).[1d,6] With one-third and two-thirds of an equivalent of hexamethylphosphoramide (HMPA) present, a new set of signals appeared in direct proportion to the amount added (Figure 1 (parts B and C)). The signals for PhLi·THF were unaffected except for their intensity. After 1 equiv

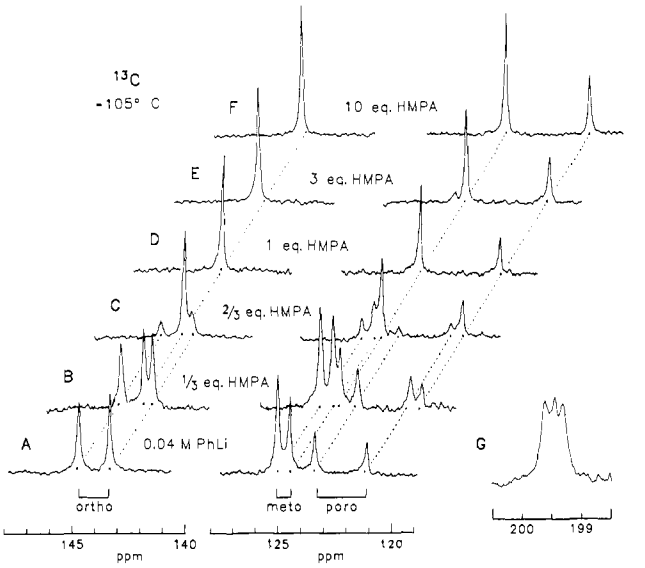

Figure 1. Carbon-13 NMR spectra (90.56 MHz) of THF solutions at −105 °C. A: DEPT-90 spectrum of 0.04 M PhLi. The upfield signal of each pair is $(PhLi)_1$. B–F: DEPT-90 spectra containing 0.013, 0.027, 0.04, 0.12, and 0.4 M HMPA. G: ipso carbon signal of 0.12 M Ph^6Li, 0.08 M HMPA in THF/dimethyl ether (2/1) at −120 °C. The 1:1:1 ^{13}C–^6Li splitting is 13 Hz.

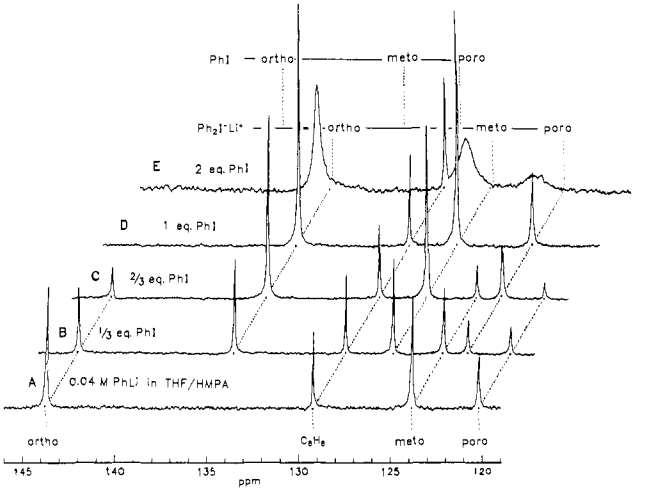

Figure 2. A–E: 90.56 MHz ^{13}C NMR spectra at −105 °C of solutions 0.04 M PhLi, 0.4 M HMPA, containing 0, 0.013, 0.027, 0.04, and 0.08 M PhI. Spectra A–D are DEPT-90 spectra; E is a normal single pulse spectrum.

Table I

δ ^{13}C (−105 °C, THF)	ipso	ortho	meta	para	δ ^7Li
$(PhLi)_1$·THF	196.68	143.24	124.28	120.83	1.05
$(PhLi)_2$·THF	188.48	144.60	124.81	123.18	1.43
$(PhLi)_1$·HMPA	201.90	143.79	123.68	120.0	0.93
$Ph_2I^-Li^+$ (HMPA)	166.51	135.23	126.62	122.51	−0.37
PhI	96.65	138.08	131.36	128.07	

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