formylmethyl derivative **4b** (as hydrate).

Chloroform Medium. Chloroacetaldehyde (**2**) monomer was prepared from the commercial aqueous solution by extraction with ethanol-free chloroform. The extracts were dried over $MgSO_4$ and filtered, and the filtrate evaporated by a slow stream of dry nitrogen into a dry ice trap. The condensate was stored over 3A molecular sieves at -20 °C and quantitated by ^1H NMR using a known weight of toluene as internal standard. A 2-mL deuteriochloroform solution containing 1 mmol each of **3b** and **2** monomer was left standing at 0 °C overnight: ^1H NMR ($CDCl_3$) δ 7.35 (s, NH), 5.0 (m, CH, CH), 3.78 (s, CH_3O), 3.75 (d, J = 4.5, CH_2Cl), 3.15 (d, J = 5.6, CH_2S), 2.10 (s, $COCH_3$). This is consistent with the assignment as the $SCH(OH)CH_2Cl$ derivative (**7**). Upon further standing at room temperature and monitoring by ^1H NMR, **7** was gradually replaced by S-CH_2CHO **4b** (its spectrum is described above for **4b** derived from **3b** and **1**). This conversion was also effected with 1 equiv of triethylamine at -20 °C in 15 min. The thiazine **6b** was the final product when a chloroform solution of **4b** was kept overnight at room temperature.

Reaction of 3,4-Dichlorobenzenethiol with Chlorooxirane (1). Aqueous Medium. A solution containing 274 mg (1.53 mmol) of 3,4-dichlorobenzenethiol (**8**) in 5 mL of 3:1 acetonitrile–water was adjusted to pH 7 by adding 0.5 N sodium hydroxide solution. To this solution was added **1** (1.53 mmol) in 1.0 mL of acetonitrile, and the solution was stirred under nitrogen at room temperature. The pH was maintained at 7 by a pH stat using 3 mL of 0.5 N sodium hydroxide in 4 min. The reaction mixture was analyzed by normal-phase HPLC: retention volume (mL) of **8**, 3.9; **8** as disulfide, 3.45; **9**, 7.25 The third peak was identified as [(3,4-dichlorophenyl)thio]acetaldehyde (**9**), and the ratio of **8** to **9** was 1:4.3, 81% yield.

An authentic sample of **9** was prepared as follows. To a solution of potassium *tert*-butoxide (3 mmol) in 20 mL of dry dimethyl sulfoxide was added 179 mg (1 mmol) of **8**. This was followed by the addition of 152 mg (1 mmol) of chloroacetaldehyde diethylacetal, and the solution was stirred for 48 h at room temperature. Water (40 mL) was added, and the reaction mixture was extracted with 3 × 10 mL of methylene chloride. The combined extracts were dried, concentrated, and applied to a silica gel column. Elution with hexane–methylene chloride yielded [(3,4-dichlorophenyl)thio]acetaldehyde diethylacetal (**10**) in 50% yield: ^1H NMR ($CDCl_3$) δ 1.1 (t, J = 6.7, 2 CH_3), 2.96 (d, J = 5.3, CH_2), 3.49 (m, 2 CH_2), 4.5 (t, J = 5.3, CH), 7.37 (m, phenyl 3 H). The diethylacetal was hydrolyzed in 2 N hydrochloric acid at 25 °C for 12 h to the known[16] aldehyde **9**, which was purified by silica gel chromatography as above: ^1H NMR ($CDCl_3$) δ 9.54 (t, J = 3.4, CHO), 7.39 (m, phenyl 3 H), 3.63 (d, J = 3.4, CH_2); ^{13}C NMR ($CDCl_3$) δ 193.8 (CHO), 133–129.6 (phenyl), 43.8 (CH_2).

Chloroform Medium. A solution containing 0.84 mmol each of the thiol **8** and **1** in 2 mL of chloroform was kept under static nitrogen at room temperature. The reaction was monitored by GC on 5% OV-17, T_c 235 °C (programmed at 50 °C for 8 min followed by 5 °C/min increase), and 24 h later the chromatogram showed the following peaks: 3,4-dichlorobenzenethiol, R_T = 16.2 min; the corresponding disulfide, R_T = 33.5 min; and an emerging peak for [(3,4-dichlorophenyl)thio]acetaldehyde (**9**), R_T = 20.2 min, as identified by co-injection with authentic samples; GC-MS (chemical ionization mode) of **9**, m/e 219 ($^{35}Cl_2C_6H_3SCH_2CO^+$), 193 ($^{35}Cl_2C_6H_3SCH_2^+$). The reaction was less than 30% complete, by integration of GC peaks and ^1H NMR [δ 3.48 (s, SH), 2.92 (m, CH_2 of **1**)] after 2 days and was about complete after 7 days.

Reaction of 3,4-Dichlorobenzenethiol with Chloroacetaldehyde (2). Aqueous Medium. The thiol **8**, 0.179 g (1 mmol), was dissolved in 3 mL of acetonitrile. To it was added a solution of 3 mL of acetonitrile and 2 mL of water containing 1 mmol of **2** at room temperature. The initial pH of the mixture was adjusted to 7.0 by adding 0.1 N NaOH, which did not change after 1 h. Analysis of the reaction mixture by ^1H NMR and HPLC (ODS column) showed no sign of **9**, although some disulfide of **8** was detected.

Chloroform Medium. A solution of **2** monomer in ethanol-free, dry chloroform, 1 mmol in 7 mL, was prepared as above. To it was added 0.179 g (1 mmol) of the thiol **8** in 2 mL of chloroform at room temperature under nitrogen. After 15 h and evaporation of the solvent, 0.26 g (100%) of the thiohemiacetal **11** was obtained as a viscous oil: ^1H NMR ($CDCl_3$) δ 7.65 (m, benzene H-2), 7.39 (m, benzene H-5,6), 5.26 (t, J = 5.5, CH), 3.80 (dd, J = 5.5, 2, CH_2), and 2.70 (S, OH, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$) δ 47.5 (CH_2), 79.1 (CH), 126.4–132.3 (phenyl); IR ($CDCl_3$) 3580 cm^{-1} (OH) and no carbonyl absorption. GC analysis showed reversion to **2** and **8** due to decomposition of **11** at the injection port. Upon heating the chloroform solution at 50 °C, as monitored by ^1H NMR, the starting materials **2** and **8** as well as the aldehyde **9** were produced, the latter increasing with time. An attempt to chromatograph an aliquot of the reaction mixture (before heating) on silica gel with hexane–chloroform resulted in isolation of the thiol **8** only. When 1 equiv of pyridine was added to the chloroform solution containing **11** and this allowed to stand at room temperature overnight, the S-acetaldehyde **9** was formed as evidenced by the above ^1H NMR.

Registry No. 1, 7763-77-1; **2**, 107-20-0; **3a**, 616-91-1; **3b**, 7652-46-2; **4a**, 123751-48-4; **4b**, 123751-54-2; **5a**, 123751-49-5; **5b**, 123751-55-3; **6a**, 123751-50-8; **6b**, 123751-56-4; **7**, 123751-51-9; **8**, 5858-17-3; **8** disulfide, 4235-78-3; **9**, 55251-69-9; **10**, 123751-52-0; **11**, 123751-53-1; $ClCH_2CH(OEt)_2$, 621-62-5.

Template-Controlled Oligomerization Support Studies. Template Synthesis and Functionalization

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Received May 30, 1989

The rigid organic template **8** can be rapidly assembled via double Diels–Alder cycloaddition of methyl 9-anthracenecarboxylate (**7**) and *trans-anti-trans*-norbornadiene trimer **5**. Subsequent manipulation leads to differentially functionalized templates capable of mediating the oligoselective polymerization of acrylate monomers. Lactonization studies with template diol **10** provide a useful measure of the "effective molecular size" of the template.

The utilization of rigid organic molecules as templates for imparting selectivity into chemical transformations has led to impressive accomplishments in the areas of regio-, diastereo-, and enantiochemical control of bond forma-

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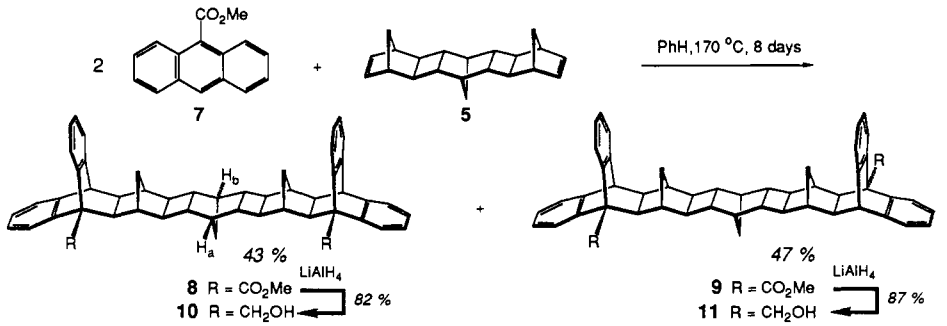
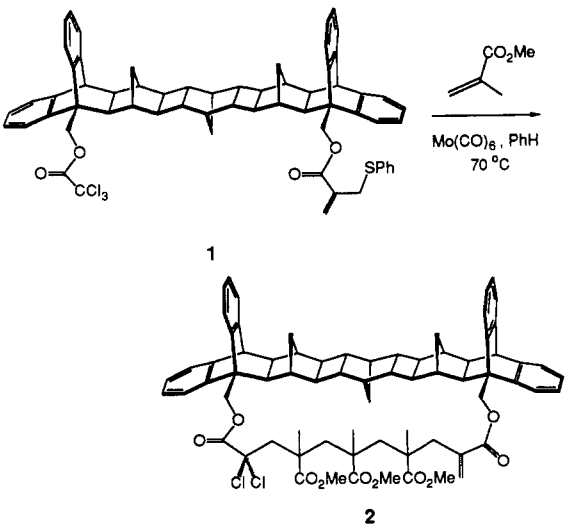
Scheme I



tion.[1,2] For example, the binaphthol-based chiral Lewis acids of Kelly[2o] and Yamamoto[2aa] afford Diels–Alder adducts with high enantioselectivity, while the molecular clefts designed by Rebek[2z] can be utilized for chemo- and regioselective epoxidation. One common theme that underlies many of these studies involves exploitation of the steric bulk of the template, either covalently attached[1] or transiently bound[2] to the substrate, to influence addition of an external reagent toward one preferred location out of several possible sites. In other instances, the geometry and architecture of the template, more than any particular steric interactions, dictate reactivity preferences.[2x,y] In all cases, the template must be capable of engaging in at least some primitive level of recognition with the substrate in order to achieve acceptable discrimination between competing reaction pathways.

One type of selectivity in a chemical transformation distinct from those mentioned above can be described as *oligoselectivity* in a polymerization process.[3] In this case, selectivity is not related to spatial control of reagent addition to a substrate, rather it is critically dependent upon *temporal* control of the three stages (initiation, propagation, termination) of the polymerization reaction. A plausible strategy for effecting this control might rely on confining the location of the polymerization process to a gap defined by specific polymerization initiation and termination functionalities held at precise locations on a rigid template molecule. In principle, then, termination will occur only when the growing oligomeric chain is long enough to reach across the gap and interact with the resident terminating functionality. In fact, employing the template system **1**,[14c] we have successfully demonstrated that methyl methacrylate can be oligoselectively trimerized under conditions that would ordinarily lead to high polymer (eq 1).[4]



(1)

Details of the synthesis and characterization of template **1**, as well as related species, are described in this paper.

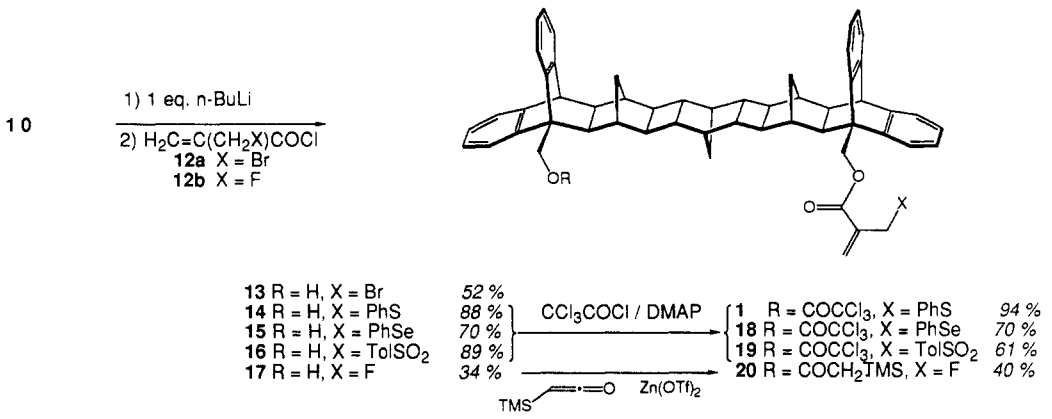
(1) (a) Lutomski, K. A.; Meyers, A. I. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3. (b) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3. (c) Oppolzer, W.; Dudfield, P.; Stevenson, T.; Godel, T. *Helv. Chim. Acta* **1985**, *68*, 212. (d) Liebeskind, L. S.; Welker, M. E.; Fengl, R. W. *J. Am. Chem. Soc.* **1986**, *108*, 6328. (e) Davies, S. G.; Walker, J. C. *J. Chem. Soc., Chem. Commun.* **1986**, 495. (f) Enders, D. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984, Vol. 3. (g) Seebach, D.; Imwinkelreid, R.; Weber, T. *Modern Synth. Methods* **1986**, *4*, 128. (h) Schollkopf, U. *Pure Appl. Chem.* **1983**, *55*, 1799. (i) Braun, M.; Devant, R. *Tetrahedron Lett.* **1984**, *25*, 5031. (j) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 5919. (k) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (l) Meyers, A. I.; Sohda, T.; Loewe, M. F. *J. Org. Chem.* **1986**, *51*, 3108. (m) Johnson, W. S.; Elliot, R.; Elliot, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2904. (n) Mash, E. A.; Nelson, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 8256. (o) Posner, G. H.; Weitzberg, M.; Hamill, T. G.; Asirvatham, E.; Cun-Heng, H.; Clardy, J. *Tetrahedron* **1986**, *42*, 2919. (p) Oppolzer, W.; Loher, H. J. *Helv. Chim. Acta* **1981**, *64*, 2808. (q) Whitesell, J. K.; Bhattacharya, A.; Buchanan, C. M.; Chen, H. H.; Deyo, D.; James, D.; Liu, C.-L.; Minton, M. A. *Tetrahedron* **1986**, *42*, 2993. (r) Meyers, A. I.; Fleming, S. A. *J. Am. Chem. Soc.* **1986**, *108*, 306.

(2) (a) Dolling, U.-H.; Davis, P.; Gravowski, E. J. J. *J. Am. Chem. Soc.* **1984**, *106*, 446. (b) Regan, A. C.; Staunton, J. *J. Chem. Soc., Chem. Commun.* **1987**, 520. (c) Simpkins, N. S. *J. Chem. Soc., Chem. Commun.* **1986**, 88. (d) Mukaiyama, T.; Iwasawa, N.; Stevens, R. W.; Haga, T. *Tetrahedron* **1984**, *40*, 1381. (e) Paterson, I.; Lister, M. A.; McClure, C. K. *Tetrahedron Lett.* **1986**, *27*, 4787. (f) Masamune, S.; Sato, T.; Kim, B. M.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279. (g) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405. (h) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615. (i) Imwinkelried, R.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 765. (j) Guette, M.; Capillon, J.; Guette, J. P. *Tetrahedron* **1973**, *29*, 3659. (k) Seebach, D.; Beck, A. K.; Roggo, S.; Wonnacott, A. *Chem. Ber.* **1985**, *118*, 3673. (l) Mazaleyrat, J. P.; Cram, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 4585. (m) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071. (n) Corey, E. J.; Naef, R.; Hannon, F. J. *J. Am. Chem. Soc.* **1986**, *108*, 7114. (o) Kelly, T. R.; Whiting, A.; Chandrakumar, N. S. *J. Am. Chem. Soc.* **1986**, *108*, 3510. (p) Chapuis, C.; Jurczak, J. *Helv. Chim. Acta* **1987**, *70*, 436. (q) Sakane, S.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1985**, *26*, 5535. (r) Haubenstock, H. *Top. Stereochem.* **1983**, *14*, 231. (s) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551. (t) ApSimon, J. W.; Collier, T. L. *Tetrahedron* **1986**, *42*, 5157. (u) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5. (v) Wolfe, J.; Nemeth, D.; Costero, A.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 983. (w) Breslow, R. *Science* **1982**, *218*, 532. (x) Breslow, R. *Chemtracts* **1988**, *1*, 333. (y) Collman, J. P.; Brauman, J. I.; Meunier, B.; Hayashi, T.; Kodadek, T.; Raybuck, S. A. *J. Am. Chem. Soc.* **1985**, *107*, 2000. (z) Rebek, J., Jr.; Marshall, L.; McManis, J.; Wolak, R. *J. Org. Chem.* **1986**, *51*, 1649. (aa) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310. (bb) Groves, J. T.; Nuemann, R. *J. Org. Chem.* **1988**, *53*, 3891.

(3) Representative examples of non-selective oligomerization can be found in the following. (a) Telomerization: Kumieda, T.; Takazawa, T. *Heterocycles* **1977**, *8*, 661. (b) Formose reaction: Okano, T.; Ito, H.; Konishi, H.; Kiji, J. *Chem. Lett.* 1986, 1731. (c) Condensation polymerization: Margolin, A. L.; Crenne, J. Y.; Klibanov, A. M. *Tetrahedron Lett.* **1987**, *28*, 1607. Kammerer et al. have reported the controlled oligomerization of two or three methacrylate units which themselves are all covalently linked to the same polycyclic aromatic template. In these cases, termination typically relied on radical–radical combination events. (d) Kammerer, H.; Steiner, V.; Gueniffey, H.; Pinazzi, C. P. *Makromol. Chem.* **1976**, *177*, 1665. (e) Kammerer, H.; Shulka, J. S. *Makromol. Chem.* **1968**, *116*, 62.

(4) Feldman, K. S.; Lee, Y. B. *J. Am. Chem. Soc.* **1987**, *109*, 5850.

Scheme II

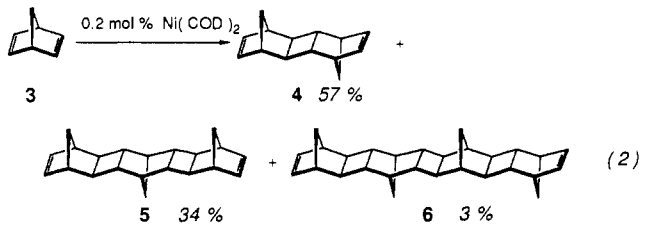


Salient features of this approach include a facile route to a C_s symmetric template precursor **8** and desymmetrization of this species to provide the differentially functionalized templates **1** and **18–20**. In addition, the results of bis-lactonization experiments with the template diols **10**/**11** and α,ω-bis(carboxylic acid)-substituted hydrocarbon chains are discussed. These studies contribute to an appreciation of the "effective molecular size" of the initiator/terminator gap for the template system.

Results and Discussion

Template Synthesis. At the outset of our studies, it was not clear which particular initiator and terminator functionalities might be most effective in controlling oligoselectivity for a given polymerization. Consequently, our strategy for template synthesis had to permit facile interchange of potential initiator/terminator pairs. The template C_s diol **10** was chosen as an initial target, with the intention of utilizing simple acylation chemistry for the sequential attachment of the desired functionality.

The synthesis of the crucial *trans-anti-trans*-norbornadiene trimer spacer unit **5**[14a] from norbornadiene (**3**) follows from procedures reported in the patent literature (eq 2).[5] This nickel(0)-catalyzed *uncontrolled* polymer-



ization process can, in principle, lead to a broad range of oligomeric products. In practice, however, the sparing solubility of the higher oligomers (n = 3, 4) under these reaction conditions serves as a crude but effective control element, and most of the monomer is incorporated as dimeric **4**, trimeric **5**, and tetrameric **6** products. Fractional sublimation and recrystallization serves to separate oligomers and remove small amounts (≈5–10%) of stereoisomers, resulting in isolation of 40–50 g of the desired trans-anti-trans trimer **5** from **170** g of norbornadiene.

With an adequate supply of trimer **5** in hand, the C_s template diol **10**[14b] can be prepared in two steps as shown in Scheme I. Double Diels–Alder cycloaddition of methyl 9-anthracenecarboxylate (**7**) with trimer **5** occurs smoothly to furnish a 1:1 mixture of the C_s and C_2 symmetric template isomers **8** and **9**, respectively, in good yield. These isomers can be separated chromatographically and can be distinguished by virtue of symmetry considerations in the ^1H and ^{13}C NMR spectra. Specifically, H_a and H_b resonances in the C_s isomer **8** are distinct and appear at δ 1.63 and 1.73, respectively, while the hydrogens at the same positions in the C_2 isomer **9** are chemically equivalent and resonate at δ 1.67 (500 MHz). The undesired C_2 isomer **9** was partially recycled by thermal equilibration (200 °C) to produce a mixture of the C_2 and C_s isomers (ca. 10% C_s diester **8** recovered). Unfortunately, the intervention of destructive reaction processes competitive with the desired retro-Diels–Alder/Diels–Alder equilibration sequence limits the value of this recycling strategy. Both C_s and C_2 isomers **8** and **9** could be reduced to provide the C_s and C_2 diols **10** and **11**, respectively, in high yield.

Selective functionalization of one of the two alcohol units in diol **10** was required for preparation of the desired bifunctional template system. Formation of the monobromomethacrylate derivative **13** (Scheme II) was our initial goal, as subsequent replacement of bromine with other functional groups would lead to a range of terminators potentially useful for arresting either free radical or anionic (group transfer[6]) polymerizations. Thus, treatment of template diol **10** with 1 equivalent of *n*-BuLi, followed by addition of bromomethacryloyl chloride (**12a**) at reflux in THF, led to production of the monoester **13** in 50–55% yield along with 10–20% of the corresponding diester and ca. 20–30% of recovered starting diol. These unusually harsh reaction conditions were necessary for esterification because product formation did not occur upon attempted condensation of the neopentyl alcohol moiety in **10** with milder reagent systems (acid chloride/DMAP; acid/DCC; acid/carbonyldiimidazole).

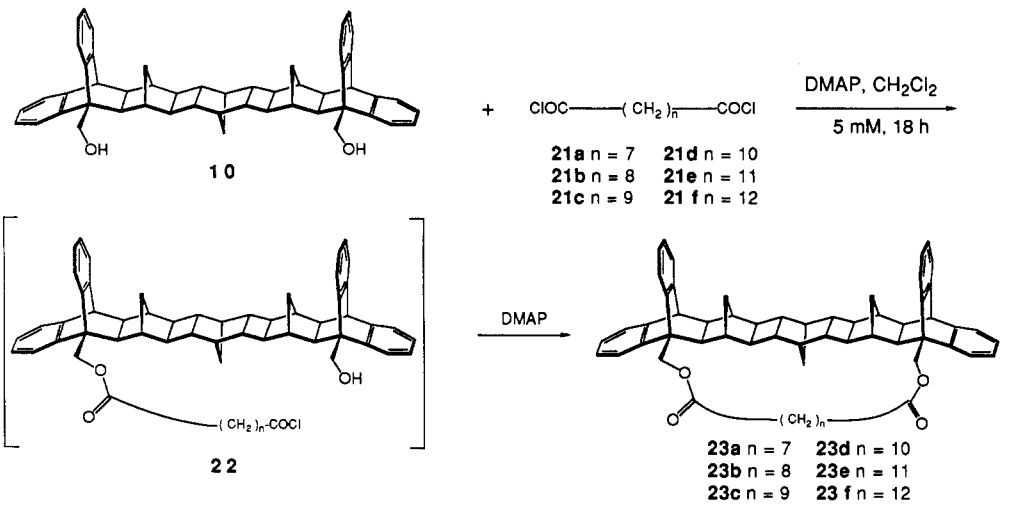
With the key monobromomethacrylate derivative **13** in hand, displacement of bromine with phenylthio, phenylseleno, and toluenesulfonyl nucleophiles furnished the substituted monomethacrylates **14–16**, respectively, in the yields indicated. Trichloroacetylization of the phenylthio, **14**, phenylseleno, **15**, and toluenesulfonyl, **16**, species afforded the differentially functionalized templates, **1**, **18** and **19**, respectively, capable of mediating the oligoselective free-radical polymerization of methyl methacrylate.[4] The detailed molecular structure of the phenylthio species **1** was ascertained through single-crystal X-ray analysis.[7] The fluoride-containing template **17**, prepared in 34% yield by fluoromethacryloyl chloride esterification of the lithium alkoxide derived from C_s diol **10**, was condensed

(5) Pruett, R. L.; Rick, E. A. U.S. Patent 3 440 294, April 22, 1969.

(6) Webster, O. W.; Hertler, W. R.; Sogah, D. Y.; Farnham, W. B.; Rajanbabu, T. V. *J. Am. Chem. Soc.* **1983**, *105*, 5706.

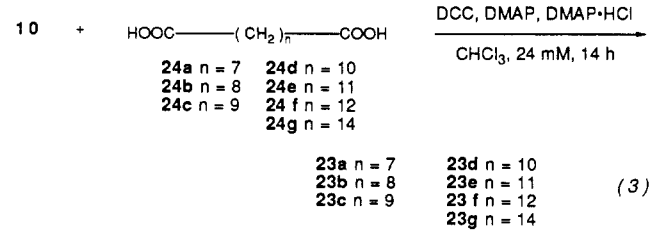
(7) For information regarding the X-ray structural analysis of **1**, contact Dr. M. Parvez at the above address.

Scheme III



with trimethylsilyl ketene[8] in the presence of $Zn(OTf)_2$ to afford the (trimethylsilyl)acetate–fluoromethacrylate template **20**. Other Lewis acids proved less effective in mediating this condensation: $BF_3{\cdot}Et_2O$ led to substantial amounts of desilylation of the product acetate, while $MgBr_2{\cdot}Et_2O$ resulted in formation of the products of Br/F exchange in the methacrylate moiety. The utilization of this particular template in the oligoselective group transfer polymerization of acrylate monomers is under current study, and results will be reported in due course.

Lactonization Studies. Bislactonization experiments with diol **10** and the acid chlorides **21a–f** and acids **24a–g** probed the issue of macrocyclization efficiency with this template system. Specifically, we had hoped to model the macrocyclization event, which would constitute termination in an actively polymerizing system, with the macrolactonization reactions shown in Scheme III and eq 3. We



(3)

believed that if any particular chain length (n) for the bifunctional substrates **21** and **24** led to efficient macrolactonization as a consequence of the intrinsic architecture of the template, then this preference might permit prediction of favored oligomer size in the controlled polymerization experiment. The lactonization reactions were run under two distinct sets of experimental conditions: (dimethylamino)pyridine-mediated coupling of the bis(acid chlorides) **21** (Scheme III), and modified Steglich[9] esterification conditions with the diacids **24** (eq 3). Each series of experiments was run under identical conditions, with the reaction being quenched after a specific length of time and product bislactone **23** isolated by silica gel chromatography. We feel that this approach effectively measures the relative efficiencies of macrolactonization (Scheme III, **22** → **23**), since the rate of formation of the initial ester linkage (**10** → **22**) should be independent of chain length n.

The macrocycle yield data collected from the diacid chloride and diacid lactonization studies are shown in

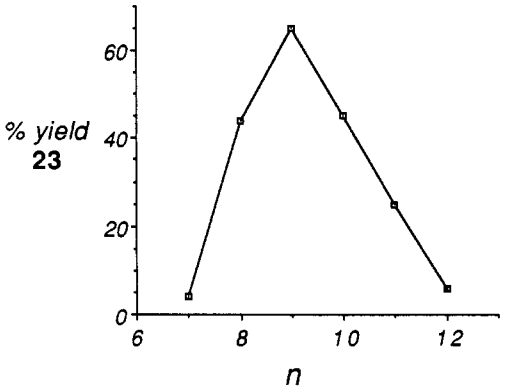


Figure 1. Yield of macrobislactonization of bis(acid chlorides) **21** and template diol **10**.

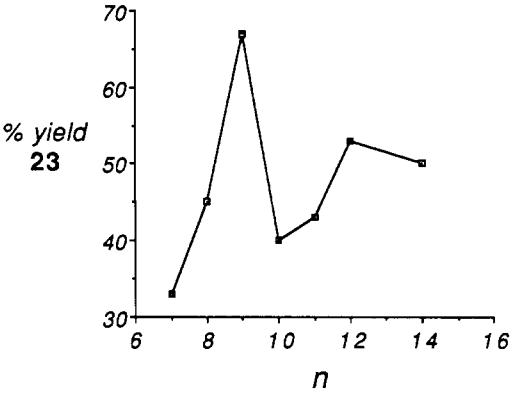


Figure 2. Yield of macrobislactonization of bisacids **24** and template diol **10**.

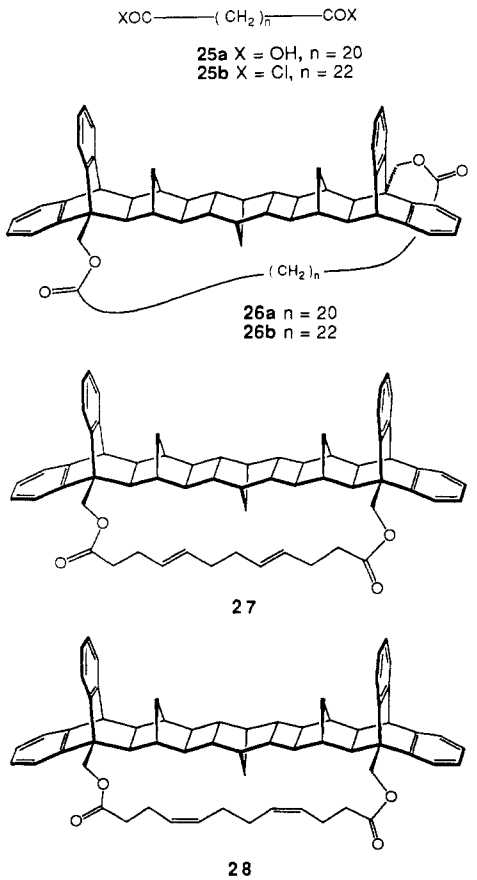
Figures 1 and 2, respectively. In both cases, the maximum yield is obtained when n = 9. Inspection of Drieding models reveals that while hydrocarbon chains of seven methylene units can, in fact, bridge the diol gap, at least one destabilizing s-cis ester conformation is required. Once the optimum "fit" is exceeded (n = 10–14), the yield drops sharply, perhaps reflecting the energetic penalty associated with the gauche interactions that necessarily must arise in the hydrocarbon chain as the reactive end groups come together. In the diacid experiments, which rely on carbonyl activation through a putative acylurea intermediate, a second smaller maximum at n = 12 was detected. In contrast, the acid chloride substrates, which presumably react through a cationic DMAP–acyl intermediate, apparently do not have access to a similar low energy chain

(8) Ruden, R. A. *J. Org. Chem.* **1974**, *39*, 3607.
(9) Boden, E. P.; Keck, G. E. *J. Org. Chem.* **1985**, *50*, 2394.

conformation in the $n = 12$ case. At the very least, these well-defined macrolactonization profiles, obtained under two quite different sets of esterification conditions, are suggestive of very specific spanning requirements for this template system. These requirements ($n = 9$) have been met in the selective trimerization of methyl methacrylate under free radical conditions, eq 1,[4] and may have further predictive value in other oligomerization systems currently under study.

Exploratory studies designed to probe the scope of these bis lactonization reactions led to successful macrocyclization with the C_2 template diol **11**. Furthermore, in a separate series of reactions, unsaturated hydrocarbon chains were coupled with the C_s template diol **10** in analogy with the saturated species described earlier. For substrates **26a**, **27**, and **28** the modified Steglich esterification protocol (eq 3) proved superior to the acid chloride route (Scheme III) with regard to both yield and ease of product isolation.

Thus, combination of either the C_{22} diacid **25a** or the C_{24} diacid chloride **25b** with diol 11 under a modification of the conditions described earlier (additional solvent required to dissolve substrates) led to formation of the C_2 symmetric template bislactones 26a (14%) and 26b (9%), respectively. In both cases, varying amounts of compounds tentatively assigned as dimeric structures based on ^1H NMR and FABMS spectra (two templates linked by two bisester chains) were isolated as well. These remarkable bislactonization reactions leading to 38–40-membered rings emphasize the overriding importance of the rigidity of the template structure in controlling subsequent chemistry.[10]



The *E,E* and *Z,Z* template diene diesters **27** and **28** were readily prepared by union of the diol **10** with either (*E,E*)-deca-4,8-diene-1,10-dicarboxylic acid (**29**) or (Z,Z)-deca-4,8-diene-1,10-dicarboxylic acid (**30**), respectively, in moderate yield (**27**, 53%; **28**, 40%). These diene substrates have the potential to engage in various addition reactions (i.e., bisepoxidation) with high levels of remote relative asymmetric induction. Thus, this template molecule, by virtue of its rigidity and disposition of functionality, may prove to be a valuable auxiliary for diastereoselectivity in chemical transformations. Investigation of these reaction processes are in progress.

(10) Menger, F. M. *Acc. Chem. Res.* **1985**, *18*, 128, and references cited therein.

Conclusion

Bifunctional rigid organic templates of the general structure **1** can be readily assembled from simple precursors. Template diol **10** serves as a key intermediate in the synthesis of several more highly functionalized species equipped with substituents capable of mediating the oligoselective polymerization of acrylate monomers. Furthermore, the C_s diol **10** and the C_2 diol **11** engage in macrobislactonization reactions with suitably activated α,ω-bis(carboxylic acid) derivatives to afford a range of functionalized template diesters. Incorporation of alkene functionality in the linking chain of these bislactones offers the opportunity to explore template-directed remote relative asymmetric induction. Selectivity in chemical transformations mediated by these species appears to be a direct consequence of the rigidity, architecture, and functionality of the template moiety.

Experimental Section

Liquid (flash)[11] chromatography was carried out by using 32–63-μm silica gel (Woelm-Pharma) and the indicated solvent. Analytical thin-layer chromatography was performed by using precoated silica gel (60 F_{254}) plates (E. Merck). High-pressure liquid chromatography (HPLC) was performed on a semipreparative instrument equipped with a refractometer and UV detector, using a ZORBAX-SIL silica gel column (25 cm × 20 mm, Dupont). Ether, tetrahydrofuran, and benzene were purified by distillation from sodium benzophenone under nitrogen, while methylene chloride was distilled from CaH_2 under nitrogen. Moisture-sensitive reactions were carried out in predried glassware and under an inert atmosphere (N_2, Ar). The purity of all title compounds was judged to be ≥90% by ^{13}C NMR determinations. Satisfactory elemental analyses could not be obtained for the compounds **8**, **9**, **11**, **13**, **17**, **1**, **20**, **23a**, **26a**, and **27**, possibly due to solvent inclusion upon crystallization. Nickel bis(cyclooctadiene) was purchased from Alfa Products, Danvers, MA, and used without purification.

***trans-anti-trans*-Norbornadiene Trimer 5.**[5,14a] Norbornadiene (3) (85.4 g, 927 mmol) was added to a stirring solution of nickel bis(cyclooctadiene) (1.3 g, 4.73 mmol) in 100 mL of 1,4-dioxane. The resulting dark red/brown solution was allowed to stir at room temperature for 22 h, resulting in formation of

(11) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(12) Prepared through a variation of Vyas, G. N.; Shah, N. M. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 836.
(13) The bis(acid chlorides) used in this study were prepared by reaction of the corresponding bisacids with oxalyl chloride in CH_2Cl_2 containing a catalytic amount of DMF.
(14) (a) The systematic *Chemical Abstracts* name for **5** is: 1,4,4a,4b,5,5a,5b,6,9,9a,9b,10,10a,10b-tetradecahydro-1,4:5,10:6,9-trimethanobenzo[3,4]cyclobuta[1,2-*b*]biphenylene. (b) The systematic *Chemical Abstracts* name for **10** is: (5aα,6β,6aα,6bβ,7α,7aβ,7bα,8β,8aα,14aα,15β,15aα,15bβ,16α,16aβ,16bα,17β,17aα)-6,6a,6b,7a,7b,8,8a,14,14a,15,15a,15b,16,16a,16b,17,17a,18-octadecahydro-5,18[1′,2′]:9,14[1″,2″]-dibenzeno-6,17:7,16:8,15-trimethanobenzo[1″,2″:3,4;4″,5″:3′,4′]dicyclobuta[1,2-*b*:1′,2′-*b*′]dianthracene-5,9(5a*H*,7*H*)-dimethanol. (c) The systematic *Chemical Abstracts* name for **1** is: 2-propenoic acid, 2-[(phenylthio)methyl], (5aα,6β,6aα,6bβ,7α,7aβ,7bα,8β,8aα,14aα,15β,15aα,15bβ,16α,16aβ,16bα,17β,17aα) [6,6a,6b,7,7a,7b,8,8a,9,14,14a,15,15a,15b,16,16a,16b,17,17a,18-eicosahydro-9-[[(trichloroacetyl)oxy]methyl]-5,18[1′,2′]:9,14[1″,2″]dibenzeno-6,17:7,16:8,15-trimethanobenzo[1″,2″:3,4;4″,5″:3′,4′]dicyclobuta[1,2-*b*:1′,2′-*b*′]dianthracen-5-(5a*H*)-yl]methyl ester.

a white precipitate. A second portion of norbornadiene (85.4 g, 927 mmol) was then added to the reaction mixture, which was heated at 50–55 °C for 48 h and at 40 °C for an additional 16 h. The reaction mixture was then allowed to cool to room temperature and concentrated in vacuo to give a solid residue. This white solid was separated into dimer, trimer, and tetramer fractions by sublimation at ≈0.05 Torr and the following temperatures: dimer **4**, 60–70 °C (96.6 g, 57%); trimer **5**, 155–165 °C (59.2 g, 34%); tetramer **6**, ≈240 °C (5.8 g, 3.4%). The trimer **5** was further purified by recrystallization from isopropyl alcohol to afford 47.8 g (28%) of fluffy white crystals: mp 198–201 °C (lit.[5] mp 201 °C); IR ($CDCl_3$) 3035 (alkene C—H), 1610 (C=C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.93 (s, 4 H, C=CH), 2.59 (s, 4 H, terminal bridgehead H), 1.89–1.12 (m, 16 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 135.3, 44.2, 41.8, 41.6, 40.6, 28.9; MS *m/z* (relative intensity) 276 (100, M^+); HRMS calcd for $C_{21}H_{24}$ 276.1879, found 276.1890.

Template C_s and C_2 Diesters 8 and 9. A stirring solution of *trans-anti-trans*-norbornadiene trimer **5** (11 g, 40 mmol), methyl 9-anthracenecarboxylate (**7**)[12] (20 g, 85 mmol), and 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide (20 mg, 0.06 mmol) in 50 mL of benzene was heated to 170 °C in a medium-pressure reactor for 200 h. At that time, the solution was allowed to cool to room temperature and concentrated in vacuo. The resulting yellow solid was purified by flash chromatography with 75% benzene/hexane as the eluent to afford 12.5 g (43%) of the desired template C_s diester **8**, along with 13.5 g (47%) of the template C_2 diester **9**, both as white powders which decomposed upon heating above 256 and 338 °C, respectively.

Template C_s diester 8: IR ($CDCl_3$) 1730 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.51–6.96 (m, 16 H, Ar H), 4.17 (d, *J* = 2.2 Hz, 2 H, bridgehead H), 4.05 (s, 6 H, OCH_3), 2.04–1.05 (m, 22 H), –0.61 (d, *J* = 10.2 Hz, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 172.7, 143.7, 142.7, 141.6, 139.1, 126.5, 126.2, 126.0, 125.5, 124.3, 124.0, 123.0, 121.8, 58.8, 51.9, 49.4, 48.6, 48.4, 47.1, 47.0, 42.6, 42.30, 42.28, 41.5, 41.3, 41.2, 29.0, 27.6; FABMS *m/z* (relative intensity) 747 (22, M – H^+).

Template C_2 diester 9: IR ($CDCl_3$) 1730 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.46–6.96 (m, 16 H, Ar H), 4.16 (d, *J* = 2.3 Hz, 2 H, bridgehead H), 4.04 (s, 6 H, OCH_3), 2.01–1.04 (m, 22 H), –0.63 (d, *J* = 11.0 Hz, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 172.7, 143.7, 142.8, 141.8, 139.1, 128.3, 126.5, 126.2, 126.0, 125.5, 124.4, 124.0, 123.0, 121.8, 58.8, 51.8, 49.4, 48.6, 48.4, 47.1, 47.0, 42.6, 42.3, 41.6, 41.2, 29.0, 27.6; FABMS *m/z* (relative intensity) 749 (100, M + H^+).

Template C_s Diol 10.[14b] A solution of template C_s diester **8** (2.94 g, 3.93 mmol) in 75 mL of THF was slowly added to a stirring, ice-cooled suspension of lithium aluminum hydride (298 mg, 7.85 mmol) in 50 mL of dry THF. After addition, the ice bath was removed, and the solution was brought to reflux for 18 h. At that time, the reaction solution was allowed to cool to room temperature before being poured into ice-cold 1 M H_3PO_4 and extracted with 3 × 100 mL of ether. The combined organic layers were washed sequentially with saturated $NaHCO_3$ and brine, dried over sodium sulfate, filtered, and dried in vacuo to afford 2.20 g (82%) of template C_s diol **10** as a white solid, which decomposed upon heating above 286 °C: IR ($CDCl_3$) 3610 cm^{-1} (OH); ^1H NMR (200 MHz, $CDCl_3$) δ 7.47–7.05 (m, 16 H, Ar H), 4.82 (dd, *J* = 10.8, 4.1 Hz, 2 H, OC(*H*)H), 4.61 (dd, *J* = 10.8, 4.1 Hz, 2 H, OC(H)*H*), 4.15 (d, *J* = 2.4 Hz, 2 H, bridgehead H), 1.79–0.88 (m, 24 H), –0.49 (d, *J* = 10.2 Hz, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 145.4, 143.7, 142.9, 141.5, 125.9, 125.5, 125.4, 124.3, 123.1, 122.1, 121.8, 63.4, 49.5, 48.8, 48.5, 48.3, 47.0, 46.9, 42.4, 42.23, 42.19, 41.2, 41.1, 39.4, 31.5, 29.0, 28.1; FABMS *m/z* (relative intensity) 691 (100, M – H^+). Anal. Calcd for $C_{51}H_{48}O_2$: C, 88.40; H, 6.98. Found: C, 88.15; H, 7.06.

Template C_s Diol Monobromomethacrylate 13. A solution of *n*-butyllithium in hexane (3.2 mL of a 1.6 M solution, 5.0 mmol) was slowly added to a stirring ice-cooled solution of C_s diol **10** (3.5 g, 5.0 mmol) in 100 mL of THF. After 30 min, bromomethacryloyl chloride (1.14 g, 6.1 mmol) was added, and the solution was brought to reflux and held there for 9 h. The reaction solution was allowed to cool to room temperature before being poured into ice-cold 1 M H_3PO_4 and extracted with 3 × 10 mL of Et_2O. The combined organic layes were washed sequentially with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting white solid was purified by flash chromatography with 4:1 CH_2Cl_2/hexane as eluent to afford 2.2 g (52%) of the monobromomethacrylate ester **13** as a light brown solid, which decomposed upon heating above 228 °C, 0.5 g (10%) of the dibromomethacrylate ester, and 1.3 g (37%) of recovered C_s diol **10**: IR ($CDCl_3$) 3115 (OH), 1725 (C=O), 1645 (C=C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.47–7.02 (m, 16 H, Ar H), 6.30 (s, 1 H, C=C(*H*)H), 5.92 (s, 1 H, C=C(H)*H*), 5.30–5.23 (m, 2 H, OCH_2), 4.79 (d, *J* = 11.2 Hz, 1 H, HOC(*H*)H), 4.59 (d, *J* = 11.2 Hz, 1 H, HOC(H)*H*), 4.17 (d, *J* = 2.5 Hz, 1 H, bridgehead H), 4.15–4.13 (m, 3 H, bridgehead H′ and CH_2Br), 1.83–0.85 (m, 23 H), –0.44 to –0.48 (m, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 164.9, 145.4, 144.9, 143.7, 143.3, 142.9, 142.5, 141.5, 140.6, 137.1, 129.6, 126.1, 126.0, 125.9, 125.6, 125.4, 125.2, 124.3, 124.2, 123.1, 122.0, 121.8, 121.5, 64.5, 62.4, 49.6, 48.8, 48.6, 48.5, 48.4, 48.3, 47.7, 47.0, 46.7, 42.5, 42.4, 42.1, 41.2, 41.1, 39.5, 39.4, 29.6, 29.2, 29.0, 28.1; FABMS *m/z* (relative intensity) 839 (61, M – H^+).

Template C_s Diol Monophenylthiomethacrylate 14. Freshly distilled thiophenol (90 μL, 0.88 mmol) was added to a hexane-washed slurry of NaH (35 mg (60%), 0.88 mmol) in 5 mL of THF under a nitrogen atmosphere at 0 °C. Monobromomethacrylate **12** (0.67 g, 0.80 mmol) in 20 mL of THF was added to this homogeneous solution, and the reaction mixture was heated to reflux and held there for 12 h. At that time, the solution was cooled to room temperature, poured into 50 mL of 1 M HCl, and extracted with 3 × 50 mL of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel using CH_2Cl_2 as eluent to furnish 0.61 g of mono(phenylthio)methacrylate **14** (88%) as a white solid, which decomposed upon heating above 218 °C: IR ($CDCl_3$) 3620 (OH), 1720 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.47–7.02 (m, 21 H, Ar H), 6.10 (s, 1 H, C=C(*H*)H), 5.45 (s, 1 H, C=C(H)*H*), 5.26 (d, *J* = 11.6 Hz, 1 H, C(*H*)HO), 5.18 (d, *J* = 11.6 Hz, 1 H, C(H)*H*O), 4.79 (d, *J* = 11.3 Hz, 1 H, C(*H*)HOH), 4.57 (d, *J* = 11.3 Hz, 1 H, C(H)*H*OH), 4.14 (m, 2 H, bridgehead H), 3.74 (s, 2 H, CH_2S), 1.77–1.06 (m, 22 H), –0.47 (m, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.2, 145.5, 145.0, 143.7, 143.4, 143.0, 142.6, 141.5, 141.0, 135.9, 135.1, 131.2, 130.1, 129.0, 128.8, 127.4, 126.9, 126.7, 126.1, 125.9, 125.6, 125.5, 125.4, 124.3, 123.1, 123.0, 122.0, 121.8, 121.6, 64.3, 62.5, 49.7, 48.8, 48.6, 48.5, 48.4, 48.3, 47.8, 47.1, 46.9, 42.5, 42.4, 42.2, 41.3, 41.2, 39.6, 39.4, 35.9, 29.0, 28.1; FABMS *m/z* (relative intensity) 868 (100, M + H^+).

Template C_s Diol Monofluoromethacrylate 17. A solution of *n*-butyllithium (375 μL of a 1.6 M solution in hexane, 0.60 mmol) was slowly added to a stirring, ice-cooled solution of C_s diol **9** (346 mg, 0.50 mmol) in 6 mL of THF. The solution was stirred for 0.5 h before 2-fluoromethacryloyl chloride **12b** (51 mg, 0.42 mmol) was added. After addition, the ice bath was removed, and the solution was brought to reflux and held there for 20 h. The reaction solution was allowed to cool to room temperature before being poured into ice-cold 1 M H_3PO_4 and extracted with 3 × 20 mL of Et_2O. The combined organic layers were washed sequentially with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting white solid was purified by flash chromatography with 1:1 CH_2Cl_2/hexane as eluent to afford 134 mg (34%) of monofluoromethylacrylate **17** as a white solid, which decomposed upon heating above 210 °C, 62 mg (14%) of the difluoromethylacrylate ester, and 146 mg (42%) of recovered C_s diol **9**: IR ($CDCl_3$) 3120 (OH), 1735 (C=O), 1635 (C=C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.47–7.04 (m, 16 H, Ar H), 6.39 (s, 1 H, C=C(*H*)H), 5.95 (s, 1 H, C=C(H)*H*), 5.27–5.17 (m, 2 H, OCH_2), 5.07 (d, *J* = 46.5 Hz, 2 H, CH_2F), 4.82 (d, *J* = 11.8 Hz, 1 H, HOC(*H*)H), 4.59 (d, *J* = 11.1 Hz, 1 H, HOC(H)*H*), 4.18 (d, *J* = 2.7 Hz, 1 H, bridgehead H), 4.15 (d, *J* = 2.6 Hz, 1 H, bridgehead H′), 1.78–0.88 (m, 23 H), –0.46 to –0.50 (m, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 164.9 (d, *J* = 5.3 Hz, O=*C*CCF), 145.5, 145.0, 143.4, 143.3, 143.0, 142.6, 141.5, 140.6, 135.7 (d, *J* = 16.6 Hz, C=*C*CF), 127.7 (d, *J* = 9.4 Hz, *C*=CCF), 126.1, 125.9, 125.6, 125.5, 125.4, 124.4, 123.2, 122.1, 121.7, 121.4, 80.8 (d, *J* = 170 Hz, CF), 64.3, 62.6, 49.7, 48.9, 48.6, 48.54, 48.47, 47.7, 47.1, 47.0, 42.5, 42.2, 41.3, 41.2, 39.6, 39.4, 29.7, 29.0, 28.1; FABMS *m/z* (relative intensity) 778 (77, M^+).

Template C_s Diol Mono(phenylthio)methacrylate Monotrichloroacetate 1.[14c] Trichloroacetyl chloride (0.40 g, 2.2 mmol) was added to a stirring solution of monobromomethacrylate **13**

(1.40 g, 1.6 mmol) and 4-(dimethylamino)pyridine (0.27 g, 2.2 mmol) in 50 mL of THF at −78 °C under a nitrogen atmosphere. The solution was warmed to room temperature and stirred for 12 h. The mixture was poured into 10 mL of 1 M HCl and extracted with 3 × 20 mL of CH_2Cl_2. The combined extracts were washed with saturated $NaHCO_3$ solution and then brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel using 1:1 hexane–Et_2O as eluent to furnish 1.53 g (94%) of diester **1** as a white solid which decomposed upon heating above 264 °C. Crystals suitable for X-ray analysis were obtained through vapor diffusion crystallization with toluene/hexane: IR (CH_2Cl_2) 1761, 1715 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.34–7.0 (m, 21 H, Ar H), 6.12 (s, 1 H, C=C(*H*)H), 5.49 (s, 1 H, C=C(H)*H*), 5.37 (s, 2 H, OCH_2), 5.23 (m, 2 H, OCH_2), 4.18 (m, 2 H, bridgehead H), 3.75 (s, 2 H, SCH_2), 1.77–0.83 (m, 22 H), −0.45 (d, 2 H, *J* = 10.7 Hz, 2 H, H over Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.2, 162.1, 145.0, 144.8, 143.4, 142.6, 142.5, 142.4, 141.0, 140.2, 135.9 135.1, 131.1, 128.8, 127.4, 126.9, 126.3, 126.0, 125.8, 125.5, 125.4, 124.5, 124.3, 123.2, 123.1, 121.9, 121.6, 121.5, 121.3, 68.5, 64.3, 48.6, 48.5, 48.3, 47.7, 47.6, 46.9, 42.5, 42.2, 39.6, 35.8, 29.0, 28.1; FABMS (in dithiothreitol) *m/z* (relative intensity) 1016, 1015, 1014, 1013, 1012 (30, 65, 45, 65, 42 M^+, M^+ + 1).

Template C_s Diol Monofluoromethacrylate Mono(trimethylsilyl)acetate 20. Trimethylsilyl ketene[9] (27 mg, 0.24 mmol) was added to a stirring mixture of monofluoromethacrylate **17** (156 mg, 0.20 mmol) and zinc triflate (21 mg, 0.06 mmol) in 15 mL of CH_2Cl_2 at room temperature under N_2. After 5.5 h, TLC indicated the presence of starting alcohol **17**, and so more trimethylsilyl ketene (27 mg, 0.24 mmol) was added. After an additional 14 h, TLC indicated almost total consumption of starting material, and so the reaction mixture was filtered to facilitate removal of the zinc residue and concentrated in vacuo. The resulting white solid was purified by flash chromatography with 10% CH_2Cl_2/hexane as eluent to afford 70 mg (40%) of diester **20** as a white solid, which decomposed upon heating above 206 °C: IR ($CDCl_3$) 1730 (C=O), 1640 (C=C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.24–7.03 (m, 16 H, Ar H), 6.39 (s, 1 H, C=C(*H*)H), 5.94 (s, 1 H, C=C(H)*H*), 5.28–5.02 (m, 4 H, OCH_2), 5.07 (d, *J* = 46.3 Hz, 2 H, CH_2F), 4.18–4.15 (m, 2 H, bridgehead H), 2.01–0.85 (m, 24 H), 0.15 (s, 9 H, $Si(CH_3)_3$), −0.47 (d, *J* = 10.9 Hz, 2 H, H over Ar); ^{13}C NMR (90 MHz, $CDCl_3$) δ 173.3, 164.8, 145.1, 145.0, 143.6, 143.3, 142.6, 142.5, 141.2, 140.8, 135.7 (d, *J* = 16.9 Hz, C=*C*CF), 127.6 (d, *J* = 9.0 Hz, *C*=CCF), 126.1, 126.0, 125.8, 125.6, 125.5, 125.4, 125.2, 124.4, 124.2, 123.2, 123.0, 121.9, 121.8, 121.3, 80.8 (d, *J* = 170 Hz, CF), 64.3, 63.4, 48.6, 48.5, 48.4, 48.3, 47.7, 47.4, 47.1, 46.9, 42.6, 42.5, 42.2, 41.3, 41.2, 36.9, 29.0, 28.1, 26.9, −1.1; FABMS *m/z* (relative intensity) 892 (98, M^+).

Lactonization Studies: General Procedure A. The appropriate bis(acid chloride) **21**[13] (0.10 mmol, 1 equiv) was added to a stirring solution of template C_s diol **10** (69 mg, 0.10 mmol) and (dimethylamino)pyridine (28 mg, 0.23 mmol) in 20 mL of dichloromethane at room temperature under a N_2 atmosphere. After 18 h, the reaction solution was washed with 10 mL of 1 M HCl, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel with dichloromethane as eluent to furnish the bislactones **23** in the indicated yields (Figure 1).

General Procedure B.[9] A solution of template C_s diol **10** (100 mg, 0.14 mmol) and diacid **24** (0.14 mmol, 1 equiv) in 0.5 mL of THF and 0.5 mL of ethanol-free chloroform was added via motor-driven syringe over 12 h to a refluxing mixture of dicyclohexylcarbodiimide (127 mg, 0.62 mmol), (dimethylamino)pyridine (113 mg, 0.92 mmol), and (dimethylamino)pyridine hydrochloride (97 mg, 0.61 mmol) in 5 mL of ethanol-free chloroform. After addition, the solution was allowed to reflux another 5 h. At this time, the reaction solution was cooled to room temperature, and methanol (185 μL) and acetic acid (35 μL, 0.62 mmol) were added. Following 40 min of stirring, the solution was concentrated, 5 mL of ether was added, the solution was filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on silica gel with dichloromethane as eluent to furnish the bislactones **23** in the indicated yields (Figure 2).

23a: IR (CCl_4) 1734 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 7.2–7.0 (16 H, Ar H), 5.63 (d, *J* = 11.6 Hz, 2 H, C(*H*)HO), 5.00 (d, *J* = 11.6 Hz, 2 H, C(H)*H*O), 4.15 (d, *J* = 2.0 Hz, 2 H, bridgehead H), 2.55–2.25 (m, 4 H, CH_2CO_2), 1.9–1.0 (m, 32 H), −0.31 (m, 2 H, H over Ar); ^{13}C (90 MHz, $CDCl_3$) δ 173.8, 145.4, 143.8, 142.6, 141.4, 126.0, 125.8, 125.6, 125.3, 124.3, 123.1, 121.4, 120.9, 62.4, 49.1, 48.5, 48.0, 47.9, 47.7, 47.6, 42.4, 41.9, 41.7, 41.3, 41.0, 39.5, 34.3, 32.7, 30.5, 28.7, 28.3, 26.4; FABMS *m/z* (relative intensity) 845 (10, M^+ + H).

23b: IR (KBr) 1740 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.31–7.06 (m, 16 H, Ar H), 5.57 (d, *J* = 11.6 Hz, 2 H, C(*H*)HO), 4.89 (d, *J* = 11.6 Hz, 2 H, C(H)*H*O), 4.17 (s, 2 H, bridgehead H), 2.42–2.35 (m, 4 H, CH_2CO_2), 1.81–1.0 (m, 34 H), −0.34 (d, *J* = 11.2 Hz, 2 H, H over Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.9, 145.4, 143.9, 142.6, 141.3, 126.1, 125.9, 125.5, 125.3, 124.4, 123.1, 121.4, 121.1, 62.2, 48.6, 48.5, 47.9, 47.7, 47.5, 47.0, 42.5, 41.7, 41.5, 41.3, 39.2, 35.0, 30.9, 30.5, 28.6, 28.3, 26.3; MS *m/z* (relative intensity) 858 (17, M^+). Anal. Calcd for $C_{61}H_{62}O_4$: C, 85.28; H, 7.27. Found: C, 84.82; H, 7.41.

23c: IR (KBr) 1734 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.32–7.02 (m, 16 H, Ar H), 5.59 (d, *J* = 11.5 Hz, 2 H, C(*H*)HO), 4.88 (d, *J* = 11.5 Hz, 2 H, C(H)*H*O), 4.16 (s, 2 H, bridgehead H), 2.38–2.33 (m, 4 H, CH_2CO_2), 1.78–1.0 (m, 36 H), −0.40 (d, *J* = 11.1 Hz, H over Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.6, 143.9, 142.8, 141.4, 126.0, 125.9, 125.5, 125.3, 124.3, 123.1, 121.8, 121.1, 96.1, 62.2, 48.5, 48.3, 47.3, 47.2, 46.8, 42.7, 42.1, 42.0, 41.4, 41.2, 39.4, 34.7, 31.5, 30.7, 29.9, 28.8, 28.2, 26.0; MS *m/z* (relative intensity) 872 (10, M^+). Anal. Calcd for $C_{62}H_{64}O_4$: C, 85.28; H, 7.39. Found: C, 85.02; H, 7.66.

23d: IR (KBr) 1732 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.31–7.06 (m, 16 H, Ar H), 5.25 (d, *J* = 11.5 Hz, 2 H, C(*H*)HO), 5.07 (d, *J* = 11.5 Hz, 2 H, C(H)*H*O), 4.17 (d, *J* = 2.4 Hz, 2 H, bridgehead H), 2.44–2.36 (m, 4 H, CH_2CO_2), 1.81–1.0 (m, 38 H), −0.39 (d, *J* = 11.2 Hz, 2 H, H over Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.0, 145.3, 143.9, 142.7, 141.3, 126.1, 125.9, 125.5, 125.3, 124.3, 123.1, 121.6, 121.1, 96.1, 62.9, 48.5, 48.1, 47.3, 47.2, 47.0, 46.9, 42.8, 42.1, 42.0, 41.4, 39.4, 35.1, 29.4, 29.3, 28.9, 28.2, 25.8; MS *m/z* (relative intensity) 886 (90, M^+). Anal. Calcd for $C_{63}H_{66}O_4$: C, 85.29; H, 7.50. Found: C, 85.26; H, 7.53.

23e: IR (KBr) 1735 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.25–7.04 (m, 16 H, Ar H), 5.30 (d, *J* = 11.5 Hz, 2 H, C(*H*)HO), 5.04 (d, *J* = 11.6 Hz, 2 H, C(H)*H*O), 4.12 (s, 2 H, bridgehead H), 2.51–2.17 (m, 4 H, CH_2CO_2), 1.8–1.0 (m, 40 H), −0.42 (d, *J* = 11.1 Hz, 2 H, H over Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.8, 145.4, 143.9, 142.9, 141.4, 126.0, 125.9, 125.4, 125.3, 124.3, 123.1, 121.9, 121.0, 62.9, 48.5, 48.0, 47.1, 47.0, 46.8, 42.9, 42.5, 42.4, 41.3, 41.2, 39.5, 35.0, 29.9, 29.4, 29.1, 29.0, 28.9, 28.2, 25.2; MS *m/z* (relative intensity) 900 (42, M^+). Anal. Calcd for $C_{64}H_{68}O_4$: C, 85.29; H, 7.61. Found: C, 85.58; H, 7.52.

23f: IR (KBr) 1738 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.2–6.9 (m, 16 H, Ar H), 5.09 (s, 4 H, CH_2O), 4.10 (d, *J* = 2.3 Hz, 2 H, bridgehead H), 2.39–2.31 (m, 4 H, CH_2CO_2), 1.81–1.0 (m, 42 H), −0.49 (d, *J* = 11.1 Hz, 2 H, H over Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.9, 145.4, 143.9, 142.9, 141.4, 126.1, 125.9, 125.5, 125.3, 124.3, 123.1, 121.6, 121.0, 62.9, 48.5, 48.1, 47.2, 47.1, 47.0, 46.9, 42.9, 42.4, 42.3, 41.4, 39.5, 34.6, 29.0, 28.5, 28.4, 28.3, 28.2, 24.8; MS *m/z* (relative intensity) 914 (51, M^+).

23g: IR (CCl_4) 1745 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 7.2–7.0 (m, 16 H, Ar H), 5.17 (s, 4 H, CH_2O), 4.16 (d, *J* = 2.4 Hz, 2 H, bridgehead H), 2.40 (t, *J* = 8.0 Hz, 4 H, CH_2CO_2), 1.9–1.1 (m, 46 H), −0.40 (d, *J* = 11 Hz, 2 H, H over Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 145.4, 143.8, 142.8, 141.4, 126.0, 125.9, 125.5, 125.3, 124.3, 123.1, 121.6, 121.0, 62.9, 48.5, 48.1, 47.2, 47.0, 42.8, 42.3, 42.2, 41.4, 39.5, 34.3, 29.1, 28.6, 28.4, 28.2, 24.5; FABMS *m/z* (relative intensity) 943 (73, M^+).

C_s Template (*E,E*)-Deca-4,8-diene-1,10-dicarboxylate 27. By use of general procedure B, template C_s diol **10** (1.00 gm, 1.45 mmol) and (*E,E*)-deca-4,8-diene-1,10-dicarboxylic acid (**29**) (0.33 gm, 1.46 mmol) were coupled to afford 672 mg of bislactone **27** (53%) following flash chromatography on silica gel with CH_2Cl_2 as eluent; IR (CCl_4) 1740 (C=O), 940 (*E*-CH=CH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.26–7.04 (m, 16 H, Ar H), 5.40–5.28 (m, 6 H, C*H*=C*H*, C(*H*)HO), 5.04 (d, *J* = 11.5 Hz, 2 H, C(H)*H*O), 4.18 (s, 2 H, bridgehead H), 2.45–2.30 (m, 4 H, CH_2CO_2), 2.0–1.08 (m, 30 H), −0.36 (d, *J* = 10.3 Hz, 2 H, H over Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 145.2, 143.9, 142.6, 141.3, 131.4, 128.2, 126.0, 125.9, 125.5, 125.3, 124.3, 123.1, 121.2, 121.1, 63.1, 48.4, 48.2, 47.4, 47.3, 47.0, 42.6, 42.0, 41.9, 41.5, 41.4, 39.5, 35.0, 32.5, 28.9, 28.6, 28.2; FABMS *m/z* (relative intensity) 883 (20, M^+ + H).

C_s Template (Z,Z)-Deca-4,8-diene-1,10-dicarboxylate 28. By use of general procedure B, template C_s diol **10** (200 mg, 0.29 mmol) and (Z,Z)-deca-4,8-diene-1,10-dicarboxylic acid (**30**) (65 mg, 0.29 mmol) were combined to furnish 103 mg of bislactone **28** (40%) following flash chromatography on silica gel with CH_2Cl_2 as eluent: IR (CCl_4) 1743 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 7.27-7.05 (m, 16 H, Ar H), 5.48-5.30 (m, 6 H, C*H*=CH, C(*H*)HO), 5.00 (d, J = 11.5 Hz, 2 H, C(H)*H*O), 4.17 (s, 2 H, bridgehead H), 2.48-2.36 (m, 4 H, CH_2CO_2), 2.10-1.06 (m, 30 H), -0.37 (d, J = 11.3 Hz, 2 H, H over Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 145.3, 143.8, 142.6, 141.2, 130.4, 127.6, 126.1, 125.9, 125.5, 125.3, 124.3, 123.1, 121.5, 121.0, 62.6, 48.4, 48.3, 47.6, 47.4, 47.2, 46.9, 42.6, 41.9, 41.7, 41.6, 41.5, 39.3, 34.6, 28.8, 28.3, 27.1, 23.6; FABMS m/z (relative intensity) 882 (70, M^+).

C_2 Template Docosanedioate 26a. By use of general procedure B, template C_2 diol **11** (100 mg, 0.14 mmol) and docosanedioic acid (53 mg, 0.14 mmol) were coupled to deliver 21 mg of bislactone **26a** (14%) following flash chromatography on silica gel with CH_2Cl_2 as eluent: IR (CCl_4) 1740 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 7.21-7.03 (m, 16 H, Ar H), 5.25 (d, J = 11.3 Hz, 2 H, C(*H*)HO), 5.11 (d, J = 11.3 Hz, 2 H, C(H)*H*O), 4.16 (s, 2 H, bridgehead H), 2.43-2.39 (m, 4 H, CH_2CO_2), 1.79-1.09 (m, 58 H), -0.40 (d, J = 10.6 Hz, 2 H, H over Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 145.3, 143.8, 142.9, 141.4, 126.0, 125.9, 125.5, 125.3, 124.3, 123.1, 121.7, 121.0, 62.8, 48.5, 48.2, 47.2, 47.0, 42.8, 42.3, 42.2, 41.3, 39.5, 34.8, 29.7, 29.4, 29.2, 29.0, 28.9, 28.8, 28.7, 28.2, 25.1; FABMS m/z (relative intensity) 1027 (97, M^+ + H).

C_2 Template Tetracosanedioate 26b. By use of general procedure A, template C_2 diol **11** (69 mg, 0.10 mmol), (dimethylamino)pyridine (28 mg, 0.23 mmol), and tetracosanedioyl chloride (44 mg, 0.10 mmol) were combined to yield 9 mg of bislactone **26b** (9%) following flash chromatography on silica gel with 1:1 hexane/dichloromethane as eluent: IR (CCl_4) 1736 cm^{-1} (C=O); ^1H NMR (300 MHz, $CDCl_3$) δ 7.26-7.03 (m, 16 H, Ar H), 5.2 (d, J = 11.5 Hz, 2 H, C(*H*)HO), 5.12 (d, J = 11.5 Hz, 2 H, C(H)*H*O), 4.17 (s, 2 H, bridgehead H), 2.41 (t, J = 7.2 Hz, 4 H, CH_2CO_2), 1.79-1.09 (m, 62 H), -0.41 (d, J = 11.1 Hz, 2 H, H over Ar); ^{13}C NMR (50 MHz $CDCl_3$) δ 173.9, 145.3, 143.7, 142.8, 141.3, 126.0, 125.9, 125.8, 125.3, 124.3, 123.1, 121.6, 121.2, 48.6, 48.3, 47.4, 47.3, 47.26, 47.2, 42.8, 42.3, 42.2, 41.4, 39.6, 34.7, 34.5, 29.5, 29.4, 28.38, 28.7, 25.3, 20.7; FABMS m/z (relative intensity) 1055 (64, M^+ + H).

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Supplementary Material Available: Copies of ^{13}C NMR spectra for **8**, **9**, **11**, **13**, **17**, **1**, **20**, **23a**, **26a**, and **27** and experimental details/spectroscopic characterization for **11**, **12b**, **15**, **16**, **18**, **19**, **29**, and **30** (18 pages). Ordering information is given on any current masthead page.

Transition Structures for the Aldol Reactions of Anionic, Lithium, and Boron Enolates

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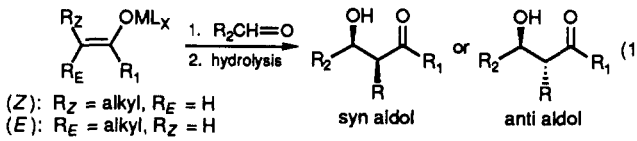
Transition structures for the reactions of acetaldehyde enolate and lithium and boron enolates of acetaldehyde with formaldehyde have been located with ab initio molecular orbital calculations. For the reaction of acetaldehyde enolate with formaldehyde, three transition structures were located. The transition structure for the reaction of lithium enolate with formaldehyde has a half-chair conformation, with the lithium, oxygens, and adjacent carbons in a plane. Both chair and twist-boat transition structures have been located for the reaction of boron acetaldehyde enolate with formaldehyde. The chair is 1.4 kcal/mol higher in energy than the twist-boat for the parent reaction, while methyl substituents at various positions alter these relative conformational energies. The perference for chair transition structures is large for Z-enolates, while twist-boat transition structures are only slightly less stable than the chair for reactions of E-enolates.

Introduction

Aldol reactions of metal enolates with carbonyl compounds in solution are among the most useful methods of carbon-carbon bond formation.[2,3] As shown in eq 1, the reactions of metal enolates with aldehydes can give either syn or anti aldols. The formation of a CC bond to give products with desirable functionality, frequently with stereocontrol, has made this reaction an extremely useful process.



The stereochemistries of reactions of substituted enolates with aldehydes have led to qualitative inferences about transition state geometries.[3-15] As described below,

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