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Template-Controlled Oligomerization. The Search for Bimolecular Termination

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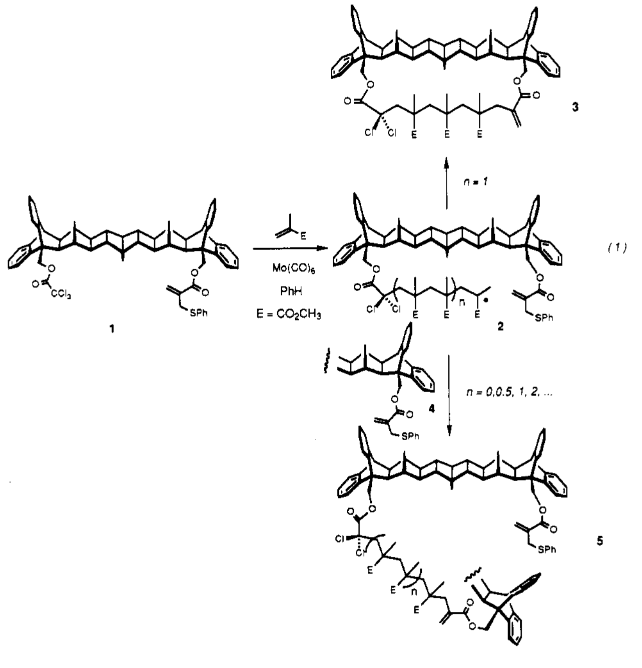
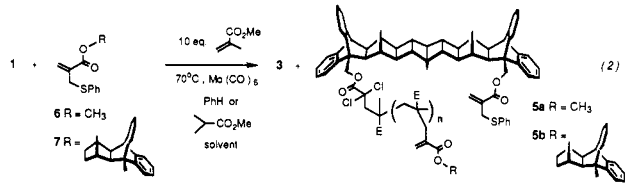
Summary: Bimolecular termination was probed in benzene and in methyl isobutyrate using exogenous terminator and a previously described template system effective in controlling oligoselectivity in the free-radical-mediated polymerization of methyl methacrylate. As expected, increasing amounts of added terminator led to a decrease in intramolecular termination (cyclization). However, differences in reactivity profiles with different added terminators in the two solvents are consistent with the intervention of solvent-enforced control of chain–template dynamics.

Enforcing oligoselectivity in a polymerization reaction represents one promising approach for obtaining short repeating molecular segments which may have interesting properties characteristic of both small molecules and larger polymers. We have been exploring the prospect that such selectivity might emerge from tethering the growing oligomer chain to a large rigid template molecule. In principle, then, oligoselectivity in the template-mediated free-radical polymerization of methyl methacrylate (MMA) will result from largely confining the polymerization process to the gap defined by the template-bound trichloroacetate initiator and phenylthiomethacrylate terminator, cf. 1. Prior studies have shown that the template-bound MMA trimer **3** could be isolated (as a mixture of stereoisomers) in yields over 40%, eq 1.[1] The successful execution of this strategy is critically dependent upon suppression of unwanted *bimolecular* termination events between a carbon radical bound to one template (e.g., **2**) and the terminating functionality of a second template (e.g., **4**). In this paper, we report the results of a detailed study into the structural and electronic factors which influence the competition between this yield-limiting bimolecular termination and the desired intramolecular (macrocyclizing) termination.



Although bimolecular termination seemed like a plausible culprit in limiting the yield of **3**, we were frustrated in our attempts to obtain prima facie evidence via isolation of any material of the type **5** from polymerization reaction mixtures. Thus, we sought indirect means to garner evidence for the intervention of this yield limiting process as a prelude, hopefully, to manipulating reaction conditions in order to suppress this competition for **2**. The "terminator challenge" experiments outlined in eq 2 are designed to address this goal, and in addition, probe the consequences of solvent variation on bimolecular termination. Specifically, the template-controlled oligomerization reaction was run as indicated in eq 1, but in independent trials, varying amounts of exogenous terminators **6** and **7** were included. These reactions were run in both benzene, a solvent in which the yield of **3** is maximized,[1] and methyl isobutyrate, a solvent chosen for its resemblance to the growing MMA oligomer chain in **2**. The outcome of these studies is shown in Figures 1 and 2 where the yield of **3** is normalized to 100%.[2] Each data point resulted from averaging two or three independent runs, and the yield of **3** in each case was determined by product isolation following HPLC.



Inspection of these figures leads to several interesting observations. Clearly, the yield of product macrocycle **3** diminishes as more added terminator is present, a result entirely consistent with a scenario where **6** or **7** siphon off intermediate **2** via bimolecular termination. Beyond this obvious conclusion, the differential effects of **6** and **7** in the two solvents reveal some subtleties concerning the role that the medium may play in fostering or suppressing bimolecular termination. Thus, to the extent that yield loss of **3** can be attributed to bimolecular termination,[3] for both added terminators, this process appears to be suppressed to a significantly greater extent (~20%) in benzene than in methyl isobutyrate. Furthermore, the model template ester terminator **7** is marginally less effective than the methyl ester terminator **6** at intercepting intermediate radicals (e.g., **2**) in benzene relative to this same comparison in methyl isobutyrate.

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

(2) The actual chemical yields of isolated product **3** in the blank runs typically hovered around 17%. In addition, 60–70% of unreacted template **1** could be recovered from these crude reaction mixtures following chromatography. The maximum chemical yield for this process approaches 50% (unpublished observations), although in this instance periodic charges of Mo(CO)$_6$ were added to the reaction over its 9-day course. For the experiments described in this work, we deemed reproducibility from run to run to be more important than yield optimization, and so we used just a single initial charge of molybdenum catalyst in a sealed reaction vessel for each experiment. In this way, the yield of **3** should not reflect exposure to adventitious oxygen or other impurities.

(3) The chain-transfer constants to solvent for MMA radical polymerization are small and similar in the two solvents (benzene 4×10^{-6}, methyl isobutyrate 3×10^{-5}): Brandrup, J., Immergut, E. H., Eds. *Polymer Handbook*, 2nd Ed.; J. H. Wiley and Sons: New York, 1975.

0022-3263/92/1957-4573$03.00/0

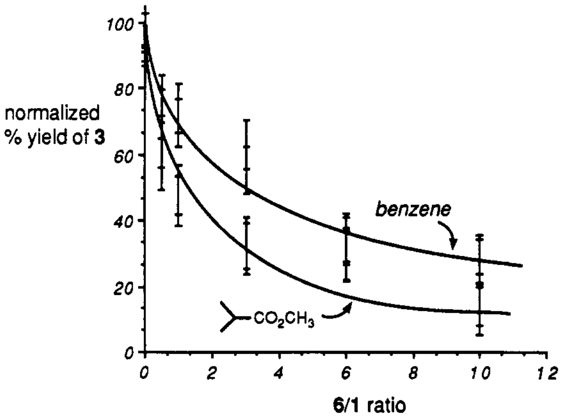


Figure 1. Yield of macrocycle 3 as a function of added methyl ester terminator 6.

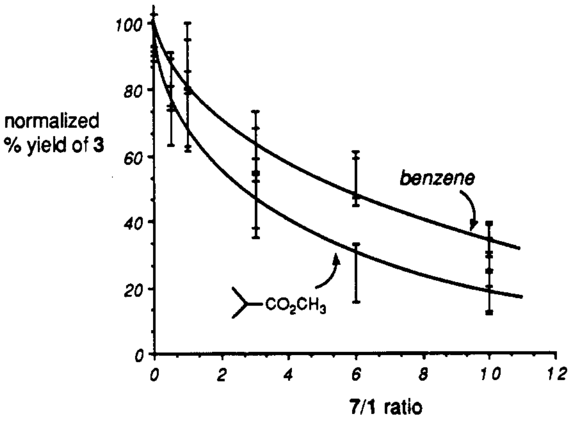
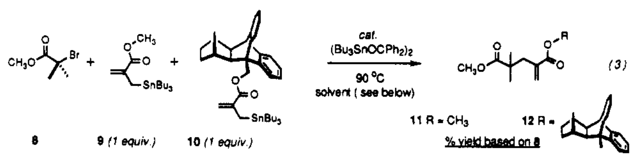


Figure 2. Yield of macrocycle 3 as a function of added model template ester terminator 7.



		% yield based on 8	
benzene	0.1 equiv. 8	50	50
	0.2 equiv. 8	43	48
methyl isobutyrate	0.1 equiv. 8	49	49
	0.2 equiv. 8	50	50

The interpretation of these data is not entirely straightforward. The control experiment shown in eq 3, which uses a simple MMA radical derived from 8 as a model for template bound radical 2 ($n = 0$ or 1), narrows the range of possible explanations. Thus, the formation of adducts 11 and 12 in essentially equal yields provides unequivocal evidence that the two terminators (modeled by 9 and 10) exhibit identical *reactivity* with the simple MMA radical derived from 8 in either solvent. Our current working hypothesis to rationalize these observations focuses on the possibility that a "solvophobic effect"[4] conspires to force the growing oligomeric chain against the template to a greater extent in benzene than in the structurally similar (to the growing oligomeric chain) solvent methyl isobutyrate. Once packed against the template, interception of an intermediate radical by external terminator (i.e., bimolecular termination) may then be suppressed for steric reasons with the bulkier 7 more so than the smaller 6, and hence, the opportunities for (desirable) intramolecular termination will be enhanced. Thus, a *solvent induced* steric effect may underlie the differential reactivity of the growing chain radical with the two terminators in the two solvents. Experiments designed to exploit these unusual solvent effects as a means for maximizing production of macrocycle 3 are planned.

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Supplementary Material Available: Experimental procedures and compound characterization data (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(4) (a) Abraham, M. H. *J. Am. Chem. Soc.* 1982, *104*, 2085. (b) Dunams, T.; Hoekstra, W.; Pentaleri, M.; Liotta, D. *Tetrahedron Lett.* 1988, *29*, 3745. (c) Breslow, R.; Guo, T. *J. Am. Chem. Soc.* 1988, *110*, 5613. (d) Ito, M. M.; Kato, J.; Takagi, S.; Wakashiro, E.; Sato, T.; Yamada, Y.; Saito, H., Namiki, T.; Takamura, I.; Watasuki, K.; Suzuki, T.; Endo, T. *J. Am. Chem. Soc.* 1988, *110*, 5147.

Vinylcyclopropane Oxygenation. Anti Diastereoselectivity through an Unexpected Transition-State Geometry

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Summary: Ester-substituted vinylcyclopropanes react with molecular oxygen via a radical-mediated [3-atom + 2-atom] addition to form 1,2-dioxolanes with predominantly anti stereochemistry. The degree of anti stereoselectivity can be controlled by the electronic nature of the radical stabilizing substituent R.

Molecular oxygen can be combined with substituted vinylcyclopropanes to furnish 1,2-dioxolanes via a radical-mediated [3-atom + 2-atom] addition.[1] The reaction is believed to occur by the mechanism shown in Scheme I in which dioxolane stereochemistry is set during ring closure of substituted 5-hexenylperoxy radical 5. With 1, R = Ph or CH=CHCO$_2$Me, high levels of syn dioxolane product are observed (Table I, entries **a** and **b**). In this paper we report recent advances in this chemistry which (1) give further insight into the transition-state structures and attendant steric interactions which accompany cy-

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(1) Feldman, K. S.; Simpson, R. E. *J. Am. Chem. Soc.* 1989, *111*, 4878.