Communications to the Editor

Regio- and Enantioselective Molybdenum-Catalyzed Alkylations of Polyenyl Esters

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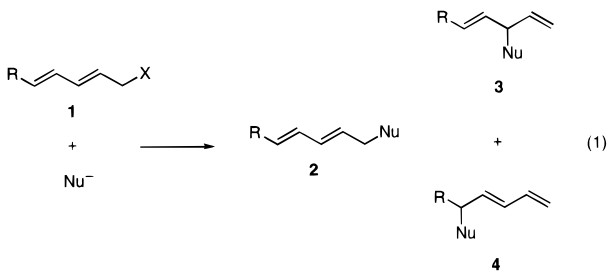
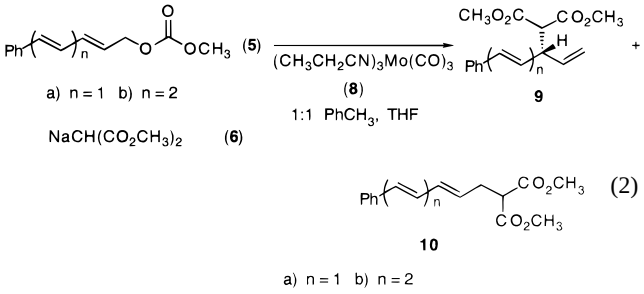
The use of polyene substrates in allylic alkylations can be complicated by the issue of regioselectivity, as illustrated in eq 1, as well as reversibility.[1,2] Thus, although much work in



asymmetric palladium-catalyzed allylic alkylations has been done,[3] the utilization of polyenes has not been explored. One of the reasons clearly stems from the anticipated selectivity for formation of the achiral product **2**.[1d,e] On the other hand, switching to molybdenum should favor either **3** or **4** over **2**.[4,5] The recent success in effecting an asymmetric alkylation with cinnamyl substrates[6] induced us to explore its potential with polyene systems.

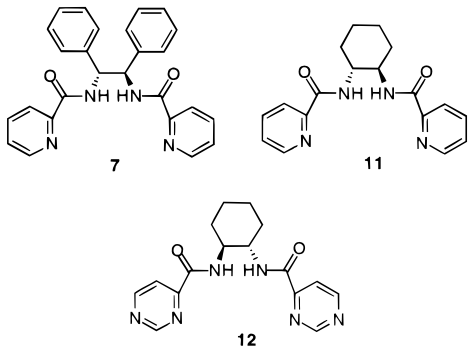
Our initial studies examined the reaction of 5-phenylpentadienyl methyl carbonate, **5a** (eq 2), and dimethyl sodiomalonate, **6**, using



a catalyst formed in situ from the bis-picolinylamide **7** and the molybdenum complex **8**. Only two alkylation products were observed—the branched one, **9a**[2], and the linear one, **10a**[1e], in 6.1:1 ratio in 95% isolated yield. None of the product derived from attack at the benzylic position was observed. Using chiral HPLC, the ee of **9a** was established as 98% (er 99:1). Interestingly, extending the conjugation as in **5b** led to virtually the same results—only the two products **9b**[2] and **10b**[2] in a 5.3:1 ratio were formed (58% yield, 92% brsm[7]), and the ee of **9b** was 97%. Switching to ligand **11** led to slight improvements: **9b** and **10b** were obtained in a 6.1:1 ratio (68% yield) and the ee of **9b** was >99%.

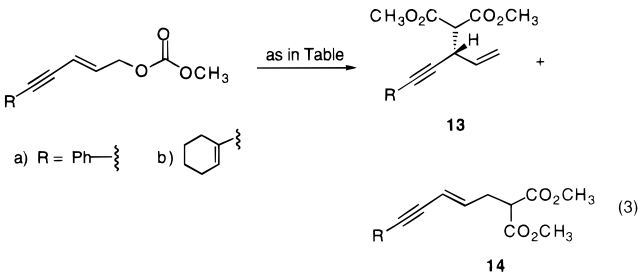
With this background, a series of polyenyl substrates as summarized in Table 1 was examined. While the proximal double bond must be only disubstituted, the remote double bond can bear any number of substituents.

Generally, trisubstitution on the distal double bond, notably as in entries 3, 4, 6, and 8, gave higher ee's than terminal disubstitution as in entry 7 or disubstitution as in entry 5. The use of the enol ether as in entry 8 is particularly useful for further transformations. The trienyl substrates of entries 9 and 10 still produce only two regioisomeric products with good regioselectivity (∼10−12:1) and excellent ee (97 and 98%).



In examining the role of the linker heterocycle, we prepared the 4-pyrimidinecarbonyl ligand **12**[9] to decrease the σ-donation to the molybdenum. This new ligand system gave slight improvements in either ratio or ee in the two cases examined, entries 6 and 7. Further evaluation of this ligand is underway.

Conjugation of the allyl carbonate with an alkyne also led to no involvement of the triple bond as shown in eq 3. In both cases,



the major product (**13a**:**14a** 5.3:1, **13b**:**14b** 7.3:1) was the branched one with excellent ee (**13a** 99% ee, **13b** 99% ee). In

(1) (a) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1998**, *120*, 70. (b) Nilsson, Y. I. M.; Andersson, P. G.; Backvall, J.-E. *J. Am. Chem. Soc.* **1993**, *115*, 6609. (c) Andersson, P. G.; Backvall, J.-E. *J. Org. Chem.* **1991**, *56*, 5349. (d) Trost, B. M.; Lautens, M.; Hung, M.-H.; Carmichael, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 7641. (e) Trost, B. M.; Urch, C. J.; Hung, M.-H. *Tetrahedron Lett.* **1986**, *27*, 4949.

(2) Trost, B. M.; Hung, M.-H. *J. Am. Chem. Soc.* **1984**, *106*, 6837.

(3) For reviews, see: Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395; Hayashi, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH Publishers: New York, 1993; pp 325−365.

(4) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590; Trost, B. M.; Lautens, M. *Tetrahedron* **1987**, *43*, 4817; Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1987**, *109*, 1469; **1982**, *104*, 5543. Also see: Faller, J. W.; Lambert, C.; Mazzieri, M. R. *J. Organomet. Chem.* **1990**, *383*, 161; Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670.

(5) For work on stoichiometric π-allylmolybdenum alkylations, see: Adams, R. D.; Chodosh, D. F.; Faller, J. W.; Rosan, A. M. *J. Am. Chem. Soc.* **1979**, *101*, 2570; McCleverty, J. A.; Murray, A. J. *J. Organomet. Chem.* **1978**, *149*, C29; Rubio, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 891.

(6) Trost, B. M.; Hachiya, I. *J. Am. Chem. Soc.* **1998**, *120*, 1104. Also see: Glorius, F.; Pfaltz, A. *Org. Lett.* **1999**, *1*, 141.

(7) brsm = based upon reacted starting material.

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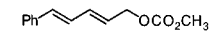
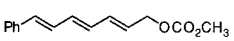
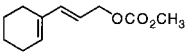
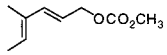
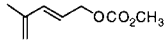
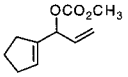
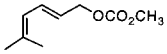
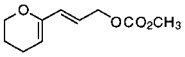
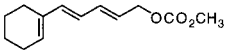
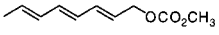
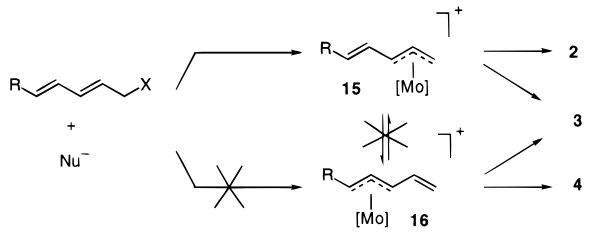
Table 1. Regio- and Enantioselective Alkylations of Polyenyl Carbonates[a] with Dimethyl Malonate

Entry		Time	Yield[b]	Ratio[c] **3**:**2**	ee (er)[d] **3**
1		3 h[e]	95	6.1:1	98 (99:1)
2		4 h[e]	58 (92)	5.3:1	97 (98.5:1.5)
		3.5 h	68	6.1:1	>99 (>99:1)
3		3 h	91	11.5:1	94 (97:3)
4		3 h	89 (94)	49:1	98 (99:1)
		6 h[e]	87 (95)	15.7:1	97 (98.5:1.5)
5		3 h	81 (89)	8.1:1	80 (90:10)
6		2 h	94	11.5:1	87 (93.5:6.5)
		1.5 h[f]	88	13.3:1	86 (7:93)
7		2 h	96	15.7:1	86 (93:7)
		2 h[f]	94	15.7:1	91 (4.5:95.5)
8[g]		1.5 h	93	13.3:1	96 (98:2)
9		2 h	70 (79)	11.5:1	97 (98.5:1.5)
10		3 h	81 (85)	10.1:1	98 (99:1)

[a] All reactions performed using 10 mol % **8**, 15 mol % **11**, 1 equiv of allyl carbonate, 2.2 equiv of dimethyl malonate, and 2.0 equiv of sodium hydride in 1:1 $PhCH_3$/THF at 80−90 °C. [b] Isolated yields; yields in parentheses based upon recovered starting material. [c] Determined by ^1H NMR spectroscopy of the isolated products; also see ref 8. [d] Determined by chiral HPLC. [e] Ligand **7** employed in this run. [f] For this run, ligand **12** was employed; therefore, the enantiomeric product from that obtained with ligand **11** is formed. [g] For this run, 20 mol % of **8** and 30 mol % of **11** employed.

the latter case, better results were obtained with 20 mol % of catalyst than with 10 mol %.

The lack of participation of the additional unsaturation is both surprising and satisfying. The regioselectivity suggests that π-allyl complex **16** is not involved in the sequence, otherwise detectable amounts of regioisomer **4** would have been expected. This conclusion then states that initial ionization must occur to give **15** exclusively and, furthermore, that **15** does not equilibrate to **16** to any appreciable extent. While it can be argued that (a) complexes **15** and **16** are in dynamic equilibrium and (b) complex **15** might be the kinetically more active complex in the alkylation step to rationalize the results, it is not obvious that complex **16** should really be significantly less reactive especially since attack at the benzylic position in cinnamyl systems is preferred. The types of products can be quite useful for further structural elaboration. For example, the chiral 1,3-dienes resulting from



triene substrates in entries 2, 9, and 10 may participate in subsequent Diels−Alder reactions.[1d] On the other hand, the products are also of interest in their own right. The stereochemistry is assigned by analogy to the cinnamyl substrates[6] and thus must be considered tentative at present. Future studies are intended to elucidate the exact nature of the active catalyst.

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Supporting Information Available: A sample experimental procedure for the asymmetric alkylation as well as the characterization data for all of the compounds described in the Table 1, as well as for **13a** and **13b** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) All new compounds have been characterized spectroscopically and elemental compositions established by combustion analysis or high-resolution mass spectrometry.

(9) Prepared in standard fashion from the diamine and 4-pyrimidinecarboxylic acid [Gabriel, S.; Colman, J. *Chem. Ber.* **1899**, *32*, 1525].