Reactions of Cobalt-Complexed Acetylenic Aldehydes with Chiral (γ-Alkoxyallyl)boranes: Enantioselective Synthesis of 3,4-Dioxy 1,5-Enynes and Stereoselective Entry to Polyfunctional Building Blocks

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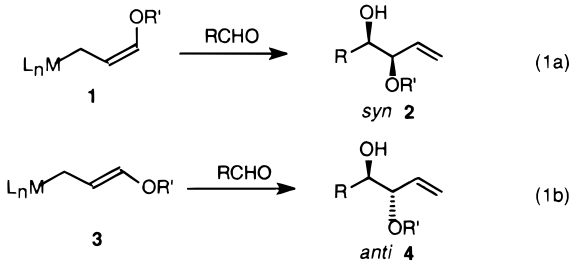
Received October 16, 1996[⊗]

Toward the goal of developing enantioselective routes to polyfunctional building blocks using Co-based technology, the reactions of (*Z*)- and (*E*)-(*γ-alkoxyallyl*)diisopinocampheylboranes (**8**, **13**) with acetylenic aldehydes and their $-Co_2(CO)_6$ complexes (**10a**−**c**) have been investigated. Whereas phenylpropynal reacts with (*Z*)-**8** with poor efficiency (<10% yield) and moderate enantioselectivity, the corresponding Co derivatives **10** undergo high-yielding (65−76%), diastereoselective (88−>95% de), and enantioselective (>96% ee) reactions, producing *syn*-(3,4-dioxy 1,5-enyne)$Co_2(CO)_6$ **11a**−**f**. Similarly, the newly prepared (*E*)-boranes **13** also react efficienctly with the complexed aldehydes, affording the corresponding (*anti*-3,4-dioxy 1,5-enyne)$Co_2(CO)_6$ complexes **15a**−**c** with virtually complete diastereo- and enantioselectivity, while phenylpropynal itself reacts inefficiently and with lower enantioselectivity. Oxidative demetalation of the complexed adducts affords the 3,4-dioxy 1,5-enynes **17** with complete maintenance of stereochemical integrity. Osmium-catalyzed dihydroxylation of a representative dioxy enyne, i.e., **17c**, proceeds with high diastereoselectively (9:1), favoring addition *anti* to the allylic alkoxy group. Although epoxidation of enynediol **25** by *t*-BuOOH/$VO(acac)_2$ occurs stereoselectively, it is accompanied by epimerization of the diol unit.

Introduction

The development of stereocontrolled methods for the construction of acyclic structures containing multiple asymmetric centers has received much attention because of its importance for the efficient synthesis of highly functionalized, biologically active molecules.[1] Methodology that leads to the stereoselective formation of *syn*- or *anti*-1,2-diol units with the simultaneous generation of carbon−carbon bonds has been very attractive in this context. Among the most important methods for producing such functionality are pinacol coupling[2] and α-alkoxyallylation of aldehydes by (*γ*-alkoxyallyl)metal reagents, with boron[3] and tin[4] derivatives receiving the most attention (eq 1 a,b). Among the boron-based reagents, excellent *syn* diastereoselectivity has been observed in the reactions of [(*Z*)-*γ*-alkoxyallyl]boranes[5] and boronates[6] with aldehydes. Additionally, good to excellent enantioselectivity has been demonstrated in reactions of aldehydes with homochiral [(*Z*)-alkoxyallyl]boronates[7] and diisopinocampheylboranes[8]



The stereocontrolled synthesis of *anti* diol derivatives by this approach (eq 1b) has been less widely studied, in part because of the configurational instability of (*E*)-*γ*-alkoxyallyl anions.[9] This problem was overcome by Hoffmann's group,[10] who synthesized achiral (*E*)-*γ*-alkoxy-substituted allylboronates (**3**) at low temperature and found that they add to aldehydes, giving *anti*-1,2-diols with excellent diastereoselectivity. Prior to the present report, enantioselective variants of this methodology were not available.

Recently, our group has been interested in the potential utility of 3,4-dioxy enyne derivatives **6** and **7** as building blocks for the stereoselective synthesis of complex molecules possessing multiple adjacent stereocenters. The inherently unsymmetrical, chiral, and multifunctional nature of these compounds offers promise for chemo-, regio-, and enantioselective functionalization of the unsaturated units. Moreover, the opportunity to compare in one system the relative reactivity of the double and triple bonds and to assess the stereodirecting effects of the hydroxy versus alkoxy groups is also of interest. At the inception of this project we envisioned that these compounds could be prepared *via* the addition of (*γ*-

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[⊗] Abstract published in *Advance ACS Abstracts*, February 15, 1997.

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(6) Hoffmann, R. W.; Kemper, B. *Tetrahedron Lett.* **1982**, *23*, 845.

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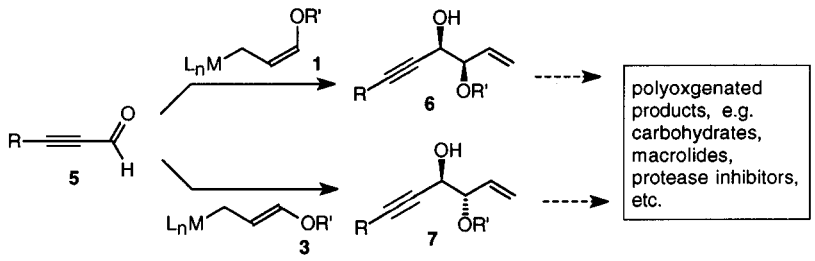
S0022-3263(96)01938-X CCC: $14.00

Scheme 1



alkoxyallyl)metal reagents to acetylenic aldehydes (Scheme 1). Prior studies in our laboratory[11] and others[12] have demonstrated that cobalt complexes of acetylenic aldehydes and acetals, (RC≡CCHO)$Co_2(CO)_6$ and [RC≡CCH-$(OR)_2$]$Co_2(CO)_6$, undergo highly diastereoselective aldol reactions with silyl enol ethers. In a related development Roush and Park found enhanced *enantioselectivity* in the asymmetric allyl- and crotylboration of complexed acetylenic and propargylic aldehydes relative to the uncomplexed aldehydes.[13]

We report herein the results of a study of the reactions of (*Z*)- and (*E*)-(γ-alkoxyallyl)diisopinocampheylboranes **8** and **13** with acetylenic aldehydes and their $-Co_2(CO)_6$ complexes. Whereas the free acetylenic substrates react with poor efficiency and limited enantioselectivity with **8** and **13**, the corresponding cobalt derivatives undergo efficient regio-, diastereo-, and *enantio*selective reactions, producing 3,4-dioxy 1,5-enynes (after demetalation); a preliminary study of the reactions with (*Z*)-**8** has been reported.[14] Also described is an investigation of two representative functionalization reactions of the dioxy enyne adducts, i.e., dihydroxylation and epoxidation. High chemo- and diastereoselectivity has been found in both cases, underscoring the potential of these intermediates for the selective synthesis of molecular targets containing multiple adjacent stereocenters. Unexpectedly, however, epoxidation by $VO(acac)_2$ is accompanied by epimerization of the diol unit.

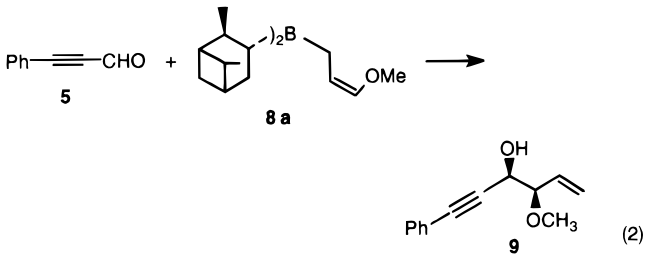
Results and Discussion

Additions of [(*Z*)-γ-Alkoxyallyl]diisopinocampheylboranes to Alkynyl Aldehydes and Their Cobalt Complexes. [(*Z*)-γ-Alkoxyallyl]diisopinocampheylboranes **8** were prepared by metalation of the corresponding allyl ethers and subsequent treatment with *B*-methoxy-(+)- or -(−)-diisopinocampheylborane.[8] The reactions of 2-butynal and 3-phenylpropynal with borane **8** were carried out by treatment of the borane with 1.3 equiv of BF_3·Et_2O in THF at −78 °C followed by addition of the aldehyde. After workup, the 3,4-dioxy 1,5-enyne derivatives **9** were isolated in poor yields (5−10%), apparently the result of polymerization of the acetylenic aldehydes (formation of a gelatinous, insoluble residue) under the reaction conditions. NMR and GC/MS analysis suggested the presence of a single diastereomer in each case, but chiral GC[15] and Mosher ester[16] analysis of the products indicated only moderate enantioselectivity (65% ee).

Table 1. Preparation of (*syn*-3,4-Dioxy 1,5-enyne)$Co_2(CO)_6$ 11

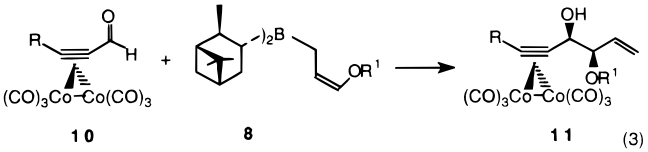
aldehyde complex	borane	adduct complex	% yield[a]	% de[b]	% ee
10a (R = Ph)	**8a** (R = Me)	**11a**	75	>95	>98[c]
10a	**8b** (R = Me)[d]	**11b**[d]	75	>95	>98[c]
10a	**8c** (R = CH_2OMe)	**11c**	62	>95	>96[e]
10b (R = Me)	**8a**	**11d**	73	>95	>96[e]
10b	**8c**	**11e**	65	>95	>96[e]
10c (R = H)	**8a**	**11f**	76	88	>96[e,f]

[a] Yield after chromatography. [b] Determined by ^1H and ^{13}C NMR. [d] Determined by chiral GC on cyclodextrin. [d] Enantiomer of **8a** and **11a**. [e] Determined by ^{19}F NMR of Mosher ester derivative. [f] % ee of major diastereomer.



(2)

Reactions of the corresponding $-Co_2(CO)_6$ complexes of the acetylenic aldehydes provided a dramatic improvement in efficiency and selectivity. Compounds **10** were prepared in good yield by complexation of the readily available acetylenic acetals ($Co_2(CO)_8$/20 °C) followed by Amberlyst-catalyzed hydrolysis (acetone/H_2O) at room temperature.[11,17] The reactions of **10** with (alkoxyallyl)-boranes **8**, when carried out as for the free aldehyde, gave dark red (3-alkoxy-4-hydroxy-1-en-5-yne)$Co_2(CO)_6$ complexes **11** in good yield (eq 3, Table 1).[14]



(3)

The ^1H and ^{13}C NMR spectra of the product complexes **11** indicated the presence of a single diastereomer (>97%) that was tentatively assigned the *syn* stereochemistry on the basis of literature precedent and the characteristic chemical shift of the −OH proton (*vide infra*).[10] This assignment was confirmed by an X-ray structure determination of the major isomer of **11f**.[14] Only in the addition of **8a** to the parent complex **10c** (R = H) was any of the *anti*-diastereomer detected.

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(13) (a) Roush, W. R.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 1143. (b) Roush, W. R.; Park, J. C. *Tetrahedron Lett.* **1991**, *32*, 6285.

(14) Ganesh, P.; Nicholas, K. M. *J. Org. Chem.* **1993**, *58*, 5587.

(15) Chiral GC analysis was performed on a cyclodextrin B column (30 m), 70 °C (5 min) → 0 °C 5°/min.

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(18) Roush, W. R.; Michaelides, M. R.; Tai, D. F.; Lesur, B. M.; Chong, W. K. M.; Harris, D. J. *J. Am. Chem. Soc.* **1989**, *111*, 2984 and references therein.

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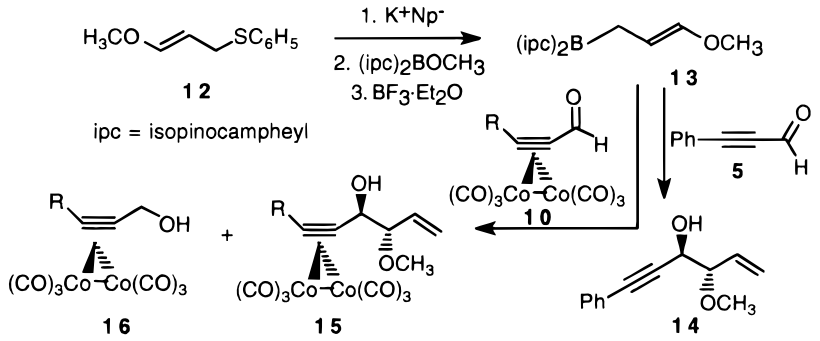
Scheme 2



Moreover, analysis of **11a**−**f** using chiral NMR shift reagent Eu(hfacam)$_3$ pointed to the formation of a single enantiomer (≥95%) in each case as well. This conclusion was confirmed by a combination of Mosher ester ^{19}F NMR characterization and chiral GC (cyclodextrin B) studies of the demetalated compounds (*vide infra*). Furthermore, reaction of (+)- or (−)-borane **8** with **10a** (Table 1, entries 1 and 2) gave opposite enantiomers of comparable optical purity. Although the reactions with MOM derivative **8c** resulted in somewhat lower yields, the high *syn* selectivity and enantioselectivity were still preserved. It is noteworthy that the enantioselectivities found in the present study are somewhat higher than those reported by Roush and Park for the corresponding reactions of **5** with tartrate-derived crotylboranes.[13] However, whether this modest effect is derived from differences in the chiral group of the borane, the γ-alkoxy vs alkyl group, or the differing acetylenic substituents is unclear.

Preparation and Additions of [(*E*)-γ-Alkoxyallyl]-diisopinocampheylboranes to Alkynyl Aldehydes and Their Cobalt Complexes. We then sought access to the unknown [(*E*)-γ-methoxyallyl]diisopinocampheylboranes **13**, which could lead to the *anti* adducts **15**. Hoffmann's procedure for synthesizing (*E*)-γ-alkoxyallylboronates was adapted to gain entry to **13**. (*E*)-1-Methoxy-3-(phenylthio)propene (**12**) was reduced with 2 equiv of potassium naphthalenide at −120 °C followed by reaction with *B*-methoxydiisopinocampheylborane; the resulting [(*E*)-methoxyallyl]-diisopinocampheylborane solution was treated first with BF_3·Et_2O at −78 °C followed by addition of phenylpropynal (**5**) and gradual warming to 25 °C (Scheme 2). After ethanolamine workup and chromatography, the adduct **14** was obtained in low yield (15%), as with the additions of the [(*Z*)-γ-alkoxyallyl]-boranes to the uncomplexed aldehyde **5**. Isolation of **14** also was complicated by the similarity of its R_f value to the coproduct (*E*)-1-methoxy-3-(phenylthio)propene. This problem was overcome by complexation of crude **14** with cobalt octacarbonyl; separation of the cobalt complex **15a** by flash chromatography and subsequent demetalation (Ce(IV)) gave pure **14**. Although the yield of **14** was low, a single diastereomer apparently was produced, judged to be *anti* by ^{1}H NMR by comparing the complexed product of **14** and **15a**. Its enantiomeric purity was determined to be 89% ee by ^{19}F NMR analysis of its Mosher ester.

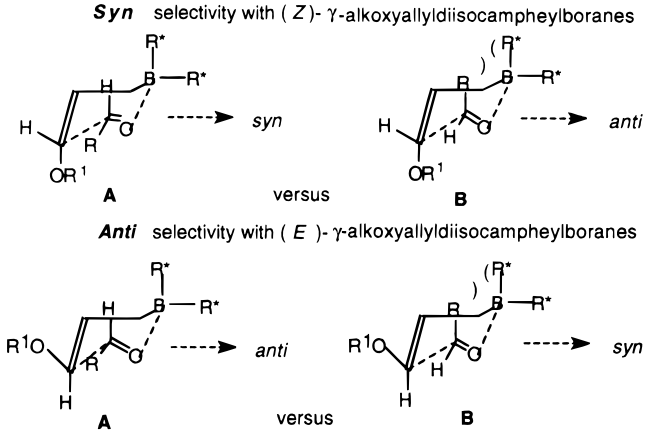
Corresponding reactions between (*E*)-**13** and the complexed acetylenic aldehydes **10a**−**c** proved more efficient, affording moderate yields (Table 2) of the complexes **15a**−**c**, accompanied by variable amounts (25%) of alcohol complexes **16** derived from aldehyde reduction. Accordingly, the yields obtained in the *E*-borane series were somewhat lower than from the corresponding [(*Z*)-γ-methoxyallyl]diisopinocampheylboranes. The alcohol complexes **16** presumably arise from competing β-hydride transfer from the borane reagent. ^{1}H and ^{13}C NMR analysis of the crude reaction products detected only a single diastereomer (>97% de) in each case, assigned the *anti* stereochemistry. The hydroxy proton resonances of the isolated **15** were uniformly found 0.7−1.0 ppm upfield from those of the *syn* adducts **11**, a feature seen for a related series of compounds.[10] The enantiomeric purity of **15a**−**c** was determined by chiral NMR shift reagent analysis and by ^{19}F and ^{1}H NMR analysis of the Mosher esters of the demetalated adducts. In all cases, high enantiomeric excesses were observed (>95%).

Table 2. Preparation of (*anti*-3,4-Dioxy 1,5-enyne)$Co_2(CO)_6$ (15)

aldehyde	borane	product	% yield[a]	% de[b]	% ee
10a (R = Ph)	**13** (R = Me)	**15a**	50	>95	>95[c]
10b (R = Me)	**13**	**15b**	44	>95	>95[c]
10c (R = H)	**13**	**15c**	20	>95	>95[c]

[a] Yield after chromatography. [b] Determined by ^{1}H and ^{13}C NMR. [c] Determined by ^{19}F NMR of Mosher ester derivative and Eu(hfacam)$_3$ analysis.

Scheme 3



The diastereoselectivities observed in these reactions can be explained satisfactorally by the familiar six-membered chelated transition state model for allylmetal additions to carbonyl compounds[10,20] (Scheme 3). Thus, of the transition states involving the [(*Z*)-alkoxyallyl]-borane, that leading to the *syn* adduct (i.e., **A**) avoids a 1,3-diaxial interaction between the bulky (alkynyl)Co_2-$(CO)_6$ and isopinocampheyl units. Conversely, with the [(*E*)-alkoxyallyl]borane additions the more stable transition state (**A′**) is that leading to the *anti* product. The somewhat lower diastereoselectivity obtained from the addition of (*Z*)-**8** to the parent complex **10c** (R = H) may reflect its lesser steric requirement derived from the bent

(20) Bhat, K. S.; Brown, H. C. *J. Am. Chem. Soc.* **1986**, *108*, 5919.

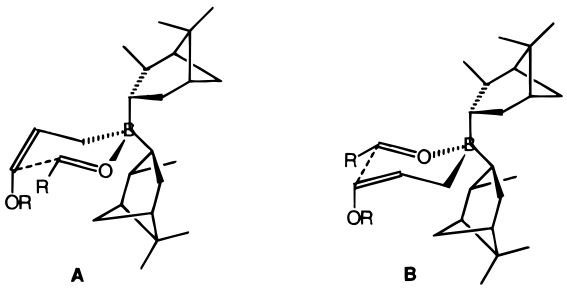
Table 3. Decomplexation of Enyne Complexes by $(NH_4)_2Ce(NO_3)_2$

complex	R	X	Y	product	% yield	% ee
11a	Ph	OMe	H	**17a**	72	>98[a,b]
11b	Ph	OMe	H	**17b**	70	≥98[a]
11c	Ph	OCH_2OMe	H	**17c**	70	≥98[b]
11d	CH_3	OMe	H	**17d**	64	≥98[b]
11e	CH_3	OCH_2OMe	H	**17e**	60	≥98[b]
11f	H	Me	H	**17f**	50	≥98[b]
15a	Ph	H	OMe	**18a**	70	≥98[b]
15b	CH_3	H	OMe	**18b**	65	≥98[b]
15c	H	H	OMe	**18c**	40	≥98[b]

[a] GC analysis on cyclodextrin B. [b] ^{19}F NMR analysis of Mosher ester.

geometry of the coordinated alkyne.[19] This effect has been noted in the reactions of silyl enol ethers with **10**[11] and the related $[(RC{\equiv}CCR_2)Co_2(CO)_6]^+$ complexes.[12] Although the low yield obtained in the addition to the uncomplexed acetylenic aldehyde clouds the issue, it is perhaps surprising that the diastereoselectivity is so high in this case given the limited steric demand of the "skinny" linear alkynyl unit.

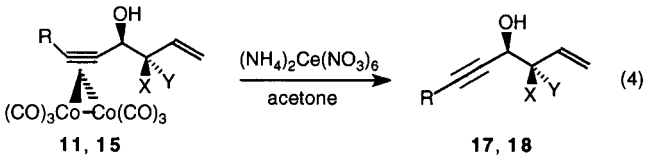
The origin of the increased enantioselectivity in the reactions of the complexed aldehydes is less apparent. Indeed, a detailed analysis of the transition states for additions of the (γ-alkoxyallyl)diisopinocamphenylborane additions to aldehydes is lacking.[20] Once again, assuming chairlike transition states, the basis for enantioselection presumably lies in the asymmetry created by the conformational preferences of the bulky, chiral isocampheyl units. Examination of hand-held and computer-generated (MMX) models suggest that by minimizing the steric interactions between the isocampheyl units a chiral pocket is created on the side of the boron at which the reacting allyl and aldehyde fragments are assembled (**A**, **B** below). The methano bridge of the pseudoequatorial



isocampheyl unit appears to be the primary stereodifferentiating element by its relative steric and electronic interactions with the nearby allyl methylene group (greater in **B**) vs the aldehyde oxygen (lesser in **A**). The greater enantioselectivities found for the cobalt complexes relative to the free aldehydes may derive from the stronger gauche interaction between the bulky (alkynyl)-$Co_2(CO)_6$ group of the complexed aldehyde and the alkoxy group of the allyl unit compared to the smaller alkynyl unit; this would cause distortion of the chair, magnifying the stereodifferentiating interactions with the campheyl units.

Decomplexation of the adducts **11** and **15** was accomplished conveniently and with no loss in enantiomeric purity upon treatment with $(NH_4)_2Ce(NO_3)_6/Et_3N$/acetone (−78 to 20 °C, Table 3).[11] In most cases, enantiomeric excesses were determined by NMR analysis of the corresponding Mosher esters.

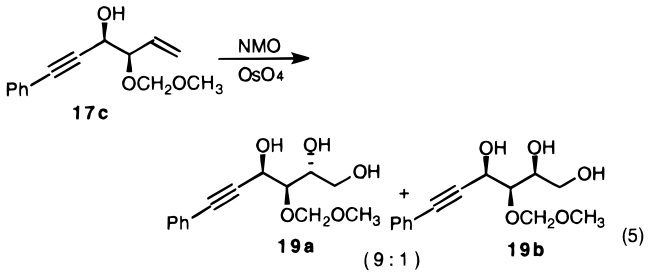
Reactivity Studies of 3,4-Dioxy 1,3-Enynes. Dihydroxylation. Osmium-promoted dihydroxylation has



11, 15 **17, 18** (4)

gained prominence for the diastereo- and enantioselective elaboration of C−C double bonds.[21] In the former cases, Kishi[22] and later others[23] have found that high diastereoselectivity is obtained with substrates possessing allylic alkoxy or hydroxy groups, with preferential introduction of the hydroxyl groups *anti* to the oxygenated group. It thus appeared that the dioxy enyne intermediates would be excellent candidates for stereoselective dihydroxylation of the C−C double bond. It has been observed that triple bonds have lower reactivity than double bonds; the dihydroxylations of conjugated enynes occur exclusively at the double bond giving rise to ynediols.[24]

The osmylation of the selected enyne adduct **17c** was carried out by adding OsO_4 (5 mol %) and 2 equiv of *N*-methylmorpholine *N*-oxide to **17c** in acetone/water (5:1) with stirring at 0−25 °C for 12 h.[25] After complete conversion was confirmed by TLC, chromatographic isolation gave crude triol **19** as an oil (75%, eq 5). The



(5)

^1H NMR spectrum of **19** indicated an 85:15 mixture of diastereomers; decreasing the reaction temperature to 0 °C increased the diastereoselectivity to 90:10. Unfortunately, the isomeric triols **19a**,**b** could not be separated by TLC. The ^1H NMR spectrum of the mixture showed an apparent triplet at 4.85 for the propargylic proton and multiplets at 4.02 ppm (1H) and at 3.8 ppm (3H) for the methylene and methine protons of the diol unit, respectively, of the major isomer.

Since the relative stereochemistry of **19a**,**b** was uncertain on the basis of the NMR analysis, separable, crystalline derivatives were sought. Acetylation of **19a**,**b** (Ac_2O, pyridine) occurred quantitatively to give a 9:1 mixture of oily triacetates **20a**,**b**, but these, too, were inseparable by TLC/flash chromatography (Scheme 4). Likewise, complexation of triols **19a**,**b** with $Co_2(CO)_8$ also produced an inseparable mixture. Finally, the cobalt carbonyl complexes of triacetate **20** were prepared and separated (**21a**,**b** Scheme 4). ^1H NMR analysis of crude **21a**,**b** reconfirmed the diastereomeric ratio (9:1). Im-

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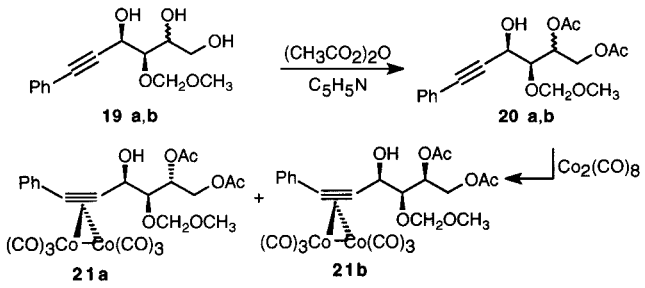
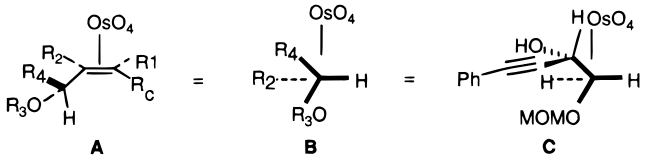
(22) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247.
(23) (a) Evans, D. A.; Kaldor, S. W. *J. Org. Chem.* **1990**, *55*, 5424. (b) Smith, D. A.; Wang, Z.; Schreiber, S. L. *Tetrahedron* **1990**, *46*, 4793. (c) Seletsky, B. M.; Luke, G. P.; Marshall, J. A. *J. Org. Chem.* **1994**, *59*, 3413. (d) Brimacombe, J. S.; Kabir, A. K. M. S. *Carbohydr. Res.* **1988**, *179*, 21. (e) Saito, S.; Morikawa, Y.; Moriwake, T. *J. Org. Chem.* **1990**, *55*, 5424.
(24) Jeong, K. S.; Sjo, P.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *27*, 1992.
(25) Cha, D. Y.; Kelly, R. C.; Van Rheenen, V. *Tetrahedron Lett.* **1976**, *23*, 1973. Sharpless, K. B.; Schroder, G.; Mungall, W. S.; Marko, I.; Jacobsen, E. R. *J. Am. Chem. Soc.* **1988**, *110*, 1968.

Scheme 4



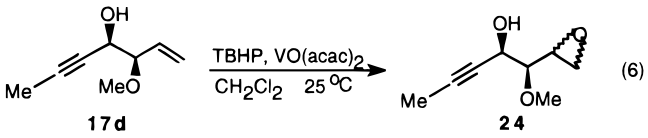
portantly, the isomers **21a**,**b** were separable by preparative TLC and obtained as red oils. The stereochemistry assigned to the major product **19a** was based on the vicinal coupling constants between the hydrogens on the MOM-bearing carbon (C3) and on the adjacent acetate-bearing carbon (C2) of **21a**,**b**, these being 4.0 Hz (for major isomer **21a**) and 3.0 Hz (minor isomer **21b**), respectively. NMR data for a number of reported related compounds[26,27] reveal a higher coupling constant for the *anti* diastereomers relative to the *syn* derivatives. PC Model MMX calculations on **20a**,**b** also support this assignment, the major conformation of *syn* **20b** being predicted to have a coupling constant of 2 Hz, that for *anti* **20a** calculated to be 7 Hz.

The observed preferred dihydroxylation *anti* to the preexisting allylic alkoxy group is consistent with the empirical rule formulated by Kishi for osmylation of allylic-substituted substrates.[22,23] This transition-state model, illustrated for substrate **17c** in structure **C**, is reactant like, closely resembling the ground-state conformation of allylic ethers **A**, which minimizes allylic strain. The presence of the *syn* homoallylic hydroxyl group apparently does not override this preference.

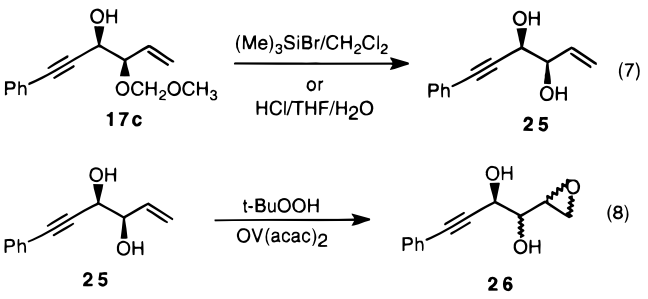


Epoxidation. Epoxidation of allylic alcohols is a generally useful approach to stereocontrolled generation of multiple stereocenters.[28] Although the peracid epoxidation of cyclic allylic alcohols is well-known to give high *syn* stereoselectivity, the selectivity for acyclic allylic substrates is much more variable.[29] Similarly, metal-catalyzed epoxidation with peroxides generally exhibit high *syn* stereoselectivity with cyclic allylic alcohols but the selectivity for acyclic substrates is more complex, depending considerably on both the catalyst (e.g., Mo vs V) and the substrate.[30] Generally, moderate to high *anti* selectivity relative to an allylic or *syn* relative to a homoallylic hydroxyl group has been observed. However, few substrates having both allylic and homoallylic OH-(R) groups as in the dioxy enynes **17** and **18** have been epoxidized. Accordingly, we examined the reactivity of various epoxidizing reagents with representative 3,4-dioxy enynes. The following epoxidizing systems were tested: (1) *m*-chloroperbenzoic acid (*m*-CPBA);[31] (2) VO(acac)$_2$/*t*-BuOOH;[32] (3) magnesium monoperphthalate;[33] and (4) Mo(CO)$_6$/*tert*-butyl hydroperoxide.[34] *m*-CPBA was found to be ineffective for epoxidizing **17d** between 25 and 80 °C in dichloromethane. Similarly, magnesium monoperphthalate also failed to produce any desired product from substrate **17d** as indicated by TLC. Reaction of **18a** with Mo(CO)$_6$/*t*-BuOOH at 25−60 °C led to polymerized material.

tert-Butyl hydroperoxide/vanadyl acetylacetonate did successfully epoxidize 3,4-alkoxy en-yne **17d**; however, the conversion was less than 20% at room temperature after 48 h; increasing the temperature to 70 °C produced no significant improvement, instead causing extensive decomposition. The ^{1}H NMR spectrum of the resulting epoxide **24** suggested formation of a single diastereomer, but complete characterization was deferred in search of increased reactivity. To test whether the relative stereochemistry of the hydroxy and alkoxy groups was a major factor in determining the reactivity toward epoxidation, *anti*-3,4-dioxy enyne **18a** was subjected to typical epoxidation conditions with VO(acac)$_2$/*tert*-butyl hydroperoxide, but only starting material was recovered.



Since monosubstituted double bonds are relatively unreactive toward metal-catalyzed epoxidation, we sought to increase the reactivity of the substrate by unmasking the allylic hydroxy group.[35] The MOM derivative **17c** was therefore deprotected using trimethylsilyl bromide at room temperature, providing diol **25**, albeit in low yield (25%).[36] After considerable experimentation, deprotection of **17c** by HCl/H$_2$O/THF[37] was found to be superior (90%, eq 7). Diol **25** successfully underwent epoxidation



by VO(acac)$_2$−*t*-BuOOH (eq 8) at 0−20 °C over several hours; chromatography afforded a 7:3 mixture of diastereomeric epoxides **26** (45% yield) as indicated by NMR; reaction at 0 °C for 48 h enhanced the stereoselectivity to ≥90% de. Thus, the diol **25**, in contrast to the MOM-protected adduct **17c**, undergoes epoxidation with high conversion and acceptable rate. Although the ^{1}H NMR

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(31) Eustache, J.; Bernardon, M.; Shroot, B. *Tetrahedron lett.* **1987**, *28*, 4861.
(32) Mihelich, E. D.; Daniel, K.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 7690.
(33) Brougham, P.; Looper, M. S.; Cummerson, D. A.; Heaney, H.; Thompson, N. *Synthesis* **1987**, 1015.
(34) Duke, R. K.; Richards, R. W. *J. Org. Chem.* **1984**, *49*, 1898.
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(37) Panek, J.; Cirillo, C. *J. Org. Chem.* **1994**, *59*, 3057.

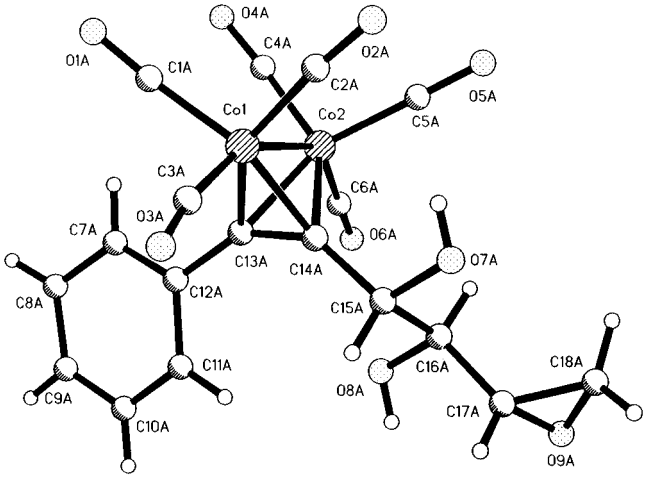
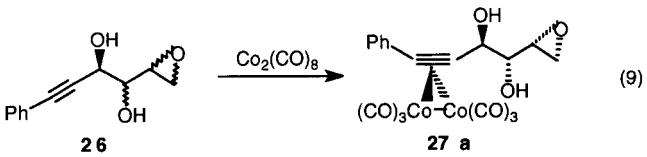


Figure 1. X-ray structure of **27a**.

and mass spectra of **26** supported its formulation as a diol epoxide(s), spectral overlap and our inability to separate the isomers prompted us to derivatize it.

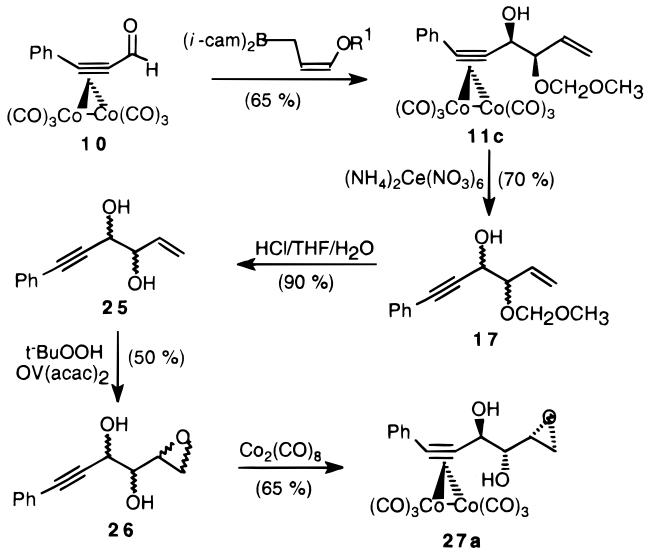
For the purpose of stereochemical determination, we sought a crystalline derivative of **26** by the following methods: acetylation (Ac_2O, pyridine);[38] formation of an acetonide (2,2-dimethoxypropane/*p*-toluenesulfonate);[39] conversion to a *tert*-butyldimethylsilyl derivative;[40] and complexation with $Co_2(CO)_8$. The first three approaches resulted in decomposition of the sensitive epoxide but the last proved successful. Since dicobalt octacarbonyl is known to deoxygenate epoxides at room temperature,[41] the crude epoxide **26** was treated with an equimolar quantity of dicobalt octacarbonyl at 0 °C (eq 9). Chromatography on neutral alumina gave the cobalt complex **27a**,**b**, but separation of the isomers by regular silica, alumina, or reversed-phase TLC methods failed. The ^{1}H NMR spectrum of the major epoxide showed a doublet of doublets at 5.0 ppm (J = 7.5, 4.9 Hz) for the propargylic protons, an apparent triplet at 3.55 ppm (J = 3.4, 3.3 Hz) for the homopropargylic protons, and a multiplet at 3.34 ppm for the methylenic protons of the oxirane, but an unambiguous stereochemical assignment was not possible on the basis of the NMR spectrum. Finally, fractional crystallization of **27a**,**b** by pentane vapor diffusion into a CH_2Cl_2 solution afforded an X-ray quality crystal of the major epoxide isomer **27a**. Examination of the X-ray structure of **27a** (Figure 1) led to two important conclusions: (1) epoxidation had occurred *syn* to the allylic hydroxy group; and, remarkably, (2) the two hydroxyl groups were disposed *anti* to each other, apparently having inverted from the original adduct **25**.



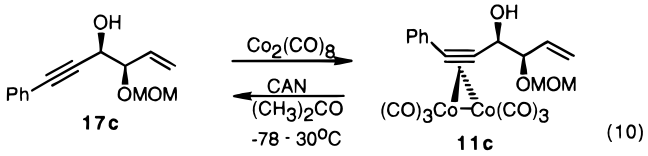
(9)

In order to investigate this unexpected stereochemical result, we probed in detail the stereochemistry of each of the steps leading to **27a**. The sequence of reactions

Scheme 5

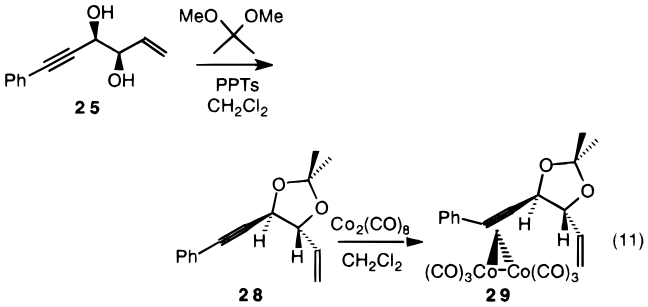


leading to **27** along with the yields are shown in Scheme 5; stereochemistry in question is indicated by wiggly lines. The *syn* stereochemistry at C3,4 assigned to **11c** was supported by the 3.2 ppm chemical shift of the hydroxyl proton of **11c** in the region characteristic of the *syn*-adducts[10] and by the X-ray proven structure of the corresponding methoxy derivative **11f**. To establish that decomplexation of **11c** by ceric ammonium nitrate did not cause epimerization, the alkyne **17c** was recomplexed with $Co_2(CO)_8$ to produce complex **11c** having an R_f value and ^{1}H NMR spectrum identical to those of the original complex.



(10)

In order to rule out the possibility that epimerization occurred during the MOM deprotection step, the stereochemistry of diol **25** was established by its conversion to the corresponding acetonide **28** (90%) using dimethoxypropane/pyridinium *p*-toluenesulfonate (PPTs, eq 11).



(11)

The ^{1}H NMR spectrum of **28** indicated that it had the *trans* geometry, as was expected being derived from the *syn* diol. This assignment is based on the nearly coincident methyl resonances of the acetonide ($\Delta\delta$ = 0.015 ppm), indicative of approximate C_2 symmetry. Ample literature data[42,43] show a much smaller chemical shift difference for the methyl groups of *trans* acetonides (ca.

(38) *Reactions and Synthesis in the Organic Chemistry Lab*; Tietze L. F., Eicher, Th., Eds.; University Science Books: Mill Valley, CA, 1988.
(39) Mori, K.; Maemoto, S. *Liebigs Ann. Chem.* **1987**, 863.
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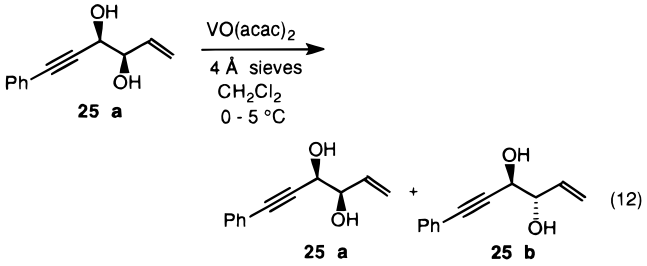
(43) Miyaura, N.; Suzuki, A.; Moriya, T. *Tetrahedron Lett.* **1995**, *36*, 1889.

0.01 ppm) compared to those of *cis* acetonides (ca. 0.17 ppm). Additionally, since the protons of the stereocenters of **28** had very similar chemical shifts, the acetonide was complexed with dicobalt octacarbonyl (90%) in order to resolve the stereogenic proton resonances and to facilitate NOE and NOESY experiments. The *trans* structure assigned to **29** (and hence to **28**) was thus supported by difference NOE and NOESY experiments with weak NOE effects (less than 1%) being observed for the two stereogenic ring protons. Hence, epimerization at C3/C4 does not occur during removal of the MOM group.

Finally, to assess the possibility that epimerization of the diol **25** occurred in the epoxidation reaction itself, a control experiment was performed by stirring **25** with $VO(acac)_2$ and 4 Å molecular sieves under typical epoxidation conditions. Indeed, preparative TLC afforded a diastereomeric mixture of diols **25a** and **25b** (eq 12), apparent in both the ^1H and ^{13}C NMR spectra of **25a**,**b**.



(12)

The doublet at 4.60 and apparent triplet at 4.32 ppm in the original spectrum of **25** now appeared as multiplets at 4.60 ppm and at 4.32 ppm; two sets of stereogenic ^{13}C NMR resonances were also observed. Thus, the diol undergoes epimerization under the epoxidation conditions. We have found no previous reports of $OV(acac)_2$-promoted epimerization of allylic or propargylic alcohols, though few epoxidations have been carried out on polyoxygenated substrates with less reactive monosubstituted double bonds.[44,45] $VO(acac)_2$ presumably functions as a Lewis acid, promoting reversible ionization of an OH group (via chelation?). It is not a simple acid-catalyzed epimerization since deprotection of **17d** under aqueous acidic conditions did not cause epimerization.

If epimerization procedes epoxidation, selective formation of epoxide **26** from the *anti* diol is unexpected given the general preference for an allylic OH to direct *anti* epoxidation and a homoallylic OH to favor *syn* addition. However, as noted earlier, very few diols that are both allylic and homoallylic have been epoxidized.[46] Because of the uncertainty introduced by epimerization, it is premature to speculate about a detailed transition state to account for the observed selectivity. Additional studies that eliminate this complication and that explore a wider variety of substrates are needed.

Conclusions/Summary

The addition of [(*Z*)-alkoxyallyl]diisopinocampheylboranes to cobalt-complexed acetylenic aldehydes occurs efficiently and with excellent regio-, diastereo- (*syn*), and enantioselectivity in contrast to the corresponding poorly yielding reactions of free acetylenic aldehydes. [(*E*)-Alkoxyallyl]diisopinocampheylboranes, prepared for the first time, likewise react moderately efficiently and highly stereoselectively with the complexed aldehydes producing the corresponding *anti*-3,4-dioxy enyne adducts. Demetalation of these complexes provides access to all four stereoisomeric families of 3,4-dioxy 1,5-enynes, attractive building blocks for the synthesis of target molecules possessing multiple adjacent stereocenters. Dihydroxylation of a representative *syn*-dioxy enyne occurs selectively at the carbon−carbon double bond and preferentially (9:1) *anti* to the allylic alkoxy group. When the highly enantio- and diastereoselective addition of γ-alkoxyallyl boranes to cobalt-complexed acetylenic aldehydes is combined with the stereoselective dihydroxylation of the resulting dioxy enynes, a highly enantioselective entry to molecules with four adjacent tetraoxygenated centers is provided, of considerable potential in carbohydrate synthesis. Epoxidation of a representative *syn*-dioxy enyne also occurs selectively but is complicated by epimerization of the starting material, affording an *anti*-diol epoxide, with epoxidation occurring *syn*- to the allylic hydroxyl group. In conclusion, we note the key roles played by the $-Co_2(CO)_6$ moiety in these transformations. First, it serves a protective function for the triple bond, blocking potentially competing addition/polymerization reactions. Second, there is a considerable stereocontrolling effect of complexation, presumably reflecting the greatly increased steric demand of the bulky, bent $-(alkynyl)Co_2(CO)_6$ moiety relative to the linear, "skinny" alkyne. Efforts to expand the scope of this methodology and to demonstrate the synthetic potential of the derived 3,4-dioxy 1-en-5-ynes in natural products synthesis are underway.

Experimental Section

General Methods/Materials. Deuterated solvents were dried over 4 Å molecular sieves and stored and handled under N_2. ^1H NMR spectra were obtained at 300 MHz using $CDCl_3$ or C_6D_6 as solvent; ^{13}C NMR spectra were measured at 75.4 MHz. Preparative TLC was carried out on silica gel E. Merck (G-60$PF_{254-366}$) with 20 × 20 cm glass plates (1 mm). Analytical TLC was performed on silica gel IB-F plates. Flash chromatography was conducted by the method of Still using E. Merck silica gel (230−400 mesh) under 20 psi of N_2.[46] Organolithium reagents were titrated before use.[47] Melting points (uncorrected) of solid cobalt complexes were determined in sealed capillaries. All reactions were conducted in oven- or flame-dried glassware under an atmosphere of nitrogen. Transfers were made by syringe or cannula. Methylene chloride, dichloroethane, pyridine, and triethylamine were distilled from CaH_2; benzene, toluene, THF, and diethyl ether were distilled from sodium benzophenone ketyl; acetic anhydride was distilled from P_2O_5; ethanolamine was azeotropically distilled using benzene. Elemental analyses were performed by Midwest Microlabs, Indianapolis, IN. Those new compounds that were not characterized by elemental analysis (typically oils) were judged to be ≥95% pure by ^1H and ^{13}C NMR analysis. X-ray diffraction was carried out by Dr. M. Khan, the O.U. staff crystallographer.

Allyl methyl ether,[48] methoxymethyl allyl ether,[49] methoxyallene,[50] α-methoxy-3,3,3-trifluoropropanoyl chloride,[51] (acetylenic acetal)$Co_2(CO)_6$,[11] and Mosher esters of the alcohols[52] were prepared using literature procedures. (*E*)-1-Methoxy-3-

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(45) Roush, W. R.; Michaelides, M. R. *Tetrahedron Lett.* **1986**, *27*, 3353.
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(52) (a) Dale, T. A.; Dull, L. D.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) Kabuto, K.; Yasuhara, F.; Yamaguchi, S. *Tetrahedron Lett.* **1980**, *21*, 307.

(phenylthio)propene was obtained using a modification of Hoffmann's method by conducting the reaction at −30 °C.[10]

(3*R,4*R**)-4-Methoxy-1-phenyl-5-hexenyn-3-ol (9).** To a flame-dried sidearm flask equipped with a stir bar was added 0.40 mL (3.8 mmol) of allyl methyl ether using a syringe followed by 50 mL of freshly distilled THF. The solution was cooled to −78 °C, 3.4 mL (3.1 mmol) of *sec*-butyllithium was added slowly through a syringe, and the resulting yellow solution was stirred at −78 °C for 15 min to 30 min. In a flame-dried flask 0.970 g (3.1 mmol) of (−)-*B*-methoxydiisopinocampheylborane was weighed inside the drybox. Freshly distilled THF (15 mL) was added to the (−)-*B*-methoxydiisopinocampheylborane, and the solution was cooled to −78 °C before canulation into the solution of lithiated allyl methyl ether. The yellow color was immediately discharged, and the solution was stirred at −78 °C for 1 h. To the solution of the ate complex was added 0.50 mL (4.1 mmol) of $BF_3{\cdot}Et_2O$ to form [(*Z*)-γ-methoxyallyl]diisopinocampheylborane (**8**). Meanwhile, 0.400 g (3.07 mmol) of phenylpropargyl aldehyde dissolved in 20 mL of THF at −78 °C was slowly added to the solution of **8** and stirred at −78 °C for 3 h and then 12 h at room temperature. The solution was concentrated under vacuum, and the residue was dissolved in 150 mL of freshly distilled diethyl ether and then filtered into a flame-dried side-arm flask with a magnetic stirrer using a Teflon tube. The solution was cooled to 0 °C, and 0.19 mL (3.1 mmol) of distilled ethanolamine was added. The mixture was stirred at 0 °C for 1 h and at 20 °C for 24 h and then filtered. The product was subjected to Kugelrohr distillation (bp 100 °C; 5 mm) and then purified by flash column chromatography on silica (3:1 hexane/ethyl acetate) to yield 50 mg (0.25 mmol) of **9** (8%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49 (m, 2H), 7.29 (m, 3H), 5.83 (m, 1H), 5.46 (dd, *J* = 17.6, 8.14 Hz, 1H), 4.51 (d, *J* = 7.1 Hz, 1H), 3.77 (pseudo triplet, *J* = 7.5, 7.2 Hz, 1H), 3.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 134.3, 132.2, 132.2, 128.9, 128.8, 128.6, 86.2, 86.0, 66.0, 57.5; MS (DIP, 70 eV) *m/e* 171.0 (M − 31, 3), 131.0 (M − 71, 43), 115 (M − 87, 12), 103 (M − 99, 27), 77 (M − 125, 48), 71 (M − 131, 100).

Determination of the Enantiomeric Purity of 9. (a) By Gas Chromatography with a Chiral Cyclodextrin Stationary Phase. Temperature program: T_i = 70 °C; t_i = 5 min; 5 °C per min; T_f = 220 °C, t_f = 20 min. The retention time of major enantiomer was 40.4 min, integration 1.3; that of the minor was 40.6 min (0.26); ee = 65%.

(b) Mosher Ester Analysis. In a flame-dried side-arm flask equipped with a stir bar was added 120.0 mg of freshly prepared Mosher chloride. Dry methylene chloride (5 mL), 0.90 mL (10 mmol) of dry pyridine, and 8 mg of (dimethylamino)pyridine (DMAP) were added to the Mosher chloride. In a dry round-bottom flask, 68.0 mg (0.340 mmol) of **60** dissolved in 5 mL of dry CH_2Cl_2 was canulated into the side-arm flask containing the Mosher chloride. The solution was stirred at room temperature for 2 days. 3-(Dimethylamino)propylamine (0.100 mL, 0.795 mmol) was added to the reaction product and the mixture stirred for 15 min. The solution was then diluted with 20 mL of CH_2Cl_2, washed with saturated Na_2CO_3 and brine, and dried over $MgSO_4$. The organic phase was then concentrated in vacuo to yield the ester. The ^{19}F NMR of the Mosher ester of **9** showed two resonances for the CF_3 groups of the diastereomers in a 7:3 ratio at 6.38 ppm (major) and 9.10 ppm (minor).

(c) Eu(hfacam)$_3$ Analysis. In the drybox, 30 mg (0.030 mmol) of Eu(hfacam)$_3$ was weighed into a flame-dried flask. In an oven-dried vial, 10 mg of **9** was dissolved in 2 mL of $CDCl_3$. The sample was analyzed by NMR after each addition of solid Eu(hfacam)$_3$. After addition of nearly 15 mg, the methoxy signals of **9** split into two distinct signals (70:15) indicating 65% ee.

(Alkynyl aldehyde)dicobalt Hexacarbonyl Complexes 10a−c. In a typical experiment, a side-arm flask equipped with a magnetic stirring bar, 13.9 g (32.6 mmol) of (3-butynal diethyl acetal)$Co_2(CO)_6$, 100 mL of acetone, 3 g of Amberlyst-15 resin, and 2 mL of water was added, and the solution was stirred at room temperature for 24 h with TLC monitoring (silica gel, 9:1 petroleum ether/ether). The solvent was removed by rotary evaporation, and the mixture was then loaded on a column of silica gel and separated by flash chromatography (95:5 petroleum ether/ether) to obtain 9.60 g (27.2 mmol) of the aldehyde complex **10b** (84%).

10a: ^{1}H NMR ($CDCl_3$) δ 10.5 (s, 1H), 7.35 (m, 2H), 7.25 (m, 3H); IR (CH_2Cl_2) 3060, 3980, 2980, 2880, 2090, 2050, 1660, 1480, 1060, 1010 cm^{-1}.

10b: ^{1}H NMR ($CDCl_3$) δ 10.48 (s, 1H), 2.68 (s, 3H); IR (CH_2Cl_2) 2980, 2930, 2900, 2860, 2010, 1670, 1310, 1010 cm^{-1}.

10c: ^{1}H NMR ($CDCl_3$) δ 10.5 (s, 1H), 5.99 (s, 1H); IR (CH_2Cl_2) 2980, 2900, 2860, 2090, 2040, 2010, 1690, 1100 cm^{-1}.

[(3*R*,4*R*)- and (3*S*,4*S*)-4-Alkoxy-1-substituted-5-hexenyn-3-ol]dicobalt Hexacarbonyl Complexes 11a−e. The following procedure is representative: In a flame-dried side-arm flask equipped with a stirring bar was added 0.49 mL (5.2 mmol) of allyl methyl ether followed by 50 mL of freshly distilled THF. The solution was cooled to −78 °C, and 3.2 mL (1.3M in hexane, 4.2 mmol) of *sec*-butyllithium was added; the solution immediately turned bright yellow. The solution was stirred at −78 °C for 15−30 min. Into a flame-dried flask 1.39 g (4.15 mmol) of (−)-*B*-methoxydiisopinocampheylborane was weighed inside the drybox. Freshly distilled THF (15 mL) was added to the borane, and the solution was cooled to −78 °C before canulation into the solution of lithiated allyl methyl ether. The yellow color was immediately discharged, and the solution was stirred at −78 °C for 1 h. To this mixture was added 0.70 mL (5.5 mmol) of $BF_3{\cdot}Et_2O$ to form [(*Z*)-γ-methoxyallyl]diisopinocampheylborane (**8a**). Meanwhile, 1.73 g (4.15 mmol) of (phenylpropynal)dicobalt hexacarbonyl was dissolved in 20 mL of THF, cooled to −78 °C, and slowly added to the solution of **8a** and stirred at −78 °C for 3 h and then 12 h at room temperature. The mixture was concentrated under vacuum, and the residue was dissolved in 150 mL of freshly distilled diethyl ether and then filtered into a flame-dried side-arm flask containing a magnetic stirring bar using a Teflon tube. The solution was cooled to 0 °C, and 0.70 mL (11 mmol) of distilled ethanolamine was added. The solution was stirred at 0 °C for 1 h and then at room temperature for 24 h and was filtered under nitrogen. The product was purified by flash column chromatography on silica (3:1 petroleum ether/diethyl ether) to yield 1.35 g (2.77 mmol, 67%) of **11a** as a dark red oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (m, 2H), 7.30 (m, 3H), 5.9 (ddd, *J* = 17.3, 8.1, 6.8 Hz, 1H), 5.38 (dd, *J* = 17.3, 8.1 Hz, 2H), 4.93 (apparent t, *J* = 6.4, 4.8 Hz, 1H), 3.76 (apparent t, *J* = 6.4, 6.8 Hz, 1H), 3.29 (s, 3H), 3.28 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200, 139.9, 136.8, 131.8, 130.7, 129.7, 122.4, 108.5, 87.7, 76.9, 57.8; IR (cm^{-1}, $CHCl_3$) 3550−3450, 3100, 2090−2000, 1060; MS (FAB, 3-nitrobenzyl alcohol) *m/e* 432.15 (M^+ − 2CO, 100), 404 (M^+ − 3CO, 14), 376 (M^+ − 4CO, 98), 348 (M^+ − 5CO, 96), 320 (M^+ − 6CO, 7).

11c: dark red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (m, 2H), 7.30 (m, 3H), 5.90 (ddd, *J* = 16.5, 10.4, 6.7 Hz, 1H), 5.38 (dd, *J* = 17.1, 10.2 Hz, 2H), 4.98 (apparent t, *J* = 6.9, 4.0 Hz, 1H), 4.73 (d, *J* = 6.6 Hz, 1H), 4.61 (d, *J* = 6.6 Hz, 1H), 4.08 (apparent t, *J* = 7.2, 7.4 Hz, 1H), 3.4 (d, *J* = 4.0 Hz, 1H), 3.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200, 136.0, 131.8, 130.6, 129.7, 96.1, 83.1, 76.6, 58.0; IR (cm^{-1}, $CHCl_3$) 3560−3450, 3100, 2090−2000, 1028; MS (FAB, 3-nitrobenzyl alcohol) *m/e* 434 (M^+ − 3CO, 26), 406 (M^+ − 4CO, 100), 378 (M^+ − 5CO, 33), 350 (M^+ − 6CO, 12).

11d: dark red solid; mp = 52 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.79 (ddd, *J* = 17, 9.1, 6.7 Hz, 1H), 5.44 (dd, *J* = 17.1, 9.0 Hz, 2H), 4.66 (apparent t, *J* = 5.7, 5.4 Hz, 1H), 3.53 (apparent t, *J* = 6.5, 5.5 Hz, 1H), 3.11 (s, 3H), 3.10 (d, *J* = 4.8 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200, 136.0, 130.8, 129.3, 128.3, 121.1, 86.8, 75.5, 56.5; IR (cm^{-1}, $CHCl_3$) 3560−3450, 3030, 2333, 2089−2000, 1373; MS (FAB, 3-nitrobenzyl alcohol) *m/e* 398 (M^+ − CO, 15.7), 370 (M^+ − 2CO, 100.0), 342 (M^+ − 3CO, 50), 314 (M^+ − 5CO, 64), 258 (M^+ − 6CO, 30). Anal. Calcd for $C_{14}H_{12}O_8Co_2$: C, 39.46; H, 2.84. Found: C, 39.36; H, 2.94.

11e: dark red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.8 (ddd, *J* = 16.5, 9.0, 7.8 Hz, 1H), 5.44 (dd, *J* = 16.5, 9.0 Hz, 2H), 4.93 (apparent t, *J* = 8.5, 3.0 Hz, 1H), 4.75 (d, *J* = 6.9 Hz, 1H), 4.62 (d, *J* = 6.6 Hz, 1H), 3.92 (apparent t, *J* = 8.1, 7.8 Hz, 1H), 3.37 (s, 3H), 3.18 (d, *J* = 3.3 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 134.5, 122.6, 96.1, 94.6, 94.5, 82.3, 75.2, 56.6, 22.31; IR (cm^{-1}, $CHCl_3$) 3460−3436, 2950, 2089−2012, 1366, 1018; MS (FAB, 3-nitrobenzyl alcohol) *m/e* 428 (M^+

− CO, 9.4), 400 (M^+ − 2CO, 100), 372 (M^+ − 3CO, 94), 344 (M^+ − 4CO, 79), 316 (M^+ − 5CO, 32), 288 (M^+ − 6CO, 40). Anal. Calcd for $C_{15}H_{14}Co_2O_9$: C, 39.50; H, 3.09. Found: C, 38.99; H, 3.22.

11f: light red solid; mp = 40 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.93 (s, 1H), 5.65 (ddd, J = 18, 9, 6.7 Hz, 1H), 5.25 (dd, J = 18, 9 Hz, 2H), 4.49 (apparent t, J = 6.3, 4.3 Hz, 1H), 3.34 (apparent t, J = 7.3, 6.8 Hz, 1H), 3.21 (s, 3H), 3.2 (d, J = 4.21 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 200.5, 134.1, 121.8, 94.7, 87.0, 75.5, 72.9, 56.7, 30.20; IR (cm^{-1}, $CHCl_3$) 3450, 2995, 2090−1982, 1366, 1018; MS (FAB, 3-nitrobenzyl alcohol) *m/e* 384 (M^+ − CO, 19), 356 (M^+ − 2CO, 100), 328 (M^+ − 3CO, 60), 300 (M^+ − 4CO, 44), 272 (M^+ − 5CO, 11), 244 (M^+ − 6CO, 28). Anal. Calcd for $C_{13}H_{10}Co_2O_8$: C, 37.89; H, 2.45. Found: C, 37.72; H, 2.62.

(3*R*,4*R*)- and (3*S*,4*S*)-4-Alkoxy-1-substituted-5-hexenyn-3-ol 17a−f by Demetalation of 11a−f. The following procedure is representative: To a stirred solution of **11a** (0.110 g, 0.223 mmol) in 20 mL of acetone at −78 °C was added a solution of 0.844 g (1.54 mmol) of ceric ammonium nitrate in 10 mL of acetone (until the CO ceased). The reaction was stirred for 2 h at −78 °C and then warmed to room temperature and allowed to stir for 1 h. The mixture was poured into 20 mL of saturated NaCl solution and extracted thoroughly with ether. The ether layer was washed with brine, dried over $MgSO_4$, and then evaporated to give a yellow oil. The oil was subjected to column chromatography over silica (8:2, petroleum ether/diethyl ether) to give 32.0 mg (0.158 mmol, 72%) of **17a** as a yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (m, 2H), 7.33 (m, 3H), 5.82 (m 1H), 5.4 (dd, J = 8.4, 17.9 Hz, 2H), 4.5 (d, J = 7.0 Hz, 1H), 3.73 (t, J = 7.3 Hz, 1H), 3.4 (s, 3H); MS (LCMS, 0.1 M ammonium acetate) *m/e* 220 (M^+ + 18, 100), 153 (M^+ − 17, 2).

17c: red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (m, 5H), 5.90 (m, 1H), 5.44 (dd, J = 14.1, 10.0 Hz, 2H), 4.55 (d, J = 6.0 Hz, 1H), 4.74 (d, J = 6.3 Hz, 1H), 4.59 (d, J = 5.9 Hz, 1H), 4.19 (apparent triplet, J = 6.31, 6.56 Hz, 1H), 3.43 (s, 3H), 2.80 (bs, 1H); MS (LCMS, 0.1 M ammonium acetate) *m/e* 250 (M^+ + 18, 100), 232 (M^+ + 1, 1), 215 (M^+ − 17, 9), 206 (M^+ − 27, 1), 171 (M^+ − 61, 5).

17d: yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.73 (m, 1H), 5.36 (dd, J = 11.4, 17.6 Hz, 2H), 4.26 (d, J = 6.0 Hz, 1H), 3.46 (at, J = 6.5, 6.0 Hz, 1H), 3.33 (s, 3H), 1.8 (s, 3H,); MS (LCMS, 0.1 M ammonium acetate) *m/e* 158 (M^+ + 18, 100), 123 (M^+ − 17, 10).

17e: yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.83 (m, 1H), 5.41 (dd, J = 9.3, 15.4 Hz, 2H), 4.73 (d, J = 6.7 Hz, 1H), 4.67 (d, J = 6.7 Hz, 1H), 4.29 (m, 1H), 4.06 (apparent triplet, J = 7.2, 6.3 Hz, 1H), 3.41 (s, 1H), 1.85 (s, 3H); MS (LCMS, 0.1 M ammonium acetate) *m/e* 188 (M^+ + 18, 100), 153 (M^+ − 17, 10).

17f: yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.74 (m, 1H), 5.39 (dd, J = 10.0, 14.3 Hz, 2H), 4.29 (d, J = 7.0 Hz, 1H), 3.65 (dd, J = 7.1, 7.0 Hz, 1H), 3.43 (s, 3H), 2.46 (s, 1H); MS (LCMS, 0.1 M ammonium acetate) *m/e* 144 (M^+ + 18, 100), 109 (M^+ − 17, 10).

Determination of Enantiomeric Purity of 17a−f. Chiral GC. The temperature program used in the separation of the enantiomers is as follows: initial temperature = 70 °C, initial time = 5 min, rate of heating = 5 °C/min; final temperature = 220 °C, final time = 20 min. The retention time of the only detected enantiomer of **17a** was 40.36 min; ee ≥ 99%.

Mosher Ester Analysis. The Mosher esters of all the decomplexed alcohols were prepared by the method described in the synthesis of Mosher ester of **9**. ^{19}F NMR of the Mosher esters of **17a−f** (ref CF_3COOH, $CDCl_3$, 282 MHz): **17a**, 4.01 ppm; **17c**, 4.02 ppm; **17d**, 3.89 ppm; **17e**, 3.90 ppm; **17f:** 3.87 ppm.

Eu(hfacam)$_3$ Analysis. In a flame-dried flask, 30 mg (0.03 mmol) of Eu(hfacam)$_3$ was weighed in the drybox. In a dry vial, 10 mg of the **11a** was dissolved in 3 mL of $CDCl_3$ and used in the analysis of **11a**. The sample was analyzed after each addition of Eu(hfacam)$_3$. After nearly 15 mg was added, the methoxy signals of **11a** showed a single peak, indicating that the enantiomeric excess was close to 95%.

[(3*R*,4*S*)-4-Methoxy-1-substituted-5-hexenyn-3-ol]dicobalt Hexacarbonyl 15a−c. A solution of potassium naphthalenide was prepared from 3.91 g (10.6 mmol) of potassium and 1.28 g (10.6 mmol) of naphthalene in 40 mL of dry THF by stirring for 1 h at room temperature. After addition of 10 mL of diethyl ether and 10 mL of pentane, the solution was cooled to −120 °C (liquid nitrogen and pentane). First, 1.15 g (6.36 mmol) of (*E*)-1-methoxy-3-(phenylthio)propene (**12**) and then 2.00 g (6.32 mmol) of (−)-*B*-methoxydiisopinocampheylborane dissolved in 10 mL of dry THF was added by a cannula. The mixture was stirred at −120 °C for 1 h and at −78 °C for 3 h and then filtered through a sintered glass funnel containing Celite under nitrogen at −78 °C. The solution of the ate complex was treated with 1.00 mL (8.41 mmol) of $BF_3{\cdot}Et_2O$. Meanwhile, 1.76 g (4.24 mmol) of (phenylpropynal)$Co_2(CO)_6$ dissolved in 20 mL of THF was cooled to −78 °C and slowly added to the solution of [(*E*)-γ-methoxyallyl]diisopinocampheylborane (**13**) and stirred at −78 °C for 3 h and then for 12 h at room temperature. The solution was concentrated under vacuum, and the residue was dissolved in 150 mL of freshly distilled diethyl ether and then filtered via a Teflon cannula into a flame-dried side-arm flask containing a magnetic stirring bar. The solution was then cooled to 0 °C, and 0.49 mL (8.00 mmol) of dry ethanolamine was added. The mixture was stirred at 0 °C for 1 h and then at 20 °C for 24 h and then was filtered under nitrogen. The crude product, obtained by evaporation of the filtrate, was purified by flash column chromatography on silica (3:1 petroleum/ether) to yield 1.00 g (2.04 mmol, 48.1%) of **15a** as a dark red oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 m, 2H), 7.30 (m, 3H), 5.9 (m, 1H), 5.48 (dd, J = 15.8, 11.7 Hz, 2H), 4.94 (apparent t, J = 6.4, 4.8 Hz, 1H), 3.7 (apparent t, J = 7.8, 6.9 Hz, 1H), 3.21 (s, 3H), 2.43. (d, J = 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.6, 137.9, 135.3. 130.0, 128.8, 128.5, 127.6, 122.0, 96.8, 87.3, 73.5, 55.7; IR (cm^{-1}) ($CHCl_3$) 3550−3450, 3100, 2090−2000, 1060; MS (DIP, 70 eV) *m/e* 432.15 (M^+ − 2CO, 30), 404 (M^+ − 3CO, 21), 376 (M^+ − 4CO, 70), 348 (M^+ − 5CO, 82.0), 320 (M^+ − 6CO, 72).

15b: red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.83 (ddd, J = 13.1, 9.0, 7.5, Hz, 1H), 5.48 (dd, J = 13.1, 9.0 Hz, 2H), 4.63 (apparent t, J = 7.5, 4.8 Hz, 1H), 3.54 (apparent t, J = 7.2, 7.6 Hz, 1H), 3.30 (s, 3H), 2.66 (s, 3H), 2.17 (d, J = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200, 135.63, 128.96, 121.51, 128.33, 97.69, 94.30, 87.1, 73.80, 55.874, 21.276; IR (cm^{-1}) ($CHCl_3$) 3560−3450, 3030, 2089−2000, 1373; MS (DIP, 70 eV) *m/e* 398 (M^+ − CO, 9), 370 (M^+ − 2CO, 29), 342 (M^+ − 3CO, 26), 314 (M^+ − 4CO, 6), 286.0 (M^+ − 5CO, 15), 258 (M^+ − 6CO, 61), 226 (M^+ − 6CO − OMe, 100).

15c: red oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.93 (s, 1H), 5.84 (m, 1H), 5.41 (dd, J = 10.1, 14.0 Hz, 2H), 4.94 (apparent t, J = 5.9, 5.9 Hz, 1H), 3.63 (apparent t, J = 7.0, 6.8 Hz, 1H), 3.26 (s, 3H), 2.41 (d, 1H, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) 200.5, 134.1, 121.8, 94.7, 87.0, 75.5, 72.9, 56.7, 30.2; IR (cm^{-1}) ($CHCl_3$) 3450, 2995, 2090−1982, 1366, 1018; MS (DIP, 70 eV) *m/e* 356 (M^+ − 2CO, 75), 328 (M^+ − 3CO, 46), 300 (M^+ − 4CO, 23), 272 (M^+ − 5CO, 11), 244 (M^+ − 6CO, 100).

4-Methoxy-1-phenyl-5-hexenyn-3-ol (15a) from Phenylpropynal (5). A solution of potassium naphthalenide was prepared from 0.80 g (20.4 mmol) of potassium and 2.62 g (20.4 mmol) of naphthalene in 40 mL of dry THF by stirring for 1 h at room temperature. After addition of 10 mL of diethyl ether and 10 mL of pentane, the solution was cooled to −120 °C (liquid nitrogen and pentane). First, 1.84 g (10.2 mmol) of (*E*)-1-methoxy-3-(phenylthio)propene (**12**) and then 3.23 g (10.2 mmol) (−)-*B*-methoxydiisopinocampheylborane dissolved in 10 mL of dry THF were added by a cannula. The mixture was stirred at −120 °C for 1 h and at −78 °C for 3 h and then filtered through a sintered glass funnel containing Celite under nitrogen at −78 °C. The solution of the ate complex was treated with 1.70 mL (13.6 mmol) of $BF_3{\cdot}Et_2O$ to generate [(*E*)-γ-methoxyallyl]diisopinocampheylborane. Meanwhile, 1.00 mL (8.18 mmol) of phenyl propynal dissolved in 20 mL of THF was cooled to −78 °C and slowly added to the solution of the borane (**13**) and stirred at −78 °C for 3 h and then for nearly 12 h at room temperature. The mixture was concentrated under vacuum, and the residue was dissolved in 150 mL of freshly distilled diethyl ether and then filtered into a flame-dried side-arm flask containing a magnetic stirring bar using

a Teflon cannula. The solution was cooled to 0 °C, and 0.49 mL (8.00 mmol) of dry ethanolamine was added. The mixture was stirred at 0 °C for 1 h and then at 20 °C for 24 h and then filtered under nitrogen. The crude product (1.48 g) was dissolved in 25 mL of dry diethyl ether and cannulated into a flask containing 2.51 g of dicobalt octacarbonyl. The solution was stirred at room temperature for 2 h. After rotoevaporation the product was purified by flash chromatography on silica (75:25 petroleum ethyl/diethyl ether) to yield 0.700 g (1.43 mmol, 19.1%) of **15a** (*op cit*).

(3*R*,4*S*)-4-Methoxy-1-substituted-5-hexen-yn-3-ols 18a−c via Demetalation of 15a−c. The following procedure is representative: To a stirred solution of **15a** (0.500 g, 1.02 mmol) in 20 mL of acetone at −78 °C was added dropwise a solution of 1.68 g (3.06 mmol) of ceric ammonium nitrate in 10 mL of acetone (CO evolution). The reaction mixture was stirred for 2 h at −78 °C, warmed to room temperature, and then allowed to stir for 1 h with monitoring by TLC (silica, 3:2 petroleum ether/diethyl ether). The mixture was poured into 20 mL of saturated NaCl solution and extracted thoroughly with ether. The ether layer was washed with brine, dried over $MgSO_4$, and then evaporated to give a yellow oil. The oil was subjected to column chromatography (4:1, petroleum ether/ether) to give 0.109 g (0.539 mmol, 72%) of **18a** as a yellow oil. ^{1}H NMR: ($CDCl_3$, 300 MHz) δ 7.50 (m, 2H), 7.30 (m, 3H), 5.86 (m, 1H), 5.38 (dd, J = 10.25, 10.3 Hz, 2H), 4.62 (dd, J = 3.7, 4.0 Hz, 1H), 3.82 (dd, J = 7.6, 3.8 Hz, 1H), 3.4 (s, 3H); MS (DIP, 70 eV) *m/e* 189 ($M^+ - 31$, 5), 160 ($M^+ - 60$, 9), 149 ($M^+ - 71$, 54).

18b: yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.82 (m, 1H), 5.37 (dd, J = 10.1, 9.1 Hz, 2H), 4.37 (dd, J = 4.3, 3.9 Hz, 1H), 3.69 (t, J = 3.6, 7.3 Hz, 1H), 3.67 (s, 3H), 1.8 (s, 3H); MS (DIP, 70 eV) *m/e* 158 ($M^+ + 18$, 100), 123 ($M^+ - 17$, 10).

18c: yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.74 (m, 1H), 5.39 (dd, J = 10.1, 9.3 Hz, 2H), 4.29 (t, J = 4.3 Hz, 1H), 3.65 (1H, m), 3.33 (s, 3H), 2.46 (s, 1H); MS (DIP, 70 eV) *m/e* 98 ($M^+ - 28$, 12.6), 95 ($M^+ - 31$, 33.8), 71 ($M^+ - 55$, 18.2), 70.12 ($M^+ - 56$, 100).

Determination of the Enantiomeric Purity of 18a,b. Mosher Ester Analysis. The Mosher esters of the decomplexed alcohols of **18a**,**b** were prepared as per the method described for **9.** ^{19}F NMR of **18a**,**b** (CF_3COOH ref, $CDCl_3$, 282 MHz): **18a**, 3.86 ppm; **18b**, 3.85 ppm.

Eu(hfacam)$_3$ Analysis. In a flame-dried flask 30 mg (0.03 mmol) of Eu(hfacam)$_3$ was weighed in the drybox and 300 mL of $CDCl_3$ added to prepare a 0.05 M solution. In a dry vial 10 mg of **15a−c** was dissolved in 2 mL of $CDCl_3$ and used in the analysis of **15a−c**. The sample was analyzed by NMR after each 0.1 mL addition of the Eu(hfacam)$_3$ solution. After nearly 40 μL addition, the methoxy signals of **15a−c** showed only a single peak, indicating that the enantiomeric excess was at least 95%.

Determination of the Enantiomeric Purity of 14. Mosher Ester Analysis. The Mosher esters of the decomplexed alcohols were prepared as per the method described for **9**: ^{19}F NMR of Mosher ester of **14** ($CDCl_3$, vs CF_3COOH): 3.86 ppm, 6.91 ppm. (ee = 89%).

(2*R*,3*S*,4*R*)- and (2*S*,3*S*,4*R*)-6-Phenyl-3-(methoxymethoxy)-5-hexyne-1,2,4-triol (19a,b). In a side-arm flask equipped with a magnetic stirring bar 0.232 g (1.98 mmol) of *N*-methylmorpholine *N*-oxide, 5 mL of H_2O, and 2 mL of acetone were cooled to 0 °C. To this solution was added 0.230 g (0.99 mmol) of **17d** with stirring. OsO_4 solution (0.110 mL, 0.45 M in CH_2Cl_2) was then added by syringe. The reaction was complete after stirring 15 h at 0 °C. The mixture was then poured into 20 mL of ethyl acetate, and unreacted OsO_4 was reduced by adding 1 g of sodium metabisulfite. The mixture was diluted with 10 mL of ethyl acetate and dried over $MgSO_4$. It was then filtered through a pad of Celite and concentrated to give 0.200 g of a 9:1 mixture of the triols **19a** and **19b** (75%). All glassware was cleaned with a saturated solution of sodium metabisulfite: ^{1}H NMR (**19a**) ($CDCl_3$, 300 MHz) δ 7.35−7.4 (m, 5H), 4.91 (d, J = 6.7 Hz, 1H), 4.80 (d, J = 6.7 Hz, 1H), 4.84 (d, J = 3.6 Hz, 1H), 4.02 (m, 1H), 3.8 (m, 3H), 3.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 131.7, 128.7, 128.4, 122.2, 98.3, 87.3, 86.2, 81.2, 71.4, 63.4, 56.4; MS (DIP, 70 eV) *m/e* 267 ($M^+ + 1$, 1) 221 ($M^+ - 45$, 6), 175 ($M^+ - 91$, 9); ^{1}H NMR (**19b**) ($CDCl_3$, 300 MHz) δ 7.1−7.4 (m, 5H), 4.41 (d, J = 2.6 Hz, 1H), 4.50 (d, J = 6.7 Hz, 1H), 4.31 (d, J = 6.7 Hz, 1H), 3.83 (dd, J = 5.3, 2.6 Hz, 1H), 3.65 (m, 2H), 3.00 (s, 3H).

Acetylation of 19a,b to 20a,b. To a side-arm flask containing 5 mL of pyridine and 25 mL freshly distilled acetic anhydride was added 0.200 g (0.751 mmol) of **19a**,**b**, and the mixture was stirred at room temperature for 10−12 h. The solution was evaporated, and the syrupy residue was dissolved in 100 mL of dichloromethane and then washed with water, saturated sodium bicarbonate, and brine solution. After drying over $MgSO_4$, evaporation of the organic phase gave the triacetates **20a**,**b** as a yellowish oil (0.206 g, 70%). ^{1}H NMR analysis indicated a 9:1 mixture of isomers that could not be separated by column or PTLC chromatography: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45−7.25 (m, 5H), 5.81 (d, J = 4.7 Hz, 1H), 5.34 (m, 1H), 4.94 (dd, J = 6.9 Hz, 2H), 4.77 (dd, J = 6.9 Hz, 1H), 4.54 (dd, J = 12.2, 3.2 Hz, 1H), 4.27 (dd, J = 12.0, 6.6 Hz, 1H), 4.13 (dd, J = 5.8, 4.9 Hz, 1H), 4.13 (dd, J = 5.8, 4.8 Hz, 1H), 3.43 (s, 3H), 2.05 (s, 3H), 2.15 (s, 6H).

Cobalt Complex of Triacetates 20a,b (21a,b). In a flame-dried side-arm flask equipped with a magnetic stirring bar 0.144 g (0.418 mmol) of dicobalt octacarbonyl dissolved in 50 mL of dry methylene chloride was cooled to 0 °C. Then 0.150 g (0.382 mmol) of triacetates **20a/b** dissolved in cold methylene chloride was slowly added to the solution of $Co_2(CO)_8$. The mixture was stirred at 0 °C for 8−10 h until complete complexation was observed by TLC. The dark red solution was filtered under N_2 (by cannula) through a short pad of neutral alumina, and solvent was then concentrated to give a dark red oil. The oil was purified by preparative TLC (4:1 petroleum ether/ethyl acetate) at 0 °C to give 0.203 g (79%) of **21a**,**b** (dark red oil) as a 9:1 isomeric mixture: ^{1}H NMR (**21a**) ($CDCl_3$, 300 MHz) δ 7.47 (m, 2H), 7.32 (m, 3H), 6.59 (d, J = 6.7 Hz, 1H), 5.19 (m, 1H), 4.60 (s, 2H), 4.49 (dd, J = 11.9, 4.2 Hz, 1H), 4.17 (dd, J = 6.2, 11.9 Hz, 1H), 4.02 (dd, J = 6.7, 4.0 Hz, 1H), 3.32 (s, 3H), 2.11 (s, 3H), 2.04 (s, 3H), 1.95 (s, 3H); IR (cm^{-1}, CH_2Cl_2) 2080, 2020, 2005, 1985 (s), 1755 (m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.9, 170.4, 169.4, 137.2, 129.5, 128.9, 128.00, 97.6, 92.1, 93.2, 79.5, 72.6, 70.4, 62.0, 56.1, 20.7, 92.1, 93.2; ^{1}H NMR (**21b**) ($CDCl_3$, 300 MHz) δ 7.35−7.4 (m, 5H), 6.48 (d, J = 5.9 Hz, 1H), 5.34 (m, 1H), 4.65 (dd, J = 6.9, 6 Hz, 2H), 4.37 (dd, J = 12.0, 6.6 Hz, 1H), 4.12 (dd, J = 11.5, 6.0 Hz, 1H), 4.04 (dd, J = 5.8, 3.0 Hz, 1H), 3.38 (s, 3H), 2.0 (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H).

Attempted Epoxidation of 18a. Into a flame-dried side-arm flask equipped with a stir bar and septum was added 20.0 mg (0.100 mmol) of **18a** and 5 mL of anhydrous dichloromethane. The mixture was cooled to 0 °C and then charged with 3.0 mg of $VO(acac)_2$ (0.010 mmol). This was followed by slow addition of 30.0 μL of 5 M *tert*-butyl hydroperoxide in cyclooctane (0.15 mmol); the solution immediately turned dark purple. It was then stirred at 0 °C for 1 h and then at room temperature for 48 h. TLC of the reaction mixture indicated no epoxide formation, and the starting material was recovered (3:2 petroleum ether/diethyl ether). The reaction mixture was poured into 50 mL of diethyl ether and washed with saturated sodium bisulfite. The ether extract was concentrated to give starting enyne **18a**.

(3*S*,4*R*)-1,2-Epoxy-3-methoxy-5-heptyn-4-ol (24). Into a flame-dried side-arm flask equipped with a stir bar and septum was added 70.0 mg (0.520 mmol) of **17d** and 5 mL of anhydrous dichloromethane. The mixture was cooled to 0 °C and then charged with 7.0 mg of $VO(acac)_2$ (0.26 mmol). This was followed by slow addition of 0.15 mL of 5 M *tert*-butyl hydroperoxide in cyclooctane (0.83 mmol). The solution immediately turned dark purple. It was then stirred at 0 °C for 1 h and then at room temperature for 48 h. The mixture was poured into 50 mL of diethyl ether and washed with saturated aqueous sodium bisulfite solution. The ether extract was concentrated to give a yellow oil that was chromatographed on a preparative silica plate with petroleum ether/ether eluant (4:1), giving 30 mg (0.21 mmol, 40%) of epoxide **24** (R_f = 0.32): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.37 (m, 1H), 3.53 (m, 1H), 3.34 (m, 1H), 3.51 (m, 3H), 3.21 (m, 1H), 2.8 (dd, J = 3.6, 2.4 Hz, 1H), 2.5 (d, J = 6 Hz, 1H), 2.07 (dd, J = 11.4, 2.4 Hz, 1H), 1.86 (s, 3H); IR 3600, 1250 cm^{-1}; MS (DIP, 70 eV) *m/e* 155 ($M^+ - 1$, 6) 125 ($M^+ - 31$, 32), 87 ($M^+ - 69$, 100).

(3*R*,4*R*)-1-Hexen-5-yne-3,4-diol (25). By Me_3SiBr. To a cooled (−40 °C) solution of 2.00 g (8.61 mmol) of **17c** in 10 mL of dry dichloromethane containing 4 Å molecular sieves was added slowly 4.50 mL (34.0 mmol) of trimethylsilyl bromide. The solution was stirred for 8−10 h at −30 °C until disappearance of the starting material was complete as indicated by TLC. The reaction mixture was poured into a solution of saturated sodium bicarbonate, extracted with ether, dried over anhydrous magnesium sulfate, and evaporated, and the residue was chromatographed over flash silica with petroleum ether/water (2/1) eluant to give 1.61 g (3.30 mmol) of **25** (35% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (m, 2H), 7.25 (m, 3H), 6.02 (ddd, J = 17.1, 10.7, 5.8 Hz, 1H), 5.49 (d, J = 17.1 Hz, 1H), 5.33 (d, J = 10.5 Hz, 1H), 4.8 (pseudo triplet, J = 5.6, 6.7 Hz, 1H), 4.4 (d, J = 6.6 Hz, 1H), 2.6 (bs, 2H,); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.5, 131.8, 128.7, 128.3, 122.1, 118.0, 86.8, 86.6, 75.9, 66.6; MS (DIP, 70 eV) *m*/*e* intensity 170 (M^+ − 18, 8), 154 (M^+ − 34, 8), 131 (M^+ − 57, 76), 102 (M^+ − 86, 100).

By HCl/H_2O. Into a side-arm flask equipped with a stir bar and septum was added 0.130 g (0.56 mmol) of **17c** dissolved in 1.2 mL of THF:H_2O:HCl (concd) solution (8:1:1). The solution was stirred at room temperature for 9 h until the starting material completely disappeared as indicated by TLC. The reaction mixture was then poured into a solution of saturated sodium bicarbonate, extracted with ether, and dried over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was chromatographed over flash silica (2:1 petroleum ether/ether) to afford 0.100 g (0.53 mmol) of **25** (94%).

(2*R,3*S**,4*S**)-1,2-Epoxy-6-phenyl-5-hexyne-3,4-diol (26).** To a flame-dried, jacketed, side-arm flask containing a stir bar were added 0.520 g (3.03 mmol) of **25**, 5 mL of dry dichloromethane, and 500 mg of predried 4 Å molecular sieves. The mixture was cooled to 0 °C, and 80.0 mg (0.304 mmol) of VO(acac)$_2$ was added followed by 0.85 mL of 5.5 M *t*-BuOOH solution in isooctane. The mixture was stirred for 48 h at 0 °C until complete disappearance of the starting material was indicated by TLC (1:1 petroleum ether/diethyl ether). The reaction mixture was then quenched with $Na_2S_2O_3$, and $MgSO_4$ was added. The mixture was filtered, the solvent rotary evaporated, and the residue was chromatographed (2:3 petroleum ether/ether, silica gel) to give **26** as a colorless oil (0.400g, 65%, 9:1 isomeric ratio): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.4 (m, 5H), 4.75 (d, J = 3.9 Hz, 1H), 3.39 (apparent triplet, J = 3.6, 3.3 Hz, 1H), 3.34 (m, 1H), 2.8 (d, J = 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 131.8, 129.0, 87.5, 85.7, 72.2, 65.9, 51.4, 43.6, 29.7; IR 3600, 1250 cm^{-1}; MS (DIP, 70 eV) 187 (M^+ − OH, 7), 170 (M^+ − 2OH, 59), 131 (M^+ − OH (CHOCH$_2$), 100).

[(2*R,3*S**,4*S**)-1,2-Epoxy-6-phenyl-5-hexyne-3,4-diol]-dicobalt Hexacarbonyl (27).** In a flame-dried side-arm flask equipped with a magnetic stirring bar 0.670 g (1.96 mmol) of dicobalt octacarbonyl was dissolved in 50 mL of dry methylene chloride under nitrogen and then cooled to 0 °C. In a round-bottom flask 0.400 g (1.96 mmol) of **26** dissolved in 5 mL of ice cold methylene chloride was slowly added. The mixture was stirred at 0 °C for 8−10 h until complete complexation was observed by TLC. The dark red solution was filtered under N_2 (by cannula) through a short pad of neutral alumina, and solvent was then rotary evaporated to give a dark red oil. The oil was purified by preparative TLC at 0 °C to give 0.535 g (0.981 mmol, 50%) of **27** (diastereomeric ratio 9:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.6−7.4 (m, 5H), 5.0 (dd, J = 7.5, 4.9 Hz, 1H), 3.62 (m, 1H), 3.55 (apparent triplet, J = 3.4, 3.3 Hz, 1H), 3.34 (m, 1H), 2.8 (d, J = 3.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.2, 129.6, 128.9, 128.7, 128.0, 74.1, 73.6, 52.4, 45.1, 29.7; MS (DIP, 70 eV) *m*/*e* 434 (M^+ − 2CO, 21) 406 (M^+ − 3CO, 9), 378 (M^+ − 4CO, 27), 350 (M^+ − 5CO, 29), 322 (M^+ − 6CO, 10), 304 (M^+ − H_2O, 35); IR (CH_2Cl_2) 3600, 2090, 2080, 1250 cm^{-1}.

[(4*R*,5*R*)-2,2-Dimethyl-4-ethenyl-5-(phenylethynyl)-1,3-dioxolane (28). To a stirred solution of 0.11 g (0.58 mmol) of crude diol **25** were added 2,2-dimethoxypropane (0.31 mL, 2.5 mmol) in dry methylene chloride (10 mL) and 6.2 mg (2.4 mmol) of pyridinium *p*-toluene sulfonate. The mixture was stirred for 9 h at 20 °C until the complete disappearance of starting material was indicated by TLC. The mixture was then diluted with 20 mL of diethyl ether, washed with saturated sodium bicarbonate solution and brine, dried with anhydrous magnesium sulfate, and concentrated. The residue was chromatographed over silica gel (9:1 petroleum ether/diethyl ether) producing 0.12 g (90%) of **28**: ^{1}H NMR (C_6D_6, 300 MHz) 7.45 (m, 2H), 7.0 (m, 3H), 5.83 (m, 1H), 5.43 (d, J = 17.1, Hz, 1H), 5.09 (d, J = 10.5 Hz, 1H), 4.68 (pseudo triplet, J = 7.8, 6.3 Hz, 1H), 4.61 (d, J = 7.8 Hz, 1H), 1.53 (s, 3H), 1.48 (s, 3H); MS (DIP, 70 eV) *m*/*e* 213 (M^+ − 15, 9), 182 (M^+ − 46, 2), 172 (M^+ − 56, 47).

[(4*S*,5*R*)-2,2-Dimethyl-4-ethenyl-5-(phenylethynyl)-1,3-dioxolane]dicobalt Hexacarbonyl (29). In a flame-dried side-arm flask containing a magnetic stirring bar 82.5 mg (0.241 mmol) of $Co_2(CO)_8$ was dissolved in 50 mL of dry methylene chloride under nitrogen. Then 0.050 g (0.219 mmol) of **28** dissolved in methylene chloride was added. The solution was stirred at room temperature for 2−3 h until complete complexation was indicated by TLC. The dark red solution was filtered under N_2 (by cannula) through a short pad of neutral alumina, and the solvent was concentrated to give 0.101 g of dark red oily **29** (90%): ^{1}H NMR (C_6D_6, 300 MHz) δ 7.6 (m, 2H), 7.4 (m, 3H), 5.9 (ddd, J = 17.3, 10.2, 7.3 Hz, 1H), 5.5 (d, J = 17.1 Hz, 1H), 5.35 (d, J = 10.2 Hz, 1H), 5.1 (d, J = 7.8 Hz, 1H), 4.3 (pseudo triplet, J = 7.7, 7.7 Hz, 1H), 1.49 (s, 3H), 1.51 (s, 3H).

VO(acac)$_2$-Induced Epimerization of 25. To a flame-dried flask with a jacket and side arm equipped with a stir bar were added 0.020 g (0.160 mmol) of **25** and 5 mL of anhydrous dichloromethane and 50 mg of predried molecular sieves. The solution was cooled to 0 °C, and 42.0 mg (0.016 mmol) of VO(acac)$_2$ was added to reaction mixture. The mixture was stirred for 48 h at 0−5 °C. The solution was then filtered and concentrated, and the residue was separated on preparative TLC giving 10 mg (0.080 mmoles) of **25a**,**b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (m, 4H), 7.31 (m, 6H), 6.02. (m, 2H), 5.5 (dd, J = 6.73, 17.2 Hz, 2H), 5.36 (dd, J = 10.4, 8.9 Hz, 2H) 4.62 (dd, J = 3.6, 6.8 Hz, 1H), 4.42 (pseudo triplet, J = 6.0 Hz, 1H), 4.33 (m, 1H), 4.26 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.5, 131.8, 128.7, 128.3, 118.0, 86.8, 86.6, 75.8, 75.2, 66.6, 66.5.

X-ray Structure Determination of 11f and 27a. X-ray quality crystals of **11f** were grown at 0 °C from pure pentane. Crystals of **27a** were obtained when pentane vapor was slowly diffused into a solution of **27a** in CH_2Cl_2 at −20 °C over 6−7 days. Details of the X-ray data collection and molecular and crystal data for **11f** and **27a** have been deposited with the Cambridge Crystallographic Data Centre.[53]

Acknowledgment. We are grateful for financial support provided by the National Institutes of Health (GM 34799) and the Oklahoma Center for the Advancement of Science and Technology. Determination of the X-ray structures of **11f** and **27a** by Dr. Masood Khan, O.U. Analytical Services Center, is also acknowledged.

Supporting Information Available: ^{1}H NMR spectra of all new compounds reported (22 pages). This material is contained in 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.

JO9619387

(53) The author has deposited atomic coordinates for **11f** and **27a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.