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An Approach to Pseudoguaianolides via Cobalt-Mediated Cyclopentannelation. A Stereochemical Aside

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As part of an approach to the total synthesis of pseudoguaiane sesquiterpenes a double stereoselectivity was observed in the reaction of the epimeric silyl enol ethers **4a,b** with (1-ethoxypropargylium)$Co_2(CO)_6BF_4$ (**6**). Four (of eight possible) diastereomeric adducts **8a–d** are produced in a 9:36:47:8 ratio and 75% yield. The structure of each isomer has been established by ^1H and ^{13}C NMR analyses and, in the case of **8c** and **8d**, confirmed by X-ray diffraction. All four isomers are found to possess the same relative configuration at C2 (adjacent to the carbonyl group), demonstrating a complete facial specificity in the attack of the cobalt complex on the exo face of **4a,b**. Additionally, good selectivity in the formation of the C1′ stereocenter (adjacent to the complexed triple bond) is observed as well, 3.8:1 (**8b**/**8a**) and 6:1 (**8c**/**8d**). Product isomerization studies under the reaction conditions suggest that **8b** and **8c** are kinetically favored whereas **8a** and **8c** are thermodynamically favored. Various transition-state models are proposed to account for the observed stereoselection.

Introduction

(Propargylium)$Co_2(CO)_6{}^+BF_4{}^-$ complexes have been shown to be versatile agents for carbon–carbon bond formation through their reactions with various carbon nucleophiles.[1] Key features of these reactions include: (a) regiospecific coupling to give propargylic derivatives exclusively and (b) utility with a wide variety of nucleophiles including aromatics, β-dicarbonyl compounds, enol derivatives, allyl silanes, and alkyl and alkynyl aluminums. Subsequent elaboration of the demetalated acetylenic unit opens up new synthetic possibilities. For example, we have developed a cyclopentannelation methodology combining the cobalt complexes with silyl enol ethers followed by demetalation, triple-bond hydration, and aldol condensation[2] that has been utilized in the synthesis of dihydrojasmone[3] and the guaiane sesquiterpene cyclocolorenone.[4,5]

Recently we initiated studies directed toward the synthesis of pseudoguaianolides using a variant of the above cobalt-based annelation (Scheme I). This class of sesquiterpenes has attracted several synthetic ventures[6] because of the challenging stereochemical features and significant cytotoxic and antitumoral properties of several of its members.[7] In the alkylation step, which initiates the annelation sequence, our plan called for reaction of a (1-alkoxypropargylium)$Co_2(CO)_6{}^+$ complex, i.e. **2**, with a suitably functionalized cycloheptanone derivative, e.g. **1**. In carrying out this reaction we have uncovered a high degree of stereoselectivity in the formation of the two new stereocenters. As these results may have important implications not only for the control of stereochemistry in our pseudoguaiane approach but also to the general issue of stereocontrol in alkylations by the cobalt-complexed propargyl cations,[8] we have sought to rigorously establish the stereochemical outcome of this reaction and probe the

Scheme I

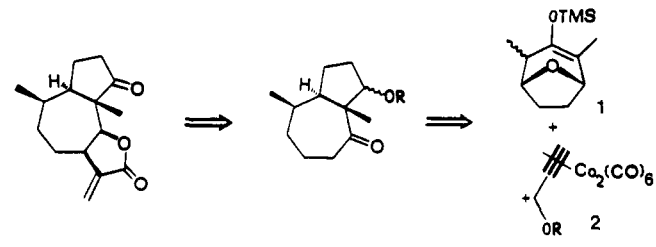

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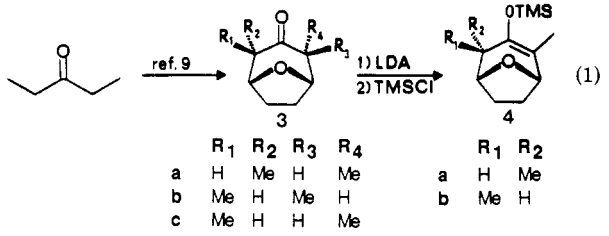
Table I. ^{1}H NMR Spectral Data of 8a–d

H1′	5.50 (s, 1 H)	5.34 (s, 1 H)	5.49 (s, 1 H)	5.39 (s, 1 H)
H3′	5.39 (s, 1 H)	5.34 (s, 1 H)	5.28 (s, 1 H)	5.24 (s, 1 H)
H6	4.10 (br dd, J_1 = 4.9, J_2 = 6.2, 1 H)	4.09 (br dd, J_1 = 2.6, J_2 = 6.0, 1 H)	3.84 (br d, J = 6.2)	3.86 (br dd, J_1 = 5.4, J_2 = 1.9, 1 H)
H3	4.44 (br d, J = 7.5, 1 H)	4.28 (br d, J = 7.3, 1 H)	4.40 (br d, J = 5.8, 1 H)	4.38 (br dd, J_1 = 2.3, J = 7.2, 1 H)
H1″	3.97 (dq, J_1 = 7.1, J_2 = 8.8, 1 H), 3.84 (dq, J_1 = 7.1, J_2 = 8.8, 1 H)	3.74 (dq, J_1 = 6.9, J_2 = 7.9, 1 H), 3.19 (dq, J_1 = 6.9, J_2 = 7.9, 1 H)	3.94 (dq, J_1 = 7.0, J_2 = 8.7, 1 H), 3.79 (dq J_1 = 7.0, J_2 = 8.7, 1 H)	3.78 (dq, J_1 = 7.0, J_2 = 8.2, 1 H), 3.33 (dq, J_1 = 7.0, J_2 = 8.2, 1 H)
H7	2.68 (br dq, J_1 = 6.6, J_2 = 6.2, 1 H)	2.80 (br dq, J_1 = 6.8, J_2 = 6.0, 1 H)	1.92 (q, J = 7.8, 1 H)	2.00 (q, J = 7.8, 1 H)
H4, H5	1.55–1.25 (m, $W_{1/2}$ = 85 Hz, 4 H)	1.60–1.30 (m, $W_{1/2}$ = 70 Hz, 4 H)	1.60–1.35 (m, $W_{1/2}$ = 75 Hz)	1.60–1.35 (m, $W_{1/2}$ = 85 Hz, 4 H)
H9	0.81 (d, J = 6.6, 3 H)	0.79 (d, J = 6.8, 3 H)	1.08 (d, J = 7.8, 3 H)	1.17 (d, J = 7.8, 3 H)
H2″	1.19 (t, J = 7.1, 3 H)	1.02 (t, J = 6.9, 3 H)	1.17 (t, J = 7.0, 3 H)	1.11 (t, J = 7.0, 3 H)
H8	1.06 (s, 3 H)	1.05 (s, 3 H)	1.05 (s, 3 H)	1.09 (s, 3 H)

origins of its stereoselectivity. Herein we report our findings.

Results

The precursor ketone **3** to the requisite silyl enol ether **4** was prepared conveniently as a mixture of isomers (**a**, cis-endo; **b**, cis-exo; **c**, trans; 45:41:14 by GC, NMR) from 3-pentanone in 82% overall yield (three steps) following Noyori's procedure[9] (eq 1). Successive treatment of **3a–c**

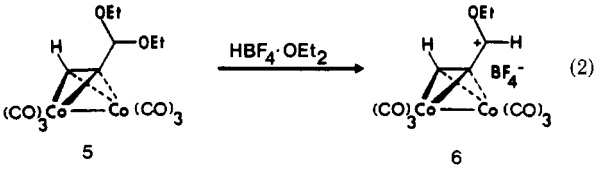


(1)

with LDA and Me_3SiCl afforded the corresponding silyl enol ehter as a mixture of C7 epimers, **4a** (endo) and **4b** (exo) (45/55). The epimers were separated by preparative GC for characterization, and their stereochemistry was established by ^{1}H NMR correlation studies, homonuclear decoupling experiments, and examination of molecular models. The most diagnostic proton resonances were those at C8, C7, and C9. Thus in **4a** (endo C9) the H7 signal appears as a broadened doubled quartet of quartets (J = 7.3, 2.2, 4.0 Hz) due to coupling with the protons at C9, C8, and H8 and weak W coupling (J < 0.9 Hz) with H5 (exo). In **4b** (exo C9) the H7 resonance appears as a quartet of quartets (J = 6.9, 1.4 Hz) due to coupling with the methyl protons at C9 and C8; no coupling is observed with H6 because the H6–H7 dihedral angle[10] (from the Dreiding model) is approximately 85°. Supporting this analysis is the higher field C7 methyl resonance in **4a** (δ 0.91) due to shielding interactions with H4 and H5 (versus a deshielding dipolar interaction of the C9 methyl with the bridging oxygen in **4b**, δ 1.19) and the correspondingly lower field H7 resonance in **4a** (δ 2.82) compared to **4b** (δ 1.72).

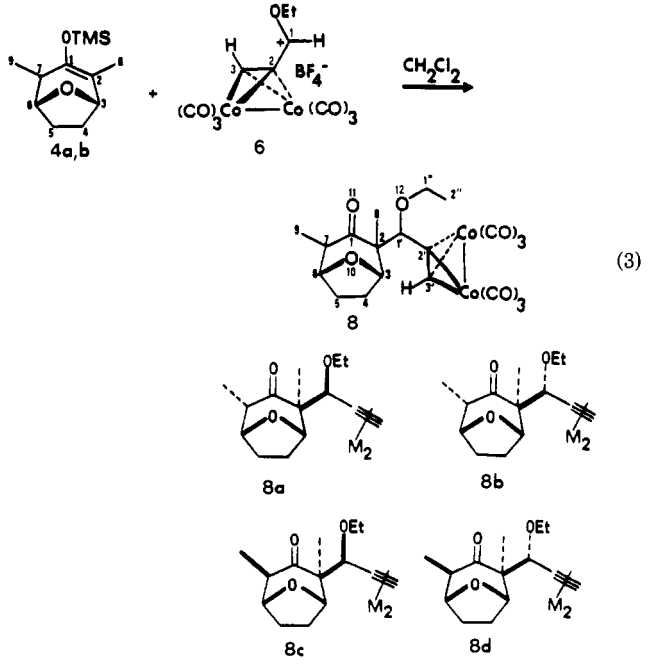
The alkoxy-substituted cation complex **6** was prepared by the general method that we have developed for the parent alkyl- and aryl-substituted complexes.[11,12]

Treatment of acetal complex **5** with HBF_4·Et_2O in propionic anhydride at −46 °C followed by ether flooding afforded **6** as a dark red moisture-sensitive solid in 85% yield (eq 2). The reaction of **6** with the epimeric mixture



(2)

of silyl enol ethers **4a,b** was carried out at −68 °C in CH_2Cl_2 over 3 h. Careful flash chromatography of the crude reaction mixture gave three very distinct dark red fractions. The least polar fraction provided a small quantity (6% of the product mixture) of $[HC{\equiv}CC(=O)H]Co_2(CO)_6$ (**5**), which results from hydrolysis of **6**. The second (and major) fraction provided the alkylated ketones **8a–d** in 75% yield (eq 3); no other isomeric products were detected in the



(3)

reaction mixture. The third and very polar fraction was composed of hydroxylated cobalt complexes derived from cleavage of the ether functions. From this last fraction a small quantity (1%) of hydroxy ketone complexes **9a,b** was

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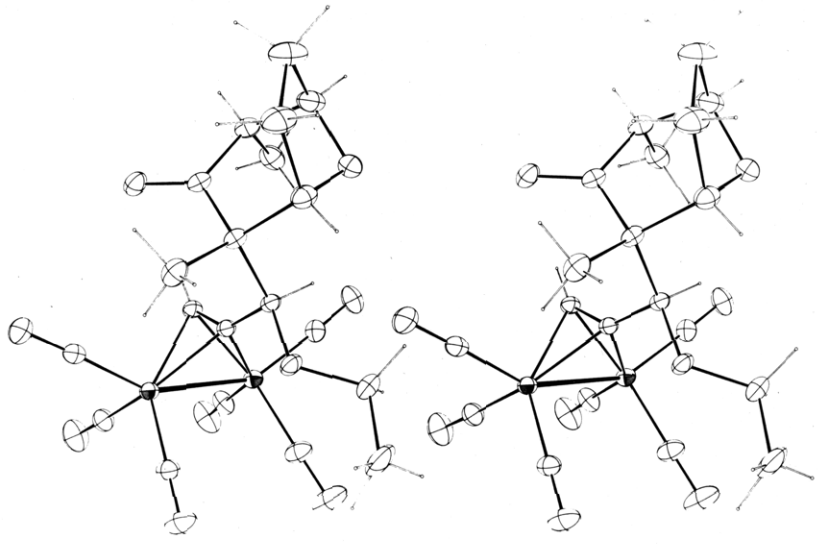

Figure 1. X-ray structures of **8c** (stereoview). Thermal ellipsoids are shown at the 50% level.

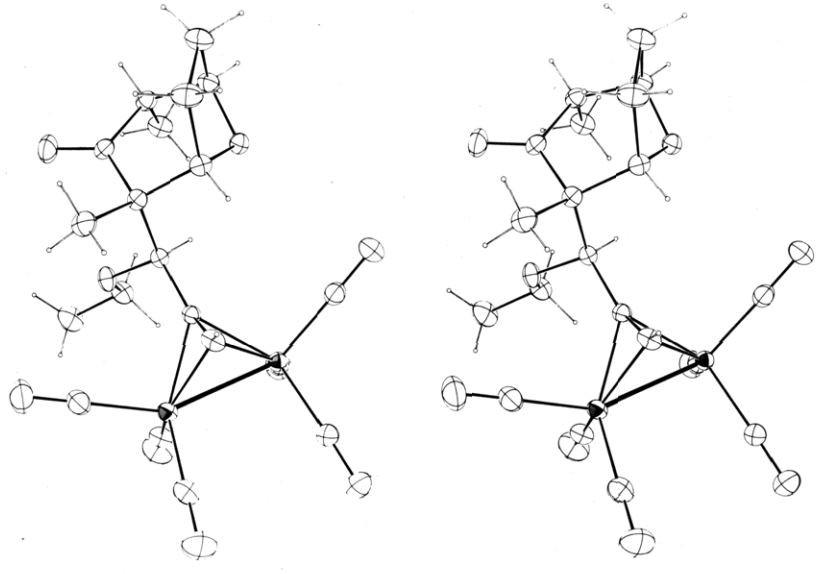

Figure 2. X-ray structure of **8d** (stereoview). Thermal ellipsoids are shown at the 50% level.

isolated and characterized as the free alkynes **10a,b** following demetalation. Compounds **10a,b** were found to have the same stereochemistry (vide infra) as **8a,b** but with an OH group in place of OEt.

The individual isomers **8a–d** (in order of elution), which could be separated by careful rechromatography and crystallization, were obtained in a relative ratio of 9:36:47:8 (by ^{1}H NMR). Their isomeric nature was apparent by comparison of their extremely similar IR and mass spectra (M^+ – CO 493.98, see the Experimental Section) and ^{1}H and ^{13}C NMR (Tables I and II). In order to establish absolute reference points for spectroscopic correlations suitable crystals of isomers **8c** and **8d** were obtained for X-ray diffraction studies. Figures 1 and 2 show the molecular structures of **8c** and **8d** determined by X-ray diffraction. Examination of these figures reveals that **8c** and **8d** differ fundamentally only in the relative configuration at C1′, the carbon adjacent to the coordinated ethynyl group. In both compounds the C7 methyl group is exo while the one at C2 is endo. Products **8c** and **8d** can thus be seen to derive from attack of complex **6** on the exo face of the silyl enol ether **4b**. In the solid-state structures of **8c** and **8d** the oxan-6-one ring adopts a chair conformation with the C7 methyl and the bulky (ethoxypropynyl)$Co_2(CO)_6$ side chain at C2 occupying pseudoaxial positions. The conformations of the C2 side chain is noticeably different in the two isomers but this could be due to crystal packing forces. All bond lengths and angles are unexceptional (Table IV, Experimental Section), both within the bicyclic system and within the cobalt cluster unit.

With the solid-state structures of **8c** and **8c** in hand it is worthwhile to compare their ^{1}H and ^{13}C NMR spectra (Tables I and II) in order to determine the spectroscopic parameters that are structurally diagnostic. The assignments shown in Table I were made by comparison of the spectra of products **8a–d** with those of the starting ketone(s) **3** and the silyl enol ethers **4a,b**, supported by homonuclear spin decoupling and phase-sensitive 2D-NOESY[13] experiments. The ^{13}C NMR assignments (Table II) were facilitated by 2D HETCOR,[14] DEPT,[15] and off-res-

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Table II. ^{13}C NMR Spectral of Data of 8a–d

carbon[a]	8a	8b	8c	8d
1	208.02	207.15	210.50	209.57
2	62.38	61.37	62.43	61.02
3	81.37	81.35	79.74	80.17
4	24.51	24.32	24.13	24.40
5	24.83	24.85	30.04	30.55
6	81.37	81.35	80.81	80.77
7	48.72	47.28	52.42	52.60
8	11.91	12.45	14.82	15.19
9	9.71	9.92	13.31	13.65
1′	81.07	83.39	80.39	82.14
2′	91.38	90.90	91.28	91.01
3′	72.85	72.56	74.17	73.86
1″	67.96	67.57	68.37	66.80
2″	14.99	15.01	17.85	19.11
Co–CO	199.82	199.82	200.21	200.14

[a] The multiplicity was established by DEPT[13] and/or off-resonance experiments and the assignment by two dimensional HETCOR[14] experiments. Quaternary carbons were identified by differential comparison of those spectra with the totally decoupled spectra.

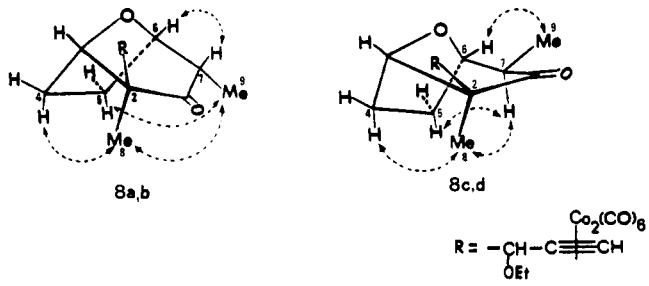


Figure 3. NOE enhancements in **8a,b** and **8c,d**. Other NOE enhancements between H4 and H5, H4 (exo) and H3, H5 (exo) and H6 were observed but are not represented for clarity. Only NOE effects with stereochemical implications are shown in the figure.

onance experiments. Consistent with the fact that **8c** and **8d** are epimeric at C1′ (but have the same relative stereochemistry at C7 and C2), both compounds exhibited similar NOE enhancements within the bicyclic portion of the molecule (Figure 3) with expectedly strong effects between H6/H9 and between H4(endo)/H9 and a weaker enhancement between H9/H7. Comparison of the proton chemical shifts of **8c** and **8d** are also informative. Very little difference is observed between the ring resonances in the two isomers ($\Delta\delta$ <0.06). However, those protons close to the differentiating C1′ stereocenter display significant differences, e.g. $\Delta\delta$ 0.10 for H1′ and 0.16 and 0.46 for the diastereotopic H1″ protons. Similarly, the ^{13}C NMR spectra of **8c** and **8d** (Table II) differ significantly (>0.5 ppm) only in the chemical shifts of the C2, 1′, 1″, and 2″ resonances ($\Delta\delta$ +1.41, −1.75, +1.57, and −1.26, respectively). It is apparent therefore that the stereochemistry at C1′ is clearly reflected in the ^1H and ^{13}C NMR chemical shifts of the nuclei at positions 2, 1′, 1″, and 2″.

Consider now the pair **8c/8a**. Peak by peak comparison of their ^1H NMR spectra (Table I) reveals negligible differences ($\Delta\delta$ <0.05) in the positions of the resonances of nuclei near the C1′ and C2 stereocenters but substantial differences ($\Delta\delta$ 0.26, 0.76, and 0.27) in the H6, H7, and H9 resonances near the C7 stereocenter. Recall that similar effects were observed in the spectra of the epimeric silyl enol ethers **4a** and **4b**. Likewise, the largest ^{13}C NMR $\Delta\delta$'s from comparison of the spectra of **8c** and **8a** are for the C5, C7, and C9 resonances (5.21, 3.70, 3.60 ppm). These observations suggest that **8a** and **8c** differ only in their relative configuration at C7. The shielding of the C9 carbon and proton resonances in **8a** relative to **8b** suggested an endo methyl configuration at C7. The endo methyl geometry assigned at C7 for **8a** also was apparent from the appearance of the H7 resonance as a somewhat broadened double quartet (J = 6.6, 6.2 Hz) by virtue of coupling to H9, H6, and a weak W coupling to H5(exo). These coupling assignments were confirmed by homonuclear spin decoupling experiments. Finally the conclusion is supported by the NOE enhancements observed for **8a** (Figure 3). Thus, strong NOE enhancements were observed between H5(endo) and H9 as well as weaker, but significant, enhancements between H8 and H9 and H6/H7.

The structure of **8b** also readily follows from its accumulated NMR data in comparison with those of **8a**, **8c**, and **8d**. Thus, the nearly identical ^1H ($\Delta\delta$ <0.10) and ^{13}C NMR ($\Delta\delta$ <1.0) chemical shifts for the 7- and 9-position nuclei in **8a** and **8b** and their similar NOE effects within the bicyclic framework point to the same relative configuration for this pair at C7, i.e. with an endo methyl. The very similar position of the C2 methyl proton resonance in all four isomers ($\Delta\delta$ <0.05) and the observations of significant NOE effects with this group is indicative of the same relative configuration at C2 in all four isomers, i.e. with the organometallic side chain exo. Finally, comparison of the ^1H NMR resonances of **8b** with the other isomers in the vicinity of the C1′ stereocenter, e.g. H1′, H1″, and H2″, reveals nearly identical shifts with **8d** ($\Delta\delta$ <0.10) but substantial differences ($\Delta\delta$ 0.15–0.65) with **8a** and **8c**. Similar correlations are observed in the ^{13}C NMR chemical shifts of **8b** and **8d**. Taken together these correlations indicate the same (2,1′-*ul*) stereochemistry for both **8b** and **8d**.

In summary, the following stereochemical features should be recognized: (1) *All four products, **8a–d**, are derived exclusively from exo face attack by complex **6** on silyl enol ether **4***. (2) The **8a/8b** pair is epimeric at C1′ and is presumably derived from reaction with **4a** whereas the **8c/8d** pair, also epimeric at C1′, is formed from reaction with **4b**. This conclusion is supported by the fact that the original **4a/4b** ratio (45:55) is *quantitatively* reflected in the (**8a** + **8b**)/(**8c** + **8d**) ratio (45:55). (3) *A moderate selectivity is observed for generation of the C1′ stereocenter from both **2a** (3.8:1) and **2b** (6.0:1) but in the opposite relative sense*, i.e. reaction of **6** with **4a** affords primarily the (2,1′-*lk*) isomer whereas **4b** gives mostly the (2,1′-*ul*) isomer.

In considering the possible origins of the observed stereoselectivity it was important to establish whether the product composition was kinetically or thermodynamically controlled. In order to address this issue each of the isomeric complexes **8a–d** was subjected to simulated reaction conditions by stirring each for 3 h in CH_2Cl_2 at −46 °C in the presence of 1:1 $BF_3{\cdot}Et_2O/Me_3SiCl$. The latter Lewis acid mixture was employed to model the behavior of the "Me_3SiBF_4" (produced when **4** and **6** react), which presumably decomposes to Me_3SiF and BF_3. The recovered **8** from each reaction was analyzed for isomeric composition by ^1H NMR and the results are summarized in eq 4–7. Because of the possible differences between

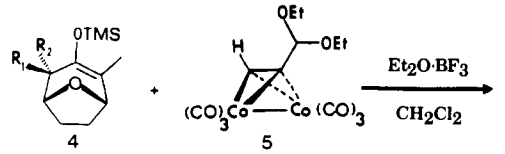
8a + $BF_3{\cdot}Et_2O/Me_3SiCl$ → **8a** (+ decomposition) (4)

8b + $BF_3{\cdot}Et_2O/Me_3SiCl$ →
8a (4) + **8b** (1) (+ decomposition) (5)

8c + $BF_3{\cdot}Et_2O/Me_3SiCl$ →
8c (85) + **8d** (1) + **8a** (1) (+ decomposition) (6)

8d + $BF_3{\cdot}Et_2O/Me_3SiCl$ →
8c (1.5) + **8d** (1) (+ decomposition) (7)

the simulated and actual reaction conditions and the fact that each of these reactions was accompanied by considerable decomposition (ca. 50%), quantitative comparisons should be avoided (i.e. the product ratios may not be truly thermodynamic). Nonetheless, it was found that isomers **8a** and **8c** were essentially unchanged under the simulated reaction conditions whereas both **8b** and **8d** were largely converted to their corresponding C1′ epimers, **8a** and **8c**. Except for a trace of **8a** observed in the reaction of **8c**, no interconversion of C7 epimers occurred nor were any C2 epimers produced. The isomerizability of **8b** and **8d** was further suggested by the diminished C1′ stereoselectivity (ca. 1.5:1 and 2.6:1) observed in the BF_3·Et_2O-promoted coupling of silyl enol ether **4a,b** with acetal complex **5** (eq 8) compared to the reaction with the isolated cation salt **6**.

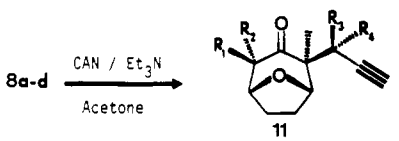


4 5

a b
R_1 H Me
R_2 Me H

8a + 8b + 8c + 8d (8)
(17%) (24%) (43%) (16%)

Demetalation of the mixture of complexes **8a–d** was carried out to advance the progress of our synthesis as well as to further support the spectroscopic correlations of structure. Because of the presence of the potentially acid epimerizable centers at C1′, C2, and C7, we modified the usual acidic Ce(IV)-induced oxidative demetalation[2] conditions for use with complexes **8a–d**. Thus when an acetone solution of **8a–d** containing added Et_3N was treated with ceric ammonium nitrate, smooth demetalation occured (CO evolution), affording the free acetylene derivatives **11a–d** in 80–95% yield (eq 9). Although the isomeric mixture was not readily separated on a preparative scale, capillary GC/MS and ^1H NMR analysis of the mixture indicated a 9:36:47:8 isomeric composition, identical with that found for the mixture of precursor complexes **8a–d**. Therefore, under these neutral/basic decomplexation conditions no isomerization occurred. Careful analysis of the 300-MHz ^1H NMR spectrum of the **11a–d** mixture augmented with 2D COSY and selective homonuclear decoupling experiments permitted assignment of almost all of the resonances in the spectrum to the individual isomers (Experimental Section). Most of the same chemical shift/stereochemical correlations could be discerned for **11a–d** as found for the corresponding complexes. For example, shielding of the H9 and deshielding of the H7 resonances characterizes the endo C7 epimers **11a,b** relative to the exo isomers **11c,d**. The characteristic shielding of the H1′, H3, and H3′ resonances of the (2,1′-*ul*) epimers **11a,c** relative to the (2,1′-*lk*) isomers **11b,d** is also observed. These results reinforce our previous stereochemical assignments and also suggest very similar conformations, especially in the bicyclic skeleton, for the corresponding complexed and uncomplexed isomers. Conversion of **11a–d** to a key pseudoguaianolide intermediate will be the subject of a forthcoming publication.[16]



11 (9)

	R_1	R_2	R_3	R_4
a	H	Me	OEt	H
b	H	Me	H	OEt
c	Me	H	OEt	H
d	Me	H	H	OEt

Discussion

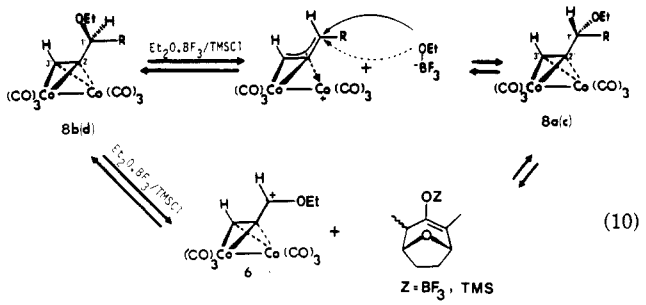
Although we first prepared alkoxy-substituted propargylium complexes such as **6** some time ago and have investigated their chemistry over the last few years,[17] the present report constitutes the first published account of one of their reactions. These dark red complexes are conveniently prepared by protonation of the acetal derivatives and can be stored for months under nitrogen. Like the corresponding alkyl-substituted relatives their IR and ^1H NMR spectra clearly indicate considerable charge delocalization onto the (alkyne)$Co_2(CO)_6$ unit. Furthermore, the substantially deshielded OCH_2 resonance in **6** relative to the precursor acetal complex **5** (+1.3 ppm) suggest that significant π-donation occurs from the ether oxygen to the adjacent electron deficient carbon.

The stereochemical course of the reaction between silyl enol ether **4a,b** and the electrophilic complex **6** has been completely elucidated. Given the X-ray structures of **8c** and **8d**, their ^1H and ^{13}C NMR spectra (including COSY,[18] NOE, and decoupling experiments), and the remarkable internal self consistency of the spectra for all four isomers **8a–d**, their assigned structures are secure. We do note that careful comparison of the corresponding ^1H and ^{13}C NMR data for **8a–d** together with molecular models suggests that in solution (in contrast to the solid state) **8c** and **8d** adopt a boatlike conformation to relieve steric interactions between the substituents at C7 and C1′ and that **8a** and **8b** adopt a deformed chairlike conformation so as to locate the 1,3-*cis*-methyl groups (at C2 and C7) far apart from one another. This model provides a complete understanding of the precise locations and coupling parameters for all the ^1H and ^{13}C NMR resonances of **8a–d**.

The key findings that should be accommodated in discussing possible origins of the observed stereoinduction include the following: (1) All four products, **8a–d**, are derived exclusively from exo face attack by complex **6** on silyl enol ether **4**. (2) A moderate selectivity is observed for generation of the C1′ stereocenter from both **4a** (3.8:1) and **4b** (6.0:1) *but in the opposite relative sense* (**4a** affords primarily the (2,1′-*ul*) isomer whereas **4b** gives mostly the (2,1′-*lk*) isomer). (3) Products **8b** and **8d** isomerize considerably (to **8a** and **8c**, respectively) under the simulated reaction conditions whereas **8a** and **8c** do not. The isomerization results indicate that the **8b**/**8a** selectivity (3.8:1) is kinetic in origin (since **8a** is more stable). Regarding the **8c**/**8d** pair, the isomerization studies suggest that **8c** is both kinetically and thermodynamically preferred in the alkylation of **4b** by **6**. The mechanism of the isomerization might likely involve either Lewis acid-promoted ethoxide extraction/readdition via a new metal-stabilized cation at C1′ or, alternatively, a dealkylation/realkylation via the intermediacy of **6**[19] (eq 10). Experiments to distinguish these alternatives are planned.

In light of these conclusions it is appropriate to attempt to account for the observed stereoselectivity in terms of

(16) Montaña, A. M.; Nicholas, K. M., manuscript in preparation.
(17) Hodes, H. D.; Varghese, V.; Nicholas, K. M., unpublished results.
(18) (a) Bax, A.; Freeman, R.; Morris, G. A. *J. Magn. Reson.* **1981**, *42*, 169. (b) Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *44*, 542. (c) Bax, R.; Freeman, R; Morris, G. *J. Magn. Reson.* **1981**, *43*, 333.
(19) We appreciate the suggestion of a referee on this point.



(10)

a transition state model for the preferred approach of cation **6** to the epimeric silyl enol ethers, **4a** and **4b**. In order to carry out the analysis, we consider the transition state to be reactant-like (the reaction is highly exoergic) so that it can be approximated by the close approach geometries of the cation **6** and each silyl enol ether. Although the structure of alkoxy-substituted propargylium complexes such as **6** have not been investigated, evidence gathered from solution NMR studies of the alkyl-derivatives by Schreiber[20,8b] and ourselves[21] provides an interesting but complex picture. In short, the (propargylium)$Co_2(CO)_6^+$ species exhibit temperature-dependent fluxionality that has been explained in terms of processes involving of hindered rotation about the C1–2 bond and interchange of the two $Co(CO)_3$ groups (Scheme II). The ease of interconversion among isomers **6a–d** is markedly dependent on the substitution at the formal cation center: ΔG^*(isom) primary > secondary > tertiary and probably reflects the decreasing demand on the cluster unit for electron donation as stabilizing alkyl groups are added. The stereochemical implication of this dynamic behavior is that for secondary, tertiary, and probably alkoxy-substituted cations interconversion of **6a–d** is rapid relative to attack by external reagents. As such, the possible transition states involving interaction of all four isomers **6a–d** should be considered with the silyl enol ethers **4a,b**.

Let us consider first the formation of the **8c,d** pair from **6** + **4b**. Examination of a molecular model of **4b** reveals a preferred conformation, which places the bulky Me_3Si group "anti" to the exo methyl at C7, i.e. on the endo side (Figure 4). This effect further shields the already crowded endo face of **4b** (from C4-H and C5-H endo), leaving the exo face open and accessible for attack by **6**, leading to **8c** and **8d**. The exclusive exo stereoselectivity could be reinforced by dipolar attraction between the electrophilic complex to the bridging O atom of the substrate.[19] Although the selectivity at C1′ indicates relatively modest transition state energy differences, inspection of molecular models of the various staggered transition states involving approach of **6a–d** to **4b** does qualitatively accommodate the results. Of the various possibilities leading to **8c**, the gauche (synclinal) transition state **12c** (utilizing rotamer **6c**) provides minimal steric repulsion by placing H1′ toward the bridging oxygen and the bulky ethoxy and (ethynyl)$Co_2(CO)_6$ groups away from the bicyclic skeleton. Of the various transition states leading to **8d** the anti arrangement **9d** (from rotamer **6d**) best minimizes the critical repulsive interactions. Comparing **12c** to **12d**, the latter transition state appears to be slightly disfavored by virtue of interaction of the C3′-H/C3-H bonds and from a dipolar repulsion between the siloxy and ethoxy oxygen atoms. Preference for **12c** (and hence **8c**) may also be enhanced

Scheme II

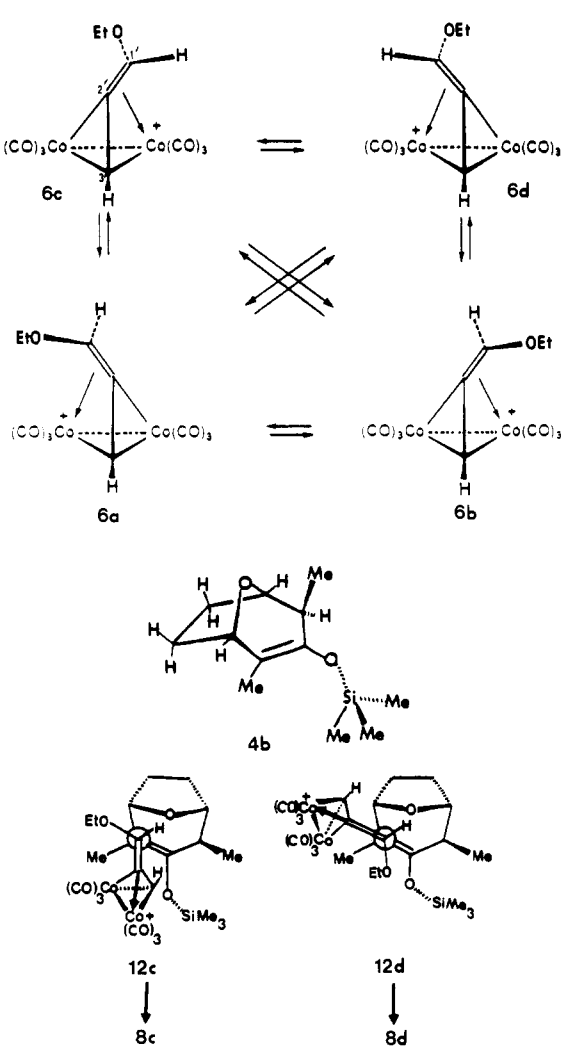


Figure 4. Conformation of **4b** and transition states **12c** and **12d**.

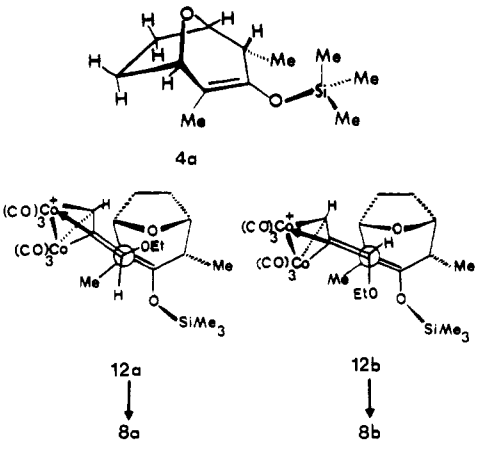


Figure 5. Conformation of **4a** and transition states **12a** and **12b**.

by stereoelectronic factors associated with the gauche arrangement.[22] A gauche approach leading to **12d** (hence **8d**) is rendered unfavorable by forcing the ethoxy group close to the bridging oxygen and the exo methyl at C7. The greater thermodynamic stability of **8c** relative to **8d** (deduced from the isomerization studies) may derive from the existence of a sterically unencumbered conformation for

(20) Schreiber, S. L.; Klimas, M. T.; Sammakia, T. *J. Am. Chem. Soc.* **1987**, *109*, 5749.

(21) Padmanabhan, S.; Nicholas, K. M. *J. Organomet. Chem.* **1983**, *268*, C-23.

(22) Seebach, D.; Golinski, J. *Helv. Chim. Acta* **1981**, *64*, 1413.

8c, which minimizes the various O/O dipolar repulsions (ascertainable from models).

Now consider the reaction of 6 with 4a to produce the 8a,b pair. The observed exo facial selectivity in this case apparently once again is the result of hindered approach by 6 to the endo face of 4a. The reason for this is somewhat less obvious here because the endo C7 methyl seems to prevent the Me_3Si group from residing on the endo face. However, with the Me_3SiO group on the exo face but tilted away from the methyl at C2 (Figure 5), access by 6 from the exo direction is relatively unimpeded. Such a placement of the Me_3SiO group also allows us to account for the interesting reversal of the sense of C1′ stereoinduction in the reactions of the epimeric silyl enol ethers. Once again examination of models for the various possible transition states involving 6a–d which lead to 8a and 8b leads us to propose arrangements 12a and 12b as the most attractive. The bulkiness of both the Me_3Si group and the $Co_2(CO)_6$ moiety causes such anti transition states to be preferred over possible gauche arrangements. Transition state 12b (which leads to product 8b) appears to be favored because only a (presumably) repulsive dipolar interaction is present between the siloxy and ethoxy oxygen atoms whereas arrangement 12a suffers from the more severe repulsions between the bridging oxygen and the ethoxy group. Once the products 8a and 8b are formed, the latter repulsions can be relieved by C2–C1′ rotation to give a conformation of 8a with maximum distance between the three oxygen atoms (which is not attainable by 8b), hence the apparently greater thermodynamic stability of 8a.

Conclusions

The reaction of ethoxy-substituted propargylium complex 6 with the epimeric mixture of silyl enol ethers 4a,b has been found to proceed with complete exo face diastereoselectivity, affording four diastereomeric adducts, 8a–d. Moderate to good diastereoselectivity (3.8:1 and 6.0:1) in generating the stereocenter adjacent to the coordinated acetylene is also observed. Isomerization experiments indicate that the selectivity is largely the result of kinetic control. The stereoselectivity can be explained in terms of a transition state model, which minimizes steric and dipolar repulsions between the silyl enol ether and various equilibrating rotamers of the cation complex 6.

Experimental Section

General Methods. ^1H and ^{13}C NMR spectra were obtained at 300 and 75.4 MHz, respectively. Deuteriated NMR solvents were dried over 4-Å molecular sieves, stored, and handled under N_2. NMR samples of cobalt complexes (10^{-2}–10^{-4} M) were prepared on a vacuum line under prepurified N_2 and filtered (dissolved in the deuteriated solvent) through a short pad of dried neutral alumina before use. For the preparation of the NMR sample of 6, the cation salt was placed into the NMR tube in the drybox, and SO_2 was condensed directly into the NMR tube before sealing it. Decoupling experiments as well as two-dimensional NOESY, HETCOR, and COSY-45 experiments were performed with use of standard Varian software. Analytical and preparative GL chromatography was carried out using 5 ft × $^1/_8$ in. and 6 ft × $^3/_8$ in. OV-101 packed columns, respectively. Preparative TLC was performed over silica gel E. Merck (G-60$PF_{254-366}$) with 20 × 20 cm glass plates (1 mm). Flash column chromatography was carried out with E. Merck silica gel (230–400 mesh) and pressure of N_2 (20 psi). Melting points of 8a–d were determined in capillaries sealed under 1 atm of CO.

Glassware was oven-dried at 120 °C overnight prior to use; solvents were purified and dried by refluxing over drying agents for 2 h prior to distillation (CH_2Cl_2, diisopropylamine, and triethylamine from CaH_2; THF, ethyl ether, pentane, and benzene from Na/benzophenone; acetone from anhydrous $MgSO_4$).

1,1-Diethoxy-2-propyne was prepared on a scale of 20 g according to ref 23 and carefully purified by distillation under reduced pressure.

2,7-Dimethyl-3,6-epoxycycloheptan-1-one (3). Ketone 3 was prepared on a 25-g scale from 3-pentanone according to ref 9 in 82% overall yield. It was purified by flash column chromatography over silica gel with a short precolumn of neutral alumina and eluting with mixtures of pentane and ether of increasing polarity. Product 3a–c is a diastereoisomeric mixture of cis diequatorial (45%), trans (14%) and cis diaxial (41%) isomers. The composition was established on the basis of ^1H NMR of their unsaturated precursors[9] and remains unchanged after hydrogenation as shown by capillary GC.

2,7-Dimethyl-3,6-epoxy-1-[(trimethylsilyl)oxy]cyclohept-1-ene (4a, 4b). A solution containing 15 mL (0.11 mol) of freshly distilled diisopropylamine and 100 mL of anhydrous THF were cooled to −78 °C with stirring under N_2, and 45 mL (0.072 mol) of a 1.6 M solution of *n*-BuLi (in hexane) was added by syringe. After 30 min 10 g (64.8 mmol) of 3a–c was added dropwise during 5 min. The dry ice/acetone bath was replaced with an ice bath, and the reaction mixture was kept at 0 °C for 2 h. Freshly distilled $ClSiMe_3$ (10 mL, 0.088 mol) was added dropwise, and after 15 min the ice bath was removed and the reaction mixture allowed to warm to room temperature for 2 h. The crude mixture was filtered by cannula under N_2 and concentrated to dryness. Dry pentane was added, and the solution was cooled to −20 °C to induce precipitation of the remaining solid. The solution was again filtered by cannula and stripped of solvent by pump (0.05 Torr, 1 h), leaving 14.7 g of a colorless oil containing 98% (by GC) of a diastereomeric mixture 4a/b (1.2/1.0, by ^1H NMR) in 98% yield. Compounds 4a and 4b were separated by preparative GC (40 °C, 1 min; 5 °C/min; 20 °C, 40 min; t_R(2a) 23.7 min, t_R(2b) 22.4 min) for their individual characterization.

4a: IR (film) 2950, 2900, 2870, 1675, 1460, 1345, 1300, 1250, 1195, 1160, 1120, 905, 890, and 755; ^1H NMR ($CDCl_3$) δ 4.23 (br dd, J_1 = 2.4, J_2 = 6.3, 1 H, H6), 4.20 (br d, J = 7.9, 1 H, H3), 2.10 (m, $W_{1/2}$ = 34 Hz, 2 H, H4), 1.88 (m, $W_{1/2}$ = 28 Hz, 2 H, H5), 1.72 (qq, J_1 = 1.4, J_2 = 6.9, 1 H, H7), 1.54 (d, J = 1.4, 3 H, H8), 1.19 (d, J = 6.9, 3 H, H9), and 0.18 (s, 9 H, $SiMe_3$); MS (EI, 70 eV, DIP), *m/e* (%) 226 (M^+, 27), 211 ($M^+ - CH_3$, 14), 198 (27), 197 (85), 183 (60), 169 (35), 157 (33), 136 (34), and 73 ($SiMe_3^+$, 100); HRMS (EI, 70 eV, DIP) calcd for $C_{12}H_{22}O_2Si$ 226.1389, found 226.1385.

4b: IR (film) 2960, 2945, 2870, 1680, 1465, 1360, 1290, 1255, 1200, 1175, 1125, 1050, 905, 895, 845, and 760; ^1H NMR ($CDCl_3$) δ 4.35 (ddd, J_1 = 4.0, J_2 = 5.5, J_3 = 1.3, 1 H, H6), 4.25 (dd, J_1 = 2.4, J_2 = 2.7, 1 H, H3), 1.87 (m, $W_{1/2}$ = 36 Hz, 4 H, H4), 2.28 (dqq, J_1 = 4.0, J_2 = 2.2, J_3 = 7.3, 1 H, H7), 1.52 (d, J = 2.2, 3 H, H8), 0.91 (d, J = 7.3, 3 H, H9), 0.18 (s, 9 H); MS (EI, 70 eV, DIP) 226 (M^+, 30), 211 ($M^+ - CH_3$, 16), 198 (22), 197 (36), 183 (58), 169 (46), 157 (45), 136 (37), and 73 ($SiMe_3^+$, 100); HRMS (EI, 70 eV, DIP) calcd for $C_{12}H_{22}O_2Si$ 226.1389, found 226.1387.

Hexacarbonyl[μ-η⁴-(1,1-diethoxy-2-propyne)]dicobalt(*Co–Co*) (5). To a solution of $Co_2(CO)_8$ (13.1 g, 38.2 mmol) dissolved in 100 ml of dry benzene was added 4.9 g (38.2 mmol) of 1,1-diethoxy-2-propyne dropwise with stirring under N_2 over 10 min. Vigorous CO evolution occurred. The reaction mixture was stirred for 3 h. The final mixture was filtered through a short pad of neutral alumina (dried into the oven at 120 °C overnight) under N_2. The resulting solution was stripped of solvent, affording a chromatographically pure, thermally unstable, dark red oil (14.6 g, 98% yield); 5 is best prepared freshly and promptly used: IR (film) 2980, 2930, 2870, 2090, 2045, 2020, 1310, 1060, 1090, and 1110; ^1H NMR (C_6D_6) δ 5.54 (s, 1 H, H1), 5.31 (s, 1 H, H3), 3.47 (dq, J_1 = 7.1, J_2 = 9.2, 2 H), 3.32 (dq, J_1 = 7.1, J_2 = 9.2, 2 H), and 1.13 (t, J = 7.1, 6 H); MS (EI, 12 eV, DIP), *m/e* (%) 414 (M^+, 1.5), 386 ($M^+ - CO$, 66), 358 ($M^+ - 2CO$, 78), 330 ($M^+ - 3CO$, 100), 302 ($M^+ - 4CO$, 96), 274 ($M^+ - 5CO$, 91), 246 ($M^+ - 6CO$, 80), 218 (16), 202 (26), 174 (2), 162 (2), 143 (8), 103 (2), and 83 (4).

Hexacarbonyl[μ-η⁴-(1-ethoxy-2-propyn-1-ylium)]dicobalt(*Co–Co*) Tetrafluoroborate (6). To a mixture of 32 g

(23) (a) Barbot, F.; Poncini, L.; Raudrianoelina, B.; Miginias, Ph. *J. Chem. Res.* **1981**, (M), 4016; (S) 343. (b) Poncini, L. *Justus Liebigs Ann. Chem.* **1984**, 1524. (c) Stetter, H.; Reske, E. *Chem. Ber.* **1970**, *103*, 643. (d) Stetter, H.; Kuhlmann, H. *Synthesis* **1975**, 379. (e) LeCoq, A.; Gorgues, A. *Org. Synth.* **1980**, *59*, 11.

(77.3 mmol) of **5** in 5 mL of freshly distilled propionic anhydride was added 5 mL of absolute ether, and the mixture was stirred and cooled to −46 °C (cyclohexanone/dry ice) under N_2. Freshly distilled $HBF_4{\cdot}OEt_2$ (21 mL, 154.5 mmol) was added at once with vigorous shaking and then stirred for 30 min. The cooling bath was replaced by ice, and the reaction mixture was quenched with 2 L of cold absolute ether (0 °C). After the cation salt precipitated, the solid was allowed to settle, and the red mother liquor was taken out by cannula. Three more 200-mL aliquots of fresh absolute ether were added and taken out successively. Finally the complex salt was dried by pumping for 1 h, resulting in 30 g (85% yield) of a brownish red solid: IR (CH_2Cl_2) 3045, 2980, 2070, 2060, 2030, 1150, and 1100; ^1H NMR (SO_2, −25 °C) δ 8.91 (s, 1 H, H-C1), 7.37 (s, 1 H, H-C3), 4.74 (q, 2 H), and 1.55 (t, 3 H).

Alkylation of 4 by Complex 6. Salt **6** (39g, 96 mmol) was disolved in 250 mL of anhydrous CH_2Cl_2 and cooled to −78 °C while stirring under N_2. Silyl ether **4** (14.6 g, 64 mmol) was then added dropwise over 5 min and the reaction mixture was warmed to −46 °C and kept under these conditions for 3 h. The cooling bath was removed, 200 mL of ether was added, and the mixture was allowed to reach room temperature (30 min). The organic solution was washed twice with aqeous $NaHCO_3$ and water to neutral pH, dried over anhydrous $MgSO_4$, and concentrated to dryness. The resulting red oil (35 g) was submitted to flash column chromatography over silica gel. Three major fractions were separated: (I) eluted with 95/5 pentane/ether, giving pure **7** (2g); (II) eluted by pentane/ether, 90/10 to 70/30, giving 25 g (75% yield) of a mixture of the four diastereomers **8a–d** (in decreasing R_f) in a ratio of 9/36/47/8 (by ^1H NMR); (III) eluted by 50/50 pentane/ether (P/E) t pure ether, giving 8 g of a mixture of hydroxylated polar complexes whose composition was studied after demetalation (vide infra).

A 2-g sample of fraction II was rechromatographed over silica gel (100g SiO_2/g of substrate). Eluting with a mixture of pentane–ether of increasing polarity it was possible to isolate pure **8a** (P/E, 90/10), **8c** (P/E 90/10), and **8d** (P/E 80/20). A fraction eluted by P/E, 90/10, and containing a mixture 1/1 of **8b** and **8c** was recrystallized in *n*-hexane at −20 °C under CO, separating the largest part of **8c** as crystals and enriching the mother liquor in **8b**: This solution was concentrated to dryness and rechromatographed (80 g of SiO_2/g of substrate) to obtain pure **8b** eluting with P/E, 70/30.

Hexacarbonyl(η^4-2-propyn-1-al)dicobalt(*Co–Co*) (7): red oil; IR (film) 3320, 3100, 2100, 2060, 2030, 1670 (CHO), 1005, 970, 860, and 780; ^1H NMR (C_6D_6) δ 9.71 (s, 1 H, CHO), 5.35 (s, 1 H, H-C3); MS (EI, 12 eV, DIP), *m/e* (%) 340 (M^+, 8), 312 (M^+ − CO, 100), 284 (M^+ − 2CO, 90), 256 (M^+ − 3CO, 72) 228 (M^+ − 4CO, 56), 200 (M^+ − 5CO, 53), 172 (M^+ − 6CO, 27), 144 (8), 143 (9), and 117 (5).

Hexacarbonyl[μ-η^4-[2,7-dimethyl-3,6-epoxy-2-(1-ethoxy-2-propyn-1-yl)cycloheptan-1-one]]dicobalt(*Co–Co*) (8a–d): ^1H NMR (Table I); ^{13}C NMR (Table II).

8a: IR (KBr) 2970, 2960, 2930, 2900, 2890, 2095, 2070, 2020, 1995, 1975, 1705, 1470, 1445, 1380, 1085, 1050, 1020, 970, and 950; MS (EI, 12 eV, 30 °C, DIP) 494 (M^+ − CO, 5), 466 (M^+ − 2CO, 46), 438 (M^+ − 3CO, 42), 410 (M^+ − 4CO, 100), 382 (M^+ − 5CO, 42), 354 (M^+ − 6CO, 80), 326 (17), 310 (16), 280 (8), 278 (10), 193 (7), 179 (8), and 83 (19); mp (benzene) red crystals 43–44 °C; HRMS (EI, 12 eV, DIP) calcd for $C_{19}H_{20}O_8Co_2$ 493.9822 (M^+ − CO), found 493.9829.

8b: IR (KBr) 2990, 2950, 2910, 2890, 2100, 2060, 2025, 2000, 1975, 1715, 1475, 1465, 1450, 1380, 1090, 1050, 1030, and 960; MS (EI, 12 eV, 30 °C, DIP), *m/e* (%) 494 (M − CO, 4), 466 (M^+ − 2CO, 80), 438 (M^+ − 3CO, 63), 410 (M^+ − 4CO, 95), 382 (M^+ − 5CO, 71), 354 (M^+ − 6CO, 100), 326 (33), 310 (10), 308 (12), 193 (7), 179 (7), and 83 (15); mp (benzene) 55–56 °C; HRMS (EI, 12 eV, DIP) calcd for $C_{19}H_{20}O_8Co_2$ 493.9822 (M^+ − CO), found 493.9846.

8c: IR (KBr) 2980, 2950, 2945, 2910, 2890, 2100, 2060, 2025, 1995, 1975, 1705, 1470, 1455, 1380, 1085, 1040, 1025, 960, and 950; MS (EI, 12 eV, 30 °C, DIP), *m/e* (%) 494 (M^+ − CO, 3), 466 (M^+ − 2CO, 46), 438 (M^+ − 3CO, 41), 410 (M^+ − 4CO, 100), 382 (M^+ − 5CO, 54), 354 (M^+ − 6CO, 73), 326 (20), 193 (8), 179 (8), and 83 (20); mp (*n*-hexane) 90–91 °C; HRMS (EI, 12 eV, DIP) calcd for $C_{19}H_{20}O_8Co_2$ 493.3822 (M^+ − CO), found 493.9831.

8d: IR (KBr) 2990, 2980, 2975, 2930, 2890, 2100, 2055, 2030, 2000, 1970, 1710, 1480, 1460, 1450, 1380, 1090, 1050, 1025, 975, and 955; MS (EI, 12 eV, 30 °C, DIP), *m/e* (%) 494 (M^+ − CO, 3), 466 (M^+ − 2CO, 53), 438 (M^+ − 3CO, 46), 410 (M^+ − 4CO, 100), 382 (M^+ − 5CO, 70), 354 (M^+ − 6CO, 97), 326 (27), 193 (18), 180 (9), 179 (18), 165 (8), 154 (8), 152 (10), 125 (8), 85 (7), and 83 (45); mp (*n*-hexane) 78–79 °C; HRMS (EI, 12 eV, DIP) calcd for $C_{19}H_{20}O_8Co_2$ 493.9822 (M^+ − CO), found 493.9804.

(2*R,3*S**,6*R**,7*S**,1*S**)- and (2*R**,3*S**,6*R**,7*S**,1′*R**)-2,7-Dimethyl-3,6-epoxy-2-(1-hydroxy-2-propyn-1-yl)cycloheptan-1-one (10a–b).** Fraction III (formed by hydroxylated cobalt complexes) of the alkylation product of **4** was demetalated with CAN by the same method described for **8a–d**, followed by flash column chromatography over silica gel (100 g of SiO_2/g of substrate, pentane–ether, 20/80), to afford 0.2 g of a white crystalline mixture (1:1.5 by ^1H NMR) of two inseparable diastereoisomers **10a** and **10b**: IR (KBr) 3600–3300, 3260, 2965, 2930, 2870, 2360, 2110, 1710, 1465, 1445, 1380 1190, 1165, 1110, 1050, 1040, 1020, 975, 945, 930, and 900; MS (EI, 70 eV, DIP), *m/e* (%) 208 (M^+, 3) 191 (20), 154 (23), 135 (30), 125 (20), 109 (30), 93 (50), 82 (30), 69 (40), and 55 (HOCHC=CH, 100); HRMS (EI, 70 eV, DIP) calcd for $C_{12}H_{16}O_3$ 208.1095, found 208.1099; ^1H NMR ($CDCl_3$) (**10a**) δ 4.79 (dd, J_1 = 2.2, J_2 = 8.6, 1 H, H1′), 4.73 (d, J = 7.6, 1 H, H3), 4.50 (br dd, J_1 = 4.5, J_2 = 6.0, 1 H, H6), 3.22 (d, J = 8.6, 1 H, OH), 2.91 (dqq, J_1 = 4.5, J_2 = 0.9, J_3 = 6.7, 1 H, H7), 2.51 (d, J = 2.2, 1 H, H3′), 1.80 (m, $W_{1/2}$ = 70 Hz, 4 H, H4, H5), 1.03 (s, 3 H, H8), and 0.96 (d, J = 6.7, 3 H, H9); (**10b**) 5.22 (dd, J_1 = 2.2, J_2 = 6.0, 1 H, H1′), 4.44 (br d, J = 7.3, 1 H, H3), 4.50 (br dd, J_1 = 4.6, J_2 = 5.9, 1 H, H6), 2.39 (d, J = 6.1, 1 H, OH), 3.04 (br dq, J_1 = 4.6, J_2 = 6.6, 1 H, H7), 2.57 (d, J = 2.2, 1 H, H3′), 1.80 (m, $W_{1/2}$ = 70 Hz, 4 H, H4 and H5), 1.07 (s, 3 H, H8), and 0.97 (d, J = 6.6, 3 H, H9).

Isomerization of 8a–d by $BF_3{\cdot}OEt_2$/ClSiMe$_3$. Pure isomer **8** (100 mg, 0.19 mmol) was placed as a solid in a 5-mL flask fitted with a rubber septum. The system was pumped and back filled with N_2 three times, 1 mL of dry CH_2Cl_2 was added by syringe, and the system cooled down to −78 °C. At that point 0.03 mL (0.29 mmol) of freshly distilled $BF_3{\cdot}OEt_2$ and 0.04 mL (0.29 mmol) of C:SiMe$_3$ were added by a microsyringe. After addition the reaction mixture was allowed to reach −46 °C and was kept under these conditions for 3 h. Solvent and remaining reagents were removed over high vacuum, and the crude mixture was dissolved in ether and filtered through a short pad of neutral alumina and finally stripped of solvent and weighed. The resulting crude mixture was analyzed by ^1H NMR in C_6D_6 and by TLC. The experiment was performed with every diastereoisomer independently, and the results provided in eq 4–7. Mass recoveries were as follows: from **8a**, 50%; from **8b**, 45%; from **8c**, 59% from **8d**, 37%.

Alkylation of 4 by Acetal Complex 5 Promoted by $BF_3{\cdot}Et_2O$. (a) One gram (4.4 mmol) of **4a,b** and 2.8 g (6.6 mmol) of **5** dissolved in 50 mL of anhydrous CH_2Cl_2 were cooled to −78 °C under N_2. $BF_3{\cdot}OEt_2$ (1.6 mL, 13.2 mmol) was added at once by syringe, and the reaction mixture was kept under these conditions for 3 h (monitoring by TLC every 30 min), quenched with aqueous $NaHCO_3$/ice, and washed twice with same and brine. The organic solution was dried over anhydrous $MgSO_4$ and concentrated to dryness, at room temperature, resulting in 3.5 g of a crude mixture formed by **3a–c**, **4a–b**, **5**, **7**, and decomposition products, but nothing at all of **8a–d**.

(b) When the reaction was performed at −46 °C but under the same other conditions, only a 10% conversion of starting material was observed after 3 h.

(c) The same reaction at 0 °C gave a 100% conversion of starting material after 3 h and a 50% yield of the diastereoisomeric mixture **8a–d** in a ratio of 1.03/1.48/2.64/1.00 (by ^1H NMR).

Demetalation of 8a–d: 2,7-Dimethyl-3,6-epoxy-2-(1-ethoxy-2-propyn-1-yl)cycloheptan-1-one (11a–d). The mixture of complexes **8a–d** (23 g, 44.2 mmol) dissolved in 300 mL of dry acetone containing 0.5 mL of Et_3N was treated with ceric ammonium nitrate (121 g, 221 mmol) portionwise at room temperature with vigorous stirring until CO evolution ceased, at which time the mixture turned from dark red to orange. The crude mixture was stripped of solvent and quenched with 300 mL of ice containing Et_3N (10 mL). After being shaken vigorously, the mixture was divided in four portions (to avoid emulsions), and each portion was extracted three times with ether in a 2-L addition funnel. All ethereal fractions were combined together and washed

Table III. Crystal Data for 8c and 8d

	8c	8d
mol formula	$C_{20}H_{20}O_9Co_2$	$C_{20}H_{20}O_9Co_2$
mol weight (g mol^{-1})	522.24	522.24
temp for data collect. (K)	295 ± 2	158 ± 2
crystal size (mm)	0.18 × 0.31 × 0.35	0.25 × 0.35 × 0.40
radiation (monochromated)	λ (Mo Kα)	λ(MoKα) = 0.71069 Å
system	triclinic	monoclinic
space group	$P\bar{1}$	$P2_1/c$
cell dimensions:		
a (Å)	8.591 (4)	7.697 (2)
b (Å)	11.327 (5)	19.106 (6)
c (Å)	12.221 (6)	14.517 (6)
α (deg)	86.19 (3)	90
β (deg)	78.01 (4)	91.52 (3)
γ (deg)	73.14 (3)	90
volume (Å^3)	1113.3	2134.3
Z	2	4
density (calcd) (g cm^{-3})	1.558	1.625
data collect. range	$3° < 2\theta < 50°$	$3 < 2\theta < 56°$
total reflns measured	3908 ($\pm h,\pm k,l$)	5135 ($\pm h,k,l$)
reflns used [$I > 2\sigma(I)$]	3114	4350
$R = \sum\|\|F_o\| - \|F_c\|\|/\sum\|F_o\|$	0.029	0.026
$R_w = [\sum w(\|F_o\| - \|F_c\|)^2/\sum wF_o^2]^{1/2}$	0.043	0.036
ρ_{max} in the final diff map (Å^{-3})	0.41	0.62

Table IV. Selected Bond Lengths (Å) and Bond Angles (deg) (std deviation, σ for last digit)

	8c	8d
C(2′)–C(3′)	1.324 (3)	1.336 (2)
C(1′)–C(2′)	1.493 (3)	1.518 (2)
C(1′)–C(2)	1.570 (3)	1.555 (2)
C(1′)–O(12)	1.419 (3)	1.423 (2)
C(1)–C(2)	1.535 (3)	1.546 (2)
C(2)–C(3)	1.551 (4)	1.542 (2)
C(2)–C(8)	1.524 (4)	1.530 (2)
C(1)–C(7)	1.517 (4)	1.523 (2)
C(6)–C(7)	1.525 (5)	1.536 (2)
C(7)–C(9)	1.523 (5)	1.532 (2)
C(6)–O(10)	1.437 (4)	1.443 (2)
C(5)–C(6)	1.522 (5)	1.526 (2)
C(3)–C(4)	1.542 (4)	1.543 (2)
C(3)–O(10)	1.428 (3)	1.436 (2)
C(1′)–C(2′)–C(3′)	145.2 (2)	143.9 (1)
C(2′)–C(1′)–O(12)	110.2 (2)	110.4 (1)
C(2)–C(1′)–O(12)	107.0 (2)	108.6 (1)
C(2)–C(1′)–C(2′)	115.6 (2)	112.6 (1)
C(1)–C(2)–C(1′)	110.8 (2)	107.9 (1)
C(1′)–C(2)–C(3)	105.9 (2)	107.9 (1)
C(1′)–C(2)–C(8)	110.4 (2)	110.7 (1)
C(1)–C(2)–C(3)	107.5 (2)	108.0 (1)
C(1)–C(2)–C(8)	111.1 (2)	109.1 (1)
C(3)–C(2)–C(8)	111.0 (2)	113.0 (1)
C(1)–C(7)–C(9)	111.1 (2)	110.0 (1)
C(6)–C(7)–C(9)	111.8 (3)	111.4 (1)

twice with $NaHCO_3$ (0.5 M) and brine. Finally the ethereal solution was dried over anhydrous $MgSO_4$, filtered through a short pad of neutral alumina, and concentrated, giving 9 g of a light yellow crystalline crude mixture. This product was submitted to a flash column chromatography over silica gel (20 g of SiO_2/g of substrate), isolating by hexane–ether, 30/70, 8.3 g (80% yield) of a white crystalline product containing a diastereomeric mixture **11a–d** (9/36/47/8 by NMR). Working on a smaller scale it is possible to obtain a 95% yield: IR (KBr) 3260, 2980, 2970, 2870, 2110, 1710, 1450, 1380, 1340, 1250, 1200, 1140, 1090, 1030, 1020, 950, 930, 900, and 840; mp 59–65 °C (hexane); HRMS (EI, 70 eV, DIP) calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1416; MS (EI, 70 eV, GC/MS: t_R(b) 10.6 min, t_R(c) 10.9 min, t_R(d) 10.3 min).

11a: ^{1}H NMR ($CDCl_3$) δ 4.86 (d, J = 2.2, 1 H, H1′), 4.47 (br dd, unresolved, 1 H, H-C6), 4.54 (d, J = 6.8, 1 H, H3), 3.84 (dq, J_1 = 2.2, J_2 = 71, 1 H, H1″), 3.50 (dq, J_1 = 2.2, J_2 = 7.1, 1 H, H1″), 2.80 (br dq, J_1 = 4.9, J_2 = 6.7, 1 H, H7), 2.37 (d, J = 2.2, 1 H, H3′), 2.20–1.60 (m, $W_{1/2}$ = 100 Hz, 4 H, H4 and H5), 0.93 (d, J = 6.7, 3 H, H9), 1.24 (t, J = 7.1, 3 H, H2″), 1.05 (s, 3 H, H8); GC/MS 80 °C, 2 min, 10 °C/min, 270 °C; t_R 11.1 min, m/e (%) 236 (M$^+$, 0.3), 221 (M$^+$ – CH_3, 3), 207 (M$^+$ – Et, 4), 193 (M$^+$ – CO – Me, 23), 191 (M$^+$ – EtO, 2), 180 (12), 179 (24), 165 (12), 152 (11), 93 (20), 91 (13), and 83 (100).

11b: ^{1}H NMR ($CDCl_3$) δ 4.98 (d, j = 2.0, 1 H, H1′), 4.46 (br dd, unresolved, 1 H, H6), 4.55 (d, J = 7.1, 1 H, H3), 3.76 (dq, J_1 = 2.5, J_2 = 7.1, 1 H, H1″), 3.38 (dq, J_1 = 2.5, J_2 = 7.1, 1 H, H1″), 2.92 (br dq, J_1 = 4.6, J_2 = 6.7, 1 H, H7), 2.51 (d, J = 2.0, 1 H, H-C3′), 2.20–1.60 (m, $W_{1/2}$ = 100 Hz, 4 H, H4 and H5), 0.93 (d, J = 6.7, 3 H, H9), 1.11 (t, J = 7.1, 3 H, H2″), 1.07 (s, 3 H, H8); GC/MS [t_R 10.6 min], m/e (%) 236 (M$^+$, 0.2), 221 (M$^+$ – CH_3, 2), 207 (M$^+$ – Et, 3), 193 (M$^+$ – CO – Me, 15), 191 (M$^+$ – EtO, 2), 180 (8), 179 (16), 107 (13), 93 (22), 91 (17), and 83 (EtOCH≡CH, 100).

11c: ^{1}H NMR ($CDCl_3$) δ 4.82 (d, J = 2.1, 1 H, H1′), 4.44 (br dd, unresolved, 1 H, H6), 4.31 (d, J = 6.6, 1 H, H3), 3.84 (dq, J_1 = 2.2, J_2 = 7.1, 1 H, H1″), 3.50 (dq, J_1 = 2.2, J_2 = 7.1, 1 H, H1″), 2.28 (q, J = 7.6, 1 H, H7), 2.41 (d, J = 2.1, 1 H, H3′), 2.20–1.60 (m, $W_{1/2}$ = 100 Hz, 4 H, H4 and H5), 1.29 (d, J = 7.6, 3 H, H9), 1.23 (t, J = 7.1, 3 H, H2″), and 1.07 (s, 3 H, H8); GC/MS [t_R 10.6 min], m/e (%) 236 (M$^+$, 0.2), 221 (M$^+$ – CH_3, 3), 207 (M$^+$ – Et, 4), 193 (M$^+$ – CO – Me, 23), 191 (M$^+$ –EtO, 2), 190 (M$^+$ – EtOH, 2), 180 (14), 139 (25), 165 (13), 152 (14), 151 (10), 109 (16), 107 (21), 93 (32), 91 (21), and 83 (EtOCHC≡CH, 100).

11d: ^{1}H NMR ($CDCl_3$) δ 4.94 (d, J = 2.1, 1 H, H1′), 4.44 (br dd, unresolved, 1 H), 4.33 (d, J = 6.3, 1 H, H3), 3.76 (eq, J_1 = 2.5, J = 7.1, 1 H, H1″), 3.38 (dq, J_1 = 2.5, J_2 = 7.1, 1 H, H1″), 2.30 (q, J = 7.6, 1 H, H7), 2.49 (d, J = 2.0, H3′), 2.20–1.60 (m, $W_{1/2}$ = 100 Hz, 4 H, H4 and H5), 1.29 (d, J = 7.6, 3 H, H9), 1.13 (t, J = 7.1, 3 H, H2″), and 1.10 (s, 3 H, H8); GC/MS [t_R 10.9 min], m/e (%) 236 (M$^+$, 0.2), 221 (M$^+$ – CH_3, 2), 207 (M$^+$ – Et, 3), 193 (M$^+$ – CO – Me, 15), 191 (M$^+$ – EtO, 2), 190 (M$^+$ – EtOH, 2), 179 (20), 152 (10), 121 (10), 111 (10), 110 (10), 109 (15), 107 (20), 93 (20), 91 (20), and 83 (EtOCHC≡CH, 100).

X-ray Analysis of 8c and 8d. Single crystals of **8c** and **8d** suitable for X-ray analysis were obtained in n-hexane at –20 °C under CO. The crystals selected were mounted on a glass fiber, and the data were collectd on an Enraf-Nonius CAD-4 automatic X-ray diffractometer fitted with a liquid N_2 low temperature device, using Mo Kα radiation (λ 0.71069 Å) by the methods standard in this laboratory.[24] Unit cell dimensions were refined by least-squares analysis of the diffractometer angular setting of 25 well-centered reflections (2θ range = 30–40°). The data were corrected for Lorentz and polarization effects; no absorption correction was applied since it was deemed to be negligible. The atomic scattering factors were obtained from ref 25. Both structures were solved by the heavy atom method and refined by least-squares analysis (SHELX-76),[26] miminizing $\Sigma w(|F_o| - |F_c|)^2$. All the non-hydrogen atoms were refined anisotropically, and all the hydrogen atoms were refined isotropically. Data regarding collection and refinement are summarized in Table III. Selected bond angles and lengths are given in Table IV.

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Supplementary Material Available: Complete listings of bond lengths and angles, thermal parameters, and atomic coordinates for **8c** and **8d** (23 pages). Ordering information is given on any current masthead page.

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