Synthesis of 11-Oxatricyclo[5.3.1.$0^{2,6}$]undecane Derivatives via Organometallic Cyclizations

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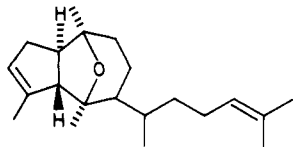
A number of substituted and functionalized derivatives of the title compounds have been prepared by $Co_2(CO)_8$-catalyzed cocyclizations of alkynes with various 8-oxabicyclo[3.2.1]oct-6-ene derivatives. The latter, in turn, were ultimately derived from the $Fe_2(CO)_9$-promoted cyclizations of furans with tetrabromoacetone. The success of the cobalt cyclization process is found to be dependent upon the steric environment of the alkene. Regio- and stereochemical preferences in the reaction are interpreted as resulting from steric interactions as well, and a mechanism consistent with these observations is formulated.

The 11-oxatricyclo[5.3.1.$0^{2,6}$]undecane ring system appears in at least three natural products, the algal diterpene dictyoxide (**1**)[1] and the furanosequiterpenoid fungal metabolites furanether A (**2**) and B (**3**).[2] Although little



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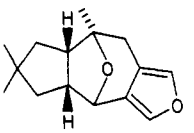

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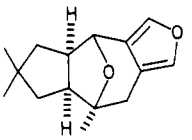

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synthetic work aimed at these types of systems has been reported, inadvertant formation of the 2,6-oxygen-bridged hydrazulene skeleton has been described in connection with synthetic efforts in the guaianolide area.[3]

We report here an efficient synthetic entry to highly functionalized derivatives of this ring system, as well as studies aimed at ascertaining their potential as precursors for synthesis of several types of natural products.

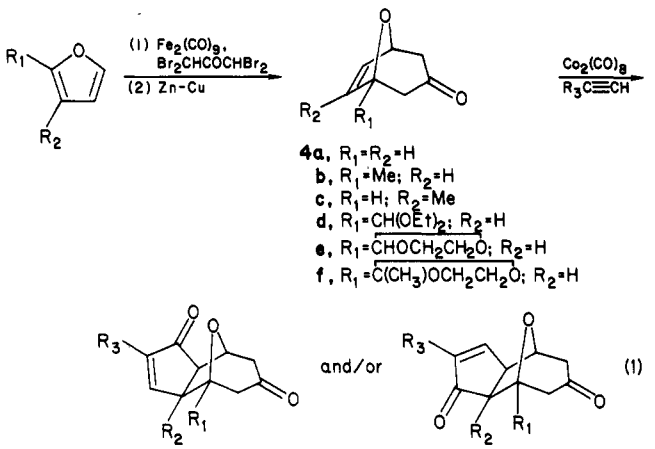
Results and Discussion

Strategic Considerations. As a general entry into the system we felt that octacarbonyldicobalt-catalyzed cyclization of 8-oxabicyclo[3.2.1]oct-6-ene derivatives **4** with alkynes would be suitable. It seemed reasonable to expect that the double bond of the bicyclic would possess reactivity in this process similar to that demonstrated by other moderately strained alkenes, e.g., norbornene and norbornadiene, in the work of Pauson and Khand.[4] The bicyclic precursors could, in turn, be obtained through cyclization of furans with polyhalogenated ketones under reducing conditions. For the latter process the Noyori method using nonacarbonyldiiron was chosen due to its demonstrated wide scope.[5] Equation 1 summarizes the general plan.

Table I. DIBAL Reduction of Ketones 4[a]

ketone	endo/exo product ratio
4a	85:15
4b	80:20
4d	65:35
4e	65:35
4f	75:25

[a] Conditions: 1:1 THF–hexane; −78 °C.



In the course of this study several basic questions were addressed: functional group tolerance of both cyclization reactions, steric effects of R_1 and R_2 on the cobalt cyclization, regioselectivity of the cobalt cyclization as a function of R_1, and general aspects of functional group interconversions on both the bicyclic and tricyclic ring systems. The latter point was of special interest because this general synthetic approach affords products in which virtually every position is either functionalized or adjacent to a functional group. Potentially, therefore, these could serve as excellent precursors to highly functionalized guaianolide or pseudoguaianolide systems.

Preparation of 8-Oxabicyclo[3.2.1]oct-6-ene Derivatives. The unsubstituted,[5a] 1-methyl,[6] and 6-methyl[7] ketones (**4a**, **4b**, and **4c**, respectively) were prepared by literature methods. Acetals **4d** and **4e** were prepared in

(1) Amico, V.; Oriente, O.; Piatelli, M.; Tringali, C. *Phytochemistry* **1979**, *18*, 1895.
(2) Battaglia, R.; De Bernardi, M.; Fronza, G.; Mellerio, G.; Vidari, G.; Vita-Finsi, P. *J. Nat. Prod.* **1980**, *43*, 319. Also see: Sterner, O.; Bergman, R.; Kihlberg, J.; Oluwadiya, J.; Wickberg, B.; Vidari, G.; De Bernardi, M.; De Mardis, F.; Fronza, G.; Vita Finzi, P. *J. Org. Chem.* **1985**, *50*, 950.
(3) Rigby, J. H.; Wilson, J. Z. *J. Am. Chem. Soc.* **1984**, *106*, 8217.
(4) (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977. (b) Khand, I. U.; Pauson, P. L. *J. Chem. Soc., Perkin Trans. 1* **1976**, 30. (c) Pauson, P. L.; Khand, I. U. *Ann. N. Y. Acad. Sci.* **1977**, *295*, 2.
(5) (a) Takaya, H.; Makino, S.; Hayakama, Y.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1765. (b) Takaya, H.; Hayakama, Y.; Makino, S.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1778.
(6) Sato, T.; Watanabe, M.; Noyori, R. *Tetrahedron Lett.* **1979**, 2897.
(7) Sato, T.; Kobayaski, H.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1971.

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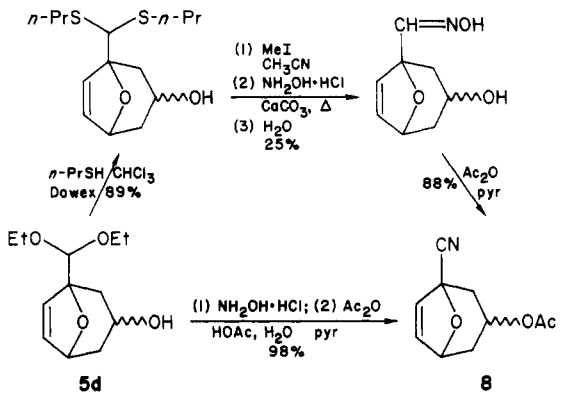
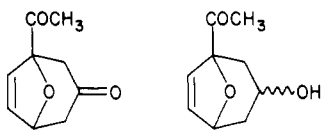
Scheme I



30% and 15% yields, respectively, from the corresponding furfural derivatives and tetrabromoacetone by using the Noyori methodology. In addition, ketal **4f** was similarly obtained in 16% yield from the ethylene ketal of 2-acetylfuran (Cf. ref 8). Although the yields of these three compounds are poor, the procedure is still practical due to its simplicity and the availability of the starting materials.

A number of functional group transformations were carried out on ketones **4a–f**. We felt that ketone reduction prior to cobalt cyclization would provide more clear-cut and useful functional group differentiation later on. Therefore, the alcohols (**5a,b,d–f**) corresponding to **4a,-b,d–f** were prepared. It was incidentally found that the best stereoselectivity upon reduction resulted from the use of diisobutylaluminum hydride at −78 °C (Table I).

Also of potential interest was the amenability of the protected carbonyl groups in **4d–f** and **5d–f** to selective refunctionalization. Hydrolyses of the ketal groups in **4f** and **5f** were readily achieved with 10% H_2SO_4 in dimethoxyethane, affording diketone **6** and keto alcohol **7** in yields of 73% and 86%, respectively. In contrast, we



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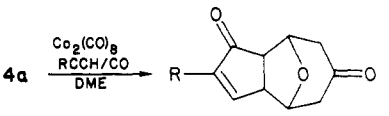
had no success in generating free aldehydes from **4d**, **4e**, **5d**, or **5e** by a number of standard methods. Several attempts using aqueous acids under several sets of homogeneous or heterogeneous conditions gave only varying ratios of recovered starting materials and olefinic, furanoid, or polymeric decomposition products. Nor was any success to be found using ketal exchange procedures. The obviously limited stability of these aldehydes led us to attempt direct functional group interconversions on the diethyl acetal **5d** itself, bypassing the aldehyde altogether. Several sequences were investigated, two of which are summarized in Scheme I. A multistep procedure involving transketalization with 1-propanethiol, oximation, and elimination afforded low yields of nitrile acetate **8**. Subsequently, conditions for a very efficient one-pot conversion were empirically established: reaction of **5d** with 3.7 equiv of hydroxylamine hydrochloride in acetic acid leads only to slow esterification of the alcohol at room temperature. However, addition of 20 equiv of water results in rapid conversion to the oxime, which, upon gentle heating with acetic anhydride in pyridine, is converted to **8** in nearly quantitative yield. Successful preparation of **8** provides a potential leaving group at C(1) as well as access to carboxylic acid derivatives at this position.

Finally, Baeyer–Villiger oxidation of keto alcohol **7** was attempted. Baeyer–Villiger oxidation of an analogue of **7** lacking the alcohol and alkene functionality has been reported,[8] thus providing ready access to systems in which the oxygen bridge has been opened. Unfortunately, the ketone of **7** is singularly resistant to attack by peracids. Using buffered MCPBA under conditions that are known to usually be selective for ketones over strained double bonds[9] only olefin epoxidation is observed. Even warming in the presence of excess peracid fails to affect the ketone. Presumably steric effects slow down attack at the carbonyl group, but the major problem probably lies in the combined inductive effects of the remaining functional groups in the molecule, reducing the migratory aptitude of the bicyclic system as a whole.

In summary, this work resulted in the preparation of 14 derivatives of 8-oxabicyclo[3.2.1]oct-6-ene, potential substrates for the cobalt carbonyl promoted cyclopentenone synthesis.

Cyclization of 8-Oxabicyclo[3.2.1]oct-6-ene Derivatives with Alkynes and CO. A. Symmetrical 8-Oxabicyclo[3.2.1]oct-6-en-3-ones. The successes of Pauson and Khand[2] at reacting norbornadiene with alkynes, carbon monoxide, and cobalt octacarbonyl to give cyclopentenones led us to explore the cyclization chemistry of the related 8-oxabicyclo[3.2.1]oct-6-enyl system. The potential for sufficient reactivity of this system was supported by the work of Houk[10] who found that bicyclo[3.2.1]oct-6-ene did indeed show reactivity toward conventional cycloaddition reactions comparable with that of norbornene. Successful cyclization would provide a rapid entry into the 11-oxatricyclo[5.3.1.$0^{2,6}$]undecyl ring system.

When a solution of **4a** in DME was heated with 1 equiv of cobalt octacarbonyl under 1 atm of a 1:1 mixture of acetylene and carbon monoxide, we obtained a solid product **9a** in 45% yield (eq 2). By analogy with reactions



(2)

9a, R = H
9b, R = C_6H_5
9c, R = n-C_4H_9

of norbornadiene, we anticipated the formation of an exo ring-fused product. The NMR spectrum of **9a** supported this assignment. The spectrum displayed doublets of doublets at δ 7.61 and 6.27 characteristic of the β- and α-protons of a cyclopentenone and a multiplet at δ 2.9–2.4 for the other five protons α to the ketones. Signals at δ 4.80 (br d) and 4.53 (br d) and at δ 3.38 (m) corresponded to the two oxygen bridgehead protons and the cyclopentenone γ-proton, respectively. Decoupling experiments revealed that the coupling constants between the cyclopentenone γ- and δ-hydrogens and the oxygen bridgehead hydrogens were very small, consistent with an exo ring fusion where the dihedral angles between the relevant C–H bonds approach 90°.

The reactivity of olefin **4a** with substituted acetylenes in the presence of cobalt octacarbonyl was also studied. Reaction of **4a** with 1 equiv of phenylacetylene and cobalt octacarbonyl under 1 atm of carbon monoxide gave α-

(8) White, J. D.; Fukuyama, Y. *J. Am. Chem. Soc.* **1979**, *101*, 226.

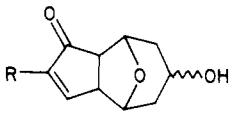
(9) Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675.

(10) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Mareda, J.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4974.

phenyl enone **9b** (42%). The position of the phenyl group exclusively α to the carbonyl, in accord with Pauson's findings for the norbornyl system, was clear from the absence of a signal for an enone α-hydrogen. The enone β-hydrogen was visible as a doublet partially buried beneath the phenyl multiplet.

A reaction of **4a** with 1-hexyne proceeded in comparable yield (40%) to give the *n*-butyl analogue **9c**.

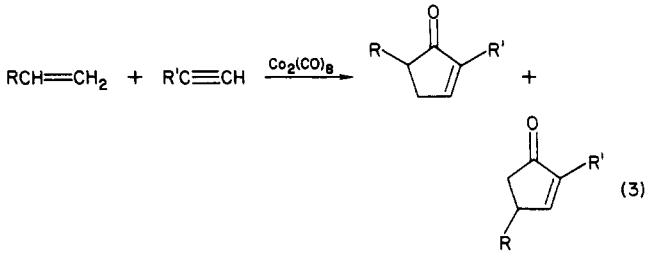
B. 8-Oxabicyclo[3.2.1]oct-6-en-3-ols. The ability of the cobalt-mediated cyclization to proceed even in the presence of a free hydroxyl group was demonstrated by the reactions of hydroxy olefin **5a** with acetylene, phenylacetylene, and 1-hexyne. When **5a** was reacted with acetylene under the conditions described above, enone **10a** was obtained in 52% yield. Similarly, reaction with phenylacetylene and 1-hexyne gave enones **10b** (57%) and **10c** (43%), respectively. As was found for compounds **9** the



10a, R=H
10b, R=C_6H_5
10c, R=*n*-C_4H_9

NMR spectra of compounds **10** failed to display any substantial coupling between the oxygen bridgehead proton and the cyclopentenone ring fusion protons, strongly suggesting that the products again contained exclusively the exo ring fusion.

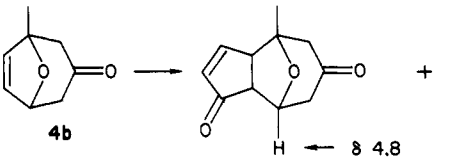
C. Unsymmetrically Substituted 8-Oxabicyclo[3.2.1]oct-6-ene Derivatives. Pauson and Khand[11] found that the cyclization of acetylenes with acyclic olefins containing simple alkyl substituents gave mixtures of γ- and δ-substituted products in approximately equal amounts (eq 3).



(3)

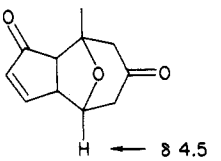
When we reacted methyl substituted olefin **4c** with acetylene, carbon monoxide, and cobalt octacarbonyl at 65 °C in DME, an NMR of the crude product mixture after filtration through silica indicated the formation of several enone containing products. Further investigation, however, revealed that none of the products incorporated **4c**. Instead, these products were found to be derived from the cyclization of acetylene and carbon monoxide in various proportions. The formation of small amounts of cyclic enones from acetylene, carbon monoxide, and cobalt octacarbonyl, also observed in other cyclizations described below, has been investigated fully and reported in detail elsewhere.[12] Evidently steric hindrance renders the trisubstituted double bond incapable of competing with a second acetylene for a coordination site on the dicobalt–monoacetylene catalyst precursor. By way of comparison, note that trisubstituted alkenes do participate in intramolecular versions of this cyclopentenone synthesis.[13]

The reaction of the less hindered **4b** under the same conditions was more successful. The crude product was concentrated onto silica and placed at the top of a silica gel column. Elution with hexane removed nonpolar organometallic species, and then elution with ether gave recovered **4b** (56%) and two isomeric product enones in an approximately 3:2 ratio in 21% combined yield. Taking the amount of recovered starting material into account, the products were formed in 49% yield at 44% conversion. An NMR of the major isomer displayed a broad doublet at δ 4.8, and the minor isomer a corresponding doublet at δ 4.5, for the residual proton at the oxygen bridgehead.



4b H ← δ 4.8

11a, major



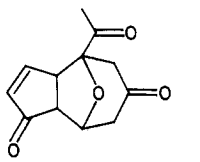
H ← δ 4.5

11s, minor

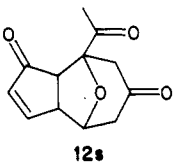
The lack of a significant coupling between the ring fusion and oxygen bridgehead protons makes it difficult to definitely assign the isomeric bridgehead hydrogens relative to the enone carbonyl. A tentative assignment of structure **11a** to the major isomer was made on the basis of an expected deshielding effect of the carbonyl group on the bridgehead hydrogen. This was later confirmed crystallographically (vide infra).

Attempts to cyclize several of the other bridgehead-substituted alkenes in this series met with mixed results. An attempt to cyclize ketal **4f**, containing a much bulkier substituent at the bridgehead position, resulted in an 85% recovery of this relatively stable starting material, with no evidence for product formation. Similarly, ethylene acetal **4e** failed to give useful amounts of cyclized products. Although traces (<1%) of product could be detected by NMR, only starting material (40%) and a complex mixture of aromatic decomposition products were recovered.

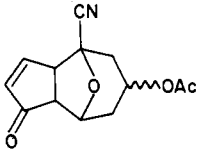
The less hindered acetyl derivative **6** gave somewhat more favorable results when subjected to the usual cyclization conditions. Chromatographic workup of the crude reaction mixture gave recovered **6** (28%), and a 3:1 ratio of the two isomeric products **12a** (bridgehead proton δ 4.8) and **12s** (bridgehead proton δ 4.6) in 17% combined yield.



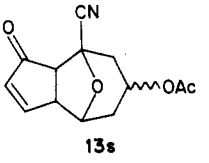
12a



12s



13a



13s

(11) Khand, I. U.; Pauson, P. L. *J. Chem. Res., Miniprint* **1976**, 0168.
(12) Schore, N. E.; La Belle, B. E.; Knudsen, M. J.; Hope, H.; Xu, X.-J. *J. Organomet. Chem.* **1984**, *272*, 435.
(13) Knudsen, M. J.; Schore, N. E. *J. Org. Chem.* **1984**, *49*, 5025.

Table II. Results of Cobalt-Catalyzed Cyclization Reactions

alkene[a]	alkyne	product(s)	yield,[b]	anti/syn ratio[c]
4a	HC≡CH	**9a**	45	
	PhC≡CH	**9b**	42	
	n-BuC≡CH	**9c**	40	
5a	HC≡CH	**10a**	52	
	PhC≡CH	**10b**	57	
	n-BuC≡CH	**10c**	43	
4b	HC≡CH	**11a/s**	21 (49)	3:2
6	HC≡CH	**12a/s**	17 (24)	3:1
8	HC≡CH	**13a/s**	40 (68)	2:1

[a] Alkenes **4c**, **4e**, and **4f** gave little or none of the expected cyclopentenone product. [b] Isolated yields; yields in parentheses are based on unrecovered starting material. [c] Refers to relative disposition of enone carbonyl and bridgehead substituent.

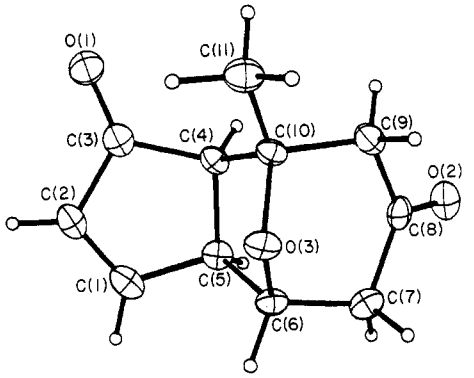


Figure 1. Computer-generated representation of **11s**.

Again, this NMR-based assignment was considered to be tentative, although it was supported in this case by NOE data obtained at 500 MHz. Proof of structure had to again rely on a crystallographic determination, presented in the next section.

The bicyclo[3.2.1]oct-6-enyl substrate with the smallest substituent other than hydrogen to be investigated was the nitrile **8**. This compound reacted surprisingly well under the standard cyclization conditions to give, after chromatographic workup on silica gel, a 40% combined yield of a 2:1 ratio of the two isomeric products **13a** and **13s**. In addition, 41% of the starting material was recovered. Based on consumed **8**, the yield was 68%. As in the cases of **11** and **12**, the NMR of the major isomer, assigned structure **13a**, displayed a signal for the oxygen bridgehead hydrogen downfield of the corresponding hydrogen of the minor isomer. Table II summarizes the results of all the cobalt cyclization reactions carried out in this study.

X-ray Crystal Structures of 11s and 12s. In order to unambiguously settle the regiochemical question posed by the products of cyclization of **4b**, **6**, and **8**, crystal structure determinations were carried out on two systems, the more readily crystallized minor isomers of **11** and **12** (assumed on the basis of NMR to have structures **11s** and **12s**). The decision to solve two structures was made to eliminate the possibility that the electronic difference between methyl (in **11**) and either acetyl (in **12**) or cyano (in **13**) might make spectroscopic generalization from a single structure risky.

In the event, the results in both cases confirmed the tentative assignments previously made. The minor isomer of **11** possesses the syn orientation **11s** with, as expected, an exo ring fusion and a typical half-chair conformation for the 4-pyranone portion of the tricyclic (Figure 1). Similar features were revealed for acetyl derivative **12s** as well (Figure 2). Noteworthy in both these structures is

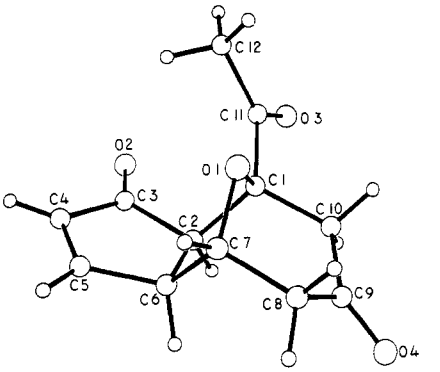
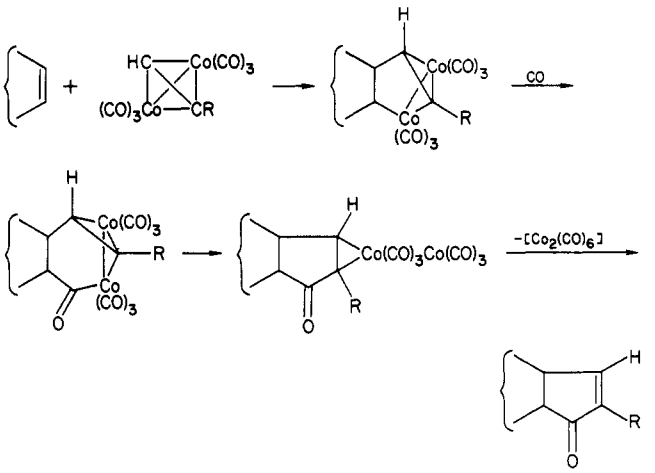


Figure 2. Computer-generated representation of **12s**.

Scheme II



the steric congestion between the bridgehead substituent and the enone carbonyl oxygen. Indeed, one of the hydrogens on C(11) of **11s** is within 2.60 Å of the enone oxygen. Although we do not have a structure of an anti regioisomer, the relatively close approach between the hydrogens on C(1) and C(6) of **11s** (2.64 Å) implies that substituents on C(6) experience a certain degree of crowding as well. These interactions certainly bear on our inability to isolate cyclization products from alkenes **4e** and **4f**. In fact, in the latter case models suggest that neither syn nor anti cyclization products can exist at all without severe distortion of the rather rigid tricyclic system (vide infra).

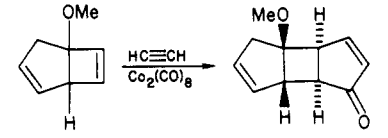
Regiochemical Considerations and the Cyclization Mechanism. The first step of the Pauson–Khand cyclopentenone synthesis is alkyne complexation to form the well-known hexacarbonyldicobalt–alkyne species. Although to our knowledge no intermediates have ever been either isolated or observed along the pathway from this complex to product, the stereo- and regiochemical preferences of this reaction may be accommodated by means of a reasonably straightforward working hypothesis. We suggest that the product-determining step is insertion of the alkene moiety into one of the formal alkyne carbon–cobalt bonds of the tetrahedrane-like cobalt–alkyne complex. This is followed by migratory insertion of CO into a metallocycle Co–C bond and reductive elimination (Scheme II).[14] This mechanism accounts for the well-known tendencies of this process to place the larger alkyne

(14) The identical mechanism has been formulated by Magnus on the basis of stereochemical results in intramolecular cyclizations: Magnus, P., personal communication. **Note added in proof**: see Magnus, P.; Principe, L. M. *Tetrahedron Lett.* **1985**, *26*, 4851.

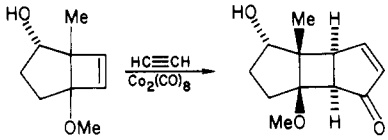
substituent α to the new enone carbonyl and to form the exo ring fusion with bicyclic alkenes. Both results arise naturally from insertion of the less hindered face of the alkene into the less hindered cobalt–carbon bond of the alkyne complex.

The mechanism also allows rationalization of the syn/anti preferences seen in the cyclizations of **4b**, **6**, and **8**. Considering only insertion at the exo face of the alkene, there are four modes of approach of $Co_2(CO)_6(HC{\equiv}CH)$ to the unsymmetrical substrate (Scheme III). Those marked syn-1 and syn-2 differ only in the orientation of the uninvolved, "back" carbon and cobalt atoms, a difference that has no ultimate effect on the organic product which is syn in either case. The two other approaches, anti-1 and anti-2, likewise are effectively indistinguishable, both leading to the anti product. The observed preference for anti products may be rationalized as resulting from steric interaction in the syn intermediates between the bridgehead substituent R and one of the three carbonyl groups on the nearby pseudooctahedral cobalt center. Although simple molecular models make this interaction appear to be quite severe, the actual anti/syn ratios imply that there is enough flexibility in the cobalt coordination sphere to reduce the relevant $\Delta\Delta G^{\ddagger}$ to the 0.3–0.6 kcal/mol range required by the results. The reason the reaction fails entirely for the bulkier R groups in **4e** and **4f** is presumably the additional pseudo-1,3-diaxial interaction in either anti intermediate, raising $\Delta G^{\ddagger}$ to the point that alkene insertion in either direction becomes noncompetitive with insertion of a second alkyne.

The regiochemical result found in these bicyclo[3.2.1]-oct-6-ene systems appears to be generalizable to other rigid bicyclic alkenes with unsymmetrical allylic substitution. In one particularly telling comparison, Pauson has found that diene **14** cyclizes with acetylene to give ketone **15** exclusively,[15] while we have carried out the same reaction with alkene **16**, obtaining **17** as the sole product.[16] In each case the larger of the two ring-fusion substituents winds up anti to the new enone carbonyl.[17]



14 15



16 17

Conclusions. Readily available derivatives of the 8-oxabicyclo[3.2.1]oct-6-ene ring system participate to varying extents in the $Co_2(CO)_8$-promoted cyclopentenone synthesis, leading to relatively complex, highly functionalized oxa-bridged hydrazulenes. When successful the reaction proceeds in moderate yields with predictable stereo- and regiochemical results. Current efforts are aimed at converting these compounds into several types of natural products and further exploring the generality and predictive value of the mechanistic hypotheses outlined above.

Experimental Section

General. Solvents. For procedures carried out under anhydrous conditions, tetrahydrofuran, ether, benzene, and dimethoxyethane were distilled from sodium benzophenone ketyl. Dichloromethane, hexane, and chloroform were dried over 4-Å molecular sieves before use. All other solvents were stored under argon and bubbled with argon immediately before use.

Reagents. Acetic anhydride and pyridine were dried by distillation and storage over molecular sieves. Diisobutylaluminum hydride in hexane (Aldrich), furan (Aldrich), Dowex 50W-X8 cation-exchange resin (Bio-Rad), dicobalt octacarbonyl (Pressure Chemical), furfural (Aldrich), 2-furaldehyde diethyl acetal (Aldrich), 2-acetylfuran (Aldrich), and 2-methylfuran (Aldrich) were used as received. 8-Oxabicyclo[3.2.1]oct-6-en-3-one (**4a**),[5a] 1-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**4b**),[6] and 6-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**4c**)[7] were prepared by the literature methods. Unless otherwise noted, other materials were obtained commercially and used without further purification.

Separation and Purification. Silica gel (Baker) for column chromatography was used as received. Commercially prepared silica gel columns (LiChroprep Si60, EM Reagents) were used for medium-pressure liquid chromatography with an FMI Lab Pump (Model RP SY), a Waters Differential Refractometer detection system (Model R403), and a Gilson Micro Fractionator. Other chromatographic separations were carried out on a Chromatotron (Harrison Research; centrifugally accelerated, radial, thin-layer chromatograph) using silica gel with calcium sulfate binder (E. Merck). Analytical thin-layer chromatography was done on fluorescent indicating silica gel sheets (Merck). Iodine was used to visualize nonchromatophoric bands.

Unless otherwise noted, all reactions were carried out under an atmosphere of dry argon. Organic product solutions were dried by stirring over anhydrous sodium sulfate under argon. Solutions were concentrated on a Büchi Rotavapor R rotary evaporator under a water aspirator vacuum. Purified reaction products were stored under argon.

Analysis. Melting points were determined with a Thomas Hoover Capillary melting point apparatus and are uncorrected. Analytical samples were purified by chromatography on a Chromatotron or MPLC.

Nuclear magnetic resonance spectra (^{1}H) were taken on a Varian EM-390 spectrometer. In addition, spectra of all compounds isolated were recorded at 360 or 500 MHz (Nicolet NT-360 and NM-500 instruments), confirming ≥98% purity in all cases.

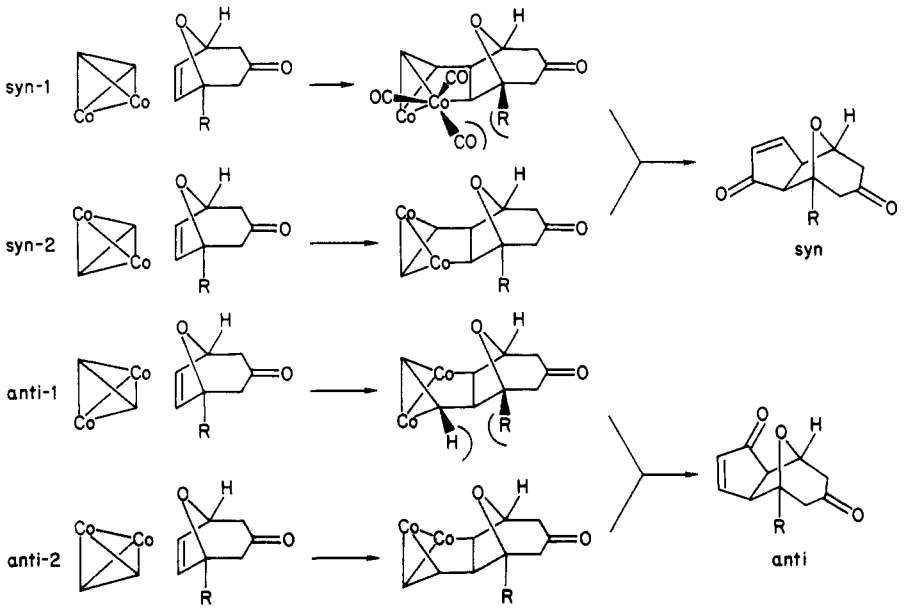
Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Significant NMR data are given in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constants (in hertz), and number of protons (by integrated intensity).

IR spectra were recorded on Beckman IR-8 or Perkin-Elmer 180 spectrophotometers. High-resolution mass spectral data were determined at the U.C. Davis Facility for Advanced Instrumentation or at the U.C. Berkeley Mass Spectrometry Facility. Microanalyses were performed by the facility at the University of California, Berkeley.

1-(Diethoxymethyl)-8-oxabicyclo[3.2.1]oct-6-en-3-one (4d). Following the general procedures of Noyori,[5] a mixture of tetrabromoacetone (22.79 g, 61 mmol), diiron nonacarbonyl (22.40 g, 61 mmol), and 2-furaldehyde diethyl acetal (12.00 g, 70 mmol) in 250 mL of benzene was stirred at 65 °C for 2 days. Water (250 mL) and ethyl acetate (150 mL) were added, the reaction mixture was filtered through Celite, and the layers were separated. The aqueous layer was extracted four times with 150 mL of ethyl acetate, and the combined organic layers were dried over sodium sulfate. Concentration gave a dark brown oil, which was reacted with zinc–copper (25 g) in 400 mL of a saturated solution of ammonium chloride in methanol for 2.5 h at room temperature. The reaction was quenched with saturated disodium EDTA (200 mL), filtered, and extracted four times with 100 mL of dichloromethane. The combined organic layers were dried over sodium sulfate and concentrated to give crude **4d** (2.91 g). Purification by chromatography on silica gel with a 1:1 mixture of ethyl acetate and hexane gave **4d** (2.39 g, 15%) as an oil: NMR

(15) Khand, I. U.; Pauson, P. L. *J. Chem. Res., Miniprint* **1977**, 0153.
(16) Schore, N. E.; Sampath, V., unpublished results.
(17) We recognize that the comparison between 14 and 16 is imperfect due to the other functional groups. However, both give exclusively exo cyclization, making it very unlikely that these remote groups can have a directing effect on the reaction.

Scheme III



($CDCl_3$, 90 MHz) δ 6.28 (s, 2 H), 5.15 (br d, J = 5 Hz, 1 H), 4.63 (s, 1 H), 4.0–3.6 (m, 4 H), 2.9–2.2 (m, 4 H), 1.6–1.2 (m, 6 H); IR (mineral oil) 1710 cm^{-1} (s); high-resolution mass spectrum, calcd for $C_{12}H_{18}O_4$ 226.1205, found 226.1201.

1-(2-Dioxolanyl)-8-oxabicyclo[3.2.1]oct-6-en-3-one (4e). A mixture of diiron nonacarbonyl (45.0 g, 0.124 mol), tetrabromoacetone (50.0 g, 0.134 mol), and 2-(2-furyl)-1,3-dioxolane[18] (20.0 g, 0.143 mol) in 300 mL of dry, oxygen-free benzene was stirred at 65 °C for 48 h. Saturated sodium bicarbonate (300 mL) and dichloromethane (300 mL) were added, the mixture was filtered, and the layers were separated. The organic layer was washed with saturated sodium bicarbonate (150 mL) and brine (150 mL), dried, and concentrated. Ammonium chloride saturated methanol (200 mL) and zinc–copper couple (50 g, 0.77 mol) were added, and the mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated Na_2EDTA (200 mL), dichloromethane (200 mL) was added, and the insoluble materials were removed by filtration through a pad of Celite. The organic layer was separated and the aqueous layer extracted five times with 200 mL of dichloromethane. The combined organic extracts were dried and concentrated. Chromatography on silica gel with a 10:10:0.1:0.1 mixture of ether–dichloromethane–ethyl acetate–methanol gave **4e** (7.32 g, 30% yield) as a viscous oil: NMR ($CDCl_3$, 90 MHz) δ 6.27 (dd, J = 7, 2 Hz, 1 H), 6.15 (d, J = 7 Hz, 1 H), 5.10 (d with additional fine splittings, J = 5 Hz, 1 H), 5.03 (s, 1 H), 4.00 (m, 4 H), 2.9–2.2 (m, 4 H); IR (mineral oil) 1710 cm^{-1}; high-resolution mass spectrum, calcd for $C_{10}H_{12}O_4$ 196.0735, found 196.0731.

1-(2-Methyl-2-dioxolanyl)-8-oxabicyclo[3.2.1]oct-6-en-3-one (4f). To a mixture of diiron nonacarbonyl (20.3 g, 55.8 mmol) and tetrabromoacetone (20.8 g, 55.8 mmol) was added 2-(2-furyl)-2-methyl-1,3-dioxolane[8] (7.20 g, 46.8 mmol) in 100 mL of benzene. The mixture was stirred overnight at 65 °C. Water (100 mL) and ethyl acetate (100 mL) were added, the solids were removed by filtration through a pad of Celite, and the pad was washed thoroughly with ethyl acetate. The organic layer was separated, dried, and concentrated to give a brown oil. The crude oil was reacted with excess zinc–copper couple in ammonium chloride saturated methanol (200 mL) at room temperature for 2 h. Saturated Na_2EDTA (200 mL) and dichloromethane (100 mL) were added, the mixture was filtered through a pad of Celite, and the organic layer was separated and dried. Concentration gave **4f** as a crude brown oil, which was extracted thoroughly with ether. The combined ether soluble material was concentrated to give unreacted acetylfuran ketal (1.309 g, 18% recovery), acetylfuran (0.760 g), and **4f** (1.339 g, 13% yield) as determined by NMR spectroscopy. Ketal **4f** was readily purified for further reactions by chromatography (Chromatotron) on silica gel with ether. An analytical sample was obtained by recrystallization from hexane: mp 59–60 °C; NMR ($CDCl_3$, 90 MHz) δ 6.10 (narrow m, 2 H), 5.02 (br d, J = 5 Hz, 1 H), 3.90 (narrow m, 4 H), 2.8–2.2 (m, 4 H), 1.27 (s, 3 H); IR (mineral oil) 1710 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.88; H, 6.69.

8-Oxabicyclo[3.2.1]oct-6-en-3-ol (5a). A solution of **4a** (0.25 g, 2.0 mmol) in 1 mL of dry, oxygen-free THF was cooled to −78 °C, and 11 mL of a 1 M solution of diisobutylaluminum hydride in hexane (11 mmol) was added dropwise. The mixture was stirred at −78 °C for 26 h and then allowed to warm to room temperature. Water (0.5 mL) was added dropwise over several minutes, and 1 mL of a 4:1 mixture of THF and water was added slowly; then the mixture was allowed to stand for 30 min, during which time a voluminous gel formed. Ethyl acetate (15 mL) was added, the mixture was filtered through a pad of Celite, and the pad washed thoroughly with ethyl acetate. Combined ethyl acetate washings were dried and concentrated to give (by NMR) an 85:15 ratio of endo and exo alcohols **5a** (0.178 g, 70% combined yield) as a clear oil. The endo isomer was separated from the mixture and purified by chromatography on silica gel using 10:10:1:1 CH_2Cl_2–Et_2O–EtOAc–MeOH. The same chromatographic conditions could be applied to the separation of endo–exo mixtures of **5f** and **5d**, below, as well: NMR ($CDCl_3$, 90 MHz) [endo alcohol] δ 6.30 (s, 2 H), 4.60 (m, 2 H), 3.85 (m, 1 H), 2.86 (br s, 1 H), 2.12 (d of m, 2 H), 1.54 (br d, J = 15 Hz, 2 H); IR (neat) 3300 cm^{-1}; high-resolution mass spectrum, calcd for $C_7H_{10}O_2$ 126.0681, found 126.0702.

1-(2-Methyl-2-dioxolanyl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (5f). To a solution of **4f** (0.315 g, 1.50 mmol) in 25 mL of dry, oxygen-free THF at −78 °C was added dropwise a 0.5 M solution of diisobutylaluminum hydride in hexane (8 mL, 4.00 mmol). The mixture was stirred at −78 °C for 3.5 h, allowed to warm to room temperature for 1 h, cooled to 0 °C, and quenched with water (0.75 mL) in 5 mL of THF. A voluminous gel slowly formed, which was mixed with Celite and filtered. The Celite pad was washed thoroughly with dichloromethane, and the combined washings were dried and concentrated to give **5f** (0.317 g, 99%) as a 3:1 ratio of endo–exo alcohols: NMR ($CDCl_3$, 90 MHz) [endo alcohol] δ 6.33 (dd, J = 6, 2 Hz, 1 H), 6.19 (d, J = 6 Hz, 1 H), 4.80 (m, 1 H), 4.1–3.8 (m, 5 H), 2.70 (br d, J = 7 Hz, 1 H), 3.2–1.2 (m, 7 H containing singlet at δ 1.26), [exo alcohol] 6.03 (dd, J = 6, 2 Hz, 1 H), 5.90 (d, J = 6 Hz, 1 H), 4.80 (m, 1 H), 4.1–3.8 (m, 5 H), 3.20 (br s, 1 H), 2.3–1.2 (m, 7 H containing singlet at δ 1.23); IR ($CHCl_3$) 3400 cm^{-1} (br). Anal. [of the corresponding acetate (pyridine/acetic anhydride, reflux, 15 min, quantitative)] Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.25; H, 7.02.

In a similar manner, 1-(2-dioxolanyl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (**5e**) was prepared from **4e** in 93% crude yield as a 2:1 mixture of endo and exo alcohols and used without further pu-

(18) Salmi, E. J.; Jansson, I. J. *Suom. Kemistil. B* **1939**, *12*, 28. See also: Astle, M. J.; Zaslowsky, J. A.; Lafyatis, P. G. *Ind. Eng. Chem.* **1954**, *46*, 787.

rification in attempts at removal of the protecting group: NMR ($CDCl_3$, 90 MHz) [endo alcohol] δ 6.33 (dd, J = 5.5, 2 Hz, 1 H), 6.16 (d, J = 5.5 Hz, 1 H), 4.80 (m, 2 H), 4.1–3.4 (m, 5 H), 2.3–1.3 (m, 5 H); [exo alcohol] δ 6.03 (dd, J = 5.5, 2 Hz, 1 H), 5.86 (d, J = 5.5 Hz, 1 H), 4.80 (m, 2 H), 4.1–3.4 (m, 5 H), 2.3–1.3 (m, 5 H); IR (neat) 3300 cm^{-1}.

1-Acetyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (6). A solution of **4f** (1.68 g, 8.00 mmol) in 50 mL of 10% H_2SO_4 plus sufficient DME for complete solubility was stirred at reflux overnight. Dichloromethane (100 mL) was added, the layers were separated, and the organic layer was back-extracted twice with water (100 mL). The organic layer was dried and concentrated to give crude **6** (0.974 g, 73%), which could be further purified by chromatography (Chromatotron) on silica gel with 10:10:1:1 ether–dichloromethane–ethyl acetate–methanol to give **6** as a clear oil: NMR ($CDCl_3$, 90 MHz) δ 6.33 (dd, J = 6, 1.6 Hz, 1 H), 6.13 (d, J = 6 Hz, 1 H), 5.15 (m, 1 H), 2.8–2.2 (m, 7 H); IR (mineral oil) 1720 cm^{-1} (vs); high-resolution mass spectrum, calcd for $C_9H_{10}O_3$ 166.0630, found 166.0630.

***endo*-1-Acetyl-8-oxabicyclo[3.2.1]oct-6-en-3-ol (7).** A solution of *endo*-**5f** (0.488 g, 2.30 mmol) in 10 mL of 15% sulfuric acid plus 15 mL of DME was stirred at 65 °C overnight, neutralized with saturated sodium bicarbonate, and extracted twice each with dichloromethane (50 mL) and ethyl acetate (50 mL). The combined organic extracts were washed with brine, dried, and concentrated to give crude **7** (0.331 g, 86%), which could be further purified by chromatotron with 10:10:1:1 CH_2Cl_2–Et_2O–EtOAc–MeOH to give **7** as a clear oil: NMR ($CDCl_3$, 90 MHz) δ 6.42 (dd, J = 6, 2 Hz, 1 H), 6.20 (d, J = 6 Hz, 1 H), 4.86 (m, 1 H), 4.02 (m, 1 H), 2.8–1.4 (m, 7 H); IR ($CHCl_3$) 3300, 1720 cm^{-1}. Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.93; H, 7.17.

1-(Diethoxymethyl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (5d). To a solution of **4d** (0.397 g, 1.76 mmol) in 75 mL of dry, oxygen-free ether at −78 °C was added dropwise 50 mL of diisobutylaluminum hydride (0.5M in hexane, 25 mmol). The solution was stirred at −78 °C for 3 h, allowed to warm to room temperature, and stirred at room temperature for an additional 30 min. The reaction was quenched with water (4 mL) in THF (50 mL) and allowed to stand for 30 min until the solution gelled. Celite and dichloromethane (100 mL) were added, the mixture was filtered through a pad of Celite, and the pad was washed thoroughly with dichloromethane. Combined washings were dried and concentrated to give **5d** (0.388 g, 97%) as a 2:1 ratio of endo–exo alcohols (clear oil): NMR ($CDCl_3$, 90 MHz) [endo alcohol] δ 6.36 (m, 2 H), 4.82 (m, 1 H), 4.37 (s, 1 H), 4.2–3.4 (m, 5 H), 2.4–1.1 (m, 11 H), [exo alcohol] δ 6.03 (m, 2 H), 4.82 (m, 1 H), 4.41 (s, 1 H), 4.2–3.4 (m, 5 H), 2.4–1.1 (m, 11 H); IR ($CHCl_3$) 3350 cm^{-1} (br); high-resolution mass spectrum, calcd for $C_{12}H_{20}O_4$ 228.1362, found 228.1366.

***endo*-1-Cyano-3-acetoxy-8-oxabicyclo[3.2.1]oct-6-ene (8).** In a reaction monitored by NMR, a solution of *endo*-**5d** (0.035 g, 0.16 mmol), hydroxylamine hydrochloride (0.040 g, 0.58 mmol), and D_2O (0.060 g, 3.0 mmol) in 0.5 mL of acetic acid-d_1 was allowed to react at room temperature. After 1 h an NMR spectrum showed an integrated intensity for the acetal methine proton (δ 4.4) 60% that of the oxygen bridgehead proton. After 3 h at room temperature, there was no acetal methine proton visible in an NMR spectrum. The reaction mixture was combined with pyridine (0.2 mL), and the solution was concentrated under high vacuum. Pyridine (0.5 mL) and acetic anhydride (0.10 mL) were added, and the mixture was stirred at room temperature overnight and then at 60 °C for 1 h. The solution was concentrated under high vacuum and the residue passed through a silica gel column with carbon tetrachloride and then ether to give **8** (0.029 g, 98%), which was purified for analysis by crystallization from ether–carbon tetrachloride: mp 90–92 °C; NMR ($CDCl_3$, 90 MHz) δ 6.40 (dd, J = 7, 2 Hz, 1 H), 6.20 (d, J = 7 Hz, 1 H), 5.11 (m, 1 H), 4.87 (m, 1 H), 2.6–1.5 (m, 7 H); IR ($CHCl_3$) 2250 (weak), 1740 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74; N, 7.25. Found: C, 61.95; H, 5.80; N, 7.09.

Attempted Baeyer–Villiger Oxidation of *endo*-1-Acetyl-8-oxabicyclo[3.2.1]oct-6-en-3-ol (7). In a reaction monitored by NMR, a mixture of **7** (0.025 g, 0.15 mmol), solid sodium bicarbonate (0.050 g, 0.60 mmol), and *m*-chloroperbenzoic acid (85% pure, 0.038 g, 0.2 mmol) in 0.5 mL of $CDCl_3$ were allowed to react at room temperature. After 5 min, the integrated intensity of the olefinic (δ 6.3) and oxygen bridgehead (δ 4.9) NMR signals had decreased by 50% relative to that of the alcohol methine proton (δ 4.0). New signals were visible at δ 4.3 (br d, 0.5 H) and 3.7 (s, 1 H). After several hours, NMR signals corresponding to the olefinic and bridgehead protons were no longer visible and the signals at δ 4.3 and 3.7 had grown in integrated intensity to one and two protons, respectively. The spectrum could be interpreted as corresponding to a simple epoxide with the signal at δ 4.3 being the oxygen bridgehead proton and the signal at δ 3.7 being the epoxide protons. The addition of additional sodium bicarbonate (0.050 g, 0.60 mmol) and *m*-chloroperbenzoic acid (0.038 g, 0.22 mmol) did not result in any further changes in the NMR at room temperature. Heating at 60 °C resulted in the NMR spectrum gradually becoming complex and signals slowly broadening as decomposition occurred. No attempt was made to separate the decomposition mixture.

Cobalt Cyclization Reactions. 11-Oxatricyclo[5.3.1.0^{2,6}]-undec-4-ene-3,9-dione (9a). A solution of **4a** (2.05 g, 16.5 mmol) and dicobalt octacarbonyl (2.23 g, 6.5 mmol) in 100 mL of dry, oxygen-free DME was stirred at 65 °C for 42 h under 1 atm of a 1:1 mixture of acetylene and carbon monoxide. The mixture was poured onto silica, concentrated, and placed at the top of a silica gel column. Elution with hexane removed nonpolar impurities. Elution with ethyl acetate then gave crude **9a**, which was further purified by silica gel chromatography with ether to yield 1.31 g (45%) of **9a**: NMR ($CDCl_3$, 60 MHz) δ 7.63 (dd, J = 6, 3 Hz, 1 H), 6.16 (dd, J = 6.2 Hz, 1 H), 4.65 (br d, J = 5 Hz, 1 H), 4.43 (br d, J = 5 Hz, 1 H), 3.26 (m, 1 H), 2.9–2.2 (m, 5 H); IR ($CHCl_3$) 1700 cm^{-1} (vs); high-resolution mass spectrum, calcd for $C_{10}H_{10}O_3$: 178.0630, found 178.0639. Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.41; H, 5.71.

4-Phenyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-ene-3,9-dione (9b). A solution of **4a** (1.06 g, 8.55 mmol), phenylacetylene (0.885 g, 8.68 mmol), and dicobalt octacarbonyl (2.88 g, 8.43 mmol) in 50 mL of DME was stirred at 60 °C for 40 h. The reaction mixture was concentrated onto silica and placed at the top of a silica gel column. Elution with hexane removed nonpolar organometallic species and then elution with ether gave **9b** (0.921 g, 42%) as a white solid: mp 188–190 °C; NMR ($CDCl_3$, 90 MHz) δ 7.70 (m, 3 H), 7.40 (m, 3 H), 4.87 (br d, J = 5 Hz, 1 H), 4.57 (br d, J = 5 Hz, 1 H), 3.36 (m, 1 H), 3.0–2.3 (m, 5 H); IR ($CHCl_3$) 1700 cm^{-1} (vs); high-resolution mass spectrum, calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0953. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.40; H, 5.68.

4-*n*-Butyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-ene-3,9-dione (9c). A solution of dicobalt octacarbonyl (2.76 g, 8.1 mmol) and 1-hexyne (0.661 g, 8.1 mmol) in 50 mL of dry, oxygen-free DME was stirred at room temperature for 30 min under 1 atm of carbon monoxide. **4a** (1.0 g, 8.1 mmol) was added, and the solution was stirred at 65 °C for 2 days under a CO atmosphere. The reaction mixture was concentrated onto silica and the resulting material placed at the top of a silica gel column. Elution with hexane removed nonpolar impurities, and then elution with ethyl acetate gave an organic fraction. Chromatography of this fraction with ether gave **9c** (0.755 g, 40%): NMR ($CDCl_3$, 90 MHz) δ 7.15 (m, 1 H), 4.73 (br d, J = 5 Hz, 1 H), 4.44 (br d, J = 5 Hz, 1 H), 3.20 (m, 1 H), 2.9–2.2 (m, 7 H), 1.6–0.9 (m, 7 H); IR ($CHCl_3$) 1700 cm^{-1} (vs); high-resolution mass spectrum, calcd for $C_{14}H_{18}O_3$ 234.1256, found 234.1229.

***endo*-9-Hydroxy-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (10a).** A solution of *endo*-**5a** (0.465 g, 3.69 mmol) and dicobalt octacarbonyl (1.78 g, 5.20 mmol) in 50 mL of DME was stirred at 65 °C for 36 h under 1 atm of a 1:1 mixture of CO and acetylene. The reaction mixture was concentrated onto silica and the silica placed at the top of a silica gel column. Elution with hexane removed nonpolar side products, and then elution with ether gave **10a** (0.360 g, 52% yield): NMR ($CDCl_3$, 90 MHz) δ 7.58 (dd, J = 6, 3 Hz, 1 H), 6.27 (dd, J = 6, 2 Hz, 1 H), 4.41 (m, 1 H), 4.13 (m, 2 H), 3.87 (m, 1 H), 3.20 (d, J = 6 Hz, 1 H), 2.3–1.5 (m, 5 H); IR ($CHCl_3$) 3450 (br), 1700 cm^{-1}; high-resolution mass spectrum, calcd for $C_{10}H_{12}O_3$ 180.0786, found 180.0783.

***endo*-9-Hydroxy-4-phenyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (10b).** A solution of *endo*-**5a** (1.50 g, 11.9 mmol), phenylacetylene (1.21 g, 11.9 mmol), and dicobalt octacarbonyl (4.07 g, 11.9 mmol) in 100 mL of DME was stirred at 65 °C for

Table III. Crystal Data

	$C_{11}H_{12}O_3$ (11s)	$C_{12}H_{12}O_4$ (12s)
mol wt	192.22	220.22
d_{calcd} (140 K), g cm^{-3}	1.38	1.44
max cryst dim, mm	0.20 × 0.43 × 0.85	1.00 × 0.75 × 0.13
space group	$P2_1/c$	$P2_1/n$
molecules/unit cell	4	4
radiation[a]	Mo Kα (λ = 0.71069 Å)	Cu Kα (λ = 1.54178 Å)
cell constants		
a, Å	11.598 (2)	6.002 (1)
b, Å	8.290 (2)	23.169 (1)
c, Å	9.819 (3)	7.667 (1)
β, deg	78.73 (2)	108.20 (1)
cell vol, Å^3	925.8 (4)	1012.7 (1)
abs coeff μ, cm^{-1}	0.9	9.2

[a] T = 140 K, graphite monochromator.

1 day under 1 atm of carbon monoxide. Chromatographic workup on silica gel with hexane and then ether gave **10b** (1.65 g, 57% yield): NMR ($CDCl_3$, 90 MHz) δ 7.70 (m, 3 H), 7.30 (m, 3 H), 4.50 (m, 1 H), 4.20 (m, 2 H), 3.80 (m, 1 H), 3.40 (d, J = 6 Hz, 1 H), 2.3–1.6 (m, 5 H); IR ($CHCl_3$) 3450 (br), 1700 cm^{-1}; high-resolution mass spectrum, calcd for $C_{16}H_{16}O_3$ 256.1110, found 256.1130.

***endo*-4-*n*-Butyl-9-hydroxy-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (10c).** A solution of *endo*-**5a** (0.506 g, 4.02 mmol), 1-hexyne (0.477 g, 5.82 mmol), and dicobalt octacarbonyl (2.04 g, 5.96 mmol) in 25 mL of DME was stirred at 65 °C for 1 day under 1 atm of carbon monoxide. Chromatographic workup on silica gel with hexane and then ether gave **10c** (0.409 g, 43% yield): NMR ($CDCl_3$, 90 MHz) δ 7.16 (m, 1 H), 4.40 (m, 1 H), 4.3–4.0 (m, 2 H), 3.78 (m, 1 H), 3.26 (d, J = 6 Hz, 1 H), 2.5–0.9 (m, 14 H); IR ($CHCl_3$) 3450 (br), 1700 cm^{-1}; low-resolution mass spectrum, m/e 236 (M^+), 163, 121, 81. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.21; H, 8.29.

7-Methyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-ene-3,9-dione (11a) and 1-Methyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-ene-3,9-dione (11s). A solution of **4b** (0.356 g, 1.85 mmol) and dicobalt octacarbonyl (0.871 g, 2.55 mmol) in 50 mL of DME was stirred at 65 °C for 64 h under a 1:1 ratio of carbon monoxide and acetylene. The reaction mixture was concentrated onto silica, and placed on top of a silica gel column. Elution with hexane removed nonpolar organometallic side products, and then elution with ether gave recovered **4b** (0.201 g, 56% recovery) and a 2:1 ratio of **11a** and **11s** (0.106 g, 21% combined yield, 49% yield based on consumed **4b**). The two isomers were separated by careful column chromatography with ether.

11a: NMR ($CDCl_3$, 90 MHz) δ 7.57 (dd, J = 6, 3 Hz, 1 H), 6.25 (dd, J = 6, 2 Hz, 1 H), 4.76 (m, 1 H), 3.25 (m, 1 H), 2.9–2.2 (m, 5 H), 1.40 (s, 3 H); IR ($CHCl_3$) 1710 cm^{-1} (br); high-resolution mass spectrum, calcd for $C_{11}H_{12}O_3$ 192.0786, found 192.0784.

11s: NMR ($CDCl_3$, 90 MHz) δ 7.55 (dd, J = 6, 3 Hz, 1 H), 6.20 (dd, J = 6, 2 Hz, 1 H), 4.60 (m, 1 H), 3.36 (m, 1 H), 2.9–2.2 (m, 5 H), 1.45 (s, 3 H); IR ($CHCl_3$) 1710 cm^{-1} (br).

7-Acetyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-ene-3,9-dione (12a) and 1-Acetyl-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-ene-3,9-dione (12s). A solution of **6** (0.301 g, 1.81 mmol) and dicobalt octacarbonyl (0.721 g, 2.11 mmol) in 100 mL of DME was stirred at 65 °C for 2 days under 1 atm of a 1:1 mixture of CO and acetylene. The crude reaction mixture was concentrated onto silica and placed on top of a silica gel column. Elution with hexane removed nonpolar organometallic species. Elution with ether gave recovered **6** (0.084 g, 28% recovery) and then **12a** and **12s** in a 3:1 ratio (0.066 g, 17% combined yield, 24% based on consumed **6**). The two isomers were separated by careful chromatography (10:10:1:1 ether–dichloromethane–ethyl acetate–methanol).

12a: NMR ($CDCl_3$, 90 MHz) δ 7.43 (dd, J = 6, 3 Hz, 1 H), 6.28 (dd, J = 6, 2 Hz, 1 H), 4.89 (m, 1 H), 3.56 (m, 1 H), 3.0–2.3 (m, 5 H), 2.23 (5, 3 H); IR ($CHCl_3$) 1710 cm^{-1} (br).

12s: NMR ($CDCl_3$, 90 MHz) δ 7.66 (dd, J = 6, 3 Hz, 1 H), 6.23 (dd, J = 6, 2 Hz, 1 H), 4.68 (m, 1 H), 3.39 (m, 1 H), 3.1–2.3 (m, 5 H), 2.16 (s, 3 H); IR ($CHCl_3$) 1710 cm^{-1} (br).

Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.44; H, 5.50. Found: C, 65.53; H, 5.50.

***endo*-9-Acetoxy-6-cyano-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (13a) and *endo*-9-Acetoxy-1-cyano-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (13s).** A solution of **8** (0.029 g, 0.15 mmol) and dicobalt octacarbonyl (0.090 g, 0.26 mmol) in 35 mL of DME was stirred at 65 °C for 19 h under 1 atm of 1:1 mixture of CO and acetylene. The reaction mixture was concentrated onto silica and placed at the top of a silica gel column. Elution with hexane removed nonpolar organometallic species, and then elution with ether gave an organic fraction which was subjected to thin-layer chromatography (70:30:1:1 hexane–ether–acetone–methanol, three elutions) to give recovered **8** (0.012 g, 41% recovery, R_f 0.25), **13a** (0.010 g, 27%, 45% based on consumed **8**, R_f 0.05–0.10), and **13s** (0.005 g, 14%, 23% based on consumed **8**, R_f <0.05).

13a: NMR ($CDCl_3$, 90 MHz) δ 7.77 (dd, J = 6, 3 Hz, 1 H), 6.40 (dd, J = 6, 2 Hz, 1 H), 5.19 (m, 1 H), 4.58 (m, 1 H), 3.95 (m, 1 H), 3.09 (d, J = 6 Hz, 1 H), 2.6–1.6 (m, 7 H, with s at δ 2.08); IR ($CHCl_3$) 1700 cm^{-1}.

13s: NMR ($CDCl_3$, 90 MHz) δ 7.59 (dd, J = 6, 3 Hz, 1 H), 6.29 (dd, J = 6, 2 Hz, 1 H), 5.18 (m, 1 H), 4.33 (m, 1 H), 3.77 (m, 1 H), 3.26 (d, J = 6 Hz, 1 H), 2.6–1.6 (m, 7 H with s at δ 2.07); IR ($CHCl_3$) 1700 cm^{-1}.

High-resolution mass spectrum, calcd for $C_{13}H_{13}NO_4$ 247.0845, found 247.0835.

X-ray Crystallography. General. Crystals of **11s** and **12s** were grown from dichloromethane. Data were collected on a Syntex $P2_1$ diffractometer equipped with a low-temperature apparatus. No loss in intensity of two standard reflections was observed in either case. Computer programs were those of SHELXTL, version 4.[19] Scattering factors were from common sources.[20] Absorption corrections were not applied. Crystal data are collected in Table III.

X-ray Crystal-Structure Determination for 11s. Intensity data were collected to $2\theta_{max}$ of 55° in the quadrant $h,k,+l$ by using an ω scan of 1° width at 60° min^{-1} [21] and a 1° offset for background counts. The space group was determined by a series of axial photographs and preliminary fast scans showing the conditions $0k0$, $k = 2n$, and $h0l$, $l = 2n$. A total of 2123 unique reflections were collected of which 386 were suppressed as unobserved ($I < 1.7\sigma(I)$), leaving 1737 for solution and refinement of the structure. The structure was solved by direct methods. No difficulty was encountered in the location of all the atoms, including hydrogen atoms. In the final cycles of refinement, non-hydrogen atoms were assigned anisotropic thermal parameters, while hydrogen atoms were refined by using isotropic thermal parameters. The final difference map showed no feature larger than 0.50 e Å^{-3}. A weighting scheme of $w = 1/(\sigma^2(F) + 0.001F)$ was used. Final agreement factors were R = 0.067 and R_w = 0.070 (175 parameters).

X-ray Crystal-Structure Determination for 12s. Intensity data were collected to $2\theta_{max}$ of 130° in the quadrant $h,k,+l$ by using an ω scan of 1.2° width at 20° min^{-1} and a 1° offset for background counts. The space group was determined as for **11s**, from the conditions $0k0$, $k = 2n$, and $h0l$, $h + l = 2n$. A total of 1708 unique reflections were collected of which 78 were suppressed as unobserved ($I < 3\sigma(I)$), leaving 1630 for solution and refinement. Procedures were as for **11s**. The final agreement factors were R = 0.039 and R_w = 0.053 (195 parameters).

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Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond lengths, and bond angles for **11s** and **12s** (10 pages). Ordering information is given on any current masthead page.

(19) Obtained from Nicolet Instruments, Cupertino, CA, 1983.
(20) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. IV.
(21) Hope, H.; Nichols, B. G. *Acta Crystallogr., Sect. B* **1981**, *B37*, 158.