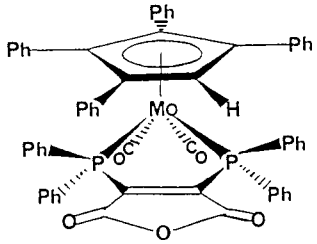
phosphorus atoms (185 °C, Figure 1f). Upon cooling, the spectral changes reversed.[11]

A crystal structure of the complex showed that it has a "four-legged piano stool" structure as shown schematically below.[12]



Because the C_5Ph_4H ring is unsymmetrically substituted, the phosphorus atoms are inequivalent, as shown. Rotation of the ring will "exchange" the phosphorus atoms, and fast rotation of the ring will make the two phosphorus atoms magnetically equivalent. Therefore, we attribute the dynamic ESR spectrum to rotation of the C_5Ph_4H ring. By approximating the effect of the ring rotation as a "two-site exchange" case,[13] we were able to calculate the rate constants for the ring rotation. (Table I in the Supplementary Material lists the rate constants at various temperatures.) A plot of $\ln(k/T)$ vs $1/T$ yielded the following activation parameters: $\Delta H^{\ddagger} = 2.2 \pm 0.1$ kcal mol^{-1}, $\Delta S^{\ddagger} = -22.9 \pm 0.3$ cal K^{-1} mol^{-1}.

To confirm our assumption that ring rotation caused the dynamic ESR spectrum of the $(\eta^5\text{-}C_5Ph_4H)Mo(CO)_2L_2$ complex, we synthesized the 19-electron $(\eta^5\text{-}C_5Ph_5)Mo(CO)_2L_2$ complex (note the symmetrically substituted C_5 ring).[14] The ESR spectrum of this complex was a 1:2:1 triplet, consistent with a structure in which the two phosphorus atoms are magnetically equivalent because the ring is symmetrically substituted.

The rotation of cyclopentadienyl and other rings in organometallic complexes has been widely reported.[15] In general, the energy barrier to ring rotation is very small. That barrier which does exist is generally attributed to intermolecular forces. In contrast, the activation barrier observed for C_5Ph_4H ring rotation in $(\eta^5\text{-}C_5Ph_4H)Mo(CO)_2L_2$ is largely due to unfavorable intramolecular steric interactions. Molecular models of the complex showed that the major barrier comes from the interaction between the phenyl rings on the C_5 ring and the phenyl rings bonded to the phosphorus atoms. For the C_5 ring to rotate freely, the phenyl groups on the C_5 ring and on the phosphorus atoms must rotate cooperatively in a "gearing" fashion.[16] Such a dynamic process would require a transition state of highly organized structure, resulting in a large negative activation entropy. The molecular models also showed that the alternative phosphorus-exchange pathway involving a trigonal-bipyramidal transition state was unlikely because of unfavorable steric interactions between the phenyl groups on the C_5 ring and the phenyl groups on the phosphorus atoms. The large negative activation entropy can also rule out a phosphorus-exchange mechanism that takes place via the dissociation of one end of the chelate ligand; this type of dissociative mechanism would result in a positive, rather than a negative, activation entropy.

Acknowledgment is made to the National Science Foundation for the support of this research. D.R.T. acknowledges the Alfred P. Sloan Foundation for a fellowship.

Supplementary Material Available: A listing of the calculated rate constants at various temperatures, a table of coupling constants at various temperatures, and a plot of $\ln(k/T)$ vs $1/T$ (3 pages). Ordering information is given on any current masthead page.

(10) Castellani, M. P.; Wright, J. M.; Geib, S. J.; Rheingold, A. L.; Trogler, W. C. *Organometallics* **1986**, *5*, 1116-1122.

(11) The complex decomposed slowly in *o*-dichlorobenzene at temperatures above about 155 °C. The spectrum of the sample on cooling was therefore less intense than on warming if spectra above 155 °C were measured. The qualitative features of the spectra were identical (and reversible) on warming and cooling, however. There was no diminuation of the spectrum intensity if 155 °C was not exceeded, and the spectral features were quantitatively reversible.

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(14) This molecule was prepared in a manner analogous to that of the $(\eta^5\text{-}C_5Ph_4H)Mo(CO)_2L_2$ complex.[7]

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Conversion of Epoxides to Rhodium Enolates: Direct Evidence for a Mechanism Involving Initial C-H Activation

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We wish to report the reaction of a low-valent metal complex with ethylene oxide that is phenomenologically related to metal-induced oxirane reactions reported earlier.[1-10] However, in the present case direct detection of an intermediate demonstrates that the reaction takes place by initial C-H activation, rather than by attack at a ring C-O bond, leading to a metalated oxirane. In addition, we have found that conversion of the metalated intermediate to the final reaction product, a C-bond rhodium enolate, involves predominant 1,2-rearrangement of hydrogen rather than rhodium.

In analogy to the photochemical reaction of $Cp^*(L)RhH_2$ (**1**, $Cp^* = (\eta^5\text{-}C_5Me_5)$; L = PMe_3) with alkanes,[11] irradiation of **1** in ethylene oxide at −60 °C also leads to products too sensitive to survive warming to 25 °C, and these materials have therefore been characterized by low-temperature spectroscopy. Thus, when **1** was irradiated for 3 h in excess ethylene oxide (**2a**) in a sealed NMR tube held at temperatures below −60 °C, and the tube transferred into a spectrometer probe precooled to this temperature, we observed the clean formation of the two disastereomeric (both the rhodium center and α-carbon atom are stereocenters) metalated epoxides $Cp^*(L)Rh(H)(CHCH_2O)$, **3a**, in over 95%

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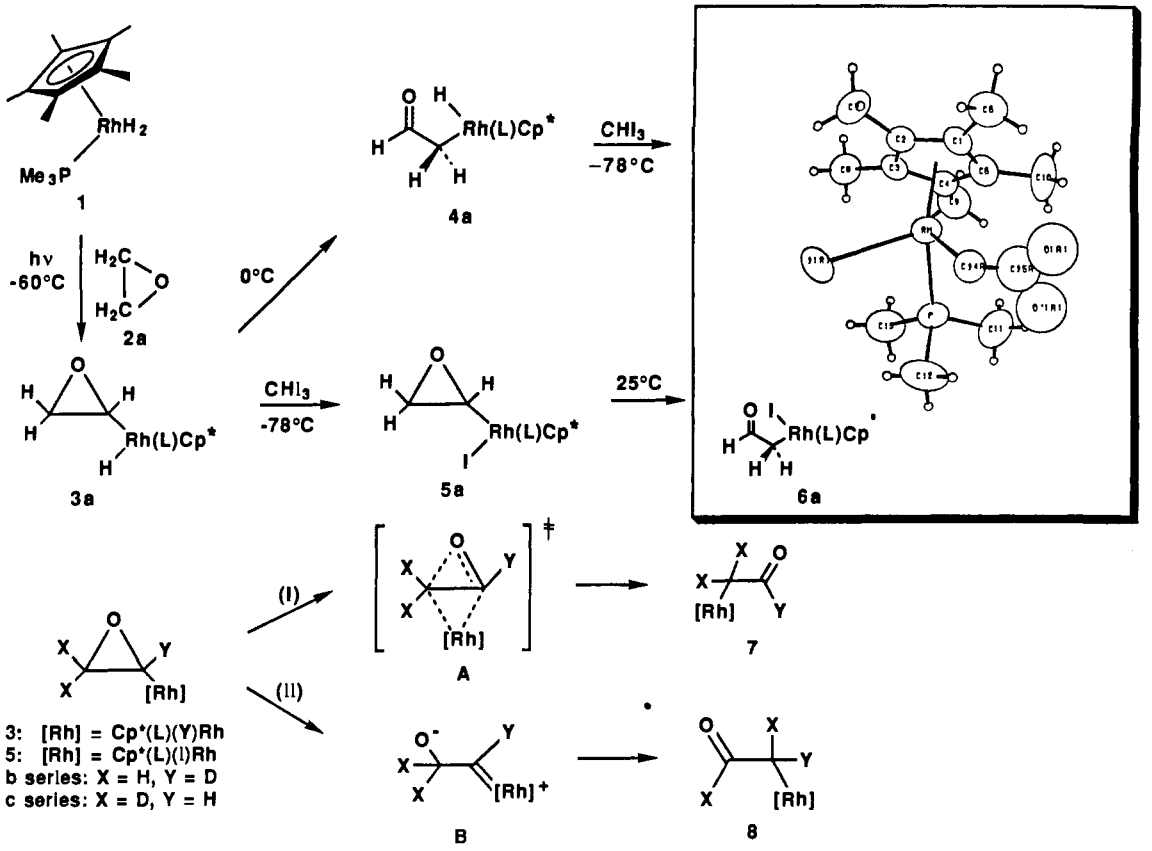
Scheme I



NMR yield (NMR data provided as Supplementary Material). Warming the tube slowly to 0 °C induces the rearrangement of **3a** to a ring-opened product (80% yield by ^{1}H NMR) whose structure is assigned on the basis of spectroscopic properties as the carbon-bound metal enolate Cp*(Me_3P)Rh(H)(CH_2CHO), **4a** (Scheme I).[12] The rearrangement also occurs when ethylene oxide is removed at low temperature and replaced by toluene solvent. This demonstrates that the hydrido enolate is formed by intramolecular rearrangement of **3a**, rather than by reversible reductive elimination to generate free epoxide and Cp*RhL, followed by a slower conversion of these species to **4a**.[13,14]

Addition of CHI_3 to a solution of **3a** at −78 °C results in replacement of the hydride ligand by iodide, leading to Cp*(Me_3P)Rh(I)($CHCH_2O$) **5a**. The chemistry of **3a** and **5a** are also analogous: at room temperature, **5a** rearranges to the iodorhodium enolate Cp*(Me_3P)Rh(I)(CH_2CHO), **6a** (81% yield by NMR). At this stage, material stable at room temperature is finally reached, and **6a** can be isolated in 36% yield after two recrystallizations from Et_2O/hexanes. This complex has been characterized by conventional methods as well as by X-ray diffraction;[15] an ORTEP diagram of the complex is illustrated in Scheme I.

Treatment of hydride rearrangement product **4a** with CHI_3 also leads to **6a** (68% NMR yield), identical with material obtained in the rearrangement of **5a**.

The above experiments demonstrate clearly that **3a** is an obligatory intermediate in the conversion of dihydride **1** and ethylene oxide to hydrido enolate **4a** and that **5a** undergoes an analogous rearrangement to **6a**. Thus the conventional mechanism involving initial attack of Rh on the C–O bond (to give either a ring-opened zwitterion[10a,b] or a four-membered oxametallacycle[1,6,16]) cannot operate in this case. Two general classes of mechanism for the second step in the reaction (the conversion of metalated epoxide to enolate) are illustrated at the bottom of Scheme I. In path (i), 1,2-metal migration assists C–O bond cleavage, and rearrangement takes place via a transition state such as A. In path (ii), rhodium-assisted C–O bond cleavage occurs initially to give zwitterionic intermediate B, and then 1,2-hydrogen shift gives the final product **8**.

As shown in Scheme I, isotope labeling can be used to distinguish these two pathways. Irradiation of **1** in the presence of ethylene oxide-*1,1-*d_2 (98.3% d_2, 1.5% d_1, 0.2% d_0 by mass spectral analysis) gave a mixture of **3b** and **3c** (ratio = 40:60); these in turn were converted with iodoform to a mixture of **5b** and **5c**. Rearrangement of each of these mixtures was allowed to occur, and then the products were analyzed by ^{1}H NMR spectrometry. Analysis of the pattern attributable to the aldehyde hydrogen in the rearranged product, along with spin decoupling experiments, allowed us to determine that at least 93% (and possibly all) of the product of rearrangement of the **5b**/**5c** mixture is formed by hydrogen-migration path (ii) in Scheme I. Examination of the NMR spectrum of the product formed from rearrangement of the mixture of **3b** and **3c** gives similar results: the data are once again consistent with a predominant or exclusive preference for 1,2-hydrogen rather than 1,2-rhodium migration.[17,18]

(12) For an earlier observation of the conversion of epoxides to rhodium hydrido enolates, see ref 10b.

(13) Control experiments demonstrated that irradiation of **1** in the presence of 2 equiv of ethylene oxide in toluene-d_8 solution gave essentially exclusively toluene insertion products and little or none of **3** or its rearrangement product **4**.

(14) No free acetaldehyde was formed during the conversion of **3a** to **4a**. Allowing solutions of **4a** to warm to room temperature gave a complex mixture of products, but again NMR analysis indicated that acetaldehyde was not among them.

(15) The structure of **6a** was solved by Dr. F. J. Hollander of the UC Berkeley College of Chemistry X-ray diffraction facility (CHEXRAY). Serious disorder problems were encountered for the iodine atom and the small organic ligand. The disorder found in the carbonyl group is illustrated in the ORTEP diagram; for clarity the additional disorder in the structure is not represented in the drawing. Structural data for **6a**: space group *Pbca*; a = 16.0047 (21) Å, b = 12.7997 (16) Å, c = 18.0965 (23) Å. R = 3.99%, R_w = 6.03%, GOF = 2.87. Details of the structure determination are provided as Supplementary Material.

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The sensitivity of hydride **3** frustrated attempts to study this reaction kinetically. However, rearrangement of the somewhat better behaved iodides gave reproducible rate data, and these provided support for a ring-opening mechanism involving polar zwitterionic intermediates such as B. The rate of conversion of **5a** to **6a** was measured by UV-vis spectroscopy. The rearrangement is first order in [**5a**] and is accelerated by polar solvents (rate constrants at 20 °C in toluene, THF, and acetone, respectively: 2.1, 4.4, and 10×10^{-4} s^{-1}; estimated error ±10%). In toluene solution, the reaction has a large negative entropy of activation,[19] further supporting the intervention of a change-separated transition state.[20]

In summary, our results demonstrate that epoxides react similarly to cyclopropanes[11,21] with the intermediate generated photochemically from dihydride **1** by initial oxidative addition of rhodium into a three-membered ring C-H bond. Once metalated, however, the small ring compounds lead to different final products: the cyclopropylrhodium compound gives metallacyclobutane,[21] while the expoxyrhodium complex rearranges to an enolate, apparently by a hydrogen-shift rather than a rhodium-shift mechanism.[22] Whatever the precise mechanism of the **3a** → **4a** and **5a** → **6a** rearrangements, however, the experiments described here demonstrate that at least in some instances, overall metal-induced ring-opening reactions of small heterocyclic organic compounds need not begin by cleavage of the ring.

Acknowledgment. This work was supported by the Director, Office of Energy Research, Office of Basic Energy Sciences, Chemical Sciences Division of the United States Department of Energy under contract No. DE-AC03-76SF00098. We are grateful to Prof. Bruce Rickborn (University of California, Santa Barbara) for helpful discussions regarding rearrangements of alkali-metalated epoxides. We acknowledge Dr. F. J. Hollander, Director of the U. C. Berkeley College of Chemistry X-ray Diffraction Facility, for carrying out the X-ray structure determination, and we also appreciate a generaous gift of rhodium chloride from the Johnson-Matthey Co. Metal Loan program.

Supplementary Material Available: Spectroscopic data supporting the structural assignments of **3a**, **4a**, **5a**, and **6a** and full details of the X-ray diffraction study, including ORTEP stereodrawings and tables of crystal and data collection parameters, positional parameters, anisotropic thermal parameters, intramolecular distances and angles, and least-squares planes (15 pages); table of calculated and observed structure factors (15 pages). Ordering information is given on any current masthead page.

(17) A referee has asked us to mention that C-H oxidative addition was suggested in an early paper (ref 8) as the initial step in a rhodium-catalyzed rearrangement of stilbene oxides to deoxybenzoins at high temperature (150-210 °C). However, the second step postulated in the previous mechanism involved 1,3-transfer of rhodium-bound hydride to the epoxide carbon atom to open the ring, followed by extrusion of the metal. This mechanism cannot be operating in the **3a** to **4a** rearrangement, because it would lead to products that are not observed (an acyl hydride or acetaldehyde), nor can it be operating in the rearrangement of iodide **5a** to **6a**, since in this case iodide, rather than hydride, is attached to rhodium. We suggest that a hydrogen-migration mechanism analogous to the one described here may also operate in the stilbene oxide-to-deoxybenzoin rearrangement.

(18) Interestingly, a similar mechanism has been postulated to occur through a carbenoid species in the rearrangement of alkali-metalated epoxides to enolates; cf.: (a) Thummel, R. P.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 3919. (b) Crandall, J. K.; Apparu, M. *Org. React.* **1983**, *29*, 345, and references cited therein.

(19) Activation parameters in toluene solvent were determined by measuring rate constants over the temperature range from 0-35 °C: $\Delta H^{\ddagger} = 12.0$ Kcal/mol; $\Delta S^{\ddagger} = -34.5$ eu.

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(22) A referee has inquired about the products formed on irradiation of $Cp^*(L)RhH_2$ with methyl-substituted epoxides. We have briefly investigated the reaction with 2,2-dimethyloxirane; observation by low-temperature NMR indicates that insertion occurs into both the methyl and ring C-H bonds (as it does with cyclopropane), but warming leads to a complex mixture of products. Because of this and the fact that photochemical conversions were lower than with ethylene oxide itself, this reaction has not been investigated further.

The Cyclization of Calicheamicin-Esperamicin Analogues: A Predictive Biradicaloid Transition State

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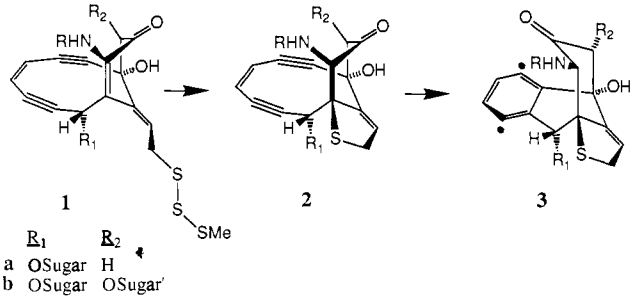
A family of exceptionally potent antitumor agents were recently isolated from soils found in Texas and Argentina. Elegant structural and mechanistic studies by Lederle[1] and Bristol-Myers/Cornell[2] teams have characterized the active agents as the highly unsaturated bicyclics calicheamicin γ_1 (**1a**) and esperamicin A_2 (**1b**), respectively. Biological action is intimately linked to double-stranded DNA cleavage.[3,4] Nicolaou and co-workers have prepared a highly simplified monocyclic analogue of **1** (**4**, Z = $(CHCH_2OH)_2$) and shown it both to cyclize in benzene and to cause scission of a variant of DNA at 37 °C.[5] Other total synthetic efforts are likewise underway.[6] The current mechanistic hypothesis[1-3] is that **1** binds to the minor groove of the double strand, undergoes Michael addition to give **2**, and finally experiences spontaneous Bergman ring closure[7] to the fugitive but lethal biradical **3**. The latter is thought to abstract hydrogen from the DNA polymer to produce oligonucleotide fragments and the corresponding benzannelated structures as intermediate metabolites.



	R_1	R_2
a	OSugar	H
b	OSugar	OSugar'

In an attempt to define the pathway from **4** to **7**, the present work describes a quantum mechanical model for cyclization to the biradicaloid transition state **5**. Two important questions concern (1) the degree of biradical character in **6** and (2) whether the pathway is least motion or not. The transformation of several

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