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Kinetic Isotope Effects in Cycloreversion of Rhenium (V) Diolates

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Abstract: Cycloreversion of 4-methoxystyrene from the corresponding Tp′Re(O)(diolato) complex (Tp′ = hydrido-tris-(3,5-dimethylpyrazolyl)borate) was measured competitively for various isotopomers at 103 °C. Primary ($^{12}C/^{13}C$) and secondary ($^{1}H/^{2}H$) kinetic isotope effects were determined. The primary KIEs were $k_{12C}/k_{13C} = 1.041 \pm 0.005$ at the α position and 1.013 ± 0.006 at the β position. Secondary KIEs were $k_H/k_D = 1.076 \pm 0.005$ at the α position and 1.017 ± 0.005 at the β position. Computational modeling (B3LYP/LACVP*+) located a transition state for concerted cycloreversion of styrene from TpRe(O)(OCH_2-CHPh) exhibiting dramatically different C−O bond lengths. A Hammett study on cycloreversions of substituted styrenes from a series of Tp′Re(O)(diolato) showed dichotomous behavior for electron donors and electron-withdrawing groups as substituents: $\rho = -0.65$ for electron donors, but $\rho = +1.13$ for electron-withdrawing groups. The data are considered in light of various mechanistic proposals. While the extrusion of 4-methoxystyrene is concluded to be a highly asynchronous concerted reaction, the Hammett study reflects a likelihood that multiple reaction mechanisms are involved.

Introduction

Cycloaddition chemistry has from its discovery invited mechanistic controversy over whether any particular reaction is concerted or proceeds via an intermediate.[1] The issue is complicated by the fact that the primary probe for concertedness, stereospecificity with regard to substituents, presumes that an intermediate capable of single-bond rotation will undergo that low-energy process (barriers usually <5 kcal/mol)[2] faster than the subsequent bond-forming reaction of the intermediate. However, if this presumption is not valid, a reaction that is actually stepwise will appear to be concerted. Likewise, if one probes symmetry properties of the transition state, the structural modifications needed to make the test may themselves create aspects of asymmetry that would make a concerted reaction appear as if the bond reorganization at two sites was proceeding in an asynchronous fashion.

The general problem is compounded if transition metals are involved. Classical organic cycloadditions are mechanistically constrained in terms of the types of intermediates that can serve as candidates for stepwise mechanistic proposals; in most situations the question is limited to whether a process is concerted or whether a biradical has properties that would mimic concertedness. However, the ability of transition metals to serve as templates for bond-forming processes opens a number of new mechanistic possibilities. The history of mechanistic investigation of osmylation and related reactions illustrates the challenges.[3] For many years, kinetic and stereochemical investigation was unable to distinguish two major proposals. Both a concerted [3 + 2] process[4] and a stepwise mechanism proceeding via a metallaoxetane[5] were capable of rationalizing reaction outcomes. The advent of enantioselective asymmetric dihydroxylation[6] raised the importance of the distinction in that very different processes for molecular recognition and enantiotopic facial discrimination were required by the two proposals. The issue was apparently resolved in 1997 by the observation[7] that oxidation of *tert*-butylethylene showed, within experimental error, identical primary and secondary kinetic isotope effects (KIEs) at the two olefinic positions when high level calculations predicted significantly different KIEs arising from the involvement of a metallaoxetane.

Our work with rhenium diolate chemistry has attempted to probe the issue from a different perspective. The general approach has been to examine diolate cycloreversion and tie the observations to C−O bond-forming processes via the principle of microscopic reversibility. This assertion is supported by the observation that cycloreversions are nearly thermoneutral,

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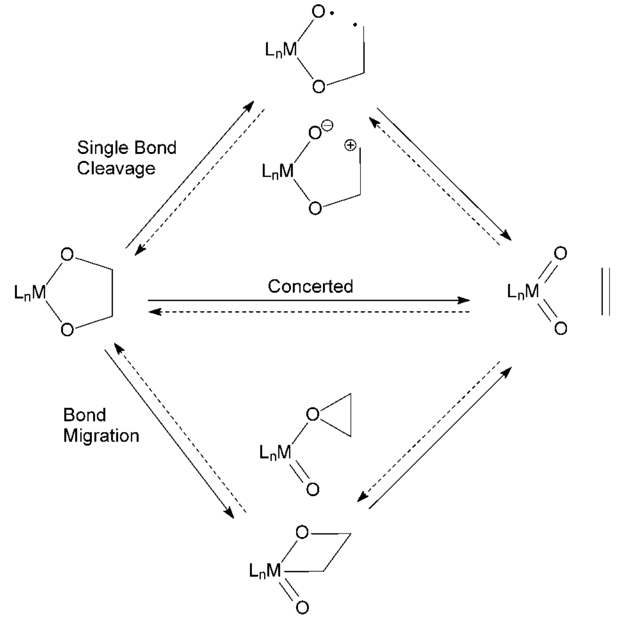
Scheme 1



driven by entropy, and that incorporation of some strain into the alkene C═C bond can favor cycloaddition to $LReO_3$ in the same fashion as alkenes add to OsO_4.[8] A series of mechanisms considered for these reactions is seen in Scheme 1.

The high degree of stereospecificity[9] (to the limit of detection, taken as >95% by NMR) suggests that the first two of these, homolytic and heterolytic cleavage of a C−O bond, are unlikely. However, the standard restriction applies in that if either of these intermediates were to cleave the second C−O bond faster than bond rotation occurs, stereospecificity would be observed. However, several further arguments mitigate against these proposals. First, substituents such as a phenyl group would be expected to stabilize the intermediate and lengthen its lifetime sufficiently for bond rotation to occur; this is not seen. Second, diolates of *trans*-cycloalkanediols are thermally stable, while the isomeric *cis*-cycloalkanediolates fragment.[10,26] Were a radical to be produced, it would invert readily and collapse to the *cis*-cycloalkene or at the very least isomerize to the *cis*-cycloalkanediolate, which would then fragment. Similar arguments discount the ionic mechanism, as does the absence of any significant solvent effect and the relatively small Hammett ρ value observed for extrusion of styrenes from Cp*Re(O)(diolato) complexes (Cp* = η-pentamethylcyclopentadienyl).[11]

The remaining possibilities are either the concerted mechanism, or two stepwise processes involving migration of carbon. One of the latter would form a metallaoxetane by migration to the metal, or a coordinated epoxide[12] via a migration to the second diolate oxygen. Either would be a frontside migration of carbon with retention of stereochemistry and would conclude with a rapid concerted loss of alkene from the intermediate after the initial rate-determining step.

Experiments to date have suggested that cleavage of only one of the two C−O bonds occurs to any extent in the transition state. The effect of strain in the C═C bond is expected to have a significant impact on relative transition-state energies for either cycloaddition or cycloreversion, due to the rehybridization of the reacting carbon. However, this effect was observed only for cycloaddition; furthermore, the quantitative impact on $\Delta H^{\ddagger}$ implied a complete relief of strain at the cycloaddition transition state. The invariance of $\Delta H^{\ddagger}$ for cycloreversion of strained and unstrained disubstituted alkenes agrees that strain is not evident by the cycloreversion transition state. Both observations are consistent with a transition-state structure that lacks sp^2 character. That at least one C−O bond is cleaved at or before the transition state is confirmed by the observation of a significant secondary deuterium KIE on extrusion of ethylene; k_H/k_{D4} = 1.25 at 100 °C. This value by itself could be rationalized with either the concerted (KIE per D = 1.06) or stepwise (KIE per D = 1.13) mechanisms; efforts to perform a Thornton analysis[13] by measuring the KIE for extrusion of ethylene-d_2 were stymied by analytical complications arising from fragmentation during mass spectrometry.[14] However, the combination of the strain effects with the KIE strongly suggested a highly asynchronous and probably stepwise process in which reorganization to an intermediate preceded development of the new C═C π bond.

Further experiments agreed with this conclusion. Conformational analysis of a series of diolates suggested that a staggered form enhanced the reaction rate, whereas a concerted reaction presumably would be enhanced by an eclipsed geometry that would allow proper orbital overlap in the incipient C═C π bond. Such an effect is evidence that orientation of a C−O bond with an orbital on rhenium is important. While a Hammett study on styrene extrusion was uninformative, the curved behavior seen for stilbene extrusion again suggested a competition between (asynchronous) cleavage of the two different C−O bonds.

However, in the intervening years, application of high-level computational methods to our system has strongly and consistently suggested that the concerted process should be energetically favored over formation or fragmentation of a metalla-

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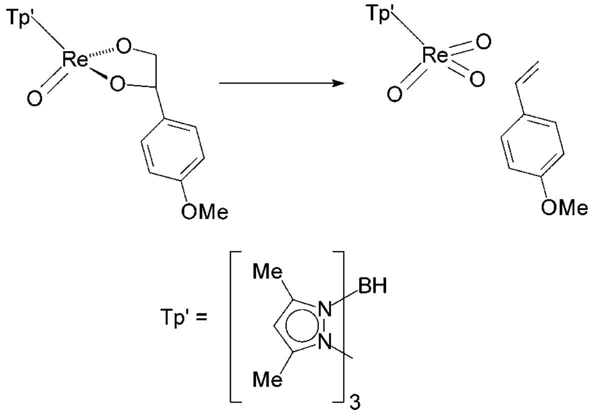
oxetane.[15] The methods and conclusions parallel a large amount of similar work in osmylation.[16] Thus, it became necessary to reconsider the earlier conclusions and revisit the issue. The value of measuring KIEs lies in presenting a rigorous picture of symmetry in the transition state and rigorously testing whether one or both reaction sites undergoes bonding reorganization. The work on osmylation reflected the advantage of considering both primary (^{12}C/^{13}C) and secondary (H/D) effects in creating a picture of the transition state structure. This report describes measurement of these kinetic isotope effects for a representative rhenium diolate.

Results

Experimental Design The experiment involved examining a known mixture of isotopomers, reacted to a known degree of conversion. Unreacted diolate was reisolated and analyzed for the increase in the slower-reacting isotopomer. We felt NMR provided an adequate means of measuring isotopic distribution, from which the KIEs would be determined. This methods avoids complications in mass spectrometric analysis due to fragmentation of molecular ions that is commonly seen in these diolates.[18] The Singleton methodology[17] normally relies on using natural abundance isotopomers as the substrates for investigation, and incorporates several controls to correct for potential systematic errors in peak integration. This has the advantage of eliminating the need for synthesis of isotopically enriched material, but imposes a significant cost in instrumental time because of low signal-to-noise ratios, particularly for deuterium. Use of enriched material would ease analysis while maintaining the advantages of NMR as a nondestructive means of measuring isotopic distribution.

We were faced with two fundamental choices in designing the substrate for this experiment. Most of the mechanistic investigations on rhenium diolate cycloreversion involved use of Cp* as an ancillary ligand on rhenium. The pyrazolylborate complexes were easier to prepare in high yield, and were marginally easier to handle due to enhanced air-stability. Earlier work[18,19] had shown strong similarities between these systems and those using Tp′. As a control, a Hammett study was performed (see below).



The second choice was more critical. Ideally, an alkyl substituent would provide less bias toward any asymmetry, however, synthesis of an appropriately labeled reference compound for R = *tert*-butyl is significantly involved. Use of a substituted phenyl group provides an easier synthesis, but imposes the potential to bias even a concerted transition state toward an asynchronous structure. Given that extremely significant electronic perturbation—cyano group(s)—is required to induce substantial asynchronicity in Diels-Alder cycloadditions,[20] the synthetic advantages of using R = 4-methoxyphenyl outweighed the risks. Further, a similar experiment has been reported for osmylation,[21] and while asymmetry was noted, substantial primary KIEs were observed at both carbons. While not a primary design consideration with regard to the KIE study, use of a phenyl substituent does allow more systematic exploration of electronic effects than would any other aliphatic substituent.

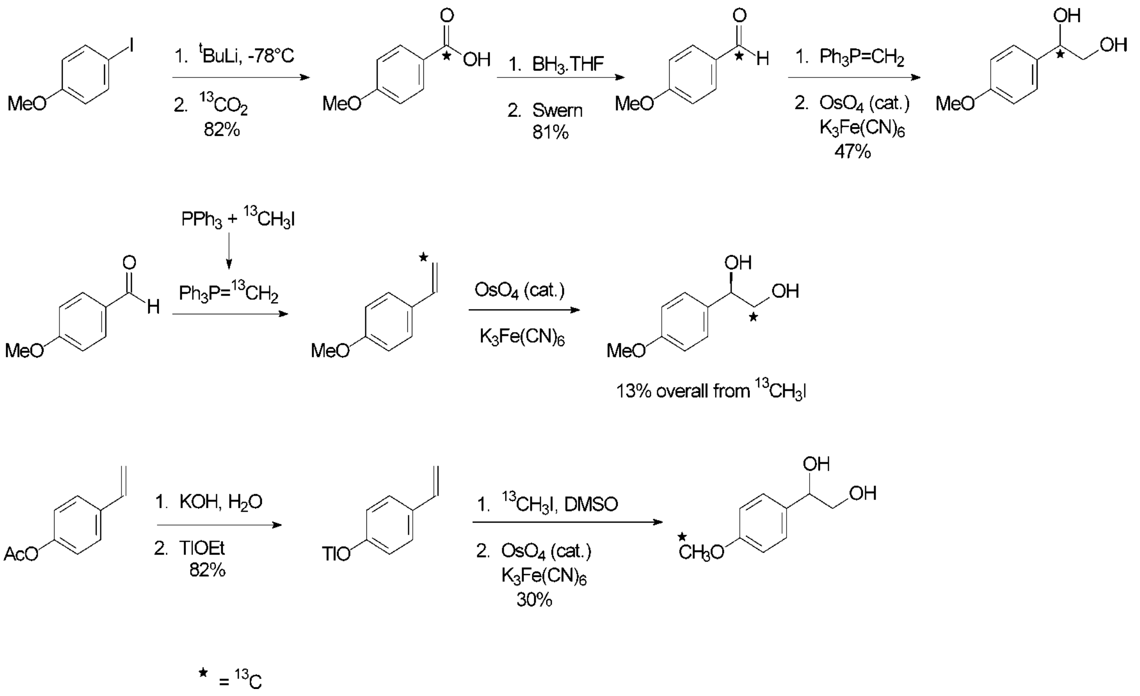
Synthesis of labeled diolates. Syntheses of required diolate complexes is shown in Schemes 2 and 3. Each experiment required diols labeled at each of the reacting carbons; incorporation of label at a reference position was performed to provide a marker for material unlabeled at the reacting carbons. All of these syntheses were straightforward. The ^{13}C-labeled materials were generally produced via a Wittig reaction[22] to methylenate 4-methoxybenzaldehyde followed by osmylation. The α-labeled compound involved producing α-^{13}C-4-methoxybenzaldehyde from a Grignard reagent and ^{13}CO$_2$[23] followed by reduction. The *β*-labeled styrene was formed from labeled Wittig reagent prepared from ^{13}CH$_3$I. Placing the reference label in the methoxy group was problematic because of the lability of 4-vinylphenoxide; generation from 4-acetoxystyrene followed by immediate in-situ conversion to the thallium salt gave a much more tractable species which was easily alkylated. On the basis of ^{1}H NMR spectra, each diol was found to be >98 atom % ^{13}C.

Synthesis of the deuterated compounds was likewise straightforward. The reference isotopomer required mere substitution of deuteriomethyl iodide. The alpha label was incorporated by LiAlD$_4$ reduction of methoxybenzoyl chloride; reoxidation allowed isolation of the deuterated aldehyde. The *β* label was most easily incorporated via metalation and D$_2$O quench of the *β*-bromo-4-methoxystyrene.[24] On the basis of ^{1}H NMR spectra, each diol was found to be >98.5 atom % D.

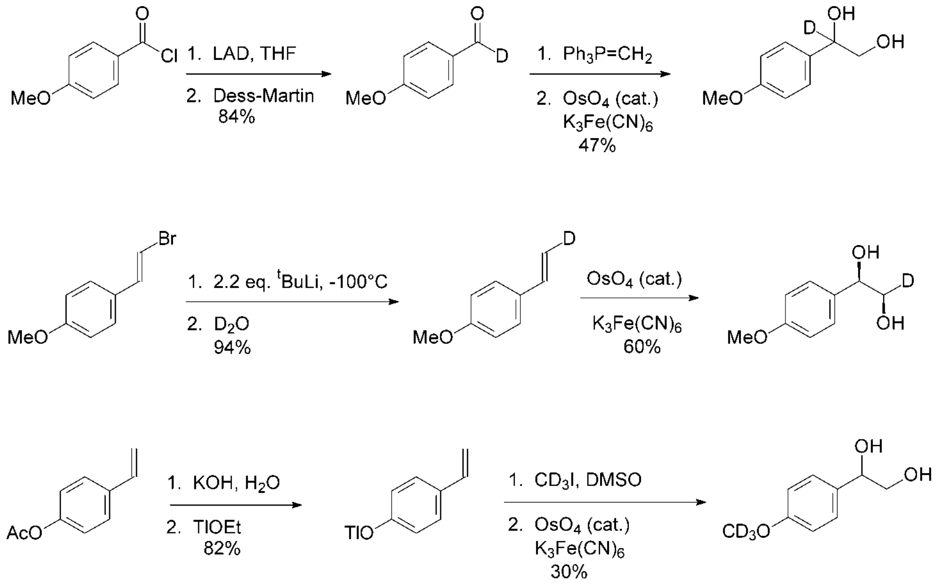
Rhenium diolate complexes were prepared from the diols via the published procedure involving in situ reduction of Tp′ReO$_3$ with PPh$_3$ and cyclocondensation with the diol.[18] Two isomers were formed in a 10:1 ratio and were assigned respectively as the *anti*- and *syn*-diastereomers at the benzylic carbon. (Syn or anti is defined on the basis of the orientation of the aromatic ring versus the pyrazole trans to the terminal oxo ligand.) This was confirmed by the observation of nOe between the methyl signal at 2.47 ppm and the diolate signals at 6.23 and 5.65 ppm. The minor isomer, on the other hand, showed only one nOe between a diolate signal at 5.42 and the pyrazolyl methyl at 2.23 ppm; enhancement was also observed for the ortho aromatic protons at 7.63 ppm. DEPT of the major isomer confirmed the identity of α and *β* carbons at 95.9 and 94.5 ppm, respectively; a 2-D HSQC spectrum confirmed assignment of the proton signals. See Supporting Information for details.

Kinetic Analysis Evaluation of the KIEs via competition requires as one component an accurate estimation of the extent of reaction for the parent (unlabeled) molecule. Thus, extrusion of 4-methoxystyrene from the corresponding diolate in toluene-d_8 was followed at several temperatures to establish the activation parameters. Like the extrusion of styrene, this was found to be cleanly first-order to >4 half-lives by ^{1}H NMR.

Scheme 2



Scheme 3



Between 100 and 120 °C, $\Delta H^{\ddagger} = 29.1 \pm 0.4$ kcal/mol and $\Delta S^{\ddagger} = 0.46 \pm 1.03$ cal/(mol K) were found. The Eyring plot is shown in Figure 1.

The minor diastereomer was evaluated kinetically at 120 °C; its rate of cycloreversion was only one-fourth that of the anti isomer (2.15×10^{-4} s^{-1} for the syn vs 8.00×10^{-4} s^{-1} for the anti).

Given the change in ancillary ligand from the earlier work, an abbreviated Hammett study was performed with five different substituted phenylethanediolates. The result is shown in Figure 2; two different slopes were observed depending on the electronic nature of the substituent. Electron donors show $\rho = -0.65$, but $\rho = +1.13$ for electron-withdrawing groups. Plotting against σ^{+} yields a similar relationship, but the small number of data points precludes any quantitative comparison.

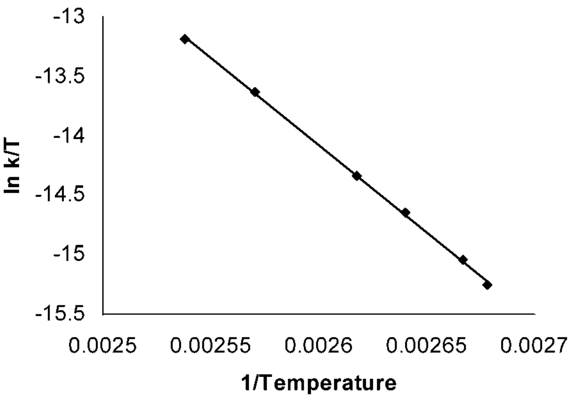


Figure 1. Eyring plot for cycloreversion of 4-methoxystyrene. $\Delta H^{\ddagger} = 29.1 \pm 0.4$ kcal/mol; $\Delta S^{\ddagger} = 0.46 \pm 1.03$ cal/mol K; $r^2 = 0.999$.

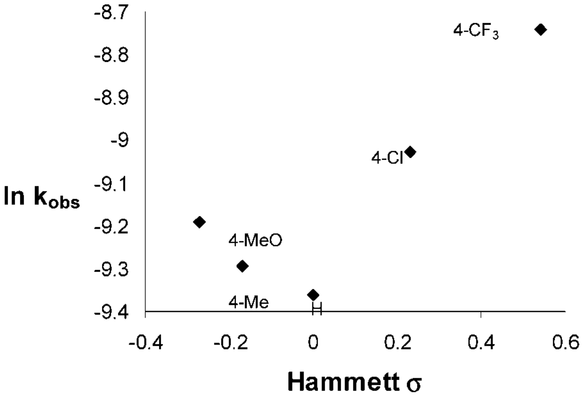


Figure 2. Hammett plot for cycloreversion of substituted phenylethanediolates.

Measurement of Isotope Effects. All experiments involved estimating the ratios of isotopic content at each of the reacting sites (α and β) relative to that at a nonreacting reference position (the methoxy group); the latter would serve as a marker for the amount of compound "unlabeled" ($^{12}C_2$ or $^1H_3$) at the reacting sites. A spectrum of the initial mixture was collected; after reaction for a known amount of time (and thus a known extent of reaction) the diolate was isolated from the reaction mixture and its spectrum recorded again. The isotope effects were all calculated from these ratios according to the equation[25]

$$\mathrm{KIE} = \frac{\ln(1-F)}{\ln((1-F)R/R_0)} \qquad (1)$$

(F = extent of reaction; R = isotopic ratio vs reference at extent of reaction F; R_0 = initial isotopic ratio vs reference).

Uncertainty in the KIE was derived by propagation of error from that in the ratios and extent of reaction, expressed as 95% confidence intervals.

To measure primary ^{12}C/^{13}C KIEs, integration of ^{13}C spectra was performed in accord with conditions laid out by Singleton.[17] The spectral window was restricted to the signals of interest; the use of enriched material ameliorated problems arising from foldover of other signals into this narrow window. Inverse gated decoupling was used; a relaxation delay of 5 times the longest ^{13}C T_1 value was used. The spectra were zero-filled to 128 K; the narrowest peak had a minimum of 10 data points. Enough transients were collected to give a minimum signal-to-noise ratio of 100:1 for the broadest peak when transformed with no line broadening correction. Care was taken to provide correct phase correction and consistent baseline correction.

Despite these precautions, multiple runs gave significant scatter in the results. Several samples appeared to show larger KIEs at the β position, and some even showed an inverse KIE at one or both positions. Several aspects of our system are likely origins of the problem. First, the diolate signals are both significantly broadened compared to other signals in the spectrum (see Figure 3). We have observed this behavior in other rhenium diolates.[26] Although conformational flexibility of the diolate ring is one potential cause, the failure to observe any sharpening in the line either on heating or cooling the sample suggests that the nuclear quadrupole of rhenium (for ^{185}Re, this is 2.18 and for ^{187}Re, 2.07 barn; compare ^{2}H at 0.00286 barn)[27] is a more likely cause. In any event, all lines need to be integrated over a region of at least 10 half-height line-widths, and in this case the signals are close enough to make correct integration impossible. Further, it was impossible to prevent small amounts of the minor diastereomer from contaminating some samples; while the diolate signals were fairly well separated, the reference methoxy carbons were so close as to be inseparable for the purpose of integration. Recall that the minor diastereomer reacted more slowly, thus we experienced the buildup of this impurity as the reaction proceeded. Since slightly different conversions were used in each experiment, this provided another variable that was impossible to factor out. In retrospect, we were fortunate to have prepared isotopically enriched compounds, as the standard integration of ^{13}C signals beginning with the natural abundance distribution would have failed completely.

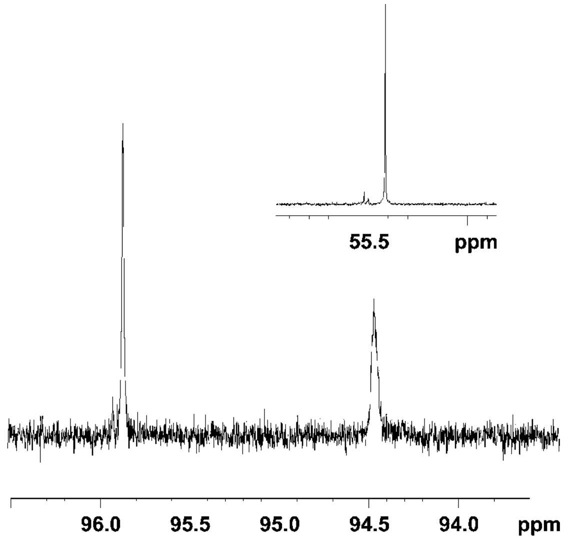


Figure 3. ^{13}C NMR lines for diolate carbons (95.9; $\nu_{1/2}$ = 1.35 Hz; 94.5; $\nu_{1/2}$ = 4.38 Hz). Inset: methoxy carbon line on a similar scale; $\nu_{1/2}$ = 0.34 Hz.

Table 1. Primary ^{12}C/^{13}C Kinetic Isotope Effects on Extrusion of 4-Methoxystyrene

run	F	R/R_0 (α)	R/R_0 (β)	KIE, α	KIE, β
1	0.905	1.083	1.020	1.035	1.008
2	0.836	1.083	1.023	1.046	1.013
3	0.903	1.100	1.040	1.043	1.017
average				1.041	1.013

Table 2. Secondary ^{1}H/^{2}H Kinetic Isotope Effects on Extrusion of 4-Methoxystyrene

run	F	R/R_0 (α)	R/R_0 (β)	KIE, α	KIE, β
4	0.888	1.160	1.036	1.073	1.016
5	0.812	1.122	1.012	1.074	1.007
6	0.896	1.178	1.060	1.080	1.027
average				1.076	1.017

We investigated several means of line fitting to provide better estimates of isotopic composition. However, all gave the same degree of scatter as the numerical integrations, and we concluded that the quadrupolar interactions were creating enough significant difficulties with the raw data that use of the ^{13}C spectra was inadvisable. Fortunately, the ^{1}H spectrum provided an alternative, in that the ^{13}C satellites of the enriched isotopomers provided an indirect but potentially more accurate estimate of

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(27) Lide, D. E., Ed. *CRC Handbook of Chemistry and Physics*,78th ed.; CRC Press: New York, 1997; Chapter 9, pp 85−87.

Table 3. Energies for Optimized Structures at the B3LYP/LACVP*+ Level

quantity	styrene	$TpReO_3$	$TpRe(O)(OCHPhCH_2O)$	transition state	ΔE_{rxn} (kcal/mol)	$\Delta E^{\ddagger}$ (kcal/mol)
E, Hartree	−309.6605	−1007.2715	−1316.9567	−1316.8998	+15.5	35.7
ZPE, kcal/mol	89.79	149.58	243.05	233.18		
ZPE corrected ΔE					+11.8	25.8

the isotopic composition at each position. Note that this method inadvertently overdetermines these measurements by permitting independent comparison of the isotopic composition at each position with the ratio of α-^{13}C or β-^{13}C to methoxy-^{13}C. Results for each run are presented in Table 1; according to eq 1 the KIEs are $k_{12C}/k_{13C} = 1.041 \pm 0.005$ at the α position, and 1.013 ± 0.006 at the β position.

Estimation of the deuterium content by direct NMR measurement was similarly complicated by the width of the signals and the corresponding peak overlap and loss of adequate signal-to-noise ratio. Again, though, the relatively well-resolved ^1H spectrum contained the necessary information. Each of the three signals in the ^1H spectrum is composed of contributions from different isotopomers. Solution of appropriate simultaneous equations for the contribution to different signals allowed the isotopomeric composition to be calculated. (Correction for the small amount of signal arising from less than 100 atom % labeling showed no discernible impact.) Results are shown in Table 2; from these data secondary KIEs were $k_H/k_D = 1.076 \pm 0.005$ at the α position, and 1.017 ± 0.005 at the β position.

Computational Modeling. Quantum mechanical modeling of the reaction was undertaken to discover whether a transition state could be located and if so, whether its properties predicted KIEs in accord with the experimental observations. The commercial package Jaguar was used.[28] The hybrid DFT method B3LYP was chosen on the basis of its previous success in modeling related rhenium compounds. The LACVP*+ basis set was selected on the basis of the following considerations. This uses a fairly standard 6-31G basis set for all first- and second-row heavy atoms and hydrogen. An effective core potential is used for rhenium that implements corrections for relativistic effects; again, this has been shown to be successful for the third row transition elements. Use of d-type polarization functions on heavy atoms has been shown to be critical to achieving good energies in related systems,[15c] but since the bond reorganization does not significantly involve hydrogens, p-type polarization functions were omitted from hydrogens. Finally, because the modeling of a transition state involves partial bonding, diffuse orbital functions were added to the heavy atoms. Two structural simplifications were implemented to minimize computational cost: an unsubstituted phenyl ring was used, and the ancillary ligand was abbreviated to the parent Tp rather than the methylated Tp′.

To benchmark the system, calculations were performed on the overall reaction thermodynamics. Both $TpReO_3$ and the corresponding phenylethanediolate converged to reasonable structures that were stationary points based on vibrational analysis, with no imaginary frequencies. Energies and relevant metrics are in Tables 3 and 4. For the trioxide, Re═O bonds in the optimized structure were 1.719 Å, compared to an experimental value of 1.707−1.720 Å in $TpReO_3$.[29] The vibrational frequency of the main rhenium oxo stretch (scaled by 0.9614, based on the 6-31G* correction)[30] was computed to be 909 cm^{-1}, compared to the observed value of 913 cm^{-1} for $TpReO_3$ and 907 for $Tp'ReO_3$. The diolate converged on a structure that shared several features with Santos' structures of $TkRe(O)(OMe)_2$ and $TkRe(O)(OCH_2CH_2O)$ (Tk = tetrakis-pyrazolylborate):[31] the rhenium-oxo bond length was 1.694 Å; Re−N bonds cis to the oxo were shorter (2.173 and 2.131 Å) than that trans to the oxo ligand (2.341 Å). The computational methodology is sufficient to replicate the gross structure of the coordination sphere of rhenium. C−O bonds are similar (1.434, 1.423 Å); thus, the phenyl group perturbs neither the ground-state structure of the diolate ring nor any other aspect of coordination sphere of rhenium to any significant extent. Again, the scaled vibration for the terminal Re−O stretch was computed to be 931 cm^{-1}, compared to an actual value of 922 cm^{-1} in $Tp'Re(O)(OCHPhCH_2O)$.[18]

Table 4. Structural data for calculated structures (B3LYP/LACVP*+)

	$TpReO_3$	$TpRe(O)(OCH_2CHPh)$	styrene	transition state
Re═O	1.719	1.694		1.703
Re−O		1.955, 1.938		1.794, 1.768
Re−N	2.300	2.335, 2.170, 2.127		2.313, 2.271, 2.240
CH_2−O		1.434		1.880
CHPh-O		1.423		2.112
C−C		1.537	1.342	1.403

The reaction energetics were in agreement with our earlier qualitative observations. ΔE based on electronic energies was calculated to be +15.5 kcal/mol for styrene cycloreversion; application of a correction for zero-point energy differences decreases this to +11.8 kcal/mol. Note that these quantities all assume gas-phase reaction; in solution we observe cycloreversion for unstrained alkenes, but preferred cycloaddition of strained alkenes (e.g., norbornene) to $Tp'ReO_3$. The experimental observations were previously interpreted to suggest a ΔH_{rxn} near zero,[8,18] and no more positive than about +5 kcal/mol. Comparison between theory and experiment are further clouded by the fact that $Tp'ReO_3$ is poorly soluble in most organic solvents, complicating the thermochemistry due to its unknown heat of crystallization.

A transition state search resulted in the location of structure c in Figure 4. This converged to a proper saddle point with one imaginary frequency. The transition state energy, +35.7 kcal/mol relative to the reactant phenylethanediolate (+25.7 kcal/mol after factoring in ZPE differences), is in reasonable accord with the observed $\Delta H^{\ddagger}$ of 27.6 kcal/mol for the Tp′ complex. Substantial asymmetry in the cleavage of the C−O bonds is observed; the difference in bond lengths is almost 0.25 Å. The

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(28) Jaguar 4.1, Schrödinger, Inc., Portland, OR, 1991−2000.

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(30) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502−16513.

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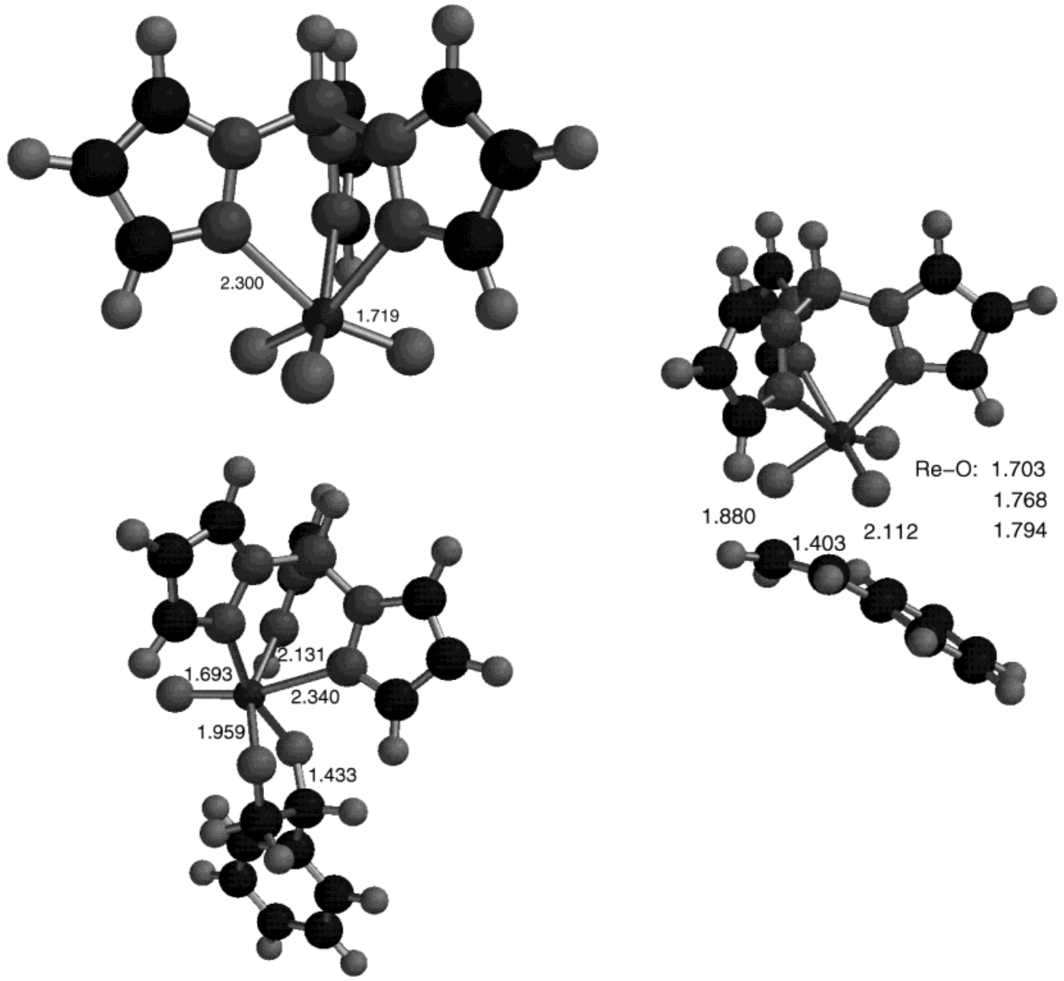

Figure 4. Optimized structures at the B3LYP/LACVP*+ level.

C−C bond is substantially shortened to 1.403 Å (from 1.537 Å in the phenylethanediolate). The β diolate carbon is still somewhat pyramidalized (sum of bond angles = 351°), while the α carbon appears to have substantially rehybridized (sum of bond angles = 358°).

Analysis of charge reorganization on going to the transition state is revealing. A diagram showing atomic charges derived from electrostatic potentials[32] is seen in Figure 5. While the rhenium unsurprisingly gains some positive character, the oxygens show remarkably little change in charge density. The carbons of the alkene, however, adopt substantial polarization; the α carbon gains substantial positive charge, while the β carbon becomes significantly more negative.

Quantitative estimation of kinetic isotope effects from vibrational analysis has become common; however, in most cases the simplest congener of a reaction type is used to minimize the impact of inaccuracies in the specific frequencies used. In this case the size of the molecule and in particular the number of normal modes that were unrelated to the reaction coordinate made such quantitative estimation unwieldy and of dubious value. However, a qualitative estimation based on our transition state structure is in all facets consistent with observed KIEs; the bond reorganization is more extensive at the α position, predicting substantially larger primary and secondary KIEs at that position. Perhaps of some surprise is that the experimental KIEs at the β position are as small as they are given the still substantial bond cleavage to that site and the degree of C−C bond contraction.

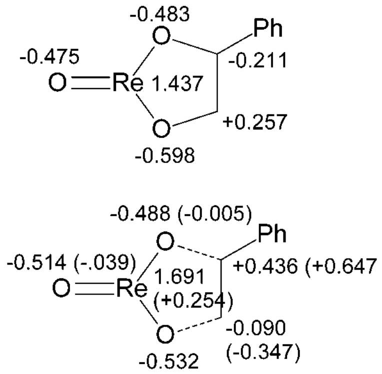

Figure 5. Atomic charges derived from electrostatic potentials for the ground-state diolate (top) and the transition-state (bottom); changes are in parentheses.

Discussion

Primary and secondary kinetic isotope effects for production of 4-methoxystyrene clearly and consistently show asymmetry in the transition state. However, the observation of KIEs that

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are significantly greater than unity (even if not by much) at the β position demonstrate some degree of bond cleavage at that site. The mechanistic conclusions must be drawn from a consideration of different types of reaction processes.

Stepwise Migrations. From the perspective of KIEs, the migratory mechanisms to form either a coordinated epoxide or a metallaoxetane are very similar. One position should show both large primary and secondary effects; the other should show a much smaller effect which ought to be very close to unity for a k_{12C}/k_{13C}. The secondary effect at the β position may be nonnegligible, depending on the specific changes in zero-point energies that accompany bond reorganization, but in general one expects negligible changes for a site that undergoes no change in bonding by the transition state. It is reasonable to assume that because the electronic effect of phenyl substitution is to increase reaction rate, the substituted α carbon will migrate in the rate-limiting step of either mechanism and show the large KIEs.

Observation of a significant primary KIE at the β carbon is inconsistent with the expectations of these two mechanisms. It is possible that competition between migration of the α and β carbons could lead to observation of primary KIEs at both sites, but a quantitative model makes this all but impossible. Consider that the rate ratio for styrene vs ethylene extrusion at 100 °C is 61.4;[18] this should be to a first approximation the rate differential for migration of substituted and unsubstituted positions. The expressions for the unlabeled and labeled rate constants are:

unlabeled:

$$k_{\mathrm{obs}}(\rho) = k_{\mathrm{benzyl}} + k_{\mathrm{CH2}} = 62.4\ k_{\mathrm{CH2}}$$

α-labeled:

$$k_{\mathrm{obs}}(\alpha) = k_{\mathrm{benzyl}}/z_\alpha + k_{\mathrm{CH2}} = \{(61.4 + z_\alpha)/z_\alpha\}\ k_{\mathrm{CH2}}$$

β-labeled:

$$k_{\mathrm{obs}}(\beta) = k_{\mathrm{benzyl}} + k_{\mathrm{CH2}}/z_\beta = (61.4 + 1/z_\beta)\ k_{\mathrm{CH2}}$$

Here k_{obs} is the observed rate constant for any particular isotopomer, k_{benzyl} is the rate of migration of a phenyl-substituted carbon, and k_{CH2} is the rate of migration of an unsubstituted carbon. Mechanistic isotope effects z_α and z_β ought to be similar if not identical, but solving the observed phenomenological KIEs ($k_{\mathrm{obs}}(\rho)/k_{\mathrm{obs}}(\alpha)$ and $k_{\mathrm{obs}}(\rho)/k_{\mathrm{obs}}(\beta)$) for z_α and z_β give, respectively $z_\alpha = 1.0367$ and $z_\beta = 7.25$. The latter is clearly unreasonable for a primary ^{13}C effect. Considering that 4-methoxystyrene extrusion is faster than styrene extrusion requires an even larger z_β. A similar approach assuming each mechanistic KIE to be about 1.04 and solving for the rate differential demands that k_{benzyl} be only 1.5 times k_{CH2}, inconsistent with the rates of ethylene vs styrene (or 4-methoxystyrene) extrusion. It is thus impossible to reconcile the observed kinetic effect of aryl substitution with the relative magnitudes of the KIEs at the two positions.

The only part of this study that initially pointed to a stepwise migration was the highly curved Hammett plot. As with our earlier study of stilbene extrusion from Cp*Re(O)(diolato) complexes, the curvature hinted at a balanced competition between cleavage of the two C−O bonds. However, this model predicts that the slope of one leg of this plot should be near-zero reflecting an attenuated electronic impact on CH_2 migration. The increase in rate on both sides of the Hammett plot suggests two different compensatory electronic effects. Initially, we envisioned this as a "push" from electron donors making the benzylic oxygen more nucleophilic in a migration of the β-carbon to form a coordinated epoxide, and a "pull" by electron-deficient groups making the benzylic carbon more electrophilic for an α-carbon migration. However, this model would demand large β KIEs and small α KIEs and therefore cannot be operating for extrusion of 4-methoxystyrene. Notably, the KIEs reported here apply only to the substrate with a fairly electron-donating methoxy group; the consequences for less electron-rich styrenes will be discussed below.

One important aspect of the new observations lies in the magnitude of the secondary KIE. Recall from above that cycloreversion of Cp*Re(O)(OCD_2CD_2O) occurred with a d_4-KIE of 1.25, which could be interpreted as either a per-ρ KIE of 1.13 on migration of a single carbon, or 1.06 on concerted fragmentation of the diolate. The magnitude of the α effect from the current study, 1.076, is not large enough to be consistent with the demands of the earlier experiment for a stepwise migration, but fall in line with expectations from a concerted model. (Of course, this assumes mechanistic congruence between compounds with different ancillary ligands.)

Concerted Cycloreversion. The most straightforward explanation of the results is that the extrusion of 4-methoxystyrene is concerted, but that there are different degrees of bond cleavage for the two C−O bonds at the transition state. The consistency of the primary and secondary KIEs argues strongly for this viewpoint. Location of a computationally modeled transition state structure that agrees with this proposal further supports the hypothesis, particularly insofar as the predicted activation barrier and reaction energy are consistent with observation.

However, the Hammett study provides curious additional information regarding this possibility. In a concerted process, the Hammond postulate leads to the prediction that there should be a relationship between $\Delta G^\ddagger$ and ΔG° for reactions of different substrates.[33] A relatively electron-rich alkene such as 4-methoxystyrene will have a less-favorable ΔG° for cycloreversion than will styrene and more electron-deficient styrenes. Presumably, $\Delta G^\ddagger$ should become larger as ΔG° gets less favorable. Thus, the more electron-rich an alkene (the easier it is to oxidize), the harder it should be to extrude from a diolate complex. While this behavior is observed for electron-deficient styrenes, the *opposite* behavior is observed for electron-rich styrenes. (The fact that $\Delta H^\ddagger$ increases slightly for the methoxy compound might suggest that free energy is not the appropriate measure in that entropy changes for different substituents can have a nontrivial impact.)

The electronic effects for electron donors are consistent with a transition-state structure that has some positive charge buildup at the benzylic site, but electron-deficient styrenes must be extruded via a transition state that has considerably different charge distribution. This opens the possibility, consistent with standard arguments, that two different mechanisms are in competition. As noted previously, it may be the case that concerted mechanisms with different electron demands could be in competition.[34] However, this would require that HOMO−

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[33] Isaacs, N. *Physical Organic Chemistry*, 2nd. ed.; Addison Wesley Longman: Edinburgh, 1995; pp 118−123.

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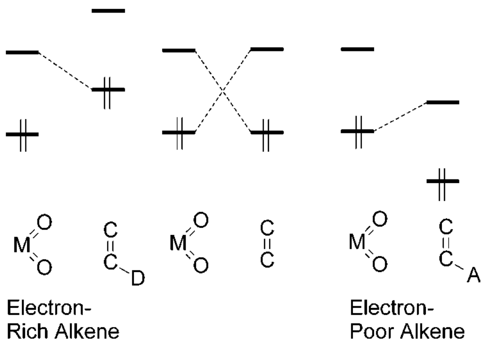

Figure 6. Possible variation in metal oxo/alkene HOMO−LUMO interactions as a function of alkene electron demand.

LUMO interactions (Figure 6) were perfectly balanced for the unsubstituted styrene extrusion and that both electron donors and electron-withdrawing groups distort the balance and encourage one HOMO−LUMO interaction in the transition state. This might explain why the Cp* complexes show this balanced behavior for stilbene extrusion and not for styrene extrusion, but the Tp′ complexes are balanced for styrene extrusion.

A more attractive interpretation is to conclude that for electron-rich styrenes, the transition state is concerted but highly asynchronous, with a significant degree of polar character. The electronic structure of this transition state would appear to be specifically induced by the electron-donating nature of the 4-methoxyphenyl substituent. A competing transition state structure would then be necessary for electron-deficient styrenes; this could be a concerted process with different electron demand, or it could be one of the stepwise reactions. The calculated transition state is consistent with the experimental behavior of electron donors in that the benzylic carbon becomes substantially more electron deficient, and obviously donors on the ring will accelerate development of this electron distribution (cf. Figure 5). More work will be necessary to test whether an electron-deficient substituent can induce a different charge reorganization in the transition state.

The degree of asynchronicity described by the computed transition state structure is extreme, and on the same order as noted for Diels−Alder reactions of dicyanoethylene[20a,b] and acrolein−BH_3 complex.[20c] (Ozonolysis of styrene, another reaction accepted to be concerted, shows almost identical per-ρ α and β deuterium KIEs.[35] The impact of the aryl group by itself on synchronicity can thus be judged to be minimal.) Particularly given that very little net charge development is evident (determined on the basis of the absence of significant solvent effects),[11] this is surprising and suggests that the concerted transition state is extremely malleable in accommodating the demands of the particular system. This to some extent rationalizes our earlier results in that (for example) in extruding a strained alkene, the system would avoid developing sp^2 character at both positions until after the transition state. Thus, the ability of this reaction to easily alter the extent of synchronous bond cleavage highlights the risk that any probe of concertedness will create the appearance of a nonconcerted process. This possibility has been noted previously.[15a] The advantage of using isotope effects to probe the system is that they provide the most minimal perturbation of steric and electronic interactions. It remains to confirm that electron acceptors create a complementary perturbation of the electronic structure in this system; these experiments are underway.

Conclusions

Cycloreversion of 4-methoxystyrene from Tp′Re(O)(OCHPhCH$_2$O) proceeds via a significantly asynchronous but concerted transition state. Primary ^{13}C and secondary ^2H kinetic isotope effects are consistent with each other in pointing to significantly more bond breaking to the α carbon than to the β carbon. Quantitative analysis of the KIEs coupled with the observed impact of aryl substitution on the rate of cycloreversion rigorously excludes the possibility of competing single bond-cleaving (stepwise) processes being responsible for the observed KIE values. DFT calculations locate a transition-state structure for styrene extrusion that agrees with this picture. However, the changes in electron distribution calculated for this transition state disagree with the observed acceleration of cycloreversion for electron-rich substituents. The Hammett behavior suggests that different substituents can induce shifts in the direction of electron flow during initial bond cleavage; this indicates that the transition-state structure (physically and electronically) is quite flexible. Such a description explains earlier work that strongly suggested stepwise cleavage of the C−O bonds during diolate cycloreversion.

Experimental Section

General Procedures. All reactions were performed using either standard benchtop or inert atmosphere techniques in a nitrogen-filled glovebox (Vacuum-Atmospheres Co. HE 493) or on a double-manifold Schlenk line. Solvents were purified by vacuum distillation prior to use; ether and THF were distilled from Na/benzophenone, hexane and benzene from K/Na alloy; dimethyl sulfoxide and toluene were dried with molecular sieves. Molecular sieves (4Å, Fisher) were activated by heating under vacuum (0.01 mbar) at 300 °C for at least 4 h prior to use. Infrared spectra were run on a Nicolet Magna-IR560.

A general method for preparation of the Tp′ diolates have been described previously. Tp′ReO$_3$ was synthesized by a published procedure.[36] Triphenylphosphine was recrystallized from ethanol. $^{13}CO_2$, $^{13}CH_3I$, and CD_3I were purchased from Aldrich. All diols were obtained from osmylation of the corresponding styrene.[11] Unlabeled *p*-chloro-, *p*-trifluoromethyl-, *p*-methyl-, and *p*-methoxystyrenes were used as received from Aldrich. Synthesis of ^{13}C- and D-labeled substituted styrenes are described in Supporting Information. General procedures for kinetic studies have been described elsewhere.[18] The general method employed in KIE studies was described in refs 25 and 17.

Synthesis of Hydrido-tris-(3,5-dimethylpyrazolyl)borato(oxo)-rhenium (V) (4-Methoxyphenyl)-ethane-1,2-diolate. A representative preparation is described here. The syntheses of labeled compounds were all accomplished in the same manner; yields and characterization are below. Yields were not optimized given the need for maximum purity.

A round-bottom flask was charged with Tp′ReO$_3$ (2.34 g, 4.40 mmol), 1-(4-methoxyphenyl)ethane-1,2-diol (0.620 g, 3.69 mmol), triphenylphosphine (1.90 g, 7.30 mmol), *p*-toluenesulfonic acid (36 mg, 78 mmol). THF (50 mL) was vacuum transferred onto the solids and the mixture stirred at room temperature for 24 h. The blue mixture was filtered and the filtrate reduced to a solid in vacuo. The residue was chromatographed on silica using CH_2Cl_2/acetone (gradient elution). The *syn*-diolate is eluted first followed by the *anti*-diastereomer. Removal of the solvent and recrystallization from chloroform/hexane gave 0.83 g (28%) of the *anti*- and 0.13 g (4.4%) of the *syn*-diolates.

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[36] Matano, Y.; Northcutt, T. O.; Brugman, J.; Bennett, B. K.; Lovell, S.; Mayer, J. M. *Organometallics* **2000**, *19*, 2781−2790.

***anti*-Diastereomer:** ^{1}H NMR (CDCl$_3$, δ, ppm): 7.37 (d, $J = 8.1$ Hz, 2H), 6.88 (d, $J = 8.1$ Hz, 2H), 6.23 (dd, $J = 6.6$, 9.6 Hz, 1H), 5.97 (s, 1H), 5.96 (s, 1H), 5.65 (dd, $J = 6.6$, 10.3 Hz, 1H), 5.53 (s, 1H), 4.59 (t, 9.6 Hz, 1H), 3.81 (s, 3H), 2.67 (s, 3H), 2.54 (two unresolved s, 6H), 2.50 (s, 3H), 2.47 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (CDCl$_3$, δ, ppm): 159.2, 157.5, 156.8, 153.7, 147.7, 146.9, 143.0, 138.7, 128.9, 113.6, 108.2, 107.6, 107.5, 95.9, 94.5, 55.4, 14.5, 14.4, 14.0, 12.7, 12.6, 12.5. MS: ($M^+ + 1$) 667. ***syn*-Diastereomer**: ^{1}H NMR (CDCl$_3$, δ, ppm): 7.63 (d, $J = 8.2$ Hz, 2H), 6.98 (d, $J = 8.2$ Hz, 2H), 6.02 (s, 1H), 5.99 (s, 1H), 5.87 (dd, $J = 7.7$, 10.6 Hz, 1H), 5.78 (t, $J = 9.53$ Hz, 1H), 5.50 (s, 1H), 5.42 (t, $J = 9.88$ Hz, 1H), 3.85 (s, 3H), 2.67 (s, 3H), 2.65 (3H), 2.57 (s, 3H), 2.55 (s, 3H), 2.23 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (CDCl$_3$, δ, ppm): 158.8, 157.5, 157.0, 154.0, 147.7, 147.1, 143.2, 135.0, 127.5, 113.9, 107.9, 107.8, 107.3, 98.0, 89.1, 55.5, 15.5, 14.2, 13.8, 12.7, 12.6, 12.5. MS: ($M^+ + 1$) 667.

Cycloreversion of ^{13}C- and D-Labeled Hydrido-*tris*-(3,5-dimethylpyrazolyl)-borato(oxo)rhenium (V) (4-Methoxyphenyl)-ethane-1,2-diolates. Typically, a 12 × 75 mm glass vessel was charged with ~150 mg of an equimolar mixture of the α, β, and *p*-OMe isotopomers. 3 mL of toluene was vacuum transferred, and the vessel was sealed under vacuum. This was heated in a thermostated bath to 103 °C; temperature was measured with calibrated thermometers to ±0.1 °C. The percent conversion was estimated by timing the reaction. Upon completion, the vessel was opened and the mixture was chromatographed (SiO$_2$, CH$_2$Cl$_2$) to reisolate unreacted diolate.

NMR Measurements. NMR spectra were obtained on either a Bruker DP300 (operating at 300.133 MHz for proton or 75.469 MHz for ^{13}C) or a Bruker DPX400 (operating at 400.134 MHz for proton or 100.614 MHz for ^{13}C). All chemical shifts are referenced either to residual protons or to carbons in solvent and are expressed in ppm downfield from tetramethylsilane. A T_1 determination was done for each signal of interest using the inversion−recovery method. For quantitative NMR work the digital resolution of 19 pts/Hz (^{1}H) and 12 pts/Hz (^{13}C) was used. A relaxation delay of 25 s ($>5T_1$) was used in both cases. All FIDs and Fourier transformed spectra were baseline corrected. For quantitative ^{13}C NMR work an inversed gated decoupling pulse sequence was used. Line shapes were assumed to be Lorenzian, integrations were determined numerically using a constant integral region set at 3.08 times the peak width at half-height (80% total peak area).[37] Uncertainties were determined as previously described.[38]

Acknowledgment. We thank the NSF for financial support (CHE0078505).

Supporting Information Available: Additional experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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