New Molybdenum Catalysts for Alkyl Olefin Epoxidation. Their Implications for the Mechanism of Oxygen Atom Transfer

Judith M. Mitchell and Nathaniel S. Finney*

Contribution from the Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093-0358

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Abstract: We report here the design, synthesis, and characterization of new (dioxo)Mo(VI) epoxidation catalysts based on monoanionic tridentate ligands. Two important features distinguish these catalysts from those previously reported. First, their coordination environment remains well-defined during the epoxidation reaction. Second, the ligand design does not permit simultaneous coordination of olefin and alkyl hydroperoxide. Based on the study of these new catalysts, we conclude that direct oxygen atom transfer from coordinated alkyl peroxide to olefin remains the simplest mechanism consistent with the available data. We discuss literature discrepancies in this regard.

Introduction

Molybdenum-catalyzed epoxidation is an important process for the production of both bulk and fine chemicals: it remains the basis for the industrial production of propylene oxide, and is a convenient laboratory method for the epoxidation of more complicated alkyl olefins.[1,2] Despite its long history and industrial relevance, the mechanism of Mo(VI)-catalyzed epoxidation of olefins with alkyl hydroperoxides remains a subject of debate.[2] Certain details of the mechanism—formation of a Mo(VI) alkyl peroxide and transfer of the distal oxygen atom of the alkyl peroxide rather than an oxo ligand—are generally agreed upon. However, it remains a point of contention whether the reaction proceeds by direct oxygen atom transfer or via the formation of a Mo(VI)−olefin complex (Scheme 1). Our efforts to resolve this mechanistic ambiguity are described herein.

Background

The conflicting mechanisms are summarized in Scheme 1. The direct oxygen atom transfer mechanism (Path A) involves a concerted single-step process in which an olefin nucleophile attacks a Mo(VI)-coordinated alkyl hydroperoxide electrophile, producing epoxide and metal alkoxide. The alternative mechanism (Path B) involves reversible binding of the olefin to a Mo(VI) alkyl hydroperoxide complex (**B**). In the most commonly discussed variation, **B** undergoes rearrangement to peroxymetallacycle **C**, which fragments into epoxide and metal alkoxide.[3]

The arguments in favor of direct oxygen atom transfer may be summarized as follows.[4] Direct transfer depicts the olefin as a nucleophile reacting with an electrophilic oxygen center, and thus easily explains the observation that electron-rich olefins react more quickly than electron-poor olefins. It is also consistent with the observation that allylic alcohols are epoxidized more rapidly than unfunctionalized olefins: rapid precoordination of the Lewis-acidic metal center to the hydroxyl group accelerates the epoxidation by making it an intramolecular process.[5] The enhanced reactivity of allylic alcohols relative to alkyl olefins in Mo(VI) and V(V) systems has also been used to argue against the intermediacy of peroxometallacycles such as **C**, as simultaneous hydroxyl coordination and metallacyle formation would lead to a highly strained bicyclic intermediate. Finally, and perhaps most importantly, direct oxygen atom transfer is the simpler of the two mechanisms and must be preferred in the absence of contrary evidence.

Contrary evidence does, however, exist: there are kinetic data indicating that many Mo(VI)-mediated epoxidations exhibit a non-first-order dependence on olefin concentration, which cannot be accounted for by the direct oxygen atom transfer mechanism. The intermediacy of Mo(VI)−olefin complexes was first invoked to explain the kinetic profile of stoichiometric epoxidations mediated by $MoO(O_2)_2$·L complexes (L = HMPA, DMF, etc.).[6] The observation of saturation kinetics as olefin concentration was increased led to the proposal of reversible formation of **B**. At low olefin concentration, formation of **B** would be rate limiting, while at high olefin concentration this preequilibrium would be saturated (reminiscent of Michaelis−Menten kinetics), leading to a rate-determining step that is no longer dependent on olefin concentration. Similar kinetic studies of catalytic epoxidations based on both (dioxo)Mo(VI) and oxo(bisperoxo)Mo(VI) complexes are also consistent with the formation of Mo(VI)−olefin intermediates.[7] In the context of

(1) (a) Landau, R.; Sullivan, G. A.; Brown, D. D. *Chemtech* **1979**, 602−607. (b) Sheldon, R. A. In *Aspects of Homogeneous Catalysis;* Ugo, R., Ed.; D. Reidel: Boston, 1981; Vol. 4.

(2) (a) Mimoun, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 734−750. (b) Di Furia, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853−1866. (c) Mimoun, H. *Catal. Today* **1987**, *1*, 281−295. (d) Jørgensen, K. A. *Chem. Rev.* **1989**, *89*, 431−458. (e) Schurig, V.; Betschinger, F. *Chem. Rev.* **1992**, *92*, 873−888.

(3) Other pathways for the conversion of **B** to epoxide can be envisioned. As this work focuses on the formation of **B** rather than subsequent steps, this point will not be addressed further.

(4) (a) Sharpless, K. B.; Townsend, J. M.; Williams, D. R. *J. Am. Chem. Soc.* **1972**, *94*, 295−296. (b) Chong, A. O.; Sharpless, K. B. *J. Org. Chem.* **1977**, *42*, 1587−1590.

(5) While most commonly associated with V(V) catalyst systems (Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370, and references therein), it has also been observed with Mo(VI): Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136−6137.

(6) (a) Mimoun, H.; de Roch, I. S.; Sajus, L. *Tetrahedron* **1970**, *26*, 37−50. (b) Arakawa, H.; Moro-oka, Y.; Ozaki, A. *Bull. Chem. Soc. J.* **1974**, *47*, 2958−2961.

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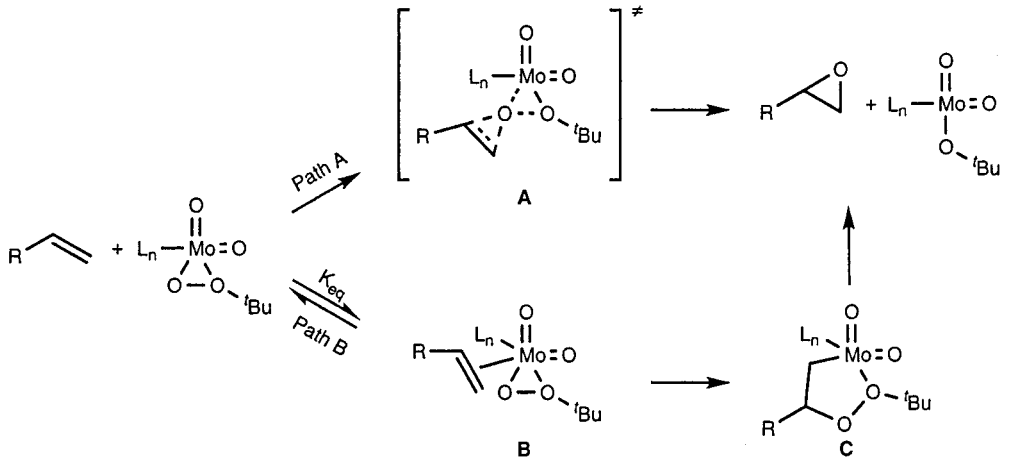
Scheme 1. Possible Epoxidation Mechanisms



Path B, the greater reactivity of more electron-rich olefins is explained by enhanced precoordination to the electron-deficient Mo(VI) center. The increased reactivity of allylic alcohols has been addressed by arguing that formation of epoxide via a bicyclic intermediate is either less unfavorable than intuition might suggest or reflects kinetic rather than thermodynamic control.[8]

While it is clear that, in its simplest form, direct oxygen atom transfer cannot account for the observed non-first-order kinetics, two important caveats must be made regarding these kinetic data. First, while the data may demonstrate that Mo(VI)−olefin complexes do form, this does not prove they are essential for oxygen atom transfer. Second, unlike the stoichiometric $MoO(O_2)_2$·L oxidations, virtually all of the catalytic epoxidations for which kinetic characterization has been reported involve multiple catalytically active Mo(VI) species, as a result of either uncontrolled ligand exchange or the use of a Mo(0) catalyst precursor.[9,10,11] While some of these systems, as noted above, display non-first-order olefin kinetics, others are reported to be linearly dependent on olefin concentration.[12] Whether the formation of Mo(VI)−olefin complexes is integral or incidental to the catalytic cycle thus remains an open question.

Experimental Design

Our approach to addressing this mechanistic issue relies on (dioxo)Mo(VI) epoxidation catalysts designed to preclude simultaneous coordination of olefin and bidentate alkyl peroxide. We began by analyzing common features of the coordination environments of transition state **A** and intermediate **B** (Scheme 1). Taking into account the presence of two cis spectator oxo ligands, the required formation of a triangularly coordinated monoanionic bidentate alkyl peroxide,[13] and the propensity for Mo(VI) to become seven-coordinate,[14] three coordination sites and one valence remain available for association of ligand and/or olefin. Transition structure **A** should be able to accommodate a tridentate monoanionic ligand. In contrast, intermediate **B**, which requires a vacant coordination site for the olefin, should not be able to accommodate such a ligand. Thus, if Mo(VI) complexes of monoanionic tridentate ligands proved catalytically active, it would provide prima facie evidence that the reaction does not require olefin precoordination.[15,16]

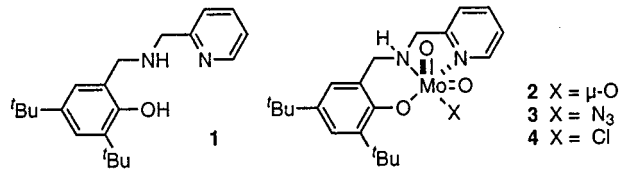


Figure 1.

Synthesis and Characterization of Molybdenum Complexes. Among the many possible topologies for monoanionic tridentate ligands—a ligand class largely unexplored in transition metal catalysis—we selected the readily available compound **1** and the corresponding Mo(VI) complexes **2**−**4** for study (Figure 1). The syntheses of ligand **1** and Mo(VI) complex **2** are illustrated in Scheme 2. Formation of the imine derived from 3,5-di-*tert*-butyl salicylaldehyde and 2-methylaminopyridine

(7) Su, C.-C.; Reed, J. W.; Gould, E. S. *Inorg. Chem.* **1973**, *12*, 337−342.

(8) Mimoun, H. *J. Mol. Catal.* **1980**, *7*, 1−29.

(9) For demonstration of the presence of multiple catalytically active Mo(VI) species, see: (a) Sheldon, R. A. *Recl. Trav. Chim.* **1973**, *92*, 253−266. (b) Sheldon, R. A. *Recl. Trav. Chim.* **1973**, *92*, 367−373. (c) Talsi, E. P.; Shalyaev, K. V.; Zamaraev, K. I. *J. Mol. Catal.* **1993**, *83*, 329−346. (d) Talsi, E. P.; Klimov, O. V.; Zamaraev, K. I. *J. Mol. Catal.* **1993**, *83*, 347−366.

(10) For a discussion of the kinetic implications of the presence of multiple catalytically active species (including Mo(VI)−olefin complexes), see: (a) Di Furia, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853−1866. (b) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G.. *J. Mol. Catal.* **1983**, *19*, 331−343. (c) Sapunov, V. N. *J. Mol. Catal.* **1980**, *7*, 149−158.

(11) For representative studies on an exceptionally well-characterized catalytic epoxidation system based on 7-coordinate $MoO(O_2)_2$·L complexes bearing neutral bidentate ligands, see: (a) Thiel, W. R.; Priermeier, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1737−1738. (b) Thiel, W. R. *J. Mol. Catal. A* **1996**, *117*, 449−454. (c) Thiel, W. R.; Eppinger, J. *Chem. Eur. J.* **1997**, *3*, 696−705. (d) Hroch, A.; Gemmeker, G.; Thiel, W. R. *Eur. J. Org. Chem.* **2000**, 1107−1114 and references therein.

(12) (a) Sheng, M. N.; Zajacek, J. G. *J. Org. Chem.* **1970**, *35*, 1839−1843. (b) Howe, G. R.; Hiatt, R. R. *J. Org. Chem.* **1971**, *36*, 2493−2497. (c) Baker, T. N., III; Mains, G. J.; Sheng, M. N.; Zajacek, J. G. *J. Org. Chem.* **1973**, *38*, 1145−1148.

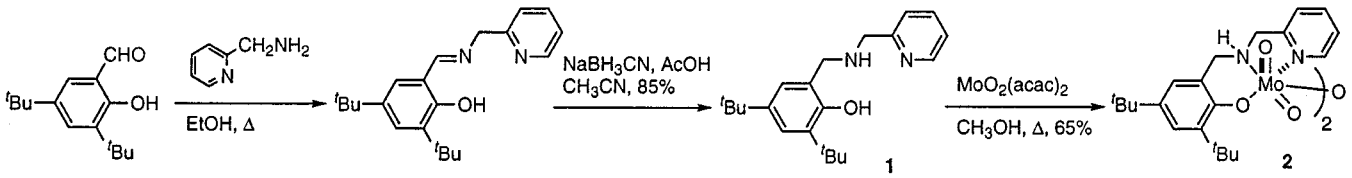
(13) "Triangular" coordination is an accepted prerequisite for oxygen-atom transfer, and is consistent with both the solution and crystal structures of oxovanadium alkyl hydroperoxide complexes, as well as theoretical models of oxygen atom transfer: (a) Mimoun, H.; Chaumette, P.; Mignard, M.; Saussine, L. *Nouv. J. Chim.* **1983**, 467−475. (b) Mimoun, H.; Mignard, M.; Brechot, P.; Saussine, L.; Rueil-Malmaison, F. *J. Am. Chem. Soc.* **1986**, *108*, 3711−18. (c) Bach, R. D.; Wolber, G. J.; Coddens, B. A. *J. Am. Chem. Soc.* **1984**, *106*, 6098−6099.

(14) For representative overviews of the extensive coordination chemistry of Mo(VI), see: (a) Stiefel, E. I. *Prog. Inorg. Chem.* **1977**, *22*, 1−223. (b) Holm, R. H. *Chem. Rev.* **1987**, *87*, 1401−1449. (c) Syamal, A.; Maurya, M. R. *Coord. Chem. Rev.* **1989**, *95*, 183−238.

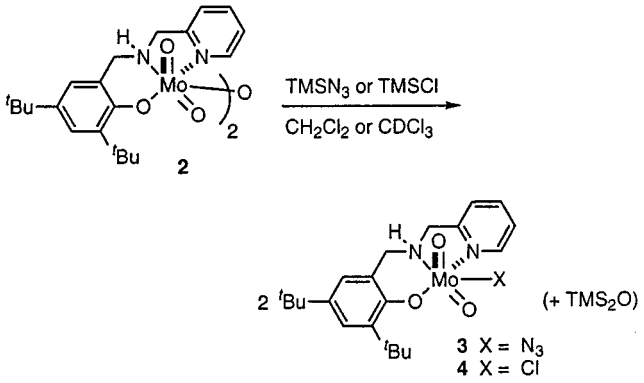
(15) To the our knowledge, no 20-electron Mo(VI) complexes have been reported. For transient electrochemical generation of an unstable, low-valent 20-electron Mo complex, see: Ballivet-Tkatchenko, D.; Boughriet, A.; Brémard, C. *Inorg. Chem.* **1986**, *25*, 826−831.

(16) For work with coordinatively saturated oxo(porphyrin)Mo(V) and oxo(porphyrin)Ti(IV) catalysts, see: (a) Ledon, H. J.; Durbut, P.; Varescon, F. *J. Am. Chem. Soc.* **1981**, *103*, 3601−3603. (b) Ledon, H. J.; Varescon, F. *Inorg. Chem.* **1984**, *23*, 2735−2737.

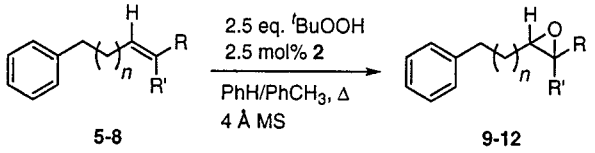
Scheme 2



Scheme 3



Scheme 4



proceeded in essentially quantitative yield under standard conditions; acidic reduction then provided **1** in 85% yield. Refluxing a slight excess of this ligand with 1 equiv of $MoO_2(acac)_2$ in methanol led, after cooling and filtration, to the isolation of **2** (65%) as an orange crystalline solid. Complex **2** was identified as a μ-oxo dimer by X-ray crystallographic analysis (Figure 2);[17,18] while the formation of a dimer was not anticipated, it is reminiscent of the low solubility of (porphyrin)Mo(V) μ-oxo dimers.[19] The location of the neutral donor atoms opposite the two oxo substituents and the anionic ligands opposite one another is typical of (dioxo)Mo(VI) species. The lability of this complex is demonstrated by the formation of the corresponding monomeric azide (**3**) upon treatment with $TMSN_3$, or the chloride (**4**) upon treatment with TMSCl (Scheme 3).

Epoxidation of Alkyl Olefins. Complexes **2**−**4** are active catalysts for the epoxidation of alkyl olefins **5**−**8**, chosen as representative epoxidation substrates (Scheme 4, Table 1). Epoxidations were carried out in benzene with anhydrous *tert*-butyl hydroperoxide as the terminal oxidant.[20] Reactions were typically followed by HPLC (see Experimental Details), but

Table 1. Epoxidation of Olefins **9**−**12**

substrate	product	R	R′	n	temp (°C)	time (h)	yield (%)[a]
5	**9**	H	H	1	55	28	75
6	**10**	CH_3	H	2	40	8	75
7	**11**	H	CH_3	1	40	24	75
8	**12**	CH_3	CH_3	1	30	25	90

[a] Reaction yields were determined by HPLC; see Experimental Section for details.

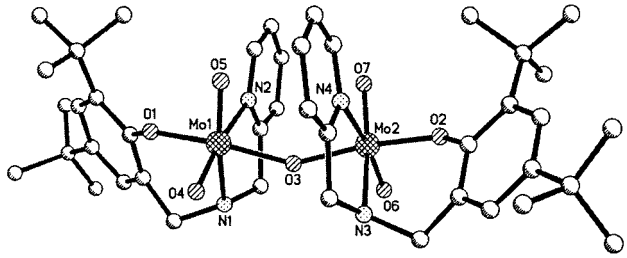


Figure 2. X-ray structure of **2**.

could also be monitored by TLC or ^{1}H NMR. Catalysts **2**, **3**, and **4** exhibit virtually identical activity, indicating that the μ-oxo dimer**,** the azide, and the chloride are readily converted to a common active monomer under the reaction conditions.[21] As a matter of convenience, the majority of our studies have been carried out on **2**.

The yields for epoxidation of **5**−**8** mediated by **2** are shown in Table 1. As anticipated, the trisubstituted olefin **8** is more reactive than the disubstituted olefins **6** and **7**, and all three are more reactive than **5**. The reaction is stereospecific: **6** gives rise exclusively to epoxide **10**, and **7** produces **11** as the sole product. That the trans olefin **6** reacts more quickly than the cis olefin **7** is somewhat surprising, in light of the kinetic preference for cis olefins exhibited by most epoxidation catalysts,[22] and presumably reflects geometric details of the active Mo(VI)−alkyl peroxide complex. The use of excess *tert*-butyl hydroperoxide is necessary to minimize product inhibition by *tert*-butyl alcohol; even with 2.5 equiv of peroxide, the epoxidation begins to slow noticeably after 60−70% conversion.[23]

In the absence of 4 Å molecular sieves, epoxides **9**−**12** underwent partial conversion to the corresponding diols, evidence of Mo(VI)-catalyzed hydrolysis.[24] Under comparable conditions employing $MoO_2(acac)_2$ as the Mo(VI) source, we

(17) Single crystals of **2** were grown from CH_3OH/CH_2Cl_2. Crystallographic analysis was carried out by Dr. Joseph Ziller at the University of California, Irvine. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 133407. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223−336−033; e-mail: deposit@ccdc.cam.ac.uk).

(18) In some cases, we have isolated a mixture of **2** and a compound tentatively identified as the terminal methoxide complex. Formation of the latter can be avoided by the addition of a small amount of water to the reaction mixture.

(19) Ledon, H. J.; Bonnet, M. C.; Brigandat, Y.; Vaescon, F. *Inorg. Chem.* **1980**, *19*, 3488−3491.

(20) Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3607−3608.

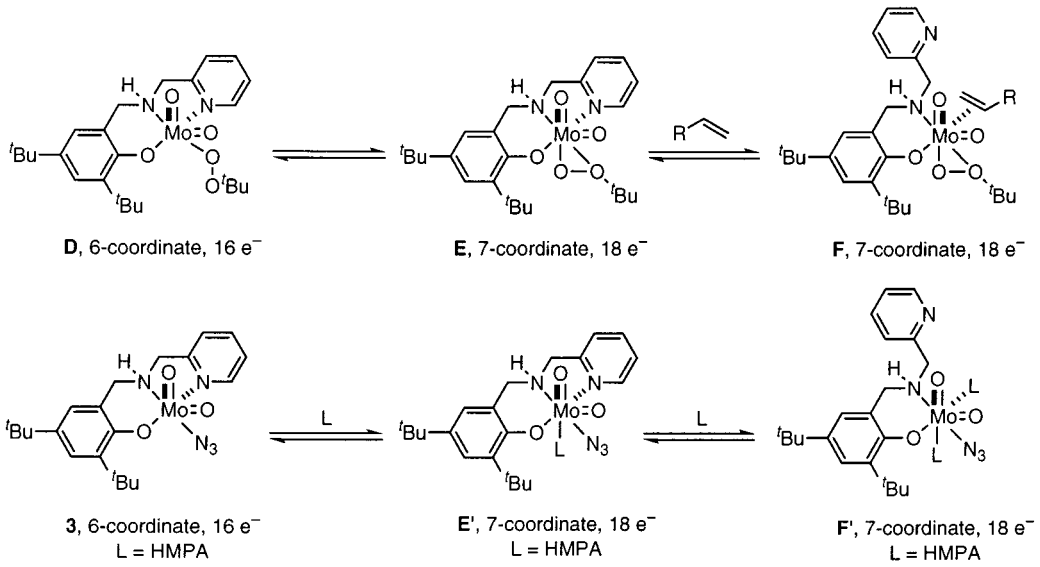
(21) Efforts to isolate the intermediate Mo(VI)−*tert*-butyl hydroperoxide complex have not yet been successful.

(22) The ordering of Z vs E reactivity is the reverse of that observed with (porphyrin)M- and (salen)M-catalyzed epoxidation reactions (M = Cr, Fe, Mn). See: (a) Jacobsen, E. N. In *Comprehensive Organometallic Chemistry II*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Hegedus, L. S., Eds.; Pergamon: New York, 1995; Vol. 12, Chapter 11.1. (b) Katsuki, T. *Coord. Chem. Rev.* **1995**, *140*, 189−214.

(23) The addition of excess (>10 equiv) of *tert*-butyl alcohol completely suppresses catalytic activity, consistent with extensive literature precedent. See, for instance: Sheng, M. N.; Zajacek, J. G. *Adv. Chem. Ser.* **1968**, *76*, 418.

(24) Conversion of epoxide to diol is a common side reaction in Mo(VI)-catalyzed epoxidation systems. For an archetypal case, in which a glycol chelate of Mo(VI) was isolated and characterized, see ref 9b.

Scheme 5. Putative Ligand Displacement



observe slightly higher catalytic activity but significantly less hydrolysis, which leads us to conclude that Lewis acidity and catalytic activity are not necessarily correlated. Another observation highlighting the Lewis acidity of these new molybdenum catalysts is that the addition of 10 equiv of triethylamine or HMPA is sufficient to suppress epoxidation completely, suggesting that these donor ligands occupy the seventh coordination site and prevent η^2-coordination of the alkyl hydroperoxide.[25]

On the basis of the observation that complexes **2**−**4** are effective catalysts for the epoxidation of alkyl olefins, we conclude that Mo(VI)−olefin complexes are not essential participants in the catalytic cycle. To reinforce this conclusion, we carried out the additional experiments described in the following section.

Ligand Dissociation and Epoxidation Kinetics. Our ligand design and the interpretation of our results are based on the assumption that the tridentate monoanionic ligand does not dissociate from the Mo(VI) center during the epoxidation, and therefore no vacant coordination site for the olefin is available. However, we have considered a scenario in which olefin manages to avail itself of a coordination site otherwise occupied by ligand. This hypothesis is illustrated in Scheme 5: if a coordination site is opened by or for the olefin as a result of partial ligand dissociation (formation of **F**),[26] it should be possible to induce similar ligand dissociation in **3** by addition of a stronger donor ligand such as HMPA (formation of **F′**). HMPA is a known inhibitor of stoichiometric $MoO(O_2)_2$·L epoxidations as well as various Mo(VI)-catalyzed epoxidations—including the present one. Further, in the context of mechanistic proposals involving Mo(VI)−olefin complexes, such inhibition has been taken as evidence that HMPA binds much more strongly to Mo(VI) than does olefin.[2]

Coordination of ligand **1** to Mo(VI) results in pronounced changes in the chemical shifts of the pyridine ring protons (Figure 3), and pronounced diasterotopicity of the two sets of methylene protons. These ^{1}H NMR signals should thus serve as a good indicator of whether the pyridine remains ligated to the Mo(VI) center of **3** in the presence of HMPA. The results of a ^{1}H NMR titration of **3** in $CDCl_3$ with up to ∼15% v/v HMPA are shown in Figure 3A. Only modest changes in the chemical shifts of the pyridine ring protons occur upon addition of HMPA; the diastereotopic methylene protons (not shown) exhibit a similar change in chemical shift, but no appreciable change in line width. Similar changes occur in the spectrum of the ligand by itself (Figure 3B), indicating that these variations derive from the change in solvent composition rather than the formation of **F′**. This in turn reasonably excludes the possibility that much weaker donor ligands such as olefin would be able to induce such ligand dissociation, and argues against the formation of an intermediate such as **F**. As an alternative probe for pyridine dissociation, we have tried to trap the free pyridine nitrogen by treatment of **2** in $CDCl_3$ with an excess of methanesulfonic acid. Again, no changes in the signals of the pyridine ring protons are observed. Finally, we note that NMR spectra of **3** at higher temperature (70 °C) provide no evidence of fluctional behavior in the ligand: the signals for the pyridine ring and diastereotopic methylene protons do not exhibit any appreciable change in line width or chemical shift.

Ultimately, the invocation of Mo(VI)−olefin intermediates derives from the kinetic profile of certain epoxidation systems. Assuming that, as concluded above, Mo(VI)−olefin complexes are not involved in the catalytic cycle, the epoxidation of **8** should be rigorously first order in olefin. Kinetic analysis of the epoxidation was carried out under the conditions indicated in Scheme 4 and Table 1, employing olefin concentrations (0.4−1.6 M)[27] in the range where nonlinear dependence on olefin concentration has previously been observed. As the data in Figure 4 indicate, the individual concentration runs all follow first-order kinetics, and lead to the extraction of a common absolute rate constant, $k = (2.9 \pm 0.5) \times 10^{-3}$ M^{-1} s^{-1}.[28] While lack of evidence is not proof, kinetic analysis of our system, in

(25) The widely accepted assumption of η^2 alkyl peroxide coordination (ref 13) is central to our interpretation, and we are unaware of any Mo(VI)/*tert*-butyl hydroperoxide epoxidations in which only η^1 alkyl peroxide coordination has been proposed. In support of this assumption, preliminary ^{1}H NMR experiments *en route* to isolating a Mo(VI) alkyl peroxide complex lead us to assign the chemical shift ($CDCl_3$, 300 MHz) of the η^2-coordinated *tert*-butyl peroxide as 1.40 ppm, 0.17 ppm downfield from the signal for free *tert*-butyl hydroperoxide. This is very similar to the chemical shifts reported for η^2 V(V) *tert*-butyl peroxide complexes (ref 13b).

(26) The ^{1}H NMR spectra of **3** do not exhibit any change in the presence of an excess of styrene or olefin **8**. The ^{1}H NMR spectra of crude epoxidation reaction mixtures show no free ligand, arguing against displacement of the ligand by *tert*-butyl peroxide and/or *tert*-butyl alcohol.

(27) At 1.6 M, the reaction is approximately 5% v/v olefin.

(28) This rate constant is at the lower end of those previously reported for Mo(VI)-mediated alkene epoxidations, both stoichiometric and catalytic, reflecting the relatively low reactivity of the present system. See ref 12.

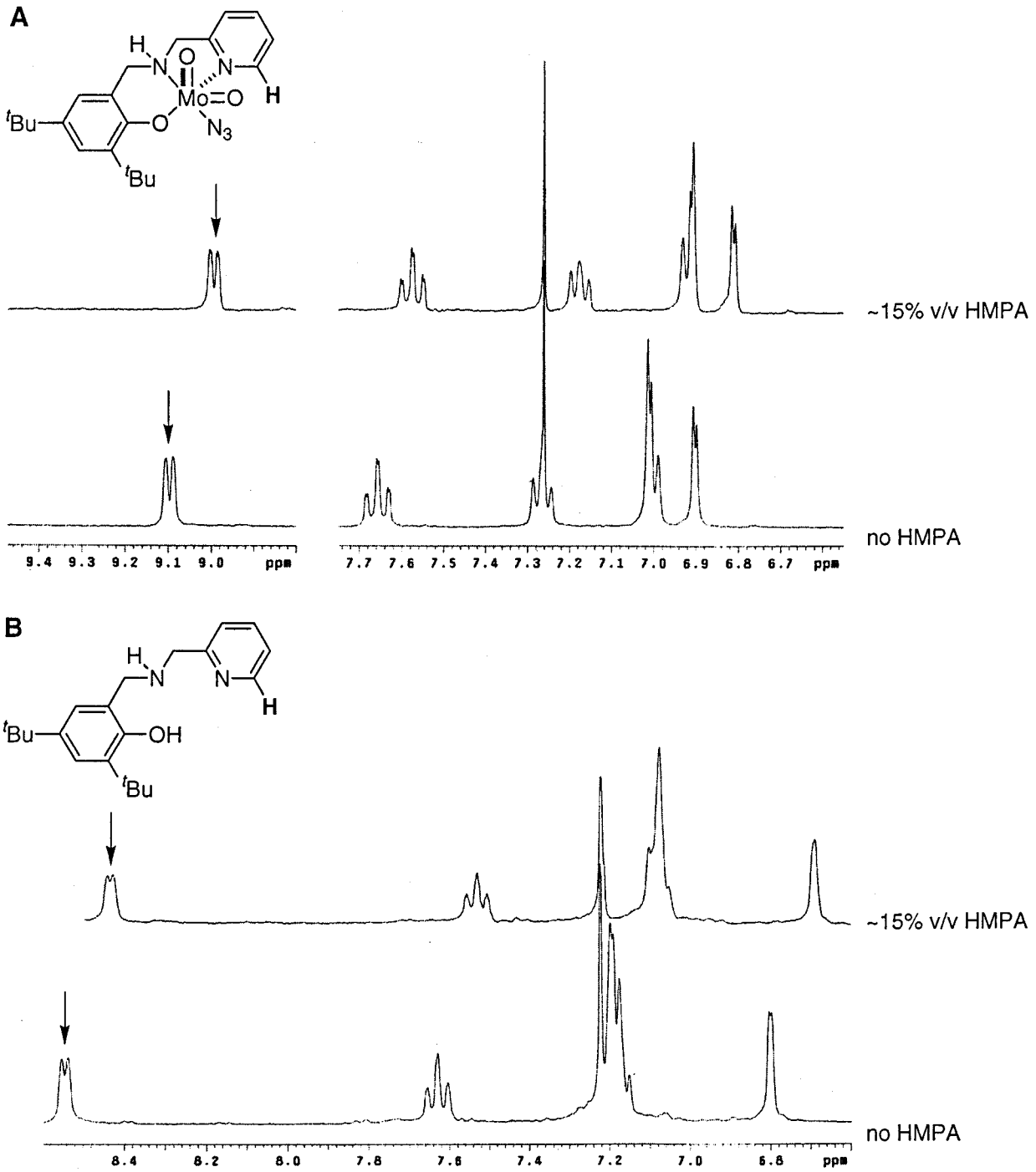


Figure 3. Titration of **3** with HMPA.

which even incidental olefin coordination should be precluded, is entirely consistent with the conclusion that metal−olefin complexes are not involved in the epoxidation reaction.

Olefins as Epoxidation Inhibitors. We have not yet been successful in isolating a Mo(VI) alkyl peroxide (e.g., **13**, Figure 5).[29] This precludes the most definitive experiment: kinetic analysis of a stoichiometric epoxidation with such a complex. Such experiments have previously been carried out with oxo(bisperoxo)Mo(VI) and (oxo)V(V) alkylperoxo complexes (**14** and **15**, Figure 5), and appear to contradict our conclusion that metal−olefin complexes are not essential intermediates in the epoxidation process. For both **14** and **15**, nonlinear rate dependence on olefin concentration is reported, and particular attention is paid to the presence of an open coordination site for olefin coordination. In the case of **14**, these reports are the origin of the argument in favor of olefin coordination and oxametallacycle formation.

These observations do not, however, necessarily contradict our conclusion. Although seldom discussed, a simple alternative interpretation of the behavior of **14** is that oxygen atom transfer is mediated by the uncomplexed oxo(bisperoxo)Mo(VI) species (**14**, L = vacant). If the HMPA and olefin complexes, which should have a less electrophilic metal center, are significantly less reactive than the uncoordinated peroxometal complex, the observed kinetic data are satisfactorily explained without

(29) To our knowledge, no Mo(VI) alkyl peroxide has ever been isolated and characterized. Efforts to prepare peroxo metal complexes, either by treatment of **2** with H_2O_2 or incubation of **1** with $MoO(O_2)_2$·DMF (ref 6a), have likewise been unsuccessful.

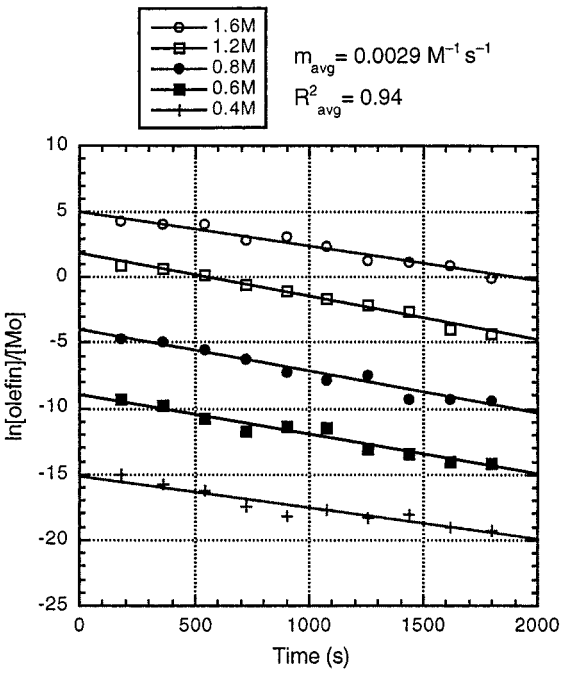


Figure 4. Kinetic analysis of the epoxidation of **8** at several concentrations.

requiring that Mo(VI)−olefin complexes appear directly in the catalytic cycle.[30] The apparent requirement for a vacant coordination site on the Mo(VI) center thus does not derive from a need to coordinate olefin, but rather the enhanced reactivity of coordinatively unsaturated Mo(VI) species.[31] In the case of **15**, if one assumes that both olefin and HMPA are capable of displacing the weakly bound second oxygen of η^2-coordinated alkyl peroxide (formation of **16**), it is not surprising that both serve as inhibitors of oxygen atom transfer. In this context, it appears that Mo(VI) complexes such as **13** are sufficiently sterically hindered to prevent olefin coordination, although coordination to smaller donors such as the oxygen center of HMPA is still possible.

Conclusion

In conclusion, we have reported the first members of a new class of Mo(VI) epoxidation catalysts based on nonlabile monoanionic tridentate ligands. Designed to preclude simultaneous coordination of olefin and bidentate alkyl peroxide, the activity of these catalysts supports an epoxidation mechanism involving direct oxygen atom transfer to olefin. This in turn leads us to conclude that previous reports of nonlinear olefin concentration dependence may be ascribed to complex kinetics resulting from the presence of multiple catalytically active species, or the formation of tangential Mo(VI)−olefin complexes which complicate kinetic analysis. While this conclusion leads to discontinuity with the mechanism of other catalytic processes in which d^0-olefin complexes or metallacycles are established intermediates (olefin metathesis and polymerization, e.g.),[32] it is in keeping with recent mechanistic studies of two other important catalytic oxidation systems: the Jacobsen epoxidation and the Sharpless asymmetric dihydroxylation.[33] Future work will focus on the isolation of Mo(VI)−alkyl peroxide intermediates and the application of **2**−**4** and related catalysts to other reactions.

Experimental Details

General Notes and Procedures. Melting points were obtained in open capillary tubes with a Thomas Scientific Uni-Melt melting point apparatus, and are uncorrected. ^{1}H NMR spectra were obtained on Varian HG-300 (300 MHz) or HG-400 (400 MHz) spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent ($CHCl_3$, s, δ 7.26). Multiplicities are given as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets), m (multiplet). Proton-decoupled ^{13}C NMR spectra were obtained on Varian HG-300 (75 MHz) or HG-400 (100 MHz) spectrometers. ^{13}C chemical shifts are reported relative to $CDCl_3$ (t, δ 77.0). IR stretches are given in cm^{-1}; spectra were obtained on a Nicolet 550 Series II Spectrophotometer. Mass spectroscopic analyses were provided by the facility at The Scripps Research Institute, with the exception of **2**, for which analysis was carried out by JEOL, Inc. (Peabody, MA).

High-pressure liquid chromatographic (HPLC) analyses were carried out on a Hewlett-Packard Series 1100 HPLC system equipped with a diode array UV detector. UV detection was performed at 210 nm. Silica gel chromatographic purifications were performed by flash chromatography with silica gel (Selecto, 32−63 μm) packed in glass columns; eluting solvent for each purification was determined by thin-layer chromatography (TLC). Analytical TLC was performed on aluminum plates coated with 0.25 mm silica gel using UV light, ethanolic *p*-anisaldehyde, or aqueous potassium permanganate for visualization.

Manipulations under an inert atmosphere were carried out with standard Schlenk line techniques. Tetrahydrofuran (THF), CH_2Cl_2, Et_2O, and benzene were dried by passage through a column of activated alumina.[34] Toluene solutions of anhydrous *tert*-butyl hydroperoxide were prepared by the method of Sharpless et al.[20] All other reagents and solvents were reagent grade and were used without further purification unless otherwise specified.

Epoxidation: Representative Procedure. In a typical epoxidation reaction, **2** (0.015 g, 0.032 mmol) and *tert*-butyl hydroperoxide (0.470 mL of a 4.26 M solution in toluene, 2.000 mmol) were combined in benzene (0.500 mL) containing 4 Å molecular sieves (ca. 0.100 g) and benzophenone (0.020 g, 0.110 mmol) as an internal standard. The resulting mixture was warmed to 30 °C under nitrogen and allowed to stir 30 min, at which time **8** (0.120 mL, 0.800 mmol) was added.

Reactions were monitored qualitatively by TLC and quantitatively by ^{1}H NMR or HPLC. For NMR analysis, samples were concentrated and epoxide quantified by integration vs benzophenone. For HPLC analysis, samples were obtained by removing a reaction aliquot and filtering through silica gel (15% *i*-PrOH−hexanes eluent) to remove Mo(VI) complexes. The sample was then diluted with 15% *i*-PrOH−hexanes, and epoxide quantified by integration vs benzophenone (210 nm, 1 mL/min, 2% *i*-PrOH−hexanes, 4.6 mm × 200 mm Waters Spherisorb S5CN). For preparative reactions, the reaction mixture was concentrated and chromatographed directly on silica gel (20% EtOAc−hexanes).

Kinetic Analyses. Kinetic data were obtained for the epoxidation of **8** according to the above procedure, at varying initial concentrations of olefin. Reaction progress was monitored by HPLC, as described

(30) Kinetic analysis of the stoichiometric epoxidation of 1-methylcyclohexene with $MoO(O_2)_2$·HMPA suggests that the uncomplexed oxo(peroxo)Mo(VI) species is 10−60 times as reactive as the HMPA complex (ref 10b). A similar (albeit attenuated) effect for olefin complexation follows as a logical inference.

(31) Recent work on catalytic epoxidations with oxo(bisperoxo)Mo(VI) (**14**, L = neutral bidentate ligand; ref 11) indicate that the apparent need for a vacant coordination site on the metal center derives from a requirement for η^2-coordination of the alkylperoxide terminal oxidant.

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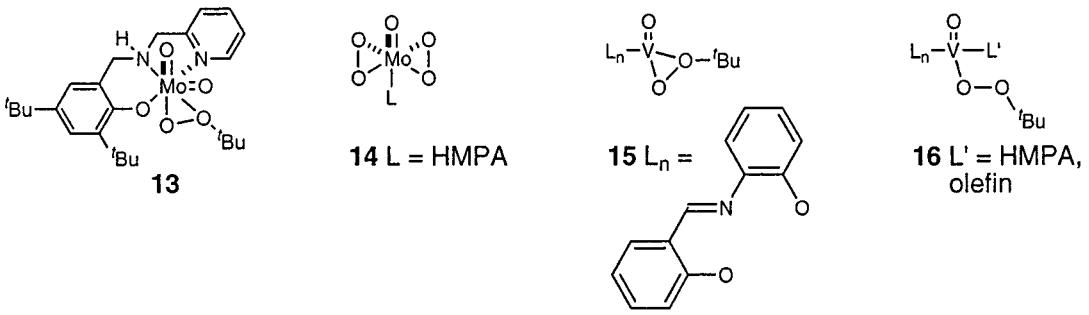

Figure 5.

above. All data presented in Figure 4 are the average of three experimental runs.

Compound Characterization. *N*-(2-Pyridyl)methyl-2-hydroxy-3,5-di-*tert*-butylbenzaldimine: To a solution of 2-hydroxy-3,5-di-*tert*-butylbenzaldehyde (1.13 g, 4.82 mmol) in CH_3OH (10 mL) was added neat 2-aminomethylpyridine (0.50 mL, 4.85 mmol, 1.01 equiv). The solution was allowed to stir for 2 h, whereupon concentration and drying in vacuo afforded the corresponding imine as a yellow solid in quantitative yield. **1**: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.57−8.59 (m, 2H), 7.69 (dt, J = 8, 8, 2 Hz, 1H), 7.43 (d, J = 2 Hz, 1H), 7.38 (d, J = 8 Hz, 1H), 7.18−7.20 (m, 1H), 7.17 (d, J = 2 Hz, 1H), 4.94 (s, 2H), 1.47 (s, 9H), 1.33 (s, 9H). IR (KBr) ν 2957, 1632. HRMS ($C_{21}H_{28}N_2O$): calcd 325.2280, obsd 325.2268 [M^+].

***N*-(2-Pyridyl)methyl-2-hydroxy-3,5-di-*tert*-butylbenzylamine (1):** A solution of the imine (1.56 g, 4.82 mmol) in CH_3CN (20 mL) was treated with $NaBH_3CN$ (0.76 g, 12.10 mmol, 2.51 equiv) and allowed to stir for 15 min, at which time acetic acid (1 mL) was added. After 2 h, the reaction mixture was diluted with Et_2O (20 mL) and washed with 1 M NaOH (2 × 40 mL) and brine (1 × 40 mL). The organic phase was dried over Na_2SO_4 and concentrated to afford an orange oil, which was purified by chromatography on silica gel (1% $CH_3OH-CH_2Cl_2$) to afford the ligand as a pale yellow oil (1.33 g, 4.10 mmol, 85%). **1**: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.58 (d, J = 5 Hz, 1H), 7.67 (dt, J = 8, 8, 2 Hz, 1H), 7.19−7.24 (m, 3H), 6.84 (d, J = 2 Hz, 1H), 3.99 (s, 2H), 3.94 (s, 2H), 1.43 (s, 9H), 1.29 (s, 9H). IR (KBr) ν 3250−3400, 2955. HRMS ($C_{21}H_{30}N_2O$): calcd 327.2436, obsd 327.2435 [M^+].

Complex 2: $MoO_2(acac)_2$ (1.33 g, 4.10 mmol) was added in one portion to a hot (50 °C) solution of **1** (1.33 g, 4.10 mmol) in CH_3OH (5 mL). The reaction was maintained at 50 °C for 2 h, during which time a bright orange crystalline solid precipitated. Complex **2** (0.81 g, 2.65 mmol, 65%) was isolated by filtration of the hot reaction mixture, followed by washing with CH_3OH (2 × 5 mL) and drying in vacuo. **2**: mp 232−235 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.69 (d, J = 5 Hz, 1H), 7.49 (dt, J = 8, 8, 2 Hz, 1H), 6.98−7.01 (m, 1H), 6.94 (d, J = 2 Hz, 1H), 6.90 (d, J = 8 Hz), 6.83 (d, J = 2 Hz, 1H), 5.47−5.49 (m, 1H), 5.16 (dd, J = 16, 8 Hz, 1H), 4.72 (dd, J = 13, 3 Hz, 1H), 3.92 (d, J = 16 Hz, 1H), 3.82 (dd, J = 13, 3 Hz, 1H), 1.23 (s, 9H), 1.18 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 157.9, 156.9, 150.5, 141.8, 138.5, 137.5, 123.8,123.5, 122.2, 121.6, 121.0, 54.5, 53.3, 34.9, 34.2, 31.7, 30.2. IR (KBr): ν 3431, 2955, 920 (Mo═O), 880 (Mo═O). Elemental Analysis: calcd ($C_{42}H_{58}N_4O_7Mo_2$) C 54.67%, H 6.33%, N 6.07%, obsd C 54.33%, H 6.06%, N 6.00%. MS (70 eV): *m*/*z* (%) 455 (50) [(ligand)MoO_2^+]. HRMS ($C_{21}H_{29}N_2O_3Mo$): calcd 455.1232, obsd 455.1236 [[(ligand)MoO_2]$^+$].

Complexes 3 and 4: The preparation of complex **3** is representative. To a solution of **2** (0.020 g, 0.02 mmol) in dry CH_2Cl_2 (1.5 mL) was added $TMSN_3$ (100 μL, 0.76 mmol, 37.7 equiv). The reaction was allowed to stir and sealed with a septum and Parafilm, at room temperature for 90 h, at which time volatiles were removed under vacuum, affording **3** as an unstable hygroscopic orange powder. As an alternative, the reaction may be carried out in $CDCl_3$, allowing spectroscopic characterization without concentration. **3**: mp >200 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 9.10 (d, J = 6 Hz, 1H), 7.66 (dt, J = 8, 8, 2 Hz, 1H), 7.20−7.40 (m, 1H), 6.95−7.05 (m, 2H), 6.91 (d, J = 2 Hz. 1H), 5.15−5.25 (m, 1H), 4.76 (d, J = 12 Hz, 1H), 4.58 (dd, J = 16, 8 Hz, 1H, CH_2), 4.00 (d, J = 16 Hz, 1H), 3.89 (d, J = 12 Hz, 1H), 1.23 (s, 9H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 157.1, 156.4, 151.1, 143.5, 139.6, 137.7, 124.1, 124.0, 123.1, 122.0, 121.5, 54.0, 43.1, 34.8, 34.3, 31.6, 30.1. IR (thin film) ν 3209, 2956, 2089 (N_3), 924 (Mo═O), 896 (Mo═O). MS (70 eV): *m*/*z* (%) 455 (100) [(ligand)MoO_2^+]. HRMS ($C_{21}H_{29}N_2O_3Mo$): calcd 455.1232, obsd 455.1226 [[(ligand)MoO_2]$^+$].

***E*-1-Phenyl-3-pentene (6):** To a solution of 6-phenyl-2-hexyne (3.3 g, 20.8 mmol) in liquid ammonia (10 mL) was added small pieces of sodium metal (0.97 g, 42.0 mmol, 2.02 equiv). The blue solution was stirred vigorously at −33 °C for 2 h, after which dry THF (5 mL) was added and the ammonia was allowed to evaporate. Solid NH_4Cl was then added cautiously to quench the reaction. The resulting solution was diluted with hexanes (75 mL) and washed with saturated NH_4Cl (3 × 75 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to afford a yellow oil, which was purified by flash column chromatography (100% hexanes) to yield olefin **6** (2.23 g, 66%) as a colorless liquid. **6**: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 7.17−7.30 (m, 5H), 5.43−5.46 (m, 2H), 2.60 (t, 2H, J = 8 Hz), 1.99−2.04 (m, 2H), 1.65−1.70 (m, 5H). IR (neat) ν 3040, 2922, 2848, 1604, 1500, 1451, 964, 710.

***Z*-1-Phenyl-3-pentene (7):** *n*-Butyllithium (32 mL, 51 mmol) was added dropwise via syringe over 10 min to a suspension of ethyltriphenylphosphonium iodide (22.5 g, 54 mmol, 1.05 equiv)[35] in dry THF (150 mL) at −78 °C. After the reaction mixture was stirred under a nitrogen atmosphere for 2 h, a solution of 3-phenylpropionaldehyde (7.6 mL, 58 mmol, 1.13 equiv) in THF (15 mL) was added dropwise via syringe over 5 min. The reaction mixture was warmed to room temperature and stirred for 12 h, then filtered through a pad of silica with hexanes. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (100% hexanes) to yield olefin **7** (4.97 g, 63%) as a colorless liquid. **7**: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.17−7.31 (m, 5H), 5.40−5.51 (m, 2H), 2.67 (t, 2H, J = 8 Hz), 2.37 (q, 2H, J = 8 Hz), 1.61 (s, 3H). IR (neat) ν 3016, 2925, 2855, 1604, 1496, 1454, 698.

1-Phenyl-3,4-dimethyl-3-pentene (8): *n*-Butyllithium (40 mL, 64 mmol, 1.01 equiv) was added dropwise via syringe over 10 min to a suspension of 2-propyltriphenylphosphonium bromide (24.3 g, 63.1 mmol)[26] in dry Et_2O (150 mL). After the reaction mixture was stirred under a nitrogen atmosphere for 2 h, a solution of 3-phenylpropionaldehyde (10 mL, 76 mmol, 1.2 equiv) in Et_2O (25 mL) was added dropwise via syringe over 5 min. The reaction mixture was refluxed for 12 h, then filtered through a pad of silica with hexanes. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (100% hexanes) to yield olefin **8** (5.17 g, 51%) as a colorless liquid. **8**: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.27−7.32 (m, 2H), 7.19−7.22 (m, 3H), 5.18 (t, 1H, J = 8 Hz), 2.63 (t, 2H, J = 8 Hz), 2.30 (q, 2H, J = 8 Hz), 1.69 (s, 3H), 1.57 (s, 3H). IR (neat) ν 3025, 2969, 2925, 2856, 1725, 1606, 1500, 1463, 1375, 760, 700.

Epoxides 9−12: The preparation of 4-Phenyl-1-butene oxide (**9**) is representative. *m*-Chloroperbenzoic acid (70% w/w, 0.21 g, 0.73 mmol, 1.09 equiv) was added to a solution of 4-phenyl-1-butene (**5**, 0.1 mL,

(35) Ethyl- and 2-propyltriphenylphosphonium bromide were prepared by heating the corresponding alkyl bromide with 1 molar equiv of triphenylphosphine in a sealed tube. The salts were used without further purification.

Table 2. Summary of Crystallographic Data for **2**

empirical formula	$C_{42}H_{58}Mo_2N_4O_7$
formula weight	922.80
temperature	158(2) K
wavelength	0.71073 Å
crystal system	monoclinic
space group	$P2_1/n$
unit cell dimensions	$a = 13.4504(11)$ Å, $\alpha = 90°$ $b = 8.5521(7)$ Å, $\beta = 95.630(2)°$ $c = 38.577(3)$ Å, $\gamma = 90°$
volume	4416.1(6) Å^3
Z	4
density (calcd)	1.388 Mg/m^3
absorption coeff	0.618 mm^{-1}
F(000)	1912
crystal size	0.21 × 0.16 × 0.06 mm^3
θ range for data collection	1.06 to 28.32°
index ranges	$-17 \le h \le 14$, $-10 \le k \le 11$, $-50 \le l \le 49$
no. of reflcns collected	28422
no. of independent reflcns	10587 [R(int) = 0.0570]
completeness to $\theta = 28.32°$	96.2%
absorption correction	semiempirical (Bruker SADABS)
max and min transmission	0.9639 and 0.8811
refinement method	full-matrix least-squares on F^2
no. of data/restraints/parameters	10587/0/497
goodness-of-fit on F^2	1.196
final R indices [$I > 2\sigma$(I)]	$R1 = 0.0529$, $wR2 = 0.0979$
R indices (all data)	$R1 = 0.0829$, $wR2 = 0.1064$
extinction coefficient	0.00024(4)
largest diff peak and hole	0.964 and −1.019 e·Å^{-3}

0.67 mmol) in chloroform (4 mL) at 0 °C, and the solution was warmed to room temperature. After the solution was stirred for 12 h, CH_2Cl_2 (20 mL) was added, and the reaction mixture was washed with 2.5 M NaOH (4 × 25 mL). The organic phase was dried over sodium sulfate and concentrated under reduced pressure to afford **9** (0.093 g, 95%) as a colorless liquid. **9**: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.21−7.36 (m, 5H), 2.96−3.02 (m, 1H), 2.74−2.92 (m, 3H), 2.51 Hz (dd, 1H, J = 5, 3.0 Hz), 1.83−1.99 (m, 2H). IR (neat) ν 3033, 2986, 2919, 2858, 1602, 1501, 1461, 1266.

***E*-1-Phenyl-3-pentene oxide (10):** ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.16−7.31 (m, 5H), 2.74 (dq, 1H, J = 5, 2 Hz), 2.63−2.69 (m, 3H), 1.67−1.89, 1.48−1.66, 1.29 (d, 3H, J = 5 Hz). IR (neat) ν 3027, 2981, 2929, 1606, 1496, 1454, 1380, 1029, 859, 747, 700.^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 141.9, 128.3, 128.2, 125.7, 59.6, 54.5, 35.7, 31.6, 27.8, 17.8. MS (70 eV): m/z (%) 176 (50) [M$^+$].

***Z*-1-Phenyl-3-pentene oxide (11):** ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.21−7.36 (m, 5H), 2.70−3.10 (m, 4H), 1.77−1.98 (m, 2H), 1.18 (d, 3H, J = 5 Hz). IR (neat) ν 3060, 2963, 2919, 2850, 1600, 1500, 1463, 1394, 756, 700.

1-Phenyl-3,4-dimethyl-3-pentene oxide (12): ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.21−7.31 (m, 5H), 2.71−2.94 (m, 3H), 1.78−2.01 (m, 2H), 1.31 (s, 3H), 1.17 (s, 3H). IR (neat) ν 2963, 2925, 1731, 1600, 1500, 1456, 1375, 1119, 700.

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Supporting Information Available: Tables of crystal data, structure solution and refinement, atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for **2** (PDF) and an X-ray crystallographic file (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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