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Enantioselective Oxidation of Di-*tert*-Butyl Disulfide with a Vanadium Catalyst: Progress toward Mechanism Elucidation†

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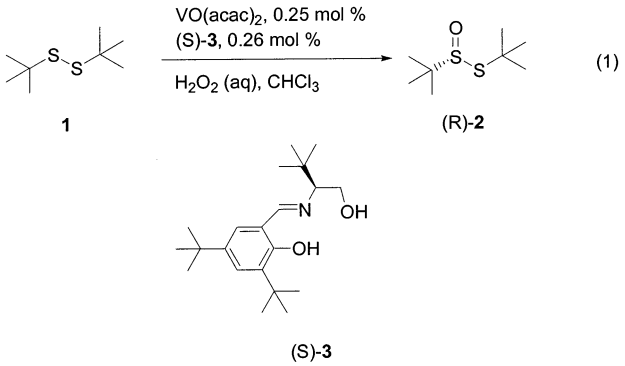
The mechanism of the oxidation of di-*tert*-butyl disulfide (**1**) to the chiral thiosulfinate (**2**) by H_2O_2 catalyzed by bis(acetylacetonato)oxovanadium and a chiral Schiff-base ligand (**3**) has been investigated. Techniques included ^{51}V NMR spectroscopy, solvent effects on reaction enantioselectivity, and the isolation and full characterization of a 2:1 ligand-to-vanadium catalyst precursor. A model for the dramatic solvent effect on the enantioselectivity of this reaction was developed, based on the identification of a competing nonselective oxidation pathway. From this model, strategies for limiting this competing pathway were developed.

Introduction

Chiral sulfinyl groups have been used as auxiliaries in a variety of highly diastereoselective carbon−carbon bond-forming reactions, including the syntheses of chiral α-branched amines,[1−4] α- and β-amino acids,[5] aziridines,[6−8] and aminophosphonic acids.[9−11] Many of these transformations used arenesulfinyl auxiliaries because practical methods for their preparation had been developed.[12−14]

In 1997, we reported the biphasic oxidation of di-*tert*-butyl disulfide (**1**) to the corresponding chiral thiosulfinate (**2**) (89% yield, 91% ee) with cost-effective hydrogen peroxide (30% aq), employing catalytic amounts of bis(acetylacetonato)oxovanadium ($VO(acac)_2$) and a chiral Schiff-base ligand (**3**) derived from *tert*-leucinol and 3,5-di-*tert*-butylsalicylaldehyde (eq 1).[3,15] This reaction was based on the Bolm protocol for oxidation of thioethers.[16,17] Thiosulfinate **2** does not undergo further oxidation under the reaction conditions. Furthermore, these conditions can be efficiently used for mole-scale reactions. Thiosulfinate **2** has proven to be a versatile intermediate for the synthesis of *tert*-butanesulfinamides[18−21] and *tert*-butyl sulfoxides[22,23] that have seen widespread use in organic synthesis.



The mechanism of this oxidation is interesting from both practical and fundamental standpoints. Mechanistic

† This paper is dedicated to the memory of Prof. Henry Rapoport, whose dedication to chemical research and education illuminated our department for many years.

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insight may aid in the design of an efficient industrial scale-up of this reaction to the ton scale, since the current biphasic conditions become inefficient on a multimole scale. Additionally, insight into this system will contribute to a broader understanding of vanadium-catalyzed oxidations employing O,N-donor ligands and stoichiometric peroxide oxidants. Other such processes include epoxidation of allylic alcohols,[24−29] development of biomimetic analogues of vanadium bromoperoxidase,[30−33] functionalization of alkanes,[34,35] and asymmetric oxidation of thioethers.[36−44]

Our progress toward elucidating the mechanism of the vanadium-catalyzed enantioselective oxidation of **1** using H_2O_2 and ligand **3** is discussed herein. In particular, we discuss isolation and X-ray crystallographic characterization of two catalyst precursors, and describe a significant solvent effect in which biphasic conditions are necessary for high enantioselectivity. Analysis of this effect led to the discovery that slow addition of H_2O_2 under fully soluble conditions results in dramatic increases in reaction enantioselectivity.

Results and Discussion

Effect of Solvent and Slow H_2O_2 Addition on Enantioselectivity. The biphasic nature of the optimized di-*tert*-butyl disulfide oxidation system complicates mechanistic studies and industrial scale-up. For these reasons, we investigated potential homogeneous reaction conditions. We observed that all reactions in which the organic cosolvent was fully miscible with the aqueous H_2O_2 yielded racemic product. Furthermore, a screen of organic cosolvents revealed an inverse relationship between the enantiopurity of **2** and the miscibility of that cosolvent with water (Figure 1). In the absence of vanadium catalyst, oxidation of **1** was slow under both biphasic and homogeneous conditions, yielding less than 5% of **2** after 7 h. Enantioselectivities of the biphasic systems were found to vary slightly (±10%) with interface area (i.e., flask shape and reaction scale).

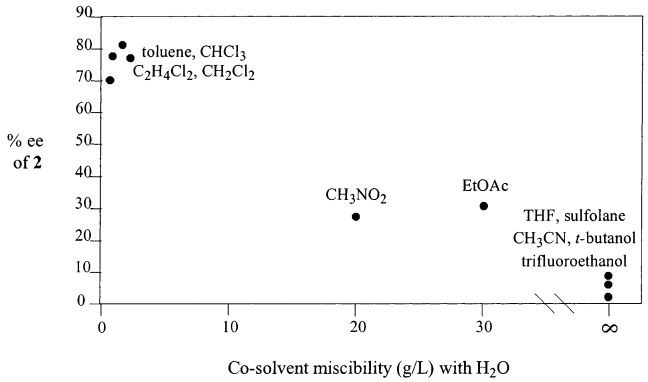

FIGURE 1. Organic cosolvent solubility (g/L) with H_2O vs ee. All reactions were run with 0.025 equiv of $VO(acac)_2$ and **3**, 1 mmol **1** scale.

TABLE 1. Increase in Reaction Enantioselectivities upon Slow H_2O_2 Addition

solvent	fast addition H_2O_2 ee (%)	slow addition H_2O_2 ee (%)
CH_3CN[a]	0	72
CF_3CH_2OH[a]	0	74
i-PrOH[a]	0	54
t-BuOH[b]	11	64
THF[b]	9	46
$CHCl_3$[b]	87	87

[a] Reaction is homogeneous. [b] Reaction is biphasic.

These results are consistent with the operation of a nonstereoselective catalytic pathway at high H_2O_2 concentrations, perhaps involving displacement of all or part of ligand **3** from the vanadium center by excess H_2O_2 to form a nonselective oxidant. As this model predicts, adding H_2O_2 slowly via syringe pump over 12 h under fully miscible conditions resulted in dramatic increases in reaction enantioselectivity to as high as 72% ee, compared to 0% ee if the oxidant is added in one portion (Table 1). No additional increase in enantioselectivity was observed with longer addition times. Slow addition of H_2O_2 into highly soluble but still biphasic cosolvents such as THF and *tert*-butyl alcohol also resulted in large increases in reaction enantioselectivities, whereas slow addition into the sparingly soluble $CHCl_3$ system did not affect the reaction enantioselectivity. Modest increases in enantioselectivity in the oxidation of thioethers under biphasic conditions upon slow H_2O_2 addition have been reported recently by Karpyshev and co-workers.[36] Specifically, portionwise addition of H_2O_2 into the biphasic CH_2Cl_2 system increased enantioselectivities from at most 29% (one portion) to 44% ee (slow addition). No homogeneous conditions, however, were reported. Homogeneous conditions that limit the nonselective pathway are particularly attractive since they may provide an efficient method for ton-scale synthesis. Because slow addition of

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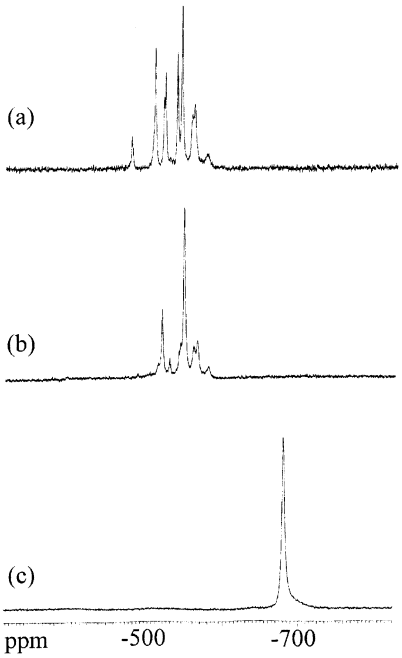


FIGURE 2. ^{51}V NMR spectra of $VO(acac)_2$ and ligand **3** (1:1) (a) with 100 equiv of H_2O_2 in CD_2Cl_2, (b) with 1 equiv of H_2O_2 in THF-d_8, and (c) with 100 equiv of H_2O_2 in THF-d_8.

H_2O_2 maintains a low peroxide concentration even under homogeneous conditions, these results are consistent with a stereoselective catalytic pathway operating at low peroxide concentrations and a competing nonstereoselective catalytic pathway operating at high peroxide concentrations. This provides an explanation for the strong dependence of enantioselectivity on the solvent system.

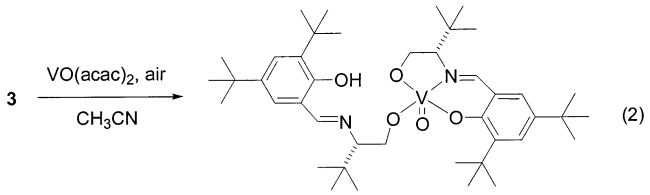
We considered that using stoichiometric amounts of ligand **3** may prevent formation of the nonstereoselective catalyst that forms under homogeneous conditions. Use of a stoichiometric amount of ligand relative to H_2O_2 (0.05:1:1:1, $VO(acac)_2$:**1**:**3**:H_2O_2) in CH_3CN, however, still produces racemic **2**. Addition of 10 equiv of **3** relative to H_2O_2 at 40% $VO(acac)_2$ catalyst loading in CH_3CN inhibits oxidation and results in the formation of only trace amounts of **2**.

Dependence of Vanadium Species on H_2O_2 Concentration. Analysis of reaction mixtures by ^{51}V NMR spectroscopy provided further insight into the dramatic solvent dependence on enantioselectivity. ^{51}V NMR spectra revealed that different species in observable diamagnetic oxidation states (+5) are present under biphasic conditions than under homogeneous conditions. A ^{51}V NMR spectrum of the organic layer of a solution of $VO(acac)_2$ and ligand **3** in CD_2Cl_2 (biphasic) with 100 equiv H_2O_2 layered on top showed nine resonances from δ −460 to −580 ppm (Figure 2a). In contrast, a ^{51}V NMR spectrum of the same materials in THF-d_8 (homogeneous) shows only one peak, at δ −680 ppm (Figure 2c). Importantly, a ^{51}V NMR spectrum of $VO(acac)_2$ and ligand **3** with only one equiv H_2O_2 in THF-d_8 (homogeneous) is similar to the spectrum obtained under biphasic conditions in CD_2Cl_2, and shows multiple peaks from δ −500 to −580 ppm, and no upfield peak (Figure 2b). This implies that the difference in spectra obtained under biphasic and homogeneous conditions is a result of the increase in H_2O_2 concentration and not an effect of changing solvent.

We initially considered that some of the nine peaks observed under low H_2O_2 concentrations were oxo−peroxo complexes (**4**) with ligand **3** bound to the metal center (Scheme 1). Vanadium oxo−peroxo complexes with N,O-donor ligands derived from amino acids and alcohols have been isolated previously and characterized by X-ray diffraction.[30] Such complexes have also been suggested to play a role in oxidation of thioethers, based on ^{51}V NMR spectroscopy.[36,45] Typical ^{51}V NMR resonances for such complexes appear between δ −500 and −600 ppm, in agreement with our observation. Unfortunately, attempts to isolate and characterize these presumed peroxo complexes were unsuccessful.

The signal at δ −680 ppm observed at high H_2O_2 concentrations likely results from a complex formed by full displacement of ligand **3** by H_2O_2. The resulting achiral oxo-diperoxo complex, $VO(O_2)O_2H$ (**5**) (Scheme 1),[46] could nonselectively oxidize **1** to give racemic **2**. Formation of complex **5** has been previously linked to a loss of enantioselectivity in the oxidation of thioethers.[36] Additional evidence for formation of **5** is that addition of H_2O_2 to $VO(acac)_2$ in the absence of ligand **3** results in formation of the species that gives rise to the peak at δ −680 ppm. Furthermore, nonenantioselective oxidation of **1** occurs in the absence of ligand **3** in CH_3CN and in ^{i}PrOH (homogeneous).

Isolation of a Catalyst Precursor. Aerobic oxidation of $VO(acac)_2$ in the presence of **3** in CH_3CN produces red crystals of a 2:1 ligand-to-vanadium complex, VOL^*_2H (**6**) (eq 2). An X-ray diffraction study revealed a square pyramidal vanadium complex of the *endo* isomer, where the oxo ligand and the *tert*-butyl group of the tridentate ligand are located on opposite sides of the plane of the square pyramid, presumably for steric reasons.



(2)

6

Addition of 2.5% catalyst **6** to **1** and H_2O_2 in $CHCl_3$ under biphasic conditions results in the formation of **2** with high conversion and ee (92%, 89% ee). This yield and enantioselectivity are similar to those obtained using $VO(acac)_2$ and **3**.

Spectroscopic Studies of Catalyst Precursor. Dissolution of crystalline **6** in CD_2Cl_2 resulted in the observation of multiple species by ^{51}V NMR (Figure 3) and ^1H NMR spectroscopy. Due to the complexity of the ^1H NMR spectra, ^{51}V NMR spectroscopy was used as the primary tool to monitor the behavior of **6** in solution. Importantly, the six resonances observed by ^{51}V NMR spectroscopy match six of the nine signals observed when

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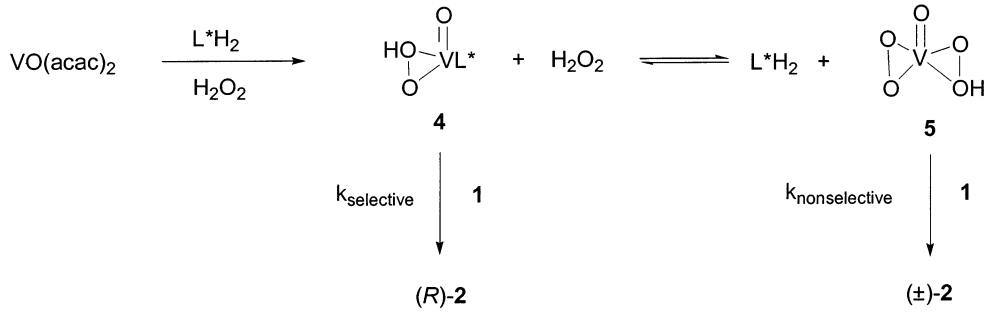
SCHEME 1. Model for the Observed Loss of Enantioselectivity at High H_2O_2 Concentrations



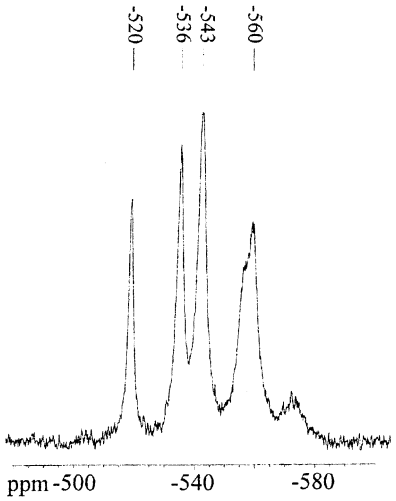


FIGURE 3. ^{51}V NMR spectrum of **6** in $CDCl_3$ at 298 K.

H_2O_2 (100 equiv) is added to $VO(acac)_2$ and ligand **3** in CD_2Cl_2 (vide supra). Thus, **6** dissolves to give most of the major species present under oxidation conditions, in the absence of other potential ligands (peroxide or acetylacetonate). Solutions of **6** exhibit temperature- and concentration-dependent spectra. Reversible coalescence of some peaks at higher temperatures suggest these vanandium(V) species are in rapid equilibrium on the NMR time scale. Rapid change of spectra upon dilution in CD_2Cl_2 suggests the presence of aggregates. Signals may also be from both endo and exo isomers, despite the fact that only the endo isomer is observed by X-ray crystallography.

The three remaining unaccounted for signals observed when H_2O_2 (100 equiv) is added to $VO(acac)_2$ in CD_2Cl_2 (δ −474, −504, −516 ppm) are assigned to vanadium oxoperoxo complexes with ligand **3** bound, based on analogy to the literature.[30,36,45] To confirm that the new peaks formed upon addition of H_2O_2 (30% aq) were from species with incorporated peroxide and not water, additional H_2O (100 equiv) was added to a solution of H_2O_2 (1 equiv), $VO(acac)_2$, and **3** in CH_3CN. The peaks at δ −474, −504, and −516 ppm did not increase in intensity, nor were any new peaks observed. ^{51}V NMR spectra of $VO(acac)_2$ and **3** in CH_3CN with H_2O, in the absence of peroxide, show no resonances since $VO(acac)_2$ is a paramagnetic vanadium(IV) complex. Addition of H_2O to **6** in THF does not result in formation of new species. This further suggests that the changes in the ^{51}V NMR spectra arise from reaction with peroxide and not H_2O.

Spectroscopic Studies of Homogeneous Oxidation of Disulfide. Addition of H_2O_2 (0.5 equiv) to solutions of $VO(acac)_2$ (0.1 equiv), **3** (0.11 equiv), and disulfide **1** (1.0 equiv) in CH_3CN (homogeneous) at 22 °C results in the formation of multiple short-lived vanadium(V) species, as monitored by ^{51}V NMR spectroscopy (δ −620 to −690 ppm, broad). These species decompose to give the characteristic multiple resonances formed on dissolution of crystalline **6** after three minutes, at which time oxidation of **1** is complete. Analysis of the oxidized product showed it to have 0% ee. Addition of another portion of H_2O_2 (0.5 equiv) re-forms the species that give rise to the short-lived signals, and again these revert to species present prior to addition of the second portion of H_2O_2 within three minutes, at which time oxidation of **1** is complete (0% ee). This shows that all the short-lived species are capable of accessing the nonstereoselective oxidation pathway.

Model for Solvent and Slow H_2O_2 Addition Effect. Information from ^{51}V NMR spectroscopy, the considerable dependence of enantioselectivity on the solvent system, and the dramatic increase in enantioselectivity upon slow H_2O_2 addition into homogeneous systems strongly support a model in which a nonselective oxidant is the dominant reactive species at high H_2O_2 concentrations (Scheme 1). The relative ratio of enantioselective oxidation to nonenantioselective oxidation depends both on the relative concentrations of **4** and **5** and on their relative oxidation rates. This model also rationalizes the similar solvent dependence of enantioselectivity observed by Bolm when this catalyst system is used in the oxidation of thioethers.[47]

Effect of $H_2{}^{18}O$. To determine whether the original oxo group exchanged with water during the oxidation reaction, $H_2{}^{18}O$ was used. Addition of $H_2{}^{18}O$ to a solution of **6** in THF did not result in incorporation of ^{18}O into the oxovanadium complex, in the absence or presence of (unlabeled) H_2O_2. Addition of $H_2{}^{18}O$ to standard oxidations of **1** did not result in ^{18}O incorporation into product **2**.

Isolation of a Second Catalyst Precursor. Due to the complexity of the mixture of species formed upon dissolution of catalyst precursor **6**, we desired to synthesize a catalyst precursor that dissolved to give a simpler mixture, ideally a single species. Additionally, we wanted to examine the ease of exchange of the monodentate ligand in **6**, since it is likely that this ligand exchanges

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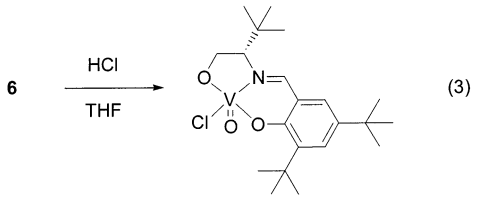
with peroxide in order to initiate the catalysis. Accordingly, one equivalent of HCl was added to **6**. ^{51}V NMR spectroscopy shows conversion to a single new vanadium(V) species in CD_2Cl_2 solution. A X-ray structure of crystals grown from this solution shows the chloride complex, **7** (eq 3). The crystals redissolve to give a solution that exhibits a ^{51}V NMR spectrum identical to the spectrum of the solution from which they initially crystallized. No reaction was observed upon addition of HBr or HI to **6**.



(3)

7

Use of **7** as the precatalyst in the oxidation of disulfide **1** resulted in conversions and enantioselectivities similar to those produced with the catalyst that is formed in situ upon addition of $VO(acac)_2$ and ligand **3** separately. Monitoring the oxidation reaction by ^{51}V NMR spectroscopy shows that **7** is the major vanadium-containing species throughout the reaction. Two weak new low-field signals appear upon addition of H_2O_2 to **7**. The multiple resonances from **6** gradually appear, leaving open the possibility that catalysis proceeds through one of the species responsible for these absorptions.

Summary and Conclusion. The mechanism of the vanadium-catalyzed enantioselective oxidation of disulfide **1** to thiosulfinate **2** has been studied. A 1:2 complex of a vanadium(V) fragment and chiral ligand **3** has been isolated and shown to be a catalyst precursor. Dramatic increases in reaction enantioselectivity under homogeneous conditions result when the H_2O_2 oxidant is added slowly. Additionally, a rationale for the observed dependence of enantioselectivities of **2** on solvent has been offered and experimentally supported. Different species observed by ^{51}V NMR spectroscopy at low and high H_2O_2 concentrations, an inverse relationship between organic cosolvent miscibility with water and enantioselectivity, and the dramatic increase in enantioselectivity upon slow H_2O_2 addition support the competitive displacement of all or part of **3** by H_2O_2 to form nonstereoselective catalysts.

Experimental Section

General Methods. All ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded on 400 and 500 MHz spectrometers. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of tetramethylsilane, and referenced to the residual protiated solvent peak. ^{51}V NMR spectra were recorded at 131.53 MHz and referenced against an external $VOCl_3$ standard (δ 0 ppm). X-ray structural analysis was performed by Dr. Fred Hollander and Dr. Allen Oliver in the University of California, Berkeley CHEXRAY facility. X-ray diffraction measurements were made on a SMART CCD area detector with graphite monochromated Mo−Kα radiation. Schiff-base ligand **3** was prepared according to previously published syntheses.[3] Di-*tert*-butyl disulfide was distilled prior to use. Bis(acetylacetonato)oxovanadium ($VO(acac)_2$) was purchased from Strem Chemical Company and used as received. $H_2{}^{18}O$ (95−98%) was purchased from Cambridge Isotope Laboratories and used as received. All manipulations were performed in air unless otherwise mentioned.

Caution: Vanadium-catalyzed H_2O_2 decomposition can result in O_2 release. Therefore, care should be taken to use only vented reaction vessels.

Typical Procedure for Synthesis of *tert*-Butane *tert*-Butylthiosulfinate (2). Ligand **3**, $VO(acac)_2$, and di-*tert*-butyl disulfide **1** were dissolved in the desired solvent, giving a pale green solution. The specified amount of H_2O_2 (30% aq) was added and the solution turned deep red or brown immediately. Gentle bubbling was often observed, presumably from O_2 evolution. Conversion was monitored by ^{1}H NMR spectroscopy. ^{1}H NMR of **2** (400 MHz, $CDCl_3$): δ 1.38 (s, 9H), 1.56 (s, 9H). Identity was established by comparison with literature ^{1}H NMR data.[15] The enantiomeric excess was determined by chiral HPLC analysis (Diacel Chiralpak AS column, 97:3 hexanes:2-propanol; 1 mL/min, 258 nm; (*R*)-**2**, t_R = 6.8 min; (*S*)-**2**, t_R = 8.4 min).

A blank reaction in CH_3CN (homogeneous) with no added $VO(acac)_2$ showed less than 5% conversion to **2** by ^{1}H NMR spectroscopy after 7 h. A reaction carried out in CH_3CN (homogeneous) with no ligand **3** showed 92% conversion to **2** by ^{1}H NMR spectroscopy after 6 h.

Procedure for Formation of 2 via Slow H_2O_2 Addition. Ligand **3** (10 mg, 0.030 mmol), $VO(acac)_2$ (5 mg, 0.02 mmol), and **1** (98 μL, 0.51 mmol) were dissolved in CH_3CN to give a pale green solution. The H_2O_2 (30% aq) (58 μL, 0.65 mmol) was added dropwise via syringe pump over the specified time (3−15 h) with rapid stirring. Upon addition of the first drop of H_2O_2 the solution turned deep brown. Aliquots were removed at the specified times and analyzed by HPLC. t = 3 h, 68% ee; t = 7 h, 76% ee; t = 12 h, 66% ee, t = 15 h, 70% ee.

Effect of Excess Ligand 3. Ligand **3** (183 mg, 0.55 mmol), $VO(acac)_2$ (3 mg, 0.01 mmol), and **1** (30 μL, 0.17 mmol) were dissolved in CH_3CN (0.5 mL) to give a yellow oil. The H_2O_2 (30% aq) (5.5 μL, 0.055 mmol) was added in one portion to produce a brown solution. While stirring over 21 h the solution gradually turned orange and a pale precipitate formed. Four drops of $CHCl_3$ were added, dissolving the precipitate. Analysis of an aliquot showed starting material **1** and ligand **3**, but no **2**. To be certain the ligand signal was not obscuring the signal from **2**, the remaining solution was frozen at −196 °C and the volatile materials were removed under vacuum. The solution was then heated to 37 °C and distilled into a round-bottom flask submerged in liquid nitrogen, over 2 h. The distillate was concentrated in vacuo to a clear residue and by HPLC showed starting material **1**, but no **2**.

Procedure for Monitoring Addition of H_2O_2 to VO(acac)$_2$ and 3 (Homogeneous Conditions) by ^{51}V NMR Spectroscopy. Ligand **3** (17 mg, 0.050 mmol) and $VO(acac)_2$ (12 mg, 0.045 mmol) were dissolved in THF-d_8 (~0.5 mL) to give a pale green solution. The solution was transferred to a NMR tube, at which time the specified amount of H_2O_2 (30% aq) was added. The solution immediately turned brown. For H_2O_2 (1.0 equiv): ^{51}V NMR (295 K, THF-d_8) δ −505, −515, −514, −525, −537, −544, −556, −562, −576 ppm. For H_2O_2 (10 equiv): ^{51}V NMR (295 K, THF-d_8) δ −437, −559, −619, −626, −692, −712, −735 ppm. For H_2O_2 (100 equiv): ^{51}V NMR (295 K, THF-d_8) δ −680 ppm.

Procedure for Monitoring Addition of H_2O_2 to VO(acac)$_2$ and 3 (Heterogeneous Conditions) by ^{51}V NMR Spectroscopy. Ligand **3** (6.3 mg, 0.019 mmol) and $VO(acac)_2$ (5.0 mg, 0.019 mmol) were dissolved in CD_2Cl_2 (0.5 mL) to give a pale green solution. The solution was transferred to a NMR tube, at which time the specified amount of H_2O_2 (30% aq) was added as a second layer. The solution was mixed, and the organic layer immediately turned brown. ^{51}V NMR spectra on the organic layer were recorded while the aqueous layer remained on top. For H_2O_2 (1.0 and 4.0 equiv): ^{51}V NMR (295 K, CD_2Cl_2) δ −476, −504, −520, −536, −545, −560 ppm. For

H_2O_2 (100 equiv): ^{51}V NMR (295 K, CD_2Cl_2) δ −474, −504, −516, −518, −527, −533, −540, −557, −573 ppm.

VOL*$_2$H (6). Ligand **3** (1.02 g, 3.05 mmol) and $VO(acac)_2$ (403 mg, 1.52 mmol) were dissolved in CH_3CN (40 mL) to give a green solution, and the flask was loosely capped. Over the course of 5 days the solution turned brown with accompanying formation of red crystals. The brown mother liquor was removed by pipet and the remaining X-ray quality crystals were washed with CH_3CN and air-dried to afford 812 mg (73%) of VOL*$_2$H (**6**). A second crop of crystals was collected by slow evaporation of the mother liquor over 4 days to half the original solvent volume, affording 68 mg of crystals for a total yield of 880 mg (79%). ^{1}H NMR, ^{13}C{^{1}H} NMR, and ^{51}V NMR (CD_2Cl_2) analysis showed a complex mixture of species. ^{1}H NMR (500 MHz, 295 K, 0.11 M, CD_2Cl_2): δ 14.02 (s), 13.99 (s), 13.74 (s), 8.54 (s), 8.49 (s), 8.39 (s), 8.26 (s), 8.23 (s), 7.66 (d, J = 2 Hz), 7.64 (d, J = 2 Hz), 7.42 (d, J = 2 Hz), 7.39 (d, J = 2 Hz), 7.36 (d, J = 2 Hz), 7.34 (d, J = 2 Hz), 7.20−7.18 (m), 6.91 (d, J = 2), 4.01 (d, J = 6 Hz), 3.94 (d, J = 11 Hz), 3.73 (t, J = 11 Hz), 3.35 (dd, J = 3, 9 Hz), 3.14 (dd, J = 2, 9 Hz), 2.95 (dd, J = 3, 9 Hz), 1.48 (s), 1.47 (s), 1.46 (s), 1.37 (s), 1.36 (s), 1.34 (s), 1.33 (s), 1.23 (s), 1.10 (s), 1.09 (s), 1.05 (s), 1.01 (s), 0.89 (s) ppm. ^{51}V NMR (295 K, 0.03 M, CD_2Cl_2): δ −518, −533, −538, −551, −556, −573 ppm. Mp: 231−232 °C. Anal. Calcd for $C_{42}H_{67}N_2O_5V$: C, 69.01; H, 9.24; N, 3.83. Found: C, 69.19; H, 9.31; N, 3.84.

X-ray Crystal Structure of 6. X-ray quality crystals were grown according to the above-described method. For X-ray crystallographic analysis, a deep red tablet-shaped crystal of **6** having approximate dimensions of 0.22 × 0.18 × 0.08 mm was mounted on a glass fiber using Paratone N hydrocarbon oil. The structure was solved by direct methods and expanded using Fourier techniques. The vanadium, oxygen, nitrogen and methyl carbon atoms were refined anisotropically, while the rest of the carbon atoms were refined isotropically. Hydrogen atoms were included in calculated positions but were not refined.

^{51}V NMR Studies of Reaction Mixtures. Ligand **3** (24 mg, 0.072 mmol), $VO(acac)_2$ (17 mg, 0.065 mmol), and **1** (124 μL, 0.65 mmol) were dissolved in CD_3CN (0.8 mL) to give a pale green solution. The solution was transferred to a NMR tube at which time H_2O_2 (30% aq) (32 μL, 0.28 mmol) was added, resulting in a brown solution. The solution was mixed and ^{51}V NMR spectra were obtained. ^{51}V NMR (295 K, CD_3CN) δ t = 2 min: −507, −533 (sharp), −600 to −700 (very broad), −641 (sharp), −680 ppm. t = 3 min: −480 to −540 (very broad), −510, −520, −533 (sharp), −642, −650 ppm. t = 5 min: −507, −520 (broad), −533 (sharp), −540 ppm.

Test for ^{18}O Incorporation into 6 from $H_2{}^{18}O$. Complex **6** (4 mg, 0.006 mmol) was dissolved in THF (0.1 mL) to produce an opaque dark red solution. The $H_2{}^{18}O$ was added with no color change. An aliquot was removed after 6 h and dissolved in CH_3CN. A mass spectrum showed no isotopic enrichment in **6**. MS (ESI): m/z 731 $[M + H]^+$.

The experiment was repeated, with the exception that (unlabeled) H_2O_2 (30% aq) (1.1 μL, 0.011 mmol) was added. An aliquot was removed after 6 h and showed no isotopic enrichment in **6**. MS (ESI): m/z 731 $[M + H]^+$.

VOL*Cl (7). To a deep red solution of **6** (100 mg, 0.140 mmol) in THF (6 mL) was added HCl (1.0 M in ether) (140 μL, 0.14 mmol). The solution immediately turned black. A ^{51}V NMR spectrum of an aliquot taken after 30 min showed a single vanadium(V) species. The reaction mixture was concentrated in vacuo to a black gum. Hexane (4 mL) was added. The solution was allowed to sit undisturbed for 2 h, at which time removal of the red-brown mother liquor revealed clusters of black needle-shaped crystals coated with a white film (presumably amine salts) and mixed with a minor amount of crystalline **6**. The crystals were washed with 3 portions of pentane and air-dried. ^{51}V NMR spectroscopy of the crystals showed the same signal as that observed on the aliquot taken earlier, and trace signals from **6**. ^{51}V NMR (295 K, CD_2Cl_2): δ −432 ppm. ^{1}H NMR (500 MHz, 295 K, CD_2Cl_2): δ 8.62 (s, 1H), 7.78 (d, J = 4 Hz, 1H), 7.38 (d, J = 4 Hz, 1H), 5.61 (m, 1H), 5.21 (m, 1H), 4.22 (m, 1H), 1.51 (s, 9H), 1.35 (s, 9H), 1.17 (s, 9H) ppm. Mp: 193−194 °C. HRMS (EI): m/z calcd ($C_{21}H_{33}VNO_3Cl$) 433.1589, found 433.1596 [M+].

X-ray Crystal Structure of 7. X-ray quality crystals of **7** were grown by addition of ether to the black gum described above to produce a black solution, followed by complete evaporation of the ether solvent over 1 h. For X-ray crystallographic analysis, a fragment of a black columnar crystal of **7** having approximate dimensions of 0.03 × 0.10 × 0.19 mm was mounted on a glass fiber using Paratone N hydrocarbon oil. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined.

^{51}V NMR Spectroscopy of Addition of H_2O_2 to 7. Complex **7** (15 mg, 0.035 mmol) was dissolved in CD_2Cl_2 to produce an opaque black solution, H_2O_2 (30% aq) (32 μL, 0.32 mmol) was added with no color change, and the solution was transferred to a NMR tube. A ^{51}V NMR spectrum obtained after 45 min showed two new minor peaks at low field (δ −252, −264 ppm). In a ^{51}V NMR spectrum obtained after 3 d those two minor peaks are no longer present, and signals from **6** increased. ^{51}V NMR (295 K): δ −432 (1.00), −540, −554, −556, −573 (0.55 total) ppm.

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Supporting Information Available: X-ray crystallographic data for **6** and **7**, variable-temperature ^{51}V NMR spectra of **6**, and a ^{51}V NMR spectrum of **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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