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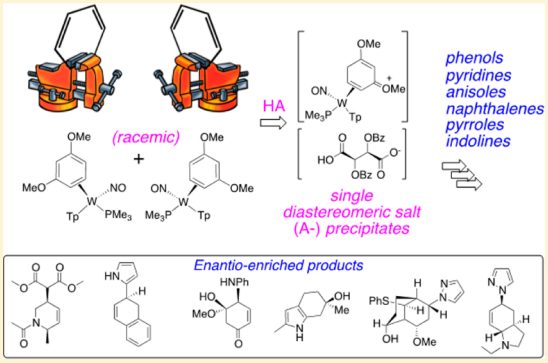
Enantioenrichment of a Tungsten Dearomatization Agent Utilizing Chiral Acids

Andrew W. Lankenau,[†] Diana A. Iovan,[‡] Jared A. Pienkos,[†] Rebecca J. Salomon,[†] Sisi Wang,[†] Daniel P. Harrison,[†] William H. Myers,[‡] and W. Dean Harman*[,†]

[†]Department of Chemistry, University of Virginia, Charlottesville, Virginia 22904, United States
[‡]Department of Chemistry, University of Richmond, Richmond, Virginia 23173, United States

Supporting Information

ABSTRACT: A method is described for the resolution of the versatile dearomatization reagent TpW(NO)(PMe_3)(η^2-benzene), in which the 1,3-dimethoxybenzene (DMB) analogue of this complex is synthesized. In turn, the coordinated arene of TpW(NO)(PMe_3)(DMB) is protonated with either D or L dibenzoyl tartaric acid ($DBTH_2$) in a butanone/water or 2-pentanone/water solution. Sustained stirring of this mixture results in the selective precipitation of a single form of the diastereomeric salt [TpW(NO)(PMe_3)(DMBH)](DBTH). After isolation, the salt can be redissolved, and the DMB ligand can be deprotonated and exchanged for benzene to produce the desired product TpW(NO)(PMe_3)(η^2-benzene) in either its *R* or *S* form. The absolute configuration of the tungsten stereocenter in TpW(NO)(PMe_3)(η^2-benzene) can be determined in either case by substituting the naturally occurring terpene (*S*)-β-pinene for benzene and evaluating the 2D NMR spectrum of the corresponding β-pinene complex.



INTRODUCTION

Over the past decade, the π-basic dearomatization fragment {TpW(NO)(PMe_3)} has proven to be a viable and versatile synthetic tool.[1] This organometallic fragment can bind to a wide variety of aromatic molecules through two carbon atoms (η^2) and activate these carbo- and heterocycles toward tandem electrophile/nucleophile addition and cycloaddition reactions.[2−4] Afterward, the aromatic-derived product may be liberated from the tungsten by a suitable oxidant. These transformations have led to the synthesis of dozens of diverse molecular frameworks, including natural product cores and new biologically active compounds.[5−10] As shown in Scheme 1, these addition reactions are highly regio- and stereoselective (typically > 95), with virtually all reagents adding to the ring-face *anti* to the metal complex. However, the organic compounds produced in this manner are obtained as racemic mixtures, owing to the lack of a method to synthesize the universal precursor TpW(NO)(PMe_3)(η^2-benzene) (**1**) in enantioenriched form.[2,11]

Although success was reported for a rhenium-based predecessor, TpRe(CO)(MeIm)(η^2-benzene),[12] attempts to control the absolute stereochemistry of {TpW(NO)(PMe_3)} through chiral ligand substitutions have been only moderately successful, and plagued by low yields.[13] The use of chiral aromatic substrates or chemical reagents was considered, but these approaches would need to be tailored for a specific chemical reaction. Modification of the ancillary ligands of {TpW(NO)(PMe_3)} (e.g., chiral phosphines) seemed plausible, but the stringent electronic and steric requirements for aromatic binding make such a strategy equally unappealing.[1] Organic chemists have long used the acid−base chemistry of diastereomeric salts to resolve racemic amines and carboxylic acids,[14] and it was our hope that this approach could be adapted to organometallic systems, such as the versatile dearomatization agent **1**.

RESULTS AND DISCUSSION

Previous studies have shown that an aromatic ligand coordinated to {TpW(NO)(PMe_3)} may be protonated with relatively weak acids (e.g., diisopropylammoniumtriflate, pK_a = 11.0) when electron donor groups are incorporated into the arene (e.g., anisole, phenol, aniline).[15−18] Therefore, we envisioned a method in which an electron-rich arene complex was protonated with a chiral acid, producing two diastereomeric salts that could be separated on the basis of solubility differences. Upon isolation, the cationic tungsten complex could be deprotonated and the electron-rich arene exchanged for benzene, providing **1** in an enantioenriched state. The 1,3-dimethoxybenzene complex TpW(NO)(PMe_3)(5,6-η^2-1,3-dimethoxybenzene) (**2**) was an attractive target because of the scale of its reported synthesis (6.5 g; 41%) and the relative thermal and chemical stability of its conjugate acid (triflate salt).[18] In solution, **2** exists as a 3:1 equilibrium ratio of

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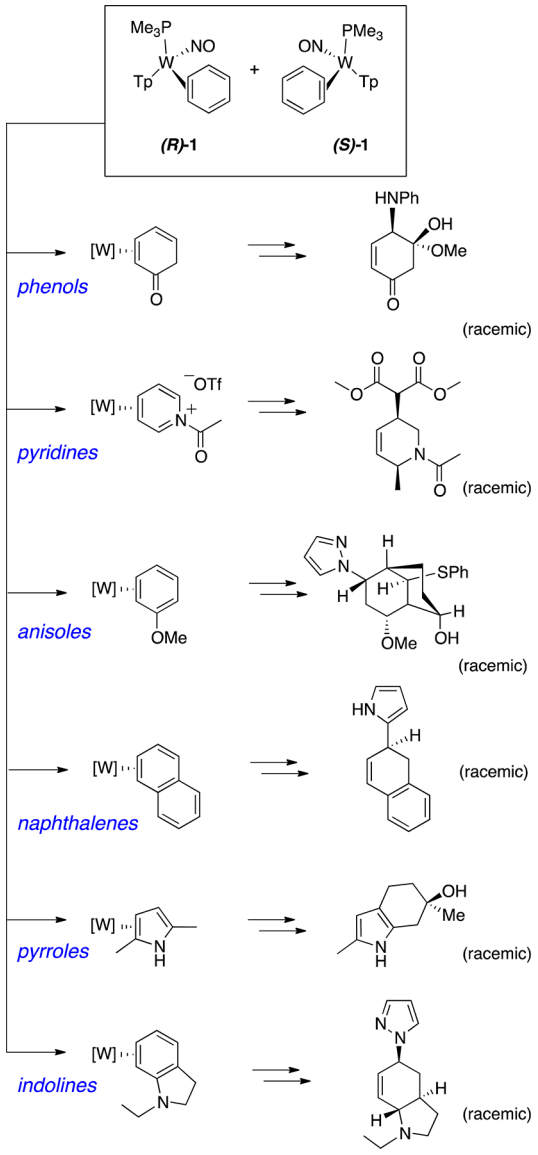
Scheme 1. Benzene Complex 1, a Universal Precursor for Dihapto-Coordinated Aromatic Chemistry[a]



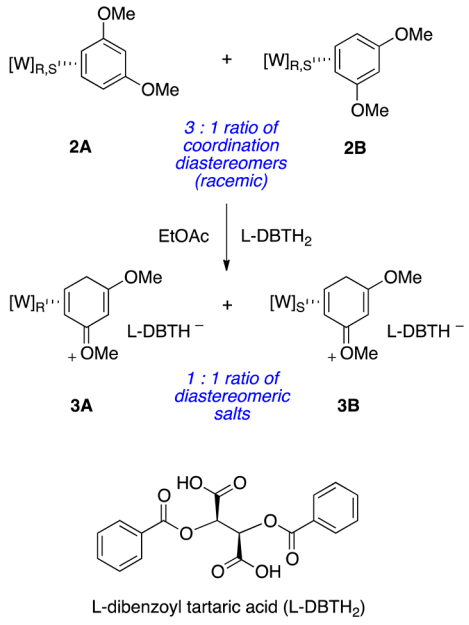
[a][W] = {TpW(NO)(PMe_3)}.

coordination diastereomers (**2A**, **2B**; Scheme 2). However, when this mixture is protonated by an achiral acid (e.g., HOTf), only the 4*H*-1,3-dimethoxybenzenium isomer is observed. Hence, protonation of **2** was investigated with a handful of chiral acids including D-camphorsulfonic acid, L-cysteic acid, L-tartaric acid, L-di-*p*-toluoyl tartaric acid, and L-dibenzoyl tartaric acid (L-$DBTH_2$), in a range of solvents of differing polarity (methanol, ethyl acetate, acetone, acetonitrile, chloroform, tetrahydrofuran).

Following the reaction of **2** (^{1}H NMR) with L-cysteic acid, L-di-*p*-toluoyl tartaric acid, or L-tartaric acid, it was found that the protonation did not reach completion, nor could a product salt be cleanly isolated. In the case of D-camphorsulfonic acid, the resultant salts were easily synthesized (^{31}P, ^{1}H NMR) but could not be resolved despite numerous selective precipitation and crystallization attempts.

In a similar vein, when L-$DBTH_2$ was combined with an ethyl acetate solution of **2** and stirred for 3 h, an orange precipitate formed that upon isolation was shown to contain a 1:1 mixture

Scheme 2. Protonation of the 1,3-Dimethoxybenzene Complex (2A+2B) with L-$DBTH_2$ Yields a Single Coordination Diastereomer but Is Isolated as a 1:1 Ratio of Diastereomeric Salts (3A+3B)



of the two diastereomeric salts **3A** and **3B** (Scheme 2). The ^{1}H NMR spectrum of this precipitate displayed a single set of resonances corresponding to the trispyrazoylborate, trimethylphosphine, and dimethoxybenzenium ligands with the exception of two distinct downfield doublets appearing at 7.78 and 7.77 ppm. These two signals, individually integrating to 0.5 protons compared to other signals, were determined via NOE interactions to represent the 5-position hydrogen of the pyrazoyl ring *cis* to the trimethylphosphine and 1,3-dimethoxybenzium ligands of **3A** and **3B**. Similarly, the ^{31}P NMR spectrum of this mixture revealed two individual resonances at −8.26 and −8.29 ppm corresponding to the *R* and *S* configurations of the tungsten center, respectively (Figure 1).

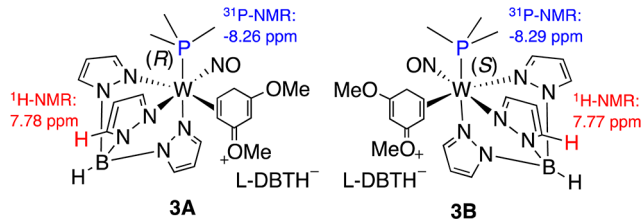


Figure 1. Distinguishing ^{31}P and ^{1}H NMR signals for diastereomeric salts **3A** and **3B**.

In contrast, when a butanone/water solution was used as the solvent for the L-$DBTH_2$ protonation, NMR spectra indicated that the salt **3A** selectively precipitated with 0.5 equiv of the free acid L-$DBTH_2$, while **3B** remained dissolved. The diastereomeric enrichment of **3A**, as well as the yield of this salt, was largely dependent on the water concentration and reaction stir time. The data from a few of these protonation reactions are summarized in Table 1. As shown by the first two entries in Table 1, increasing the concentration of water resulted in a higher yield of **3A** (41% vs 29%), but the product was less enriched than when lower concentrations of water

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Table 1. Effect of Water Concentration and Stir Time on Yield and Diastereomeric Ratio of L-DBTH$_2$ Enrichment Protonation

	solvent	[H_2O] (M)	stir time (h)	yield (%)	dr
1	butanone	0.12	22	29	90:10
2	butanone	0.82	20	41	86:14
3	butanone	0.67	46	36	92:8
4	butanone	0.89	47	38[a]	94:6[a]
5	2-pentanone	0.23	48	43	91:9
6	2-pentanone	0.30	139	24	96:4
7	ethyl acetate	0.20	44	47	64:36
8	butanone	–	3	13[a]	1:1[a]
9	ethyl acetate	–	3	91	1:1

[a] D-DBTH$_2$ was used.

were used (dr = 86:14 vs 90:10). However, when these high water concentration reactions were stirred for ∼48 h, the corresponding precipitate was significantly more enriched (dr = 92:8; 94:6) and could be collected in relatively high yields (36%; 38%; entries 3 and 4).

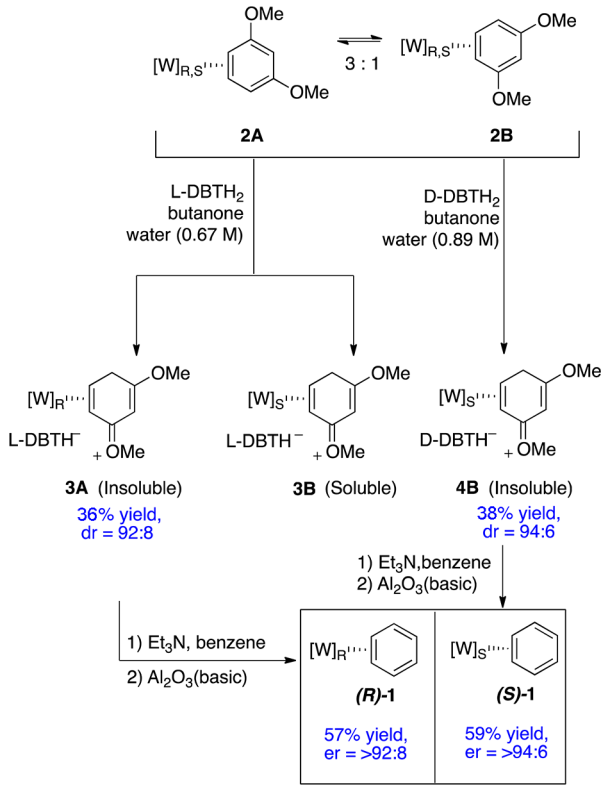
While acetone was ineffective as a solvent, the butanone data were very encouraging, and we wondered if reducing the polarity of the solvent further could optimize the yields and stereoselectivity of the protonation. Thus, 2-pentanone was pursued (entries 5 and 6). With 2-pentanone as the solvent, the salt **3A** was collected in the highest observed yields (43%) and in nearly the same diastereomeric enrichment as seen for butanone (dr = 91:9). A much longer stir time in 2-pentanone was also explored (entry 6). While the precipitate from this experiment (**3A**) was the most enriched of all the trials (dr = 96:4), this selectivity came at the sacrifice of yield (24%), presumably due to the gradual decomposition of the complex in the presence of water. Note that, for both 2-pentanone reactions, lower concentrations of H_2O were used because of the poor miscibility of water in 2-pentanone. Nevertheless, highly enriched precipitates could still be obtained.

When the same protonation reactions were performed in anhydrous butanone, the resulting orange precipitate was formed in low yield and contained no diastereomeric separation (13%; dr = 1:1; entry 8). Because neither butanone nor 2-pentanone was observed in the ^{1}H NMR spectrum of the isolated solid, we suspect that water is incorporated in the solid-state structure of **3A**. Initially, the involvement of water in this precipitation was unexpected because past studies have indicated that water leads to the decomposition of **2**.[18] However, it appears that, at low concentrations (<1 M H_2O), **2** and **3** are stable. A follow-up study of an ethyl acetate/water solution also resulted in enriched precipitates but in lower yields and selectivity when compared to butanone and 2-pentanone (47%; dr = 64:36; entry 7). For reference, the dry ethyl acetate protonation illustrated in Scheme 2 is also included (entry 9).

Following isolation of **3A**, the homogeneous filtrate was stirred for 5 h and evaporated to dryness. Due to the relatively high yield and selectivity of **3A**, it was expected that the protonated complex remaining in the filtrate would be enhanced in **3B**. However, contrary to this prediction, spectroscopic analysis (^{1}H NMR) of the remaining residue indicated a 1:1 mixture of **3A** to **3B**. Thus, it appears that either **3B** has a lower kinetic stability than **3A** or an *in situ* racemization of the tungsten center is possible under the acidic reaction conditions used. Hence, we pursued a scenario where more than half of the originally racemic mixture could be recovered as only the *R* enantiomer. Unfortunately, these efforts were ultimately unsuccessful, as were efforts to precipitate the *S* enantiomer from the filtrate with the opposite hand of the acid (D-DBTH$_2$).

To generate the benzene complex **1**, the salt **3A** was stirred with triethylamine in 1:1 THF:benzene solution. A white precipitate (believed to be triethylammoniumdibenzoyltartrate) was removed by flushing the heterogeneous solution through activated basic alumina, followed by a THF rinse. The resulting golden filtrate was then stirred for 16 h to allow for the conversion of enriched DMB complex (***R***)-**2** to the benzene complex (***R***)-**1**. The final product, obtained by concentrating the filtrate and inducing precipitation with hexanes, was the enantioenriched benzene complex (***R***)-**1** (er = >92:8; Scheme 3). Here we note that the degree of resolution was retained between **3A** and (***R***)-**1**.

Scheme 3. Synthesis of Enantioenriched Benzene Complex 1 from Racemic 2A+2B



As expected, when D-dibenzoyl tartaric acid was used, **4B** (the enantiomer of **3A**) precipitated out of a butanone/water solution in comparable yields and degree of enrichment as **3A** (38% of available epitope, dr = 94:6; see Table 1). Like **3A**, **4B** could be deprotonated and exchanged with benzene to obtain enriched (***S***)-**1** (er = 94:6; 59% yield). Thus, either enantiomer of {TpW(NO)(PMe_3)} may be retrieved when the appropriate enantiomer of dibenzoyl tartaric acid is used.

Analysis of Absolute Stereochemistry. The enantiomeric and diastereomeric ratios reported herein, as well as the absolute configuration of the tungsten center, were determined by substituting the chiral terpene (*S*)-*β*-pinene for benzene in enriched samples of (***R***)-**1** and (***S***)-**1**. Studies indicate that (*S*)-*β*-pinene binds with equal efficiency to each enantiomer of

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{TpW(NO)(PMe_3)} when starting with a racemic mixture of **1**, allowing this ligand to serve as a probe for enantioenrichment of the tungsten stereocenter.[19] However, the stereochemistry of each diastereomer was never determined. Given that the tungsten-coordinated alkene bond will be parallel to the W−P bond to effect efficient backbonding,[20] there are four coordination isomers possible for each configuration of the tungsten stereocenter (ring up, ring down, bridgehead in, bridgehead out). However, only one stereoisomer is observed for each metal configuration, presumably due to differing steric interactions. For both *R* and *S* metal configurations, the geminal dimethyl group points away from the tungsten center, while the cyclohexane ring is oriented distal to the bulky phosphine ligand (Figure 2). The assigned proton resonances

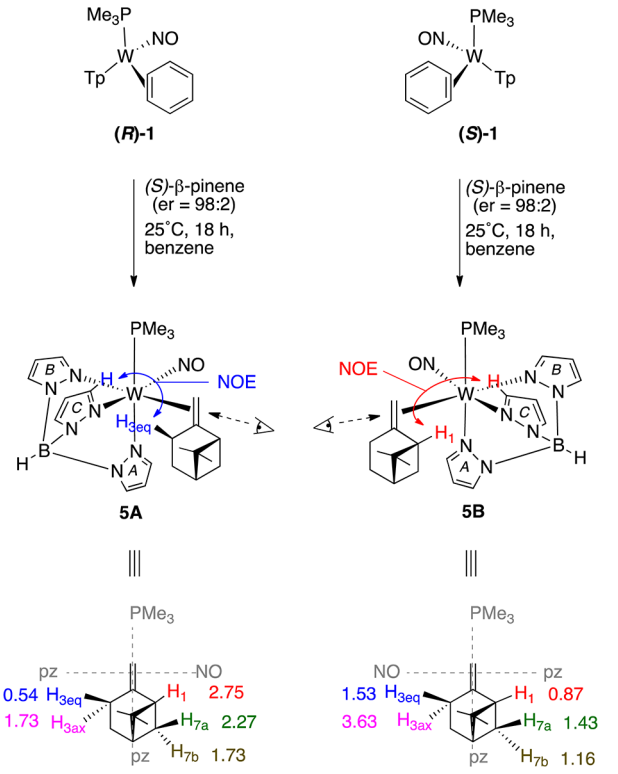

Figure 2. Quadrant analysis of (*S*)-*β*-pinene complexes **5A** and **5B**. Proton shifts reported in ppm. Note shielded protons in pz/pz quadrants.

were largely determined by comparing the ^{1}H NMR features of the coordinated pinene to those of the free ligand. Aside from the bound carbons and their associated hydrogens, the proton coupling constants and carbon chemical shifts were nearly identical between the coordinated and uncoordinated (*S*)-*β*-pinene, thus facilitating the unambiguous characterization of all observed resonances.

As depicted in Figure 2, H_{3eq} and H_{3ax} of **5A** are shifted upfield due to their position between two pyrazoyl (pz) rings. This "Tp pocket" formed between the A and C pyrazole rings shifts these resonances much further upfield than in **5B** owing to the magnetic anisotropy of the pyrazole rings. Conversely, H_1, H_{7a}, and H_{7b} of **5B** are shifted upfield with respect to **3A** due to the placement of these protons in the Tp pocket. Additionally, note that H_1 of **5B** has an NOE correlation with the proton on C3 of pyrazole C (H_{PzC3}), while for **5A**, H_{3eq} has an interaction with H_{PzC3}. In both **5A** and **5B**, NOE interactions were also observed between the PMe_3 and bound methylene group, confirming that the cyclohexane ring was distal to the PMe_3. Thus, the chemical shifts, as well as NOE data, are consistent with the proposed orientations for both the *R* and *S* configurations. With these data in hand, we were able to conclude that L-$DBTH_2$ precipitates the *R* configuration of the {TpW(NO)(PMe_3)} core while D-$DBTH_2$ precipitates the *S* configuration.

Controls. Exposing a 1:1 mixture of the diastereomeric salts **3A** and **3B** to a benzene/triethylamine solution containing 10 molar equivalents of (*S*)-*β*-pinene for 30 h (25 °C) yields a 1:1 mixture (^{31}P NMR) of **5A** and **5B**. Identical results were obtained starting from a racemic mixture of **1**. A sample of **5A** and **5B** from this experiment was isolated and shown to integrate 1:1 in both ^{31}P and ^{1}H NMR spectra. In contrast, when the enriched sample of benzene complex (***R***)-**1** prepared from a 92:8 mixture of **3A**:**3B** was treated with (*S*)-*β*-pinene, the resulting diastereomeric ratio via integration of the −14.42 and −15.00 ppm ^{31}P NMR resonances was 1:12, consistent with an enantiomeric ratio of 92:8 of the *R* configuration. Similarly, treatment of a sample of (***S***)-**1** with (*S*)-*β*-pinene, prepared from a 6:94 mixture of **3A**:**3B**, resulted in a 16:1 ratio of the −14.42 and −15.00 ppm signals, implying an enantiomeric ratio of 94:6 for the *S* configuration.

Detection Limits. We note that neither the (*S*)-*β*-pinene (ee 96%) nor the dibenzoyltartaric acid (99%) used during the resolution process was enantiomerically pure. Therefore, while the diastereomer ratios (dr's) reported in Table 1 and Scheme 3 are not expected to be affected, these samples may contain minor amounts of the *enantiomer* of the salt reported, which in turn would lead to contamination of either (***R***)-**1** or (***S***)-**1** by the minor enantiomer of the benzene complex. The optical purity of (*S*)-*β*-pinene used to create **5A** and **5B** is more problematic in that it compromises the detection limit for the ee of the benzene complex. Accordingly, if an analytically pure sample of (*S*)-*β*-pinene had been used, one could expect the observed dr's for **5A** and **5B** to be higher, thereby indicating a higher ee for **1**. For this reason, er values of (***R***)-**1** and (***S***)-**1** are reported as lower limits.

Racemization. To test the resiliency of the enriched (***R***)-**1**, we conducted several epimerization studies under elevated temperatures and acidic conditions. It was found that heating a homogeneous solution of (***R***)-**1** in benzene for 4 h at 50 °C resulted in no degradation of the stereochemical enrichment as determined by (*S*)-*β*-pinene substitution and analysis of the corresponding ^{31}P NMR spectrum after the sample was heated (4 h represents greater than 4 substitution half-lives at 50 °C based on ^{1}H NMR spectra). Hence, the substitution of benzene for benzene-d_6 for **1**, and by inference other substitutions described herein, appears to occur via a dissociative mechanism analogous to an earlier reported rhenium system[12] that likely involves a stereodefined five-coordinate square pyramidal intermediate. On the other hand, heating an analogous benzene solution of (***R***)-**1** at 80 °C for 10 min and subsequent treatment of (*S*)-*β*-pinene appears to result in complex epimerization (1:1 mixture of **5A** and **5B**) based on ^{31}P NMR data; however, most of the complex was found to decompose at this temperature, so these results are inconclusive. Exposure of enriched (***R***)-**1** to diisopropylaniliniumtriflate (pK_a = 11.0) for 20 h resulted in no epimerization as determined by (*S*)-*β*-pinene substitution. However, addition of the stronger acid aniliniumtriflate (pK_a = 4.6) to (***R***)-**1** resulted in decomposition. Therefore, we conclude that, under

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moderate temperatures and acidic conditions, the stereochemistry of benzene complex **1** is retained, even over the course of a substitution reaction.

Resolution of Other Organometallic Complexes. A search of the literature indicates that other organometallic complexes have been resolved via chiral HPLC,[21−23] differential partition between immiscible chiral solvents,[24] ligand replacement reactions,[25,26] fractional crystallization,[27−29] enantioselective complex formation,[30] chiral cation exchange,[31] and addition of chiral nucleophiles.[32,33] Additionally, there are a few reported cases of organometallic resolution via formation of diastereomeric salts.[34,35] In one instance, an octahedral d^6 ruthenium complex was resolved using the sodium salt of dibenzoyl tartrate.[36] Of note, subsequent X-ray analysis of this ruthenium salt indicated that water molecules were incorporated into the unit cell,[37] as we speculate occurs in the procedure discussed herein. However, the aforementioned resolution procedures are impractical for synthetic purposes, owing to low yields or scales, and none utilize protonation by a chiral acid to achieve separation of enantiomers. Thus, although organic chemists have long used the acid−base chemistry of diastereomeric salts to resolve racemic amines and carboxylic acids,[14] this technique has been largely overlooked for organometallic systems.

CONCLUSION

When a racemic mixture of TpW(NO)(PMe_3)(5,6-η^2-1,3-dimethoxybenzene) is protonated with L-dibenzoyl tartaric acid in butanone/water or 2-pentanone/water solutions, two diastereomeric salts are created. Over the course of 48 h, the conjugate acid for the *R* configuration of the metal center selectively precipitates while the *S* configuration remains dissolved. Subsequent deprotonation of the isolated salt in the presence of benzene affords a highly enantioenriched form of TpW(NO)(PMe_3)(η^2-benzene) (**1**), the universal precursor to a plethora of known dearomatization reactions. When these procedures were repeated using D-dibenzoyl tartaric acid, the *S* configuration of the tungsten center is obtained in similar yields and degrees of enrichment. Absolute stereochemistries for **1** were determined via structural analysis of diastereomers prepared from **1** and (*S*)-β-pinene. Collectively, a dissociative substitution mechanism is indicated for ligand exchange, thus conserving the integrity of the tungsten stereocenter. Epimerization studies of the resolved tungsten stereocenter indicate that this stereochemistry is largely retained up until the point of complex decomposition. With these procedures in hand, novel organic products derived from dearomatization reactions employing the {TpW(NO)(PMe_3)} system could now be accessible in enantioenriched form. Further, given the vast array of organometallic reactions that involve protonation (e.g., formation of hydride, dihydrogen, allyl, alkyl, carbyne, and formyl complexes, elimination of alkyl, halide, hydroxide, and alkoxide complexes), the use of chiral acids to resolve chiral organometallic complexes on a practical scale may ultimately prove suitable for a broad range of applications.

EXPERIMENTAL SECTION

General Methods. NMR spectra were obtained on either a 600 or 800 MHz spectrometer. All chemical shifts are reported in ppm and are referenced to tetramethylsilane using residual ^{1}H or ^{13}C signals of the deuterated solvents as internal standards. Phosphorus NMR signals are referenced to 85% H_3PO_4 (δ = 0.00 ppm) using a triphenylphosphate external standard in acetone (δ = −16.58 ppm). Coupling constants (*J*) are reported in hertz (Hz). Resonances in the ^{1}H NMR due to pyrazole ligands are listed by chemical shift and multiplicity only (all pyrazole coupling constants are each ca. 2 Hz). Infrared (IR) spectra were recorded on an IR spectrometer as a glaze on a horizontal attenuated total reflectance (HATR) accessory. Electrochemical experiments were performed under a dinitrogen atmosphere using a potentiostat. Cyclic voltammetry data were taken at ambient temperature at 100 mV/s (25 °C) in a standard three-electrode cell with a glassy carbon working electrode using tetrabutylammoniumhexafluorophosphate (TBAH) as an electrolyte (~0.5 M) and dimethylacetamide (DMA) solvent unless otherwise noted. All potentials are reported versus normal hydrogen electrode (NHE) using cobaltocenium hexafluorophosphate ($E_{1/2}$ = −0.78 V) as an internal standard. The peak-to-peak separation was 100 mV or less for all reversible couples. High-resolution electrospray ionization mass spectrometry (ESI-MS) analyses were obtained running in ESI mode from samples dissolved in 1:3 water/acetonitrile solution containing sodium trifluoroacetate (NaTFA), and using $[Na(NaTFA)_x]^+$ clusters as an internal standard. For metal complexes, these data are reported using the five most intense peaks from the isotopic envelope for either M^+ (for monocationic complexes) or $[M + H^+]$ or $[M + Na^+]$ (for neutral complexes). These data are listed as *m*/*z* with the intensity relative to the most abundant peak of the isotopic envelope given in parentheses for both the calculated and observed peaks. The difference between calculated and observed peaks is reported in ppm. In all cases, observed isotopic envelopes were consistent with the molecular composition reported. Unless otherwise noted, all synthetic reactions were performed in a glovebox under a dry nitrogen atmosphere. All solvents were purified by passage through a column packed with activated alumina inside the glovebox. These solvents were also thoroughly purged with nitrogen prior to being brought inside the glovebox. Deuterated solvents were used as received from Cambridge Isotopes. Pyrazole (Pz) protons of the (tris-pyrazolyl)borate (Tp) ligand were uniquely assigned using two-dimensional NMR experiments unless otherwise noted.

Compound (*R*)-1. To a 100 mL round-bottom flask was added **3A** (0.610 g, 0.518 mmol) and 50 mL of a 1:1 benzene:THF mixture. To this solution was added triethylamine (0.303 g, 2.99 mmol), and the resulting mixture was allowed to stir. After 10 min, the dark yellow heterogeneous solution was loaded onto a 4.0 cm activated basic alumina plug, pre-washed with benzene, and packed in a 15 mL coarse porosity fritted disc. Once the reaction solution was loaded, a yellow band was collected via elution with THF (50 mL). Benzene (50 mL) was added to the golden yellow filtrate, which was subsequently stirred in a 250 mL round-bottom flask. After 16 h, the solution was evaporated to 20 mL at which point hexanes (20 mL) were added. The homogeneous solution was further concentrated to 10 mL, at which point more hexanes (10 mL) were added. The resulting green-yellow precipitate was collected over a 15 mL fine porosity fritted funnel and washed with 5 mL of hexanes (0.171 g, 0.294 mmol, 57% yield, er = >92:8). ^{1}H NMR ($CDCl_3$, δ): 8.29 (1H, broad s, Tp), 7.91 (1H, broad s, Tp), 7.74 (2H, broad s, 2 Tp), 7.66 (1H, broad s, Tp), 7.15 (1H, broad s, Tp), 7.08 (1H, broad s, 3), 6.83 (1H, broad s, 6), 6.25 (2H, broad s, Tp), 6.19 (1H, broad s, Tp), 6.02 (1H, broad s, 5), 5.93 (1H, broad s, 4), 4.14 (1H, broad s, 1), 2.52 (1H, broad s, 2), 1.30 (9H, d, *J* = 7.7, PMe_3).

Compound (*S*)-1. To a 100 mL round-bottom flask was added **4B** (0.623 g, 0.529 mmol) and 75 mL of a 1:2 benzene:THF mixture. To this solution was added triethylamine (0.350 g, 3.46 mmol), and the resulting mixture was allowed to stir. After 10 min, the dark yellow heterogeneous solution was loaded onto a 4.0 cm activated basic alumina plug, wet with benzene, and packed in a 15 mL coarse porosity fritted disc. Once the reaction solution was loaded, a yellow band was collected via elution with THF (65 mL). Benzene (75 mL) was added to the golden yellow filtrate, which was subsequently stirred in a 250 mL round-bottom flask. After 16 h, the solution was evaporated to 20 mL at which point hexanes (20 mL) were added. The homogeneous solution was further concentrated until 10 mL, at which point more hexanes (10 mL) were added. The resulting green-yellow precipitate was collected over a 15 mL fine porosity fritted funnel and washed with 5 mL of hexanes (0.180 g, 0.310 mmol, 59% yield, er =

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>94:6). ^{1}H NMR ($CDCl_3$, δ): 8.29 (1H, broad s, Tp), 7.91 (1H, broad s, Tp), 7.74 (2H, broad s, 2 Tp), 7.66 (1H, broad s, Tp), 7.15 (1H, broad s, Tp), 7.08 (1H, broad s, 3), 6.83 (1H, broad s, 6), 6.25 (2H, broad s, Tp), 6.19 (1H, broad s, Tp), 6.02 (1H, broad s, 5), 5.93 (1H, broad s, 4), 4.14 (1H, broad s, 1), 2.52 (1H, broad s, 2), 1.30 (9H, d, J = 7.7, PMe_3).

Compound 3A. To a 50 mL round-bottom flask was added **2** (1.00 g, 1.56 mmol) and L-dibenzoyl tartaric acid (1.12 g, 3.13 mmol). Next, a solution of butanone (20 mL) and deionized water (0.241 g, 13.4 mmol) was added to the flask. The resulting homogeneous, dark orange solution was stirred. After 20 s, a fine precipitate was observed. After 46 h, a bright yellow solid was collected over a 30 mL coarse porosity fritted funnel, washed with 4 × 15 mL hexanes, and placed under a vacuum (0.649 g, 0.551 mmol, 36% yield, dr = 92:8). ^{1}H NMR ($CDCl_3$, δ): 7.98 (4H+2H ($^1/_2$ equiv dibenzoyl tartrate), d, J = 8.4, ortho-DBTH$^-$), 7.95 (1H, d, PzB3), 7.92 (1H, d, PzC3), 7.82 (1H, d, PzC5), 7.80 (1H, d, PzB5), 7.75 (1H, d, PzA5), 7.57 (1H, d, PzA3), 7.43 (2H+1H ($^1/_2$ equiv dibenzoyl tartrate), t, J = 7.4, para-DBTH$^-$), 7.28 (4H+2H ($^1/_2$ equiv dibenzoyl tartrate), t, J = 7.8, meta-DBTH$^-$), 6.49 (1H, t, PzC4), 6.37 (1H, t, PzB4), 6.29 (1H, t, PzA4), 5.94 (2H +1H ($^1/_2$ equiv dibenzoyl tartrate), s, DBTH$^-$ methines), 5.49 (1H, s, H2), 4.80 (1H, dd, J = 21.3, 9.3, H4 *anti*), 4.03 (1H, m, H5), 3.86 (3H, s, C3 OMe), 3.49 (1H, d, J = 21.3, H4 *syn*), 3.42 (3H, s, C1 OMe), 2.62 (1H, d, J = 8.1, H6), 1.23 (9H, d, J = 8.9, PMe_3). ^{31}P NMR ($CDCl_3$, δ): −8.26 (J_{WP} = 283). IR: ν_{BH} = 2507 cm^{-1}, ν_{NO} = 1601 cm^{-1}. CV (MeCN): $E_{p,a}$ = +1.15 V. ESI-MS obsd (%), calcd (%), ppm: 640.1729 (82), 640.1727 (85), 0.3; 641.1766 (77), 641.1753 (80), 2.1; 642.1749 (100), 642.1751 (100), −0.3; 643.1798 (42), 643.1794 (42), 0.7; 644.1791 (85), 644.1783 (84), 1.2.

Compound 3A + 3B. To a 4-dram vial charged with a stirbar was added **2** (0.500 g, 0.780 mmol) and L-dibenzoyl tartaric acid (0.839 g, 2.34 mmol). Next, EtOAc (10 mL) was added and a bright orange precipitate immediately formed. The heterogeneous solution was allowed to stir. After 3 h, the orange precipitate was collected over a 15 mL medium porosity fritted funnel, washed with 3 × 15 mL hexanes, and placed under a vacuum (0.836 g, 0.709 mmol, 91% yield, dr = 50:50). ^{1}H NMR ($CDCl_3$, δ): 7.98 (4H+2H ($^1/_2$ equiv dibenzoyl tartrate), d, J = 8.4, ortho-DBTH$^-$), 7.92 (1H, broad s, PzB3), 7.82 (1H, broad s, PzC3), 7.79 (1H, broad s, PzB5), 7.78 (1H, broad s, **3A** PzC5), 7.77 (1H, broad s, **3B** PzC5), 7.74 (1H, broad s, PzA5), 7.54 (1H, broad s, PzA3), 7.44 (2H+1H ($^1/_2$ equiv dibenzoyl tartrate), d, J = 7.4, para-DBTH$^-$), 7.29 (4H+2H ($^1/_2$ equiv dibenzoyl tartrate), t, J = 7.8, meta-DBTH$^-$), 6.45 (1H, broad s, PzC4), 6.34 (1H, broad s, PzB4), 6.26 (1H, broad s, PzA4), 5.92 (2H+1H ($^1/_2$ equiv dibenzoyl tartrate), s, DBTH$^-$methines), 5.47 (1H, s, H2), 4.74 (1H, dd, J = 21.3, 9.3, H4 *anti*), 3.94 (1H, m, H5), 3.83 (3H, s, C3 OMe), 3.47 (1H, d, J = 21.3, H4 *syn*), 3.39 (3H, s, C1 OMe), 2.56 (1H, d, J = 8.1, H6), 1.18 (9H, d, J = 8.9, PMe_3). ^{13}C NMR ($CDCl_3$, δ): 169.2, 165.5 (ester and carboxylic DBTH$^-$), 144.3 (PzB3), 143.1 (PzA3), 141.7 (PzC3), 137.9 (PzC5/PzB5), 137.8 (PzA5), 133.2 (para-DBTH$^-$), 130.1 (ortho-DBTH$^-$), 128.3 (meta-DBTH$^-$), 108.2 (PzC4), 107.6 (PzB4), 107.0 (PzA4), 92.7 (C2), 71.1 (DBTH$^-$ methines), 58.4 (C1 OMe), 58.0 (C5), 57.7 (C3 OMe), 54.2 (C6), 36.2 (C4), 12.9 (d, J = 31.0, PMe_3). ^{31}P NMR ($CDCl_3$, δ): −8.26, −8.29 (J_{WP} = 283). IR: ν_{BH} = 2507 cm^{-1}, ν_{NO} = 1601 cm^{-1}. CV (MeCN): $E_{p,a}$ = +1.14 V.

Compound 4B. To a 50 mL round-bottom flask was added **2** (1.01 g, 1.58 mmol) and D-dibenzoyl tartaric acid (1.12 g, 3.13 mmol). Next, a solution of butanone (20 mL) and deionized water (0.258 g, 14.3 mmol) was added to the flask. The resulting homogeneous, dark orange solution was stirred. After 3 min, a fine precipitate was observed. After 47 h, a bright yellow solid was collected over a 30 mL coarse porosity fritted funnel, washed with 4 × 15 mL hexanes, and placed under a vacuum (0.718 g, 0.609 mmol, 39% yield, dr = 94:6). ^{1}H NMR ($CDCl_3$, δ): 7.98 (4H+2H ($^1/_2$ equiv dibenzoyl tartrate), d, J = 8.4, ortho-DBTH$^-$), 7.95 (1H, d, PzB3), 7.92 (1H, d, PzC3), 7.82 (1H, d, PzC5), 7.80 (1H, d, PzB5), 7.75 (1H, d, PzA5), 7.57 (1H, d, PzA3), 7.43 (2H+1H ($^1/_2$ equiv dibenzoyl tartrate), t, J = 7.4, para-DBTH$^-$), 7.28 (4H+2H ($^1/_2$ equiv dibenzoyl tartrate), t, J = 7.8, meta-DBTH$^-$), 6.49 (1H, t, PzC4), 6.37 (1H, t, PzB4), 6.29 (1H, t, PzA4), 5.94 (2H+1H ($^1/_2$ equiv dibenzoyl tartrate), s, DBTH$^-$ methines), 5.49 (1H, s, H2), 4.80 (1H, dd, J = 21.3, 9.3, H4 *anti*), 4.03 (1H, m, H5), 3.86 (3H, s, C3 OMe), 3.49 (1H, d, J = 21.3, H4 *syn*), 3.42 (3H, s, C1 OMe), 2.62 (1H, d, J = 8.1, H6), 1.23 (9H, d, J = 8.9, PMe_3). Anal. Calcd for $C_{39}H_{43}BN_7O_{11}PW\cdot{}^1/_2C_{18}H_{14}O_8$: C, 47.90; H, 4.28; N, 8.32. Found: C, 47.26; H, 4.67; N, 8.26.

Compound 5A. To a 4-dram vial was added (***R***)-**1** (0.149 g, 0.256 mmol), (*S*)-*β*-pinene (0.358 g, 2.58 mmol), and DME (2.03 g). The resulting homogeneous, dark yellow solution was allowed to sit overnight. After 22 h, the reaction mixture was loaded onto a 19 cm silica column wet with hexanes. A green/yellow band was eluted with 1:1 Et_2O:THF mixture (15 mL). The homogeneous filtrate was evaporated to a residue, dissolved in $CDCl_3$, and placed in a 5 mm NMR tube. ^{1}H NMR ($CDCl_3$, δ): 8.16 (1H, d, PzA3), 7.91 (1H, d, PzB3), 7.68 (1H, d, PzC5), 7.65 (1H, d, PzA5), 7.58 (1H, d, PzB5), 7.50 (1H, d, PzC3), 6.18 (1H, t, PzC4), 6.17 (1H, t, PzA4), 6.16 (1H, t, PzB4), 2.75 (1H, t, J = 5.6, H1), 2.27 (1H, m, H7a), 2.07 (1H, dd, J = 9.6, 5.4, H10R), 1.87 (1H, buried, H10L), 1.79 (1H, m, H4eq), 1.73 (1H, buried, H3ax), 1.73 (1H, d, J = 9.5, H7b), 1.70 (1H, q, J = 5.2, H5), 1.39 (1H, m, H4ax), 1.31 (9H, d, J = 8.0, PMe3), 1.24 (3H, s, Me8), 1.17 (3H, s, Me9), 0.54 (1H, dd, J = 13.5, 7.8, H3eq). ^{13}C NMR ($CDCl_3$, δ): 145.4 (PzA3), 143.5 (PzB3), 142.1 (PzC3), 136.3, 136.0 (PzA5/PzC5), 135.2 (PzB5), 105.5, 105.1, 105.0 (PzC4/PzA4/PzB4), 54.8 (C1), 51.7 (C10), 40.3 (C5), 30.5 (C3), 28.3 (C4), 27.3 (C8), 27.0 (C7), 23.8 (C9), 13.9 (d, J = 27.8, PMe_3). ^{31}P NMR ($CDCl_3$, δ): −15.00 (J_{WP} = 262). IR: ν_{BH} = 2484 cm^{-1}, ν_{NO} = 1550 cm^{-1}. CV (DMA): $E_{p,a}$ = +0.22 V.

Compound 5B. To a 4-dram vial was added (***S***)-**1** (0.151 g, 0.260 mmol), (S)-*β*-pinene (0.352 g, 2.63 mmol), and DME (2.10 g). The resulting homogeneous, dark yellow solution was allowed to sit overnight. After 18 h, the reaction mixture was loaded onto a 20 cm silica column wet with hexanes. A green/yellow band was eluted with a 1:1 Et_2O:THF mixture (13 mL). The homogeneous filtrate was evaporated to a residue, dissolved in $CDCl_3$, and placed in a 5 mm NMR tube. ^{1}H NMR ($CDCl_3$, δ): 8.40 (1H, d, PzA3), 7.93 (1H, d, PzB3), 7.68 (2H, broad s, PzA5/PzC5), 7.58 (1H, d, PzB5), 7.33 (1H, d, PzC3), 6.19 (1H, t, PzA4), 6.17 (2H, broad s, PzB4/PzC4), 3.61 (1H, m, H3ax), 2.27 (1H, dd, J = 11.2, 5.4, H10L), 2.02 (1H, m, H4ax), 1.81 (1H, m, H4eq), 1.69 (1H, q, J = 5.2, H5), 1.56 (1H, dd, J = 9.6, 5.4, H10R), 1.53 (1H, dd, J = 13.5, 7.8, H3eq), 1.43 (1H, m, H7a), 1.30 (9H, d, J = 8.0, PMe_3), 1.16 (1H, d, J = 9.5, H7b), 1.15 (3H, s, Me9), 0.90 (3H, s, Me8), 0.87 (1H, t, J = 5.6, H1). ^{13}C NMR ($CDCl_3$, δ): 143.5 (PzA3), 142.8 (PzB3), 141.4 (PzC3), 136.7, 136.2 (PzA5/PzC5), 135.3 (PzB5), 105.5, 105.4, 105.1 (PzA4/PzB4/PzC4), 53.1 (C10), 51.8 (C1), 40.7 (C5), 34.2 (C3), 28.8 (C4), 27.3 (C8), 26.2 (C7), 24.1 (C9), 13.9 (d, J = 27.9, PMe_3). ^{31}P NMR ($CDCl_3$, δ): −14.42 (J_{WP} = 266). IR: ν_{BH} = 2488 cm^{-1}, ν_{NO} = 1547 cm^{-1}. CV (DMA): $E_{p,a}$ = +0.15 V.

■ ASSOCIATED CONTENT

Supporting Information

Text giving full experimental procedures for all previously unpublished compounds, descriptions of their spectroscopic analysis, and figures giving ^{1}H and ^{13}C NMR spectra of selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*wdh5z@virginia.edu

Notes

The authors declare no competing financial interest.

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