Enantiocontrolled Synthesis of 2,3,6-Trisubstituted Piperidines Using (η^3-Dihydropyridinyl)molybdenum Complexes as Chiral Scaffolds. Total Synthesis of (−)-Indolizidine 209B

Chutian Shu, Ana Alcudia, Jingjun Yin, and Lanny S. Liebeskind*

Contribution from the Department of Chemistry, Emory University, 1515 Pierce Drive, Atlanta, Georgia 30322

Received July 5, 2001

Abstract: Enantiopure $TpMo(CO)_2$(pyridinyl) complexes were prepared using an efficient and scalable enzymatic kinetic resolution of the precursor to the molybdenum complex. A single $TpMo(CO)_2$(pyridinyl) complex can function as a chiral scaffold for the enantiocontrolled synthesis of either 2,3,6-*cis*- or 2,6-*cis*-3-*trans*-trisubstituted piperidines. The synthetic potential of this methodology was demonstrated by a total synthesis of (−)-indolizidine 209B.

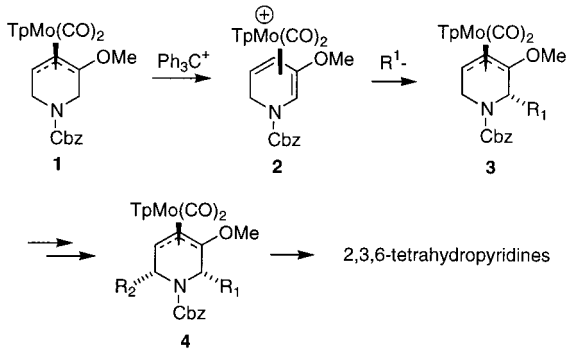
Introduction

Stoichiometric chiral, nonracemic molybdenum complexes are scaffolds for the asymmetric construction of organic molecules.[1] In particular, $TpMo(CO)_2$(pyranyl) and -(dihydropyridinyl) complexes (Tp = hydridotris(pyrazolyl)borate) are excellent chiral scaffolds for the enantiocontrolled synthesis of highly functionalized heterocycles; these and other Tp-based complexes have significantly expanded the applications of molybdenum-mediated methodologies.[2]

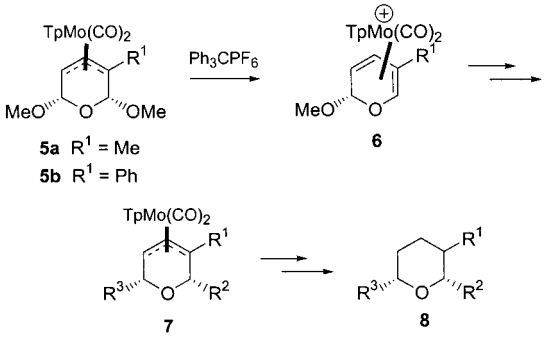
We recently reported a synthesis of 2,3,6-trisubstituted tetrahydropyridines using a regiocontrolled abstraction of hydride from (3-methoxy-η^3-dihydropyridinyl)$TpMo(CO)_2$ complex **1** as the key step.[2c] Selective abstraction of hydride with Ph_3CPF_6 gave η^4-diene cation **2** as the only product in quantitative yield. This cationic diene then reacted with a variety of nucleophiles to provide complexes **3** that, after a second hydride abstraction and nucleophilic addition, gave (2,6-disubstituted-3-methoxydihydropyridinyl)molybdenum complexes **4** (Scheme 1). Decomplexation led to 2,3,6-trisubstituted tetrahydropyridines. Unfortunately, with a 3-substituent other than methoxy (methyl or phenyl), poor regioselectivity was observed in the first hydride abstraction step.

To develop a more general approach to the selective functionalization of molybdenum complexes, we explored the possibility of selective *alkoxide* rather than *hydride* abstraction. Previous studies of the analogous (2,6-dimethoxy-3-substituted-

Scheme 1



Scheme 2

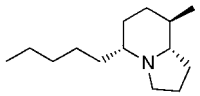


η^3-dihydropyranyl)$TpMo(CO)_2$ complexes **5** showed an unusually high selectivity for abstraction of methoxide adjacent to the 3-substituent (Scheme 2; >84:1 for **5a** where R^1 = Me, 100:0 for **5b** where R^1 = Ph).[2b] Sequential nucleophilic functionalization (**5** → **6** → **7**) followed by demetalation provided a general and enantiocontrolled route to 2,3,6-trisubstituted dihydropyrans, **8**. If this kind of selective methoxy abstraction could also be achieved with the analogous 2,6-dimethoxy-3-substituted-dihydropyridinyl complexes **9**, it would allow access to a wide range of 2,3,6-trisubstituted piperidinyl complexes **10** (Scheme 3). Stereocontrolled demetalation should selectively afford *cis*-2,3,6- and 2,6-*cis*-3-*trans*-trisubstituted piperidines, **11** and **12**, extending the scope of the original method.

(1) For reviews of stoichiometric organomolybdenum complexes in organic synthesis, see: (a) Li, C.-L.; Liu, R.-S. *Chem. Rev.* **2000**, *100*, 3127−3161. (b) Liu, R.-S. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1998; Vol. VI, p 145. (c) Pearson, A. J. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1988; Vol. I, p 1.

(2) For asymmetric synthesis using $TpMo(CO)_2$ π-allyl complexes as scaffolds, see: (a) Gómez Arrayás, R.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2001**, *123*, 6185−6186. (b) Yin, J.; Llorente, I.; Villanueva, L. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2000**, *122*, 10458−10459. (c) Moretto, A. F.; Liebeskind, L. S. *J. Org. Chem.* **2000**, *65*, 7445−7455. (d) Malinakova, H. C.; Liebeskind, L. S. *Org. Lett.* **2000**, *2*, 3909−3911. (e) Malinakova, H. C.; Liebeskind, L. S. *Org. Lett.* **2000**, *2*, 4083−4086. (f) Yin, J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1999**, *121*, 5811−5812. (g) Pearson, A. J.; Neagu, I. B. *J. Org. Chem.* **1999**, *64*, 2890−2896. (h) Pearson, A. J.; Babu, M. *Tetrahedron Lett.* **1998**, *39*, 6273−6276. (i) Pearson, A. J.; Douglas, A. R. *Organometallics* **1998**, *17*, 1446−1448.

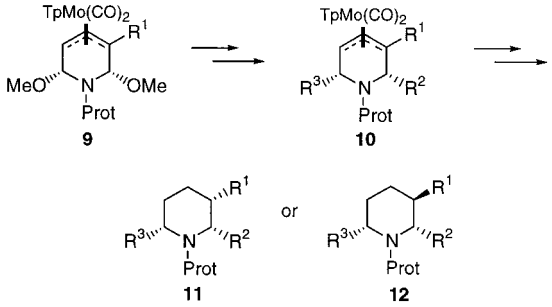
10.1021/ja011635g CCC: $20.00
Published on Web 11/22/2001



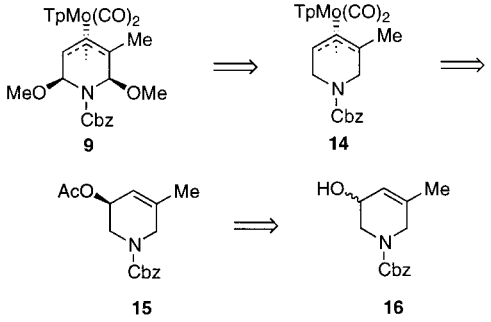
(-)-Indolizidine 209B, (**13**)

Figure 1.

Scheme 3



Scheme 4



Despite many efforts directed toward the synthesis of substituted piperidines,[3] to our knowledge no general and enantiocontrolled approach to both *cis*-2,3,6- and 2,6-*cis*-3-*trans*-trisubstituted piperidines from the same chiral starting material has been reported. On the basis of the above outlined strategy, we report here a general and enantiocontrolled synthesis of both all-*cis*-2,3,6- and 2,6-*cis*-3-*trans*-trisubstituted piperidines and, as a demonstration of its synthetic potential, the total synthesis of (−)-indolizidine 209B (**13**, Figure 1).[4] (−)-Indolizidine 209B is a member of the *dendrobatid* alkaloids isolated from the skin secretions of neotropical frogs. It has attracted the attention of synthetic organic chemists over the past decade,[5] because of its interesting chemical structure and pharmacological and medicinal activity as noncompetitive blocker of nicotine receptors channels.[6]

Results and Discussion

The required dimethoxy complex **9** should be preparable from enantiopure pyridinyl complexes **14**, which in turn could be prepared by the stereospecific oxidative addition of molybdenum[7] to the enantiopure allylic acetate **15**, obtained by enzymatic kinetic resolution of the corresponding racemic allylic alcohol **16** (Scheme 4).

To probe this strategy, we first prepared racemic dihydropyridinylmolybdenum (*rac*)-**14** (R^1 = Me) from ethyl *N*-benzyl-*N*-acetonylglycinate (**17**)[8] in six steps (Scheme 5). Intramolecular Claisen condensation of **17** using potassium *tert*-butoxide followed by trapping of the resulting enolate with acetic anhydride provided *β*-acetoxyenone **18** in 84% yield. Nucleophilic addition of methylmagnesium bromide to the carbonyl group of **18,** followed by hydrolysis of the enol acetate with aqueous NaOH, led to enone **19** in 79% yield. Exchange of the N-protecting group with benzyl chloroformate, Luche reduction[9] of the Cbz-protected piperidine enone **20**, and acetylation of the resulting allylic alcohol **16** afforded the required allylic acetate (*rac*)-**15** in good yield. Oxidative addition of $Mo(DMF)_3(CO)_3$ to (*rac*)-**15** under previously reported conditions[7] gave the racemic Mo complex (±)-**14** in 91% yield.

Both enantiomers of allylic acetate **15** were efficiently prepared in large-scale with excellent enantiopurity (99.5% ee) via lipase-catalyzed transesterification of alcohol **16**.[10] Screening experiments were conducted with alcohol (*rac*)-**16** using different lipases[11] and vinyl acetate as the acetylating agent in nonpolar aprotic solvents. Lipase AK (*pseudomonas fluorescens*, amano) gave the best results with toluene as solvent in the presence of molecular sieves.[12] The enzymatic transesterification of the alcohol (*rac*)-**16** (8 g scale) with vinyl acetate reached 50% conversion (measured by ^{1}H NMR) after 12 h. The resulting acetate (−)-**15** and the unreacted alcohol (+)-**16** were readily separated using a short pad of silica gel and isolated in 48% and 47% yield, respectively. The enantiomeric purity of the unreacted alcohol (+)-**16** (≥99.5% ee) and the acetate (−)-**15** (≥99.5% ee) were determined by chiral HPLC.[13] The allylic acetate antipode, (+)-**15**, was obtained by chemical acetylation (Ac_2O, Et_3N, DMAP) of the alcohol (+)-**16** (Scheme 6).

The antipodal acetates (−)-**15** and (+)-**15** gave rise to the corresponding η^3-dihydropyridinyl complexes (−)-**14** and (+)-**14**, respectively, in excellent enantiomeric purity (≥99.5% ee) and high yield (88%) (Scheme 7). Subsequent abstraction of hydride from (+)-**14** (≥99.5% ee) with Ph_3CPF_6, followed by deprotonation with Et_3N gave the (η^3-pyridinyl)molybdenum complex **21** in 88% yield with 99.4% ee. Treatment of **21** with

(3) For reviews, see: (a) Bailey, P. D.; Millwood, P. A.; Smith, P. D. *Chem. Commun.* **1998**, *6*, 633−640. (b) O'Hagan, D. *Nat. Prod. Rep.* **2000**, *17*, 435−446.

(4) For detection of natural indolizidine 209B, see: Daly, J. W.; Myers, C. W.; Whittaker, N. *Toxicon* **1987**, *25*, 1023−1095.

(5) For previous synthese of (−)-indolizidine 209B, see: (a) Back, T. G.; Nakajima, K. *J. Org. Chem.* **2000**, *65*, 4543−4552. (b) Michael, J. P.; Gravestock, D. *J. Chem. Soc., Perkin Trans. 1* **2000**, *12*, 1919−1928. (c) Bardou, A.; Celerier, J.-P.; Lhommet, G. *Tetrahedron Lett.* **1998**, *39*, 5189−5192. (d) Jefford, C. W.; Sienkiewicz, K.; Thorton, S. R. *Helv. Chim. Acta* **1995**, *78*, 1511−1524. (e) Aehman, J.; Somfai, P. *Tetrahedron* **1995**, *51*, 9747−9756. (f) Momose, T.; Toyooka, N. *J. Org. Chem.* **1994**, *59*, 943−945. (g) Aube, J.; Rafferty, P. S.; Milligan, G. L. *Heterocycles* **1993**, *35*, 1141−1147. (h) Satake, A.; Shimizu, I. *Tetrahedron Asymmetry* **1993**, *2*, 1405−1408. (i) Shishido, Y.; Kibayashi, C. *J. Org. Chem.* **1992**, *57*, 2876−2883. (j) Gnecco, D.; Marazano, C.; Das, B. C. *J. Chem. Soc., Chem. Commun.* **1991**, *9*, 625−626. (k) Holmes, A. B.; Smith, A. L.; Williams, S. F.; Hughes, L. R.; Lidert, Z.; Swithenbank, C. *J. Org. Chem.* **1991**, *56*, 1393−1405.

(6) Daly, J. W.; Nishizawa, Y.; Padgett, W. L.; Tokuyama, T.; Smith, A. L.; Holmes, A. B.; Kibayashi, C.; Aronstam, R. S. *Neurochem. Res.* **1991**, *16*, 1213−1218.

(7) Ward, Y. D.; Villanueva, L. A.; Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 897−898.

(8) Zymalkowski, F.; Messinger, P. *Arch. Pharm. (Weinheim)* **1967**, *300*, 91−94.

(9) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226−2227.

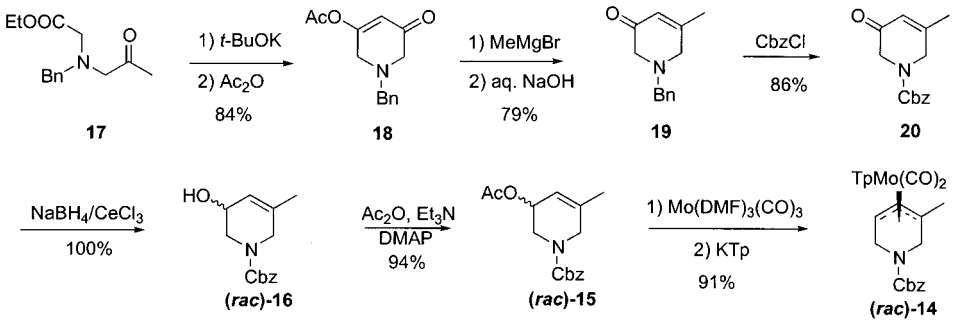
(10) For leading references in enzyme catalysis in organic synthesis, see: (a) Whitesides, G. M.; Wong, C. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 617−718. (b) Drauz, K.; Waldmann, H. *Enzyme Catalysis in Organic Synthesis*; VCH Press: Weinheim, Germany, 1995. (c) Palfreyman, M. G.; McCann, P. P.; Lovenberg, W.; Temple, J.; Sjoerdsma, A. *Enzymes as Targets for Drug Design*; Academic Press: San Diego, CA, 1989. (d) Palmer, T. *Understanding Enzymes*; Halsted Press: New York, 1985.

(11) Lipases: *Pseudomonas cepacea* (PS), *Rhizopus niveus* (F), *Candida rugosa* (CC), and *Pseudomonas fluorescens* (AK) were tested with different organic solvents (hexane, diisopropyl ether, and toluene).

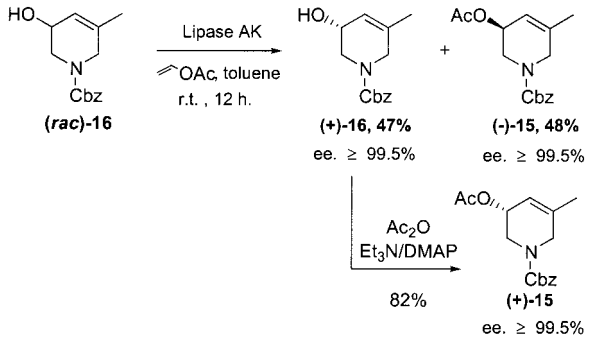
(12) Molecular sieves are necessary to reach 50% conversion; see: (a) Carretero, J. C.; Dominguez, E. *J. Org. Chem.* **1993**, *58*, 1596−1600. (b) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129−6139.

(13) The acetate (−)-**15** and alcohol (+)-**16** were converted into the corresponding UV-active allylic benzoates prior to analysis of the ee's by chiral HPLC.

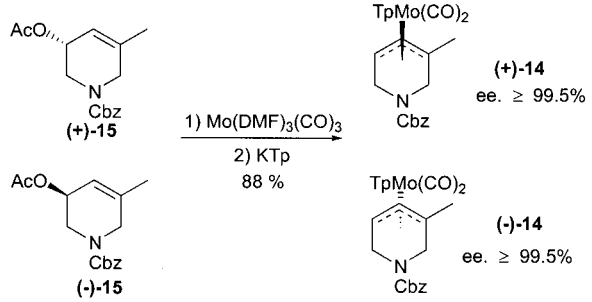
Scheme 5



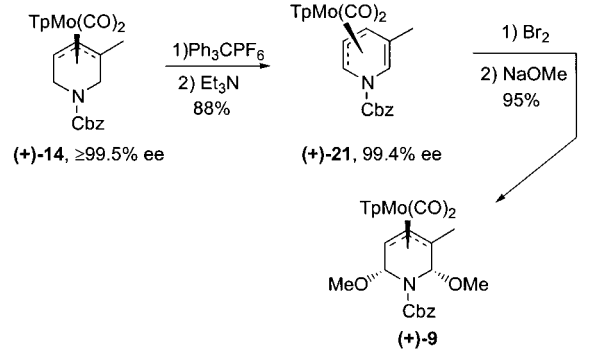
Scheme 6



Scheme 7



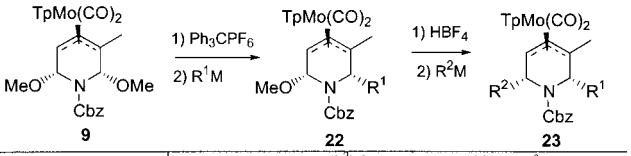
Scheme 8

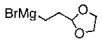
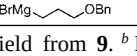


bromine followed by addition of sodium methoxide provided the desired 3-methyl-2,6-dimethoxy η^3-dihydropyridinyl (+)-**9** in 95% yield (Scheme 8). The eight-step synthesis described above can provide both enantiomers of molybdenum complex **9** in multigram scale with excellent enantiopurity (≥99% ee).

Similar to the pyranyl analogues **5a,b**, the (dimethoxydihydropyridinyl)molybdenum complex **9** underwent the anticipated regioselective, sequential methoxy abstractions and nucleophilic additions to give the (2,3,6-trisubstituted dihydropyridinyl)-molybdenum complexes **23a**−**f** in good to excellent yield with complete enantiocontrol (Table 1).[14] This suggests that the same

Table 1. Regio- and Stereocontrolled Synthesis of (2,3,6-Trisubstituted dihydropyridinyl)molybdenum Complexes



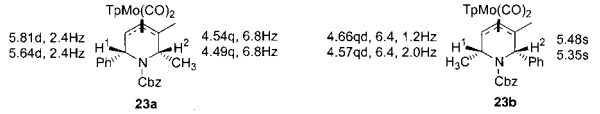
entry	R^1M	R^2M	**23**, yield[a] (%), ee (%)
1	MeMgBr	PhMgBr	**23a**, 69, --
2	PhMgBr	MeMgBr	**23b**, 65, --
3	allylMgBr	MeMgBr	**23c**, 61, --
4	vinylMgBr	3-furylLi	**23d**, 82, --
5[b]		*n*-pentylMgBr	**23e**, 85, --
6[c]		*n*-pentylMgBr	**23f**, 67, >99

[a] Overall yield from **9**. [b] Ph_3CPF_6 is used to abstract the second methoxy in order to avoid the opening of acetal ring. [c] Starting from **9** that was synthesized from **21** with 99.4% ee.

factors influence the selective abstraction in both the pyranyl and pyridinyl series. The regioselectivity ratio for abstraction of the methoxy adjacent to the 3-substitutent was determined to be greater than 49 to 1 by ^{1}H NMR analysis of the crude product. Because complexes **22** were sensitive to handling, they were only subjected to a brief workup to remove inorganic salts and volatile byproducts. Nonetheless, **22e** (precursor of **23e**) was fully characterized.

Starting from the same molybdenum π-allyl complex **23**, it is possible to generate a variety of functionalized trisubstituted tetrahydropyridines regio- and stereoselectively using three different demetalation procedures: (1) reductive demetalation using CO/NO$^+$ ligand exchange followed by nucleophilic attack;[15] (2) protodemetalation under strongly acidic conditions;[2b,16] (3) photolytic protodemetalation.[2b] Together, these three protocols constitute a powerful and versatile method to generate trisubstituted tetrahydropyridines regio- and stereoselectively from molybdenum complexes of general structure **23**.

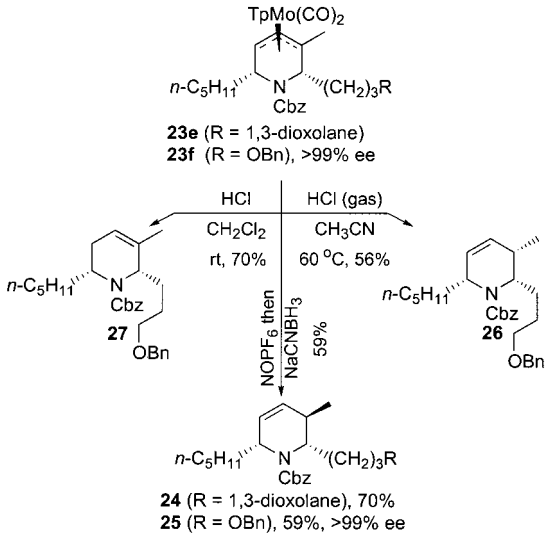
(14) The regiochemistry was established by NMR analysis. As shown below, H^1 of **23a** shows as two sets of doublets (doubling of resonances is due to *N*-Cbz rotamers), coupled only by the adjacent π-allyl hydrogen, while H^1 of **23b**, appears as two sets of quadruple doublets due to coupling by both the adjacent methyl group and π-allyl hydrogen. The coupling pattern of H^2 of **23a/b** also confirmed the depicted stereochemistry.



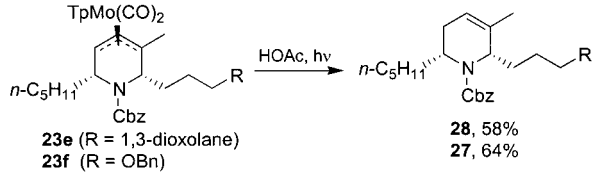
(15) (a) Faller, J. W.; Rosan, A. M. *J. Am. Chem. Soc.* **1976**, *98*, 3388−3389. (b) Faller, J. W.; Rosan, A. M. *J. Am. Chem. Soc.* **1977**, *99*, 4858−4859. (c) Villanueva, L. A.; Ward, Y. D.; Lachicotte, R.; Liebeskind, L. S. *Organometallics* **1996**, *15*, 4190−4200.

(16) Hansson, S.; Miller, J. F.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 9660−9661 (for AcOH and HCl).

Scheme 9



Scheme 10

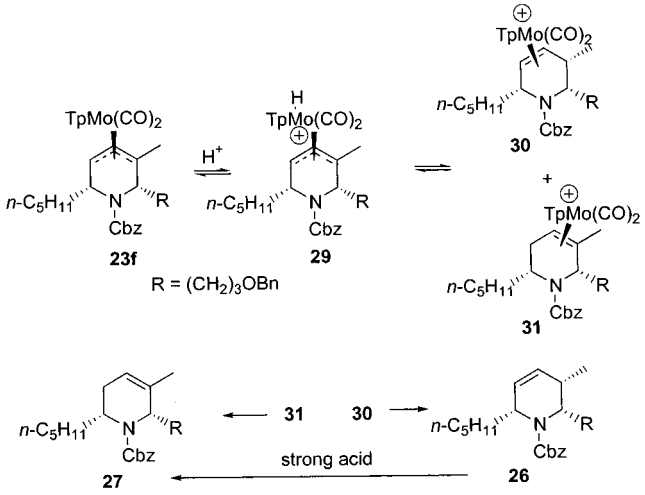


Reductive demetalation of 2,3,6-trisubstituted molybdenum complexes **23e,f** using DME as a solvent[17] gave **24** and **25** proceeded in 70% and 59% yield, respectively, with complete regio-, stereo- and enantiocontrol (Scheme 9). Protodemetalation of complex **23f** with HCl afforded unsaturated piperidines **26** and **27**, as an inseparable mixture, whose ratio was solvent dependent. When CH_3CN was used, the less substituted olefin **26** was obtained as the major product in 56% combined yield (ratio of **26**/**27**, 34:1). In contrast, the use of CH_2Cl_2 led to the more substituted olefin **27** as the major product (70% yield, ratio of **27**/**26**, 15:1).

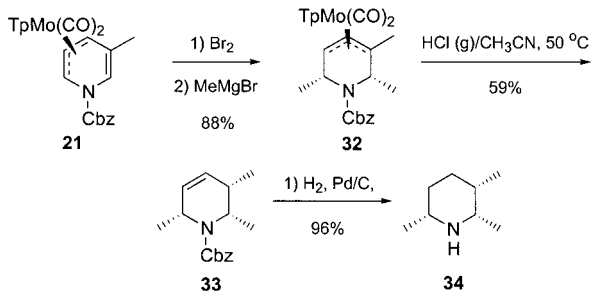
Molybdenum complexes **23e,f** were also subjected to photolytic protodemetalation to give piperidines **28** and **27**, respectively (Scheme 10). Compound **27**, which was previously obtained as a mixture of **26**/**27** by HCl-induced protodemetalation of **23f** (Scheme 9), was obtained as the only product in 64% yield using photoinduced demetalation. This HOAc-based protodemetalation protocol is useful for molybdenum complexes bearing functional groups that are sensitive to the hydrochloric acid procedure. Complex **23e** gave only decomposed product when treated with HCl; on the other hand, **28** was obtained in moderate yield (58%) using the photolytic demetalation (3% of the less substituted all-cis demetalation product was also formed but not separated).

The solvent dependence on the formation of the protodemetalation products is rationalized in Scheme 11. Metal-centered protonation of complex **23f** produces the cationic (η^3-allyl)-molybdenum complex **29**. Reductive elimination can form two regioisomeric molybdenum η^2-olefin cations, **30** or **31**, with molybdenum coordinated to either a disubstituted or trisubstituted olefin. Decomplexation leads to products **26** and **27**, respectively, in moderate yields (Scheme 11). According to this mechanism, nonbonded steric effects between the bulky TpMo-

Scheme 11



Scheme 12



$(CO)_2$ moiety and the η^2-olefin ligand should favor formation of the less hindered disubstituted olefin **26** under kinetic conditions, as is observed when HCl/CH_3CN was used as solvent. In CH_2Cl_2 HCl is a stronger acid, and acid-induced equilibration to the more substituted alkene product, **27**, can occur competitively under these conditions. Consistent with this analysis, the rate of the protodemetalation reaction was much slower in CH_3CN than in CH_2Cl_2.[18] Moreover, the conjugate base of the acid plays a role in the protonation/deprotonation isomerization of olefin **26** to **27**. Indeed the ratio of **26**/**27** dropped dramatically from 34:1 to 8:1 when aqueous hydrochloric acid was used instead of gaseous HCl. The selectivity for formation of the more substituted alkene in the photoinduced protodemetalation in acetic acid is not understood at this time.

The relative stereochemical assignments depicted in this study were confirmed by the synthesis of the known *cis*-2,3,6-trimethylpiperidine.[19] Molybdenum complex **21** was treated with bromine followed by MeMgBr to give (2,3,6-trimethyl dihydropyridinyl)molybdenum **32** (Scheme 12).[20] Complex **32** underwent the anticipated acidic protodemetalation to give 2,3,6-trimethyltetrahydropyridine (**33**)[21] which, after hydrogenation, gave the desired *cis*-2,3,6-trimethylpiperidine **34**. The structure

(17) DME has been previously described as an excellent solvent for CO/NO^+ ligand exchange: Cosford, N. D. P.; Liebeskind, L. S. *Organometallics* **1994**, *13*, 1498−1503.

(18) Reaction using CH_2Cl_2 as solvent was complete within 15 min at room temperature, while reaction with CH_3CN as solvent was not complete after 24 h at the same temperature. Raising the temperature accelerated the reaction, as the reaction was complete after 2 h at 60 °C. See the Experimental Section for details.

(19) (a) Isin, Zh. I.; Sokolov, D. V. *Izv. Akad. Nauk. Kaz. SSR, Ser. Khim.* **1974**, *24*, 76−78. (b) Lebel, N. A.; Balasubramanian, N. *J. Am. Chem. Soc.* **1989**, *111*, 3363−3368.

(20) The pyranyl trisubstituted complex analogous to **32** had been prepared under similar conditions (see ref 2b).

(21) Acidic protodemetalation of **32** gave a mixture of **33** and the more substituted alkene isomer in a ratio of 23/1.

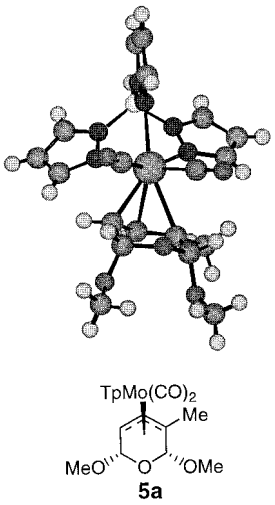


Figure 2. Chem3D representation of the X-ray crystal structure of **5a**.

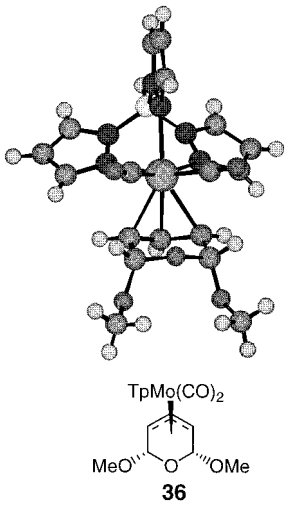
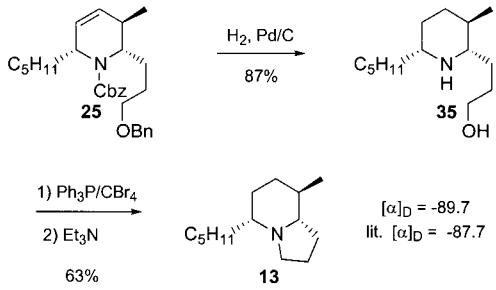


Figure 3. Chem3D representation of the X-ray crystal structure of **36**.

Scheme 13



assignment was confirmed by comparison of the NMR data for **34** and the melting point of its *N*,*N*-dimethylammonium iodide salt with those reported in the literature.[19b]

The potential of this methodology for enantiocontrolled synthesis was demonstrated by the efficient total synthesis of (−)-indolizidine 209B in enantiopure form (Scheme 13). Treatment of **25** with H_2−Pd/C resulted in N- and O-deprotection and alkene hydrogenation. Subsequent intramolecular cyclization[5i] of the resulting amino alcohol **35** gave (−)-indolizidine 209B (**13**) ($[\alpha]_D = -89.7$, $c = 0.31$, MeOH; lit.[5a] $[\alpha]_D = -87.7$, $c = 0.62$, MeOH) in 55% overall yield. Its spectroscopic data were identical to those reported in the literature. This total synthesis, in combination with the expected anti oxidative addition of molybdenum(0) to the allylic acetates (+)- and (−)-**15** shown in Scheme 7,[22] was used to deduce the absolute stereochemical assignments made throughout this work.

Finally, the origin of the highly selective abstraction of methoxide from both (2,6-dimethoxy-3-substituted-η^3-dihydropyranyl)$TpMo(CO)_2$ and the analogous pyridinyl complexes was probed. Experiments revealed that the first methoxide abstraction is extremely fast (<1 min) at low temperature (−78 °C), which means the activation energy barrier of this reaction is very low. Thus, according to the Hammond postulate[23] the structure of the transition state should be similar to that of the starting material. This suggests that the observed selectivity should arise from local differences of two different methoxy groups in the ground state. As a consequence, it was presumed that the 3-substituent adjacent to the 2-methoxy group introduces local nonbonded steric effects in the ground state that are diminished at the transition state, thus speeding the abstraction of the more hindered methoxy substituent. While nonbonded steric effects between the 3-substituent and the adjacent 2-methoxy group may well exist, X-ray crystallographic analyses of the dihydropyranyl compounds **5a** and **36** (Figures 2 and 3) indicated an additional, unexpected effect of the 3-substituent that probably amplifies the observed selectivity. Nonbonded steric effects between the Tp ligand and the 3-substituent of the η^3-allyl distorts the ground-state structure of the (2,6-dimethoxy-η^3-pyranyl)molybdenum. The more substituted end of the η^3-allyl is tilted away from the $TpMo(CO)_2$ fragment bringing the methoxy group at the 2-position closer to a *trans-anti*-parallel conformation with the Mo (Figure 4). As a result, in **5a** the torsion angle of Mo−C13−C14−O3 (165.77°) is closer to 180° than that of Mo−C11−C10−O2 (157.98°), while the crystal structure of symmetrical **36**, unperturbed by a 3-substituent, shows identical torsion angles of 160.96°. Therefore, in complex **5a** selective abstraction of the methoxy group adjacent to the 3-substituent is stereoelectronically favored, because the methoxy group adjacent to the 3-methyl substituent is closer to a *trans-anti*-parallel conformation with Mo. Similar ground-state distortions should be operative in the analogous pyridinyl complexes and account for the similar highly selective methoxy abstractions.

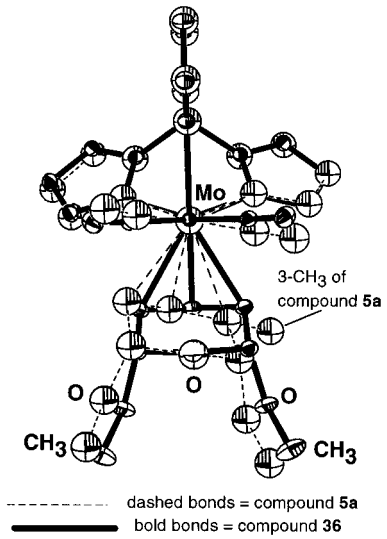


Figure 4. Mo and the three ligating nitrogen atoms from each Tp ligand were overlayed.

(22) Ward, Y. D.; Villanueva, L. A.; Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 897−898.

(23) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334−338.

Table 2. Determination of Enantiomeric Retention Times

entry	compd	column	hexanes/*i*-PrOH	mL/min	λ (nm)	(+)- (min)	(−)- (min)
1	benzoate of (±)-**16**	Chiralpack AD	80:20	1.0	254	16.8	22.4
2	(±)-**14**	Chiralpack AD	80:20	1.0	254	23.1	25.8
3	(±)-**21**	Chiralpack AD	85:15	1.0	365	10.8	7.0
4	(±)-**23f**	Chiralcel OD	98:2	1.0	370	53.7	34.7
5	(±)-**25**	(R,R)-Whelk O1	95:5	0.5	254	26.1	17.1

Conclusions

In summary, a novel and enantiocontrolled route to either 2,3,6-*cis*- or 2,6-*cis*-3-*trans*-trisubstituted piperidines starting from the same enantiopure $TpMo(CO)_2$ pyridinyl complex as a chiral scaffold has been described. Key steps include the efficient and scalable enzymatic kinetic resolution of a racemic allylic alcohol, a highly selective methoxide abstraction from 2,6-dimethoxy-3-substituted dihydropyridinyl complexes, and regio- and stereoselective demetalations of 2,3,6-trisubstituted (dihydropyridinyl)molybdenum complexes. The synthetic potential of this methodology was demonstrated by a total synthesis of (−)-indolizidine 209B.

Experimental Section

General Methods. Unless otherwise indicated, all NMR data were collected at room temperature in $CDCl_3$ with internal $CHCl_3$ as the reference (7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C) or in $(CD_3)_2CO$ with internal $(CD_3)(CD_2H)CO$ as the reference (2.05 ppm for ^{1}H and 29.92 ppm for ^{13}C). IR spectra were recorded in CH_2Cl_2 using a KCl cell on a Nicolet 510 FT-IR spectrometer or on an ASI React IR spectrometer, equipped with a silicon probe. Peaks are reported in cm^{-1}. Optical rotations were measured at 25 °C. Analytic thin-layer chromatography (TLC) was carried out on commercial Merck Silica gel 60 plates, 0.25 thickness, with fluorescent indicator (F-254). Visualization was accomplished by UV light or by staining with 5% phosphomolybdic acid in ethanol. Column chromatography was performed by the method of Still[24] with 32−63 μm silica gel (Woelm) or 135 μm activated basic alumina (Aldrich). In some cases (as indicated), silica gel was previously neutralized with Et_3N. Lipases AK, PS, F, and CC were purchased from Amano Enzyme. The enzymatic reactions were shaken in a Lab-line, L-C Shaker (model 1346) at 184 rpm. Solvents for chromatography were reagent grade and used as received. HPLC was performed on a Millipore Waters 60C HPLC spectrometer with a CHIRALPACK AD or CHIRALCEL OD or REGIS (R,R)-Whelk O1 column at room temperature using a Waters 486 UV detector (HPLC grade 2-propanol and hexanes were used). Photochemical reactions were performed in regular Pyrex glassware in a Rayonet RMR-500 photochemical reactor manufactured by the Southern New England Ultraviolet Co. All chemical reagents were used as received unless otherwise indicated. All solvents indicated "dry" were dried either with molecular sieves or by distillation, except diethyl ether that was purchased from Mallinckrodt and used as received. Unless otherwise specified, all reactions were carried out under nitrogen or argon atmosphere, and all reaction flasks were flamed or oven dried before use. Data for enantiomeric retention times are found in Table 2.

Synthesis of (Dihydropyridinyl)molybdenum Complex 14.

5-Acetoxy-1-benzyl-3-oxo-1,2,3,6-tetrahydropyridine (18). Compound **17**[8] (18.80 g, 75.41 mmol, 1.00 equiv) in THF (40 mL) was added over 30 min via a syringe pump to a solution of potassium *tert*-butoxide (8.88 g, 79.18 mmol, 1.05 equiv) in THF (120 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. It was then cooled to 0 °C again and quenched with acetic anhydride (7.46 mL, 8.08 g, 79.18 mmol, 1.05 equiv). After additional stirring at 0 °C for 1 h, the reaction mixture was diluted with ethyl acetate (300 mL) and water (300 mL). The aqueous layer was separated and washed with ethyl acetate (160 mL). The combined organic layers were washed with brine (2 × 300 mL), dried over $MgSO_4$, concentrated, and passed through a short pad of silica gel (8 × 6 cm) with 30% ethyl acetate in hexanes to afford compound **18** as a light yellow oil (15.6 g, 63.68 mmol, 84%). TLC (30% ethyl acetate in hexanes): $R_f = 0.27$. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.34−7.29 (m, 5 H), 6.09 (s, 1 H), 3.67 (s, 2 H), 3.36 (s, 2 H), 3.18 (s, 2 H), 2.16 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 196.2, 167.3, 167.0, 136.5, 129.2, 128.6, 127.8, 115.0, 60.9, 60.4, 52.9, 21.2. IR (CH_2Cl_2, KCl, cm^{-1}): 1779, 1735, 1681, 1652, 1636, 1372, 1194, 1142. Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.39; H, 6.10; N, 5.62.

1-Benzyl-5-methyl-3-oxo-1,2,3,6-tetrahydropyridine (19). To a solution of compound **18** (14.40 g, 58.8 mmol, 1.00 equiv) in THF (100 mL) at 0 °C was added MeMgBr (3.0 M in diethyl ether, 21.6 mL, 64.6 mmol, 1.1 equiv) over 5 min via syringe. After being stirred at 0 °C for 30 min, the reaction was quenched with aqueous NaOH (3.0 M, 80 mL, 240 mmol, 4.1 equiv) and stirred at room temperature for 4 h. The aqueous layer was separated and washed with ethyl acetate (2 × 300 mL). The combined organic layers were washed with brine (2 × 400 mL), dried over $MgSO_4$, and concentrated to afford **19** as a light yellow oil (9.30 g, 46.26 mmol, 79%). TLC (30% ethyl acetate in hexanes): $R_f = 0.25$. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34−7.27 (m, 5 H), 5.95 (d, $J = 1.5$ Hz, 1 H), 3.65 (s, 2 H), 3.15 (s, 2 H), 3.11 (s, 2 H), 1.93 (d, $J = 1.0$ Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.9, 160.8, 136.5, 129.1, 128.9, 128.4, 124.9, 61.6, 60.2, 56.1, 21.7. IR (CH_2Cl_2, KCl, cm^{-1}): 3053, 3033, 2809, 2752, 1674, 1640, 1455, 1439. HRMS (EI): calcd for $C_{13}H_{15}NO$ (M^+), 201.1154; found, 201.1145.

1-(Benzyloxycarbonyl)-5-methyl-3-oxo-1,2,3,6-tetrahydropyridine (20). To a solution of compound **19** (9.0 g, 44.8 mmol, 1.0 equiv) in dichloromethane (50 mL) was added benzyl chloroformate (12.74 mL, 15.21 g, 89.1 mmol, 2.0 equiv) via syringe. The reaction mixture was stirred at room temperature overnight and passed through a short pad of silica gel (8 × 6 cm), eluting first with 50% dichloromethane in hexanes to remove starting materials and byproducts and then with 30% ethyl acetate in hexanes to obtain **20** as a light yellow oil (9.45 g, 38.6 mmol, 86%). TLC (30% ethyl acetate in hexanes): $R_f = 0.20$. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33−7.29 (m, 5 H), 5.98 (q, $J = 1.5$ Hz, 1 H), 5.14 (s, 2 H), 4.15 (s, 2 H), 4.13 (s, 2 H), 1.98 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 192.4, 159.1, 154.6, 135.7, 128.4, 128.1, 127.9, 124.7, 67.5, 50.4, 46.6, 21.2. IR (CH_2Cl_2, KCl, cm^{-1}): 1704, 1681, 1643, 1445, 1428, 1235, 1225. Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.29; H, 6.17; N, 5.61.

(±)-1-(Benzyloxycarbonyl)-3-hydroxy-5-methyl-1,2,3,6-tetrahydropyridine (16). To a solution of compound **20** (9.25 g, 37.75 mmol, 1.0 equiv) and $CeCl_3 \cdot 7H_2O$ (14.05 g, 37.75 mmol, 1.0 equiv) in ethanol (200 mL) at 0 °C was added $NaBH_4$ (1.43 g, 37.75 mmol, 1.0 equiv). After being stirred at 0 °C for 3 h, the reaction mixture was diluted with ethyl acetate (400 mL) and water (400 mL). The aqueous layer was separated and washed with ethyl acetate (250 mL). The combined organic layers were washed with brine (2 × 400 mL), dried over $MgSO_4$, and concentrated to afford **16** as a light yellow oil (9.48 g, 37.75 mmol, 100%). TLC (30% ethyl acetate in hexanes): $R_f = 0.18$. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35−7.30 (m, 5 H), 5.63 (s, 1 H), 5.14 (s, 2 H), 4.20−3.85 (m, 2 H), 3.70−3.50 (m, 3 H), 1.70 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.5, 136.4, 128.3, 127.9, 123.1, 122.6, 67.2, 63.5, 47.7, 47.3, 46.9, 20.3. IR (CH_2Cl_2, KCl, cm^{-1}): 3588, 2918, 1700, 1674, 1450, 1430, 1239, 910. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.67. Found: C, 68.12; H, 6.80; N, 5.50.

(±)-3-Acetoxy-1-(benzyloxycarbonyl)-5-methyl-1,2,3,6-tetrahydropyridine (15). To a solution of **16** (6.70 g, 27.12 mmol, 1.0 equiv), triethylamine (4.92 mL, 3.58 g, 35.30 mmol, 1.3 equiv), and DMAP (66 mg, 0.55 mmol, 0.02 equiv) in dichloromethane (20 mL) was added acetic anhydride (2.80 mL, 3.04 g, 29.84 mmol, 1.1 equiv). The mixture

(24) Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

was stirred for 3 h at room temperature and passed through a short pad of silica gel (8 × 5 cm) with 10% ethyl acetate in hexanes and then 20% ethyl acetate in hexanes to give **15** as a light yellow oil (7.38 g, 25.54 mmol, 94%). TLC (30% ethyl acetate in hexanes): $R_f = 0.45$. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.36−7.31 (m, 5 H), 5.62 (d, J = 14.0 Hz, 1 H), 5.26−5.08 (m, 3 H), 4.23−4.00 (m, 2 H), 3.66−3.62 (m, 1 H), 3.35 (dd, J = 14.0, 3.0 Hz, 1 H), 2.05 (s, 1.5 H), 1.92 (s, 1.5 H), 1.76 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.6, 155.2, 138.9, 137.9, 136.5, 128.4, 127.9, 127.7, 118.6, 118.1, 67.2, 67.0, 65.8, 65.6, 46.7, 44.5, 44.2, 20.9, 20.3. IR (CH_2Cl_2, KCl, cm^{-1}): 2945, 1726, 1701, 1675, 1449, 1433, 1373, 1362, 1234. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.47; H, 6.63; N, 4.79.

(+)-3*R*-16 and (−)-3*S*-15 (Lipase-Mediated Kinetic Resolution). To a solution of the racemic alcohol **16** (8 g, 32.35 mmol, 1.0 equiv) in dry toluene (435 mL) were added 20.5 g of activated 4 Å molecular sieves, vinyl acetate (11.7 mL, 126.93 mmol, 3.9 equiv), and 4.59 g of Lipase AK. The mixture was shaken at room temperature until 50% of conversion was reached (12 h). The enzyme and the molecular sieves were filtered through a short pad (7 × 5 cm) of Celite and washed with ethyl acetate (2 × 20 mL). The organic solvent was evaporated to give a mixture of the unreacted alcohol (+)-**16** and the acetate (−)-**15** as a light yellow oil. This mixture was passed through a short pad of silica gel (2.5 × 7 cm) using first hexanes−ethyl acetate (20:1) to elute (−)-**15** (4.30 g, 48%, ≥99.5% ee), $[\alpha]_D$ −23 (c = 1.2, EtOH), and then hexanes−ethyl acetate (10:1) to elute the more polar (+)-**16** (3.76 g, 47%, ≥99.5% ee), $[\alpha]_D$ +44 (c = 1.3, EtOH).

To measure the ee of the acetate **(−)-15** and alcohol **(+)-16** by HPLC, they were converted into the corresponding UV-active allylic benzoates **(−)-3*S*-** and **(+)-3*R*-1-(benzyloxycarbonyl)-5-methyl-3-(phenylcarbonyloxy)-1,2,3,6-tetrahydropyridine,** respectively. To a solution of (+)-**16** (0.24 g, 0.97 mmol, 1.0 equiv) and DMAP (12 mg, 0.09 mmol, 0.1 equiv) in CH_2Cl_2 (5 mL) was added at room temperature Et_3N (0.20 mL, 1.45 mmol, 1.5 equiv). After 2 min, benzoyl chloride (0.16 mL, 1.16 mmol, 1.2 equiv) was added dropwise via syringe. The reaction was stirred at room temperature overnight and then quenched with HCl (5 wt % in H_2O, 1 mL). The aqueous layer was separated and washed with CH_2Cl_2 (3 × 25 mL). The organic layer was washed with a saturated aqueous solution of Na_2CO_3 (1 × 15 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (25% ethyl acetate in hexanes) to afford **(+)-3*R*-1-(benzyloxycarbonyl)-5-methyl-3-(phenylcarbonyloxy)-1,2,3,6-tetrahydropyridine** as a colorless oil (0.33 g, 96%, ≥99.5% ee), $[\alpha]_D$ +195 (c = 1.0, EtOH).

The enantiomer **(−)-3*S*-1-(benzyloxycarbonyl)-5-methyl-3-(phenylcarbonyloxy)-1,2,3,6-tetrahydropyridine** was obtained from alcohol (−)-**16** by following the same procedure.

Preparation of (−)-16. To a solution of (−)-**15** (0.30 g, 1.03 mmol, 1.0 equiv) in MeOH (2 mL) was added K_2CO_3 (0.07 g, 0.51 mmol, 0.5 equiv) at room temperature. The solution was stirred for 5 min at same temperature. The crude was then concentrated to dryness, passed through a short pad of silica, and eluted with CH_2Cl_2 (40 mL) to afford alcohol (−)-**16** (0.24 g, 0.98 mmol, 96%). Data for **(−)-3*S*-1-(benzyloxycarbonyl)-5-methyl-3-(phenylcarbonyloxy)-1,2,3,6-tetrahydropyridine:** TLC (25% ethyl acetate in hexane): $R_f = 0.35$). $[\alpha]_D$: −195 (c = 1.0, EtOH), ee = 99.5%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.12−7.85 (m, 2 H), 7.61−7.09 (m, 8 H), 5.90−5.62 (m, 1 H), 5.52−5.31 (m, 1 H), 5.50−4.95 (m, 2 H), 4.38−4.61 (m, 2 H), 3.82−3.65 (m, 2 H), 3.60−3.32 (m, 2 H), 1.78−1.75 (m, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.5, 141.8, 141.7, 139.2, 136.1, 134.6, 129.4, 128.6, 126.4, 106.1, 106.1, 105.5, 105.5, 72.1, 71.3, 67.5, 63.4, 58.0, 42.7. IR (neat, cm^{-1}): 2941, 1710, 1432, 1451, 1270, 1235, 1173, 1127, 714. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.70; H, 6.14; N, 4.10.

(−)-3*S*-, (+)-3*R*-, and (±)-Dicarbonyl[hydridotris(1-pyrazolyl)-borato][(η-3,4,5)-1-(benzyloxycarbonyl)-3-methyl-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (14). To a solution of $Mo(DMF)_3(CO)_3$ (11.8 g, 29.6 mmol, 1.4 equiv) in CH_2Cl_2 (dry and degassed, 100 mL) was added (+)-**15** (6.10 g, 21.1 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (10 mL) at 0 °C. The mixture was stirred at 0 °C for 3 h and room temperature for 1 h. KTp[25] (7.46 g, 29.6 mmol, 1.4 equiv) was then added as a solid. After being stirred overnight at room temperature, the reaction mixture was passed through a short pad of silica gel (30% EtOAc in hexanes, 8 × 6 cm) and then concentrated. The residue was further purified by chromatography (25% ethyl acetate in hexanes, 20 × 4 cm) to afford (+)-**14** as a yellow solid (11.4 g, 91%, ≥99.5% ee), $[\alpha]_D$ +260 (c = 0.5, EtOH). (−)-**14** was prepared from (−)-**15** in the same manner (11.4 g, 91%, ≥99.5% ee), $[\alpha]_D$ −260 (c = 0.5, EtOH).

Preparation of (±)-14. To a solution of $Mo(DMF)_3(CO)_3$ (11.8 g, 29.6 mmol, 1.4 equiv) in CH_2Cl_2 (dry and degassed, 100 mL) was added (±)-**15** (6.10 g, 21.1 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (25 mL) at room temperature. After the solution was stirring overnight, KTp (7.46 g, 29.6 mmol, 1.4 equiv) was added as a solid. After 1 h, the reaction mixture was passed through a short pad of silica gel (30% EtOAc in hexanes, 8 × 6 cm) and then concentrated. The residue was further purified by chromatography (25% ethyl acetate in hexanes, 20 × 4 cm) to afford (±)-**14** as a yellow solid (11.4 g, 19.2 mmol, 91%). TLC (30% ethyl acetate in hexanes): $R_f = 0.25$; mp > 109 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.50 (d, J = 1.5 Hz, 0.5 H), 8.48 (d, J = 1.5 Hz, 0.5 H), 7.76 (d, J = 1.5 Hz, 0.5 H), 7.74 (d, J = 1.5 Hz, 0.5 H), 7.65−7.60 (m, 3 H), 7.47 (d, J = 2.0 Hz, 1 H), 7.40−7.27 (m, 5 H), 6.25 (t, J = 2.0 Hz, 1 H), 6.23 (t, J = 2.0 Hz, 1 H), 6.16 (t, J = 2.0 Hz, 1 H), 5.18−5.07 (m, 2 H), 4.35−4.20 (m, 2 H), 4.07 (d, J = 7.2 Hz, 0.5 H), 4.00 (d, J = 7.2 Hz, 0.5 H), 3.86 (dd, J = 7.2, 2.0 Hz, 1 H), 3.50−3.44 (m, 1 H), 3.36 (d, J = 11.2 Hz, 0.5 H), 3.32 (d, J = 11.2 Hz, 0.5 H), 1.92 (s, 1.5 H), 1.87 (s, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 231.0, 230.4, 226.1, 225.6, 155.0, 154.8, 146.7, 145.7, 145.6, 139.5, 136.8, 136.5, 135.9, 134.2, 128.3, 128.0, 127.8, 127.7, 105.6, 105.5, 105.1, 90.5, 90.2, 71.5, 71.3, 67.1, 66.9, 56.7, 56.6, 47.2, 47.1, 41.0, 40.9, 24.0. IR (CH_2Cl_2, KCl, cm^{-1}): 3055, 2985, 2483, 1936, 1850, 1697, 1503, 1240, 1051. Anal. Calcd for $C_{25}H_{26}BMoN_7O_4$: C, 50.44; H, 4.40; N, 16.47. Found: C, 50.22; H, 4.42; N, 16.23.

Synthesis of Pyridinyl Complex 9.

(+)-3*S*-, (−)-3*R*-, and (±)-Dicarbonyl[hydridotris(1-pyrazolyl)-borato][(η-2,3,4)-1-(benzyloxycarbonyl)-1,2-dihydropyridin-5-methyl-2-yl]molybdenum (21). To a solution of (+)-**14** (802 mg, 1.35 mmol, 1.0 equiv, ≥99.5% ee) in CH_2Cl_2 (10 mL), at −15 °C, was added Ph_3CPF_6 (0.55 g, 1.42 mmol, 1.05 equiv) as a solid in one portion. After 30 min, dry Et_2O (50 mL) was added to precipitate the formed diene cation. The solvents were removed via cannula (covered with a piece of filter paper to prevent removal of the solid). The remaining orange solid was washed with dry Et_2O (2 × 30 mL), briefly dried under vacuum, redissolved in CH_2Cl_2 (15 mL), and treated at room temperature with Et_3N (0.284 mL, 2.03 mmol, 1.5 equiv). After 5 min, the reaction mixture was concentrated and the residue was purified by chromatography (10% ethyl acetate in hexanes, 12 × 2 cm) to afford (+)-**21** as a orange solid (700 mg, 1.19 mmol, 88%, 99.4% ee), $[\alpha]_D$ +183.8 (c = 2.4, CH_2Cl_2). (−)-**21** was prepared from (−)-**14** in the same manner.

Preparation of (±)-21. To a solution of (±)-**14** (4.17 g, 7.00 mmol, 1.0 equiv) in CH_2Cl_2 (25 mL), at 0 °C, was added Ph_3CPF_6 (2.72 g, 7.00 mmol, 1.0 equiv) as a solid. After 2 h at 0 °C, dry Et_2O (100 mL) was added to precipitate the formed diene cation. The diene cation was filtrated, washed with Et_2O, dried under vaccum, and treated with Et_3N in the same way as described in the preparation of (+)-**21**. After chromatography, (±)-**21** was obtained as an orange solid (3.72 g, 6.27 mmol, 90%). TLC (30% ethyl acetate in hexanes): $R_f = 0.50$; mp > 110 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.47 (d, J = 2.0 Hz, 0.5 H), 8.20 (d, J = 2.0 Hz, 0.5 H), 8.19 (d, J = 2.0 Hz, 0.5 H), 7.74 (d, J = 2.0 Hz, 0.5 H), 7.70 (d, J = 2.0 Hz, 0.5 H), 7.69 (d, J = 2.0 Hz, 0.5 H), 7.60 (t, J = 2.4 Hz, 1 H), 7.57 (d, J = 2.4 Hz, 0.5 H), 7.52 (d, J = 3.0 Hz, 1.5 H), 7.47 (d, J = 2.2 Hz, 1 H), 7.45−7.35 (m, 4 H), 7.10 (dt, J = 6.0, 1.8 Hz, 0.5 H), 6.32 (s, 0.5 H), 6.27−6.18 (m, 2.5 H), 6.16 (t, J = 2.2 Hz, 1 H), 5.87 (t, J = 2.0 Hz, 0.5 H), 5.32−5.30 (m, 2 H), 4.70−4.68 (m, 1 H), 2.79 (t, J = 6.0 Hz, 0.5 H), 2.67 (t, J = 6.0 Hz, 0.5 H), 2.07 (d, J = 1.2 Hz, 1.5 H), 2.03 (d, J = 1.2 Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 231.3, 230.6, 223.2, 222.5, 152.9, 152.8, 146.0, 145.8, 143.7, 140.1, 140.0, 136.0, 135.9, 135.8, 135.7, 135.3, 134.3, 129.2, 128.7, 128.6, 128.5, 128.3, 128.1, 122.7, 122.1, 111.6, 111.1, 105.7, 105.4, 89.8,

(25) Trofimenko, S. *J. Am. Chem. Soc*. **1967**, *89*, 3170.

88.6, 69.1, 68.3, 64.7, 64.2, 52.5, 51.9, 20.4. IR (CH_2Cl_2, KCl, cm^{-1}): 2484, 1935, 1851, 1711, 1650, 1503, 1409, 1302, 1051. Anal. Calcd for $C_{25}H_{24}BMoN_7O_4$: C, 50.61; H, 4.08; N, 16.53. Found: C, 50.71; H, 4.14; N, 16.43.

(+)-(2*S*,3*R*,6*R*)-, (−)-(2*R*,3*S*,6*S*)-, and (±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-(benzyloxycarbonyl)-2,6-dimethoxy-3-methyl-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (9). To a solution of (+)-**21** (621 mg, 1.04 mmol, 1.0 equiv) in THF (10 mL) at −78 °C was added bromine (59.5 μL, 1.15 mmol, 1.1 equiv). After 15 min, a 25 wt % solution of NaOMe in MeOH (4.375 M, 0.60 mL, 2.61 mmol, 2.5 equiv) was added. After 5 min at −78 °C the reaction was allowed to warm to room temperature. The reaction mixture was passed through a pad of neutralized silica gel (3 × 2 cm) with Et_2O to afford (+)-**9** (652 mg, 0.99 mmol, 95%) as a yellow solid. (−)-**9** and (±)-**9** were prepared in the same manner starting from (−)-**21** and (±)-**21**, $[\alpha]_D$ +167.7 (*c* = 1.17, CH_2Cl_2). TLC (30% ethyl acetate in hexanes) $R_f = 0.22$; mp = 158−161 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($(CD_3)_2CO$, 400 MHz): δ 8.44 (s, 1 H), 7.99 (s, 0.5 H), 7.98 (d, *J* = 1.6 Hz, 0.5 H), 7.94 (s, 1 H), 7.82 (d, *J* = 2.0 Hz, 1 H), 7.80 (d, *J* = 1.6 Hz, 1 H), 7.69 (s, 1 H), 7.45−7.30 (m, 5 H), 6.32 (t, *J* = 2.0 Hz, 2 H), 6.28−6.27 (m, 1 H), 5.82 (d, *J* = 2.8 Hz, 0.5 H), 5.46 (d, *J* = 2.8 Hz, 0.5 H), 5.42 (s, 0.5 H), 5.42 (s, 0.5 H), 5.25 (d, *J* = 11.6 Hz, 0.5 H), 5.20 (d, *J* = 11.6 Hz, 0.5 H), 5.12 (d, *J* = 12.4 Hz, 0.5 H), 5.01 (d, *J* = 12.4 Hz, 0.5 H), 4.40 (dd, *J* = 7.2, 2.8 Hz, 0.5 H), 4.35 (dd, *J* = 7.2, 2.8 Hz, 0.5 H), 4.11 (d, *J* = 7.2 Hz, 0.5 H), 4.10 (d, *J* = 7.2 Hz, 0.5 H), 3.49 (s, 1.5 H), 3.38 (s, 1.5 H), 3.36 (s, 1.5 H), 3.30 (s, 1.5 H), 1.96 (s, 1.5 H), 1.87 (s, 1.5 H). ^{13}C NMR ($(CD_3)_2CO$, 100 MHz): δ 233.2, 232.9, 227.1, 226.9, 156.3, 155.9, 147.6, 147.4, 147.2, 141.7, 141.5, 138.1, 137.6, 137.5, 135.8, 129.3, 129.2, 129.1, 128.9, 128.8, 106.8, 106.4, 91.6, 90.9, 86.8, 84.5, 84.3, 77.2, 76.4, 68.2, 68.0, 59.6, 58.9, 57.9, 56.7, 56.4, 56.0, 23.54, 23.48. IR (CH_2Cl_2, KCl, cm^{-1}): 2485, 1943, 1858, 1706, 1410, 1304, 1051. Anal. Calcd for $C_{27}H_{30}BMoN_7O_6$: C, 49.49; H, 4.61; N, 14.96. Found: C, 49.48; H, 4.59; N, 14.89.

General Procedure for the Synthesis of 2,3,6-Trisubstituted (Dihydropyridinyl)molybdenum Complexes 22 and 23 from 9.

To a Schlenk flask containing a solution of complex **9** (131 mg, 0.20 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL) cooled to −78 °C was added Ph_3CPF_6 (77.6 mg, 0.20 mmol, 1.0 equiv) as a solid in one portion. After 1 min, the mixture was allowed to warm to 0 °C over 5 min. Then methyl *tert*-butyl ether (MTBE) (8 mL) was added to precipitate the formed cationic diene. The solvents were removed via cannula (the tip was covered with a piece of filter paper to prevent removal of the solids), and the remaining solid was washed with MTBE (2 × 6 mL) and then briefly dried under vacuum for a few minutes. It was then cooled to −78 °C, dissolved in THF (1 mL), and treated with the first nucleophile (R^1M) (when prepared and used fresh, R^1M was added via cannula into the reaction mixture). After 15 min the reaction was warmed to 0 °C, passed through a pad of neutralized silica gel (2 × 3 cm) with Et_2O, and concentrated to provide **22** that was used for the next step without further purification. A solution of crude **22** in MTBE (8 mL) was treated at 0 °C with 54 wt % solution of HBF_4 in Et_2O (0.056 mL, 0.40 mmol, 2.0 equiv). After 5 min the solvents were removed via cannula, and the remaining solid was washed with MTBE (8 mL) and then dried under vacuum for 5 min. The cationic diene complex was then cooled to −78 °C, dissolved in THF (2 mL), and treated with the second nucleophile (R^2M). After 15 min at −78 °C, the reaction was quenched with methanol, warmed to room temperature, and diluted with ethyl acetate (2 mL) and brine (4 mL). The organic layer was separated, dried over $MgSO_4$, concentrated, and chromatographed to afford **23** as a yellow solid.

(±)-(2*S*,3*R*,6*S*)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-(benzyloxycarbonyl)-2,3-dimethyl-6-phenyl-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (23a). R^1M = MeMgBr (3.0 M in ether, 0.080 mL, 0.24 mmol, 1.2 equiv); R^2M = PhMgBr (1.0 M in THF, 0.28 mL, 0.28 mmol, 1.4 equiv). Following the general procedure, **23a** (95 mg, 0.13 mmol, 69%) was obtained after chromatography (10% ethyl acetate in hexanes, 15 × 2 cm). TLC (30% ethyl acetate in hexanes): $R_f = 0.31$; mp > 123 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.52 (d, *J* = 1.6 Hz, 0.5 H), 8.48 (d, *J* = 1.6 Hz, 0.5 H), 7.93 (s, 0.5 H), 7.91 (s, 0.5 H), 7.75−7.64 (m, 5 H), 7.48−7.45 (m, 2 H), 7.41−7.35 (m, 4 H), 7.33−7.28 (m, 3 H), 6.25−6.19 (m, 3 H), 5.81 (d, *J* = 2.4 Hz, 0.5 H), 5.64 (d, *J* = 12.4 Hz, 0.5 H), 5.25 (d, *J* = 12.4 Hz, 0.5 H), 5.24 (s, 1 H), 5.10 (d, *J* = 12.4 Hz, 0.5 H), 4.54 (q, *J* = 6.8 Hz, 0.5 H), 4.49 (q, *J* = 6.8 Hz, 0.5 H), 4.37 (dd, *J* = 7.4, 2.6 Hz, 0.5 H), 4.31 (dd, *J* = 7.2, 2.8 Hz, 0.5 H), 4.27 (d, *J* = 7.2 Hz, 0.5 H), 4.23 (d, *J* = 7.2 Hz, 0.5 H), 1.89 (s, 1.5 H), 1.86 (s, 1.5 H), 1.15 (d, *J* = 6.8 Hz, 1.5 H), 1.07 (d, *J* = 6.8 Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 232.7, 232.1, 227.1, 226.5, 155.0, 154.1, 146.7, 146.1, 146.0, 144.4, 144.0, 139.6, 136.9, 136.7, 136.6, 136.0, 134.3, 128.7, 128.4, 128.3, 128.24, 128.18, 128.13, 128.09, 128.0, 127.74, 127.66, 127.4, 105.6, 105.34, 105.26, 99.1, 98.6, 74.3, 74.0, 67.24, 67.21, 59.7, 59.5, 53.9, 53.3, 52.3, 52.1, 24.2, 22.9, 22.3. IR (CH_2Cl_2, KCl, cm^{-1}): 2484, 1936, 1849, 1688, 1503, 1410, 1305, 1051. Anal. Calcd for $C_{32}H_{32}BMoN_7O_4$: C, 56.08; H, 4.71; N, 14.31. Found: C, 56.17; H, 4.81; N, 14.16.

(±)-(2*S*,3*R*,6*R*)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-(benzyloxycarbonyl)-3,6-dimethyl-2-phenyl-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (23b). R^1M = PhMgBr (1.0 M in THF, 0.24 mL, 0.24 mmol, 1.2 equiv); R^2M = MeMgBr (3.0 M in ether, 0.10 mL, 0.30 mmol, 1.5 equiv). Following the general procedure, **23b** (89 mg, 0.13 mmol, 65%) was obtained after chromatography (10% ethyl acetate in hexanes, 15 × 2 cm). TLC (30% ethyl acetate in hexanes): $R_f = 0.31$; mp > 129 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.52 (s, 0.5 H), 8.50 (s, 0.5 H), 7.83−7.81 (m, 1 H), 7.79 (s, 0.5 H), 7.76 (s, 1.5 H), 7.65 (s, 1 H), 7.62 (s, 1 H), 7.53−7.51 (m, 1 H), 7.48 (s, 1 H), 7.39−7.23 (m, 8 H), 6.27−6.15 (m, 3 H), 5.48 (s, 0.5 H), 5.35 (s, 0.5 H), 5.16 (d, *J* = 12.4 Hz, 0.5 H), 5.10 (s, 1 H), 5.03 (d, *J* = 12.4 Hz, 0.5 H), 4.66 (dq, *J* = 6.4, 1.2 Hz, 0.5 H), 4.57 (dq, *J* = 6.4, 1.2 Hz, 0.5 H), 4.32 (d, *J* = 7.6 Hz, 0.5 H), 4.29−4.28 (m, 1 H), 4.21 (dd, *J* = 7.2, 2.4 Hz, 0.5 H), 1.65 (s, 1.5 H), 1.54 (s, 1.5 H), 1.51 (d, *J* = 6.8 Hz, 1.5 H), 1.42 (d, *J* = 6.4 Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 232.9, 232.4, 227.6, 227.2, 154.5, 154.3, 146.7, 145.9, 141.6, 141.4, 140.1, 140.0, 136.9, 136.6, 136.5, 135.9, 134.3, 129.5, 129.4, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.5, 127.4, 127.3, 105.6, 105.3, 105.2, 91.5, 91.1, 75.4, 75.2, 67.4, 66.9, 65.3, 65.0, 60.3, 59.7, 48.1, 48.0, 25.4, 25.3, 25.2, 25.1. IR (CH_2Cl_2, KCl, cm^{-1}): 2484, 1936, 1849, 1689, 1503, 1410, 1306, 1051. Anal. Calcd for $C_{32}H_{32}BMoN_7O_4$: C, 56.08; H, 4.71; N, 14.31. Found: C, 56.18; H, 4.89; N, 14.04.

(±)-(2*S*,3*R*,6*R*)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-allyl-1-(benzyloxycarbonyl)-3,6-dimethyl-1,2,3,6-tetrahydropyridin-3-y l]molybdenum (23c). R^1M = allylMgBr (1.0 M in THF, 0.24 mL, 0.24 mmol, 1.2 equiv); R^2M = MeMgBr (3.0 M in Et_2O, 0.10 mL, 0.30 mmol, 1.5 equiv). Following the general procedure, **23c** (79 mg, 0.12 mmol, 61%) was obtained after chromatography (10% ethyl acetate in hexanes, 15 × 2 cm). TLC (30% ethyl acetate in hexanes): $R_f = 0.31$; mp = 172−173 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.47 (s, 0.5 H), 8.44 (s, 0.5 H), 7.75 (s, 0.5 H), 7.73 (s, 0.5 H), 7.65 (s, 0.5 H), 7.64 (s, 0.5 H), 7.61 (s, 2 H), 7.45 (s, 1 H), 7.40−7.27 (m, 5 H), 6.23−6.16 (m, 3 H), 6.06−5.99 (m, 0.5 H), 5.81−5.73 (m, 0.5 H), 5.18−4.88 (m, 4 H), 4.60 (dd, *J* = 6.6, 2.2 Hz, 0.5 H), 4.56 (dd, *J* = 7.4, 5.8 Hz, 0.5 H), 4.50 (dd, *J* = 6.4, 2.4 Hz, 0.5 H), 4.46 (dd, *J* = 7.8, 5.6 Hz, 0.5 H), 4.10 (dd, *J* = 7.4, 2.6 Hz, 0.5 H), 4.02 (dd, *J* = 7.4, 2.6 Hz, 0.5 H), 3.89 (d, *J* = 2.0 Hz, 0.5 H), 3.87 (d, *J* = 2.0 Hz, 0.5 H), 2.85−2.73 (m, 0.5 H), 2.41−2.27 (m, 0.5 H), 1.89 (s, 1.5 H), 1.85 (s, 1.5 H), 1.53 (d, *J* = 6.8 Hz, 1.5 H), 1.48 (d, *J* = 6.4 Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 232.6, 231.9, 226.9, 226.4, 154.5, 154.3, 146.6, 145.9, 139.6, 137.1, 136.7, 136.5, 136.3, 135.8, 134.2, 128.3, 128.1, 127.7, 127.6, 127.5, 116.5, 116.3, 105.5, 95.6, 95.2, 72.9, 72.8, 67.1, 66.8, 64.6, 64.3, 56.0, 55.7, 47.4, 47.3, 44.7, 44.6, 26.5, 25.8, 24.75, 24.68. IR (CH_2Cl_2, KCl, cm^{-1}): 2484, 1934, 1848, 1688, 1503, 1410, 1051. Anal. Calcd for $C_{29}H_{32}BMoN_7O_4$: C, 53.64; H, 4.97; N, 15.10. Found: C, 53.89; H, 5.10; N, 15.00.

(±)-(2*S*,3*R*,6*S*)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-(benzyloxycarbonyl)-2-vinyl-3-methyl-6-(3-furyl)-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (23d). R^1M = vinylmagnesium bromide (1.0 M in THF, 0.24 mL, 0.24 mmol, 1.2 equiv); R^2M = 3-furyllithium (0.40 mmol, 2.0 equiv), which was prepared by stirring

3-furyl-tri-*n*-butyltin[26] (157 mg, 0.44 mmol, 2.2 equiv) and *n*-BuLi (1.53 M in hexanes, 0.26 mL, 0.40 mmol, 2.0 equiv) for 20 min at −78 °C. In this case reverse addition was used for the addition of the second nucleophile: the cationic diene solution was added into a solution of 3-furyllithium at −100 °C via cannula. After 1 min the reaction was quenched with methanol (1 mL) at −100 °C. After chromatography (10% ethyl acetate in hexanes, 15 × 2 cm), **23d** was obtained as a yellow solid (113 mg, 0.16 mmol, 82%), mp > 122 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.53 (d, J = 1.6 Hz, 0.5 H), 8.50 (d, J = 1.6 Hz, 0.5 H), 7.78 (d, J = 1.2 Hz, 0.5 H), 7.77 (d, J = 1.6 Hz, 0.5 H), 7.74 (s, 0.5 H), 7.71−7.65 (m, 3 H), 7.58 (s, 0.5 H), 7.49 (s, 1 H), 7.46−7.31 (m, 6 H), 6.67 (d, J = 0.8 Hz, 0.5 H), 6.48 (d, J = 0.8 Hz, 0.5 H), 6.27−6.18 (m, 3 H), 5.59 (d, J = 2.4 Hz, 0.5 H), 5.49 (d, J = 2.4 Hz, 0.5 H), 5.45−5.32 (m, 1.5 H), 5.27−5.06 (m, 3 H), 4.80 (dd, J = 9.8, 1.8 Hz, 0.5 H), 4.77 (d, J = 8.8 Hz, 0.5 H), 4.69 (d, J = 9.6 Hz, 0.5 H), 4.40 (dd, J = 7.2, 2.8 Hz, 0.5 H), 4.34 (dd, J = 7.2, 2.8 Hz, 0.5 H), 4.13 (d, J = 7.2 Hz, 0.5 H), 4.12 (d, J = 7.6 Hz, 0.5 H), 1.84 (s, 1.5 H), 1.79 (s, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 232.1, 231.5, 226.7, 226.1, 154.8, 153.6, 146.6, 146.0, 145.9, 142.8, 142.7, 140.4, 140.2, 139.4, 139.1, 138.6, 136.65, 136.62, 136.5, 136.0, 134.3, 129.8, 129.7, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 118.8, 118.2, 110.9, 110.7, 105.6, 105.25, 105.18, 93.9, 93.3, 73.0, 72.8, 67.2, 60.1, 59.8, 59.5, 59.4, 46.1, 45.8, 24.5, 24.4. IR (CH_2Cl_2, KCl, cm^{-1}): 2484, 1938, 1852, 1691, 1502, 1410, 1305, 1051. Anal. Calcd for $C_{31}H_{30}BMoN_7O_5$: C, 54.17; H, 4.40; N, 14.26. Found: C, 54.20; H, 4.48; N, 14.01.

(±)-(2*S*,3*R*,6*R*)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(*η*-3,4,5)-1-(benzyloxycarbonyl)-2-(3,3-(ethylenedioxy)propyl)-6-methoxy-3-methyl-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (22e) and (±)-(2*S*,3*R*,6*R*)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(*η*-3,4,5)-1-(benzyloxycarbonyl)-2-(3,3-(ethylenedioxy)propyl)-3-methyl-6-*n*-pentyl-1,2,3,6-tetrahydropyridin-3-yl]molybdenum (23e). R^1M = 3,3-(ethylenedioxy)propylmagnesium bromide[27] (0.36 M in THF, 0.83 mL, 0.30 mmol, 1.5 equiv); R^2M = *n*-pentylmagnesium bromide (2.0 M in ether, 0.15 mL, 0.30 mmol, 1.5 equiv). **22e** was prepared by following the general procedure and was dissolved in CH_2Cl_2 (1 mL) and treated with Ph_3CPF_6 (77.6 mg, 0.20 mmol, 1.0 equiv) at −78 °C. After 1 min, the reaction mixture was slowly warmed to 0 °C over 5 min. Then methyl *tert*-butyl ether (MTBE) (8 mL) was added to precipitate the formed cationic diene. The solvents were removed via cannula (covered with a piece of filter paper to prevent removal of the solid). The remaining solid was washed with MTBE (2 × 6 mL) and then briefly dried under vacuum for a few minutes. The reaction mixture was then cooled to −78 °C, dissolved in THF (1 mL), and treated with the second nucleophile (R^2M). After 15 min at −78 °C, the reaction was quenched with methanol, brought to room temperature, and diluted with ethyl acetate (2 mL) and brine (4 mL). The organic layer was separated, dried over $MgSO_4$, concentrated, and chromatographed (10% ethyl acetate in hexanes, 15 × 2 cm) to give **23e** as a yellow solid (130 mg, 0.17 mmol, 85%).

Data for 22e: TLC (50% ethyl acetate in hexanes) R_f = 0.26; mp = 142−145 °C with decomposition (Et_2O/hexanes); ^{1}H NMR ((CD_3)$_2$CO, 400 MHz) δ 8.42 (s, 1 H), 7.95 (s, 0.5 H), 7.91 (d, J = 1.6 Hz, 1.5 H), 7.81 (d, J = 1.6 Hz, 1 H), 7.79 (s, 1 H), 7.68 (s, 1 H), 7.46−7.31 (m, 5 H), 6.30−6.26 (m, 3 H), 5.63 (d, J = 2.4 Hz, 0.5 H), 5.52 (d, J = 2.8 Hz, 0.5 H), 5.17 (d, J = 12.4 Hz, 0.5 H), 5.16 (d, J = 12.4 Hz, 0.5 H), 5.07 (d, J = 12.4 Hz, 0.5 H), 4.96 (d, J = 12.4 Hz, 0.5 H), 4.82 (t, J = 4.6 Hz, 0.5 H), 4.78−4.74 (m, 0.5 H), 4.45 (td, J = 7.8, 3.6 Hz, 0.5 H), 4.32 (dd, J = 7.2, 2.8 Hz, 0.5 H), 4.28 (dd, J = 7.2, 2.8 Hz, 0.5 H), 4.06 (d, J = 7.2 Hz, 0.5 H), 4.02 (d, J = 7.2 Hz, 0.5 H), 3.92−3.84 (m, 2 H), 3.80−3.73 (m, 2 H), 3.39 (s, 1.5 H), 3.30 (s, 1.5 H), 2.16−2.08 (m, 1 H), 1.99−1.68 (m, 2 H), 1.94 (s, 1.5 H), 1.85 (s, 1.5 H), 1.61−1.56 (m, 0.5 H), 1.44−1.40 (m, 0.5 H); ^{13}C NMR ((CD_3)CO, 100 MHz) δ 234.1, 233.7, 227.8, 227.7, 156.3, 155.1, 147.5, 147.3, 141.7, 141.5, 138.0, 137.9, 137.7, 137.2, 135.9, 129.23, 129.19, 129.1, 128.8, 128.7, 106.7, 106.4, 105.2, 105.04, 104.98, 100.2, 99.1, 85.6, 85.3, 76.3, 75.8, 67.9, 67.7, 66.2, 65.42, 65.36, 59.7, 58.9, 56.9, 56.65, 56.57, 56.3, 34.7, 32.4, 32.0, 31.8, 31.7, 30.8, 24.8, 24.7; IR (CH_2Cl_2, KCl, cm^{-1}) 2951, 2886, 2484, 1939, 1852, 1697, 1506, 1410, 1305, 1051. Anal. Calcd for $C_{31}H_{36}BMoN_7O_7$: C, 51.33; H, 5.00; N, 13.52. Found: C, 51.25; H, 5.08; N, 13.41.

Data for 23e: TLC (30% ethyl acetate in hexanes) R_f = 0.19; mp = 93−95 °C with decomposition (ether/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (s, 0.5 H), 8.44 (s, 0.5 H), 7.75 (s, 0.5 H), 7.74 (s, 0.5 H), 7.64−7.61 (m, 3 H), 7.46 (d, J = 1.2 Hz, 1 H), 7.42−7.29 (m, 5 H), 6.24 (s, 1 H), 6.22 (s, 1 H), 6.16 (s, 1 H), 5.16−5.03 (m, 2 H), 4.91 (t, J = 4.6 Hz, 0.5 H), 4.75 (t, J = 4.6 Hz, 0.5 H), 4.52−4.47 (m, 1 H), 4.41−4.34 (m, 1 H), 4.22 (dd, J = 7.6, 2.4 Hz, 0.5 H), 4.12 (dd, J = 7.6, 2.4 Hz, 0.5 H), 3.97−3.75 (m, 5 H), 2.28−2.13 (m, 1 H), 1.92 (s, 1.5 H), 1.87 (s, 1.5 H), 2.05−1.46 (m, 6.5 H), 1.41−1.25 (m, 4.5 H), 0.93 (t, J = 7.2 Hz, 1.5 H), 0.84 (t, J = 7.2 Hz, 1.5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 232.3, 231.6, 227.4, 226.8, 155.1, 154.9, 146.6, 145.8, 139.6, 136.9, 136.6, 136.5, 135.8, 134.2, 128.6, 128.2, 128.1, 128.0, 127.7, 127.5, 105.5, 105.24, 105.16, 104.4, 104.1, 95.9, 95.4, 73.2, 73.0, 67.3, 67.0, 64.8, 64.7, 64.6, 63.04, 62.98, 55.6, 55.3, 51.82, 51.76, 40.8, 40.6, 33.7, 32.3, 32.00, 31.95, 31.6, 30.2, 27.2, 27.1, 24.6, 24.5, 22.6, 22.5, 14.1, 14.0; IR (CH_2Cl_2, KCl, cm^{-1}) 2957, 2484, 1934, 1848, 1688, 1409, 1305, 1124, 1051. Anal. Calcd for $C_{35}H_{44}BMoN_7O_6$: C, 54.91; H, 5.79; N, 12.81. Found: C, 54.70; H, 5.84; N, 12.81.

(+)-(2*S*,3*R*,6*R*)- and (±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(*η*-3,4,5)-1-(benzyloxycarbonyl)-2-(3-benzyloxypropyl)-3-methyl-6-*n*-pentyl-1,2,3, 6-tetrahydropyridin-3-yl]molybdenum (23f). R_1M = (3-(benzyloxy)propyl)magnesium bromide (0.40 M in THF, 0.75 mL, 0.30 mmol, 1.5 equiv);[28] R_2M = *n*-pentylmagnesium bromide (2.0 M in ether, 0.15 mL, 0.30 mmol, 1.5 equiv). Following the general procedure starting from (+)-**9**, (+)-**23f** (111 mg, 0.13 mmol, 67%, >99% ee) was obtained after chromatography (10% ethyl acetate in hexanes, 15 × 2 cm), $[\alpha]_D$ +136.0 (c = 0.5, CH_2Cl_2). (±)-**23f** was prepared in the same manner starting from (±)-**9**. TLC (30% ethyl acetate in hexane): R_f = 0.60; mp = 88−90 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.49 (s, 0.5 H), 8.45 (s, 0.5 H), 7.74 (d, J = 4.8 Hz, 1 H), 7.62 (s, 3 H), 7.46 (s, 1 H), 7.42−7.20 (m, 10 H), 6.22 (d, J = 12.4 Hz, 2 H), 6.17 (s, 1 H), 5.14 (t, J = 13.0 Hz, 1.2 H), 5.04 (t, J = 13.0 Hz, 0.8 H), 4.58−4.45 (m, 2 H), 4.45−4.32 (m, 2 H), 4.22 (dd, J = 7.3, 2.2 Hz, 0.5 H), 4.13 (dd, J = 7.3, 2.2 Hz, 0.5 H), 3.88 (d, J = 6.3 Hz, 1 H), 3.62−3.46 (m, 1 H), 3.44−3.28 (m, 1 H), 2.28−2.10 (m, 1 H), 1.92 (s, 1.5 H), 1.87 (s, 1.5 H), 2.00−1.14 (m, 11 H), 0.93 (t, J = 6.8 Hz, 1.5 H), 0.84 (t, J = 6.8 Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 232.4, 231.7, 227.6, 226.9, 155.2, 155.0, 146.6, 145.9, 145.8, 139.7, 138.8, 138.6, 137.0, 136.7, 136.5, 135.8, 134.2, 105.5, 105.3, 105.2, 96.5, 95.9, 73.1, 73.0, 72.52, 72.46, 70.4, 70.1, 67.2, 67.0, 63.0, 62.9, 55.8, 55.6, 51.9, 51.8, 40.9, 40.7, 36.7, 36.5, 32.0, 31.7, 28.1, 28.0, 27.22, 27.16, 24.64, 24.55, 22.6, 22.5, 14.1, 14.0. IR (CH_2Cl_2, KCl, cm^{-1}): 3054, 1933, 1847, 1418, 1269, 1265, 1259. Anal. Calcd for $C_{40}H_{48}BMoN_7O_5$: C, 59.05; H, 5.95; N, 12.05. Found: C, 58.75; H, 5.90; N, 11.85.

Demetalation of (Dihydropyridinyl)molybdenum Complexes.

(±)-(2*R*,3*S*,6*S*)-1-(Benzyloxycarbonyl)-2-(3,3-(ethylenedioxy)propyl)-3-methyl-6-*n*-pentyl-1,2,3,6-tetrahydropyridine (24). To a solution of **23e** (0.20 g, 0.26 mmol, 1.0 equiv) in DME (2 mL) at −15 °C was added $NOPF_6$ (136 mg, 0.78 mmol, 3.0 equiv) as a solid in one portion. The reaction was slowly warmed to 0 °C over 30 min, and a solution of $NaCNBH_3$ in THF (1.0 M, 1.30 mL, 1.30 mmol, 5.0 equiv) was added. The mixture was stirred at room temperature for 1 h. Then ethyl acetate (10 mL) and water (10 mL) were added. The

(26) Pinhey, J. T.; Roche, E. G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2415.

(27) To a suspension of Mg turnings (486 mg, 20 mmol, 2.0 equiv; ground to generate fresh surface) in THF (20 mL) was added 2-(2-bromoethyl)-1,3-dioxolane (1.17 mL, 1.81 g, 10 mmol, 1.0 equiv) via syringe at room temperature over 5 min. After 4 h the Grignard reagent was transferred to a Sure-Seal bottle and stored in a refrigerator. The concentration was measured to be ca. 0.36 M by titration of an aqueous solution of the quenched Grignard reagent with 0.10 M HCl solution.

(28) To a suspension of Mg turnings (0.486 g, 20 mmol, 2.0 equiv; ground to generate a fresh surface) in THF (20 mL) was added benzyl 3-bromopropyl ether (1.77 mL, 2.29 g, 10 mmol, 1.0 equiv) via syringe at room temperature over 5 min. After 2 h at room temperature, the Grignard reagent was transferred to a Sure-Seal bottle and stored in a refrigerator. The concentration was measured to be ca. 0.40 M by titration of an aqueous solution of the quenched Grignard reagent with 0.10 M HCl solution.

aqueous layer was washed with ethyl acetate (2 × 5 mL). The combined organic layers were washed with water (15 mL) and brine (15 mL), dried over $MgSO_4$, and evaporated. The residue was purified by chromatography (10% diethyl ether in hexanes, 2 × 10 cm) to afford **24** (73 mg, 0.18 mmol, 70%) as a colorless oil. TLC (30% ethyl acetate in hexanes): $R_f = 0.58$. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35−7.28 (m, 5 H), 5.77−5.65 (m, 1.5 H), 5.61 (d, $J = 4.7$ Hz, 0.3 H), 5.58 (d, $J = 4.7$ Hz, 0.2 H), 5.24−5.04 (m, 2 H), 4.88 (t, $J = 4.4$ Hz, 0.5 H), 4.81 (t, $J = 4.4$ Hz, 0.5 H), 4.37−4.28 (m, 0.5 H), 4.28−4.17 (m, 1 H), 4.17−4.08 (m, 0.5 H), 3.99−3.88 (m, 2 H), 3.88−3.70 (m, 2 H), 2.17 (pent, $J = 7.0$ Hz, 0.5 H), 2.11 (pent, $J = 7.0$ Hz, 0.5 H), 1.80−1.16 (m, 12 H), 0.98 (d, $J = 7.2$ Hz, 1.5 H), 0.94 (d, $J = 7.2$ Hz, 1.5 H), 0.88 (t, $J = 6.8$ Hz, 1.5 H), 0.83 (t, $J = 6.8$ Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.6, 156.1, 137.0, 136.9, 128.4, 128.0, 127.8, 127.7, 127.5, 125.0, 124.4, 104.3, 104.2, 67.1, 66.9, 64.8, 55.1, 54.6, 52.1, 51.9, 36.6, 35.7, 34.1, 33.8, 31.7, 31.6, 31.1, 30.9, 29.7, 28.9, 26.5, 22.6, 22.5, 19.9, 14.0. IR (CH_2Cl_2, KCl, cm^{-1}): 3036, 2959, 2929, 2868, 1686, 1450, 1416, 1305, 1095. HRMS (FAB): calcd for $C_{24}H_{35}O_4NLi$ (M + Li^+), 408.2726; found, 408.2716.

(−)-(2*S*,3*R*,6*R*)- and (±)1-(Benzyloxycarbonyl)-2-(3-benzyloxypropyl)-3-methyl-6-*n*-pentyl-1,2,3,6-tetrahydropyridine (25). To a solution of (+)-**23f** (146 mg, 0.18 mmol, 1.0 equiv, >99% ee) in DME (2 mL) at −15 °C was added $NOPF_6$ (94.6 mg, 0.54 mmol, 3.0 equiv) as a solid in one portion. The reaction was slowly warmed to 0 °C over 30 min, and a solution of $NaCNBH_3$ in THF (1.0 M, 0.90 mL, 0.90 mmol, 5.0 equiv) was added. The mixture was stirred at room temperature for 1 h, and then it was diluted with EtOAc (10 mL) and H_2O (10 mL). The aqueous layer was washed with EtOAc (2 × 5 mL). The combined organic layer was washed with H_2O (15 mL) and brine (15 mL) and dried over $MgSO_4$. After concentration, the residue was purified by chromatography (5% ethyl acetate in hexanes, 2 × 10 cm) to afford (−)-**25** as a colorless oil (47.7 mg, 0.11 mmol, 59%, >99% ee), $[\alpha]_D$ −109.4 ($c = 2.7$, CH_2Cl_2). (±)-**25** was prepared in the same manner starting from (±)-**23f**. TLC (30% ethyl acetate in hexanes): $R_f = 0.73$. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.44−7.22 (m, 10 H), 5.78−5.64 (m, 1.5 H), 5.62 (d, $J = 4.7$ Hz, 0.3 H), 5.58 (d, $J = 4.7$ Hz, 0.2 H), 5.22−5.04 (m, 2 H), 4.49 (s, 1 H), 4.43 (s, 1 H), 4.32 (t, $J = 7.0$ Hz, 0.5 H), 4.23 (t, $J = 7.0$ Hz, 1 H), 4.11 (t, $J = 7.0$ Hz, 0.5 H), 3.49 (q, $J = 6.8$ Hz, 1 H), 3.42 (q, $J = 6.8$ Hz, 1 H), 2.20−2.05 (m, 1 H), 1.80−1.16 (m, 12 H), 0.97 (d, $J = 7.2$ Hz, 1.5 H), 0.94 (d, $J = 7.2$ Hz, 1.5 H), 0.88 (t, $J = 6.8$ Hz, 1.5 H), 0.84 (t, $J = 6.8$ Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.6, 156.1, 138.6, 138.5, 137.0, 136.9, 128.4, 128.3, 128.0, 127.8, 127.7, 127.7, 127.5, 127.4, 124.9, 124.4, 72.74, 72.70, 70.1, 69.9, 67.0, 66.8, 55.0, 54.6, 52.1, 51.8, 36.6, 35.7, 34.0, 33.7, 31.8, 31.6, 31.4, 31.2, 29.7, 27.0, 26.9, 26.8, 26.5, 22.6, 22.5, 19.9, 14.1, 14.0. IR (CH_2Cl_2, KCl, cm^{-1}): 3032, 2955, 2924, 2858, 1685, 1455, 1414, 1347, 1306, 1096. Anal. Calcd for $C_{29}H_{39}NO_3$: C, 77.47; H, 8.74; N, 3.12. Found: C, 77.48; H, 8.82; N, 3.16.

(±)-(2*R*,3*R*,6*S*)-1-(Benzoxycarbonyl)-2-(3-benzyloxypropyl)-3-methyl-6-*n*-pentyl-1,2,3,6-tetrahydropyridine (26) and (±)-(2*R*,6*S*)-1-(Benzoxycarbonyl)-2-(3-benzyloxypropyl)-3-methyl-6-*n*-pentyl-1, 2,5,6-tetrahydropyridine (27).

Protodemetalation in CH_2Cl_2. To a solution of **23f** (104 mg, 0.13 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL) at room temperature was added HCl (37 wt % in H_2O, 0.32 mL, 3.8 mmol, 30 equiv) over 2 min. After 20 min, the mixture was cooled to 0 °C and Et_3N (0.89 mL, 6.39 mmol, 50 equiv) was added. It was diluted with EtOAc (20 mL) and H_2O (20 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$, and evaporated. The residue was purified by chromatography (5% EtOAc in hexanes, 1.5 × 12 cm) to afford an inseparable mixture of **27**/**26** (ratio of **27**/**26** = 15/1) as a colorless oil (40.0 mg, 0.09 mmol, 70%).

Protodemetalation in CH_3CN. To a solution of **23f** (117 mg, 0.14 mmol, 1.0 equiv) in CH_3CN (2 mL) at 60 °C was added HCl in CH_3CN (2.28 M, 1.56 mL, 4.33 mmol, 30 equiv)[29] over 2 min. After 2 h, the reaction was cooled to 0 °C, and Et_3N (1.0 mL, 7.22 mmol, 50 equiv) was added. The reaction mixture was diluted with EtOAc (20 mL) and H_2O (20 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$, and evaporated. The residue was purified by chromatography (5% EtOAc in hexanes, 1.5 × 12 cm) to afford an inseparable mixture of **26**/**27** (ratio of **26**/**27** = 34/1) as a colorless oil (36.3 mg, 0.08 mmol, 56%).

Photolytic Protodemetalation. Complex **23f** (82.2 mg, 0.10 mmol, 1.0 equiv), HOAc (11.6 μL, 0.20 mmol, 2.0 equiv), and CH_3CN (10 mL) were placed in a high-pressure-proof tube under nitrogen and subject to UV irradiation (350 nm) for 24 h. The crude mixture was concentrated, and the residue was purified by chromatography (5% EtOAc in hexanes, 1.5 × 12 cm) to afford **27** (28.9 mg, 0.06 mmol, 64%) as a colorless oil.

Data for 26: TLC (30% ethyl acetate in hexanes) $R_f = 0.73$; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.23 (m, 10 H), 5.74−5.68 (s, 0.5 H), 5.68−5.56 (s, 0.5 H), 5.49−5.39 (s, 1 H), 5.20−5.10 (s, 2 H), 4.52−4.16 (m, 4 H), 3.53−3.33 (m, 2 H), 2.61−2.46 (s, 1 H), 1.81−1.10 (m, 12 H), 0.99 (d, $J = 7.0$ Hz, 1.5 H), 0.97 (d, $J = 7.0$ Hz, 1.5 H), 0.88 (t, $J = 7.0$ Hz, 1.5 H), 0.83 (t, $J = 7.0$ Hz, 1.5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.0, 138.7, 136.8, 128.6, 128.4, 128.3, 128.0, 127.9, 127.5, 127.4, 125.7, 125.2, 72.7, 70.2, 70.1, 67.1, 66.9, 53.2, 52.7, 52.4, 52.1, 36.2, 35.5, 33.0, 32.7, 31.8, 31.6, 29.7, 26.6, 26.1, 23.6, 23.4, 22.6, 17.5, 14.0; IR (CH_2Cl_2, KCl, cm^{-1}) 3048, 2960, 2925, 2853, 2361, 2336, 1692, 1450, 1414, 1260, 1255. Anal. Calcd for $C_{29}H_{39}NO_3$: C, 77.47; H, 8.74; N, 3.12. Found: C, 77.58; H, 8.86; N, 3.24.

Data for 27: TLC (30% ethyl acetate in hexanes) $R_f = 0.73$; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.23 (m, 10 H), 5.41−5.33 (s, 1 H), 5.15−5.10 (s, 2 H), 4.60−4.15 (m, 4 H) 3.65−3.23 (m, 2 H), 2.40−2.22 (br m, 1 H), 1.71 (s, 3 H), 1.98−1.14 (m, 13 H), 0.86 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.1, 138.7, 128.4, 128.3, 127.9, 127.5, 127.4, 118.2, 117.8, 72.7, 70.2, 67.1, 55.0, 48.8, 34.6, 31.7, 31.4, 29.7, 27.6, 26.8, 22.6, 21.5, 14.1; IR (CH_2Cl_2, KCl, cm^{-1}) 3052, 2955, 2924, 2858, 1685, 1454, 1419. Anal. Calcd for $C_{29}H_{39}NO_3$: C, 77.47; H, 8.74; N, 3.12. Found: C, 77.64; H, 8.93; N, 3.13.

(±)-(2*R*,6*S*)-1-(Benzoxycarbonyl)-2-(3,3-ethylenedioxypropyl)-3-methyl-6-*n*-pentyl-1,2,5,6-tetrahydropyridine (28) and (±)-(2*R*,3*R*,-6*S*)-1-(Benzoxycarbonyl)-2-(3,3-(ethylenedioxy)propyl)-3-methyl-6-*n*-pentyl-1,2,3,6-tetrahydropyridine (28′). Complex **23e** (76.5 mg, 0.10 mmol, 1.0 equiv), HOAc (57.2 μL, 1.00 mmol, 10 equiv), and CH_3CN (10 mL) were placed in a high-pressure-proof tube under nitrogen and subjected to UV irradiation (350 nm) for 24 h. The crude mixture was then concentrated, and the residue was purified by chromatography (10% Et_2O in hexanes, 1.5 × 12 cm) to afford an inseparable mixture of **28**/**28′** (ratio of **28**/**28′** = 19/1) (24.5 mg, 0.06 **m**mol, 61%) as a colorless oil. TLC (30% ethyl acetate in hexane): $R_f = 0.58$. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.40−7.27 (br m, 5 H), 5.42−5.35 (br m, 1 H), 5.18−5.07 (m, 2 H), 4.92−4.72 (m, 1 H), 4.56−4.16 (br m, 2 H), 4.00−3.88 (br s, 2 H), 2.40−2.22 (br m, 1 H), 2.00−1.76 (m, 3 H), 1.72 (s, 3 H), 1.68−1.16 (m, 10 H), 0.86 (t, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.1, 1376.9, 128.4, 128.0, 127.9, 125.7, 118.4, 104.4, 67.1, 64.83, 64.79, 54.9, 48.8, 34.6, 31.7, 29.7, 28.8, 22.6, 21.5, 14.1. IR (CH_2Cl_2, KCl, cm^{-1}): 3053, 2981, 2950, 2930, 2300, 1685, 1414, 1265. Anal. Calcd for $C_{24}H_{35}NO_4$: C, 71.79; H, 8.79; N, 3.49. Found: C, 71.99; H, 8.97; N, 3.39. The minor isomer, **28′**, was not separated but was assigned on the basis of representative peaks in the ^{1}H NMR spectrum: 5.74−5.66 (m, 0.5 H, olefinic hydrogen), 5.66−5.58 (m, 0.5 H, olefinic hydrogen), 5.50−5.38 (m, 1 H, olefinic hydrogen), 2.60−2.50 (m, 1 H, allylic hydrogen).

Synthesis of cis-2,3,6-Trimethylpiperidine (34).

(±)-(2*S*,3*R*,6*R*)-Dicarbonyl[hydrotris(1-pyrazolyl)borato][(η-3,4,5)-1-(benzyloxycarbonyl)-1,2,3,6-tetrahydropyridin-2,3,6-trimethyl-3-yl]molybdenum (32). To a solution of (±)-**21** (246 mg, 0.41 mmol, 1.0 equiv) in THF (2 mL) at −78 °C was added bromine (23.5 μL, 0.45 mmol, 1.1 equiv). After 15 min, 0.346 mL of MeMgBr (3.0 M in diethyl ether, 1.03 mmol, 2.5 equiv) was added, and the mixture was stirred at −50 °C for another 5 min. The reaction mixture was passed through a pad of silica gel (3 × 2 cm) with Et_2O and concentrated to give (±)-**32** (227 mg, 88%) as a yellow solid. TLC (30% ethyl acetate in hexanes): $R_f = 0.42$; mp = 138−141 °C with decomposition (Et_2O/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46

(29) HCl gas was bubbled for 30 min through degassed and dried CH_3CN (200 mL) in a three-neck flask. The obtained solution was then sealed with rubber septum and stored in the dark. The concentration was measured to be ca. 2.78 M by titration of this solution with 0.100 M NaOH aqueous solution.

(s, 0.5 H), 8.44 (s, 0.5 H), 7.73 (d, J = 1.8 Hz, 1 H), 7.68−7.58 (m, 3 H), 7.45 (s, 1 H), 7.42−7.27 (m, 5 H), 6.27−6.13 (m, 3 H), 5.24−5.04 (m, 2 H), 4.57 (qd, J = 6.6, 2.2 Hz, 0.5 H), 4.49 (qd, J = 6.6, 2.2 Hz, 0.5 H), 4.46−4.37 (m, 1 H), 4.11 (dd, J = 7.3, 2.2 Hz, 0.5 H), 4.04 (dd, J = 7.3, 2.2 Hz, 0.5 H), 3.87 (dd, J = 7.3, 2.5 Hz, 1 H), 1.87 (s, 1.5 H), 1.83 (s, 1.5 H), 1.51 (d, J = 6.6 Hz, 1.5 H), 1.48 (d, J = 6.6 Hz, 1.5 H), 1.47 (d, J = 6.7 Hz, 1.5 H), 1.44 (d, J = 6.7 Hz, 1.5 H). ^{13}C NMR ($CDCl_3$, 100 Mz): δ 232.9, 232.2, 227.0, 226.4, 154.3, 153.9, 146.7, 146.0, 145.9, 139.6, 137.13, 137.07, 136.5, 135.9, 134.2, 128.3, 128.0, 127.7, 127.66, 127.58, 105.55, 105.49, 105.3, 105.2, 97.4, 96.9, 72.8, 72.6, 67.0, 66.8, 63.6, 63.4, 51.8, 51.7, 47.5, 47.4, 26.5, 26.0, 24.7, 24.0. IR (CH_2Cl_2, KCl, cm^{-1}): 3053, 2985, 2484, 1929, 1842, 1683, 1505, 1414, 1305, 1046. HRMS (FAB): calcd for $C_{27}H_{30}N_7O_4$-BMo (M^+), 622.2511; found, 622.2511.

(±)-(2*R*,3*R*,6*S*)-1-(Benzyloxycarbonyl)-1,2,3,6-tetrahydro-2,3,6-trimethylpyridine (33) and (±)-(2*R*,6*S*)-1-(Benzyloxycarbonyl)-1,2,5,6-tetrahydro-2,3,6-trimethylpyridine (33′). To a solution of **32** (168 mg, 0.27 mmol, 1.0 equiv) in CH_3CN (2 mL) was added the freshly prepared solution of HCl in CH_3CN (2.78 M, 2.9 mL, 8.09 mmol, 30 equiv).[29] The solution was stirred at 50 °C for 1 h and cooled to 0 °C, and Et_3N (1.9 mL, 13.5 mmol, 50 equiv) was added. The reaction mixture was diluted with EtOAc (20 mL) and H_2O (20 mL). The aqueous layer was washed with EtOAc (2 × 15 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, and concentrated. The residue was purified by chromatography (3% ethyl acetate in hexanes, 1.5 × 12 cm) to afford an inseparable mixture of **33** and **33′** (ratio of **33**/**33′** = 23/1) as a colorless oil (41 mg, 0.16 mmol, 59%). TLC (30% ethyl acetate in hexanes): R_f = 0.76. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42−7.20 (m, 5 H), 5.62−5.46 (s, 1 H), 5.42 (d, J = 5.1 Hz, 1 H), 5.17 (s, 2 H), 4.70−4.20 (m, 2 H), 2.60−2.42 (s, 1 H), 1.28 (d, J = 7.0 Hz, 3 H), 1.04 (d, J = 7.0 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.0, 137.0, 128.4, 128.2, 127.8, 127.7, 66.8, 48.3, 47.5, 32.3, 21.5, 20.8, 17.4, 15.0. IR (CH_2Cl_2, KCl, cm^{-1}): 1685, 1414, 1322, 1107. Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.09; H, 8.22; N, 5.40. The minor isomer, **33′**, not separated, was assigned on the basis of representative peaks in the ^{1}H NMR spectrum: 2.42−2.30 (m, 1 H, allylic hydrogen), 1.73−1.68 (s, 3 H, methyl), 1.30 (d, J = 6.8 Hz, 3 H, methyl), 1.19 (d, J = 6.8 Hz, 3 H, methyl).

(±)-(2*R*,3*R*,6*S*)-2,3,6-Trimethylpiperidine (34). To a solution of **33** (10.2 mg, 0.04 mmol, 1.0 equiv) in HCOOMe (4 mL) at room temperature was added Pd (10 wt % on activated carbon, 0.01 mmol, 0.2 equiv). After being stirred under H_2 (1 atm) for 7 h, the reaction mixture was passed through a pad of Celite and concentrated at 0 °C to afford **34** (4.8 mg, 0.04 mmol, 96%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.03 (oct, J = 3.3 Hz, 1 H), 2.88−2.76 (m, 1 H), 1.79−1.70 (m, 1 H), 1.69−1.58 (m, 2 H), 1.52−1.36 (m, 2 H), 1.18 (d, J = 6.4 Hz, 3 H), 1.12 (d, J = 6.7 Hz, 3 H), 0.97 (d, J = 7.3 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 54.7, 53.1, 31.2, 31.0, 26.9, 20.9, 18.4, 11.2.

The *N,N*-dimethylammonium iodide was prepared, mp = 270−272 °C (lit.[19b] mp 271−273 °C).

Synthesis of (−)-Indolizidine 209B.

(−)-(2*S*,3*R*,6*R*)- and (±)-2-(3-Hydroxypropyl)-3-methyl-6-*n*-pentylpiperidine (35). To a solution of (−)-**25** (65.0 mg, 0.1447 mmol, 1.0 equiv) in ethanol (5 mL) was added Pd/C (10 wt %, 46.2 mg, 0.0434 mmol, 0.3 equiv), and the mixture was stirred at room temperature under H_2 (1 atm) for 24 h. The reaction mixture was passed through a pad of Celite, and the filtrate was concentrated to give (−)-**35** as a colorless oil (29.4 mg, 0.126 mmol, 87%), $[\alpha]_D$ −44.1 (c = 1.4, MeOH). (±)-**35** was prepared in the same manner starting from (±)-**25**. TLC (50% ethyl acetate in hexanes): R_f = 0.01. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.64−3.48 (m, 2 H), 2.57−2.42 (m, 1 H), 2.22 (ddd, J = 9.4, 6.3, 2.4 Hz, 1 H), 1.86−1.48 (m, 6 H), 1.46−1.18 (m, 10 H), 1.14−1.02 (m, 2 H), 0.87 (t, J = 6.7 Hz, 3 H), 0.85 (d, J = 6.3 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 62.9, 62.2, 56.7, 36.9, 34.6, 33.9, 33.3, 32.6, 31.9, 29.3, 25.6, 22.5, 18.5, 14.0. IR (CH_2Cl_2, KCl, cm^{-1}): 2960, 2924, 2852, 1270. HRMS (FAB): calcd for $C_{14}H_{30}NO$ (M + H^+), 228.2327; found, 228.2329.

(−)- and (±)-Indolizidine 209B (13). To a solution of crude (−)-**35** in CH_2Cl_2 (0.5 mL) at 0 °C in a Schlenk flask were added Ph_3P (48 mg, 0.18 mmol, 1.5 equiv) and CBr_4 (49 mg, 0.14 mmol, 1.2 equiv). After 30 min, Et_3N (0.3 mL) was added. The mixture was stirred at 0 °C for 10 min and warmed to room temperature. The solvent was removed by evaporation, and the resulting oily mixture was extracted with petroleum ether (4 × 10 mL). The extract was concentrated and purified by chromatography (basic alumina, 1% ethyl acetate in hexanes, 7 × 0.4 cm) to afford (−)-**13** as a colorless oil (12.4 mg, 0.06 mmol, 63%). $[\alpha]_D$ −89.7 (c = 0.31, MeOH); lit.[5a] $[\alpha]_D$ −87.7 (c = 0.6, MeOH). (±)-**13** was prepared in the same manner starting from (±)-**35**. TLC (30% ethyl acetate in hexanes, R_f = 0.20). IR (CH_2Cl_2, KCl, cm-^{1}): 2966, 2925, 2863, 2776, 1460, 1373, 1096, 1004, 805. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.26 (dt, J = 8.8 Hz, 2.4 Hz, 1 H), 2.00−1.17 (m, 19 H), 1.00−0.91 (m, 1 H), 0.88 (t, J = 7.2 Hz, 3 H), 0.86 (d, J = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 71.3, 63.5, 51.9, 36.6, 34.6, 33.7, 32.3, 31.3, 29.1, 25.5, 22.6, 20.3, 18.9, 14.1. HRMS (EI): calcd for $C_{14}H_{27}N$ (M^+), 209.2144; found, 209.2142.

Synthesis of 36 for Structural Comparison to 5a.

(±)-(2*R*,6*S*)-Dicarbonyl[hydrotris(1-pyrazolyl)borato][η-(3,4,5)-2,6-dimethoxy-2,3-dihydropyran-3-yl]molybdenum (36). To a solution of (2*S*,3*R*)-dicarbonyl[hydridotris(1-pyrazolyl)borato][η-(3,4,5)-2,3-dihydropyran-2-ethoxy-3-yl]molybdenum (**37**)[30] (0.49 g, 0.99 mmol, 1.0 equiv) in CH_2Cl_2 (8 mL) was added Ph_3CPF_6 (406 mg, 1.04 mmol, 1.05 equiv) in one portion at 0 °C. After 10 min, Et_2O (15 mL) was added to precipitate the diene cation. The solvent was filtrated, and the remaining orange solid was washed with Et_2O (2 × 10 mL) and then dried under vacuum. The resulting diene cation was redissolved in CH_2Cl_2 (8 mL) and treated with Et_3N (0.275 mL, 2.0 mmol, 2.0 equiv) at room temperature. After 5 min, the solution was concentrated and passed through a pad of silica gel (2 × 3 cm) using Et_2O as eluent, to afford a yellow solid. The yellow solid was then dissolved in THF (2 mL) and treated with bromine (0.056 mL, 1.1 mmol, 1.1 equiv) at −78 °C. The mixture was stirred at −78 °C for 15 min and then treated with a 25 wt % solution of NaOMe in MeOH, (4.375 M, 0.57 mL, 2.5 equiv). After 5 min at −78 °C, the reaction mixture was warmed to 0 °C and passed through a pad of neutralized silica gel (2 × 3 cm) using Et_2O as eluent to afford **36** (478 mg, 0.94 mmol, 94%) as a yellow solid. TLC (30% ethyl acetate in hexanes) R_f = 0.25; mp > 200 °C with decomposition (Et_2O/hexanes). ^{1}H NMR (($CD_3)_2CO$, 400 MHz): δ 8.61 (d, J = 2.2 Hz, 1 H), 8.06 (d, J = 1.9 Hz, 2 H), 7.79 (d, J = 1.9 Hz, 3 H), 6.44 (t, J = 2.2 Hz, 1 H), 6.27 (t, J = 2.2 Hz, 2 H), 4.65 (s, 2 H), 4.30 (d, J = 7.2 Hz, 2 H), 3.90 (t, J = 7.2 Hz, 1 H), 3.41 (s, 6 H). ^{13}C NMR (($CD_3)_2CO$, 100 MHz): δ 227.1, 147.9, 143.4, 137.5, 136.0, 107.3, 106.6, 98.6, 66.8, 66.2, 56.3. IR (CH_2Cl_2, KCl, cm^{-1}): 2930, 1941, 1865, 1834, 1813. Anal. Calcd for $C_{18}H_{21}BMoN_6O_5$: C, 42.55; H, 4.17; N, 16.54. Found: C, 42.59; H, 4.19; N, 16.56.

Acknowledgment. This work was supported by Grant No. GM43107, awarded by the National Institute of General Medical Sciences, DHHS. We thank our colleagues Drs. Kenneth Hardcastle and Karl Hagen for their skilled and efficient assistance with X-ray crystallography. A.A. thanks NATO for a postdoctoral fellowship.

Supporting Information Available: Complete X-ray crystallographic information for compounds **5a** and **36** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA011635G

(30) Ward, Y. D.; Villanueva, L. A.; Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 897−898. The synthesis and characterization data of complex **37** were included in the Supporting Information.