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Molybdenum-Promoted Synthesis of Isoquinuclidines with Bridgehead CF_3 Groups

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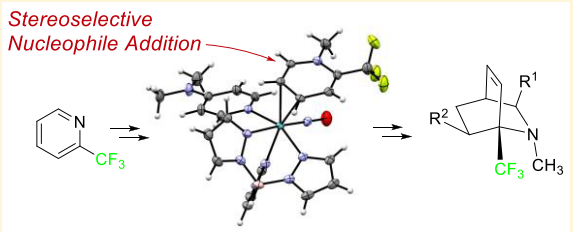
Supporting Information

ABSTRACT: The preparation of the complex MoTp(NO)(DMAP)(4,5-η^2-(2-trifluoromethyl)pyridine) (DMAP = 4-(dimethylamino)pyridine; Tp = tris(pyrazolyl)borate) is described. The CF_3 substituent is found to preclude κ-N coordination, allowing for direct coordination without protection of the nitrogen. The dihapto-coordinate complex can be isolated as a single diastereomer, methylated, and reacted with a range of nucleophiles. Oxidative decomplexation affords the free dihydropyridines in good yield (75−90%). As a demonstration of synthetic utility, a series of novel bridgehead CF_3-substituted isoquinuclidines was prepared from these decomplexed dihydropyridines.



INTRODUCTION

The coordination of an arene to a transition metal can have a profound effect upon its reactivity, a feature which has often been exploited in organic synthesis. Examples include nucleophilic addition reactions to $Cr(CO)_3(\eta^6$-benzene) or $[Mn(CO)_3(\eta^6$-benzene)$]^+$, and electrophilic additions to $[Os(NH_3)_5(\eta^2$-benzene$)]^{2+}$, ReTp(CO)(MeIm)(η^2-naphthalene) (MeIm = *N*-methylimidazole; Tp = tris(pyrazolyl)borate), or WTp(NO)(PMe_3)(η^2-benzene).[1−3] However, transition-metal-promoted dearomatization has been much less explored for aromatic heterocycles, with pyridines often proving to be especially challenging due to the thermodynamic preference for κ-N coordination.[4] One exception has been the π-basic dearomatization agent {WTp(NO)(PMe_3)}, which has been shown to promote tandem addition and cycloaddition reactions to pyridine, following the dihapto-coordination of this heterocycle.[5,6] The success of this chemistry relies on the blockage of nitrogen, either by substitution at the 2-position or by boronation of the nitrogen prior to coordination. To date, the functionalization of pyridines promoted by dihapto-coordination has only been observed with tungsten. While the molybdenum agent {MoTp(NO)(DMAP)} (DMAP = 4-(dimethylamino)pyridine) can also bind benzene, the substitution half-life (∼20 s at 25 °C) and susceptibility to oxidation of the resulting complex has precluded its use in organic synthesis.[7] However, the advantages of cost and scale compared to its heavy metal analog, and the paucity of examples of dihapto-coordinated heterocycles with other transition metals compelled a deeper exploration.

Attempts to combine the {MoTp(NO)(DMAP)} synthon MoTp(NO)(DMAP)(η^2-PhCF$_3$) with [pyMe]OTf resulted in immediate metal oxidation, signaled by formation of a green paramagnetic material. Efforts to prepare a stable complex with pyridine-borane were more promising, as a cyclic voltammogram (CV) of the reaction solution (100 mV/s) showed an anodic peak at 0.05 V (NHE) (cf. WTp(NO)(PMe_3)($pyBH_3$), $E_{p,a}$ = +0.47 V), but isolation of the desired complex could not be accomplished free of impurities due to its thermal instability. Attempts to bind 2-methyl-, 2-ethyl-, and 2-isopropyl-pyridine were also unsuccessful. These reactions resulted in species with $E_{1/2}$ values measured near −0.9 V, consistent with the formation of κ−N complexes. In contrast, 2-phenylpyridine produced a complex which appeared to be dihapto-coordinate by cyclic voltammetry ($E_{p,a}$ at −0.1 V) and ^{1}H NMR data, though this complex could not be isolated cleanly, perhaps due to decomposition during isolation.

In earlier work with {MoTp(NO)(DMAP)} arene complexes,[7] it was shown that while the benzene analog was impractically fragile, the incorporation of a CF_3 arene substituent dramatically enhanced the stability of the corresponding molybdenum complex, enough to enable organic modifications of the aromatic ring.[7] Thus, we posited that a CF_3 group at the 2-position of pyridine (i.e., 2-(trifluoromethyl)pyridine) would not only block nitrogen coordination but also might stabilize a purported molybdenum η^2-pyridine complex enough to carry out heterocycle-based organic reactions (Figure 1). Further, given the significant role fluorine plays in modern medicinal chemistry,[8] the anticipated organic products could serve as novel precursors to pharmacologically relevant compounds. Hence, the aim of this initial phase of our investigation into molybdenum η^2-pyridine complexes is the metal-mediated stereoselective conversion of an η^2-(2-trifluoromethyl)pyridine) to novel 1,2-dihydropyridines, which in turn could be elaborated into isoquinuclidines bearing an angular CF_3 group.

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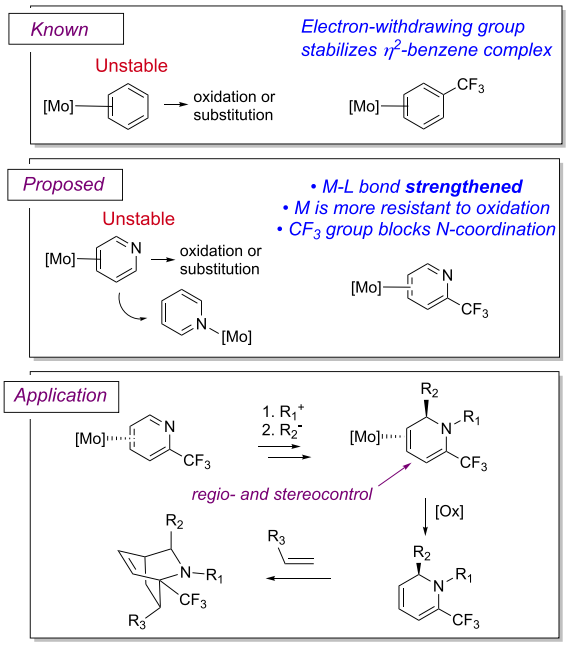


Figure 1. Proposed stabilization of a dihapto-coordinated molybdenum-pyridine complex by a CF_3 group and the enabled stereoselective synthesis of novel isoquinuclidines.

RESULTS AND DISCUSSION

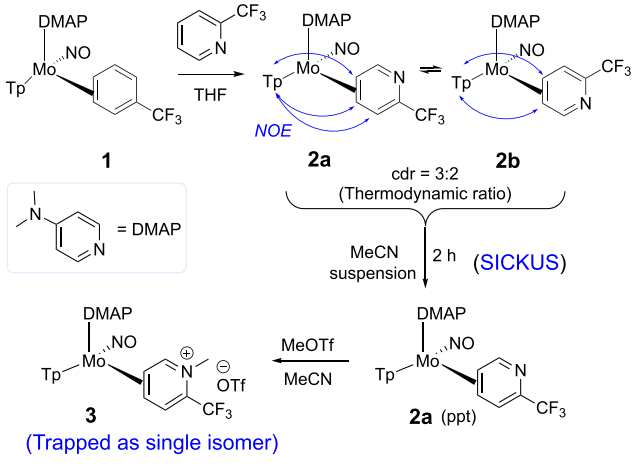
Stirring the previously reported complex MoTp(NO)(DMAP)(η^2-PhCF$_3$) (**1**)[7] in a THF solution of 2-(trifluoromethyl)pyridine (TFP) generates two new compounds, shown to be coordination diastereomers differentiated by which face of the pyridine ligand is bound by the metal (**2a** and **2b**; coordination diastereomer ratio (cdr) = 3:2 Scheme 1). These diastereomers were characterized by ^{1}H, ^{13}C, COSY, and NOESY NMR data and were identified by NOE correlations of the pyridine ring protons to the Tp ligand (Scheme 1).[9] A cyclic voltammogram of this mix of diastereomers (**2**) in MeCN solution shows an $E_{p,a}$ of −0.08 V (NHE) at 100 mV/s, and an IR absorption spectrum of **2** indicates a ν(NO) of 1584 cm^{-1}. These features are consistent with an η^2-aromatic complex of {MoTp(NO)(DMAP)}.[4,7]

The inability to selectively bind a single face of the pyridine ring would limit the ability to control the absolute stereochemistry of organic transformations to the heterocycle. This problem was addressed by taking advantage of differential stability of the two diastereomers (**2a** and **2b**) in the solid state (solid-state induced control of kinetically unstable stereoisomers (SICKUS)).[10] Hence when this mixture of coordination diastereomers was stirred as a suspension in MeCN for 2 h, a single coordination diastereomer (**2a**) was recovered as the precipitate in 70% percent yield (7.0 g scale). Although **2a**/**2b** isomerization occurs within seconds in solution at 20 °C (^{1}H NMR), the diastereomer present in crystalline form (**2a**) could be selectively reacted by adding the solid to a solution of MeOTf in MeCN. Once "trapped" through methylation, the greatly strengthened back-bonding interaction of the molybdenum with the pyridinium ion dramatically slows the interfacial isomerization, and even heating **3** in MeCN for 24 h at 40 °C fails to produce an observable coordination diastereomer of **3**.

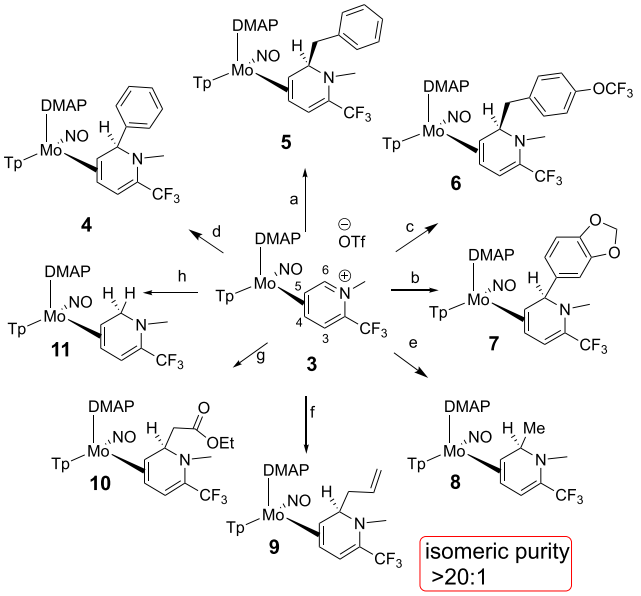
Methylation also was expected to increase the reactivity of the complex toward nucleophiles, allowing for further modification of the ligand. While similar pyridinium complexes could be prepared via protonation (triflic acid in MeOH) or Michael addition (MVK) to the nitrogen, these reactions were subsequently found to be reversible in the presence of basic nucleophiles (vide infra).

A wide range of Grignard reagents, including those with pharmacologically relevant functionalities (e.g., benzodioxole, trifluoromethoxy),[11,12] were found to add to pyridinium complex **3** stereo- and regioselectively, and in good yields (Scheme 2). As typically seen only for free pyridinium salts reacting with hard nucleophiles,[13,14] nucleophilic addition was found to occur exclusively at C6, with no addition to C4 observed. The stereochemistry of nucleophilic addition was

Scheme 1. Synthesis of TFP Complex 2, the NOE Correlations That Differentiate the Two Diastereomers, 2a and 2b, and the Selective Conversion to a Single Diastereomer of the Methylated Pyridinium Complex 3



Scheme 2. Addition of Various Nucleophiles to the Methylated Pyridine Complex 3[a]



[a] a: BnMgCl; b: $C_7H_5O_2MgBr$; c: p-(trifluoromethoxy)benzylMgBr; d: PhMgBr; e: MeMgBr; f: C_3H_5Br, Zn; g: $BrCH_2COOEt$, Zn; h: KBH_4.

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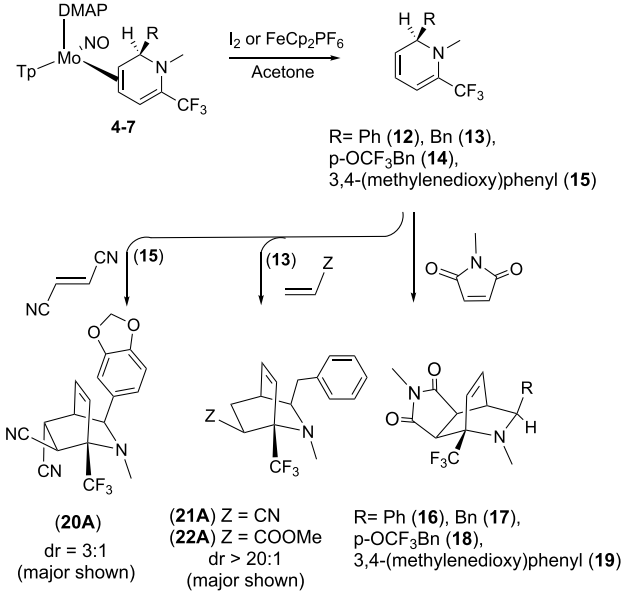
determined through NOESY data: in every case, addition was found to take place anti to the metal, as indicated by an NOE correlation between proton H2 and the H2/H6 protons of the DMAP ligand. Subsequently, these results were confirmed by single-crystal X-ray diffraction (SC-XRD) experiments (Supporting Information). The attempted addition of a Grignard reagent to the neutral TFP complex **2a** resulted in no reaction, and addition of BnMgCl to the organic methylated TFP gives mostly C4 addition (vide infra). To our knowledge, there is only one report of TFP (or its pyridinium analog) reacting with an organometallic reagent to form a 1,2-dihydropyridine (DHP); in that disclosure, *t*-BuLi reacted at C2 to form a quaternary carbon,[15] and this compound rapidly decomposed at ambient temperature. In contrast, halogenated, trifluoromethylated pyridines have been used in coupling reactions to make other pyridines.[16]

Although further functionalization of the bound dihydropyridine ligand may be achievable, efforts were directed toward isolation of the free dihydropyridines (DHPs), with the goal of using these compounds as precursors to novel isoquinuclidines.[17] The phenyl and benzyl derivatives **4**−**7** were chosen as models for further elaboration. It was found that the free organic could be obtained in good yield (70−90%) via oxidative decomplexation by treating complexes **4**−**7** with $[FeCp_2]PF_6$ in acetone (Scheme 3). Alternatively, I_2 could be

Scheme 3. Decomplexation of DHP and Its Elaboration to Isoquinuclidines



used, which afforded the recovery of MoTp(NO)(DMAP)(I) (92%). In contrast to literature reports,[15] the resulting organic trifluoromethylated DHPs were readily purified by chromatography on silica under ambient conditions and characterized by ^1H and ^{13}C NMR data (Figure 2).

To demonstrate the potential utility of these novel fluorinated DHPs in organic synthesis, the released dienes **12**−**15** were combined with a dienophile: over the course of 24 h, with mild heating, they reacted with *N*-methylmaleimide to form endo cycloadducts **16**−**19**. In addition, when compound **15** was heated in the presence of fumaronitrile, cycloadduct **20** was isolated as a 3:1 ratio of two diastereomers (**20A**/**B**). A significantly weaker dienophile, acrylonitrile, was

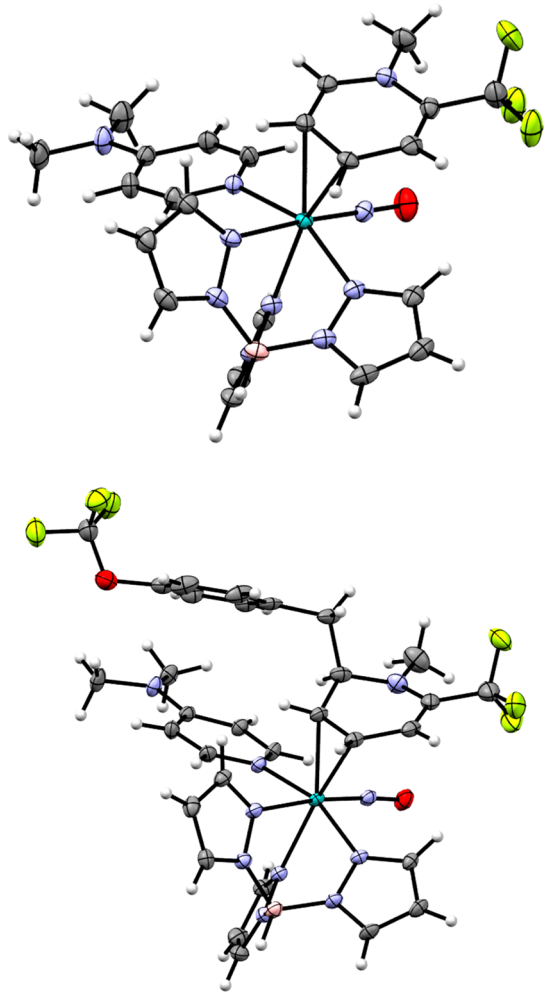


Figure 2. ORTEP diagram (50% probability) of a single diastereomer of the methylated TFP complex **3** (top) and its addition product **6** (bottom). For both structures, the anion and solvent are omitted for clarity.

also found to undergo a Diels−Alder reaction with **13**, at 77 °C, producing cycloadduct (**21A**/**B**) in 96% yield (dr = 95:5). These novel isoquinuclidines were characterized by 2D NMR techniques and high-resolution mass spectrometry. Further, the structures of the cycloadducts **17**, **19**, and **20A** were confirmed with SC-XRD.

Control Experiments. Molybdenum-free reactions were explored to establish whether the same reactivity occurs in the absence of the metal. Hence free 2-(trifluoromethyl)pyridine was methylated in good yield with MeOTf in Et_2O. The resulting methylpyridinium salt was then reacted with benzylmagnesium chloride under a range of conditions varying both in temperature (20 °C and −60 °C) and solvent (Et_2O and THF). In each case, the 1,2-dihydropyridine product was produced as a minor species, with the 1,4-dihydropyridine dominating (Figure 3). Ratios of 1,4-DHP to 1,2-DHP ranged from 5:1 in Et_2O at 20 °C to 3:1 in THF at 20 °C. Small amounts (∼5%) of two other unidentified minor species were also produced.

To determine if the analogous tungsten system, {TpW(NO)(PMe_3)}, would provide similar reactivity, TpW(NO)(PMe_3)(4,5-η^2-(2-trifluoromethyl)pyridine) was prepared via exchange from TpW(NO)(PMe_3)(η^2-benzene).[18] Methylation, Grignard addition, and oxidative decomplexation were

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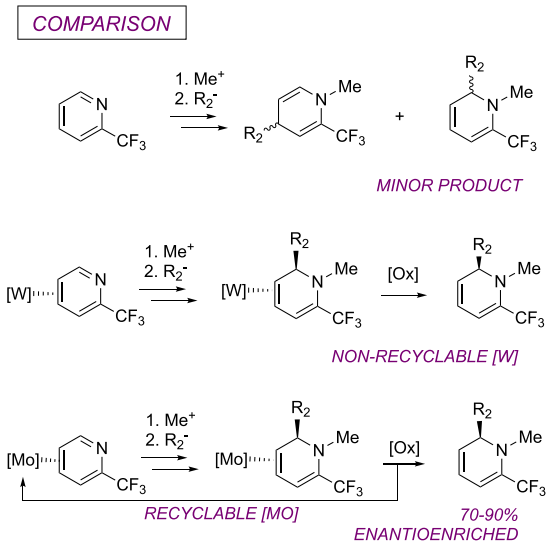
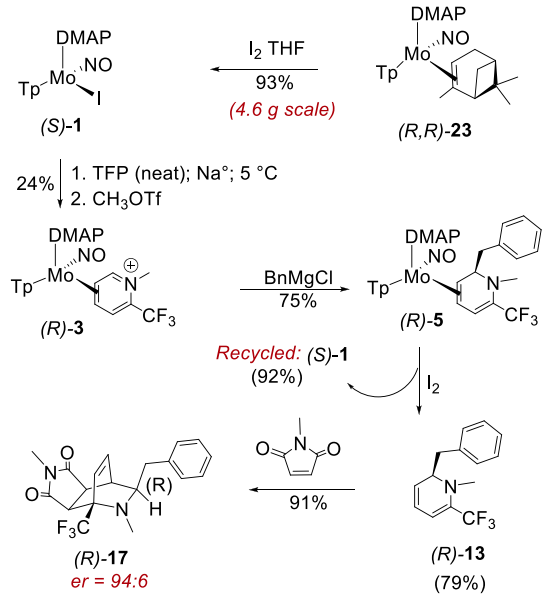


Figure 3. A comparison of several methods used to generate 6-(trifluoromethyl)-1,2-dihydropyridines.

carried out, and the same products were isolated in comparable yield (Figure 3). However, unlike with molybdenum, oxidative decomplexation required $FeCp_2PF_6$, with I_2 resulting in no reaction. The tungsten byproducts were thus not recyclable (vide infra).

Enantioenriched Variation. Previous studies have shown the ability of molybdenum to promote enantioselective dearomatization.[19] In this case, the complex must be synthesized by reduction instead of ligand exchange, as the pentacoordinate Mo(0) intermediate rapidly epimerizes. Although it was feared that the required sodium metal would react with the free pyridine ligand, preventing synthesis of a molybdenum complex via reduction, a dihapto 2-(trifluoromethyl)pyridine complex was successfully produced from the α-pinene complex **23**, via TpMo(NO)(DMAP)I, (*S*)-**1**, by reduction in neat ligand in usable yield (28%; Scheme 4).

Scheme 4. Enantioenriched Preparation of Isoquinuclidine from α-Pinene Precursor



The pyridine complex was methylated to generate (*R*)-**3** (24% overall), and this pyridinium salt was reacted with benzylmagnesium chloride. Oxidative decomplexation with I_2 released the enantioenriched DHP (*R*)-**13** with almost quantitative recovery of the molybdenum complex (92%). Meanwhile, (*R*)-**13** was allowed to undergo a Diels–Alder reaction with NMM to form a cycloadduct (*R*)-**17**. The final enantiomeric ratio of this product was determined to be 94:6 by ^{1}H NMR in benzene at +6 °C using 5.0 equiv of α-methoxy-α-(trifluoromethyl)phenylacetic acid (Mosher's acid).[20] The absolute configuration of (R)-17 was confirmed by X-ray crystallography (absolute structure parameter is −0.02(15)). Thus, in principle any of the products characterized herein may be be synthesized with high enantioenrichment.

Dihydropyridines may be synthesized by several alternative methods, the simplest of which is nucleophilic addition to acyl or alkyl pyridinium salts.[21,22] 1,2 addition tends to predominate with harder nucleophiles, such as Grignard reagents, whereas 1,4 addition is generally favored for softer nucleophiles (e.g., organocuprates). However, the products are usually formed as a mixture of 1,2- and 1,4-isomers, the ratio of which is highly dependent upon the nucleophile, the N-substituent, and any additional functional groups on the pyridine. Additionally, weaker nucleophiles often require acyl activation or the presence of electron-withdrawing substituents on the pyridine in order for addition to be successful. The use of chiral auxiliaries at nitrogen, or more uncommonly at another position of a substituted pyridine, allows for the enantioselective synthesis.[23] An alternative approach utilizes a rhodium-catalyzed C–H alkenylation/electrocyclization to produce 1,2-dihydropyridines from α,β-unsaturated imines and alkynes, and these products have also been employed in the synthesis of isoquinuclidines.[17,24,25] Furthermore, 1,2-dihydropyridines have also been synthesized by rhodium-catalyzed hydroboration.[26]

Given the reaction scale and potential diversity of Grignard nucleophiles, the chemistry demonstrated herein presents a practical synthesis of molecules of potential pharmacological interest, including isoquinuclidines with a CF_3-subsituted bridgehead position. Carbobicyclics and heterobicyclics of any kind with CF_3-subsitituted bridgehead positions are uncommon, with only a few examples reported as being formed via cycloaddition.[27−29] Further, although isoquinuclidines constitute the structural nucleus of several classes of biologically active natural products (e.g., iboga alkaloids, dioscorine, and cannivonines) and are important in medicinal chemistry,[30] this appears to be the first report of an isoquinuclidine with a bridgehead CF_3 group. Roughly one-quarter of all drugs contain at least one fluorine,[8] with notable CF_3-containing examples including Sustiva, Prozac, and Celebrex. Thus, the ability to prepare isoquinuclidines with a bridgehead CF_3 group and alkene and carboxyl functional groups for further elaboration creates exciting possibilities for new druggable chemical space (Figure 4).[31]

CONCLUSIONS

Previous studies from our group have outlined the potential of tungsten as an η^2-pyridine dearomatization agent,[6,32−35] but this is the first report that extends this concept to another metal. The ability to prepare the precursor MoTp(NO)(DMAP)(η^2-PhCF$_3$) on a 37 g scale[7] and recycle the metal[36] are key advantages over its heavy metal cousin. We note that

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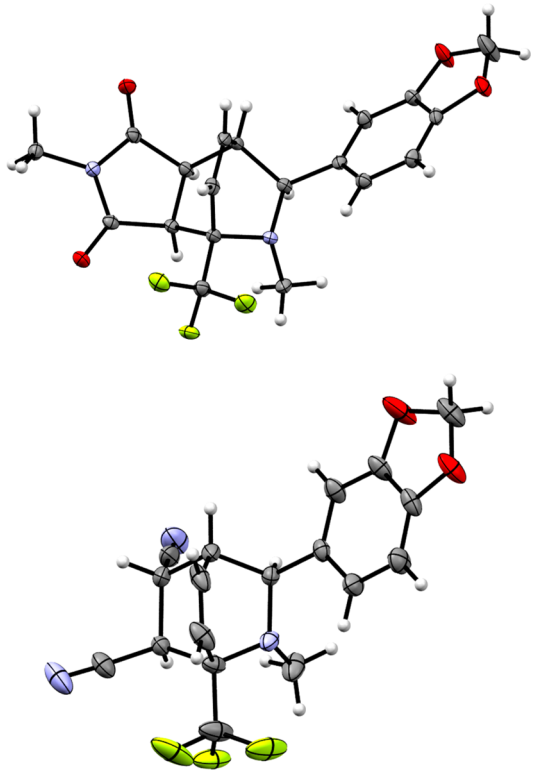

Figure 4. ORTEP diagram (50% probability) of isoquinuclidine compounds **17** (top) and **20A** (bottom) (50% probability).

the use of stoichiometric molybdenum in the synthesis of pyridine-derived alkaloids was pioneered by the Liebeskind group, who used enantioenriched 3-oxopyridinylmolybdenum scaffolds to access biologically relevant heterocyclic cores.[37] The metal-mediated reactions described herein offer a complementary reactivity manifold to explore.

EXPERIMENTAL SECTION

General Methods. NMR spectra were obtained on a 600 or 800 MHz spectrometer (22−25 °C). All chemical shifts are reported in ppm, and proton and carbon shifts are referenced to tetramethylsilane (TMS) utilizing residual 1H or 13C signals of the deuterated solvents as an internal standard. Coupling constants (J) are reported in hertz (Hz). Infrared spectra (IR) were recorded as a glaze on a spectrometer fitted with a horizontal attenuated total reflectance (HATR) accessory or on a diamond anvil ATR assembly. Electrochemical experiments were performed under a nitrogen atmosphere. Cyclic voltammetry data were taken at ambient temperature (22−25 °C) at 100 mV/s in a standard three-electrode cell with a glassy carbon working electrode, *N*,*N*-dimethylacetamide (DMA) or acetonitrile (MeCN) solvent, and tetrabutylammonium hexafluorophosphate (TBAH) electrolyte (approximately 0.5 M). All potentials are reported versus NHE (normal hydrogen electrode) using cobaltocenium hexafluorophosphate ($E_{1/2}$ = −0.78 V), ferrocene ($E_{1/2}$ = +0.55 V), or decamethylferrocene ($E_{1/2}$ = +0.04 V) as an internal standard. The peak-to-peak separation was less than 100 mV for all reversible couples. Unless otherwise noted, all synthetic reactions were performed in a glovebox under a dry nitrogen atmosphere. Deuterated solvents were used as received. Pyrazole (Pz) protons of the (trispyrazolyl)borate (Tp) ligand were uniquely assigned (e.g., "Pz3B") using a combination of two-dimensional NMR data and (dimethylamino)pyridine−proton NOE interactions. When unambiguous assignments were not possible, Tp protons were labeled as "Pz3/5 or Pz4". All J values for Pz protons are 2 (±0.2) Hz. BH 1H NMR peaks (around 4−5 ppm) are not identified due to their quadrupole broadening; IR data are used to confirm the presence of a BH group (around 2500 cm^{-1}).

*TpMo(NO)(DMAP)(3,4-η²-2-(trifluoromethyl)pyridine) (**2**).* Compound **1**, TpMo(NO)(DMAP)(η^2-PhCF$_3$) (8.28 g, 13.6 mmol), followed by 2-(trifluoromethyl)pyridine (31.9 g, 217 mmol) and THF (85.0 mL) was added to a 250 mL round-bottom flask charged with a stir bar. This orange mixture was stirred for 4 h. The resulting brown heterogeneous mixture was added slowly to stirring pentane (900 mL). The resulting precipitate was isolated on a 150 mL fine porosity fritted disc, washed with Et_2O (3 × 50 mL), and desiccated to yield a tan solid, **2** (7.50 g, 90.4%). CV (MeCN) $E_{p,a}$ = +0.08 V (NHE). IR: ν_{NO} = 1584 cm^{-1}. Two coordination diastereomers. **A:B** = 3:2 ^{1}H NMR (d_6-acetone, δ): **A** 8.15 (d, J = 3.4 Hz, 1H, H6), 8.09 (d, 1H, PzC5), 7.99 (d, 1H, PzA5), 7.93 (d, 1H, PzB5), 7.88 (d, 1H, PzA3), 7.79 (broad s, 2H, DMAP A), 7.61 (d, 1H, PzC3), 7.24 (d, J = 6.4 Hz, 1H, H3), 6.97 (d, 1H, PzB3), 6.74 (d, 2H, DMAP B), 6.41 (t, 1H, PzC4), 6.41 (t, 1H, PzA4), 6.16 (t, 1H, PzB4), 3.68 (dd, 1H, H5), 3.11 (t, 1H, H4), 3.11 (s, 6H, DMAP Me). **B** 8.54 (d, J = 3.5 Hz, 1H, H6), 8.09 (d, 1H, Pz3/5), 7.98 (d, 1H, Pz3/5), 7.95 (d, 1H, Pz3/5), 7.93 (d, 1H, Pz3/5), 7.79 (broad s, 2H, DMAP A), 7.56 (d, 1H, PzC3), 6.97 (d, 1H, Pz3/5), 6.89 (d, J = 6.3 Hz, 1H, H3), 6.74 (d, 2H, DMAP B), 6.41 (t, 1H, Pz4), 6.41 (t, 1H, Pz4), 6.16 (t, 1H, Pz4), 3.65 (m, 1H, H5), 3.17 (m, 1H, H4), 3.11 (s, 6H, DMAP Me). ^{13}C NMR (d_6-acetone, δ): **A** 165.3 (C6), 155.4 (DMAP C), 150.3 (DMAP A), 142.6 (Tp3/5), 142.3 (Tp3/5), 141.7 (Tp3/5), 137.8 (Tp3/5), 137.1 (Tp3/5), 136.1 (Tp3/5), 130.5 (C2), 127.1 (C3), 123.5 (CF_3), 108.5 (DMAP B), 107.1 (Tp4), 106.7 (Tp4), 106.5 (Tp4), 75.0 (C5), 73.5 (C4), 39.1 (DMAP Me). **B** 165.8 (C6), 155.1 (DMAP C), 150.8 (DMAP A), 144.0 (Pz3/5), 142.7 (Pz3/5), 141.7 (Pz3/5), 137.8 (Pz3/5), 137.0 (Pz3/5), 136.1 (Pz3/5), 130.1 (C2), 126.4 (C3), 108.5 (DMAP B), 107.1 (Pz4), 106.7 (Pz4), 106.6 (Pz4), 75.9 (C4), 72.8(C5), 39.1 (DMAP Me). Calculated for $C_{22}H_{24}BF_3MoN_{10}O$: C, 43.44; H, 3.98; N, 23.03. Found: C, 43.15; H, 4.09; N, 22.99.

*Preparation of **2A**.* **2** (7.23 g, 11.9 mmol) and MeCN (70.0 mL) were added to a 100 mL round-bottom flask charged with a stir bar. The resulting suspension was stirred for 2 h at ambient temperature and then filtered through a 60 mL fine porosity fritted funnel. The isolated solid was washed with MeCN (10 mL) followed by Et_2O (2 × 20 mL). The washed solid was desiccated to yield **2A** as a light orange solid (5.06 g, 70.0%).

*Enantioenriched Preparation of **2**.* Compound **1**, (S)-TpMo(NO)(DMAP)(I) (2.01 g, 3.42 mmol),[19] followed by 2-(trifluoromethyl)pyridine (25.0 g, 0.170 mol) was added to a 250 mL jacketed round-bottom flask cooled to +5 °C with circulating chilled ethylene glycol and charged with a stir bar. This mixture was stirred for 15 min to cool, and then sodium 35% (w/w) dispersion in toluene, diameter < 0.1 mm (10.0 g, 0.152 mol), was added to the reaction mixture. The reaction mixture was stirred vigorously for 16 h and then filtered through a Celite plug in a 30 mL medium porosity fritted funnel to remove sodium. The filtrate was loaded onto a column of basic alumina (100 mL) prepared as a slurry with hexanes in a 150 mL medium porosity fritted funnel. The free pyridine was eluted with hexanes (500 mL), then a yellow-orange product was eluted with Et_2O (300 mL). The eluent was evaporated to dryness, and the residue was redissolved in DCM (3 mL). EtOAc (6 mL) was added until the complex was nearly saturated, followed by hexanes (100 mL). The suspension was evaporated to half volume under vacuum, and the precipitate was isolated on a 30 mL fine porosity fritted funnel. The solid was washed with hexanes (3 × 20 mL) and desiccated under vacuum to yield **2** as a pale orange solid (582 mg, 28%).

*[TpMo(NO)(DMAP)(3,4-η²-2-(trifluoromethyl)-N-methylpyridinium)]⁺ (OTf) (**3**).* MeOTf (1.72 g, 10.5 mmol) and MeCN (9.0 mL), both of which had been cooled to −30 °C, were added to a 4-dram vial charged with a stir bar. **2A** (4.70 g, 7.73 mmol) was then immediately added to the reaction mixture. The resulting solution was allowed to stir for 15 min and subsequently added dropwise to a stirring mixture of Et_2O (350 mL) and pentane (150 mL). The resulting precipitate was isolated on a 60 mL fine porosity fritted disc,

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washed with Et_2O (4 × 25 mL), and desiccated to yield a magenta solid, **3** (5.01 g, 83.9%). CV (DMAc) $E_{p,a}$ = +0.87 V (NHE). IR: ν_{NO} = 1623 cm^{-1}. ^1H NMR (d_6-acetone, δ): 8.42 (d, J = 5.2 Hz, 1H, H6), 8.03 (d, 1H, PzC5), 7.96 (d, 1H, PzA5), 7.85 (d, 1H, PzB5), 7.72 (broad s, 2H, DMAP A), 7.68 (d, 1H, PzA3), 7.63 (d, J = 6.8 Hz, 1H, H3), 7.53 (d, 1H, PzC3), 7.17 (d, 1H, PzB3), 6.63 (d, 2H, DMAP B), 6.43 (t, 1H, PzC4), 6.41 (t, 1H, PzA4), 6.17 (t, 1H, PzB4), 4.10 (s, 3H, H7), 3.89 (dd, J = 7.0 Hz, 5.2 Hz, 1H, H5), 3.46 (dd, J = 7.0 Hz, 6.8 Hz, 1H, H4), 3.02 (s, 6H, DMAP Me). ^{13}C NMR (d_6-acetone, δ): 172.3 (C6), 155.8 (DMAP C), 151.0 (DMAP A), 143.3 (PzB3), 142.5 (PzC3), 142.2 (PzA3), 138.8 (PzC5), 138.2 (PzA5), 137.0 (PzB5), 136.6 (C3), 109.3 (DMAP B), 108.0 (PzA4), 107.6 (PzC4), 107.2 (PzB4), 74.4 (C4), 73.3 (C5), 43.6 (C7), 39.5 (DMAP Me). Calculated for $C_{24}H_{27}BF_6MoN_{10}O_4S$: C, 37.32; H, 3.52; N, 18.14. Found: C, 37.61; H, 3.46; N, 18.00.

*TpMo(NO)(DMAP)(3,4-η²-2-(trifluoromethyl)-6-phenyl-N-methyldihydropyridine) (**4**).* Compound **3** (1.00 g, 1.29 mmol) and THF (16.0 mL), which had previously been cooled to −40 °C, were added to a 25 mL flame-dried round-bottom flask charged with a stir bar. A 1.0 M solution of phenylmagnesium bromide in THF (3.0 mL, 3.0 mmol) was added dropwise to the solution of **3**. The reaction mixture changed from vivid magenta to golden yellow over the course of the addition. The reaction mixture was stirred for 5 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (30 mL) and extracted with saturated $NaHCO_3$ (2 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in DCM (8 mL) and added dropwise to stirring pentane (100 mL). The precipitate was isolated on a 30 mL fine porosity fritted disc, washed with pentane (3 × 10 mL), and desiccated to yield a yellow solid, **4** (633 mg, 70.0%). CV (MeCN) $E_{p,a}$ = +0.13 V (NHE). IR: ν_{NO} = 1576 cm^{-1}. ^1H NMR (d_6-acetone, δ): 8.22 (bs, 2H, DMAP A), 8.01 (d, 1H, PzA3), 7.92 (d, 1H, PzC5), 7.86 (d, 1H, PzA5), 7.80 (d, 1H, PzB5), 7.51 (d, 1H, PzC3), 7.27 (d, 1H, PzB3), 7.23 (m, 2H, H8), 7.21 (m, 2H, H9), 7.13 (m, 1H, H10), 6.79 (d, 2H, DMAP B), 6.30 (t, 2H, PzC4/PzA4), 6.15 (t, 1H, PzB4), 5.96 (d, J = 6.8 Hz, 1H, H3), 4.34 (s, 1H, H6), 3.11 (s, 3H, DMAP Me), 2.98 (s, 3H, H7), 2.88 (d, J = 9.7 Hz, 1H, H5), 2.47 (dd, J = 9.7 Hz, 6.4 Hz, 1H, H4). ^{13}C NMR (d_6-acetone, δ): 155.1 (DMAP C), 151.1 (DMAP A), 148.8 (C8a), 143.9 (PzA3), 142.3 (PzB3), 141.4 (PzC3), 137.4 (PzA5), 136.6 (PzC5), 135.9 (PzB5), 128.9 (C8), 127.4 (C9), 127.0 (C10), 124.4 (q, J = 28.6 Hz, C2), 124.0 (q, J = 270 Hz, CF_3), 109.4 (q, J = 7.0 Hz, C3), 108.7 (DMAP B), 106.8 (PzC4), 106.3 (PzA4), 106.2 (PzB4), 82.0 (C5), 67.7 (C6), 56.3 (C4), 39.2 (DMAP Me), 38.1 (C7). Calculated for $C_{29}H_{32}BF_3MoN_{10}O$: C, 49.73; H, 4.61; N, 20.00. Found: C, 49.75; H, 4.76; N, 19.82.

*TpMo(NO)(DMAP)(3,4-η²-2-(trifluoromethyl)-6-benzyl-N-methyldihydropyridine) (**5**).* Compound **3** (2.57 g, 3.33 mmol) and THF (45.0 mL), which had previously been cooled to −40 °C, were added to a 100 mL flame-dried round-bottom flask charged with a stir bar. A 1.0 M solution of benzylmagnesium chloride in Et_2O (3.50 mL, 3.50 mmol) was added dropwise to the solution of **3**. The reaction mixture changed from vivid magenta to golden yellow over the course of the addition. The reaction mixture was stirred for 5 min and subsequently filtered through a 1 cm Celite column prepared in a 30 mL fine porosity fritted disc. The filtrate was diluted with DCM (50 mL) and extracted with saturated $NaHCO_3$ (2 × 50 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in minimal DCM and added dropwise to stirring pentane (250 mL). The precipitate was isolated on a 30 mL fine porosity fritted disc, washed with pentane (3 × 15 mL), and desiccated to yield a yellow solid, **5** (1.78 g, 75%). CV (MeCN) $E_{p,a}$ = +0.10 V (NHE). IR: ν_{NO} = 1567 cm^{-1}. ^1H NMR (d_6-acetone, δ): 7.96 (broad s, 2H, DMAP A), 7.95 (d, 1H, PzA3), 7.90 (d, 1H, PzC5), 7.83 (d, 1H, PzA5), 7.78 (d, 1H, PzB5), 7.30 (d, 1H, PzC3), 7.21 (d, 1H, PzB3), 7.19 (m, 2H, H10), 7.13 (m, 1H, H11), 7.05 (m, 2H, H9), 6.64 (d, 2H, DMAP B), 6.30 (t, 1H, PzC4), 6.27 (t, 1H, PzA4), 6.12 (t, 1H, PzB4), 5.96 (d, J = 6.1 Hz, 1H, H3), 3.42 (dd, J = 7.2 Hz, 6.4 Hz, 1H, H6), 3.11 (s, 3H, DMAP Me), 3.01 (dd, J = 12.7 Hz, 6.4 Hz, H8), 2.96 (s, 3H, H7), 2.87 (d, J = 9.9 Hz, 1H, H5), 2.75 (dd, J = 12.7 Hz, 7.2 Hz, 1H, H8′), 2.34 (dd, J = 9.9 Hz, 6.1 Hz, 1H, H4). ^{13}C NMR (d_6-acetone, δ): 155.0 (DMAP C), 150.9 (DMAP A), 143.8 (PzA3), 142.2 (PzB3), 141.7 (H9a), 141.1 (PzC3), 137.4 (PzA5), 136.5 (PzC5), 135.8 (PzB5), 130.2 (H10), 128.8 (H9), 126.2 (H11), 124.1 (q, J = 272 Hz, CF_3), 124.0 (q, J = 28.7 Hz, C2), 110.3 (q, J = 6.6 Hz, C3), 108.5 (DMAP B), 106.6 (PzC4), 106.3 (PzA4), 106.1 (PzB4), 81.7 (C5), 66.2 (C6), 56.5 (C4), 42.1 (C8), 39.2 (DMAP Me), 38.0 (C7). Calculated for $C_{30}H_{34}BF_3MoN_{10}O$: C, 50.44; H, 4.80; N, 19.61. Found: C, 50.43; H, 4.83; N, 19.46.

*TpMo(NO)(DMAP)(3,4-η²-2-(trifluoromethyl)-6-(4-trifluoromethoxy)benzyl-N-methyldihydropyridine) (**6**).* Compound **3** (1.00 g, 1.29 mmol) and THF (16.0 mL), which had previously been cooled to −40 °C, were added to a 25 mL flame-dried round-bottom flask charged with a stir bar. A 1.0 M solution of 4-(trifluoromethoxy)benzylmagnesium bromide in Et_2O (3.0 mL, 3.0 mmol) was added dropwise to the solution of **3**. The reaction mixture changed from vivid magenta to golden yellow over the course of the addition. The reaction mixture was stirred for 5 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (30 mL) and extracted with saturated $NaHCO_3$ (2 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in minimal DCM and added dropwise to stirring hexanes (100 mL). The precipitate was isolated on a 30 mL fine porosity fritted disc, washed with hexanes (3 × 10 mL), and desiccated to yield a yellow solid, **6** (754 mg, 72%). CV (MeCN) $E_{p,a}$ = +0.13 V (NHE). IR: ν_{NO} = 1568 cm^{-1}. ^1H NMR (d_2-methylene chloride, δ): 7.94 (broad s, 2H, DMAP A), 7.93 (d, 1H, PzA3), 7.74 (d, 1H, PzC5), 7.72 (d, 1H, PzA5), 7.64 (d, 1H, PzB5), 7.17 (d, 1H, PzB3), 7.12 (d, 1H, PzC3), 7.10 (m, 2H, H9), 7.06 (m, 2H, H10), 6.42 (d, 2H, DMAP B), 6.24 (t, 1H, PzA4), 6.23 (t, 1H, PzC4), 6.07 (t, 1H, PzB4), 5.95 (d, J = 6.3 Hz, 1H, H3), 3.33 (dd, J = 7.5 Hz, 6.1 Hz, 1H, H6), 3.05 (dd, J = 12.9 Hz, 6.1 Hz, H8), 3.03 (s, 6H, DMAP Me), 2.98 (s, 3H, H7), 2.77 (dd, J = 12.9 Hz, 7.5 Hz, 1H, H8′), 2.67 (d, J = 9.7 Hz, 1H, H5), 2.38 (dd, J = 9.7 Hz, 6.3 Hz, 1H, H4). ^{13}C NMR (d_2-methylene chloride, δ): 154.4 (DMAP C), 150.7 (DMAP A), 147.6 (C10a), 143.7 (PzA3), 142.0 (PzB3), 140.7 (C9a), 140.5 (PzC3), 136.9 (PzA5), 136.2 (PzC5), 135.5 (PzB5), 131.2 (C9), 123.9 (q, J = 29.3 Hz, C2), 123.6 (q, J = 272 Hz, CF_3), 121.3 (q, J = 256 Hz, OCF_3), 121.0 (C10), 109.9 (q, J = 6.7 Hz, C3), 108.0 (DMAP B), 106.2 (PzC4), 106.0 (PzA4), 105.9 (PzB4), 81.0 (C5), 65.8 (C6), 56.6 (C4), 40.9 (C8), 39.5 (DMAP Me), 38.9 (C7). Calculated for $C_{31}H_{33}BF_6MoN_{10}O_2 \cdot 1/3\ C_6H_{14}$: C, 47.92; H, 4.59; N, 16.93. Found: C, 47.20; H, 4.20; N, 16.98.

*TpMo(NO)(DMAP)(3,4-η²-2-(trifluoromethyl)-6-(3,4-methylenedioxy)phenyl-N-methyldihydropyridine) (**7**).* Compound **3** (1.00 g, 1.29 mmol) and THF (16.0 mL), which had previously been cooled to −40 °C, were added to a 25 mL flame-dried round-bottom flask charged with a stir bar. A 1.0 M solution of 3,4-(methylenedioxy)phenylmagnesium bromide in 1:1 toluene/THF (3.0 mL, 3.0 mmol) was added dropwise to the solution of **3**. The reaction mixture changed from vivid magenta to golden yellow over the course of the addition. The reaction mixture was stirred for 5 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (30 mL) and extracted with saturated $NaHCO_3$ (2 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in DCM (8 mL) and added dropwise to stirring Et_2O (100 mL). Half of the solvent was evaporated under vacuum to yield a bright yellow precipitate. The precipitate was isolated on a 30 mL fine porosity fritted disc, washed with Et_2O (3 × 10 mL), and desiccated to yield a yellow solid, **7** (652 mg, 68%). CV (MeCN) $E_{p,a}$ = +0.14 V (NHE). ^1H NMR (d_2-methylene chloride, δ): 8.14 (bs, 2H, DMAP A), 7.98 (d, 1H, PzA3), 7.76 (d, 1H, PzC5), 7.75 (d, 1H, PzA5), 7.67 (d, 1H, PzB5), 7.40 (d, 1H, PzC3), 7.21 (d, 1H, PzB3), 6.86 (s, 1H, H10), 6.69 (d, J = 8.2 Hz, 1H, H9), 6.61 (d, J = 8.2 Hz, 1H, H8), 6.54 (d, 2H, DMAP B), 6.26 (t, 2H, PzA4), 6.22 (t, 2H, PzC4), 6.10 (t, 1H, PzB4), 5.95 (d, J = 6.2 Hz, 1H, H3), 5.89 (s, 2H, H11), 4.21 (s, 1H, H6), 3.09 (s, 6H,

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DMAP Me), 2.97 (s, 3H, H7), 2.77 (d, J = 9.7 Hz, 1H, H5), 2.53 (dd, J = 9.7 Hz, 6.4 Hz, 1H, H4). ^{13}C NMR (d_2-methylene chloride, δ): 154.5 (DMAP C), 150.8 (DMAP A), 148.2 (C10a), 146.6 (C9a), 143.8 (PzA3), 142.7 (C8a), 142.0 (PzB3), 140.9 (PzC3), 136.9 (PzA5), 136.2 (PzC5), 135.5 (PzB5), 124.3 (q, J = 28.9 Hz, C2), 123.7 (q, J = 272 Hz, CF_3), 119.8 (C8), 108.8 (q, J = 6.7 Hz, C3), 108.2 (DMAP B), 108.0 (C9), 107.8 (C10), 106.2 (PzC4), 106.0 (PzA4), 105.9 (PzB4), 101.4 (C11), 81.7 (C5), 67.0 (C6), 56.4 (C4), 39.5 (DMAP Me), 38.0 (C7). Calculated for $C_{30}H_{32}BF_3MoN_{10}O_3 \cdot 1/2\ C_4H_{10}O$: C, 49.18; H, 4.77; N, 17.92. Found: C, 49.11; H, 4.66; N, 17.97.

*TpMo(NO)(DMAP)(3,4-η^2-2-(trifluoromethyl)-6-methyl-N-methyldihydropyridine) (**8**).* Compound **3** (1.00 g, 1.29 mmol) and THF (16.0 mL), which had previously been cooled to −40 °C, were added to a 25 mL flame-dried round-bottom flask charged with a stir bar. A 1.4 M solution of methylmagnesium bromide in 1:3 THF/toluene (2.10 mL, 2.94 mmol) was added dropwise to the solution of **3**. The reaction mixture changed from vivid magenta to golden yellow over the course of the addition. The reaction mixture was stirred for 5 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (30 mL) and extracted with saturated $NaHCO_3$ (2 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in DCM (4 mL) and added dropwise to stirring Et_2O (100 mL). The precipitate was isolated on a 30 mL fine porosity fritted disc, washed with Et_2O (3 × 10 mL), and desiccated to yield a yellow solid, **8** (432 mg, 52.5%). CV (DMAc) $E_{p,a}$ = +0.06 V (NHE). IR: ν_{NO} = 1568 cm^{-1}. ^{1}H NMR (d_3-MeCN, δ): 7.97 (broad s, 2H, DMAP A), 7.90 (d, 1H, PzA3), 7.86 (d, 1H, PzC5), 7.80 (d, 1H, PzA5), 7.75 (d, 1H, PzB5), 7.59 (d, 1H, PzC3), 7.15 (d, 1H, PzB3), 6.61 (d, 2H, DMAP B), 6.31 (t, 1H, PzC4), 6.27 (t, 1H, PzA4), 6.13 (t, 1H, PzB4), 5.96 (d, J = 6.1 Hz, 1H, H3), 3.28 (qd, J = 6.2 Hz, 1.7 Hz, 1H, H6), 3.00 (s, 6H, DMAP Me), 2.99 (s, 3H, H7), 2.76 (dd, J = 9.6 Hz, 1.7 Hz, 1H, H5), 2.29 (dd, J = 9.6 Hz, 6.1 Hz, 1H, H4), 1.13 (d, J = 6.2 Hz, 3H, H8). ^{13}C NMR (d_3-MeCN, δ): 155.0 (DMAP C), 151.1 (DMAP A), 144.0 (PzA3), 142.4 (PzB3), 141.9 (PzC3), 137.8 (PzC5), 137.0 (PzA5), 136.3 (PzB5), 124.5 (C2, J_{CF} = 28.5 Hz), 124.2 (CF_3, J_{CF} = 270.1 Hz), 109.6 (C3, J_{CF} = 6.3 Hz), 108.7 (DMAP B), 107.0 (PzC4), 106.7 (PzA4), 106.6 (PzB4), 83.7 (C5), 59.1 (C6), 57.5 (C4), 39.4 (DMAP Me), 37.5 (C7), 19.6 (C8). Calculated for $C_{24}H_{30}BF_3MoN_{10}O$: C, 45.16; H, 4.74; N, 21.94. Found: C, 45.18; H, 4.85; N, 21.86.

*TpMo(NO)(DMAP)(3,4-η^2-6-allyl-2-(trifluoromethyl)-N-methyldihydropyridine) (**9**).* Compound **3** (380 mg, 0.492 mmol), THF (3.0 mL), allyl bromide (100 mg, 0.826 mmol), and zinc dust (250 mg, 3.82 mmol) were added to a 4-dram vial charged with a stir bar. The reaction mixture was stirred for 30 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (10 mL) and extracted with saturated $NaHCO_3$ (3 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in DCM (1.0 mL) and added dropwise to stirring pentane (50 mL). The precipitate was isolated on a 15 mL fine porosity fritted disc, washed with pentane (3 × 10 mL), and desiccated to yield a yellow solid, **9** (130 mg, 41.0%). CV (DMAc) $E_{p,a}$ = +0.09 V (NHE). IR: ν_{NO} = 1565 cm^{-1}. ^{1}H NMR (d_3-MeCN, δ): 7.99 (broad s, 2H, DMAP A), 7.89 (d, 1H, PzA3), 7.86 (d, 1H, PzC5), 7.80 (d, 1H, PzA5), 7.75 (d, 1H, PzB5), 7.53 (d, 1H, PzC3), 7.18 (d, 1H, PzB3), 6.61 (d, 2H, DMAP B), 6.32 (t, 1H, PzC4), 6.27 (t, 1H, PzA4), 6.13 (t, 1H, PzB4), 5.94 (q, J = 6.2 Hz, 1H, H3), 5.83 (m, 1H, H9), 4.97 (m, 1H, H10), 4.95 (m, 1H, H10′), 3.17 (td, J = 6.4 Hz, 1.4 Hz, 1H, H6), 3.09 (s, 3H, H7), 3.00 (s, 6H, DMAP Me), 2.96 (dd, J = 9.6 Hz, 1.4 Hz, 1H, H5), 2.45 (m, 1H, H8), 2.28 (dd, J = 9.6 Hz, 6.2 Hz, 1H, H4), 2.23 (m, 1H, H8′). ^{13}C NMR (d_3-MeCN, δ): 155.1 (DMAP C), 151.0 (DMAP A), 144.0 (PzA3), 142.4 (PzB3), 141.8 (PzC3), 138.2 (C9), 137.8 (PzC5), 136.9 (PzA5), 136.3 (PzB5), 124.4 (C2, J_{CF} = 28.5 Hz), 124.2 (CF3, J_{CF} = 270.1 Hz), 116.2 (C10), 110.8 (C3, J_{CF} = 6.3 Hz), 108.7 (DMAP B), 107.0 (PzC4), 106.7 (PzA4), 106.6 (PzB4), 82.7 (C5), 64.0 (C6), 56.8 (C4), 40.7 (C8), 39.4 (DMAP Me), 39.1 (C7). Calculated for $C_{26}H_{32}BF_3MoN_{10}O$: C, 47.00; H, 4.86; N, 21.08. Found: C, 46.76; H, 4.95; N 20.96.

*TpMo(NO)(DMAP)(3,4-η^2-ethyl 6-(1-methyl-2-(trifluoromethyl)-dihydropyridinyl)acetate) (**10**).* Compound **3** (380 mg, 0.492 mmol), THF (2.5 mL), ethyl bromoacetate (201 mg, 1.20 mmol), and zinc dust (250 mg, 3.82 mmol) were added to a 4-dram vial charged with a stir bar. The reaction mixture was stirred for 45 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (10 mL) and extracted with saturated $NaHCO_3$ (3 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in DCM (1.0 mL) and added dropwise to stirring Et_2O (50 mL). The precipitate was isolated on a 15 mL fine porosity fritted disc, washed with Et_2O (3 × 10 mL), and desiccated to yield a yellow solid, **10** (140 mg, 40.0%). CV (DMAc) $E_{p,a}$ = +0.14 V (NHE). IR: ν_{NO} = 1576 cm^{-1}; ν_{CO} = 1719 cm^{-1}. ^{1}H NMR (d_3-MeCN, δ): 7.97 (broad s, 2H, DMAP A), 7.88 (d, 1H, PzA3), 7.86 (d, 1H, PzC5), 7.80 (d, 1H, PzA5), 7.75 (d, 1H, PzB5), 7.48 (d, 1H, PzC3), 7.18 (d, 1H, PzB3), 6.64 (d, 2H, DMAP B), 6.32 (t, 1H, PzC4), 6.28 (t, 1H, PzA4), 6.14 (t, 1H, PzB4), 6.03 (d, J = 6.3 Hz, 1H, H3), 4.01 (m, 2H, H9), 3.60 (tdd, J = 7.1 Hz, J = 6.4 Hz, 1.4 Hz, 1H, H6), 3.08 (s, 3H, H7), 3.01 (s, 6H, DMAP Me), 2.93 (dd, J = 9.8 Hz, 1.4 Hz, 1H, H5), 2.68 (dd, J = 13.7 Hz, J = 7.1 Hz, 1H, H8), 2.41 (dd, J = 13.7 Hz, J = 6.4 Hz, 1H, H8′), 2.28 (dd, J = 9.8 Hz, 6.3 Hz, 1H, H4), 1.14 (t, J = 7.2 Hz, 3H, H10). ^{13}C NMR (d_3-MeCN, δ): 173.1 (Ester CO), 155.1 (DMAP C), 151.1 (DMAP A), 144.1 (PzA3), 142.5 (PzB3), 141.8 (PzC3), 137.9 (PzC5), 137.0 (PzA5), 136.4 (PzB5), 124.0 (CF_3, J_{CF} = 270.1 Hz), 123.6 (C2, J_{CF} = 28.5 Hz), 111.7 (C3, J_{CF} = 6.0 Hz), 108.8 (DMAP B), 107.1 (PzC4), 106.7 (PzA4), 106.7 (PzB4), 83.0 (C5), 61.4 (C6), 60.8 (C9), 56.3 (C4), 40.3 (C8), 39.4 (DMAP Me), 38.9 (C7), 13.5 (C10). Calculated for $C_{27}H_{34}BF_3MoN_{10}O_3$: C, 45.65; H, 4.82; N, 19.72. Found: C, 45.39; H, 4.62; N 19.45.

*TpMo(NO)(DMAP)(3,4-η^2-2-(trifluoromethyl)-N-methyldihydropyridine) (**11**).* Compound **3** (496 mg, 0.642 mmol) and MeOH (2.0 mL) were added to a 4-dram vial charged with a stir bar. In a separate 4-dram vial, KBH_4 (105 mg, 1.95 mmol) was added to MeOH (2.0 mL). The KBH_4 suspension was immediately added to the solution of **3**. The reaction mixture was stirred for 15 min and subsequently filtered through a 1 cm Celite column prepared in a 15 mL fine porosity fritted disc. The filtrate was diluted with DCM (10 mL) and extracted with saturated $NaHCO_3$ (3 × 20 mL). The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuo. The resulting residue was dissolved in DCM (2.0 mL) and added dropwise to stirring Et_2O (50 mL). The precipitate was isolated on a 30 mL fine porosity fritted disc, washed with Et_2O (3 × 15 mL), and desiccated to yield a yellow solid, **11** (231 mg, 57.6%). CV (DMAc) $E_{p,a}$ = +0.12 V (NHE). IR: ν_{NO} = 1570 cm^{-1}. ^{1}H NMR (d_3-MeCN, δ): 7.94 (broad s, 2H, DMAP A), 7.88 (d, 1H, PzA3), 7.86 (d, 1H, PzC5), 7.81 (d, 1H, PzA5), 7.75 (d, 1H, PzB5), 7.56 (d, 1H, PzC3), 7.15 (d, 1H, PzB3), 6.62 (d, 2H, DMAP B), 6.31 (t, 1H, PzC4), 6.29 (t, 1H, PzA4), 6.14 (t, 1H, PzB4), 6.04 (d, J = 5.8 Hz, 1H, H3), 3.74 (dd, J = 11.7 Hz, 3.4 Hz, 1H, H6b), 3.31 (dd, J = 11.7 Hz, 2.0 Hz, 1H, H6a), 3.00 (s, 6H, DMAP Me), 2.83 (s, 3H, H7), 2.66 (ddd, J = 9.5 Hz, 3.4 Hz, 2.0 Hz, 1H, H5), 2.27 (dd, J = 9.5 Hz, 5.8 Hz, 1H, H4). ^{13}C NMR (d_3-MeCN, δ): 155.1 (DMAP C), 151.0 (DMAP A), 144.1 (PzA3), 142.3 (PzB3), 141.6 (PzC3), 137.4 (PzC5), 136.5 (PzA5), 135.8 (PzB5), 126.7, (C2, J_{CF} = 28.5 Hz), 124.2 (CF_3, J_{CF} = 270.1 Hz), 112.3 (C3, J_{CF} = 6.7 Hz), 108.5 (DMAP B), 106.7 (PzC4), 106.3 (PzA4), 106.2 (PzB4), 72.5 (C5), 56.6 (C6), 56.0 (C4), 39.6 (DMAP Me), 39.1 (C7). Calculated for $C_{23}H_{28}BF_3MoN_{10}O$: C, 44.25; H, 4.52; N, 22.44. Found: C, 43.83; H, 4.48; N 21.94.

*1-Methyl-2-phenyl-6-(trifluoromethyl)-1,2-dihydropyridine (**12**).* Compound **4** (250 mg, 0.357 mmol) and acetone (7.5 mL) were combined in a 4 dram vial containing a stir bar. $FeCp_2PF_6$ (119 mg, 0.359 mmol) was dissolved in acetone (7.5 mL) in a separate 4 dram vial, and then this solution was transferred to the vial containing **4**. The reaction mixture was stirred for 15 min. The reaction mixture was then diluted with DCM (40 mL) and extracted with saturated Na_2CO_3 (2 × 30 mL). The organic layer was dried with Na_2SO_4, and

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the solids removed by filtration. The filtrate was evaporated onto silica and purified by Combiflash flash chromatography on a 4 g silica column, using a 100% hexanes mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **12** as a colorless oil (65 mg, 76%). ^{1}H NMR (d_3-acetonitrile, δ): 7.36 (m, 4H, H8+H9), 7.30 (m, 1H, H10), 6.01 (ddt, J = 9.4 Hz, 5.9 Hz, 1.0 Hz, 1H, H4), 5.51 (ddt, J = 9.4 Hz, 5.8 Hz, 1.0 Hz, 1H, H5), 5.48 (dt, J = 5.8 Hz, 1.0 Hz, 1H, H3), 5.00 (d, J = 5.9 Hz, 1H, H6), 2.89 (s, 3H, H7). ^{13}C NMR (d_3-Acetonitrile, δ): 143.2 (C8a), 133.8 (q, J = 30.2 Hz, C2), 129.6 (C8), 128.8 (C10), 127.1 (C9), 122.9 (q, J = 273 Hz, CF_3), 121.5 (C5), 121.4 (C4), 100.1 (q, J = 6.9 Hz, C3), 65.2 (C6), 38.6 (C7).

*2-Benzyl-1-methyl-6-(trifluoromethyl)-1,2-dihydropyridine (**13**).* Compound **5** (179 mg, 0.250 mmol) and acetone (5.0 mL) were combined in a 4 dram vial containing a stir bar. $FeCp_2PF_6$ (83 mg, 0.251 mmol) was dissolved in acetone (5.0 mL) in a separate 4 dram vial, and then this solution was transferred to the vial containing **5**. The reaction mixture was stirred for 15 min. The reaction mixture was then diluted with DCM (30 mL) and extracted with saturated Na_2CO_3 (2 × 20 mL). The organic layer was dried with Na_2SO_4 and the solids removed by filtration. The filtrate was evaporated onto silica, and purified by Combiflash flash chromatography on a 4 g silica column, using a 100% hexanes mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **13** as a colorless oil (51 mg, 80%). ^{1}H NMR (d-chloroform, δ): 7.30 (m, 2H, H10), 7.24 (m, 1H, H11), 7.20 (m, 2H, H9), 6.00 (dd, J = 9.1 Hz, 5.7 Hz, 1H, H4), 5.67 (d, J = 5.7 Hz, 1H, H3), 5.28 (dd, J = 9.1 Hz, 6.1 Hz, 1H, H5), 3.91 (ddd, J = 7.9 Hz, 6.2 Hz, 6.1 Hz, 1H, H6), 2.80 (dd, J = 13.2 Hz, 7.9 Hz, 1H, H8), 2.74 (s, 3H, H7), 2.61 (dd, J = 13.2 Hz, 6.2 Hz, 1H, H8′). ^{13}C NMR (d-chloroform, δ): 137.9 (C9a), 132.5 (q, J = 31.1 Hz, C2), 129.8 (C9), 128.4 (C10), 126.3 (C11), 121.7 (C4), 121.9 (q, J = 274 Hz, CF_3), 118.7 (C5), 101.7 (q, J = 6.6 Hz, C3), 63.5 (C6), 39.6 (C7), 38.3 (C8).

*1-Methyl-2-(4-(trifluoromethoxy)benzyl)-6-(trifluoromethyl)-1,2-dihydropyridine (**14**).* Compound **6** (195 mg, 0.244 mmol) and acetone (5.0 mL) were combined in a 4 dram vial containing a stir bar. $FeCp_2PF_6$ (81 mg, 0.245 mmol) was dissolved in acetone (5.0 mL) in a separate 4 dram vial, and then this solution was transferred to the vial containing **6**. The reaction mixture was stirred for 15 min. The reaction mixture was then diluted with DCM (30 mL) and extracted with saturated Na_2CO_3 (2 × 20 mL). The organic layer was dried with Na_2SO_4, and the solids removed by filtration. The filtrate was evaporated onto silica, and purified by Combiflash flash chromatography on a 4 g silica column, using a 100% hexanes mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **14** as a colorless oil (68 mg, 83%). ^{1}H NMR (d_3-acetonitrile, δ): 7.29 (m, 2H, H9), 7.21 (m, 2H, H10), 6.00 (dd, J = 9.0 Hz, 5.6 Hz, 1H, H4), 5.67 (d, J = 5.6 Hz, 1H, H3), 5.32 (dd, J = 9.0 Hz, 6.0 Hz, 1H, H5), 4.01 (dt, J = 7.9 Hz, 6.0 Hz, 1H, H6), 2.72 (dd, J = 13.2 Hz, 7.8 Hz, 1H, H8), 2.70 (s, 3H, H7), 2.64 (dd, J = 13.2 Hz, 6.0 Hz, 1H, H8′). ^{13}C NMR (d_3-acetonitrile, δ): 148.0 (C10a), 132.5 (q, J = 31.6 Hz, C2), 136.6 (C9a), 131.0 (C9), 122.0 (C4), 121.9 (q, J = 274 Hz, CF_3), 120.9 (C10), 120.7 (q, J = 256 Hz, OCF_3), 118.3 (C5), 102.1 (q, J = 6.3 Hz, C3), 63.3 (C6), 39.8 (C7), 37.5 (C8).

*2-(Benzo[d][1,3]dioxol-5-yl)-1-methyl-6-(trifluoromethyl)-1,2-dihydropyridine (**15**).* Compound **7** (316 mg, 0.424 mmol) and acetone (4.0 mL) were combined in a 4 dram vial containing a stir bar. $FeCp_2PF_6$ (140 mg, 0.424 mmol) was dissolved in acetone (7.5 mL) in a separate 4 dram vial, and then this solution was transferred to the vial containing **7**. The reaction mixture was stirred for 15 min. The reaction mixture was then diluted with DCM (30 mL) and extracted with saturated Na_2CO_3 (2 × 20 mL). The organic layer was dried with Na_2SO_4 and the solids removed by filtration. The filtrate was evaporated onto silica and purified by Combiflash flash chromatography on a 12 g silica column using a 100% hexanes mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **15** as a colorless oil (81 mg, 67%). ^{1}H NMR (d_1-chloroform, δ): 6.91 (t, J = 0.9 Hz, 1H, H10), 6.76 (d, J = 0.9 Hz, 2H, H8+H9), 5.98 (dd, J = 9.4 Hz, 5.9 Hz, 1H, H4), 5.95 (m, 2H, H11), 5.39 (d, J = 5.9 Hz, 1H, H3), 5.38 (dd, J = 9.4 Hz, 5.4 Hz, 1H, H5), 4.86 (d, J = 5.4 Hz, 1H, H6), 2.85 (s, 3H, H7). ^{13}C NMR (d_1-chloroform, δ): 148.3 (C10a), 147.5 (C9a), 136.8 (C8a), 133.5 (q, J = 30.4 Hz, C2), 123.0 (q, J = 273 Hz, CF_3), 120.8 (C5), 120.2 (C4), 119.5 (C8), 108.2 (C9), 107.3 (C10), 101.2 (C11), 98.1 (C3), 65.5 (C6), 37.9 (C7).

*2,9-Dimethyl-8-phenyl-4-(trifluoromethyl)-3a,4,7,7a-tetrahydro-1H-4,7-(epiminomethano)isoindole-1,3(2H)-dione (**16**).* Compound **12** (33.0 mg, 0.138 mmol) and NMM (250 mg, 2.25 mmol) were dissolved in MeCN (1.5 mL) in a 1 dram vial. The reaction mixture was heated at +80 °C in an oil bath for 16 h and then evaporated in vacuo onto 1 g silica. The crude product was purified by Combiflash flash chromatography on a 12 g silica column, using a 0−100% EtOAC in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **16** as a colorless oil, which spontaneously crystallized (41 mg, 85%). ^{1}H NMR (d-chloroform, δ): 7.30 (m, 4H, H11 + H12), 7.24 (m, 1H, H13), 6.45 (dd, J = 8.4 Hz, 1.3 Hz, 1H, H7), 5.96 (dd, J = 8.4 Hz, 6.5 Hz, 1H, H8), 3.73 (d, J = 8.2 Hz, 1H, H3), 3.55 (d, J = 1.4 Hz, 1H, H6), 3.43 (m, 1H, H5), 3.30 (dd, J = 8.2 Hz, 3.5 Hz, 1H, H4), 2.92 (s, 3H, H10), 2.46 (s, 3H, H9). ^{13}C NMR NMR (d-chloroform, δ): 176.6 (Imide CO), 174.5 (Imide CO), 141.6 (C11a), 130.6 (C7), 130.5 (C8), 128.3 (C12), 127.6 (C13), 127.1 (C11), 125.2 (q, J = 282 Hz, CF_3), 67.8 (C6), 63.8 (q, J = 28.6 Hz, C2), 43.3 (C4), 39.5 (C5), 38.9 (C3), 37.3 (C9), 25.2 (C10).). ESI-MS: obsd (%), calcd (%), ppm, $(M + H)^+$: 351.1318 (100), 351.1315(100), 0.8.

*8-Benzyl-2,9-dimethyl-4-(trifluoromethyl)-3a,4,7,7a-tetrahydro-1H-4,7-(epiminomethano)isoindole-1,3(2H)-dione (**17**).* Compound **13** (50.0 mg, 0.197 mmol) and NMM (219 mg, 1.97 mmol) were dissolved in MeCN (1.5 mL) in a 1 dram vial. The reaction mixture was heated at +80 °C in an oil bath for 24 h and then evaporated in vacuo onto 1 g silica. The crude product was purified by Combiflash flash chromatography on a 12 g silica column, using a 0−100% EtOAC in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **17** as a colorless oil, which was crystallized by dissolution in minimal Et_2O followed by slow evaporation (67 mg, 91%). ^{1}H NMR (d_3-acetonitrile, δ): 7.32 (m, 2H, H13), 7.25 (m, 1H, H14), 7.21 (m, 2H, H12), 6.37 (dd, J = 8.4 Hz, 1.6 Hz, 1H, H7), 6.33 (m, 1H, H8), 3.62 (d, J = 8.0 Hz, 1H, H3), 3.01 (dd, J = 8.0 Hz, 3.4 Hz, 1H, H4), 2.89 (m, 1H, H5), 2.76 (s, 3H, H10), 2.69 (dd, J = 13.4 Hz, 5.0 Hz, 1H, H11), 2.56 (ddd, J = 8.9 Hz, 5.7 Hz, 1.2 Hz, 1H, H6), 2.35 (dd, J = 13.4 Hz, 8.9 Hz, 1H, H11′), 2.33 (s, 3H, H9). ^{13}C NMR (d_3-acetonitrile, δ): 177.8 (imide CO), 175.9 (imide CO), 139.6 (C12a), 132.5 (C8), 130.4 (q, J = 3.7 Hz, C7), 130.3 (C12), 129.4 (C13), 127.3 (C14), 126.5 (q, J = 282 Hz, CF_3), 68.0 (C6), 64.6 (q, J = 27.6 Hz, C2), 43.0 (C4), 42.2 (C11), 39.6 (C3), 37.8 (C9), 35.6 (C5), 25.1 (C10). ESI-MS: obsd (%), calcd (%), ppm, $(M + H)^+$: 365.1475 (100), 365.1471 (100), 1.1.

*2,9-Dimethyl-8-(4-(trifluoromethoxy)benzyl)-4-(trifluoromethyl)-3a,4,7,7a-tetrahydro-1H-4,7-(epiminomethano)isoindole-1,3(2H)-dione (**18**).* Compound **14** (77.0 mg, 0.228 mmol) and NMM (254 mg, 2.29 mmol) were dissolved in MeCN (2.0 mL) in a 1 dram vial. The reaction mixture was heated at +80 °C in an oil bath for 24 h and then evaporated in vacuo onto 1 g silica. The crude product was purified by Combiflash flash chromatography on a 12 g silica column, using a 0−100% EtOAC in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **18** as a colorless oil, which was crystallized by dissolution in minimal Et_2O followed by slow evaporation (101 mg, 98%). ^{1}H NMR (d_6-acetone, δ): 7.41 (m, 2H, H13), 7.29 (d, J = 8.0 Hz, 2H, H12), 6.41 (m, 2H, H7+H8), 3.80 (d, J = 8.1 Hz, 1H, H3), 3.18 (dd, J = 8.1 Hz, 3.4 Hz, 1H, H4), 3.04 (m, 1H, H5), 2.77 (s, 3H, H10), 2.74 (dd, J = 12.8 Hz, 6.1 Hz, 1H, H11), 2.71 (m, 1H, H6), 2.51 (dd, J = 12.8 Hz, 7.8 Hz, 1H, H11′), 2.35 (s, 3H, H9). ^{13}C NMR (d_6-acetone, δ): 177.3 (imide CO), 175.2 (imide CO), 148.5 (C13a), 139.1 (C12a), 132.4 (C8), 132.0 (C12), 130.3 (q, J = 3.7 Hz, C7), 126.4 (q, J = 282 Hz, CF_3), 121.9 (C13), 121.5 (q, J = 255 Hz, OCF_3) 68.0 (C6), 64.5 (q, J = 27.6 Hz, C2), 42.9 (C4), 41.7 (C11), 39.6 (C3), 37.9 (C9),

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35.8 (C5), 24.9 (C10). ESI-MS: obsd (%), calcd (%), ppm, $(M + H)^+$: 449.1295 (100), 449.1294 (100), 0.2.

*8-(Benzo[d][1,3]dioxol-5-yl)-2,9-dimethyl-4-(trifluoromethyl)-3a,4,7,7a-tetrahydro-1H-4,7-(epiminomethano)isoindole-1,3(2H)-dione (**19**).* Compound **15** (56.0 mg, 0.198 mmol) and NMM (219 mg, 1.97 mmol) were dissolved in MeCN (1.5 mL) in a 1 dram vial. The reaction mixture was heated at +80 °C in an oil bath for 24 h and then evaporated in vacuo onto 1 g silica. The crude product was purified by Combiflash flash chromatography on a 12 g silica column, using a 0−100% EtOAC in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **19** as a colorless oil, which was crystallized by dissolution in minimal Et_2O followed by slow evaporation. (68 mg, 87%). ^{1}H NMR (d_2-methylene chloride, δ): 6.83 (d, J = 1.7 Hz, 1H, H11), 6.78 (dd, J = 8.0 Hz, 1.7 Hz, 1H, H13), 6.73 (d, J = 8.0 Hz, 1H, H12), 6.42 (dd, J = 8.4 Hz, 1.4 Hz, 1H, H7), 5.98 (dd, J = 8.4 Hz, 6.5 Hz, 1H, H8), 5.91 (m, 2H, H14), 3.68 (d, J = 8.1 Hz, 1H, H3), 3.47 (d, J = 1.3 Hz, 1H, H6), 3.34 (m, 1H, H5), 3.27 (dd, J = 8.1 Hz, 3.5 Hz, 1H, H4), 2.87 (s, 3H, H10), 2.42 (s, 3H, H9). ^{13}C NMR (d_2-methylene chloride, δ): 176.8 (imide CO), 174.8 (imide CO), 148.1 (C11a), 147.9 (C12a), 136.6 (C13a), 131.2 (C7), 130.8 (C8), 125.8 (q, J = 282 Hz, CF_3), 120.7 (C13), 108.3 (C11), 108.1 (C12), 101.7 (C14), 67.8 (C6), 64.2 (q, J = 28.4 Hz, C2), 43.7 (C4), 40.1 (C3), 39.3 (C9), 37.4 (C5), 25.3 (C10). ESI-MS: obsd (%), calcd (%), ppm, $(M + H)^+$: 395.1216 (100), 395.1213 (100), 0.8.

*3-(Benzo[d][1,3]dioxol-5-yl)-2-methyl-1-(trifluoromethyl)-2-azabicyclo[2.2.2]oct-7-ene-5,6-dicarbonitrile (**20A**).* Compound **15** (81 mg, 0.286 mmol) and fumaronitrile (106 mg, 1.36 mmol) were dissolved in MeCN (1.0 mL) in a small test tube containing a stir bar. The reaction mixture was placed in an oil bath at +80 °C and heated for 72 h. After heating, the reaction solution, containing a 2:1 mixture of diastereomers, was evaporated onto silica and purified by Combiflash flash chromatography on a 12 g silica column using 0−100% EtOAc in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield a colorless oil, which was crystallized to yield exclusively **20A** by dissolution in minimal Et_2O followed by slow evaporation. (48 mg, 46%). ^{1}H NMR (d_2-methylene chloride, δ): 6.79 (m, 1H, H10), 6.75 (m, 2H, H11/H12), 6.68 (dd, J = 8.4 Hz, 1.3 Hz, 1H, H7), 6.28 (dd, J = 8.4 Hz, 6.5 Hz, 1H, H8), 5.93 (m, 2H, H13), 3.97 (d, J = 1.9 Hz, 1H, H6), 3.74 (d, J = 5.2 Hz, 1H, H3), 3.17 (m, 1H, H5), 3.09 (dd, J = 5.2 Hz, 2.9 Hz, 1H, H4), 2.49 (s, 3H, H9). ^{13}C NMR (d_2-methylene chloride, δ): 148.3 (C10a), 147.8 (C12a), 134.9 (C11a), 132.7 (C8), 131.8 (C7), 125.0 (q, J = 283 Hz, CF_3), 119.5 (C11), 118.3 (CN), 117.3 (CN), 108.5 (C10), 108.0 (C12), 101.9 (C13), 63.7 (C6), 64.2 (q, J = 27.5 Hz, C2), 40.6 (C5), 36.8 (C9), 33.9 (C4), 28.3 (C3). ESI-MS: obsd (%), calcd (%), ppm, $(M + H)^+$: 362.1113 (100), 362.1111 (100), 0.6.

*3-Benzyl-2-methyl-1-(trifluoromethyl)-2-azabicyclo[2.2.2]oct-7-ene-6-carbonitrile (**21A**).* Compound **13** (158 mg, 0.624 mmol) was dissolved in neat acrylonitrile (850 mg, 16.0 mmol) in a small test tube containing a stir bar. The reaction mixture was heated in an oil bath at +77 °C for 96 h and then evaporated onto silica and purified by Combiflash flash chromatography on a 12 g silica column using 0−100% EtOAc in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **21A** as a colorless oil (118 mg, 62%). To obtain a crystal for X-ray diffraction, the hydrochloride salt of **21A** was prepared with HCl. ^{1}H NMR (d_3-MeCN, δ): 7.30 (m, 2H, H13), 7.22 (m, 1H, H14), 7.18 (m, 2H, H12), 6.63 (dd, J = 8.5 Hz, 1.4 Hz, 1H, H8), 6.53 (dd, J = 8.5 Hz, 6.9 Hz, 1H, H7), 3.56 (dd, J = 9.8 Hz, 4.3 Hz, 1H, H3), 2.53 (m, 1H, H5), 2.60 (dd, J = 13.2 Hz, 5.7 Hz, 1H, H11), 2.48 (m, 1H, H6), 2.33 (dd, J = 13.4 Hz, 8.8 Hz, 1H, H11′), 2.28 (s, 3H, H9), 2.10 (ddd, J= 13.2 Hz, 9.8 Hz, 2.6 Hz, 1H, H4), 1.59 (ddd, J= 13.2 Hz, 4.3 Hz, 3.6 Hz, 1H, H4′). ^{13}C NMR (d_3-MeCN, δ): 139.7 (C12a), 136.0 (C8), 130.2 (C12), 129.6 (q, J = 3.4 Hz, C7), 129.3 (C13), 127.2 (C14), 126.6 (q, J = 283 Hz, CF_3), 121.4 (C10), 69.1 (C6), 64.2 (q, J = 26.4 Hz, C2), 42.6 (C11), 37.9 (C9), 32.8 (C5), 30.9 (C4), 23.2 (C3).

*Methyl 3-benzyl-2-methyl-1-(trifluoromethyl)-2-azabicyclo[2.2.2]oct-7-ene-6-carboxylate (**22**).* Compound **13** (200 mg, 0.790 mmol) was dissolved in neat methyl acrylate (900 mg, 10.4 mmol) in a small test tube containing a stir bar. The reaction mixture was heated in an oil bath at +77 °C for 96 h and then evaporated onto silica and purified by Combiflash flash chromatography on a 12 g silica column using 0−100% EtOAc in hexanes gradient mobile phase. The fractions containing the desired product were evaporated in vacuo to yield **22** as a colorless oil (188 mg, 70%). To obtain a crystal for X-ray diffraction, the hydrochloride salt of **22** was prepared with HCl (dr = 97:3). ^{1}H NMR (d_3-MeCN, δ): 7.30 (m, 2H, H13), 7.21 (m, 1H, H14), 7.19 (m, 2H, H12), 6.49 (dd, J = 8.5 Hz, 6.9 Hz, 1H, H8), 6.28 (dd, J = 8.5 Hz, 1.3 Hz, 1H, H7), 3.57 (s, 3H, H10), 3.36 (dd, J = 9.4 Hz, 5.0 Hz, 1H, H3), 2.64 (dd, J = 13.1 Hz, 5.0 Hz, 1H, H11), 2.46 (m, 1H, H5), 2.40 (m, 1H, H6), 2.31 (dd, J = 13.1 Hz, 9.2 Hz, 1H, H11′), 2.35 (s, 3H, H9), 1.77 (ddd, J= 12.7 Hz, 9.4 Hz, 3.0 Hz, 1H, H4), 1.59 (ddd, J= 12.7 Hz, 5.0 Hz, 3.1 Hz, 1H, H4′). ^{13}C NMR (d_3-MeCN, δ): 174.2 (ester CO), 140.1 (C12a), 134.2 (C8), 130.2 (C12), 129.5 (q, J = 3.2 Hz, C7), 129.3 (C13), 127.1 (C14), 127.1 (q, J = 282 Hz, CF_3), 69.2 (C6), 64.8 (q, J = 26.7 Hz, C2), 52.4 (C10), 42.7 (C11), 37.2 (C9), 36.9 (C3), 33.0 (C5), 30.2 (C4).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b10781.

Compounds **3**, **4**, **6**, **7**, **8**, **9**, **10** (CIF)

Compounds **11**, **17**, (R)-**17**, **18**, **19**, **20A**, **21A·HCl**, and **22·HCl** (CIF)

^{1}H and ^{13}C NMR of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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