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Michael−Michael Ring-Closure Reactions for a Dihapto-Coordinated Naphthalene Complex of Molybdenum

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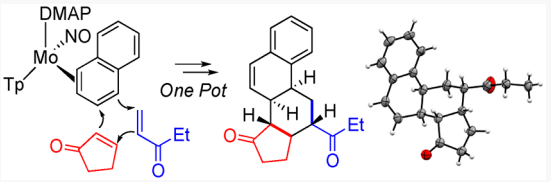
ABSTRACT: The complex MoTp(NO)(DMAP)(η^2-naphthalene) (**1**; DMAP = 4-(dimethylamino)pyridine; Tp = tris(pyrazolyl)borate) is demonstrated to undergo Michael−Michael ring-closure (MIMIRC) reactions promoted by trimethylsilyltriflate. The resulting hexahydrophenanthrenes are formed stereoselectively, with isolation of a single dominant isomer. Combining the MIMIRC sequence with an oxidative decomplexation step, the final tricyclics can be synthesized from the naphthalene complex with overall yields between 19 and 50% (for four steps). This reaction sequence is shown to be capable of producing a steroidal core directly from naphthalene, providing access to a biologically relevant carbon framework.



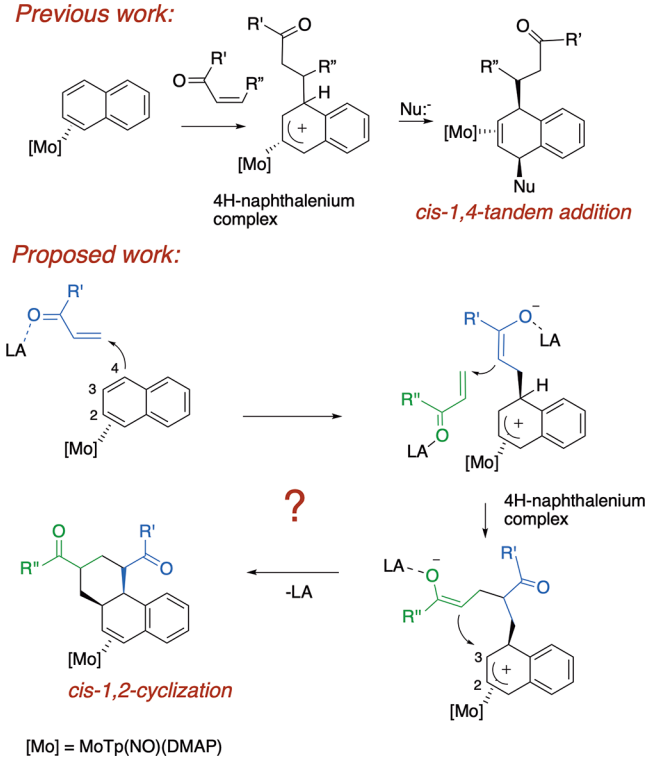
INTRODUCTION

The Michael reaction, which involves enolate addition to an α,β-unsaturated carbonyl, is one of the most useful and well-recognized C−C bond-forming reactions in organic synthesis.[1−3] Pioneering studies by Posner and others have explored a variant of this reaction where the enolate resulting from the conjugate addition undergoes a second Michael addition, and that resulting enolate terminates in a new six-membered ring.[4] These so-called Michael−Michael ring-closure (MIMIRC) reactions[5−11] are normally enolate-driven, but we questioned whether it would be possible to promote such a reaction sequence with an organometallic arene complex. We have a long-standing interest in promoting novel organic reactions of aromatic molecules through their dihapto-coordination,[12−15] and we recently investigated the ability of the complex {MoTp(NO)(DMAP)} (DMAP = 4-(dimethylamino)pyridine; Tp = tris(pyrazolyl)borate) to dearomatize naphthalene via a 1,4-tandem addition reaction sequence (Scheme 1).[16,17] We questioned whether this highly pi-basic metal complex was sufficiently electron-donating to promote a MIMIRC sequence, using this common aromatic hydrocarbon as the initial nucleophile (Scheme 1). Herein we describe our attempts to effect such reactions, both where the Michael acceptors are the same (R′ = R″) and when they are different (R′ ≠ R″), using a Lewis acid to initiate the process.

RESULTS

In order for the desired sequence to be successful, the molybdenum complex would have to sufficiently activate the naphthalene for the initial conjugate addition reaction at C4 (Scheme 1) and stabilize the 4H-naphthalenium product long enough for the second enolate to close at C3. The complex MoTp(NO)(DMAP)(η^2-naphthalene) (**1**) was prepared on a 10 g scale according to literature methods as a 3:1 mixture of

Scheme 1. Proposed Acid-Promoted Michael−Michael Ring-Closure Sequence with an η^2-Coordinated Naphthalene



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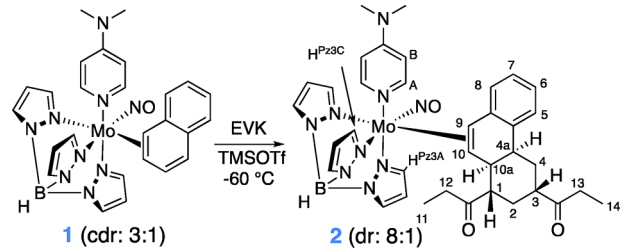
coordination diastereomers by reducing MoTp(NO)(DMAP)-(I) with magnesium or sodium in the presence of naphthalene.[16,17]

In an initial attempt to induce a MIMIRC reaction under neutral conditions, a 0.05 M solution of the naphthalene complex **1** and an excess of ethyl vinyl ketone (EVK) was stirred at 25 °C. Monitoring this reaction with cyclic voltammetry showed no change over several days. We next attempted to induce reactivity using various Lewis acids to activate the α,β-unsaturated carbonyl. The addition of either LiOTf or $BF_3{\cdot}OEt_2$ yielded only free naphthalene after treatment with an oxidant (I_2 or air). However, treating a propionitrile solution of **1** and EVK (−60 °C) with trimethylsilyltriflate (TMSOTf) generated a vivid red solution, indicative of a π-allyl complex of {MoTp(NO)-(DMAP)}.[17] After it was stirred for an additional hour, the solution was loaded onto an alumina column, and compound **2** was isolated as a yellow solid (45%). In agreement with the 1,2-dihydronaphthalene complex of {MoTp(NO)(DMAP)},[16,17] a solution of compound **2** showed a chemically irreversible anodic wave with $E_{p,a}$ = +0.16 V (100 mV/s; vs normal hydrogen electrode (NHE)), and IR absorbance data for this material included a peak corresponding to the Mo^0-NO stretch at 1567 cm^{-1}. Two-dimensional (2D) NMR data for **2** (COSY, NOESY, HSQC, HMBC) were fully consistent with the proposed MIMIRC product, present as an 8:1 mixture of diastereomers.

We anticipated that the metal complex would control the stereochemistry of the additions to the naphthalene framework (C4a and C10a), with both electrophilic addition and nucleophilic addition occurring *anti* to metal coordination. However, two additional stereocenters alpha to the carbonyl groups (C1, C3) are also formed selectively. We speculate that the latter preference is a result of an acid-catalyzed epimerization of these carbons, occurring *after* the initial C−C bond-forming event. This epimerization, via enol intermediates, would allow the carbonyl groups to adopt equatorial positions, as shown in Figure 1. This geometry was ultimately confirmed from X-ray diffraction (XRD) data. A detailed analysis of both XRD and NMR data for **2** is presented in the Supporting Information.

The MIMIRC sequence that rendered compound **2** is believed to take place by the mechanism shown in Scheme 2, wherein the α,β-unsaturated ketone is first activated via silylation of the carbonyl, followed by conjugate addition of the nucleophilic η^2-naphthalene ligand of **1** to yield **i**. The resulting silylated enolate can then undergo a second conjugate addition with tetramethylsilane (TMS)-activated EVK (R = Et) to yield intermediate **ii**. In both intermediates **i** and **ii**, the η^2-naphthalenium fragment is stabilized by molybdenum, forming a highly asymmetric π-allyl complex,[17] which can serve as the electrophile in the final step of the annulation process (Scheme 2).

The optimization of the synthesis of **2** was performed by running the reaction under various conditions (time, temperature, addition order, and concentration), then quenching any acidic species with an excess of triethylamine (TEA). The reaction mixture was then oxidized with iodine to liberate the desired product **3**, which upon purification crystallizes from solution (Figure 2). ^{1}H NMR analysis of the crude reaction mixture revealed that two substitution products (**4** and **5**, Figure 3)[18] were often formed during the course of the



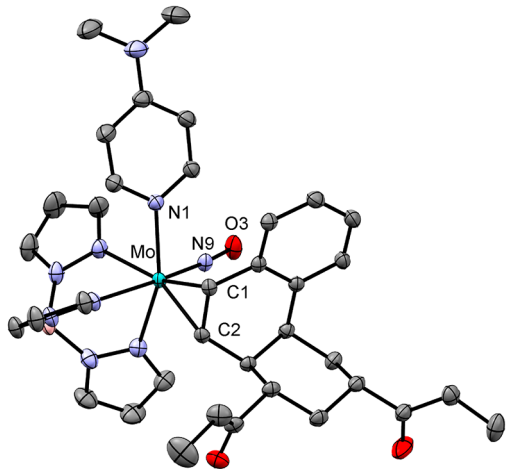
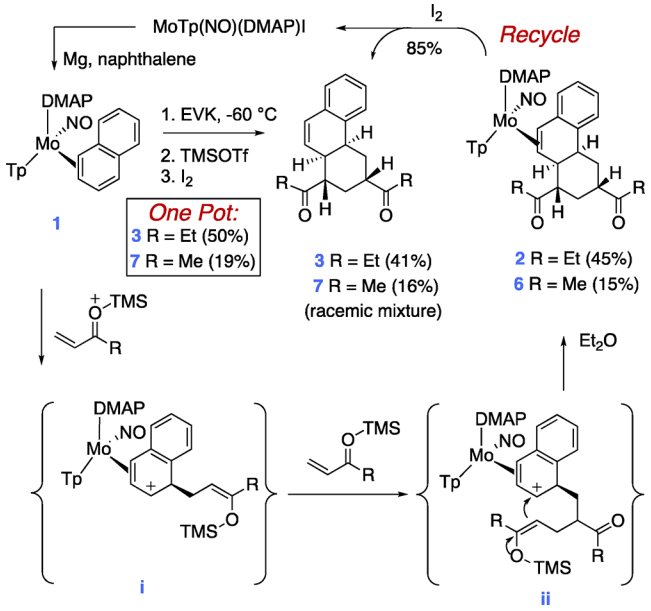


Figure 1. Synthesis, numbering scheme (major isomer; dr = 8:1), and ORTEP diagram of compound **2** (50% ellipsoidal probability, cocrystallized THF molecules and H's omitted for clarity).

Scheme 2. Proposed Mechanism of a Michael−Michael Ring Closure with EVK



reaction, along with free naphthalene and the desired product **3** (vide infra).

To confirm that the substituted naphthalene complexes **4**[18] and **5**[19] were formed during the initial reaction period and not formed from decomposition of the tricyclic **3** or its molybdenum precursor **2**, an isolated sample of **3** was stirred under similar reaction conditions and monitored via ^{1}H NMR. The absence of **4** or **5** in this experiment indicates that these

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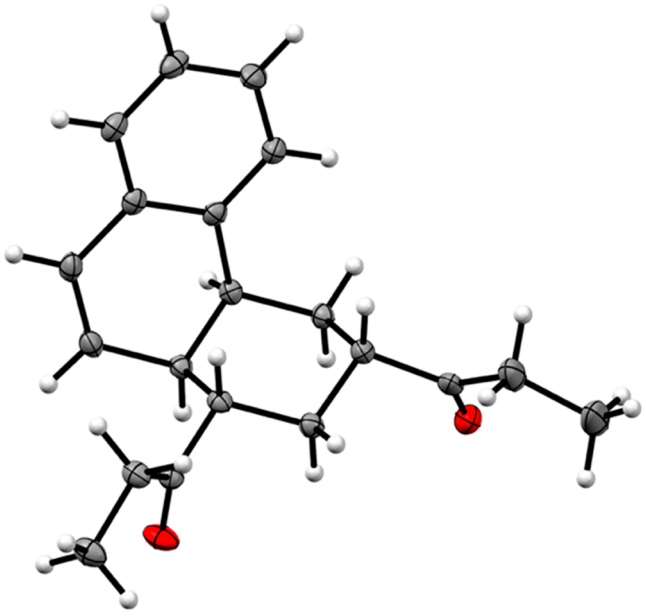

Figure 2. ORTEP diagram of compound **3** (50% ellipsoidal probability; H_2O omitted).

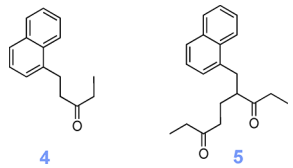

Figure 3. Side-products from the MIMIRC reaction.

compounds are formed as a result of the silyl enolate intermediates **i** or **ii** reacting with an acidic impurity such as HOTf. With the reaction stalled, subsequent treatment with base effects the deprotonation of the purported allyl species to form naphthalenes **4** and **5**. To help mitigate adventitious proton sources, 2,6-di-*tert*-butylpyridine (DTBP) was added to the reaction mixture. With this addition, the formation of **4** and **5** was minimized, and the isolated overall yield of **2** rose to 45% (77% per C−C bond formed).

With an optimized procedure developed, a variety of other ketone Michael acceptors (2-cyclopenten-1-one, 2-cyclohexen-1-one, 3-penten-2-one, 4-hexen-3-one, 3-methyl-3-buten-2-one) were screened to determine their compatibility with this procedure. Unfortunately, this MIMIRC sequence was found to be incompatible with further α-vinyl substitution or substitution at the β-position of the Michael acceptor. The additional bulk of even these sterically undemanding substituents apparently slows the conjugate addition step significantly, with the result being that the metal is oxidized before the more robust allyl species can form. The reaction also fails with α,β-unsaturated esters (methyl acrylate, α-methylene-γ-butyrolactone). In these reactions, only the starting complex was recovered, indicating that the molybdenum backbonding into the naphthalene π^* orbital is not sufficient to make it a competent nucleophile for these less electrophilic α,β-unsaturated esters. However, replacement of EVK with methyl vinyl ketone (MVK) did yield the desired tricyclic **6**, albeit in low overall yield (15%). Suspecting that metal oxidation was primarily responsible for the low yield, the MVK and EVK addition reactions were attempted with a metal system established to be more resistant to oxidation, {WTp(NO)(PMe_3)}.[20] Unfortunately, the tendency of this complex to protonate at C4 led only to the formation of the parent 4*H*-naphthalenium species.[21]

With the isolation of the complexes **2** and **6**, the liberation of their hexahydrophenanthrene organic ligands was pursued. The oxidative decomplexation of the organic products directly from **2** and **6** was accomplished using iodine, yielding **3** and **7** in modest yields (**3**: 41% **7**: 16%), but with good recovery of the Mo(I) precursor, MoTp(NO)(DMAP)(I) (85% average yield). Ultimately single-crystal (SC) XRD data confirmed the identity of **3** (Figure 2). For this compound, a substantially higher *overall* yield (50% overall from **1** for four steps; average 84% per step; 200 mg final product) can be achieved via an iodine oxidation of the evaporated reaction mixture, thereby bypassing the isolation of **2**. These observations indicate that a significant amount of product remains in solution during precipitation of the MIMIRC product complex (**2**). A similar approach with **6** provided a one-pot yield of 19% for the MVK-derived compound **7** (19% for four steps; average 66% per step).

To further explore the promise of this method, A+B MIMIRC reactions from **1** were also investigated. Our approach was to stop the reaction at enolate **i** (Scheme 2) and then introduce the second Michael acceptor to complete the ring closure. This was attempted by limiting the initial Michael acceptor (e.g., EVK) to one molar equivalent to prevent a second addition from occurring. To a −60 °C propionitrile solution of **1**, either MVK or EVK was added (1.0 equiv), along with DTBP and TMSOTf; after it was stirred at −60 °C for 1 min, a solution of either MVK, cyclopentenone, or cyclohexenone was added, and then the reaction mixture was left at −60 °C for 18 h.

The cleanest, highest yielding product of these A+B MIMIRC reactions was obtained when EVK was followed by MVK. This led to the isolation of the metal complex **8** in 30% yield. A solid-state structure of **8** was determined via single-crystal X-ray diffraction (Figure 4). As expected, the structure of **8** again shows a 1,3-diequatorial geometry of the acyl groups. Also observed is the *cis* ring fusion consistent with the C−C bond-forming reactions to naphthalene occurring *anti* to

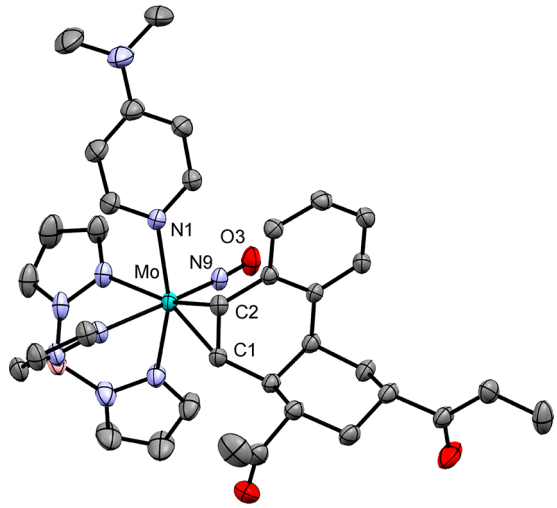

Figure 4. ORTEP diagram of **8** (50% ellipsoidal probability, cocrystallized THF molecule omitted for clarity).

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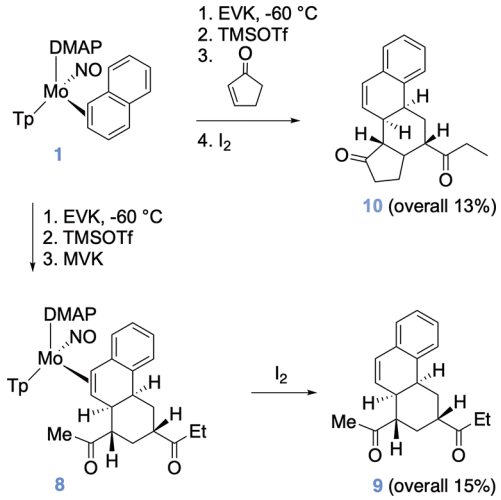
the metal center. Although the metal complex **8** can be isolated and oxidized, a higher mass recovery of the organic tricyclic **9** was accomplished by direct treatment of the reaction mixture with iodine. Compound **9** can be isolated from **1** in an *overall* yield of 15% (four steps; 62%/step average). The remaining mass is assumed to be made up from substituted naphthalenes analogous to **4** and **5** (Figure 3), but these byproducts were not pursued.

The reaction sequence was then repeated using EVK as the first Michael acceptor and cyclopent-2-en-1-one as the second (Scheme 3). Flash chromatography resulted in isolation of

Scheme 3. [A+B] MIMIRC Reactions[a]



[a]**9** and **10** are formed as racemic mixtures.

compound **10** in 13% *overall* yield as a single isomer, along with ~6% impurity of **5**. While this yield is low, we note that it still represents an average yield per step (4) of 60%.

A solid-state structure was determined from SC-XRD data (Figure 5). This structure confirms the presence of *cis*-BC and *cis*-CD ring fusions predicted by ^{1}H NMR data (Supporting Information), the trans relationship between H8 and H14, and the equatorial orientations of both acyl groups.

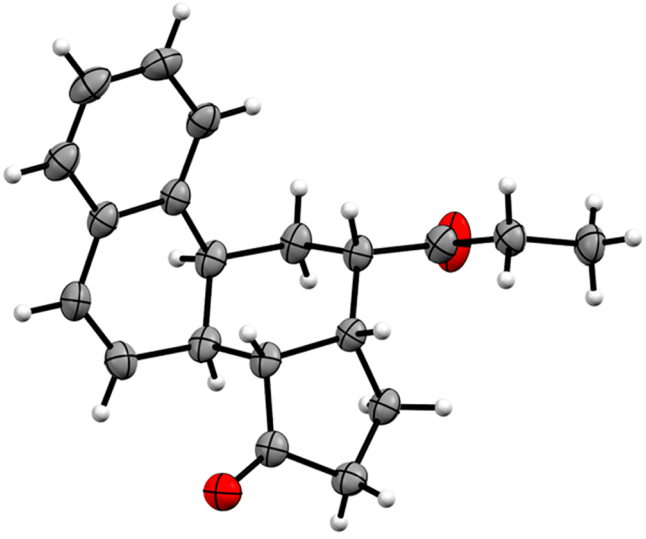


Figure 5. ORTEP diagram of **10** (50% ellipsoidal probability).

DISCUSSION

We have on rare occasion observed unintentional [A+A] MIMIRC reactions with other π-basic metal complexes of aromatic molecules. These were cases in which the aromatic ligand possessed a π-donor substituent that enhanced its nucleophilicity. For example, $[Os(NH_3)_5(\eta^2$-dimethylaniline$)]^{2+}$ undergoes a TBSOTf-promoted MIMIRC reaction with α-methylene-γ-butyrolactone to give a tetracyclic structure.[22] Similarly, $\{Os(NH_3)_5(\eta^2$-2-methylfuran$)\}^{2+}$ was shown to undergo MIMIRC reaction with furan and MVK, activated by boron trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$).[23] The resulting benzofuran skeleton was formed as a mixture of stereoisomers. Alternatively, ReTp(CO)(MeIm)(η^2-2-methoxynaphthalene) was found to undergo cyclization with methyl acrylate.[24] In this case, the stereocenters set by the metal were lost once the organic was liberated due to an elimination of the methoxy group. In none of these cases was a systematic study performed, nor was an A+B MIMIRC cyclization achieved.

To our knowledge, only one other example of the synthesis of a steroidal core from naphthalene has been reported. Berndt et al.[25] closed a pendant cyclopentanone ring using samarium diiodide. The isolation of **10** demonstrates the potential of the MIMIRC method with dihapto-coordinated aromatics. While the overall yield is moderate, *five new stereocenters and three C−C bonds are selectively formed from naphthalene* and simple enones in a one-pot procedure with average yields per step of 60−84% (four steps). Although a majority of naturally occurring steroidal cores have *trans*-BC and *trans*-CD ring fusions, steroidal cores with *cis*-fused BC rings have also attracted interest (I and II; Figure 6).[26−29] Investigations have shown that I and II have an affinity for estrogen receptors

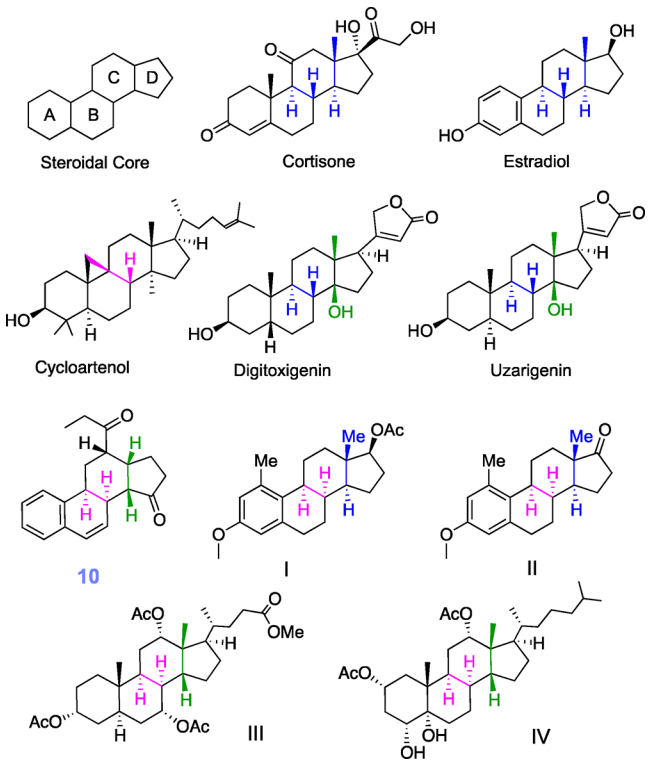


Figure 6. Examples of natural and unnatural steroid cores. Blue: *trans-B/C* and *trans-C/D* ring fusions (common); pink: *cis-B/C* ring fusion; green: *cis-C/D* ring fusion.

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while also providing osteoprotective action, a significant benefit for their use in hormone replacement therapy. Particularly noteworthy, a 2017 study found that compounds III and IV, which possess the same *cisB/C-anti-cisC/D* configuration as **10** were shown to be promising therapeutics for treatment of malaria.[30] Although this steroid configuration has not yet been widely studied, access to a library of such *cis-anticis* steroidal cores could provide insight into their potential as therapeutic agents. Furthermore, the compounds **3**, **7**, and **9** contain the same hexahydrophenanthrene core as compounds that have been studied for their efficacy as selective estrogen receptor-beta agonists.[31] These hexahydrophenanthrenes also share a similar core with aromatic abietane diterpenoids (i.e., carnosic acid, ferruginol, and abietic acid), which have been studied for their antimicrobial and antibacterial properties.[32,33]

Finally, we note that, because the molybdenum of **1** constitutes a stereogenic center, the potential exists to prepare enantioenriched variants of **3**, **7**, **9**, and **10**, as has been previously shown for molybdenum complexes of α,α,α-trifluorotoluene and 2-(trifluoromethyl)pyridine.[34,35] Unfortunately, initial attempts to form an enantioenriched form of **1** through reduction of (*S*)-MoTp(NO)(DMAP)(I) in the presence of naphthalene were unsuccessful, owing to the inability to achieve high enough concentrations of naphthalene to prevent racemization during the iodide/naphthalene exchange.[34,35]

CONCLUSION

Starting from the fully aromatic core of naphthalene, organic products with at least four new stereocenters and three new carbon−carbon bonds have been prepared and characterized. Tricyclic systems resulting from both [A+A] and [A+B] MIMIRC reactions have been performed in a one-pot procedure with average yields ranging from 60 to 84% per step. The oxidative decomplexation step regenerates a molybdenum(I) species that is the immediate precursor to the naphthalene complex (**1**). While naphthylboronic acid has been shown to undergo conjugate addition with MVK,[18] and **1** has previously been shown to react with enones,[17] this report appears to describe the first examples of naphthalene participating in a MIMIRC reaction sequence for any metal.

EXPERIMENTAL SECTION

General Methods. NMR spectra were obtained on a 600 or 800 MHz spectrometer (22−25 °C). All chemical shifts are reported in parts per million, and proton and carbon shifts are referenced to tetramethylsilane utilizing residual ^{1}H or ^{13}C 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 (DMAc) or acetonitrile (MeCN) solvent, and tetrabutylammonium hexafluorophosphate (TBAH) electrolyte (~0.5 M). All potentials are reported versus normal hydrogen electrode (NHE) 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 nuclear Overhauser effect (NOE) interactions. When unambiguous assignments were not possible, Tp protons were labeled as "Pz3/5 or Pz4". All $^{3}J_{HH}$ values for Pz protons are 2 (±0.2) Hz. BH ^{1}H NMR peaks (~4−5 ppm) are not identified due to their quadrupole broadening; IR data are used to confirm the presence of a BH group (~2500 cm^{-1}).

*Synthesis of TpMo(NO)(DMAP)(η^{2}-1,1′-((1S,3S,4aS,10aS)-1,2,3,4,4a,10a-Hexahydrophenanthrene-1,3-diyl)bis(propan-1-one)) (**2**).* Compound **1** (400 mg, 0.679 mmol), CH_3CH_2CN (15 mL), EVK (212 mg, 2.53 mmol), and DTBP (135 mg, 0.706 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (275 mg, 1.24 mmol) was added to the reaction mixture, and the resulting red solution was left stirring at −60 °C for 1 h. The reaction mixture was loaded onto 30 mL of dry basic alumina in a 60 mL coarse porosity fritted disc. The product was eluted with 1:1 Et_2O/tetrahydrofuran (THF) (100 mL) as a yellow band, collected as a yellow solution, and evaporated in vacuo. The resulting oil was dissolved in dichloromethane (DCM) (2 mL), and the product was precipitated in stirred pentane (100 mL). The precipitate was collected on a 15 mL fine porosity fritted disc, washed with pentane (3 × 10 mL), and dried for 1 h yielding the yellow solid **2** (230 mg, 45%). Cyclic voltammetry (CV) (DMAc) $E_{p,a}$ = +0.16 V (NHE). IR: ν(B−H) = 2480 cm^{-1}, ν(CO) = 1703 and 1620 cm^{-1}, ν(NO) = 1562 cm^{-1}. ^{1}H NMR (acetone-d_6, δ): 7.93 (1H, d Pz5A), 7.87 (1H, d, Pz3A), 7.79 (1H, d, Pz5B), 7.69 (1H, d, Pz3C), 7.41 (2H, bs, DMAP-A), 7.35 (1H, d, $^{3}J_{HH}$ = 7.9, H5), 6.98 (1H, d, Pz3B), 6.93 (1H, t, $^{3}J_{HH}$ = 7.5, H6), 6.86 (1H, t, $^{3}J_{HH}$ = 7.5, H7), 6.51 (2H, m, DMAP-B), 6.37 (1H, t, Pz4A), 6.35 (1H, t, Pz4C), 6.21 (1H, d, $^{3}J_{HH}$ = 7.2, H8), 6.09 (1H, t, Pz4B), 3.73 (1H, m, H4a), 3.31 (1H, d, $^{3}J_{HH}$ = 9.0, H9), 3.06 (6H, s, NMe), 2.84 (1H, m, H4), 2.77 (1H, m, H10a), 2.65 (3H, m, H3, H1, & H13/12), 2.55 (1H, m, H13/H12), 2.40 (1H, m, H13/H12), 2.30 (1H, m, H13/12), 2.07 (1H, dd, J = 9.0 and 2.6, H10), 1.87 (1H, m, H4), 1.70 (1H, m, H2), 1.52 (1H, q, $^{3}J_{HH}$ = 12.4, H2), 1.00 (3H, t, $^{3}J_{HH}$ = 7.3, H11/H14), 0.68 (3H, t, $^{3}J_{HH}$ = 7.2, H11/14). ^{13}C NMR (acetone-d_6, δ): 215.1 (CO), 213.8 (CO), 155.1 (DMAP-C), 150.7 (DMAP-A), 144.7 (Pz5), 143.6 (Pz3A), 142.1 (Pz3B), 141.2 (Pz3C), 137.6 (Pz5), 136.9 (Pz5), 135.8, 134.1, 128.1 (C8), 125.6 (C5), 125.1 (C7), 123.9 (C6), 108.3 (2C, DMAP-B), 106.9 (Pz4A/C), 106.8 (Pz4A/C), 106.5 (Pz4B), 70.9 (C10), 68.1 (C9), 55.0, 45.3, 43.1 (C10a), 39.3, 37.5, 35.9 (C4a), 34.3, 32.6 (C2), 31.0 (C4), 8.2 (C11/14), 7.8 (C11/14). SC-XRD determination details are in the Supporting Information.

*Synthesis of 1,1′-((1S,3S,4aS,10aS)-1,2,3,4,4a,10a-Hexahydrophenanthrene-1,3-diyl)bis(propan-1-one) (**3**).* Compound **1** (400 mg, 0.679 mmol), CH_3CH_2CN (15 mL), EVK (212 mg, 2.53 mmol), and DTBP (135 mg, 0.706 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (275 mg, 1.24 mmol) was added to the reaction mixture, and the resulting red solution was left to stir at −60 °C for 1 h. The reaction

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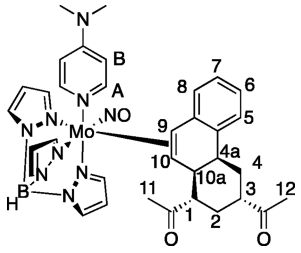
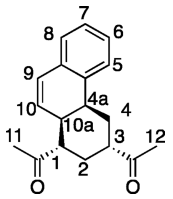
mixture was loaded onto 30 mL of dry basic alumina in a 60 mL coarse porosity fritted disc. The product was eluted with 1:1 Et_2O/THF (100 mL) as a yellow band, collected as a yellow solution, and evaporated to dryness in vacuo. The residue was dissolved in DCM (15 mL), and to this solution was added a solution of I_2 (173 mg, 0.682 mmol) in Et_2O (5 mL). The vivid green solution was evaporated in vacuo. The residue was dissolved in DCM (3 mL) and added to stirring hexanes (100 mL). The green precipitate was filtered off on a 30 mL fine porosity fritted disc, and the filtrate was removed from the glovebox and evaporated onto SiO_2 in vacuo. The product was purified using Combiflash flash chromatography on 12 g of SiO_2 column using ethyl acetate (EtOAc) in hexanes. The product eluted at 15% EtOAc. The fractions containing the product were evaporated and desiccated to yield **3** as a colorless oil (200 mg, 50%). IR: ν(CO) = 1702 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 7.28 (1H, d, $^3J_{HH}$ = 7.3, H5), 7.26 (1H, t, $^3J_{HH}$ = 7.0, H6/7), 7.21 (1H, t, $^3J_{HH}$ = 7.0, H6/7), 7.10 (1H, d, $^3J_{HH}$ = 7.3, H8), 6.45 (1H, d, $^3J_{HH}$ = 9.6, H9), 6.01 (1H, dd, $^3J_{HH}$ = 9.6 and 6.20, H10), 3.34 (1H, bs, H4a), 2.70 (2H, m, H3 & H4), 2.57 (1H, m, H10a), 2.55 (2H, m, H13), 2.42 (2H, m, H1 & H12), 2.27 (1H, dq, $^2J_{HH}$ = 18.0 & $^3J_{HH}$ = 7.3, H12), 1.85 (1H, m, H2), 1.80 (1H, m, H4), 1.43 (1H, m, H2), 1.09 (3H, t, $^3J_{HH}$ = 7.4, H14), 0.98 (3H, t, $^3J_{HH}$ = 7.2, H11). ^{13}C NMR ($CDCl_3$, δ): 213.4 (CO), 213.2 (CO), 135.4 (C8*a*/4b), 134.2 (C8*a*/4b), 131.2 (C10), 128.2 (C9), 127.9 (C6/7), 127.1 (C8), 126.7 (C6/7), 124.8 (C4), 49.3 (C1), 44.4 (C3), 37.2 (C10a), 36.5 (C12), 35.9 (C4a), 34.0 (C13), 30.9 (C2), 27.8 (C4), 7.9 (C11/14), 7.6 (C11/14). Elemental analysis (EA): Calculated for $C_{20}H_{24}O_2 \cdot 0.25\ CH_2Cl_2$: C, 76.57; H, 7.77. Found: C, 76.50; H, 7.88%.

Synthesis of TpMo(NO)(DMAP)(η^2-1,1′-((1S,3S,4aS,10aS)-1,2,3,4,4a,10a-Hexahydrophenanthrene-1,3-diyl)bis(ethan-1-one))



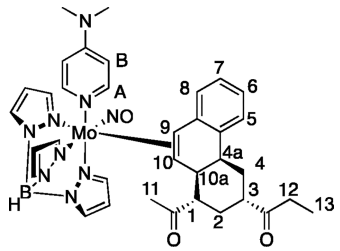
(6). Compound **1** (400 mg, 0.679 mmol), CH_3CH_2CN (15 mL), MVK (177 mg, 2.53 mmol), and DTBP (135 mg, 0.706 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (275 mg, 1.24 mmol) was added to the reaction mixture, and the resulting red solution was left to stir at −60 °C for 1 h. The reaction mixture was loaded onto 30 mL of dry basic alumina in a 60 mL coarse porosity fritted disc. The product was eluted with 1:1 Et_2O/THF (100 mL) as a yellow band, collected as a yellow solution, and evaporated in vacuo. The resulting oil was dissolved in DCM (2 mL), and the product was precipitated in stirred pentane (100 mL). The precipitate was collected on a 15 mL fine porosity fritted disc, washed with pentane (3 × 10 mL), and dried for 1 h yielding the yellow solid **6** (74 mg, 15%). CV (DMAc) $E_{p,a}$ = +0.17 V (NHE). IR: ν(B−H) = 2478 cm^{-1}, ν(CO) = 1698 and 1619 cm^{-1}, ν(NO) = 1562 cm^{-1}. ^1H NMR (acetone-d_6, δ): 7.94 (1H, d, Pz5A/C), 7.91 (1H, d, Pz3A), 7.88 (1H, d, Pz5A/C), 7.78 (1H, d, Pz5B), 7.72 (1H, d Pz3C), 7.37 (2H, bs, DMAP-A), 7.34 (1H, d, $^3J_{HH}$ = 7.5, H5), 6.98 (1H, d, Pz3B), 6.94 (1H, td, $^3J_{HH}$ = 7.5 and 1.5, H6), 6.86 (1H, t, $^3J_{HH}$ = 7.4, H7), 6.50 (2H, m, DMAP-B), 6.36 (2H, m, Pz4A&C), 6.24 (1H, dd, $^3J_{HH}$ = 7.6 and 1.0, H8), 6.09 (1H, t, Pz4B), 3.79 (1H, m, H4a), 3.32 (1H, d, $^3J_{HH}$ = 9.5, H9), 3.05 (6H, s, NMe), 2.87 (1H, m, H4), 2.79 (1H, m, H10a), 2.59 (2H, m, H3 & H1), 2.19 (3H, s, H13), 2.14 (1H, dd, $^3J_{HH}$ = 9.5 and 2.5, H10), 1.89 (3H, s, H12), 1.86 (1H, m, H4), 1.77 (1H, m, H2), 1.52 (1H, q, $^3J_{HH}$ = 12.6, H2). ^{13}C NMR (acetone-d_6, δ): 212.5 (CO), 211.0 (CO), 154.9 (DMAP-C), 151.1 (2C, DMAP-A), 144.6 (C4*b*/9a), 143.5 (Pz3A), 141.9 (Pz3B), 141.3 (Pz3C), 137.5 (Pz5A/C), 136.8 (Pz5A/C), 135.7 (Pz5B), 133.8 (C4*b*/9a), 128.0 (C8), 125.4 (C5), 124.9 (C7), 123.8 (C6), 108.1 (2C, DMAP-B), 106.9 (Pz4A/C), 106.6 (Pz4A/C), 106.3 (Pz4B), 70.4 (C10), 68.0 (C9), 55.9 (C1/3), 45.9 (C1/3), 42.7 (C10a), 39.1 (2C, DMAP-Me), 35.5 (C4a), 32.2 (C2), 30.7 (C4), 30.2 (C11), 28.1 (C12).

*Synthesis of 1,1′-((1S,3S,4aS,10aS)-1,2,3,4,4a,10a-Hexahydrophenanthrene-1,3-diyl)bis(ethan-1-one) (**7**).* Compound **1** (430



mg, 0.730 mmol), CH_3CH_2CN (24 mL), MVK (177 mg, 2.53 mmol), and DTBP (135 mg, 0.706 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (275 mg, 1.24 mmol) was added to the reaction mixture, and the resulting red solution was left to stir at −60 °C for 1 h. The reaction mixture was loaded onto 30 mL of dry basic alumina in a 60 mL coarse porosity fritted disc. The product was eluted with 1:1 Et_2O/THF (100 mL) as a yellow band, collected as a yellow solution, and evaporated to dryness in vacuo. The residue was dissolved in MeCN (15 mL), and to this solution was added a solution of I_2 (79 mg, 0.156 mmol) in Et_2O (5 mL). The yellow-green solution was evaporated in vacuo. The residue was dissolved in DCM (3 mL) and added to stirred hexanes (100 mL). The green precipitate was filtered off on a 30 mL fine porosity fritted disc, and the filtrate was removed from the glovebox and evaporated onto SiO_2 in vacuo. The product was purified using Combiflash flash chromatography on 12 g of SiO_2 column using EtOAc in hexanes. The product eluted at 20% EtOAc. The fractions containing the product were evaporated in vacuo and desiccated to yield the colorless oil **7** (37 mg, 19% yield). IR: ν(CO) = 1701 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 7.28 (1H, d, $^3J_{HH}$ = 7.3, H5), 7.27 (1H, m, H6/7), 7.22 (1H, m, H6/7), 7.10 (1H, d, $^3J_{HH}$ = 7.3, H8), 6.46 (1H, d, $^3J_{HH}$ = 9.6, H9), 1H, dd, $^3J_{HH}$ = 9.6 and 6.08, H10), 3.35 (1H, m, H4a), 2.73 (1H, m, H4), 2.70 (1H, m, H3), 2.54 (1H, m, H10a), 2.45 (1H, td, $^3J_{HH}$ = 12.2 and 3.5, H1), 2.23 (3H, s, H13), 2.07 (3H, s, H12), 1.95 (1H, m, H2), 1.77 (1H, m, H4), 1.42 (1H, q, $^3J_{HH}$ = 12.3, H2). ^{13}C NMR ($CDCl_3$, δ): 210.8 (CO), 210.6 (CO), 135.3 (C9*a*/4b), 134.2 (C9*a*/4b), 131.2 (C10), 128.2 (C9), 128.0 (C6/7), 127.1 (C8), 126.8 (C6/7), 124.8 (C5), 50.2 (C1), 45.3 (C3), 37.0 (C10a), 35.9 (C4a), 30.5 (C2), 30.2 (C11), 28.2 (C12), 27.7 (C4).

*Synthesis of TpMo(NO)(DMAP)(η^2-1-(((1S,3S,4aS,10aS)-1-Acetyl-1,2,3,4,4a,10a-hexahydrophenanthren-3-yl)propan-1-one)) (**8**).*



Compound **1** (200 mg, 0.34 mmol), CH_3CH_2CN (6 mL), EVK (33 mg, 0.4 mmol), and DTBP (54 mg, 0.3 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (0.1 mL, 0.5 mmol) was added to the reaction mixture, and the resulting red solution was stirred at −60 °C for 1 min. MVK (50 mg, 0.7 mmol) was added to the reaction mixture, which was then stirred at −60 °C for 18 h. The reaction mixture was loaded onto 30 mL of dry silica in a 60 mL coarse porosity fritted disc. The product was eluted with Et_2O (50 mL) as a yellow band, collected as a yellow solution, and evaporated to dryness in vacuo. The resulting oil was dissolved in DCM (1 mL), and the product was precipitated in stirred pentane (50 mL). The precipitate was collected on a 15 mL fine porosity fritted disc, washed with pentane (3 × 10 mL), and dried for

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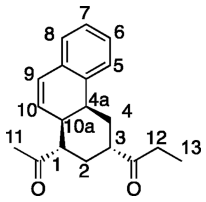
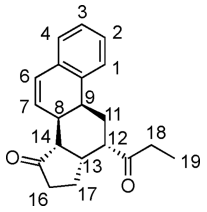
1 h yielding the yellow solid **8** (77 mg, 30%). CV (DMAc) $E_{p,a}$ = +0.16 V (NHE). IR: ν(B−H sp^2) = 2474 cm^{-1} ν(CO) = 1702 and 1618 cm^{-1}, ν(NO) = 1561 cm^{-1}. ^{1}H NMR (acetone-d_6, δ): 7.94 (1H, d, Pz5A/C), 7.91 (1H, d, Pz3A), 7.88 (1H, d, Pz5A/C), 7.78 (1H, d, Pz5B), 7.72 (1H, d, Pz3C), 7.37 (2H, bs, DMAP-A), 7.35 (1H, d, $^3J_{HH}$ = 7.4, H5), 7.00 (1H, d, Pz3B), 6.94 (1H, t, $^3J_{HH}$ = 7.4, H6), 6.86 (1H, t, $^3J_{HH}$ = 7.5, H7), 6.51 (2H, m, DMAP-B), 6.37 (1H, t, Pz4A/C), 6.36 (1H, t, Pz4A/C), 6.21 (1H, d, $^3J_{HH}$ = 7.5, H8), 6.09 (1H, t, Pz4B), 3.78 (1H, m, H4a), 3.31 (1H, d, $^3J_{HH}$ = 9.5, H9), 3.05 (6H, s, N-Me), 2.83 (1H, m, H4), 2.79 (1H, ddd, J = 10.6, 5.1, 2.4, H10a), 2.63 (2H, m, H3 & H12), 2.56 (2H, m, H1 & H12), 2.14 (1H, dd, J = 9.5, 2.5, H10), 1.88 (3H, s, H11), 1.74 (1H, d, $^3J_{HH}$ = 12.7, H2), 1.55 (1H, q, $^3J_{HH}$ = 12.7, H2), 1.01 (3H, t, $^3J_{HH}$ = 7.3, H13). ^{13}C NMR (acetone-d_6, δ): 213.7 (CO), 212.5 (CO), 155.11 (DMAP-C), 150.7 (2C, DMAP-A), 144.7 (C4*b*/9a), 143.6 (Pz3A), 142.1 (Pz3B), 141.4 (Pz3C), 137.6 (Pz5A/C), 137.0 (Pz5A/C), 135.8 (Pz5B), 133.9 (C4*b*/9a), 128.2 (C8), 125.6 (C5), 125.1 (C7), 123.9 (C6), 108.3 (2C, DMAP-B), 107.0 (Pz4A/C), 106.7 (Pz4A/C), 106.5 (Pz4B), 70.6 (C10), 68.2 (C9), 56.2 (C1), 45.2 (C3), 42.9 (C10a), 39.3 (2C, DMAP-Me), 35.7 (C4a), 34.4 (C12), 32.4 (C2), 31.0 (C4), 8.24 (C13). See SC-XRD determination details in the Supporting Information.

*Synthesis of 1-((1S,3S,4aS,10aS)-1-Acetyl-1,2,3,4,4a,10a-hexahydrophenanthren-3-yl)propan-1-one (**9**).* Compound **1** (430 mg,



0.730 mmol), CH_3CH_2CN (24 mL), EVK (66 mg, 0.784 mmol), and DTBP (135 mg, 0.706 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (275 mg, 1.24 mmol) was added to the reaction mixture, and the resulting red solution was stirred at −60 °C for 1 min. MVK (255 mg, 3.64 mmol) was added to the reaction mixture, which was then stirred at −60 °C for 1 h. The reaction mixture was loaded onto 30 mL of dry basic alumina in a 60 mL coarse porosity fritted disc. The product was eluted with MeCN (40 mL) as a yellow band, collected as a yellow solution, and evaporated to dryness in vacuo. The residue was dissolved in MeCN (15 mL), and to this solution was added a solution of I_2 (79 mg, 0.156 mmol) in Et_2O (5 mL). The solution was evaporated in vacuo. The residue was dissolved in DCM (3 mL) and added to stirred hexanes (100 mL). The brown precipitate was filtered off on a 30 mL fine porosity fritted disc, and the filtrate was removed from the glovebox and evaporated onto SiO_2 in vacuo. The product was purified using Combiflash flash chromatography on 12 g of SiO_2 column using EtOAc in hexanes. The product eluted at 18% EtOAc. The fractions containing the product were evaporated in vacuo and desiccated to yield the colorless oil **9** (27 mg, 13% yield). IR: ν(CO) = 1702 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 7.28 (1H, d, $^3J_{HH}$ = 7.3, H5), 7.26 (1H, t, $^3J_{HH}$ = 7.3, H6), 7.21 (1H, t, $^3J_{HH}$ = 7.1, H7), 7.09 (1H, d, $^3J_{HH}$ = 7.2, H8), 6.44 (1H, d, $^3J_{HH}$ = 9.6, H10), 6.08 (1H, dd, $^3J_{HH}$ = 9.6 and 5.9, H9), 3.34 (1H, bs, H4a), 2.70 (2H, m, H3 & H4), 2.58 (1H, m, H10a), 2.53 (2H, q, H12), 2.42 (1H, m, H1), 2.06 (3H, s, H11), 1.92 (1H, m, H2), 1.78 (1H, m, H4), 1.43 (1H, m, H2), 1.09 (3H, t, $^3J_{HH}$ = 7.3, H13). ^{13}C NMR ($CDCl_3$, δ): 213.2 (CO), 210.8 (CO), 135.4 (C4*b*/9a), 134.2 (C4*b*/9a), 131.2 C9), 128.1 (C10), 127.9 (C6/7), 127.1 (C8), 126.1 (C6/7), 124.8 (C5), 50.3 (C1), 44.4 (C3), 36.9 (C10a), 35.9 (C4a), 34.1 (C12), 30.6 (C2), 30.1 (C11), 27.9 (C4), 7.9 (C13).

*Synthesis of (8S,9S,12S,13S,14S)-12-Propionyl-8,9,11,12,13,14,16,17-octahydro-15H-cyclopenta[a]phenanthren-15-one (**10**).* Compound **1** (398 mg, 0.676 mmol), CH_3CH_2CN (22 mL), EVK (55 mg, 0.654 mmol), and DTBP (110 mg, 0.575 mmol) were added to a test tube. The reaction mixture was then cooled at −60 °C for 15 min. TMSOTf (275 mg, 1.24 mmol) was added to the



reaction mixture, and the resulting red solution was stirred at −60 °C for 1 min. 2-Cyclopenten-1-one (294 mg, 3.58 mmol) was added to the reaction mixture, which was then stirred at −60 °C for 18 h. The reaction mixture was loaded onto 30 mL of dry basic alumina in a 60 mL coarse porosity fritted disc. The product was eluted with MeCN (50 mL) as a yellow band, collected as a yellow solution, and evaporated to dryness in vacuo. The residue was dissolved in MeCN (15 mL), and to this solution was added a solution of I_2 (79 mg, 0.156 mmol) in Et_2O (5 mL). The solution was evaporated in vacuo. The residue was dissolved in DCM (3 mL) and added to stirred hexanes (100 mL). The brown precipitate was filtered off on a 30 mL fine porosity fritted disc, and the filtrate was removed from the glovebox and evaporated onto SiO_2 in vacuo. The product was purified using Combiflash flash chromatography on 12 g of SiO_2 column using EtOAc in hexanes. The product eluted at 25% EtOAc. The fractions containing the product were evaporated in vacuo and desiccated to yield the colorless oil **10** (27 mg, 13% yield). IR: ν(C−H sp^2) = 2932 cm^{-1}, ν(CO) = 1731 and 1703 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 7.22 (3H, m, H1, H2, & H3), 7.11 (1H, d, $^3J_{HH}$ = 7.3, H4), 6.58 (1H, d, $^3J_{HH}$ = 9.6, H6), 6.15 (1H, dd, $^3J_{HH}$ = 9.6 and 6.2, H7), 3.27 (1H, m, H9), 3.11 (1H, dt, J = 13.0 and 4.4, H12), 2.58 (2H, m, H13 & H18), 2.47 (3H, m, H11, H16, H18), 2.25 (1H, m, H8), 2.17 (2H, m, H11 & H16), 2.06 (1H, dd, $^3J_{HH}$ = 12.2 and 6.7, H14), 1.97 (1H, m, H17), 1.69 (1H, m, H17), 1.10 (3H, t, $^3J_{HH}$ = 7.2, H19). ^{13}C NMR ($CDCl_3$, δ): 218.5 (CO), 212.5 (CO), 134.6 (C5/10), 134.3 (C5/10), 130.6 (C7), 128.7 (C6), 127.9 (C2/3), 127.2 (C4), 126.8 (C2/3), 124.9 (C1), 51.1 (C14), 43.8 (C12), 37.9 (C13), 37.1 (C16), 35.2 (C9), 34.5 (C18), 30.8 (C8), 21.2 (C11), 21.0 (C17), 7.9 (C19). EA: Calculated for C20H22O2·0.25 EtOAc: C, 79.14; H, 7.68. Found: C, 78.96; H, 7.51%. SC-XRD determination details are in the Supporting Information.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.0c00110.

CIF files for compounds **2**, **3**, **8**, **10**, ^{1}H and ^{13}C NMR of all new compounds (PDF)

Accession Codes

CCDC 1976642−1976645 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

[#]Joint first authorship.

Notes

The authors declare no competing financial interest.

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