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Regio- and Stereospecific Uncatalyzed Reactions of Electron-Rich Arenes and Olefins at Organomolybdenum Enantiomeric Scaffolds

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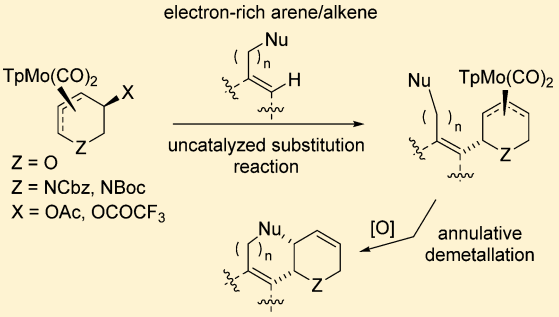
Supporting Information

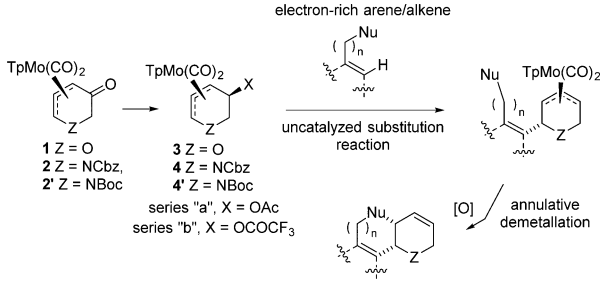
ABSTRACT: A novel uncatalyzed reaction between $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyranyl/dihydropyridinyl) complexes and electron-rich arenes/olefins is reported. The reaction proceeds under mild reaction conditions so that a variety of functional groups are tolerated. Combined with a stereospecific annulative demetalation, the new reaction provides a rapid access to polycyclic alkaloid structures. The sequential protocol was used to prepare analogues of the antimalarial agent isofebrifugine.



INTRODUCTION

Readily available enantiopure, air- and moisture-stable $TpMo(CO)_2$(5-oxo-η^3-6*H*-pyranyl)and $TpMo(CO)_2$(5-oxo-η^3-6*H*-pyridinyl) complexes, **1** and **2**, and their derivatives are synthetically useful scaffolds for the enantiocontrolled construction of substituted heterocycles (Scheme 1; Tp = hydridotris(pyrazolyl)borato).[1−24]

Scheme 1. Reaction with π-Nucleophiles Followed by an Annulative Demetalation



The preparation of multigram quantities of high-enantiopurity complexes is relatively straightforward.[6,7] For carbon−carbon and carbon−heteroatom bond constructions, both $TpMo(CO)_2$-stabilized cation[1,2,6,8,11,14−20,23] and anion[3−5,10] pathways have been observed and applied in the enantiocontrolled synthesis of natural products. The $TpMo(CO)_2$-stabilized carbocations react regio- and stereospecifically with a variety of sp^3-, sp^2-, and sp-hybridized Grignard and lithium reagents.[1,2,6,11,14−20] Complementing the stabilized cation pathway, a $TpMo(CO)_2$-mediated nucleophilic functionalization pathway was also described. These latter disclosures demonstrate the direct reaction of charge neutral $TpMo(CO)_2$(5-oxo-η^3-6*H*-pyranyl/pyridinyl) complexes, such as **1** and **2**, and $TpMo(CO)_2$(5-acetoxy-η^3-5,6-dihydropyranyl/pyridinyl) complexes, such as **3a** and **4a**, with preformed enolates or alkoxide anions.[3−5,9,10]

Herein we report a new and synthetically versatile pathway for the regio- and stereospecific functionalization of molybdenum-based organometallic enantiomeric scaffolds—an uncatalyzed direct reaction between charge neutral $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyranyl/pyridinyl) complexes, **3b** and **4b**, and electron-rich arenes and olefins (Scheme 1). Simply by tuning the nucleofugality of the 5-position leaving group, both **3** and **4** become competent electrophiles for high-yield reactions with charge neutral π nucleophiles. The charge neutral nature of the π nucleophile allows the presence of internal functional groups that can be used for the rapid regio- and stereospecific construction of functionalized polycyclic motifs. Using this principle, the sequence of an uncatalyzed reaction with π nucleophiles followed by annulative demetalation was applied to a four-step synthesis of analogues of the antimalarial natural product isofebrifugine. The reaction proceeds under mild conditions in typical organic solvents at room temperature without the addition of any activators, so that a variety of sensitive functional groups are tolerated.

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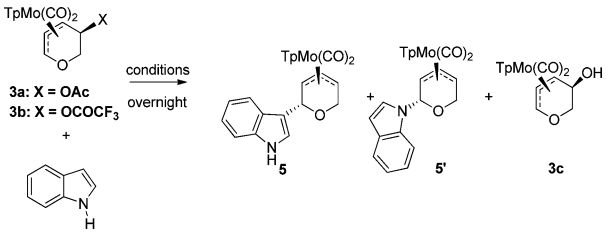
RESULTS AND DISCUSSION

We initiated our study by examining the reaction of indole with the racemic $TpMo(CO)_2$(5-acetoxy-η^3-5,6-dihydropyranyl) complex **3a** under a variety of reaction conditions (Table 1).

Table 1. Optimization of the C-Alkylation between Indole and $TpMo(CO)_2(\eta^3$-dihydropyranyl) Complexes 3a,b[a]



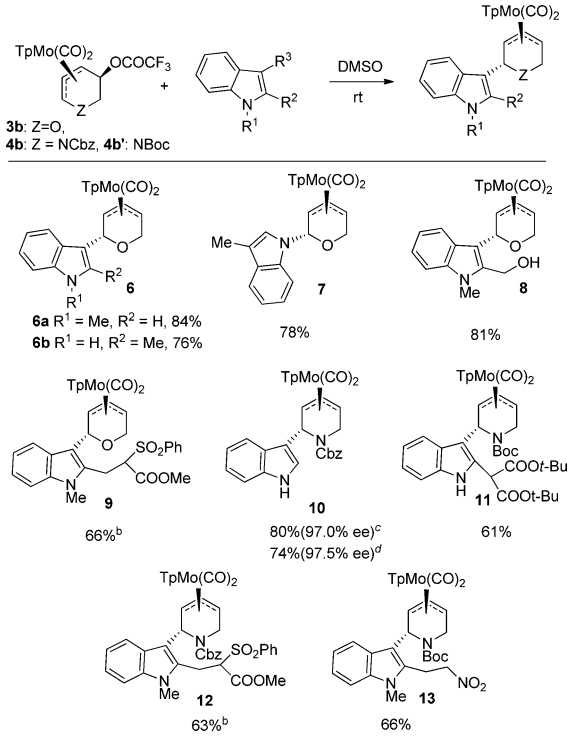
entry	substrate	conditions	yield (%) 5	5′	3c
1	**3a**	NaH/THF	0	92	0
2[b,c]	**3a**	NaH/THF/15-C-5	20	20	20
3[d]	**3a**	MeMgBr/THF	0	0	20
4	**3a**	LiO^{t}Bu/THF	0	0	90
5	**3a**	DBU/THF	0	0	90
6	**3a**	DMSO	0	0	0
7	**3a**	DMSO/NaH	0	86	0
8[b]	**3a**	DMSO/NaH/15-C-5	0	89	0
9	**3b**	THF	73	0	0
10	**3b**	CH_3CN	78	0	0
11	**3b**	DMSO	86	0	0

[a]The yield of purified product is reported. Conditions: entries 1−8, 3 equiv of indole was used; entries 9−11, 1.5 equiv of indole was used. [b]0.2 equiv 15-C-5 was added. [c]40% **3a** was recovered. [d]80% **3a** was recovered.

No reaction took place upon mixing the two substrates in THF. Under basic reaction conditions in THF (NaH, NaH with 15-crown-5-ether (15-C-5), MeMgBr, LiO^{t}Bu, or DBU) the reaction was mostly unproductive, generating varying yields of **3c**, the product of hydrolysis of the acetoxy moiety, **5′**, the undesired product of indole N-alkylation, and only a low yield (20%) of the desired product **5** when NaH was activated with 15-C-5. Complex **3a** also did not react directly with indole in DMSO at room temperature, although upon warming to 60 °C the elimination product $TpMo(CO)_2(\eta^3$-pyranyl) was observed. Reactions in DMSO in the presence of NaH or NaH with 15-C-5 were likewise unproductive, only generating the undesired product of indole N-alkylation **5′**. In contrast to the reactions of the acetoxy complex **3a**, the more activated $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyranyl) complex **3b** reacted easily with indole in THF, CH_3CN, or DMSO in the absence of base to afford the desired product of C-alkylation of the indole in good yield (Table 1, entries 9−11). The use of sulfonate esters, even better leaving groups than trifluoroacetate, did not provide stable analogues of **3a,b** and rather led to known (η^3-pyranyl)molybdenum complexes.[7,12,20]

Having observed a successful reaction of the trifluoroacetate **3b** with indole, attention was then turned to determine the scope of this process with respect to various substituted indoles (Chart 1). The electron-rich 1-methylindole reacted with **3b** in DMSO at room temperature to furnish the C-3-alkylation product **6a** in 84% yield (see the Supporting Information for details), while Cbz-protected indole failed to react with **3b** under the same reaction conditions. 2-Methylindole reacted

Chart 1. Scope of the Reaction with Indoles[a]



[a]The yield of purified product is reported; 1.2−1.5 equiv of indole derivatives was used. [b]A roughly 1:1 diastereomeric mixture at the $PhSO_2$-bearing center is formed. [c]97% ee Mo complex was used. [d]97% ee Mo complex was used in the presence of MgO.

with **3b** within minutes to form the C3-alkylation product **6b**, while the isomeric 3-methylindole reacted with **3b** to provide only the N-alkylation product **7**. 1,3-Dimethylindole failed to react with **3b** under the same conditions. The dihydropyridinyl complex system $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyridinyl) (**4b′**) also showed a facile reaction with indole to generate the C-3-substitution product **10**. When the high-enantiopurity dihydropyridinyl complex **4b′**[7] was used in the reaction (97.5% ee), the product **10** was formed with only very slight racemization (97.0% ee).[2] Moreover, the addition of MgO completely suppressed any racemization, presumably by scavenging the TFA under the reaction conditions.[2]

2-Substituted indole derivatives bearing various tethered functional groups were also suitable reaction partners. For instance, 2-(1-methylindole)methanol reacted with the dihydropyranyl complex **3b** to generate **8** in 81% yield without recourse to alcohol protecting groups (Chart 1, entry 3). The reaction between the dihydropyridinyl $TpMo(CO)_2$ complex **4b** and various indoles bearing tethered sulfonyl, malonyl, and nitro groups all took place in the absence of adverse events (see **9** and **11**−**13** in Chart 1).

In seeking to extend the reaction to π-electron nucleophiles other than indoles, DMSO did not prove to be a suitable solvent. However, a simple solvent switch to acetonitrile facilitated the reaction of $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyranyl) and $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyridinyl)-complexes with electron-rich arenes and olefins (Table 2). For example, 2-methylfuran yielded only 28% of product with $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyridinyl) (**4b**) in DMSO, while the same reaction in acetonitrile solely furnished the desired 5-substitution product in 84% yield (entry 1).

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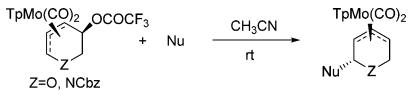
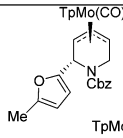
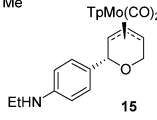
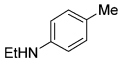
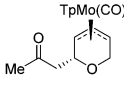
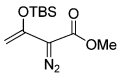
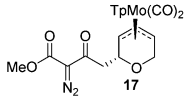
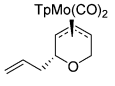
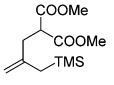
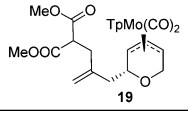
Table 2. Scope of the Reaction with Electron-Rich Arenes and Olefins[a]



Entry	Nu	Product	Yield(%)[b]
1		 **14**	84(28)
2		 **15**	56
3		—	NR
4		 **16**	80(0)
5		 **17**	77
6		 **18**	74(0)
7		 **19**	71

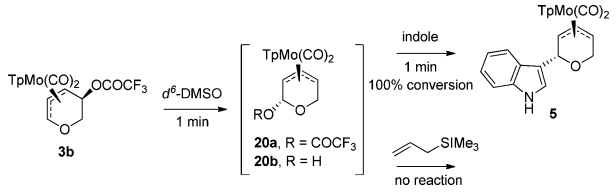
[a]The yield of purified product is reported; 1.2−1.5 equiv of nucleophile was used. [b]Values in parentheses are yields using DMSO as solvent.

N-Ethylaniline reacted with complex **3b** to produce exclusively the *para*-substituted product in 56% yield (entry 2), while no reaction was observed using 4-methyl-*N*-ethylaniline, in which the *para* position is blocked; no *ortho*-substitution product was detected (entry 3). Although silyl enol ethers and allylsilanes showed no reactivity toward molybdenum complex **3b** in DMSO, both substrate classes underwent facile reactions with **3b** in acetonitrile without requiring typical silane activators such as a fluoride source or a Lewis acid (entries 4 and 6). Moreover, amine, diazo, and malonate functional groups were all tolerated under the mild reaction conditions, demonstrating the good functional group compatibility of this system.

Intrigued by the different reactivities of the 5-trifluoroacetoxy $TpMo(CO)_2$ complex in DMSO and acetonitrile, an NMR study with the complex $TpMo(CO)_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyranyl) (**3b**) was carried out in order to gain some insight into the mechanism of this novel transformation. The complex **3b** when dissolved in d_6-DMSO rearranged within seconds to a mixture of the complexes **20a,b**, which were thereafter stable in solution even after 3 days (Scheme 2). Upon exposure to indole, this mixture of rearranged products reacted very rapidly (60 s) to afford the substitution product **5** quantitatively. In contrast, the mixture of rearranged complexes **20a,b** derived from **3b** failed to react with allyltrimethylsilane in d_6-DMSO.

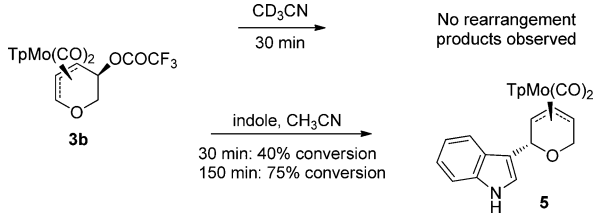
In comparison to dissolution in d_6-DMSO, no rearrangement of **3b** occurred on dissolution in CD_3CN; rather, **3b** completely

Scheme 2. ^{1}H NMR Studies in d_6-DMSO



decomposed to a complex mixture after standing overnight (Scheme 3). However, indole was mixed with **3b** in CD_3CN,

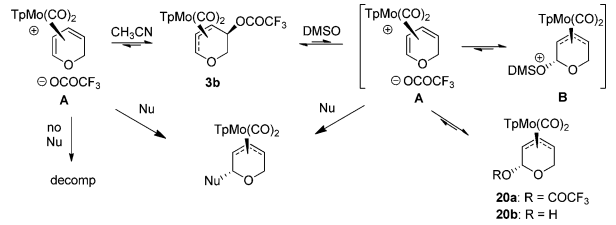
Scheme 3. ^{1}H NMR Studies in CD_3CN



the reaction proceeded to generate product (40% conversion after 30 min, 75% conversion after 2.5 h). In addition, in comparison to the complete lack of reaction of **3b** with allyltrimethylsilane in d_6-DMSO, in CD_3CN the substitution reaction proceeded uneventfully without the observable intervention of intermediates **20a,b**.

The observed reactivity differences can be understood partially on the basis of the differential donicities of DMSO and CH_3CN.[25] In order for a successful reaction to be observed, both solvents must be able to support self-ionization of **3b** to the η^4-diene cation **A**, which then reacts with π-electron-rich substrates (Scheme 4). In strongly solvating

Scheme 4. Proposed Mechanism for the Reaction in DMSO versus CH_3CN



DMSO we presume that the cation **A** is "stabilized" by solvent trapping, giving **B**, which provides a cationic system with a sufficient lifetime for the rearranged products **20a,b** to be formed and observed. Furthermore, interaction of the cation **A** with strongly solvating DMSO to form **B** lowers not only the effective concentration but also the reactivity of the active cation **A**, allowing a productive reaction to be observed only with the most potent of π-electron-rich nucleophiles, such as indoles.[26,27] In contrast, diminished solvent stabilization of the cation **A** by the much weaker donor CH_3CN presumably generates a more reactive cation that, once generated, either reacts with π-electron-rich nucleophiles when they are present or rapidly decomposes to complex mixtures when they are not. Solvent stabilization of the cationic intermediate also explains the formation of **20a,b** in d_6-DMSO but not in CD_3CN. It is trace amounts of water in the d_6-DMSO that leads to formation of **20b** (**20a**/**20b** ratio 5/1).

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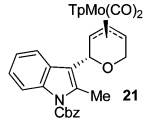
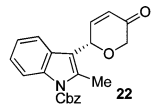
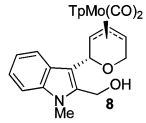
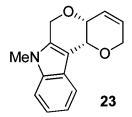
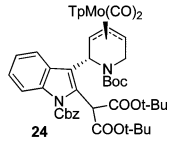
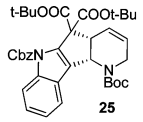
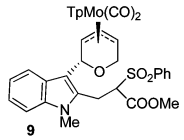
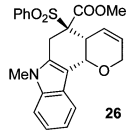
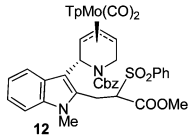
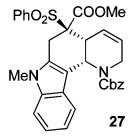
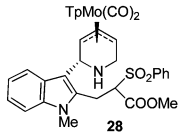
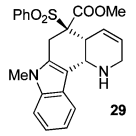
With conditions favoring the uncatalyzed reaction of π nucleophiles with molybdenum complexes in hand, we explored further development of the methodology in the context of polycyclic indole synthesis[28] (Table 3). Two

Table 3. Oxidative Demetalation of Indole-Substituted $TpMo(CO)_2$ Complexes

Entry	Substrate	Product	Yield(%)[a]
1[b]			52
2[c]			95
3[c]			67
4[c]			90
5[c]			0
6[c]			85

[a]The yield of purified product is reported. [b]The reaction was run with PDC/silica in CH_2Cl_2. [c]The reaction was run with NaH open to air in the presence of 0.2 equiv of Cu(2-ethylhexanoate)$_2$.

demetalation protocols were examined. The 2-methylindole adduct **6b** was N-protected with Cbz, providing **21**, which participated in oxidative demetalation with pyridinium dichromate to yield the unsaturated ketone **22** in a moderate yield (entry 1). For the more synthetically interesting substrates bearing tethered nucleophilic sources, a Cu(2-ethylhexanoate)$_2$-mediated annulative demetalation[5] was employed to stereoselectively induce C−Nu bond formation between a terminus of the (η^3-allyl)molybdenum moiety and an internal nucleophile. Entry 2 demonstrates a highly efficient C−O bond forming annulative demetalation generating the indole bis-pyran **23** from alcohol **8**, while entries 3, 4, and 6 depict effective and stereoselective generation of C−C bonds when stabilized enolates are used as nucleophiles. For example, the malonate anion of complex **24** (derived from molybdenum complex **11** by protection of the indole NH with Cbz) was used as the nucleophile to form product **25**, bearing a five-membered ring *cis*-fused to the piperidine ring (entry 3). In entry 4 the pyranyl complex **9** underwent annulative demetalation to furnish the single cyclization product **26** diastereoselectively in excellent yield (entry 4). The stereochemistry of the product **26** was confirmed by an X-ray crystallographic study (see the Supporting Information for details).

In contrast to the reactions shown in entries 2−4 (Table 3), attempted annulative demetalation of the Cbz-protected pyridinyl complex **12** failed to form the desired cyclization product **27** (entry 5) under conditions identical with those used to generate products **23**, **25**, and **26** in entries 2−4. However, after N-deprotection of **12**, the N-unprotected pyridinyl complex **28** underwent nucleophilic oxidative ring closure very slowly yet efficiently to form the six-membered ring closure product **29** in 85% yield (entry 6).

Irrespective of the specific mechanistic details of the nucleophilic oxidative demetalation pathway followed by entries 2−4 and 6 of Table 3,[5] we assume that maximum orbital overlap favors a chairlike transition state for attack *anti* to the molybdenum on the (η^3-allyl)molybdenum moiety by the incoming anion (or one-electron oxidized anion). Thus, although $TpMo(CO)_2$(5,6-dihydro-η-3,4,5-pyranyl)and $TpMo(CO)_2$(5,6-dihydro-η-3,4,5-pyridinyl) complexes favor a ground state conformation that orients substituents at the 2- and 6-positions axially,[14] both the 5,6-dihydropyranyl and the unprotected N−H 5,6-dihydropyridinyl molybdenum complexes can presumably achieve effective concentrations of the ring-flip conformations where the tether is situated equatorially (Figure 1). As depicted in Figure 1, an equatorially oriented

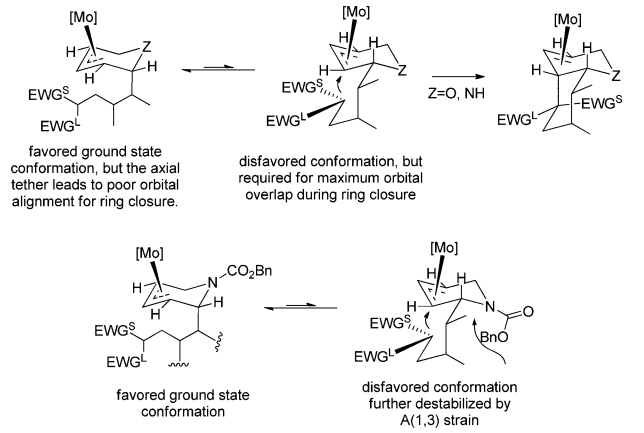


Figure 1. Stereoelectronic influences on the demetalation.

tether then places its distal functionality adjacent to the orbital back lobe of the η^3-allyl terminus, poised for a maximal orbital overlap "axial" attack ring closure and product formation, after spontaneous demetalation. This analysis also rationalizes the formation of a single diastereomer of the ring closure product, the isomer that orients the larger of the two electron-withdrawing substituents that are attached to the attacking carbon away from the (η^3-allyl)molybdenum moiety.

In contrast, the equatorial conformation required for ring closure of the N-Cbz protected dihydropyridinyl complex experiences significant *additional* destabilization because of A(1,3) strain between the carbamate and the equatorial substituent.[29,30] This added destabilization must make the requisite equatorial conformer inaccessible in concentrations sufficient to observe ring-closing reactions of the N-protected pyridinylmolybdenum complex **12**.

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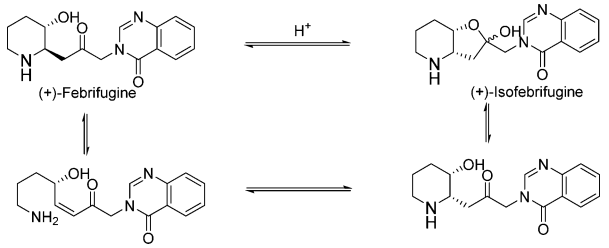
Given the effective cyclization of N-protected dihydropyridinyl substrates to generate five-membered ring closure products (such as the N-Boc bearing **24** closing to **25** in this paper or related N-Cbz bearing systems shown in an earlier publication[5]), it appears that the greater ring closure rates for five-membered vs six-membered cyclizations can compensate for the conformational bias against cyclization in the N-protected dihydropyridinyl systems.

Confirmation of the structural assignments made in this paper rests on complete analyses made earlier[5] and is further supported through an X-ray crystal structure of the demetalation product **26** (see the Supporting Information).

Application to a Concise Synthesis of Isofebrifugine Analogues. The antimalarial alkaloids febrifugine and isofebrifugine were isolated from the Chinese herb Chang Shan (*Dichroa febrifuga* Lour).[31] Because of their high antimalarial activity, the two compounds have inspired a number of total syntheses and formal syntheses.[5,32−41] However, substantial toxicity, which was presumably associated with in vivo oxidation of the quinazolinone ring and with the generation of a reactive bioalkylating enone (Scheme 5) via a

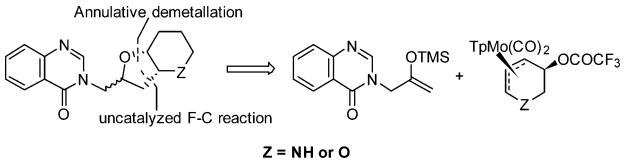
Scheme 5. Equilibration of Febrifugine and Isofebrifugine



retro-aza-Michael reaction, limited the potential efficacy of febrifugine/isofebrifugine as a drug.[42,43] Different strategies, including replacing the piperidine with a pyrolidine, repositioning the piperidine ring nitrogen,[44] and studying the activities of febrifugine metabolites[45] and of an acetone adduct,[46] have been utilized to search for a solution to lower the toxicity. No exploration of the structure−activity relationship (SAR) around the piperidine ring has been reported to date.

The diastereomers of deoxyisofebrifugine are interesting analogues of the natural product because the ether bond locks the furan ring and prevents the formation of the bioalkylating enone structure. To access the diastereomers of deoxyisofebrifugine, a highly convergent route was devised using a π-nucleophile substitution−annulative demetalation sequence (Scheme 6). Because the organometallic scaffold allows a

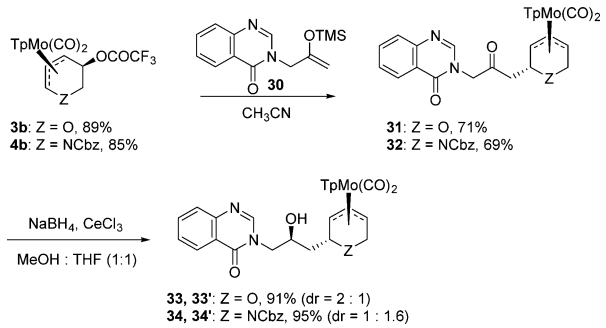
Scheme 6. Retrosynthetic Analysis of Deoxyisofebrifugine



synthetic strategy to be equally applied in both the pyranyl and pyridinyl systems, the tetrahydropyran analogues of deoxyisofebrifugine were also synthesized in order to evaluate their antimalarial activity.

The reaction between the 5-trifluoroacetate scaffolds **3b** and **4b** and electron-rich silyl enol ether **30** derived from 3-(2-oxopropyl)-4(3*H*)-quinazolinone afforded **31** and **32**, each as a single diastereomer (addition *anti* to Mo) in good yields. A nonstereoselective Luche reduction led to a mixture of two separable diastereomeric alcohols in each case (Scheme 7), an

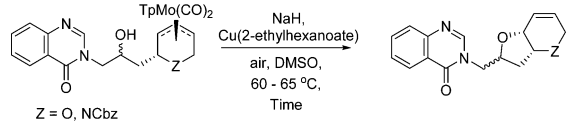
Scheme 7. Reactions with Silyl Enol Ether 30

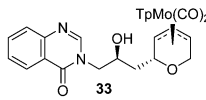
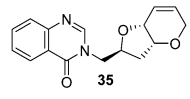
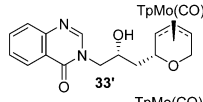
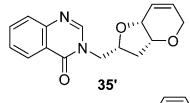
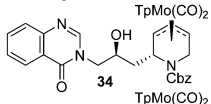
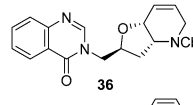
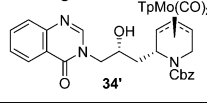
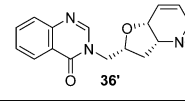


intentional tactic used to provide diastereomers for bioassay. The relative stereochemistry of alcohols **33**, **33′**, **34**, and **34′** was assigned on the basis of 1D NOE NMR experiments of the final deoxyisofebrifugine analogues **37**, **37′**, **38**, and **38′**. The relative stereochemistry was further confirmed by the X-ray crystal structure analysis of **34** and **35**. In contrast to the Luche reduction conditions, the use of $NaBH_4$ led to a sluggish reaction and resulted in a poor conversion to the alcohol. The use of other reducing agents such as DIBAL and Li- and Na-Selectride led to the reduction of the ketone accompanied by substantial over-reduction of the quinazolinone ring.[47,48]

Following the annulative demetalation protocol,[5] the alcohols were transformed to the corresponding bicyclic annulation products with excellent stereoselectivity (Table 4).

Table 4. Annulative Demetalation of Isomers of Alcohols



Entry	Substrate	Time (days)	Product	Yield(%)[a]
1	 **33**	5	 **35**	75
2	 **33'**	2	 **35'**	69
3	 **34**	10	 **36**	61
4	 **34'**	2	 **36'**	71

[a]The yield of the purified product is reported.

The structure of the product was confirmed by an X-ray crystallographic study of **35** (see the Supporting Information for details). This demetalative ring annulation protocol is efficient for the construction of 2,3-fused bicyclic pyranyl and pyridinyl derivatives, albeit only after fairly long reaction times to reach completion (days). Finally, hydrogenation of the above

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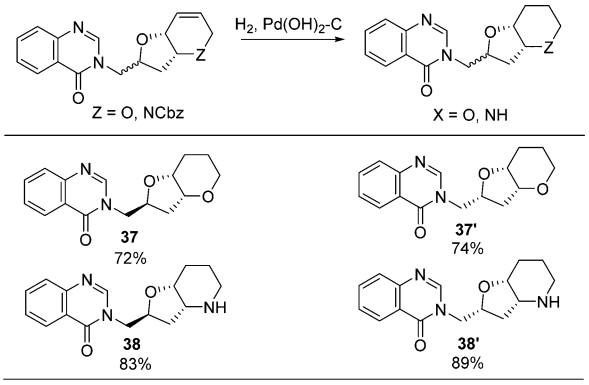
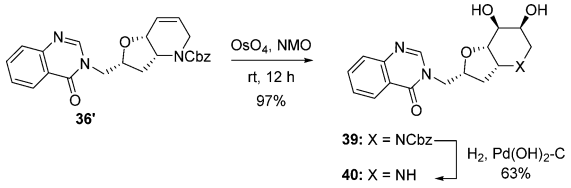
compounds delivered deoxyisofebrifugine analogues **37**, **37′**, **38**, and **38′** (Table 5).

Table 5. Deoxyisofebrifugine Analogues



The double bond was also investigated as a functional group handle to synthesize more highly elaborated deoxyisofebrifugine analogues. The double bond of the annulation product **36′** was treated with catalytic osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide, followed by hydrogenation to give **40** as a single diastereomer (Scheme 8).

Scheme 8. Functionalization of the Double Bond of 36′



None of the deoxyisofebrifugine analogues **37**, **37′**, **38**, **38′**, and **40** demonstrated any significant in vitro antimalarial activity (see the Supporting Information for details).

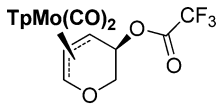
CONCLUSIONS

A novel uncatalyzed reaction of electron-rich arenes and olefins with TpMo(CO)$_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyranyl)- and TpMo(CO)$_2$(5-trifluoroacetoxy-η^3-5,6-dihydropyridinyl) complexes is reported. This reaction is sufficiently mild that it can tolerate a variety of functional groups, including amines, alcohols, esters, and diazo moieties. A subsequent nucleophilic, oxidative annulative demetalation provides a rapid access to piperidine- or pyran-embedding motifs, such as tetracyclic indole alkaloid structures. The reaction sequence was applied to a convergent synthesis of isofebrifugine analogues.

EXPERIMENTAL SECTION

All Tp molybdenum complexes decompose over 180−200 °C. Therefore, melting points of the complexes are not useful and are not provided here.

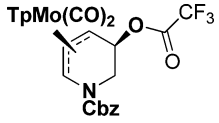
Preparation of Substrates. *(±)-Dicarbonyl[hydridotris-(1-pyrazolyl)borato][(η-2,3,4)-5-trifluoroacetoxy-5,6-dihydro-2H-pyran-2-yl]molybdenum ((±)-**3b**).*



3b

To a solution of (±)-TpMo(CO)$_2$(*syn*-5-hydroxy-η^3-5,6-dihydropyranyl)[5] (500 mg, 1.08 mmol, 1.0 equiv) in DCM (25 mL) were added TEA (165 mg, 1.62 mmol, 1.5 equiv) and TFAA (289 mg, 1.40 mmol, 1.3 equiv) at room temperature. The reaction mixture was stirred for 20 min and then loaded on the silica gel directly. Flash chromatography in under 5 min with hexanes/EtOAc (3/1) afforded (±)-**3b** (547 mg, 0.95 mmol, 88%) as a yellow solid. TLC: R_f = 0.62 (3/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 2.0 Hz, 1 H), 7.72 (d, J = 2.8 Hz, 1 H), 7.71 (d, J = 2.8 Hz, 1 H), 7.59 (d, J = 2.0 Hz, 1 H), 7.58 (d, J = 2.0 Hz, 1 H), 7.51 (d, J = 1.6 Hz, 1 H), 7.05 (dd, J = 4.4, 2.0 Hz, 1 H), 6.30 (t, J = 2.4 Hz, 1 H), 6.22 (t, J = 2.4 Hz, 1 H), 6.20 (t, J = 2.0 Hz, 1 H), 5.79 (ddd, J = 9.2, 6.0, 2.8 Hz, 1 H), 4.59 (dt, J = 7.6, 2.4 Hz, 1 H), 3.75 (dd, J = 10.8 Hz, 6.0 Hz, 1 H), 3.54 (dd, J = 8.0 Hz, 4.0 Hz, 1 H), 2.64 (dd, J = 11.6, 10.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 226.9, 224.0, 147.2, 146.8, 142.0, 141.8, 136.24, 136.21, 134.6, 134.5, 109.7, 106.1, 105.8 105.6, 73.5, 63.7, 62.8, 58.0.

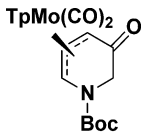
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-2,3,4)-1-benzyloxycarbonyl-5-trifluoroacetoxy-5,6-dihydro-2H-pyridin-2-yl]molybdenum ((±)-**4b**).*



4b

To a solution of (±)-TpMo(CO)$_2$(*syn*-5-hydroxy-1-benzyloxycarbonyl-η^3-5,6-dihydropyridinyl)[5] (300 mg, 0.50 mmol, 1.0 equiv) in DCM (3 mL) were added TEA (140 μL, 1.0 mmol, 2.0 equiv) and TFAA (105 μL, 0.75 mmol, 1.5 equiv) at −15 °C. The reaction mixture was stirred for 20 min and then loaded on the silica gel directly. Flash chromatography in under 5 min with hexanes/EtOAc (3/1) afforded (±)-**4b** (310 mg, 0.44 mmol, 89%) as a yellow solid. TLC: R_f = 0.65 (3/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (600 MHz, $CDCl_3$): δ 8.45 (d, J = 1.2 Hz, 0.3 H), 8.44 (d, J = 1.2 Hz, 0.7 H), 8.19 (d, J = 1.2 Hz, 1.0 H), 7.63 (d, J = 1.2 Hz, 1.0 H), 7.60 (s, 0.7 H), 7.58 (d, J = 2.4 Hz, 0.7 H), 7.56 (d, J = 2.4 Hz, 0.7 H), 7.54 (d, J = 2.4 Hz, 0.3 H), 7.51 (d, J = 2.4 Hz, 0.3 H), 7.47 (d, J = 2.4 Hz, 0.7 H), 7.45 (d, J = 2.4 Hz, 0.7 H), 7.44 (s, 0.3 H), 7.40−7.31 (m, 3 H), 7.15 (d, J = 6.0 Hz, 0.7 H), 6.90 (d, J = 6.0 Hz, 0.3 H), 6.25 (d, J = 1.8 Hz, 1.0 H), 6.22 (s, 0.7 H), 6.18−6.17 (m, 1 H), 5.91 (s, 0.3 H), 5.88−5.5.85 (m, 1 H), 5.28 (d, J = 12.0 Hz, 0.7 H), 5.19 (s, 1 H), 5.18 (d, J = 12.0 Hz, 0.3 H), 4.58 (t, J = 8.4 Hz, 1.0 H), 3.75 (dd, J = 12.8 Hz, 7.2 Hz, 0.3 H), 3.71 (dd, J = 12.4 Hz, 7.2 Hz, 0.7 H), 3.51 (t, J = 7.2 Hz, 0.7 H), 3.42 (t, J = 7.2 Hz, 0.3 H), 2.23 (dd, J = 12.0 Hz, 9.0 Hz, 0.3 H), 2.14 (dd, J = 12.0 Hz, 9.0 Hz, 0.7 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 228.2, 227.9, 223.9, 223.7, 157.4 (q, J = 43.9 Hz), 155.8, 155.4, 147.2, 147.0, 146.2, 145.2, 144.4, 144.0, 143.5, 141.1, 140.9, 136.3, 136.2, 136.1, 136.1, 134.9, 129.5, 129.2, 129.0, 128.9, 128.8, 128.6, 128.4, 128.3, 116.4 (q, J = 169 Hz), 113.4 (q, J = 169 Hz), 106.3, 106.1, 105.9, 105.8, 105.6, 105.5, 92.9, 91.7, 90.1, 89.0, 74.5, 74.3, 69.6, 69.1, 68.8, 68.4, 60.2, 60.1, 58.8, 58.3, 52.5, 51.8, 43.6, 43.5. IR (cm^{-1}): 2485 (w), 1948 (s), 1854 (s), 1780 (s), 1702 (s).

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-2,3,4)-1-tert-butoxycarbonyl-5-oxo-5,6-dihydro-2H-pyridin-2-yl]molybdenum ((±)-**2′**).*



2′

To a solution of the complex **2** (500 mg, 0.88 mmol, 1.0 equiv) in THF (25 mL) was added 10% Pd(OH)$_2$/C (90 mg, 0.09 mmol, 0.1 equiv). The reaction mixture was stirred at room temperature under a hydrogen balloon for 5 h. The mixture was filtered and then concentrated to a solid. The unpurified solid was dissolved in DCM. To the solution were added Boc_2O (249 mg, 1.14 mmol, 1.3 equiv), DMAP (11 mg, 0.09 mmol, 0.1 equiv), and triethylamine (138 mg, 1.32 mmol, 1.5 equiv). The mixture was stirred at room temperature overnight and then poured into a separatory funnel containing EtOAc (15 mL) and H_2O (15 mL), and the layers were separated. The

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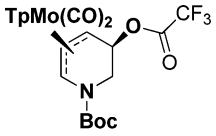
aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2/1) afforded the N-Boc protected complex (±)-TpMo(CO)$_2$(5-oxo-η^3-6H-pyridinyl) (**2′**; 434 mg, 0.77 mmol, 88%) as a yellow solid. TLC: R_f = 0.28 (2/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.41 (d, J = 2.0 Hz, 0.3 H), 8.35 (d, J = 2.0 Hz, 0.7 H), 8.29 (d, J = 1.2 Hz, 0.7 H), 8.01 (d, J = 1.6 Hz, 0.3 H), 7.77 (d, J = 1.6 Hz, 0.3 H), 7.69 (d, J = 1.4 Hz, 0.7 H), 7.65 (d, J = 2.0 Hz, 0.3 H), 7.58−7.62 (m, 1.7 H), 7.46−7.49 (m, 1.7 H), 7.32 (dd, J = 6.8 Hz, 2.0 Hz, 0.3 H), 6.27 (t, J = 1.6 Hz, 0.3 H), 6.17−6.24 (m, 2.7 H), 4.71−4.74 (m, 1 H), 3.99 (t, J = 6.0 Hz, 0.7 H), 3.94 (t, J = 6.0 Hz, 0.3 H), 3.38 (d, J = 20.0 Hz, 0.7 H), 3.36 (d, J = 20.0 Hz, 0.3 H), 3.20 (d, J = 20.4 Hz, 0.3 H), 3.17 (d, J = 20.0 Hz, 0.7 H), 1.57 (s, 2.7 H), 1.46 (s, 6.3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.5, 223.0, 222.1, 193.8, 193.6, 153.5, 152.5, 147.3, 147.1, 144.5, 142.7, 141.9, 141.2, 136.5, 136.3, 136.2, 136.1, 134.7, 106.2, 106.0, 105.8, 105.7, 96.2, 93.2, 82.4, 82.0, 64.7, 64.1, 63.7, 62.9, 48.3, 47.5, 28.1, 27.9. IR (cm^{-1}): 3420 (w), 2980 (w), 2482 (w), 1942 (s), 1845 (s), 1695 (s). HRMS (ESI): calcd for $C_{21}H_{25}BMoN_7O_5$ ([M + H]$^+$), 564.1059; found, 564.1061.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-2,3,4)-1-tert-butoxycarbonyl-5-trifluoroacetoxy-5,6-dihydro-2H-pyridin-2-yl]molybdenum ((±)-**4b′**).*

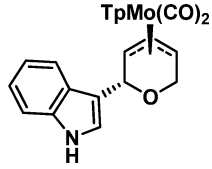


4b'

To a solution of (±)-**2′** (500 mg, 0.88 mmol, 1.0 equiv) in THF (20 mL) was added DIBAL (1.0 M in hexane, 2.2 mL, 2.18 mmol, 2.5 equiv) at 0 °C. The reaction mixture was stirred at 0 °C for 20 min and then quenched with potassium sodium tartrate tetrahydrate (760 mg, 2.56 mmol, 3.0 equiv) and H_2O (10 mL). The mixture was poured into a separatory funnel containing EtOAc (15 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 25 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2/1) afforded (±)-TpMo(CO)$_2$(*syn*-5-hydroxy-1-*tert*-butoxycarbonyl-η^3-5,6-dihydropyridinyl) (452 mg, 0.80 mmol, 91%) as an orange solid. TLC: R_f = 0.27 (2/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.42 (d, J = 1.2 Hz, 0.4 H), 8.40 (d, J = 1.2 Hz, 0.6 H), 8.18 (d, J = 1.2 Hz, 0.6 H), 7.96 (d, J = 1.2 Hz, 0.4 H), 7.82 (d, J = 0.8 Hz, 0.4 H), 7.77 (d, J = 1.2 Hz, 0.6 H), 7.62 (d, J = 2.0 Hz, 0.4 H), 7.56 (br s, 1.6 H), 7.46 (br s, 1 H), 7.20 (d, J = 5.2 Hz, 0.6 H), 7.00 (d, J = 5.6 Hz, 0.4 H), 6.23 (br s, 0.4 H), 6.11−6.16 (m, 2.6 H), 4.67−4.79 (m, 2 H), 3.75 (dd, J = 12.0 Hz, 7.2 Hz, 0.4 H), 3.63 (dd, J = 12.4 Hz, 6.8 Hz, 0.6 H), 3.31 (t, J = 6.8 Hz, 0.6 H), 3.25 (t, J = 6.8 Hz, 0.4 H), 1.75−1.85 (m, 1 H), 1.59 (s, 3.6 H), 1.47 (s, 5.4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 232.7, 231.6, 224.1, 223.8, 154.6, 154.0, 146.6, 146.4, 143.8, 142.2, 141.1, 140.6, 136.0, 135.9, 135.82, 135.76, 134.3, 105.8, 105.7, 105.5, 105.4, 105.2, 94.4, 92.2, 81.5, 81.1, 69.5, 67.9, 67.8, 67.6, 57.2, 56.6, 47.4, 46.6, 28.1, 27.9, 27.4. IR (cm^{-1}) 3420 (w), 2980 (w), 2482 (w), 1942 (s), 1845 (s), 1695 (s). HRMS (ESI): calcd for $C_{21}H_{26}BMoN_7O_5$ ([M + Na]$^+$), 588.1035; found, 588.1038.

Then, to a solution of the reduction product(±)-TpMo(CO)$_2$(*syn*-5-hydroxy-1-*tert*-butoxycarbonyl-η^3-5,6-dihydropyridinyl) (452 mg, 0.80 mmol, 1.0 equiv) in DCM (15 mL) were added TEA (122 mg, 1.20 mmol, 1.5 equiv) and TFAA (218 mg, 1.04 mmol, 1.3 equiv) at −15 °C. The reaction mixture was stirred for 20 min and then loaded on the silica gel directly. Flash chromatography in under 5 min with hexanes/EtOAc (3/1) afforded (±)-**4b′** (490 mg, 0.74 mmol, 92%) as a yellow solid. TLC: R_f = 0.63 (3/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.47 (d, J = 2.0 Hz, 0.3 H), 8.44 (d, J = 2.0 Hz, 0.7 H), 8.21 (d, J = 2.0 Hz, 0.7 H), 7.97 (d, J = 2.0 Hz, 0.3 H), 7.69 (d, J = 1.6 Hz, 0.3 H), 7.66 (d, J = 2.4 Hz, 0.7 H), 7.63 (d, J = 2.0 Hz, 0.3 H), 7.59 (d, J = 2.0 Hz, 0.7 H), 7.58 (d, J = 2.0 Hz, 0.3 H), 7.58 (d, J = 2.0 Hz, 0.7 H), 7.47−7.49 (m, 1 H), 7.25 (dd, J = 6.4 Hz, 2.0 Hz, 0.7 H), 7.06 (dd, J = 5.6 Hz, 1.6 Hz, 0.3 H), 6.18−6.27 (m, 3 H), 5.86−5.91 (m, 1 H), 4.60 (d, J = 8.8 Hz, 0.3 H), 4.59 (d, J = 7.6 Hz, 0.7 H), 3.77 (dd, J = 12.8 Hz, 7.2 Hz, 0.3 H), 3.65 (dd, J = 12.4 Hz, 7.2 Hz, 0.7 H), 3.46 (t, J = 7.2 Hz, 0.7 H), 3.39 (t, J = 7.2 Hz, 0.3 H), 2.01−2.10 (m, 1 H), 1.59 (s, 3 H), 1.49 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 228.5, 227.5, 224.0, 223.7, 157.2 (q, J = 169.6 Hz), 154.4, 153.9, 147.0, 146.8, 144.2, 142.5, 141.2, 140.7, 136.3, 136.2, 136.1, 136.1, 134.5, 114.4 (q, J = 1138 Hz), 106.1, 105.9, 105.8, 105.6, 105.5, 94.8, 92.5, 82.1, 81.9, 77.3, 77.0, 76.7, 74.7, 74.5, 60.8, 59.5, 57.5, 57.0, 43.4, 42.6, 34.6, 34.5, 31.6, 29.0, 28.2, 28.0, 25.2, 22.6, 20.7, 14.1, 11.4.

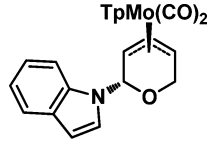
Uncatalyzed Reactions with π-Nucleophiles. *(±)-Dicarbonyl-[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(3′-indolyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**5**).*



5

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in DMSO (4 mL) was added indole (15.2 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**5** (43 mg, 0.077 mmol, 86%) as an orange solid. TLC: R_f = 0.45 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, J = 2.4 Hz, 1 H), 8.17 (br s, 1 H), 7.83 (d, J = 8.0 Hz, 1 H), 7.74 (d, J = 2.0 Hz, 1 H), 7.72 (d, J = 2.0 Hz, 1 H), 7.63 (d, J = 2.4 Hz, 1 H), 7.59 (d, J = 2.4 Hz, 1 H), 7.58 (d, J = 2.4 Hz, 1 H), 7.53 (d, J = 2.0 Hz, 1 H), 7.38 (d, J = 8.0 Hz, 1 H), 7.21 (t, J = 8.0 Hz, 1 H), 7.13 (t, J = 7.6 Hz, 1 H), 6.32 (t, J = 2.0 Hz, 1 H), 6.17(t, J = 2.0 Hz, 1 H), 6.15 (t, J = 2.0 Hz, 1 H), 5.32 (d, J = 2.0 Hz, 1 H), 4.37 (dt, J = 6.8 Hz, 2.4 Hz, 1 H), 4.03−4.11 (m, 2 H), 3.88 (d, J = 12.0 Hz, 1 H), 3.62 (dd, J = 12.8 Hz, 2.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 226.0, 225.8, 147.4, 141.9, 141.4, 136.6, 136.0, 135.9, 134.4, 127.1, 123.8, 122.5, 120.0, 119.9, 116.8, 111.0, 106.0, 105.3, 105.3, 69.8, 67.4, 65.4, 64.2, 57.5.IR (cm^{-1}): 3300 (w), 2482 (w), 1938 (s), 1849 (s), 1505 (s). HRMS (ESI): calcd for $C_{24}H_{22}BMoN_7O_3Na$ ([M + Na]$^+$), 588.0823; found, 588.0829.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(1′-indolyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**5′**).*

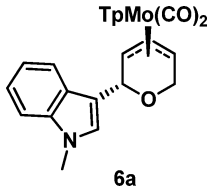


5'

The N-substituted isomer (±)-**5′** was formed when the reaction is carried out in THF under basic conditions on the 5-acetoxymolybdenum complex **3a**: to a solution of (±)-**3a**[5] (50 mg, 0.099 mmol, 1.0 equiv) in THF (4 mL) were added NaH (1.2 mg, 0.297 mmol, 3.0 equiv) and indole (38.0 mg, 0.297 mmol, 3.0 equiv). The reaction mixture was stirred at room temperature for 2 h and then quenched with saturated NH_4Cl. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted by EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (20/1) afforded (±)-**5** (51.3 mg, 0.32 mmol, 92%) as an orange solid. TLC: R_f = 0.65 (3/1 hexanes/EtOAc). ^{1}H NMR (600 MHz, DMSO): δ 8.69 (d, J = 1.2 Hz, 1 H), 8.08 (d, J = 3.0 Hz, 1 H), 7.75 (s, 1 H), 7.73 (s, 1 H), 7.65 (d, J = 7.8 Hz, 1 H), 7.62 (d, J = 7.2 Hz, 1 H), 7.61 (d, J = 7.2

Hz, 1 H), 7.56 (s, 1 H), 7.55 (d, J = 9.0 Hz, 1 H), 7.23 (t, J = 7.2 Hz, 1 H), 7.15 (t, J = 7.2 Hz, 1 H), 6.59 (d, J = 7.2 Hz, 1 H), 6.36 (t, J = 3.0 Hz, 1 H), 6.22(t, J = 2.4 Hz, 1 H), 6.18 (t, J = 2.4 Hz, 1 H), 6.17 (s, 1 H), 4.30 (t, J = 7.2 Hz, 1 H), 4.26 (d, J = 7.2 Hz, 1 H), 4.18 (d, J = 7.2 Hz, 1 H), 3.90 (d, J = 13.2 Hz, 1 H), 3.66 (dd, J = 13.2 Hz, 1.8 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO): δ 225.5, 224.5, 147.4, 142.1, 141.3, 136.8, 136.2, 136.2, 134.6, 129.3, 125.5, 122.0, 120.7, 120.3, 110.6, 106.2, 105.6, 105.5, 101.8, 77.9, 66.4, 65.1, 63.9, 57.8. IR (cm^{-1}): 3142 (w), 3053 (w), 2930 (w), 2486 (w), 1945 (s), 1861 (s).

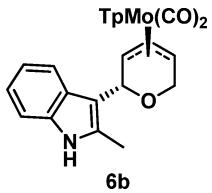
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(1′-methyl-3′-indolyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**6a**).*



6a

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in DMSO (4 mL) was added *N*-methylindole (17.1 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**6a** (43 mg, 0.075 mmol, 84%) as an orange solid. TLC: R_f = 0.38 (3/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, DMSO): δ 8.62 (d, J = 2.0 Hz, 1 H), 8.07 (d, J = 2.0 Hz, 1 H), 8.04 (d, J = 2.0 Hz, 1 H), 7.89 (d, J = 2.4 Hz, 1 H), 7.86 (d, J = 2.4 Hz, 1 H), 7.85 (d, J = 2.4 Hz, 1 H), 7.81 (s, 1 H), 7.56 (d, J = 7.6 Hz, 1 H), 7.45 (d, J = 8.4 Hz, 1 H), 7.18 (t, J = 7.2 Hz, 1 H), 7.05 (t, J = 8.0 Hz, 1 H), 6.49 (t, J = 2.0 Hz, 1 H), 6.30 (t, J = 2.0 Hz, 1 H), 6.26 (t, J = 2.0 Hz, 1 H), 5.11 (d, J = 2.4 Hz, 1 H), 4.58 (dt, J = 7.2 Hz, 2.4 Hz, 1 H), 4.39 (d, J = 6.4 Hz, 1 H), 4.00 (t, J = 7.2 Hz, 1 H), 3.84 (s, 3 H), 3.68 (d, J = 12.4 Hz, 1 H), 3.43 (dd, J = 12.0 Hz, 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO): δ 226.6, 226.2, 147.0, 142.9, 142.4, 137.1, 136.6, 135.3, 129.6, 127.2, 121.4, 118.9, 113.8, 109.8, 106.6, 105.8, 105.8, 70.2, 68.1, 64.8, 64.6, 56.9, 32.6. IR (cm^{-1}): 2957 (w), 2922 (m), 2853 (w), 2482 (m), 1942 (s), 1849 (s). HRMS (FAB): calcd for $C_{25}H_{25}BMoN_7O_3$ ([M + H]$^+$), 580.1161; found, 580.1167.

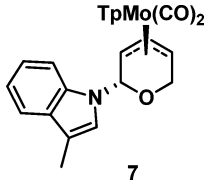
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(2′-methyl-3′-indolyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**6b**).*



6b

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in DMSO (4 mL) was added 2-methylindole (17.1 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**6b** (39 mg, 0.068 mmol, 76%) as an orange solid. TLC: R_f = 0.48 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, J = 2.0 Hz, 1 H), 8.45 (d, J = 7.2 Hz, 1 H), 7.97 (br s, 1 H), 7.81 (d, J = 2.0 Hz, 1 H), 7.70 (d, J = 2.0 Hz, 1 H), 7.60 (d, J = 2.4 Hz, 1 H), 7.57 (d, J = 2.4 Hz, 1 H), 7.54 (d, J = 2.4 Hz, 1 H), 7.32 (d, J = 7.2 Hz, 1 H), 7.10–7.17 (m, 2 H), 6.34 (t, J = 2.4 Hz, 1 H), 6.22 (t, J = 2.4 Hz, 1 H), 6.12(t, J = 2.4 Hz, 1 H), 5.24 (d, J = 2.4 Hz, 1 H), 4.40–4.43 (m, 1 H), 4.32 (d, J = 5.6 Hz, 2 H), 4.30 (d, J = 12.0 Hz, 1 H), 3.80 (d, J = 12.0 Hz, 1 H), 2.56 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 226.8, 225.8, 147.4, 141.9, 141.5, 135.9, 135.9, 135.2, 134.6, 134.4, 127.8, 121.1, 120.2, 119.7, 111.7, 110.3, 106.0, 105.3, 105.2, 71.2, 67.0, 66.5, 60.1, 12.7. IR (cm^{-1}): 3347 (m), 2957 (w), 2482 (w), 1942 (s), 1853 (s), 1602 (m). HRMS (FAB): calcd for $C_{25}H_{24}BMoNaN_7O_3$ ([M + Na]$^+$), 602.0980; found, 602.0982.

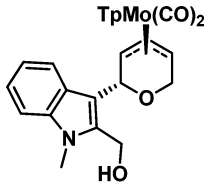
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(3′-methyl-1′-indolyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**7**).*



7

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in DMSO (4 mL) was added 3-methylindole (17.1 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (20/1) afforded (±)-7 (40 mg, 0.075 mmol, 78%) as an orange solid. TLC: R_f = 0.61 (6/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, DMSO): δ 8.65 (d, J = 2.4 Hz, 1 H), 8.19 (d, J = 2.0 Hz, 1 H), 8.09 (d, J = 2.0 Hz, 1 H), 8.00 (s, 1 H), 7.91 (d, J = 2.4 Hz, 1 H), 7.89 (d, J = 2.4 Hz, 1 H), 7.86 (d, J = 2.0 Hz, 1 H), 7.53 (d, J = 2.0 Hz, 1 H), 7.33 (d, J = 8.0 Hz, 1 H), 7.16 (t, J = 8.0 Hz, 1 H), 7.08 (t, J = 8.0 Hz, 1 H), 6.50 (t, J = 2.0 Hz, 1 H), 6.33 (t, J = 2.0 Hz, 1 H), 6.26(t, J = 2.0 Hz, 1 H), 6.02 (d, J = 2.0 Hz, 1 H), 4.59 (d, J = 7.6 Hz, 1 H), 4.49 (d, J = 6.8 Hz, 1 H), 4.30 (t, J = 7.2 Hz, 1 H), 3.68 (d, J = 12.8 Hz, 1 H), 3.48 (dd, J = 12.4 Hz, 2.0 Hz, 1 H), 2.32 (s, 3 H). ^{13}C NMR (100 MHz, DMSO): δ 226.2, 225.6, 147.0, 143.6, 142.3, 136.7, 136.7, 135.4, 129.4, 124.0, 121.5, 119.3, 118.7, 110.2, 109.5, 106.8, 106.0, 105.8, 77.3, 66.6, 65.8, 65.1, 57.5, 9.7. IR (cm^{-1}): 2957 (w), 2482 (w), 1949 (s), 1864 (s), 1505 (w). HRMS (FAB): calcd for $C_{25}H_{25}BMoN_7O_3$ ([M + H]$^+$), 580.1161; found, 580.1167.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(1′-methyl-2′-hydroxymethyl-3′-indolyl)-5,6-dihydro-2H-pyran-3-yl] molybdenum ((±)-**8**).*



8

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in DMSO (4 mL) was added the indolyl alcohol, prepared as described in the Supporting Information (20.9 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**8** (44 mg, 0.072 mmol, 81%) as an orange solid. TLC: R_f = 0.38 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.67 (d, J = 2.0 Hz, 1 H), 8.58 (d, J = 8.4 Hz, 1 H), 7.78 (d, J = 1.6 Hz, 1 H), 7.72 (d, J = 2.0 Hz, 1 H), 7.61 (d, J = 2.0 Hz, 1 H), 7.59 (d, J = 2.0 Hz, 1 H), 7.55 (d, J = 2.0 Hz, 1 H), 7.38 (d, J = 8.4 Hz, 1 H), 7.28 (dt, J = 7.2 Hz, 1.2 Hz, 1 H), 7.16 (dt, J = 7.2 Hz, 1.2 Hz, 1 H), 6.34 (t, J = 2.0 Hz, 1 H), 6.22 (t, J = 2.0 Hz, 1 H), 6.13 (t, J = 2.0 Hz, 1 H), 5.34 (d, J = 2.0 Hz, 1 H), 4.92 (d, J = 14.0 Hz, 1 H), 4.86 (d, J = 13.2 Hz, 1 H), 4.56 (dt, J = 6.4 Hz, 2.4 Hz, 1 H), 4.31–4.37 (m, 2 H), 4.22 (dd, J = 12.4 Hz, 1.6 Hz, 1 H), 3.84 (s, 3 H), 3.74 (dd, J = 12.4 Hz, 1.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 226.8, 225.9, 147.4, 142.0, 141.4, 138.6, 137.0, 136.0, 134.4, 126.3, 121.9, 121.1, 119.6, 113.3, 109.5, 106.0, 105.4, 105.3, 71.1, 67.4, 67.3, 66.7, 60.1, 54.2, 29.7. IR (cm^{-1}):

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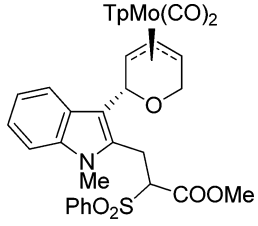
3377 (m), 3146 (w), 3053 (w), 2945 (w), 2482 (m), 1942 (s), 1845 (s), 1505 (m). HRMS (FAB): calcd for $C_{26}H_{27}BMoN_7O_4$ ([M + H]$^+$), 610.1266; found, 610.1271.

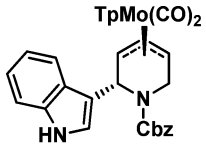
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(2′-(3″-methoxy-3″-oxo-2″-(phenylsulfonyl)propyl)-1′-methyl-1H-indol-3′-yl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**9**).*



9

To a solution of (±)-**3b** (175 mg, 0.31 mmol, 1.0 equiv) in DMSO (5 mL) was added methyl 3-(1-methyl-1*H*-indol-2-yl)-2-(phenylsulfonyl)propanoate, prepared as described in the Supporting Information (165 mg, 0.47 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**9** (180 mg, 0.224 mmol, 73%) as an orange solid. ^{1}H NMR (a mixture of two diastereomers) (600 MHz, $CDCl_3$): δ 8.68−8.65 (m, 1.5H), 8.44 (d, *J* = 7.8 Hz, 0.5H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.78 (s, 0.5H), 7.76−7.75 (m, 1.5H), 7.68−7.66 (m, 1H), 7.59 (s, 1H), 7.58 (s, 1H), 7.55 (t, *J* = 1.8 Hz, 1H), 7.53−7.52 (m, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.33−6.31 (m, 1H), 6.21−6.19 (m, 1H), 6.09−6.08 (m, 1H), 5.18 (d, *J* = 1.8 Hz, 0.5H), 5.05 (d, *J* = 1.8 Hz, 0.5H), 4.73 (dd, *J* = 3.0, 11.4 Hz, 0.5H), 4.41−4.39 (m, 0.5H), 4.34−4.32 (m, 1.5H), 4.28−4.26 (m, 2H), 4.17 (t, *J* = 7.2 Hz, 1H), 4.12 (dd, *J* = 3.6, 12.6 Hz, 1.5H), 3.79 (s, 1.5H), 3.77 (s, 1.5H), 3.73 (dd, *J* = 3.0, 13.2 Hz, 1H), 3.69 (t, *J* = 5.4 Hz, 1H), 3.66−3.65 (m, 1H), 3.64−3.63 (m, 0.5H), 3.59 (dd, *J* = 1.8, 13.2 Hz, 1H), 3.55 (s, 1.5H), 3.50 (s, 1.5H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 227.0, 226.6, 226.5, 226.2, 166.0, 165.4, 147.6, 142.7, 142.4, 141.6, 141.5, 137.7, 137.6, 137.5, 137.2, 136.2, 136.1, 134.7, 134.6, 134.5, 133.4, 129.5, 129.4, 129.2, 126.9, 126.7, 122.0, 121.7, 121.1, 121.0, 114.4, 113.3, 109.8, 109.7, 106.2, 105.6, 105.5, 72.0, 71.6, 70.6, 70.2, 67.5, 67.3, 67.1, 66.6, 66.0, 60.6, 60.1, 53.6, 53.2, 30.2, 30.1, 22.4, 21.7. IR (cm^{-1}): 2481 (w), 1938 (s), 1850 (s), 1741 (s). HRMS (FAB): calcd for $C_{35}H_{34}BMoN_7NaO_7S$ ([M + Na]$^+$), 828.1280; found, 828.1284.

*(+)- and (±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-benzyloxycarbonyl-2-(3′-indolyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((+)- and (±)-**10**).*



10

To a solution of (±)-**4b** (50 mg, 0.072 mmol, 1.0 equiv) in DMSO (4 mL) was added indole (12.6 mg, 0.11 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**10** (40 mg, 0.058 mmol, 80%) as an orange solid.

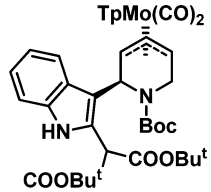
Similar treatment of (+)-**4b** (50 mg, 0.072 mmol, 1.0 equiv, 97.5% ee) in DMSO (4 mL) with indole (12.6 mg, 0.11 mmol, 1.5 equiv) afforded (+)-**10** (40 mg, 0.058 mmol, 80%, 97% ee).

Similar treatment of (+)-**4b** (50 mg, 0.072 mmol, 1.0 equiv, 97.5% ee) in DMSO (4 mL) with indole (12.6 mg, 0.11 mmol, 1.5 equiv) and MgO (8.8 mg, 0.22 mmol, 3 equiv) afforded (+)-**10** (37 mg, 0.054 mmol, 74%, 97.5% ee).

Similar treatment of (+)-**4b** (50 mg, 0.072 mmol, 1.0 equiv, 97.5% ee) in MeCN (4 mL) with indole (12.6 mg, 0.11 mmol, 1.5 equiv) afforded (+)-**10** (40 mg, 0.058 mmol, 74%, 97.5% ee). $[\alpha]_D^{20}$ = +121.1° (*c* = 0.75, CH_2Cl_2).

TLC: R_f = 0.28 (2/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 2.4 Hz, 0.5 H), 8.63 (d, *J* = 2.4 Hz, 0.5 H), 8.26 (d, *J* = 8.0 Hz, 0.5 H), 8.25 (s,0.5 H), 8.21 (s, 0.5 H), 7.81 (d, *J* = 2.0 Hz, 0.5 H), 7.79 (d, *J* = 2.0 Hz, 0.5 H), 7.73 (d, *J* = 8.0 Hz, 0.5 H), 7.72 (d, *J* = 2.4 Hz, 0.5 H), 7.69 (d, *J* = 2.0 Hz, 0.5 H), 7.60 (t, *J* = 2.4 Hz, 1 H), 7.57 (d, *J* = 2.0 Hz, 1 H), 7.53 (d, *J* = 2.0 Hz, 1 H), 7.51 (d, *J* = 2.0 Hz, 0.5 H), 7.26−7.39 (m, 6.5 H), 7.14−7.23 (m, 1.5 H), 6.94 (t, *J* = 8.0 Hz, 0.5 H), 6.32 (m, 1 H), 6.21 (t, *J* = 2.0 Hz, 1 H), 6.12 (t, *J* = 2.0 Hz, 0.5 H), 6.11 (t, *J* = 2.0 Hz, 0.5 H), 5.87 (d, *J* = 2.8 Hz, 0.5 H), 5.78 (d, *J* = 2.8 Hz, 0.5 H), 5.15 (d, *J* = 12.4 Hz, 0.5 H), 5.12 (d, *J* = 12.0 Hz, 0.5 H), 5.02 (d, *J* = 12.0 Hz, 0.5 H), 4.98 (d, *J* = 12.0 Hz, 0.5 H), 4.51 (dt, *J* = 7.2 Hz, 2.8 Hz, 0.5 H), 4.41−4.46 (m, 1 H), 4.32−4.37 (m, 1 H), 4.26 (dd, *J* = 14.4 Hz, 2.8 Hz, 0.5 H), 4.00 (t, *J* = 7.2 Hz, 0.5 H), 3.94 (d, *J* = 7.2 Hz, 0.5 H), 3.71 (d, *J* = 10.0 Hz, 0.5 H),3.68 (d, *J* = 10.0 Hz, 0.5 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.8, 225.3, 225.3, 224.9, 154.7, 154.2, 147.3, 141.9, 141.7, 136.7, 136.6, 136.5, 136.2, 136.0, 134.4, 128.4, 128.2, 128.2, 127.9, 127.8, 127.6, 126.3, 126.0, 123.8, 122.9, 122.2, 122.1, 120.9, 120.1, 119.8, 119.6, 117.7, 117.5, 111.0, 106.0, 105.4, 105.3, 105.3, 105.3, 71.2, 70.8, 67.3, 67.1, 67.0, 64.1, 63.6, 47.3, 47.1, 39.4, 39.2. IR (cm^{-1}): 3358 (m), 3123 (w), 3057 (w), 2482 (m), 1938 (s), 1857 (s), 1679 (s). HRMS (FAB): calcd for $C_{32}H_{30}BMoN_8O_4$ ([M + H]$^+$), 699.1532; found, 699.1550. HPLC: (DaicelChiralcelOD-RH column, isocratic solvent system 65% CH_3CN in H_2O (without TFA), 1.0 mL/min, λ 254 nm): (2*R*,3*R*)-(+)-**10**, t_+ = 16.6 min; (2*S*,3*S*)-(−)-**10**, t_- = 21.5 min.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-tert-butoxycarbonyl-2-(2′-malonyl-3′-indolyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**11**).*



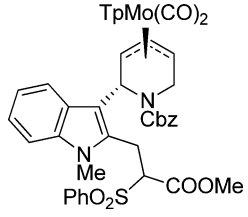
11

To a solution of (±)-**4b′** (50 mg, 0.076 mmol, 1.0 equiv) in DMSO (4 mL) were added indolyl malonate[49] (37.8 mg, 0.11 mmol, 1.5 equiv) and MgO (8.8 mg, 0.22 mmol, 3.0 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**11** (41 mg, 0.046 mmol, 61%) as an orange solid. TLC: R_f = 0.26 (2/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 9.46 (s, 0.5 H), 9.35 (s, 0.5 H), 8.64 (d, *J* = 1.6 Hz, 1 H), 8.37 (d, *J* = 8.0 Hz, 0.5 H), 8.16 (d, *J* = 8.0 Hz, 0.5 H), 7.88(br s, 1 H), 7.82 (d, *J* = 2.0 Hz, 0.5 H), 7.73 (d, *J* = 2.0 Hz, 0.5 H), 7.58−7.60 (m, 1.5 H), 7.50−7.53 (m, 2.5 H), 7.41 (s, 0.5 H), 7.39 (s, 0.5 H), 7.17−7.22 (m, 1H), 7.12−7.16 (m, 1 H), 6.29−6.31 (m, 1 H), 6.20−6.23 (m, 1 H), 6.03−6.05 (m, 1 H), 5.93 (s, 0.5 H), 5.58 (d, *J* = 2.0 Hz, 0.5 H), 5.52 (d, *J* = 2.8 Hz, 0.5 H), 5.38 (s, 0.5 H), 4.54−4.46 (m, 1 H), 4.45−4.50 (m, 1 H), 4.30−4.38 (m, 1 H), 4.27−4.31 (m, 1 H), 3.93−4.10 (m, 1 H), 1.56 (s, 4.5 H), 1.53 (s, 4.5 H), 1.46 (s, 4.5 H), 1.45 (s, 9 H), 1.36 (s, 4.5 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 226.3, 225.8, 225.2, 168.3, 167.7, 167.1, 166.1, 154.3, 153.8, 147.3, 147.3, 142.2, 142.1, 141.9, 141.8, 136.0, 136.0, 135.8, 134.3, 129.3, 128.8, 128.6, 128.5, 128.4, 128.3, 128.3, 127.0, 126.1, 125.6, 121.9, 121.6, 121.0, 119.6, 119.3, 116.9, 115.3, 111.4, 105.9, 105.8, 105.3, 105.1, 105.0, 83.2, 83.0, 82.5, 82.4, 80.3, 79.1, 70.9, 70.4, 67.0, 66.5, 66.0, 64.9, 50.8, 47.2, 46.0, 41.3, 41.0, 28.5, 28.3, 27.9, 27.9. IR (cm^{-1}): 3358 (m), 3123 (w), 3057 (w),

dx.doi.org/10.1021/om401087h | *Organometallics* 2013, 32, 7594−7611

2482 (m), 1938 (s), 1857 (s), 1679 (s). HRMS (FAB): calcd for $C_{40}H_{49}BMoNaN_8O_8$ ([M + Na]$^+$), 901.2724; found, 901.2712.

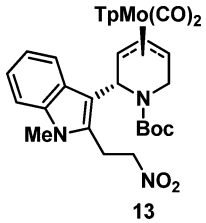
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-benzyloxycarbonyl-2-(2′-(3″-methoxy-3″-oxo-2″-(phenylsulfonyl)propyl)-1′-methyl-1H-indol-3′-yl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**12**).*



12

To a solution of (±)-**4b** (120 mg, 0.172 mmol, 1.0 equiv) in DMSO (8 mL) was added methyl 3-(1-methyl-1*H*-indol-2-yl)-2-(phenylsulfonyl)propanoate, prepared as described in the Supporting Information (92 mg, 0.26 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**12** (102 mg, 0.108 mmol, 63%) as an orange solid. TLC: R_f = 0.22 (2/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two diastereomers) (600 MHz, $CDCl_3$): δ 8.63 (d, J = 1.2 Hz, 0.5 H), 8.61 (d, J = 1.2 Hz, 0.5 H), 8.34 (d, J = 7.8 Hz, 0.5 H), 8.31 (d, J = 7.8 Hz, 0.5 H), 8.23 (d, J = 1.8 Hz, 0.5 H), 8.19 (d, J = 1.8 Hz, 0.5 H), 8.01 (d, J = 1.2 Hz, 0.5 H), 8.0 (d, J = 1.2 Hz, 0.5 H), 7.86 (d, J = 1.8 Hz, 0.5 H), 7.82 (d, J = 1.8 Hz, 0.5 H), 7.80 (d, J = 7.2 Hz, 1 H), 7.68 (d, J = 7.2 Hz, 0.5 H), 7.66 (d, J = 7.2 Hz, 0.5 H), 7.61 (d, J = 1.8 Hz, 1 H), 7.58 (d, J = 7.8 Hz, 0.5 H), 7.56 (d, J = 1.2 Hz, 1 H), 7.53 (s, 1H), 7.52 (d, J = 8.4 Hz, 0.5 H), 7.45 (d, J = 7.8 Hz, 0.5 H), 7.43 (d, J = 7.8 Hz, 0.5 H), 7.32−7.26 (m, 4 H), 7.22 (d, J = 7.8 Hz, 0.5 H), 7.20 (d, J = 7.8 Hz, 0.5 H), 7.05 (d, J = 7.2 Hz, 1 H), 6.31 (d, J = 1.8 Hz, 1 H), 6.24−6.22 (m, 1 H), 6.04 (t, J = 1.8 Hz, 0.5 H), 6.02 (t, J = 1.8 Hz, 0.5 H), 5.57 (d, J = 3.0 Hz, 0.5 H), 5.54 (d, J = 2.4 Hz, 1 H), 5.40 (d, J = 10.8 Hz, 0.5 H), 5.34 (d, J = 12.6 Hz, 0.5 H), 5.24 (d, J = 10.8 Hz, 0.5 H), 5.12 (d, J = 2.4 Hz, 0.5 H), 5.11 (s, 1 H), 5.08 (dd, J = 3.0, 12 Hz, 0.5 H), 4.87 (dd, J = 3.0, 12 Hz, 0.5 H), 4.81 (d, J = 12.6 Hz, 0.5 H), 4.75 (d, J = 12.6 Hz, 0.5 H), 4.51 (dd, J = 1.8, 7.2 Hz, 0.5 H), 4.43−4.40 (m, 1.5 H), 4.37 (br s, 0.5 H), 4.35 (br s, 0.5 H), 4.32 (dt, J = 2.4, 7.2 Hz, 0.5 H), 4.28 (dt, J = 2.4, 7.2 Hz, 0.5 H), 4.07−4.03 (m, 1.5 H), 3.98 (d, J = 13.8 Hz, 0.5 H), 3.71 (dd, J = 12.6, 15.0 Hz, 0.5 H), 3.65 (dd, J = 2.4, 15.0 Hz, 0.5 H), 3.60 (s, 1.5 H), 3.56 (s, 1.5 H), 3.50 (d, J = 6.6 Hz, 0.5 H), 3.42 (s, 1.5 H), 3.35 (s, 1.5 H), 2.80 (dd, J = 2.4, 15.0 Hz, 0.5 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 227.0, 226.6, 225.0, 224.4, 166.4, 166.3, 155.4, 154.6, 147.6, 143.6, 141.3, 138.4, 137.2, 137.1, 136.9, 136.8, 136.3, 134.7, 134.6, 133.6, 132.4, 129.6, 129.4, 129.3, 128.6, 128.5, 128.1, 127.8, 127.7, 126.3, 126.1, 122.8, 122.5, 121.4, 121.3, 120.8, 120.6, 117.5, 116.6, 109.7, 109.5, 106.2, 105.7, 105.3, 105.2, 74.1, 73.9, 72.9, 72.5, 69.7, 69.2, 66.9, 66.7, 65.7, 65.4, 63.4, 56.3, 56.2, 53.3, 53.2, 47.9, 47.6, 42.3, 41.9, 22.7, 22.6. IR (cm^{-1}): 1945 (s), 1858 (s), 1743 (s), 1692. HRMS (FAB): calcd for $C_{43}H_{41}BMoNaN_8O_8S$ ([M + Na]$^+$), 961.181; found, 961.1803.

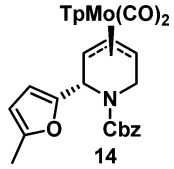
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-tert-butoxycarbonyl-2-(1′-methyl-2′-nitroethyl-3′-indolyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**13**).*



13

To a solution of (±)-**4b′** (50 mg, 0.076 mmol, 1.0 equiv) in DMSO (4 mL) were added methyl-2-(2-nitroethyl)-1*H*-indole, prepared as described in the Supporting Information (22.4 mg, 0.11 mmol, 1.5 equiv), and MgO (8.8 mg, 0.22 mmol, 3.0 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**13** (41 mg, 0.046 mmol, 66%) as an orange solid. TLC: R_f = 0.23 (2/1 hexanes/EtOAc). ^{1}H NMR (major rotamer) (400 MHz, $CDCl_3$): δ 8.62 (d, J = 2.0 Hz, 1 H), 8.30 (d, J = 8.0 Hz, 1 H), 7.87 (d, J = 2.0 Hz, 1 H), 7.82 (d, J = 2.0 Hz, 1 H), 7.60 (d, J = 2.4 Hz, 1 H), 7.53 (d, J = 2.4 Hz, 1 H), 7.51 (d, J = 2.0 Hz, 1 H), 7.33 (d, J = 8.0 Hz, 1 H), 7.26 (t, J = 7.2 Hz, 1 H), 6.30 (t, J = 2.0 Hz, 1 H), 6.23 (t, J = 2.0 Hz, 1 H), 6.08 (t, J = 2.0 Hz, 1 H), 5.58 (d, J = 2.8 Hz, 1 H), 4.96 (dt, J = 12.8 Hz, 6.8 Hz, 1 H), 4.64 (dt, J = 13.2 Hz, 6.4 Hz, 1 H), 4.47 (d, J = 4.4 Hz, 1 H), 4.22−4.35 (m, 3 H), 4.08 (t, J = 7.6 Hz, 1 H), 3.97 (d, J = 15.2 Hz, 1 H), 3.73 (s, 3 H), 3.62 (dt, J = 15.6 Hz, 6.8 Hz, 1 H), 1.37 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$)): δ 225.8, 225.7, 153.8, 147.4, 142.4, 141.6, 137.6, 136.0, 135.8, 134.3, 133.0, 125.6, 121.5, 120.9, 119.5, 115.1, 109.3, 105.9, 105.3, 79.4, 75.2, 71.4, 65.8, 65.4, 46.5, 41.5, 29.7, 28.3, 22.9. IR (cm^{-1}): 2976 (w), 2930 (w), 2482 (w), 1942 (s), 1853 (s), 1679 (m). HRMS (FAB): calcd for $C_{32}H_{36}BMoNaN_9O_6$ ([M + Na]$^+$), 774.1828; found, 774.1835.

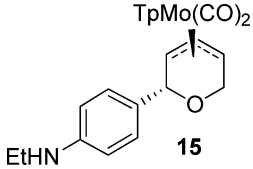
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-benzyloxycarbonyl-2-(5′-methyl-2′-furanyl)-5,6-dihydro-2H-pyridin-3-yl] molybdenum ((±)-**14**).*



14

To a solution of (±)-**4b** (50 mg, 0.072 mmol, 1.0 equiv) in MeCN (4 mL) was added 2-methylfuran (9.1 mg, 0.11 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**14** (40 mg, 0.060 mmol, 84%) as an orange solid. TLC: R_f = 0.34, 3/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.58 (br s, 1 H), 7.77 (d, J = 2.0 Hz, 0.4 H), 7.75 (br s, 1 H), 7.72 (d, J = 2.0 Hz, 0.6 H), 7.56−7.58 (m, 2 H), 7.51 (d, J = 2.0 Hz, 1 H), 7.27−7.34 (m, 5 H), 6.31 (t, J = 2.0 Hz, 1 H), 6.26 (d, J = 3.2 Hz, 0.4 H), 6.17−6.19 (m, 1 H), 6.14−6.16 (m, 1 H), 6.14 (d, J = 2.8 Hz, 0.6 H), 5.92 (d, J = 2.0 Hz, 0.4 H), 5.89 (d, J = 2.4 Hz, 0.6 H), 5.43 (d, J = 2.8 Hz, 0.4 H), 5.38 (d, J = 3.2 Hz, 0.6 H), 5.19 (d, J = 13.2 Hz, 0.6 H), 5.13 (d, J = 12.4 Hz, 0.4 H), 5.06 (d, J = 12.8 Hz, 0.4 H), 5.05 (d, J = 12.8 Hz, 0.6 H), 4.19−4.38 (m, 3 H), 3.87 (t, J = 7.2 Hz, 1 H), 3.75 (d, J = 13.2 Hz, 0.4 H), 3.67 (d, J = 13.2 Hz, 0.6 H), 2.31 (s, 1.2 H), 2.27 (s, 1.8 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.7, 225.5, 225.3, 225.0, 154.8, 153.6, 153.6, 151.8, 151.7, 147.3, 141.9, 141.7, 136.9, 136.7, 136.0, 134.4, 128.3, 128.2, 127.9, 127.7, 127.6, 127.6, 107.6, 107.5, 106.2, 106.0, 106.0, 105.4, 105.3, 68.2, 68.0, 67.2, 67.0, 67.0, 64.0, 63.9, 48.9, 48.5, 39.8, 39.4, 13.8, 13.7. IR (cm^{-1}): 3134 (w), 3030 (w), 2953 (w), 2837 (w), 2486 (m), 1945 (s), 1861 (s), 1698 (s). HRMS (FAB): calcd for $C_{29}H_{29}BMoN_7O_5$ ([M + H]$^+$), 664.1372; found, 664.1377.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(4-ethylaminophenyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**15**).*



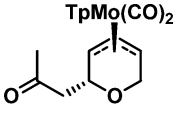
15

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in MeCN (4 mL) was added *N*-ethylaniline (25 mg, 0.18 mmol, 2 equiv). The

dx.doi.org/10.1021/om401087h | *Organometallics* 2013, 32, 7594−7611

reaction mixture was stirred at room temperature for 4 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**15** (28 mg, 0.050 mmol, 56%) as a yellow solid. TLC: R_f = 0.32 (2/1 hexanes/EtOAc).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, J = 1.9 Hz, 1H), 7.74 (d, J = 1.9 Hz, 1H), 7.70 (d, J = 1.9 Hz, 1H), 7.60 (d, J = 2.2 Hz, 1H), 7.59 (d, J = 2.2 Hz, 1H), 7.57−7.53 (m, 2H), 6.65 (d, J = 8.5 Hz, 2H), 6.33 (t, J = 2.2 Hz, 1H), 6.19 (t, J = 2.1 Hz, 1H), 6.15 (t, J = 2.1 Hz, 1H), 4.87 (d, J = 2.1 Hz, 1H), 4.23−4.17 (m, 1H), 4.17−4.10 (m, 2H), 3.97 (d, J = 12.5 Hz, 1H), 3.64 (d, J = 12.3 Hz, 2H), 3.19 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 226.1, 225.6, 148.3, 147.4, 141.8, 141.4, 135.9, 134.3, 129.7, 129.0, 112.3, 105.9, 105.3, 105.2, 72.2, 69.8, 67.2, 64.5, 57.4, 38.4, 14.9. IR (cm^{-1}): 2968 (w), 2868 (w), 2490 (w), 1942 (s), 1853 (s), 1598 (m). HRMS (ESI): calcd for $C_{24}H_{27}N_7O_3BMo$ ([M + H]$^+$), 570.1328; found, 570.1315.

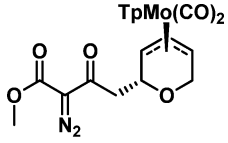
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-acetonyl-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**16**).*



16

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in MeCN (4 mL) was added 2-trimethyloxypropene (16.9 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**16** (36 mg, 0.071 mmol, 80%) as an orange solid. TLC: R_f = 0.20 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, J = 2.0 Hz, 1 H), 7.71 (d, J = 2.0 Hz, 1 H), 7.68 (d, J = 2.0 Hz, 1 H), 7.58 (br s, 2 H), 7.52 (d, J = 2.4 Hz, 1 H), 6.31 (t, J = 2.0 Hz, 1 H), 6.17−6.18 (m, 2 H), 4.35 (ddd, J = 7.6 Hz, 5.2 Hz, 2.0 Hz, 1 H), 4.14 (d, J = 12.8 Hz, 1 H), 4.06−4.12 (m, 2 H), 3.74 (t, J = 7.6 Hz, 1 H), 3.72 (dd, J = 12.4 Hz, 2.0 Hz, 1 H), 2.99 (dd, J = 14.8 Hz, 8.0 Hz, 1 H), 2.83 (dd, J = 14.8 Hz, 5.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.3, 225.2, 207.0, 147.3, 141.8, 141.4, 136.0, 134.4, 106.0, 105.3, 70.5, 67.6, 66.8, 62.9, 57.8, 50.6, 30.2.IR (cm^{-1}): 2957 (m), 2856 (w), 2490 (w), 1948 (s), 1853 (s), 1714 (s), 1625 (s). HRMS (FAB): calcd for $C_{19}H_{21}BMoNaN_6O_4$ ([M + Na]$^+$), 529.0675; found, 529.0664.

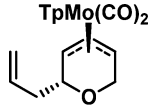
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(diazomethoxycarbonylacetonyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**17**).*



17

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in MeCN (4 mL) was added *tert*-butyldimethylsilyloxyvinyldiazoacetate[50] (33 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-7 (39 mg, 0.067 mmol, 77%) as an orange solid. TLC: R_f = 0.41 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, J = 1.6 Hz, 1 H), 7.73 (d, J = 2.0 Hz, 1 H), 7.68 (d, J = 2.0 Hz, 1 H), 7.57 (t, J = 1.6 Hz, 2 H), 7.51 (d, J = 2.4 Hz, 1 H), 6.30 (t, J = 2.0 Hz, 1 H), 6.17 (t, J = 2.4 Hz, 1 H), 4.41 (ddd, J = 7.2 Hz, 4.8 Hz, 2.0 Hz, 1 H), 4.24 (d, J = 12.8 Hz, 1 H), 4.14 (dt, J = 7.2 Hz, 2.4 Hz, 1 H), 4.08 (d, J = 7.2 Hz, 1 H), 3.86 (s, 3 H), 3.76 (d, J = 7.6 Hz, 1 H), 3.71 (dd, J = 12.8 Hz, 2.4 Hz, 1 H), 3.43 (dd, J = 14.4 Hz, 8.8 Hz, 1 H), 3.31 (dd, J = 14.8 Hz, 4.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.2, 225.2, 190.0, 161.8, 147.3, 141.9, 141.4, 135.9, 134.4, 105.9, 105.3, 70.7, 68.2, 67.0, 63.0, 57.9, 52.2, 46.5. IR (cm^{-1}): 3130 (w), 2957 (w), 2486 (m), 2138 (s), 1942 (s), 1853 (s), 1718 (s), 1648 (s). HRMS (FAB): calcd for $C_{21}H_{21}BMoNaN_8O_6$ ([M + Na]$^+$), 613.0623; found, 613.0633.

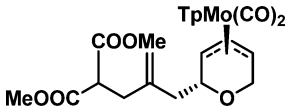
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-allyl-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**18**).*



18

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in MeCN (4 mL) was added allyltrimethylsilane (14.8 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**18** (32 mg, 0.066 mmol, 74%) as an orange solid. TLC: R_f = 0.35 (6/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.63 (d, J = 2.0 Hz, 1 H), 7.70 (d, J = 2.0 Hz, 1 H), 7.68 (d, J = 2.0 Hz, 1 H), 7.57 (d, J = 2.0 Hz, 2 H), 7.52 (d, J = 2.4 Hz, 1 H), 6.31 (t, J = 2.4 Hz, 1 H), 6.17 (t, J = 2.0 Hz, 2 H), 5.93 (ddt, J = 16.8 Hz, 10.0 Hz, 7.2 Hz, 1 H), 5.16 (dd, J = 16.8 Hz, 2.0 Hz, 1 H), 5.10 (dd, J = 10.0 Hz, 0.8 Hz, 1 H), 4.16 (d, J = 12.4 Hz, 1 H), 4.07 (d, J = 6.8 Hz, 1 H), 4.06 (d, J = 6.8 Hz, 1 H), 3.90 (ddd, J = 8.0 Hz, 5.6 Hz, 2.0 Hz, 1 H), 3.78 (t, J = 7.2 Hz, 1 H), 3.72 (dd, J = 12.4 Hz, 1.6 Hz, 1 H), 2.60 (dt, J = 14.0 Hz, 7.2 Hz, 1 H), 2.50 (dt, J = 14.0 Hz, 6.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.7, 225.3, 147.3, 141.6, 141.5, 135.9, 135.5, 134.3, 116.8, 105.9, 105.3, 71.1, 70.4, 67.4, 63.4, 57.6, 40.8. IR (cm^{-1}): 3146 (w), 2926 (m), 2853 (w), 2482 (w), 1938 (s), 1845 (s), 1640 (w). HRMS (FAB): calcd for $C_{19}H_{21}BMoNaN_6O_3$ ([M + Na]$^+$), 513.0715; found, 513.0723.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(malonylisobutenyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**19**).*



19

To a solution of (±)-**3b** (50 mg, 0.089 mmol, 1.0 equiv) in MeCN (4 mL) was added dimethyl 2-(2-((trimethylsilyl)methyl)allyl)-malonate[51] (33 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 1 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**19** (40 mg, 0.063 mmol, 71%) as an orange solid. TLC: R_f = 0.33 (3/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, J = 2.0 Hz, 1 H), 7.73 (d, J = 2.0 Hz, 1 H), 7.69 (d, J = 2.0 Hz, 1 H), 7.57 (d, J = 2.4 Hz, 2 H), 7.52 (d, J = 2.0 Hz, 1 H), 6.30 (t, J = 2.0 Hz, 1 H), 6.16−6.18 (m, 2 H), 4.98 (s, 1 H), 4.88 (s, 1 H), 4.15 (d, J = 12.4 Hz, 1 H), 4.06 (d, J = 7.2 Hz, 2 H), 4.00 (t, J = 7.2 Hz, 1 H), 3.78 (t, J = 7.6 Hz, 1 H), 3.74 (s, 6 H), 3,67−3.74 (m, 2 H), 2.74 (d, J = 7.6 Hz, 2 H), 2.58 (dd, J = 14.0 Hz, 8.4 Hz, 1 H), 2.45 (dd, J = 14.4 Hz, 4.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.5, 225.4, 169.4, 169.4, 147.3, 142.9, 141.8, 141.4, 135.9, 134.3, 113.7, 105.9, 105.3, 71.2, 69.2, 67.1, 63.2, 57.5, 52.6, 52.6, 50.4, 42.6, 34.8. IR (cm^{-1}): 2957 (m), 2926 (m), 2482 (w), 1942 (s), 1853 (s), 1733 (s), 1648 (m). HRMS (FAB): calcd for $C_{25}H_{29}BMoNaN_6O_7$ ([M + Na]$^+$), 657.1137; found, 657.1132.

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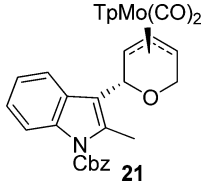
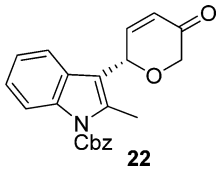
Oxidative Demetalations. *(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(1′-benzyloxycarbonyl-2′-methyl-3′-indolyl)-5,6-dihydro-2H-pyran-3-yl]molybdenum ((±)-**21**).*



21

To a solution of (±)-**6b** (110 mg, 0.19 mmol, 1.0 equiv) in THF (4 mL) were added NaHMDS (1.0 M in THF, 0.38 mL, 0.38 mmol, 2 equiv) and CbzCl (49 mg, 0.29 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature for 30 min and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**21** (95 mg, 0.13 mmol, 70%) as an orange solid. TLC: R_f = 0.33 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, J = 2.0 Hz, 1H), 8.46−8.37 (m, 1H), 8.23−8.08 (m, 1H), 7.81 (d, J = 2.0 Hz, 1H), 7.66 (d, J = 2.0 Hz, 1H), 7.60 (d, J = 2.2 Hz, 1H), 7.57 (d, J = 2.2 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.52−7.48 (m, 2H), 7.45−7.35 (m, 3H), 7.30−7.23 (m, 2H), 6.33 (t, J = 2.2 Hz, 1H), 6.22 (t, J = 2.2 Hz, 1H), 6.11 (t, J = 2.2 Hz, 1H), 5.49 (s, 2H), 5.19 (d, J = 1.8 Hz, 1H), 4.50−4.37 (m, 3H), 4.34 (t, J = 6.8 Hz, 1H), 3.90−3.78 (m, 1H), 2.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 227.1, 226.3, 152.0, 147.4, 141.9, 141.3, 136.5, 136.0, 136.0, 134.9, 134.4, 128.8, 128.7, 128.7, 128.6, 123.5, 122.8, 120.4, 119.3, 115.4, 106.0, 105.4, 105.3, 71.4, 68.7, 68.5, 67.8, 66.8, 62.2, 14.3. IR (cm^{-1}): 3150 (w), 3127 (w), 3049 (w), 2961 (w), 2856 (w), 2482 (m), 1942 (s), 1849 (s), 1733 (m). HRMS (ESI): calcd for $C_{33}H_{30}N_7O_5BMoNa$ ([M + Na]$^+$), 736.1348; found, 736.1350.

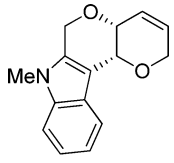
*Benzyl 2-Methyl-3-(5-oxo-5,6-dihydro-2H-pyran-2-yl)-1H-indole-1-carboxylate ((±)-**22**).*



22

To a solution of (±)-**21** (50 mg, 0.07 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) was added pyridinium dichromate (90 mg, 0.21 mmol, 3 equiv) and silica (90 mg, 0.21 mmol, 3 equiv). The reaction mixture was stirred at room temperature for 5 h, and then was passed through a plug of silica gel with ethyl acetate as the eluent. The eluant was collected and concentrated for further purification. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**22** (13 mg, 0.036 mmol, 52%) as a colorless oil. TLC: R_f = 0.33 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.49 (dd, J = 7.8, 1.6 Hz, 1H), 7.46−7.35 (m, 3H), 7.25−7.17 (m, 1H), 7.11 (dd, J = 10.4, 1.8 Hz, 1H), 6.36 (dd, J = 10.4, 2.5 Hz, 1H), 5.63 (dd, J = 4.4, 2.1 Hz, 1H), 5.48 (s, 2H), 4.44 (d, J = 16.5 Hz, 1H), 4.33 (dd, J = 16.3, 2.1 Hz, 1H), 2.66 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.3, 151.8, 151.8, 136.2, 135.7, 134.8, 128.8, 128.6, 127.8, 127.7, 124.2, 123.2, 119.0, 115.8, 115.7, 72.4, 69.5, 68.9, 14.2. IR (cm^{-1}): 3038 (w), 2968 (w), 2930 (w), 2856 (w), 1733 (s), 1698 (s). HRMS (ESI): calcd for $C_{22}H_{20}NO_4$ ([M + H]$^+$), 362.1387; found, 362.1383.

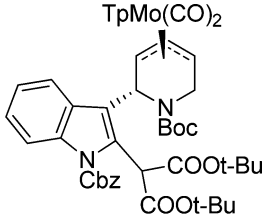
*7-Methyl-4a,6,7,11c-tetrahydro-2H-pyrano[2′,3′:5,6]pyrano[3,4-b]indole ((±)-**23**).*



23

To a solution of (±)-**8** (44 mg, 0.072 mmol, 1.0 equiv) in DMSO (4 mL) were added a 60% NaH suspension (4.3 mg, 0.11 mmol, 1.5 equiv) and copper 2-ethylhexanoate (5 mg, 0.014 mmol, 0.2 equiv). The reaction mixture was stirred at room temperature under dry air for 3 days and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (2 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (6/1) afforded (±)-**23** (16 mg, 0.068 mmol, 95%) as a colorless oil. TLC: R_f = 0.36 (4/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 1 H), 7.31 (d, J = 8.4 Hz, 1 H), 7.20 (dt, J = 8.4 Hz, 1.2 Hz, 1 H), 7.15 (dt, J = 8.0 Hz, 0.8 Hz, 1 H), 6.21 (dd, J = 10.4 Hz, 1.6 Hz, 1 H), 6.11 (ddt, J = 10.4 Hz, 4.0 Hz, 1.6 Hz, 1 H), 5.04 (d, J = 14.8 Hz, 1 H), 4.83 (dd, J = 14.8 Hz, 1.2 Hz, 1 H), 4.68 (s, 1 H), 4.32−4.43 (m, 2 H), 3.92 (dd, J = 4.4 Hz, 2.4 Hz, 1 H), 3.62 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.4, 135.7, 132.7, 126.5, 123.6, 121.7, 119.9, 118.4, 108.9, 106.8, 68.8, 67.4, 65.3, 62.6, 29.6. IR (cm^{-1}): 3042 (w), 2926 (m), 2853 (m), 1471 (s). HRMS (ESI): calcd for $C_{15}H_{16}NO_2$ ([M + H]$^+$), 242.1175; found, 242.1176.

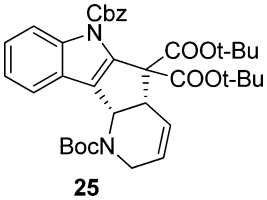
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-tert-butoxycarbonyl-2-(2′-malonyl-3′-N-benzyloxycarbonylindolyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**24**).*



24

To a solution of (±)-**11** (50 mg, 0.051 mmol, 1.0 equiv) in THF (4 mL) were added NaHMDS (1.0 M in THF, 0.10 mL, 0.10 mmol, 2 equiv) and CbzCl (14 mg, 0.092 mmol, 1.8 equiv). The reaction mixture was stirred at room temperature for 30 min and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (2.5/1) afforded (±)-**24** (45 mg, 0.045 mmol, 88%) as an orange solid. TLC: R_f = 0.27 (2/1 hexanes/EtOAc). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.59−8.61 (m, 1 H), 8.26 (dd, J = 8.8, 1.6 Hz, 0.7 H), 8.19 (dd, J = 8.8, 0.8 Hz, 0.7 H), 8.08 (d, J = 7.2 Hz, 0.3 H), 8.01 (d, J = 8.0 Hz, 0.3 H), 7.88 (d, J = 2.0 Hz, 0.7 H), 7.85 (d, J = 8.0 Hz, 0.3 H), 7.55−7.61 (m, 1 H), 7.46−7.54 (m, 4 H), 7.23−7.42 (m, 6 H), 6.32 (t, J = 2.4 Hz, 1 H), 6.21 (t, J = 2.0 Hz, 1 H), 6.10 (s, 0.7 H), 6.03 (t, J = 2.4 Hz, 1 H), 5.59 (d, J = 12.4 Hz, 0.7 H), 5.56 (d, J = 12.4 Hz, 0.3 H), 5.35−5.53 (m, 1.6 H), 5.21 (d, J = 12.4 Hz, 0.7 H), 4.47−4.54 (m, 1.3 H), 4.38 (dd, J = 15.2, 2.4 Hz, 1.0 H), 4.07−4.19 (m, 2.7 H), 4.00 (d, J = 15.6 Hz, 0.7 H), 3.89 (t, J = 6.8 Hz, 0.3 H), 1.47 (s, 2.7 H), 1.44 (s, 9 H), 1.38 (s, 6.3 H), 1.36 (s, 2.7 H), 1.35 (s, 6.3 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 227.1, 226.8, 224.6, 224.1, 166.2, 165.9, 165.6, 165.3, 154.2, 153.9, 151.7, 151.6, 147.4, 142.4, 142.2, 141.4, 141.1, 140.8, 136.5, 136.1, 136.0, 135.9, 135.8, 135.5, 135.1, 134.4, 131.4, 129.7, 128.6, 128.5, 128.4, 128.3, 127.6, 127.5, 127.0, 125.5, 124.6, 124.0, 122.8, 122.5, 122.2, 121.1, 120.9, 120.4, 115.6, 115.3, 106.0, 105.3, 105.2, 105.1, 82.2, 82.1, 81.5, 81.4, 80.8, 79.5, 68.8, 68.4, 68.1, 67.9, 67.7, 66.5, 65.4, 64.8, 51.7, 51.2, 47.5, 46.8, 41.7, 41.1, 28.3, 28.0, 27.7. IR (cm^{-1}): 3065 (w), 2961 (m), 2482 (w), 1945 (s), 1864 (s), 1741 (s). HRMS (ESI): calcd for $C_{48}H_{55}N_8O_{10}BMoNa$ ([M + Na]$^+$), 1035.3091; found, 1035.3129.

*6-Benzyl-1,5,5-tri-tert-butylpyrido[2′,3′:3,4]cyclopenta[1,2-b]-indole-1,5,5,6(2H,4aH,10cH)-tetracarboxylate ((±)-**25**).*

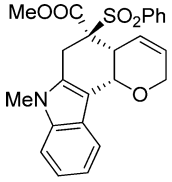


25

dx.doi.org/10.1021/om401087h | *Organometallics* 2013, 32, 7594−7611

To a solution of (±)-**24** (50 mg, 0.050 mmol, 1.0 equiv) in DMSO (2 mL) were added a 60% NaH suspension (2.97 mg, 0.075 mmol, 1.5 equiv) and copper 2-ethylhexanoate (4 mg, 0.001 mmol, 0.2 equiv). The reaction mixture was stirred at room temperature under dry air overnight and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (2 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (6/1) afforded (±)-**25** (22 mg, 0.033 mmol, 67%) as a colorless oil. TLC: R_f = 0.29 (2/1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (br s, 1H), 7.47 (dd, J = 7.8, 1.6 Hz, 2H), 7.42–7.29 (m, 4H), 7.29–7.25 (m, 1H), 7.24–7.17 (m, 1H), 6.08–5.93 (m, 1H), 5.86 (br s, 1H), 5.75–5.61 (m, 1H), 5.57–5.44 (m, 1H), 5.37–5.24 (m, 1H), 4.40–4.04 (m, 2H), 3.33 (br s, 1H), 1.56 (s, 9H), 1.42 (s, 9H), 1.31 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$): δ 167.0, 165.9, 154.7, 150.3, 139.9, 135.2, 128.7, 128.6, 128.5, 127.9, 126.9, 126.1, 125.1, 124.5, 123.1, 119.3, 119.1, 116.2, 82.1, 68.6, 66.4, 52.4, 52.0, 38.4, 29.5, 28.5, 28.0, 27.9, 27.7, 22.6, 13.9, 11.8. IR (cm^{-1}): 2976 (m), 2934 (w), 2872 (w), 1733 (s), 1698 (s). HRMS (ESI): calcd for $C_{37}H_{45}N_2O_8$ ([M + H]$^+$), 645.3170; found, 645.3163; calcd for $C_{37}H_{44}N_2O_8Na$ ([M + Na]$^+$), 667.2990; found, 667.2978.

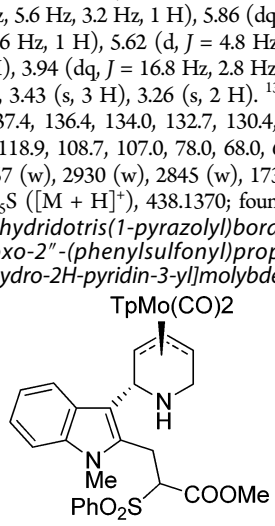
*Methyl 7-Methyl-5-(phenylsulfonyl)-2,4a,5,6,7,11c-hexahydropyrano[3,2-c]carbazole-5-carboxylate ((±)-**26**).*



26

To a solution of (±)-**9** (50 mg, 0.062 mmol, 1.0 equiv) in DMSO (4 mL) were added a 60% NaH suspension (3.74 mg, 0.094 mmol, 1.5 equiv) and copper 2-ethylhexanoate (34 mg, 0.094 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature under dry air overnight and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (2 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (6/1) afforded (±)-**26** (24 mg, 0.056 mmol, 90%) as a white solid. TLC: R_f = 0.36 (2/1 hexanes/EtOAc). Mp: 138–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (dd, J = 8.0 Hz, 1.2 Hz, 2 H), 7.68 (d, J = 8.0 Hz, 1 H), 7.52 (t, J = 7.6 Hz, 1 H), 7.36 (t, J = 8.0 Hz, 2 H), 7.14–7.17 (m, 2 H), 7.10 (ddd, J = 7.8 Hz, 5.6 Hz, 3.2 Hz, 1 H), 5.86 (dq, J = 10.4 Hz, 2.8 Hz, 1 H), 5.68 (d, J = 9.6 Hz, 1 H), 5.62 (d, J = 4.8 Hz, 1 H), 4.11 (dq, J = 16.8 Hz, 2.8 Hz, 1 H), 3.94 (dq, J = 16.8 Hz, 2.8 Hz, 1 H), 3.80 (s, 3 H), 3.78–3.80 (m, 1 H), 3.43 (s, 3 H), 3.26 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 137.4, 136.4, 134.0, 132.7, 130.4, 129.5, 128.5, 126.0, 122.5, 121.6, 119.8, 118.9, 108.7, 107.0, 78.0, 68.0, 61.5, 53.5, 37.4, 29.2, 24.7. IR (cm^{-1}): 3057 (w), 2930 (w), 2845 (w), 1737 (s). HRMS (ESI): calcd for $C_{24}H_{24}NO_5S$ ([M + H]$^+$), 438.1370; found, 438.1371.

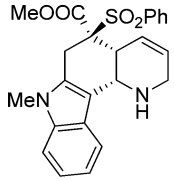
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(2′-(3″-methoxy-3″-oxo-2″-(phenylsulfonyl)propyl)-1′-methyl-1H-indol-3″-yl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**28**).*



28

A portion of 10% Pd/C (100 mg) was added to a solution of (±)-**12** (100 mg, 0.107 mmol) in MeOH/THF (3/1 v/v, 6 mL), and the mixture was exposed to hydrogen at 250 psi for 48 h. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography over silica gel with 3–5% MeOH in CH_2Cl_2 afforded (±)-**28** (60 mg, 0.075 mmol, 72%) as a yellow solid. TLC: R_f = 0.15 (9/1 CH_2Cl_2/MeOH). ^{1}H NMR (a mixture of two diastereomers) (600 MHz, $CDCl_3$): δ 8.65 (s 1 H), 8.58 (d, J = 7.8 Hz, 0.6 H), 8.40 (d, J = 7.8 Hz, 0.4 H), 7.95 (d, J = 7.8 Hz, 0.4 H), 7.93 (d, J = 7.8 Hz, 1 H), 7.89 (d, J = 7.8 Hz, 0.6 H), 7.82 (s, 0.4 H), 7.81 (s, 0.6 H), 7.71 (t, J = 7.2 Hz, 0.4 H), 7.68 (s, 0.4 H), 7.60 (s, 1 H), 7.59 (s, 0.6 H), 7.57 (s, 0.4 H), 7.55 (t, J = 1.2 Hz, 1 H), 7.54 (d, J = 1.2 Hz, 1 H), 7.51 (t, J = 7.8 Hz, 0.6 H), 7.44–7.43 (m, 1 H), 7.23 (d, J = 7.8 Hz, 0.6 H), 7.17 (t, J = 7.2 Hz, 1 H), 6.33 (s, 1 H), 6.21 (d, J = 1.8 Hz, 1 H), 6.07 (s, 0.4 H), 6.05 (s, 0.6 H), 5.56 (d, J = 11.4 Hz, 0.4 H), 5.50 (d, J = 11.4 Hz, 0.6 H), 5.47 (d, J = 11.4 Hz, 0.4 H), 5.41 (d, J = 11.6 Hz, 0.6 H), 5.06 (dd, J = 2.4, 12.0 Hz, 0.6 H), 4.74 (dd, J = 3.6, 9.0 Hz, 0.4 H), 4.49 (br s, 0.4 H), 4.42 (br m, 0.6 H), 4.38 (d, J = 7.2 Hz, 0.6 H), 4.34 (d, J = 7.2 Hz, 0.4 H), 4.29 (t, J = 7.2 Hz, 0.6 H), 4.21 (t, J = 7.2 Hz, 0.4 H), 3.75 (dd, J = 4.2, 7.2 Hz, 1 H), 3.64 (d, J = 6.6 Hz, 0.6 H), 3.61 (d, J = 6.6 Hz, 0.4 H), 3.57 (s, 1.8 H), 3.55 (s, 1.2 H), 3.37 (s, 1.8 H), 3.34 (s, 1.2 H), 3.04 (d, J = 15.0 Hz, 0.4 H), 2.99 (d, J = 15.0 Hz, 0.6 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 227.4, 226.8, 226.4, 226.3, 166.3, 166.2, 147.6, 143.2, 142.4, 141.8, 141.4, 138.4, 138.2, 137.3, 137.1, 136.3, 134.7, 134.6, 129.5, 129.4, 126.9, 122.5, 121.6, 121.5, 120.5, 109.7, 106.2, 105.9, 105.6, 105.5, 105.3, 74.1, 74.0, 69.9, 69.6, 69.2, 56.3, 53.5, 53.2, 47.5, 41.4, 22.4, 22.1. IR (cm^{-1}): 2929 (w), 1934 (s), 1845 (s), 1739 (s). HRMS (FAB): calcd for $C_{35}H_{35}BMoNaN_8O_6S$ ([M + Na]$^+$), 827.145; found, 827.1445.

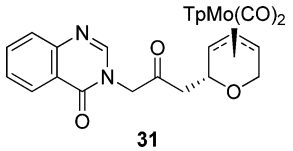
*Methyl 7-Methyl-5-(phenylsulfonyl)-2,4a,5,6,7,11c-hexahydro-1H-pyrido[3,2-c]carbazole-5-carboxylate ((±)-**29**).*



29

To a solution of (±)-**28** (59 mg, 0.062 mmol, 1.0 equiv) in DMSO (4 mL) were added a 60% NaH suspension (3.7 mg, 0.094 mmol, 1.5 equiv) and copper 2-ethylhexanoate (34 mg, 0.094 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature under dry air overnight and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (2 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with hexanes/EtOAc (6/1) afforded (±)-**29** (23 mg, 0.053 mmol, 85%) as a white solid. TLC: R_f = 0.36 (1/1 hexanes/EtOAc). Mp: 176–178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 7.29–7.18 (m, 2H), 7.15–7.01 (m, 3H), 5.86–5.71 (m, 1H), 5.40 (d, J = 10.4 Hz, 1H), 5.01 (d, J = 4.9 Hz, 1H), 3.81 (s, 3H), 3.34 (s, 3H), 3.26–3.10 (m, 3H), 3.10–2.91 (m, 1H), 2.15 (broad s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.24, 137.55, 136.98, 133.94, 132.23, 132.09, 129.60, 128.45, 126.38, 123.36, 121.43, 119.51, 119.34, 108.77, 108.28, 78.96, 53.66, 49.01, 48.99, 40.92, 38.81, 29.25, 29.22, 24.23. IR (cm^{-1}): 3360 (s), 2922 (w), 1734 (s). HRMS (ESI): calcd for $C_{24}H_{25}N_2O_4S$ ([M + H]$^+$), 437.1530; found, 437.1528.

Concise Synthesis of Isofebrifugin Analogues. *(±)-Dicarbonyl-[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(2′-oxo-3′-(4″-oxoquinazolin-3″(3″H)-yl)propyl)-5,6-dihydro-2H-pyridin-3-yl]-molybdenum ((±)-**31**).*

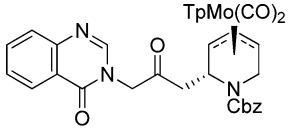


31

To a solution of (±)-**3b** (650 mg, 1.15 mmol, 1.0 equiv) in MeCN (11 mL) was added 3-[2-(trimethylsilyloxy)allyl]-3*H*-quinazolin-4-one[35] (950 mg, 3.45 mmol, 3.0 equiv). The reaction mixture was stirred at

room temperature for 12 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (25 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 25 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with CH_2Cl_2/Et_2O (3/1) afforded (±)-**31** (530 mg, 0.817 mmol, 71%) as a yellow solid. TLC: R_f = 0.22 (1/1 CH_2Cl_2/Et_2O). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.55 (d, J = 1.8 Hz, 1H), 8.24 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 8.02 (s, 2H), 7.85 (d, J = 1.8 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.82 (s, 2H), 7.69 (d, J = 7.8 Hz, 1 H), 7.55 (t, J = 7.8 Hz, 1H), 6.44 (t, J = 1.8 Hz, 1H), 6.28−6.26 (m, 2H), 5.02 (d, J = 17.4 Hz, 1H), 4.98 (d, J = 17.4 Hz, 1H), 4.42 (d, J = 7.2 Hz, 2H), 4.24 (dd, J = 3.0, 8.4 Hz, 1H), 4.15 (d, J = 12.6 Hz, 1H), 3.66 (t, J = 7.2 Hz, 1H), 3.57 (d, J = 12.6 Hz, 1H), 3.11 (dd, J = 9.0, 13.2 Hz, 1H), 3.01 (dd, J = 4.8, 13.2 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 226.9, 226.3, 202.8, 160.6, 148.8, 147.6, 143.2, 137.3, 136.0, 135.3, 127.9, 126.7, 122.1, 107.3, 106.5, 79.8, 71.3, 68.3, 67.8, 63.7, 57.8, 55.5, 46.4. IR (cm^{-1}): 1940 (s), 1853 (s), 1677 (s), 1611 (m). HRMS (FAB): calcd for $C_{27}H_{26}BMoN_8O_5$ ([M + H]$^+$), 651.1168; found, 651.1161.

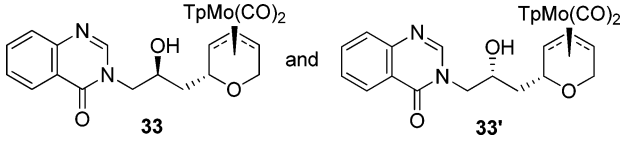
*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-benzyloxycarbonyl-2-(2′-oxo-3′-(4″-oxoquinazolin-3″(3″H)-yl)propyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**32**).*



32

To a solution of (±)-**4b** (780 mg, 1.12 mmol, 1.0 equiv) in MeCN (11 mL) was added 3-[2-(trimethylsilyloxy)allyl]-3*H*-quinazolin-4-one[35] (920 mg, 3.36 mmol, 3.0 equiv). The reaction mixture was stirred at room temperature for 12 h and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (25 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 25 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with CH_2Cl_2/Et_2O (5/1) afforded (±)-**32** (605 mg, 0.774 mmol, 69%) as a yellow solid. TLC: R_f = 0.28 (1/1 CH_2Cl_2/Et_2O). ^{1}H NMR (a mixture of two rotamers) (600 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.28 (d, J = 7.2 Hz, 0.7H), 8.25 (d, J = 7.2 Hz, 0.3H), 8.08 (s, 1H), 7.92 (d, J = 1.2 Hz, 0.3H), 7.86 (d, J = 1.2 Hz, 0.7H), 7.75 (t, J = 9.6 Hz, 1H), 7.74 (d, J = 1.2 Hz, 1H), 7.69 (d, J = 1.2 Hz, 1H), 7.58 (s, 1H), 7.56 (dd, J = 2.4, 6.0 Hz, 1H), 7.49 (d, J = 1.2 Hz, 1H), 7.47 (dd, J = 2.4, 6.0 Hz, 1 H), 7.40 (d, J = 7.2 Hz, 0.5H), 7.36 (d, J = 7.2 Hz, 0.5H), 7.35−7.27 (m, 4H), 6.28 (s, 1H), 6.17 (s, 2H), 5.23 (d, J = 12.0 Hz, 0.3H), 5.17 (d, J = 17.4 Hz, 1H), 5.14 (d, J = 12.0 Hz, 0.7H), 5.07 (d, J = 12.0 Hz, 0.3H), 5.04 (d, J = 12.0 Hz, 0.7H), 5.01 (d, J = 17.4 Hz, 1H), 4.87 (ddd, J = 3.0, 4.2, 6.0 Hz, 1H), 4.57 (d, J = 9.0 Hz, 0.3 H), 4.46 (dd, J = 3.0, 6.0 Hz, 0.3H), 4.43−4.41 (m, 1.4H), 4.30 (dd, J = 1.8, 4.8 Hz, 0.3H), 4.27 (dd, J = 2.4, 14.4 Hz, 0.3H), 4.24 (dd, J = 1.8, 4.8 Hz, 0.7H), 4.20 (dd, J = 2.4, 14.4 Hz, 0.7H), 3.72 (t, J = 7.2 Hz, 1H), 3.75 (d, J = 14.4 Hz, 0.7H), 3.58 (d, J = 14.4 Hz, 0.3H), 3.13 (dd, J = 4.8, 12.0 Hz, 1H), 2.93 (d, J = 6.0 Hz, 1H), 2.81 (dd, J = 8.4, 12.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 225.4, 225.3, 200.9, 200.4, 161.3, 155.5, 154.7, 148.5, 147.5, 147.3, 143.2, 142.6, 141.9, 141.7, 136.6, 136.4, 134.8, 134.7, 134.6, 128.8, 128.6, 128.4, 128.1, 127.9, 127.8, 127.6, 127.4, 126.9, 122.1, 106.0, 105.7, 77.0, 71.2, 67.7, 66.5, 63.2, 63.0, 54.9, 54.1, 49.4, 48.9, 48.6, 39.3, 39.1. IR (cm^{-1}): 1947 (s), 1861 (s), 1681 (s), 1612 (m). HRMS (FAB): calcd for $C_{35}H_{33}BMoN_9O_6$ ([M + H]$^+$), 784.1695; found, 784.1701.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-2-(2′-hydroxy-3′-(4″-oxoquinazolin-3″(3″H)-yl)propyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**33** and (±)-**33′**).*



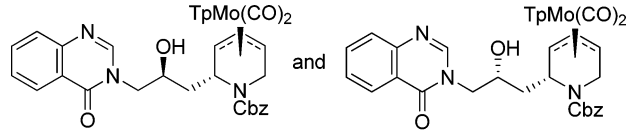
33 **33'**

To a solution of (±)-**31** (440 mg, 0.678 mmol, 1.0 equiv) in MeOH/THF (1/1 v/v, 10 mL) at 0 °C were added $CeCl_3{\cdot}7H_2O$ (250 mg, 0.678 mmol, 1.0 equiv) and $NaBH_4$ (32 mg, 0.846 mmol, 1.25 equiv). The reaction mixture was stirred at room temperature for 12 h and then quenched with saturated aqueous NH_4Cl. The mixture was poured into a separatory funnel containing EtOAc (25 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 25 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel first with toluene/EtOAc (3/1) as eluent afforded (±)-**33** (270 mg, 0.416 mmol, 61%) as a yellow solid, and then elution with toluene/EtOAc (1/1) afforded (±)-**33′** (130 mg, 0.2 mmol, 29%) as a yellow solid. The stereochemistry was confirmed by an X-ray structure analysis of **35**.

*(±)-**33**.* TLC: R_f = 0.18 (1/1 toluene/EtOAc). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.57 (d, J = 1.8 Hz, 1H), 8.30 (s, 1H), 8.29 (s, 1H), 8.18 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 1.2, Hz, 1H), 7.97 (d, J = 1.2, Hz, 1H), 7.81 (d, J = 1.8 Hz, 1H), 7.79 (s, 1H), 7.78 (dd, J = 1.2, 7.8 Hz, 1 H), 7.68 (d, J = 7.8 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 6.41 (t, J = 1.8 Hz, 1H), 6.25 (d, J = 1.8 Hz, 2H), 5.18 (br s, 1H), 4.35 (d, J = 2.4 Hz, 2H), 4.29 (dd, J = 2.4, 13.2 Hz, 1H), 4.09 (d, J = 12.6 Hz, 1H), 4.03 (t, J = 6.6 Hz, 1H), 3.78 (dd, J = 9.0, 13.8 Hz, 1H), 3.66 (t, J = 6.6 Hz, 1H), 3.58 (d, J = 11.4 Hz, 1H), 1.99−1.92 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 226.9, 226.8, 161.1, 149.5, 148.8, 147.6, 143.2, 143.0, 137.2, 135.8, 134.8, 127.8, 127.4, 126.8, 122.4, 107.2, 106.4, 79.9, 72.5, 68.7, 67.7, 66.6, 64.0, 57.8, 52.5, 41.1. IR (cm^{-1}): 3393 (w), 1938 (s), 1851 (s), 1670 (m), 1611 (m). HRMS (FAB): calcd for $C_{27}H_{28}BMoN_8O_5$ ([M + H]$^+$), 653.1324; found, 653.1316.

*(±)-**33′**.* TLC: R_f = 0.15 (1/1 toluene/EtOAc). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.54 (s, 1H), 8.30 (s, 1H), 8.27 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.02 (s, 1H), 8.0 (s, 1H), 7.84 (s, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.80 (s, 1 H), 7.67 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 6.43 (s, 1H), 6.25 (s, 2H), 5.18 (d, J = 6.0 Hz, 1H), 4.35 (d, J = 2.4 Hz, 2H), 4.19 (d, J = 13.8 Hz, 1H), 4.01−3.93 (m, 2H), 3.76 (dd, J = 8.4, 13.2 Hz, 1H), 3.63 (t, J = 7.2 Hz, 1H), 3.55 (d, J = 12.6 Hz, 1H), 1.84−1.79 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 227.3, 226.4, 161.1, 149.5, 148.8, 147.6, 143.3, 143.0, 137.2, 135.9, 134.8, 127.8, 127.5, 126.8, 122.4, 107.3, 106.4, 79.9, 72.2, 69.5, 67.2, 66.0, 64.0, 57.4, 53.0, 40.7. IR (cm^{-1}): 3394 (w), 1938 (s), 1853 (s), 1669 (m), 1610 (m). HRMS (FAB): calcd for $C_{27}H_{28}BMoN_8O_5$ ([M + H]$^+$), 653.1324; found, 653.1315.

*(±)-Dicarbonyl[hydridotris(1-pyrazolyl)borato][(η-3,4,5)-1-benzyloxycarbonyl-2-(2′-hydroxy-3′-(4″-oxoquinazolin-3″(3″H)-yl)propyl)-5,6-dihydro-2H-pyridin-3-yl]molybdenum ((±)-**34** and (±)-**34′**).*



34 **34'**

To a solution of (±)-**32** (600 mg, 0.765 mmol, 1.0 equiv) in MeOH/THF (1/1 v/v, 15 mL) at 0 °C were added $CeCl_3{\cdot}7H_2O$ (285 mg, 0.765 mmol, 1.0 equiv) and $NaBH_4$ (36 mg, 0.955 mmol, 1.25 equiv). The reaction mixture was stirred at room temperature for 12 h and then quenched with saturated aqueous NH_4Cl. The mixture was poured into a separatory funnel containing EtOAc (25 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 25 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel first with CH_2Cl/Et_2O (3/1) as eluent afforded (±)-**34** (220 mg, 0.28 mmol, 37%) as a yellow solid, and then elution with CH_2Cl_2/Et_2O (1/1) afforded (±)-**34′** (350 mg, 0.447 mmol, 58%) as a yellow solid. The stereochemistry was confirmed by an X-ray structure analysis of **34**.

*(±)-**34**.* TLC: R_f = 0.28 (1/1 CH_2Cl_2/Et_2O). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.51 (d, J = 1.2 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.23 (s, 1H), 7.74 (d, J = 6.4 Hz, 1H), 7.73 (s, 1H), 7.71 (d, J = 1.6 Hz, 1H), 7.67 (d, J = 1.6 Hz, 1H), 7.56 (d, J = 2.8 Hz, 1H), 7.55 (d, J = 2.8 Hz, 1H), 7.51−7.47 (m, 2H), 7.27 (t, J = 7.2, 2H), 7.22 (t, J = 7.2 Hz, 2H), 7.08 (t, J = 7.2 Hz, 1H), 6.26 (t, J = 2.0 Hz, 1H), 6.17−6.16 (m, 2H), 5.03 (br s, 2H), 4.76 (br s, 1H), 4.60

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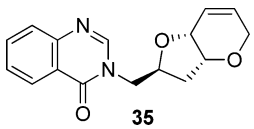
(d, J = 11.2 Hz, 1H), 4.42 (d, J = 11.2 Hz, 1H), 4.24−4.17 (m, 3H), 3.68 (t, J = 7.2 Hz, 1H), 3.61 (t, J = 8.8 Hz, 1H), 3.54 (d, J = 8.8 Hz, 1H), 1.92 (t, J = 11.6 Hz, 1H), 1.81 (t, J = 11.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.5, 224.9, 161.5, 156.6, 148.5, 148.3, 147.5, 142.2, 141.7, 136.4, 136.3, 136.2, 134.7, 134.4, 128.5, 128.3, 128.1, 127.8, 127.2, 126.9, 122.3, 106.3, 105.7, 77.0, 72.3, 68.1, 66.9, 66.2, 63.2, 51.1, 47.8, 43.0, 38.9. IR (cm^{-1}): 3392 (w), 1941 (s), 1855 (s), 1667 (s), 1609 (m). HRMS (FAB): calcd for $C_{35}H_{35}BMoN_9O_6$ ($[M + H]^+$), 786.1852; found, 786.1857.

*(±)-**34′**.* TLC: R_f = 0.20 (1/1 CH_2Cl_2/Et_2O). ^{1}H NMR (a mixture of two rotamers) (600 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.38 (d, J = 7.8 Hz, 1H), 8.20 (s, 0.7H), 7.95 (s, 0.3H), 7.80 (d, J = 1.2 Hz, 1H), 7.70 (br s, 2H), 7.67 (t, J = 7.8 Hz, 1H), 7.57 (d, J = 2.4 Hz, 0.7H), 7.56 (d, J = 1.8 Hz, 1H), 7.54 (d, J = 1.8 Hz, 0.3H), 7.50 (d, J = 1.8 Hz, 0.7H), 7.49 (d, J = 1.8 Hz, 0.3H), 7.44 (t, J = 7.2 Hz, 1 H), 7.35 (d, J = 7.8 Hz, 0.5H), 7.32−7.28 (m, 3H), 7.23 (d, J = 7.8 Hz, 0.5H), 7.19 (t, J = 7.8 Hz, 0.7H), 7.11 (t, J = 7.8 Hz, 0.3H), 6.26 (s, 1H), 6.17 (s, 0.7H), 6.16 (s, 0.3H), 6.14 (s, 0.7H), 6.01 (s, 0.3H), 5.23 (d, J = 12.0 Hz, 0.3H), 5.10 (d, J = 12.6 Hz, 0.7H), 5.06 (d, J = 12.6 Hz, 0.7H), 4.98 (d, J = 12.6 Hz, 0.3H), 4.64−4.63 (br m, 0.3H), 4.57−4.56 (br m, 0.7H), 4.44 (br s, 1H), 4.39 (dd, J = 1.2, 12.0 Hz, 1H), 4.35 (dd, J = 4.2, 6.0 Hz, 1H), 4.26 (dd, J = 3.0, 13.8 Hz, 0.7H), 4.23−4.19 (m, 3H), 4.08 (dd, J = 3.0, 13.8 Hz, 0.3H), 3.83 (dd, J = 9.0, 13.8 Hz, 1H), 3.72 (t, J = 7.2 Hz, 0.7H), 3.67 (t, J = 7.2 Hz, 0.3H), 3.63 (d, J = 13.8 Hz, 0.7H), 3.57 (d, J = 13.8 Hz, 0.3H), 3.47 (br s, 0.3H), 2.35 (s, 0.7H), 2.13 (dt, J = 4.8, 13.8 Hz, 1H), 1.93 (ddd, J = 7.8, 12.6, 13.8, Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 225.5, 225.1, 162.3, 155.9, 148.3, 148.0, 147.5, 142.3, 141.8, 136.6, 136.3, 134.6, 134.5, 128.8, 128.7, 128.6, 128.2, 128.1, 127.6, 127.3, 126.8, 122.1, 106.2, 105.6, 72.3, 69.4, 67.8, 66.5, 63.1, 52.7, 49.2, 43.0, 39.0. IR (cm^{-1}): 3397 (w), 1941 (s), 1853 (s), 1670 (s), 1610 (m). HRMS (FAB): calcd for $C_{35}H_{35}BMoN_9O_6$ ($[M + H]^+$), 786.1852; found, 786.1843.

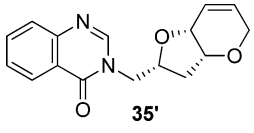
*(±)-3-((3′,3a′,5′,7a′-Tetrahydro-2′H-furo[3′,2′-b]pyran-2′-yl)-methyl)quinazolin-4(3H)-one ((±)-**35**).*



35

To a solution of (±)-**33** (70 mg, 0.107 mmol, 1.0 equiv) in DMSO (2 mL) at room temperature were added a 60% NaH suspension (9 mg, 0.214 mmol, 2.0 equiv) and copper 2-ethylhexanoate (75 mg, 0.214 mmol, 2.0 equiv). The reaction mixture was stirred at 65 °C under dry air for 5 days and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with CH_2Cl_2/Et_2O (3/1) afforded (±)-**35** (23 mg, 0.081 mmol, 75%) as a white solid. TLC: R_f = 0.32 (1/1 CH_2Cl_2/Et_2O). Mp: 112−114 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.28 (d, J = 7.8 Hz, 1H), 8.20 (s, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 6.03 (dd, J = 3.6, 10.2 Hz, 1H), 5.93 (br d, J = 8.4 Hz, 1H), 4.63−4.59 (m, 1H), 4.23 (dd, J = 3.0, 13.8 Hz, 1H), 4.14 (dd, J = 5.4, 13.8 Hz, 1H), 4.12 (dd, J = 5.4, 13.8 Hz, 1H), 4.04−3.96 (m, 3H), 2.23 (dd, J = 5.4, 13.8 Hz, 1H), 1.81−1.76 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.5, 148.2, 147.8, 134.5, 131.1, 127.6, 127.4, 127.0, 122.8, 122.2, 76.5, 76.2, 64.1, 48.7, 37.0. IR (cm^{-1}): 1667 (s), 1608 (s). HRMS (ESI): calcd for $C_{16}H_{16}NaN_2O_3$ ($[M + Na]^+$), 307.1053; found, 307.1049.

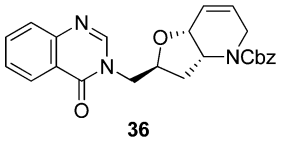
*(±)-3-((3′,3a′,5′,7a′-Tetrahydro-2′H-furo[3′,2′-b]pyran-2′-yl)-methyl)quinazolin-4(3H)-one ((±)-**35′**).*



35′

To a solution of (±)-**33′** (70 mg, 0.107 mmol, 1.0 equiv) in DMSO (2 mL) at room temperature were added a 60% NaH suspension (9 mg, 0.214 mmol, 2.0 equiv) and copper 2-ethylhexanoate (75 mg, 0.214 mmol, 2.0 equiv). The reaction mixture was stirred at 65 °C under dry air for 2 days and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with CH_2Cl_2/Et_2O (3/1) afforded (±)-**35′** (21 mg, 0.074 mmol, 69%) as a white solid. TLC: R_f = 0.35 (1/1 CH_2Cl_2/Et_2O). Mp: 108−110 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.28 (d, J = 7.8 Hz, 1H), 8.11 (s, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 6.05−5.98 (m, 2H), 4.41−4.38 (m, 1H), 4.30 (dd, J = 2.4, 13.8 Hz, 1H), 4.06 (dd, J = 7.8, 13.8 Hz, 1H), 3.99 (dd, J = 3.0, 5.4 Hz, 1H), 3.93 (s, 2H), 3.90 (dd, J = 1.2, 5.4 Hz, 1H), 2.46 (ddd, J = 5.4, 8.4, 13.8 Hz, 1H), 1.96 (dd, J = 3.0, 13.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.7, 148.3, 147.9 134.3, 131.2, 127.5, 127.1, 126.9, 122.8, 122.1 76.3, 75.8, 73.8, 64.4, 50.5, 36.6. IR (cm^{-1}): 1671 (s), 1609 (s). HRMS (ESI): calcd for $C_{16}H_{16}NaN_2O_3$ ($[M + Na]^+$), 307.1053; found, 307.1047.

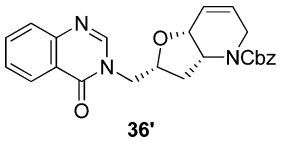
*(±)-Benzyl 2-((4′-Oxoquinazolin-3′(3′H)-yl)methyl)-3,3a,5,7a-tetrahydrofuro[3,2-b]pyridine-4(2H)-carboxylate ((±)-**36**).*



36

To a solution of (±)-**34** (145 mg, 0.185 mmol, 1.0 equiv) in DMSO (4 mL) at room temperature were added 60% NaH suspension (15 mg, 0.37 mmol, 2.0 equiv) and copper 2-ethylhexanoate (130 mg, 0.37 mmol, 2.0 equiv). The reaction mixture was stirred at 65 °C under dry air for 10 days and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with CH_2Cl_2/Et_2O (2.5/1) afforded (±)-**36** (47 mg, 0.112 mmol, 61%) as a colorless oil. TLC: R_f = 0.35 (1/1 CH_2Cl_2/Et_2O). ^{1}H NMR (a mixture of two rotamers) (600 MHz, $CDCl_3$): δ 8.27 (d, J = 8.4 Hz, 1H), 8.11 (s, 1H), 7.74 (t, J = 8.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.48 (t, J = 8.4 Hz, 1H), 7.37−7.31 (m, 5H), 5.68 (dd, J = 1.8, 10.2 Hz, 1H), 5.49 (br m, 1H), 5.15 (d, J = 12.6 Hz, 1H), 5.12 (d, J = 12.6 Hz, 1H), 5.05 (br m, 1H), 4.43 (d, J = 7.2 Hz, 1H), 4.39 (br s, 1H), 4.26 (d, J = 13.8 Hz, 1H), 4.15 (br d, J = 13.2 Hz, 1H), 3.97 (br m, 1H), 3.46 (d, J = 18.6 Hz, 1H), 2.20 (br m, 1H), 1.66 (dd, J = 10.8, 18.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.6, 155.4, 148.3, 147.8, 136.5, 134.5, 128.8, 128.4, 128.3, 127.7, 127.4, 126.9, 122.1, 76.0, 70.9, 67.7, 52.5, 50.3, 39.2. IR (cm^{-1}): 1669 (s), 1609 (s). HRMS (ESI): calcd for $C_{24}H_{23}NaN_3O_4$ ($[M + Na]^+$), 440.1581; found, 440.1584.

*(±)-Benzyl 2-((4′-Oxoquinazolin-3′(3′H)-yl)methyl)-3,3a,5,7a-tetrahydrofuro[3,2-b]pyridine-4(2H)-carboxylate ((±)-**36′**).*



36′

To a solution of (±)-**34′** (250 mg, 0.318 mmol, 1.0 equiv) in DMSO (8 mL) at room temperature were added a 60% NaH suspension (15 mg, 0.38 mmol, 1.2 equiv) and copper 2-ethylhexanoate (133 mg, 0.38 mmol, 1.2 equiv). The reaction mixture was stirred at 65 °C under dry air for 2 days and then quenched with brine. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with CH_2Cl_2/Et_2O (2.5/1) afforded (±)-**36′** (95 mg, 0.227 mmol, 71%) as a colorless oil. TLC: R_f = 0.35 (1/1 CH_2Cl_2/Et_2O). ^{1}H NMR (a mixture of two rotamers) (400 MHz, $CDCl_3$): δ 8.27 (dd, J = 1.2, 8.4 Hz, 1H), 8.10 (s, 1H), 7.73 (dt, J = 1.2, 8.4 Hz, 1H), 7.68 (dd, J = 1.2, 8.4 Hz, 1H), 7.46 (dt, J = 1.2, 8.4 Hz, 1H), 7.33−7.29 (m, 5H), 5.76 (br m, 1H), 5.56 (dd, J = 2.0, 6.4 Hz, 1H), 5.10 (br m, 2H), 4.83 (br m, 1H), 4.53 (br m, 1H), 4.34−4.33 (m, 2H), 4.16 (dd, J = 4.0,

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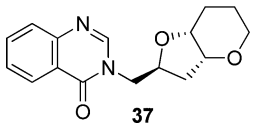
18.8 Hz, 1H), 3.76 (br m, 1H), 3.58 (br d, J = 18.4 Hz, 1H), 2.02–1.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 155.5, 148.4, 147.6, 136.5, 134.5, 128.8, 128.4, 128.2, 127.7, 127.4, 126.9, 122.2, 74.1, 71.9, 67.7, 51.5, 50.5, 39.2. IR (cm^{-1}): 1672 (s), 1610 (s). HRMS (ESI): calcd for $C_{24}H_{23}NaN_3O_4$ ([M + Na]$^+$), 440.1581; found, 440.1576.

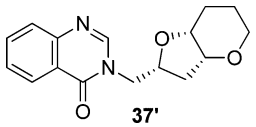
*(±)-3-((Hexahydro-2′H-furo[3′,2′-b]pyran-2′-yl)methyl)-quinazolin-4(3H)-one ((±)-**37**).*



37

A portion of 20% $Pd(OH)_2/C$ (5 mg) was added to a solution of (±)-**35** (20 mg, 0.07 mmol, 1.0 equiv) in MeOH/THF (3/1 v/v, 2 mL), and the mixture was exposed to hydrogen at 250 psi for 1.5 h with stirring. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography over silica gel with 3% MeOH in CH_2Cl_2 afforded (±)-**37** (15 mg, 0.053 mmol, 72%) as a white solid. TLC: R_f = 0.35 (5% MeOH in CH_2Cl_2). Mp: 130–132 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.29 (d, J = 7.8 Hz, 1H), 8.22 (s, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 4.65 (dt, J = 3.0, 9.0 Hz, 1H), 4.22 (dd, J = 3.0, 13.8 Hz, 1H), 4.11 (dd, J = 6.6, 13.8 Hz, 1H), 3.92 (d, J = 2.4 Hz, 1H), 3.83 (dd, J = 1.8, 11.4 Hz, 1H), 3.76 (s, 1H), 3.31 (t, J = 11.4 Hz, 1H), 2.14 (dd, J = 6.6, 13.2 Hz, 1H), 2.04 (d, J = 13.2 Hz, 1H), 1.78–1.61 (m, 3H), 1.31 (dd, J = 1.8, 13.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 148.3, 147.7, 134.5, 127.6, 127.4, 127.1, 122.2, 75.9, 66.5, 49.2, 37.5, 25.7, 20.2. IR (cm^{-1}): 1669 (s), 1609 (s) 1473 (m). HRMS (ESI): calcd for $C_{16}H_{18}NaN_2O_3$ ([M + Na]$^+$), 309.1210; found, 309.1204.

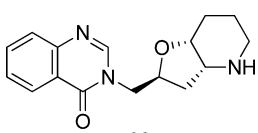
*(±)-3-((Hexahydro-2′H-furo[3′,2′-b]pyran-2′-yl)methyl)-quinazolin-4(3H)-one ((±)-**37′**).*



37′

A portion of 20% $Pd(OH)_2/C$ (5 mg) was added to a solution of (±)-**35′** (12 mg, 0.042 mmol, 1.0 equiv) in MeOH/THF (3/1 v/v, 1 mL), and the mixture was exposed to hydrogen at 250 psi for 2.5 h with stirring. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography over silica gel with 3% MeOH in CH_2Cl_2 afforded (±)-**37′** (9 mg, 0.031 mmol, 74%) as a white solid. TLC: R_f = 0.41 (5% MeOH in CH_2Cl_2). Mp: 124–126 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.29 (d, J = 7.8 Hz, 1H), 8.18 (s, 1H), 7.72 (dt, J = 1.8, 7.8 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.46 (dt, J = 1.8, 7.8 Hz, 1H), 4.41–4.37 (m, 1H), 4.34 (dt, J = 3.0, 13.8 Hz, 1H), 4.07 (dd, J = 7.8, 13.8 Hz, 1H), 3.85 (dd, J = 1.8, 4.2 Hz, 1H), 3.72 (d, J = 1.8 Hz, 1H), 3.71 (d, J = 1.8 Hz, 1H), 3.28 (dt, J = 1.8, 11.4 Hz, 1H), 2.26 (ddd, J = 4.8, 10.2, 14.4 Hz, 1H), 2.07 (dd, J = 1.8, 14.4 Hz, 1H), 1.91–1.83 (m, 2H), 1.70 (dt, J = 4.8, 14.4 Hz, 1H) 1.36 (dd, J = 3.0, 14.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 148.4, 148.3, 134.3, 127.5, 127.2, 126.9, 122.4, 76.4, 75.4, 66.7, 51.2, 37.0, 25.1, 20.7. IR (cm^{-1}): 1667 (s), 1611 (s) 1473 (m). HRMS (ESI): calcd for $C_{16}H_{18}NaN_2O_3$ ([M + Na]$^+$), 309.1210; found, 309.1205.

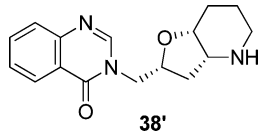
*(±)-3-((Octahydrofuro[3′,2′-b]pyridin-2′-yl)methyl)quinazolin-4(3H)-one ((±)-**38**).*



38

A portion of 20% $Pd(OH)_2/C$ (9 mg) was added to a solution of (±)-**36** (35 mg, 0.084 mmol, 1.0 equiv) in MeOH/THF (3/1 v/v, 2 mL), and the mixture was exposed to hydrogen at 250 psi for 2.5 h with stirring. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography over neutral alumina with 3% MeOH in CH_2Cl_2 afforded (±)-**38** (20 mg, 0.07 mmol, 83%) as a white solid. TLC: R_f = 0.25 (5% MeOH in CH_2Cl_2). Mp: 142–144 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.26 (d, J = 7.8 Hz, 1H), 8.22 (s, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 4.39 (d, J = 13.8 Hz, 1H), 4.30 (t, J = 9.0 Hz, 1H), 4.20 (dd, J = 5.4, 13.8 Hz, 1H), 3.71 (s, 1H), 3.18 (s, 1H), 2.82 (d, J = 12.0 Hz, 1H), 2.49 (t, J = 12.0 Hz, 1H), 2.27 (ddd, J = 5.4, 8.4, 13.8 Hz, 1H), 2.0 (d, J = 13.8 Hz, 1H) 1.66 (dd, J = 5.4, 13.8 Hz, 1H), 1.59 (dt, J = 3.0, 13.2 Hz, 1H), 1.51 (dd, J = 3.0, 13.2 Hz, 1H), 1.39 (d, J = 13.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.6, 148.5, 148.3, 134.3, 127.6, 127.1, 126.9, 122.4, 75.4, 56.3, 51.2, 45.3, 37.6, 26.5, 21.5. IR (cm^{-1}): 2934 (w), 2854 (w), 1670 (s), 1610 (s). HRMS (ESI): calcd for $C_{16}H_{20}N_3O_2$ ([M + H]$^+$), 286.1550; found, 286.1556.

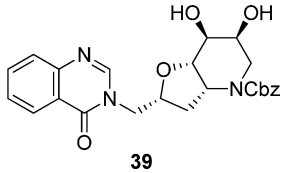
*(±)-3-((Octahydrofuro[3′,2′-b]pyridin-2′-yl)methyl)quinazolin-4(3H)-one ((±)-**38′**).*



38′

A portion of 20% $Pd(OH)_2/C$ (8 mg) was added to a solution of (±)-**36′** (30 mg, 0.072 mmol, 1.0 equiv) in MeOH/THF (3/1 v/v, 2 mL), and the mixture was exposed to hydrogen at 250 psi for 2.5 h with stirring. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography over neutral alumina with 3% MeOH in CH_2Cl_2 afforded (±)-**38′** (18 mg, 0.063 mmol, 89%) as a white solid. TLC: R_f = 0.23 (5% MeOH in CH_2Cl_2). Mp: 100–102 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.29 (dd, J = 1.2, 7.8 Hz, 1H), 8.20 (s, 1H), 7.75 (dt, J = 1.2, 7.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 4.64 (dt, J = 3.0, 9.0 Hz, 1H), 4.26 (dd, J = 3.0, 14.4 Hz, 1H), 3.98 (dd, J = 6.6, 13.8 Hz, 1H), 3.77 (t, J = 3.0 Hz, 1H), 3.23 (dd, J = 3.0, 4.0 Hz, 1H), 2.93 (d, J = 12.6 Hz, 1H), 2.51 (t, J = 10.8 Hz, 1H), 2.02 (d, J = 13.8 Hz, 1H), 1.96 (dd, J = 6.6, 13.8 Hz, 1H), 1.77 (ddd, J = 5.4, 8.4, 13.8 Hz, 1H), 1.62–1.52 (m, 2H), 1.38 (dd, J = 2.4, 13.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.6, 148.3, 147.7, 134.5, 127.7, 127.3, 127.0, 122.3, 75.9, 57.1, 49.6, 44.9, 37.5, 26.6, 21.1. IR (cm^{-1}): 2929 (w), 2850 (w), 1671 (s), 1611 (s). HRMS (ESI): calcd for $C_{16}H_{20}N_3O_2$ ([M + H]$^+$), 286.1550; found, 286.1554.

*(±)-Benzyl 6,7-Dihydroxy-2-((4′-oxoquinazolin-3′(3′H)-yl)-methyl)hexahydrofuro[3′,2′-b]pyridine-4(2H)-carboxylate ((±)-**39**).*



39

To a solution of (±)-**36′** (17 mg, 0.04 mmol, 1.0 equiv) in acetone/water (9/1 v/v, 1 mL) at room temperature were added successively *N*-methylmorpholine *N*-oxide (6 mg, 0.05 mmol, 1.25 equiv), methanesulfonamide (5 mg, 0.05 mmol, 1.25 equiv), and OsO_4 (4 wt % solution in water; 70 μL, 0.01 mmol, 0.25 equiv). The reaction mixture was stirred at room temperature for 2 days and then quenched with saturated aqueous $NaHSO_3$. The mixture was poured into a separatory funnel containing EtOAc (5 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography over silica gel with 5% MeOH in CH_2Cl_2 afforded (±)-**39** (18 mg, 0.039 mmol, 92%) as a white solid. TLC: R_f = 0.33 (5% MeOH in CH_2Cl_2). Mp: 80–82 °C. ^{1}H NMR (a mixture of two rotamers) (600 MHz, DMSO-d_6): δ 8.30 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.81 (t, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.53 (t, J = 8.4 Hz, 1H), 7.36–7.29 (m, 5H), 5.04 (br m, 1H), 4.90 (br s, 1H), 4.74 (br s, 1H), 4.69 (br m, 1H), 4.34 (br m, 1H), 4.18 (br d, J = 12.0 Hz, 1H), 3.97 (dt, J = 2.4, 7.2 Hz, 2H), 3.83 (d, J = 13.8 Hz, 1H), 3.63 (br s, 1H), 3.37 (br s, 1H), 3.05 (br s, 1H), 2.12 (q, J = 10.8 Hz, 1H), 1.88 (t, J = 10.8 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 161.0, 156.0, 149.4, 148.6, 137.6, 135.1, 129.1, 128.4, 128.1, 127.8, 127.7, 126.7, 122.2, 79.9, 77.7, 73.3, 69.8, 67.5, 66.9, 53.5, 51.0, 44.8, 30.0. IR (cm^{-1}): 3395 (w), 1672 (s), 1610 (s). HRMS (ESI): calcd for $C_{24}H_{25}NaN_3O_6$ ([M + Na]$^+$), 474.1636; found, 474.1630.

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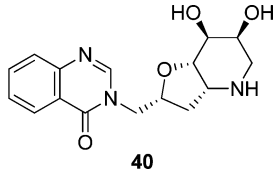
*(±)-3-((6′,7′-Dihydroxyoctahydrofuro[3′,2′-b]pyridin-2′-yl)-methyl)quinazolin-4(3H)-one ((±)-**40**).*



40

A portion of 20% $Pd(OH)_2/C$ (5 mg) was added to a solution of (±)-**39** (22 mg, 0.048 mmol, 1.0 equiv) in MeOH/THF (1/1 v/v, 1 mL), and the mixture was exposed to hydrogen at 50 psi for 3 h with stirring. The mixture was filtered through a pad of Celite, and the filtrate was concentrated. Flash chromatography over neutral alumina with 10% MeOH in CH_2Cl_2 afforded (±)-**40** (10 mg, 0.031 mmol, 63%) as a white solid. TLC: R_f = 0.2 (10% MeOH in CH_2Cl_2). Mp: 148−150 °C. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.31 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.82 (t, J = 8.4 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.54 (t, J = 8.4 Hz, 1H), 4.61 (br s, 1H), 4.43−4.40 (m, 2H), 4.11 (dd, J = 3.6, 13.8 Hz, 1H), 3.93 (dd, J = 7.8, 13.8 Hz, 2H), 3.76 (s, 1H), 3.69 (s, 1H), 3.41 (br d, J = 7.2 Hz, 1H), 3.27 (br s, 1H), 2.57 (t, J = 10.8 Hz, 1H), 2.43 (dd, J = 3.6, 12.0 Hz, 1H), 1.78 (dd, J = 6.6, 13.2 Hz, 1H), 1.66 (dd, J = 6.6, 13.2 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 161.6, 148.0, 147.9, 134.6, 127.5, 127.4, 127.0, 122.1, 80.9, 75.3, 68.1, 66.3, 62.7, 60.8, 55.1, 49.8, 49.3, 31.9, 31.5, 25.0. IR (cm^{-1}): 3397 (w), 1671 (s), 1608 (s). HRMS (ESI): calcd for $C_{16}H_{20}N_3O_4$ ($[M + H]^+$), 318.1448; found, 318.1443.

■ ASSOCIATED CONTENT

Supporting Information

Text, figures, tables, and CIF files giving additional experimental procedures, synthesis and characterization data, X-ray crystallographic study of **26**, **34**, and **35**, biological assay data, and ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

Authors Chen and Sana carried out the major portion of the experimental work described in this manuscript. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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