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Metal-mediated dearomatization leading to 2-azaspiro[4.5]decanes via tandem nucleophilic aromatic addition–Horner–Wadsworth–Emmons olefination–oxidative demetalation sequences

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ABSTRACT

A ruthenium-mediated dearomatization sequence has been developed that delivers structurally intriguing azaspirolactam products in stereoselective fashion. Treatment of (η^6-arene)Ru(cyclopentadienyl) complexes bearing *N*-benzyl-β-amido phosphonate side chains with excess NaH results in intramolecular nucleophilic aromatic addition to the *ipso* position of the coordinated arenes. Subsequent Horner–Wadsworth–Emmons (HWE) reaction with added aldehydes affords olefinated spirolactam cyclohexadienyl ruthenium complexes. Mild oxidation with $CuCl_2$ or $CuBr_2$ under CO effects removal and recovery of the CpRu(II) fragment. Substituents present on the cyclohexadienyl skeleton influence the outcome of demetalation and products obtained in this study include functionalized 2-azaspiro-[4.5]decanes and tetrahydroisoquinolinones.

1. Introduction

Arene metal complexes are versatile organometallic reactants well recognized as useful synthetic intermediates. Applications of η^6-arene complexes usually capitalize upon the ability to functionalize the coordinated arene via normally unfavorable reaction manifolds. Common transformations of arene complexes include nucleophilic aromatic addition and substitution, arene deprotonation, and benzylic deprotonation.[1] The transition metal fragment plays a dual role in these transformations by activating the arene ligand toward reaction with nucleophiles/bases while also serving as a stereocontrol element. Thus, reactions such as nucleophilic aromatic addition and benzylic deprotonation/alkylation proceed with high levels of diastereoselectivity from the face opposite the metal center. This inherent stereoselectivity has been harnessed in asymmetric syntheses employing planar chiral derivatives.[2] The most extensively investigated type of arene metal complex is that incorporating a tricarbonyl chromium fragment, and such complexes have been widely used in organic chemistry for several decades. Aside from chromium(0), metalated arenes of manganese(I), iron(II), and ruthenium(II) have also been examined in the context of organic synthesis.

While the chemistry of (η^6-arene)ruthenium complexes is not as well developed when compared to Cr(0) congeners, these materials exhibit several desirable characteristics that render them potentially attractive as synthetic building blocks. For example, arene ruthenium complexes, particularly (η^6-arene)RuCp cations (Cp=cyclopentadienyl) are readily prepared in high yield using standard bench-top techniques and, in general, are easily handled air- and moisture-stable compounds.[3] Arene ligands coordinated to a CpRu(II) fragment display a convenient level of reactivity toward a wide range of nucleophiles so that processes such as nucleophilic aromatic addition/substitution proceed efficiently under mild conditions.[4] It is also possible to recover the CpRu(II) fragment in a reusable form upon removal from a functionalized arene ligand.

As part of a program aimed at exploiting the largely untapped reactivity of (arene)Ru(II) complexes in synthesis, we have previously reported the ruthenium-mediated dearomatization of *N*-benzyl acetoacetamide complexes (e.g., **1**) to metal-free spirolactams such as **3** using a protocol that entails sequential intramolecular nucleophilic aromatic addition, enolate O-alkylation, and oxidative demetalation (Scheme 1).[5] Dearomatization reactions, particularly metal-mediated variations, possess significant synthetic potential[6] and spirolactams such as **3** represent intriguing heterocyclic building blocks. Consequently, it was disappointing to find that while a number of acetoacetamide-functionalized (η^6-arene)Ru complexes participated in the tandem spirocyclization/enolate trapping process to afford stable (cyclohexadienyl)Ru intermediates (e.g., **2**),[5a] efficient oxidative demetalation was

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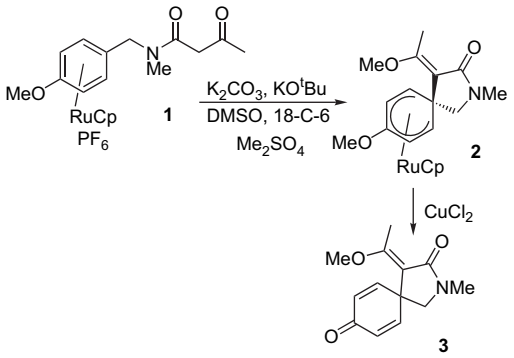
restricted to only certain electron rich derivatives.[5b–d] In addition, the requirement for enolate O-alkylation further limited the range of spirolactams accessible via this methodology. The presence of a peripheral acid-sensitive enol ether group also affects the stability of cyclohexadienyl products (**2**) and may have contributed to our inability to uncover more general demetalation procedures.



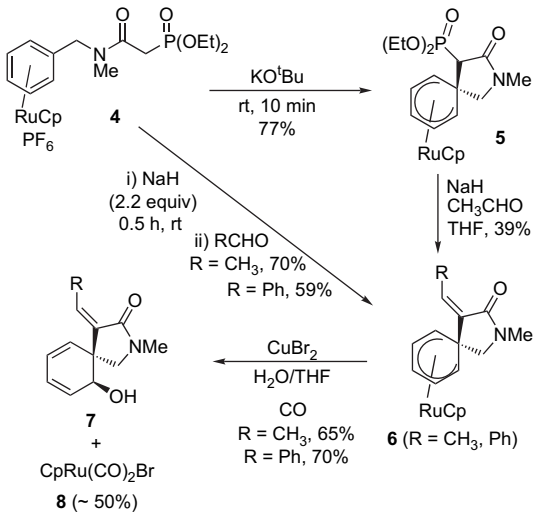
Scheme 1.

With these shortcomings in mind, alternative spirocyclization substrates were designed with the aim of accessing more substituted (hence more versatile) lactams structurally related to **3** in a stereocontrolled fashion. In this context, (arene)Ru complexes possessing β-amido phosphonate side chains were particularly intriguing as it was envisioned that such complexes may participate in intramolecular nucleophilic aromatic addition to produce phosphonate-substituted spirolactams. Subsequent Horner–Wadsworth–Emmons (HWE) olefination could then be used to introduce a variety of substituents onto the periphery of the lactam ring while avoiding generation of acid-sensitive enol ethers. Indirect precedent for the individual steps of the proposed reaction sequence can be found in reports from Müller and Martín that describe the preparation and utilization of relatively simple (η^6-benzyl phosphonate)$Cr(CO)_3$ complexes in side-chain olefination reactions with various aldehyde partners.[7,8] Müller has also reported the synthesis of more elaborate arene-metalated benzyl phosphonates through side-chain manipulations.[9] Additionally, phosphoryl-stabilized carbanions have been found to participate in intermolecular S_NAr reactions with chloroarene iron and chromium complexes, thus these anions appear to be sufficiently nucleophilic for reaction with π-coordinated arenes.[10] The feasibility of performing these individual transformations in tandem on an arene ruthenium platform, however, was unknown at the outset of our studies.

Gratifyingly, the desired reaction sequence described above proved to be largely successful as outlined in Scheme 2.[11] The preparative route was further simplified by application of a two-step/one-pot sequence for the preparation of olefinated spirolactam **6** from (η^6-arene) complex **4** without isolation of the intermediate phosphonate **5**. Moreover, **6** was found to be susceptible to stereoselective nucleophilic oxidative demetalation which, if performed under a CO atmosphere, resulted in recovery of the CpRu(II) fragment.[11] This article presents a complete account of initial investigations into the scope and limitations of these unique Ru-assisted dearomatizations involving *N*-benzyl-β-amido phosphonate complexes. The prospects for developing asymmetric dearomatization sequences are also discussed.

2. Results and discussion

The preparation of arene ruthenium complexes of the type **4** proved to be exceedingly straightforward. *N*-Methyl benzyl amines

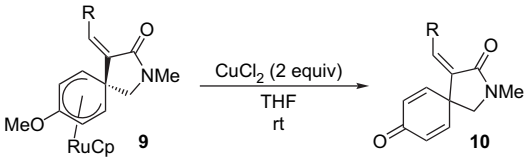


Scheme 2.

were first acylated with chloroacetyl anhydride and then subjected to Arbuzov reaction with $P(OEt)_3$. The resulting β-amido phosphonates were then treated with $[(CH_3CN)_3RuCp][PF_6]$[12] in warm 1,2-dichloroethane to afford Ru-coordinated arenes in high overall yields. An initial concern over the reaction sequence illustrated in Scheme 2 was the fate of the anion generated upon deprotonation of an amido phosphonate side chain. An unfavorable equilibrium between an uncyclized zwitterionic species (i.e., arene ruthenium cation and α-phosphonate anion) and the neutral spirocyclic cyclohexadienyl complex (such as **5**) would jeopardize the success of the overall transformation. Encouragingly, however, exposure of **4** to an equimolar amount of KO^{t}Bu in THF-d_8 rapidly and quantitatively produced the desired spirocycle **5** as evidenced by the disappearance of signals corresponding to arene hydrogens and the appearance of signals consistent with a cyclohexadienyl ligand. Additionally, the Cp hydrogens experienced an upfield shift from ~5.5 ppm in the η^6-complex to ~4.8 ppm in **5**. The phosphonate **5** appears to be relatively stable, although isolation and purification were complicated by the polar nature of the material. The difficulty encountered in purifying **5** may be responsible for the modest efficiency of subsequent HWE olefination with acetaldehyde and NaH. Consequently, a higher yielding and experimentally simpler one-pot reaction was developed. The η^6 complexes (e.g., **4**) were dissolved in THF or DMF and treated with an excess of NaH (2.2 equiv) at room temperature for 30 min. Addition of an aldehyde then produced stable cyclohexadienyl complexes in good yield.[11] As expected, nucleophilic aromatic addition occurred exclusively from the face opposite the CpRu fragment. The subsequent HWE reaction was also stereoselective, giving *Z*-configured exocyclic olefins (geometry was assigned on the basis of 2D NMR experiments).[13]

With an initial procedure for the preparation of olefinated spirolactam complexes seemingly established, suitable methods for completing the dearomatization sequence via removal of the CpRu(II) fragment were next considered. Before exploring the feasibility of nucleophilic oxidative demetalation (shown in Scheme 2) we first sought to build on previous work that had demonstrated the viability of performing oxidative demetalations on electron rich cyclohexadienyl complexes (such as **2**).[5b,c] Toward this end, several 4-methoxy-substituted cyclohexadienyl ruthenium complexes (**9**)[11] (prepared from the corresponding *p*-methoxy benzyl amide derivatives) were treated with $CuCl_2$. In each case conversion to the desired metal-free cyclohexadienone spirolactam was observed and the organic products **10a–f** were isolated in good yield (Table 1). The one exception to this trend is encountered in entry **f**

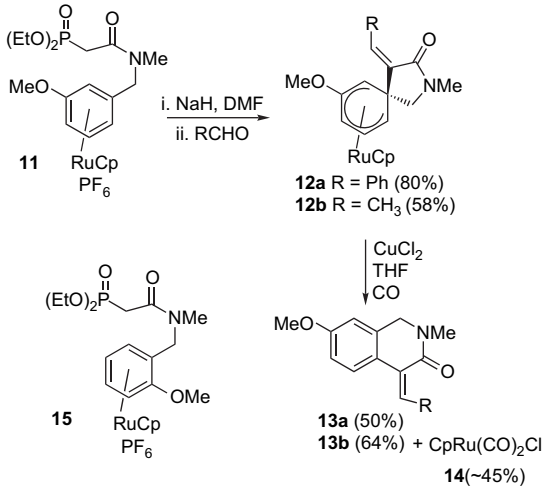
Table 1
Synthesis of azaspirodienones from cyclohexadienyl complexes **9**



Entry	R	Yield of **10** (%)
a	CH_3	60
b	H	70
c	Ph	79
d	4-$MeOC_6H_4$	85
e	4-$NO_2C_6H_4$	61
f	*E*-CH_3CH=CH	38

involving demetalation of the spiro-adduct prepared from *E*-crotonaldehyde. While the cyclohexadienyl complex **9f** was obtained in high (76%) yield,[11] this material was found to readily decompose—a characteristic that appears to adversely affect subsequent demetalation.

Other *N*-(methoxybenzyl)-β-amido phosphonate complexes were also screened for their ability to participate in tandem spirocyclization–HWE reactions. The 3-methoxy-substituted derivative **11** was successfully converted to the corresponding cyclohexadienyl adducts **12a**,**b** in good yield upon treatment with the indicated aldehydes (Scheme 3). Unlike their 4-methoxy counterparts discussed above, **12a**,**b** are unable to form tractable metal-free dienones during the course of oxidative demetalation. Instead, treatment with $CuCl_2$ initiates a skeletal rearrangement involving a 1,2-vinyl shift to produce tetrahydroisoquinolinones **13a**,**b** with reasonable efficiency.[14] Importantly, the isolated yields of **13a**,**b** improved when the oxidation was performed under a blanket of CO. The application of CO also facilitated recovery of the CpRu(II) fragment in the form of $CpRu(CO)_2Cl$ (**14**), which could be easily isolated during chromatographic purification of the crude reaction mixture.[15] The 2-methoxy-substituted arene ruthenium complex **15**, however, failed to participate in the aromatic addition–olefination sequence.

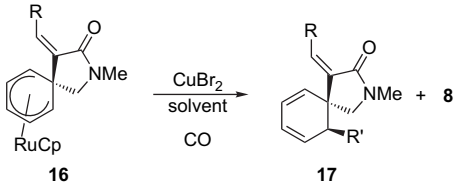


Scheme 3.

One motive for constructing metal-coordinated spirolactams via HWE reactions was to eliminate hydrolytically unstable enol ethers from the lactam periphery. It was envisioned that complexes such as **6** (Scheme 2) would be compatible with a wider range of potential demetalation reaction conditions ultimately leading to substituted azaspirocycles without the need to incorporate electron releasing methoxy groups into the ligand periphery. Oxidation of cyclohexadienyl ruthenium complexes is envisioned to produce (in a formal sense) a cyclohexadienyl cation-like species, and so the addition of a nucleophile to the cyclohexadienyl π system is presumably required in order to obtain tractable metal-free organic products.[16] Initial attempts to effect such a transformation that entailed exposing **6** (R=CH_3) to $CuCl_2$ in a nucleophilic solvent (MeOH or EtOH) were not encouraging as only complex reaction mixtures were obtained. However, switching to $CuBr_2$, an oxidizing agent with greater solubility in organic solvents, proved beneficial. Additionally, performing the reaction under an atmosphere of CO further improved the yield and allowed easy recovery of the Ru(II) fragment as the dicarbonyl complex.[15] As shown in Scheme 2, these modifications resulted in smooth demetalation in the presence of H_2O as an external nucleophile to afford **7** (R=CH_3 or Ph) as single diastereomers along with ruthenium complex **8**.[11] We speculate that oxidation of the cyclohexadienyl ruthenium complex renders the ligand receptive toward nucleophilic addition at the dienyl terminus (as has been observed in other dienyl and allyl metal complexes)[16] to initially produce a metal-coordinated diene. Thus, the CpRu fragment exerts a stereodirecting effect during the course of both phosphonate anion addition to the arene and nucleophile-assisted oxidative demetalation. Carbon monoxide serves two purposes in the reaction: it facilitates removal of the ruthenium center from the conjugated diene product and allows the CpRu fragment to be recovered in the form of a stable and easily isolable dicarbonyl halide complex.

The overall conversion of **4** to azaspirocycle **7** via the intermediacy of **6** (Scheme 2) represents a net Ru-mediated double nucleophilic addition to an (η^6-arene)metal complex accomplished under mild reaction conditions. Although sequential double nucleophilic addition to simple (arene)$Mn(CO)_3$ complexes also has been reported,[17] the Ru-based procedures described above potentially offer access to more sophisticated and synthetically versatile products. Consequently, the compatibility of the general demetalation conditions outlined in Scheme 2 with various cyclohexadienyl complexes **16** was examined, and the results are shown in Table 2. The cyclohexadienyl substrates for this study were prepared as described previously.[11] Demetalation was performed by addition of $CuBr_2$ to a solution of **16** in the indicated solvent under CO at room temperature. The corresponding methoxy- or hydroxy-substituted spirolactams were subsequently isolated in good yield along with CpRu(II) complex **8**. In each instance,

Table 2
Nucleophilic oxidative demetalation of cyclohexadienyl complexes **16**

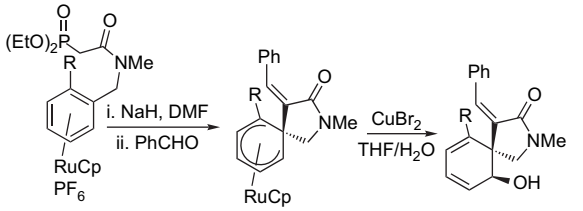


Entry	R	Solvent	Yield of **17** (%)	Yield of **8** (%)
a	Ph	MeOH	56 (R′=OCH_3)	57
b	H	MeOH	51 (R′=OCH_3)	42
c	$BnOCH_2$	THF/H_2O	54 (R′=OH)	62
d		THF/H_2O	51 (R′=OH)	43
e		THF/H_2O	nd[a]	nd[a]

[a] Not detected.

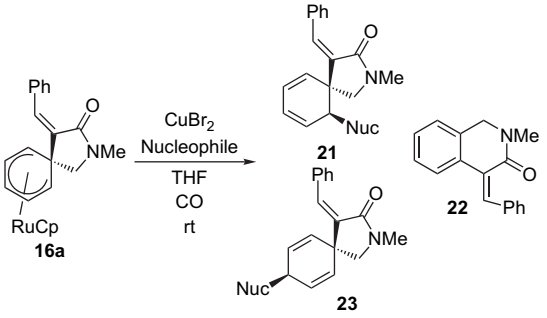
addition of the nucleophile to cyclohexadienyl complex **16** was completely stereo- and regioselective, and **17a–d** were isolated as diastereomerically pure materials. Structural assignments were made on the basis of 1D and 2D NMR spectroscopic data. Additionally, the single crystal X-ray structure of **7** (R=Ph, see Scheme 2) was secured.[18] The pyridyl-substituted complex **16e**, however, failed to deliver the corresponding diene **17e** upon attempted demetalation, presumably due to formation of pyridine-Cu adducts. Several other oxidants were examined for the ability to induce demetalation of **16a** in the presence of water or methanol, however, none of these reagents (CAN, DDQ, $PhI(OAc)_2$, and $[Cp_2Fe][PF_6]$) were as effective as Cu(II) halides.

Additional substituted (arene)Ru(II) complexes were screened for their compatibility with the cyclization–demetalation sequence outlined in Table 2. While the 2-methoxy-substituted arene complex **15** did not afford isolable cyclohexadienyl complexes (see Scheme 3), the 2-methyl and 2-chloro analogues were found to be viable participants (Scheme 4). Each of these η^6-arene complexes was converted to the corresponding cyclohexadienyl spirolactam after HWE reaction with benzaldehyde. Exposure of **19a** to $CuBr_2$-based oxidative demetalation reaction conditions in aqueous THF under a CO atmosphere afforded dienol **20a** in 53% isolated yield (along with dicarbonyl ruthenium complex **8** in 57% yield). Evidently, the presence of the methyl group at a terminal position of the cyclohexadienyl ligand directs addition of water to occur regioselectively at the unsubstituted terminus. Likewise, demetalation of **19b** also proceeded in a regioselective fashion to give **20b**.



Scheme 4.

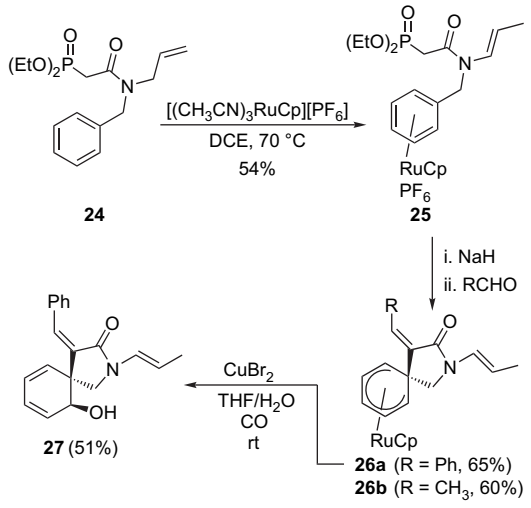
Potential nucleophiles other than water were examined as demetalation adjuvants, albeit with limited success. The results of this study are shown in Scheme 5. Cyclohexadienyl complex **16a** was dissolved in THF containing ~5 equiv of the indicated nucleophile (except in the case of AcOH as noted). The reaction mixtures were then exposed to standard demetalation conditions ($CuBr_2$, CO, rt). As can be seen, most of the nucleophiles employed were not incorporated into the metal-free products isolated from these reactions. Instead, oxidation-induced rearrangement afforded tetrahydroisoquinolinone **22** in varying amounts.[19] The use of NaI, however, did give spirodiene **21** as a minor by-product. Interestingly, demetalation performed in the presence of AcOH gave a small amount of symmetrical diene **23a** (Nuc=OAc) along with **22**, while the presence of azide ion resulted in formation of **23b** (Nuc=N_3) as the sole isolable organic product in good yield. Nucleophilic addition to cyclohexadienyl metal complexes usually occurs at a terminal position,[20] and we speculate that this is also the case with acetate and azide addition to **16a**. Sigmatropic rearrangement of these initially formed adducts then provides the observed products (**23**).[21] Despite the limited number of nucleophiles examined, the data in Scheme 5 seem to indicate that steric factors may play an important role in successful addition, perhaps accounting for the failure of cyclohexanol and phenol to participate in the reaction. Steric effects, however, should minimally impact the reactivity of NaCN. The nucleophilicity of cyanide anion may be such that the rate of addition to **16a** is simply not competitive with bond reorganization leading to **22**.



Nucleophile	Ratio **21**:**22**:**23**	% Yield
NaI (5 equiv)	27:73:0	55% (**21** Nuc = I)
phenol (5 equiv)	0:100:0	30%
cyclohexanol (5 equiv)	0:100:0	25%
NaCN (5 equiv)	0:100:0	45%
AcOH (1:4 v/v in THF)	0:87:13	77% (**23a** Nuc = OAc)
NaN_3 (5 equiv)	0:0:100	70% (**23b** Nuc = N_3)

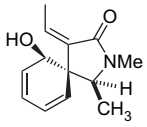
Scheme 5.

All the β-amido phosphonates discussed above feature a methyl protecting group attached to the amide nitrogen. Several alternative *N*-protecting groups have been examined as well. *N*-Benzyl β-amido phosphonate ruthenium complexes analogous to **4** functionalized with carbamate protecting groups (such as $CO_2{}^tBu$ and CO_2Me) failed to undergo tandem phosphonate addition–HWE olefination. Likewise, an unprotected secondary β-amido phosphonate complex also proved to be unreactive under our standard spirocyclization conditions. Better results were obtained with *N*-allyl functionalized complexes. Specifically, coordination of the CpRu(II) fragment to arene ligand **24** afforded the corresponding η^6-complex **25** (the allyl group was completely isomerized to the 2-propenyl derivative during the course of this reaction—Scheme 6). Conversion of **25** to spirolactam complexes **26a**,**b** proved to be straightforward. Complex **26a** was further manipulated to metal-free dienol **27**. Thus, the allyl/propenyl moiety serves as a potentially removable *N*-protecting group that is compatible with this Ru-mediated dearomatization process.



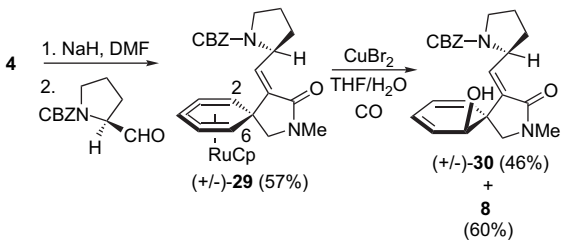
Scheme 6.

Finally, approaches toward chiral non-racemic spirolactams designed to exploit the inherent diastereoselectivity of Ru-mediated HWE spirocyclization–nucleophilic oxidative demetalation have been explored. We previously demonstrated that a pre-existing benzylic chiral center could influence the course of subsequent nucleophilic addition to the metal-dienyl fragment. Specifically, commercially available (*S*)-(−)-α-methyl benzylamine was ultimately converted to optically pure (−)-**28** via the corresponding amido phosphonate η^6-ruthenium complex, tandem spirocyclization–HWE olefination in the presence of acetaldehyde, and oxidative demetalation in an aqueous solvent mixture.[11]



(-)-28

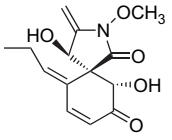
It was anticipated that a remote stereocenter introduced into the cyclohexadienyl complex via the aldehyde reaction partner would also be capable of influencing the regioselectivity of nucleophilic addition. When combined with the stereodirecting effect of the CpRu(II) fragment, the use of chiral aldehyde reactants would then offer an additional entry to non-racemic spirolactams. As a test of this strategy, **4** was treated with CBZ-protected (*S*)-proline aldehyde[22] under our standard spirocyclization–HWE reaction conditions (Scheme 7) and the expected cyclohexadienyl complex **29** was isolated in good yield. Subsequent oxidative demetalation in the presence of H_2O afforded a spirodienol product **30** as a *single diastereomer*. Unfortunately, **30** proved to be devoid of optical activity and chiral HPLC analysis confirmed the presence of a racemic mixture. Evidently, the proline aldehyde and/or **29** suffered racemization under the reaction conditions. Nonetheless, demetalation proceeded completely diastereoselectively. The origin of this stereoselectivity was probed with a molecular modeling study (Spartan, AM1) in which a cyclohexane ring was used in place of the cyclohexadienyl ruthenium fragment in order to construct a simplified surrogate for complex **29**. The lowest energy conformer that emerged from this study features the pyrrolidine C–H bond directed toward the lactam carbonyl (as shown in Scheme 7). As a consequence, the CBZ group extends over one side of the six-membered ring, leaving only one unobstructed site for nucleophilic addition (C6 in **29**). Rotation about the C(alkene)–C(pyrrolidine) bond generates a higher energy conformer ($\Delta E \sim 4.4$ kcal mol^{-1}) in which the CBZ group is positioned over C6 (thereby increasing the accessibility of C2). Since we do not obtain **30** as a mixture of diastereomers (as would result if addition of H_2O occurred at both C2 and C6 irrespective of pyrrolidine configuration), we conclude that demetalation of **29** must proceed via regioselective nucleophilic addition, and that the regioselectivity (hence stereoselectivity) of this process is controlled by conformational preferences of the remote pyrrolidine substituent (as we had hoped). The result depicted in Scheme 7 seemingly validates the feasibility of this approach for the construction of chiral spirolactams and we are now investigating alternative conditions for effecting spirocyclization–HWE reactions between **4** and chiral aldehydes so that racemization of **29** (and structurally related materials) is avoided. Subsequent demetalation should then afford enantiomerically pure products.



Scheme 7.

3. Conclusions

In summary, we have demonstrated that arene ruthenium complexes possessing β-amido phosphonate side chains can be converted to a range of functionalized 2-azaspiro[4.5]decane derivatives in a stereoselective fashion. The CpRu(II) fragment serves two roles in these transformations: it activates the coordinated arene toward *exo*-selective nucleophilic attack by a stabilized phosphonate anion (resulting in formation of cyclohexadienyl complexes that can be trapped by HWE olefination with aldehydes) and influences the stereoselectivity of subsequent oxidative demetalation leading to spirodienol products. While the range of nucleophiles that successfully participate in demetalation appears limited, these transformations proceed under mild conditions and are compatible with substituted arene and functionalized aldehyde reaction partners. This approach to azaspirodecanes complements our recently reported (arene)Ru variant of the Morita–Baylis–Hillman reaction[23] and provides access to potentially versatile synthetic building blocks. Benzylic substitution and structurally elaborate aldehydes are compatible with the reaction sequence and provide potentially general means for accessing chiral non-racemic spirolactams. Research along these lines along with application of these Ru-based synthetic methods for the construction of heterocyclic ring systems found in various alkaloid natural products (such as the spirostaphylotrichins[24]) are subjects of current investigations.



Spirostaphylotrichin A

4. Experimental

4.1. General

All commercially available reagents and solvents were used as received unless otherwise noted. Tetrahydrofuran and CH_2Cl_2 were purified by passage through packed alumina columns immediately prior to use. DMF was purified by passing through two columns of molecular sieves. All reactions were performed in oven-dried glassware under a blanket of dry argon unless otherwise noted. Thin-layer chromatography was performed on silica gel 60 glass-backed TLC plates (250 μm). All reactions were monitored by TLC for consumption of starting substrate. Radial chromatography was performed using 2 mm plates coated with TLC grade silica. ^{1}H and ^{13}C NMR spectra were obtained at 300 or 500 MHz as indicated. Chemical shifts (δ) are reported relative to residual solvent peaks. IR spectra were recorded on a spectrophotometer equipped with an ATR attachment. Melting points were determined using a capillary melting point apparatus and are uncorrected. High resolution mass spectra were obtained using electron impact ionization (EI) or electro-spray ionization (ESI).

4.2. General procedure for demetalation of methoxy-substituted cyclohexadienyl ruthenium complexes 9 (Table 1)

*4.2.1. Spiro-dienone **10a***

To a stirred solution of **9a**[11] (50 mg, 0.13 mmol) in ~5 mL THF, $CuCl_2$ (53 mg, 0.39 mmol) was added at room temperature. A dark

brown solid formed in the reaction. The reaction was monitored by TLC and after 30 min all the starting material was consumed. The precipitate was removed by filtration and the filtrate was partitioned between CH_2Cl_2 and water. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to afford yellow oil, which was then purified by flash column chromatography (SiO_2, EtOAc) to give **10a** (17 mg, 60%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.19 (d, J=7.0 Hz, 3H), 2.94 (s, 3H), 3.71 (s, 2H), 5.85 (q, J=7.0 Hz, 1H), 6.28 (d, J=6.0 Hz, 2H), 6.81 (d, J=6.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 30.0, 45.9, 54.4, 128.2, 130.1, 136.7, 150.0, 167.0, 185.5. IR (neat) ν (cm^{-1}) 1633, 1657. HRMS (ESI): calcd for $C_{12}H_{14}NO_2$ 204.1020 $[M+H]^+$, found 204.1026.

*4.2.2. Spiro-dienone **10b***

Using the procedure described above, **10b** was obtained from complex **9b**[11] in 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.04 (s, 3H), 3.51 (s, 2H), 5.30 (s, 1H), 6.14 (s, 1H), 6.34 (d, J=12.0 Hz, 2H), 6.80 (d, J=12.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.4, 45.2, 54.6, 119.7, 128.7, 140.3, 148.9, 168.2, 185.3. IR (neat) ν (cm^{-1}) 1605, 1683. HRMS (EI): calcd for $C_{11}H_{11}NO_2$ 189.0784 $[M]^+$, found 189.0780.

*4.2.3. Spiro-dienone **10c***

Obtained in 79% yield from **9c**.[11] ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.03 (s, 3H), 3.57 (s, 2H), 6.37 (d, J=10.0 Hz, 2H), 6.46 (s, 1H), 6.94 (d, J=10.0 Hz, 2H), 7.33 (m, 3H), 7.89 (dd, J=7.5, 2.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 47.0, 54.4, 128.2, 128.7, 129.7, 131.4, 133.5, 138.0, 149.8, 165.6, 185.5. IR (neat) ν (cm^{-1}) 1677, 1666. HRMS (FAB, NBA) calcd for $C_{17}H_{16}NO_2$ 266.1181 $[M+H]^+$, found 266.1181. Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.69; H, 5.84; N, 5.04.

*4.2.4. Spiro-dienone **10d***

Obtained in 85% yield from demetalation of **9d**.[11] ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.93 (s, 3H), 3.46 (s, 2H), 3.73 (s, 3H), 6.27 (m, 3H), 6.81 (dd, J=22.5, 7.5 Hz, 4H), 7.89 (d, J=6.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 47.0, 54.3, 55.4, 113.6, 126.5, 128.5, 133.6, 137.7, 150.2, 160.8, 166.1, 173.4, 185.6. IR (neat) ν (cm^{-1}) 1509, 1607, 1657. HRMS (ESI): calcd for $C_{18}H_{18}NO_3$ 296.1281 $[M+H]^+$, found 296.1288.

*4.2.5. Spiro-dienone **10e***

Obtained in 61% yield from complex **9e**.[11] ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.06 (s, 3H), 3.49 (s, 2H), 6.42 (d, J=12.0 Hz, 2H), 6.53 (s, 1H), 6.96 (d, J=12.0 Hz, 2H), 7.55 (d, J=9.0 Hz, 2H), 8.19 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 47.1, 54.4, 113.6, 126.5, 126.6, 128.5, 133.7, 137.8, 150.3, 160.9, 166.1, 185.7. IR (neat) ν (cm^{-1}) 1624, 1651. HRMS (ESI): calcd for $C_{17}H_{15}N_2O_4$ 311.1026 $[M+H]^+$, found 311.1036.

*4.2.6. Spiro-dienone **10f***

Isolated in 38% yield from demetalation of **9f**.[11] ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.78 (d, J=6.0 Hz, 3H), 2.90 (s, 3H), 3.41 (s, 2H), 5.85 (m, 1H), 6.00 (d, J=12.0 Hz, 1H), 6.22 (d, J=12.0 Hz, 2H), 6.74 (d, J=12.0 Hz, 2H), 7.50 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 30.2, 45.7, 54.5, 125.4, 128.3, 131.5, 137.4, 139.7, 149.9, 163.5, 190.8. IR (neat) ν (cm^{-1}) 1621, 1662. HRMS (ESI): calcd for $C_{14}H_{16}NO_2$ 230.1175 $[M+H]^+$, found 230.1179.

4.3. Spirocyclization and oxidative demetalation of 3-methoxy-substituted arene ruthenium complexes (Scheme 3)

*4.3.1. Preparation of (η^6-arene)ruthenium complex **11***

N-(3-Methoxybenzyl)-*N*-methylacetamide-β-phosphonic acid diethyl ester (1.00 g, 3.04 mmol) was combined with $[(MeCN)_3RuCp][PF_6]$[12] (1.32 g, 3.04 mmol) in Ar-saturated 1,2-dichloroethane (20 mL). The resulting dark orange solution was stirred in a 70 °C oil bath for 36 h. After this time the solvent was evaporated to give a dark oily residue, which was dissolved in acetone and passed through a short column of neutral alumina. The filtrate was evaporated in vacuo to give brown oily product, which was then again dissolved in a minimum amount of acetone and reprecipitated by addition of anhydrous ether to give **11** as a tan solid (1.91 g, 98%) after collection by vacuum filtration. ^{1}H NMR (300 MHz, acetone-d_6) δ 1.32 (dt, J=6.0, 4.0 Hz, 6H), 3.21 (d, J=6.0 Hz, 1H), 3.29 (d, J=6.0 Hz, 1H), 3.37 (s, 3H), 3.89 (s, 3H), 4.17 (dq, J=8.0, 2.2 Hz, 4H), 4.67 (d, J=6.0 Hz, 2H), 5.53 (s, 5H), 6.34 (m, 4H). ^{13}C NMR (75 MHz, acetone-d_6) δ 16.6, 32.6, 38.0, 50.0, 58.0, 63.1, 74.2, 74.7, 81.4, 84.2, 101.8, 135.1, 166.7. IR (neat) ν (cm^{-1}) 1630, 1642, 1662. HRMS (FAB, NBA) calcd for $C_{20}H_{29}NO_5PRu$ 496.0826 $[M]^+$, found 496.0829. Anal. Calcd for $C_{20}H_{29}NO_5PRu\cdot PF_6$: C, 37.44; H, 4.55; N 2.18. Found: C, 37.26; H, 4.36; N, 2.33.

*4.3.2. 3-Methoxy cyclohexadienyl ruthenium complex **12a***

The procedure used for the preparation of **12a** is representative for all spirocyclization–HWE olefination reactions. A solution of **11** (250 mg, 0.39 mmol) in ~4 mL THF was added to NaH (60%, 34.4 mg, 0.86 mmol) at room temperature. The resulting mixture was maintained for 30 min, during which time the reaction turned golden yellow. Benzaldehyde (207 mg, 1.95 mmol) was added via syringe and the reaction was stirred at room temperature for another 30 min. The reaction was quenched with a few drops of H_2O and the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a yellow solid. Purification by flash column chromatography gave **12a** (139 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62 (d, J=6.0 Hz, 1H), 2.92 (s, 3H), 3.03 (m, 1H), 3.34 (s, 3H), 3.42 (d, J=6.0 Hz, 2H), 4.50 (t, J=4.5 Hz, 1H), 4.81 (s, 5H), 5.88 (d, J=6.0 Hz, 1H), 6.22 (s, 1H), 7.25 (m, 3H), 7.80 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.3, 30.1, 37.3, 50.1, 55.6, 64.5, 65.3, 68.3, 71.8, 75.1, 127.0, 127.6, 128.1, 129.1, 130.7, 134.6, 141.3, 166.3. IR (neat) ν (cm^{-1}) 1638. HRMS (EI): calcd for $C_{23}H_{23}NO_2Ru$ 447.0766 $[M]^+$, found 447.0768.

*4.3.3. 3-Methoxy cyclohexadienyl ruthenium complex **12b***

Using the procedure given above, **11** and acetaldehyde gave **12b** in 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99 (d, J=6.0 Hz, 3H), 2.54 (d, J=6.0 Hz, 1H), 2.87 (s, 3H), 2.92 (br s, 1H), 3.31 (br s, 2H), 3.34 (s, 3H), 4.41 (t, J=6.0 Hz, 1H), 4.81 (s, 5H), 5.55 (q, J=7.0 Hz, 1H), 5.84 (d, J=6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 29.3, 29.7, 37.8, 48.6, 55.5, 64.3, 68.2, 71.6, 75.4, 128.8, 132.7, 142.0, 167.2. IR (neat) ν (cm^{-1})1670. HRMS (EI): calcd for $C_{18}H_{21}NO_2Ru$ 385.0615 $[M]^+$, found 385.0618.

*4.3.4. Tetrahydroisoquinolinone **13a***

To a stirred solution of **12a** (76 mg, 0.17 mmol) in 6 mL of THF was added $CuCl_2$ (62 mg, 0.46 mmol) and the reaction was stirred under 1 atm of CO (balloon) for 2 h. The solvent was evaporated and residue was dissolved in CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to give a yellow oil, which was purified by flash column chromatography (SiO_2, 1:1 EtOAc/hexanes) to give **13a** (23 mg, 50%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 3H), 3.83 (s, 3H), 4.48 (s, 2H), 6.70 (s, 1H), 7.26 (d, J=3.0 Hz, 1H), 7.34 (m, 4H), 7.55 (q, J=9.0 Hz, 1H), 7.66 (d, J=6.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.9, 52.8, 55.6, 110.1, 114.3, 125.4, 127.9, 128.0, 128.1, 128.7, 130.2, 132.8, 134.8, 136.1, 159.3, 164.8. IR (neat) ν (cm^{-1}) 1659. HRMS (EI): calcd for $C_{18}H_{17}NO_2$ 279.1253 $[M]^+$, found 279.1248.

*4.3.5. Tetrahydroisoquinolinone **13b***

Application of the procedure described above to **12b** gave **13b** in 64% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.28 (d, J=6.0 Hz, 3H), 3.12 (s, 3H), 3.81 (s, 3H), 4.33 (s, 2H), 6.39 (q, J=7.0 Hz, 1H), 6.64

(d, J=3.0 Hz, 1H), 6.83 (m, 1H), 7.35 (d, J=12.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 34.5, 52.8, 55.6, 110.0, 114.2, 117.6, 124.9, 128.0, 128.6, 131.5, 158.9, 165.8. IR (neat) ν (cm^{-1}) 1632. HRMS (EI): calcd for $C_{13}H_{15}NO_2$ 217.1097 $[M]^+$, found 217.1090.

*4.3.6. (Arene)ruthenium complex **15***

Using the procedure given for the preparation of **11**, complex **15** was obtained from the corresponding *o*-methoxy-substituted ligand and $[(CH_3CN)_3RuCp][PF_6]$ in 95% isolated yield. ^{1}H NMR (300 MHz, acetone-d_6) δ 1.28 (t, J=15.0 Hz, 6H), 2.84 (s, 1H), 3.13 (d, J=3.0 Hz, 1H), 3.29 (s, 3H), 3.84 (s, 3H), 4.15 (q, J=8.0 Hz, 4H), 4.25 (d, J=18.0 Hz, 1H), 4.95 (d, J=18.0 Hz, 1H), 5.49 (s, 5H), 6.04 (d, J=6.0 Hz, 1H), 6.19 (t, J=6.0 Hz, 1H), 6.46 (d, J=6.0 Hz, 1H), 6.50 (d, J=6.0 Hz, 1H). ^{13}C NMR (75 MHz, acetone-d_6) δ 16.8, 32.7, 34.4, 38.3, 47.3, 58.0, 63.0, 72.0, 81.6, 82.7, 84.4, 93.8, 133.5, 167.0. IR (neat) ν (cm^{-1}) 1628. HRMS (FAB$^+$, NBA) calcd for $C_{20}H_{29}NO_5PRu$ 496.0826 $[M]^+$, found 496.0823. Anal. Calcd for $C_{20}H_{29}NO_5PRuP_2F_6$: C, 37.44; H, 4.55; N, 2.18. Found: C, 37.86; H, 4.49; N, 2.27.

4.4. Demetalation of cyclohexadienyl ruthenium complexes 16 (Table 2)

*4.4.1. Spirodiene **17a***

Cyclohexadienyl complexes **16** were prepared as described previously.[11] To a stirred solution of **16a** (50 mg, 0.12 mmol) in ~5 mL methanol under 1 atm of CO (balloon), $CuBr_2$ (86 mg, 0.39 mmol) in 1 mL methanol was added dropwise via syringe. The reaction initially turned dark red and then gradually changed to pale yellow over a period of 2 h. The solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to give a yellow oil. Purification by flash column chromatography gave **17a** (18.9 mg, 56%) as a colorless oil along with $RuCp(CO)_2Br$ (**8**, 57%) as yellow needles whose spectral properties matched those previously reported.[15] ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.90 (s, 3H), 3.27 (d, J=9.0 Hz, 1H), 3.36 (s, 3H), 3.39 (d, J=9.0 Hz, 1H), 3.71 (d, J=6.0 Hz, 1H), 5.79 (d, J=9.0 Hz, 1H), 6.08 (m, 1H), 6.12 (m, 2H), 6.81 (s, 1H), 7.31 (m, 3H), 7.89 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0, 47.4, 54.4, 58.7, 79.8, 87.4, 124.4, 124.6, 127.7, 128.3, 130.8, 131.6, 133.4, 134.7, 136.8, 166.8. IR (neat) ν (cm^{-1}) 1635. HRMS (EI): calcd for $C_{18}H_{19}NO_2$ 281.1416 $[M]^+$, found 281.1419.

*4.4.2. Spirodiene **17b***

Using the procedure given above, **16b** afforded **17b** in 51% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94 (s, 3H), 3.23 (d, J=10.0 Hz, 1H), 3.35 (s, 3H), 3.38 (d, J=10.0 Hz, 1H), 3.82 (d, J=3.75 Hz, 1H), 5.58 (s, 1H), 5.67 (m, 1H), 5.95 (m, 1H), 6.05 (m, 2H), 6.13 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1, 31.1, 56.5, 58.1, 80.7, 118.7, 124.2, 125.2, 125.3, 133.9, 140.9, 167.6. IR (neat) ν (cm^{-1}) 1645. HRMS (EI): calcd for $C_{12}H_{15}NO_2$ 205.1102 $[M]^+$, found 205.1101.

*4.4.3. Spirodiene **17c***

Spirodiene **17c** was prepared as described above except that THF was used as the solvent (in place of MeOH) and the $CuBr_2$ was added as an aqueous solution. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.80 (s, 3H), 3.18 (d, J=12.0 Hz, 1H), 3.32 (d, J=12.0 Hz, 1H), 4.08 (m, 1H), 4.47 (s, 2H), 4.75 (q, J=6.0 Hz, 2H), 5.55 (d, J=12.0 Hz, 1H), 5.73 (m, 1H), 5.94 (m, 2H), 6.14 (t, J=6.0 Hz, 1H), 7.23 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.9, 46.5, 56.2, 66.8, 71.5, 73.1, 124.6, 127.8, 128.1, 128.6, 131.5, 133.0, 137.1, 138.3, 167.4. IR (neat) ν (cm^{-1}) 1625, 1680, 3320. HRMS (ESI): calcd for $C_{19}H_{22}NO_3$ 312.1594 $[M+H]^+$, found 312.1592.

*4.4.4. Spirodiene **17d***

The material was prepared in 51% isolated yield using the procedure given for **17c**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.93 (s, 3H), 3.33 (d, J=9.0 Hz, 1H), 3.45 (d, J=9.0 Hz, 1H), 4.22 (d, J=9.0 Hz, 1H), 5.71 (d, J=9.0 Hz, 1H), 5.86 (m, 1H), 6.12 (m, 2H), 6.48 (m, 1H), 6.75 (s, 1H), 7.43 (d, J=3.0 Hz, 1H), 7.92 (d, J=3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.9, 47.7, 55.8, 71.7, 87.5, 112.9, 116.8, 123.6, 125.0, 127.3, 127.6, 133.1, 143.3, 150.8, 167.1. IR (neat) ν (cm^{-1}) 1628, 1710, 3351. HRMS (ESI): calcd for $C_{15}H_{16}NO_3$ 258.1124 $[M+H]^+$, found 258.1129.

4.5. Spirocyclization–demetalation of *o*-substituted amido phosphonate ruthenium complexes (Scheme 4)

*4.5.1. (η^6-Arene)ruthenium complexes **18a** and **18b***

These arene complexes were prepared using the procedure given for **11**. Complex **18a**: 71%, ^{1}H NMR (300 MHz, acetone-d_6) δ 1.30 (t, J=12.0 Hz, 6H), 2.44 (s, 3H), 3.25 (d, J=21.0 Hz, 1H), 3.30 (s, 3H), 3.37 (d, J=21.0 Hz, 1H), 4.16 (q, J=8.0 Hz, 4H), 4.55 (d, J=15.0 Hz, 1H), 4.88 (d, J=15.0 Hz, 1H), 5.45 (s, 5H), 6.31 (m, 4H). ^{13}C NMR (75 MHz, acetone-d_6) δ 16.6, 18.4, 32.5, 34.2, 37.9, 48.8, 63.1, 82.1, 84.2, 84.8, 85.7, 86.9, 87.2, 88.6, 101.4, 101.9, 166.6. IR (neat) ν (cm^{-1}) 1639, 1651. HRMS (ESI): calcd for $C_{20}H_{29}NO_4PRu$ 480.0872 $[M]^+$, found 480.0878. Complex **18b**: 82%, ^{1}H NMR (300 MHz, acetone-d_6) δ 1.32 (t, J=7.5 Hz, 6H), 3.25 (m, 2H), 3.42 (s, 3H), 4.19 (m, 4H), 4.48 (d, J=18.0 Hz, 1H), 5.15 (d, J=18.0 Hz, 1H), 5.59 (s, 5H), 6.32 (m, 2H), 6.61 (d, J=6.0 Hz, 1H), 6.81 (d, J=6.0 Hz, 1H). ^{13}C NMR (75 MHz, acetone-d_6) δ 16.5, 32.4, 34.1, 38.1, 49.2, 63.1, 81.1, 83.8, 84.3, 85.4, 86.4, 86.9, 88.4, 102.2, 105.3, 167.0. IR (neat) ν (cm^{-1}) 1638, 1646, 1658. HRMS (EI): calcd for $C_{19}H_{26}NO_4PClRu$ 500.0325 $[M]^+$, found 500.0326.

*4.5.2. Cyclohexadienyl ruthenium complexes **19a** and **19b***

Spirocyclization–HWE olefination of **18a**,**b** was effected in the presence of benzaldehyde using the procedures given above for the preparation of **12a**. Complex **19a**: 90%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 3H), 2.67 (d, J=6.0 Hz, 1H), 2.94 (s, 3H), 3.27 (d, J=12.0 Hz, 1H), 3.86 (d, J=12.0 Hz, 1H), 4.42 (d, J=3.0 Hz, 1H), 4.52 (t, J=3.0 Hz, 1H), 4.76 (s, 5H), 5.72 (t, J=3.0 Hz, 1H), 6.21 (s, 1H), 7.23 (m, 3H), 7.80 (d, J=6.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 30.0, 37.6, 48.3, 52.1, 61.3, 75.8, 76.2, 78.4, 79.3, 128.1, 130.8, 133.7, 135.0, 139.8, 166.9. IR (neat) ν (cm^{-1}) 1683. HRMS (EI): calcd for $C_{23}H_{23}NORu$ 431.0811 $[M]^+$, found 431.080. Complex **19b**: 40%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94 (s, 3H), 3.09 (d, J=6.0 Hz, 1H), 3.39 (d, J=9.0 Hz, 1H), 4.11 (d, J=9.0 Hz, 1H), 4.75 (t, J=3.0 Hz, 1H), 4.89 (s, 5H), 4.99 (d, J=6.0 Hz, 1H), 5.75 (t, J=3.0 Hz, 1H), 6.25 (s, 1H), 7.25 (m, 4H), 7.80 (d, J=6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.4, 35.6, 42.2, 55.1, 61.6, 67.2, 76.0, 78.4, 117.2, 126.9, 129.9, 138.4, 143.3, 147.5, 165.8. IR (neat) ν (cm^{-1}) 1643. HRMS (EI): calcd for $C_{22}H_{20}NOClRu$ 451.0271 $[M]^+$, found 451.0278.

*4.5.3. Spirodienols **20a** and **20b***

Using the demetalation procedure given for the preparation of **17c**, cyclohexadienyl complexes **19a** and **19b** were converted to the corresponding dienols **20a** and **20b** in 53 and 40% isolated yield, respectively. Dienol **20a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 3H), 2.91 (s, 3H), 3.38 (d, J=12.0 Hz, 1H), 3.53 (d, J=12.0 Hz, 1H), 4.25 (m, 1H), 5.90 (m, 1H), 5.92 (m 1H), 6.01 (m, 1H), 6.79 (s, 1H), 7.31 (m, 4H), 7.88 (d, J=12.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.0, 28.5, 52.9, 56.9, 68.4, 125.5, 125.7, 126.0, 127.9, 128.7, 130.4, 131.4, 132.0, 132.4, 134.2, 165.8. IR (neat) ν (cm^{-1}) 1635, 3325. HRMS (ESI): calcd for $C_{18}H_{19}NO_2$ 281.1416 $[M+H]^+$, found 281.1419. Dienol **20b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.93 (s, 3H), 3.32 (d, J=12.0 Hz, 1H), 3.69 (d, J=12.0 Hz, 1H), 4.75 (br s, 1H), 5.84 (d, J=6.0 Hz, 1H), 5.87 (m, 1H), 5.94 (m, 1H), 6.54 (s, 1H), 7.31 (m, 3H), 7.90 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.5, 46.5, 54.2, 70.2, 123.3, 124.8, 126.6, 127.8, 128.7, 131.0, 131.4, 133.1, 134.2, 137.1, 166.4. IR (neat) ν (cm^{-1}) 1610, 3320. HRMS (ESI): calcd for $C_{17}H_{17}NO_2Cl$ 302.0942 $[M+H]^+$, found 302.0940.

4.6. Oxidative demetalation of 16a in the presence of alternative nucleophiles (Scheme 5)

4.6.1. Iodo-diene *21* and tetrahydroisoquinolinone *22*

Cupric bromide (86 mg, 0.39 mmol) was added to a stirred solution of **16a** (50 mg, 0.12 mmol) and NaI (90 mg, 0.60 mmol) in 4 mL THF under 1 atm of CO (balloon). The reaction initially turned dark red and then gradually changed to pale yellow over a period of 2 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to give a yellow oil. Purification by flash column chromatography gave **21** (6.8 mg) and **22** (12 mg) in combined isolated yield of 55%. Iodo-diene **21**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.97 (s, 3H), 3.32 (d, J=9.0 Hz, 1H), 3.45 (d, J=9.0 Hz, 1H), 4.16 (d, J=6.0 Hz, 1H), 5.77 (d, J=9.0 Hz, 1H), 5.92 (m, 1H), 6.14 (m, 2H), 6.86 (s, 1H), 7.35 (m, 4H), 7.94 (d, J=9.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0, 47.4, 54.4, 79.8, 87.4, 124.4, 124.7, 127.7, 128.3, 130.8, 131.6, 133.4, 134.7, 136.8, 166.8. IR (neat) ν (cm^{-1}) 1680. HRMS (ESI): calcd for $C_{17}H_{17}INO$ 378.0355 $[M+H]^+$, found 378.0352. Tetrahydroisoquinoline **22**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.17 (s, 3H), 4.52 (s, 2H), 7.14–7.72 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.9, 52.8, 110.1, 114.3, 125.4, 127.9, 128.0, 128.1, 128.7, 130.2, 132.8, 134.8, 136.2, 159.3, 164.9. IR (neat) ν (cm^{-1}) 1623. HRMS (ESI): calcd for $C_{17}H_{16}NO$ 250.1232 $[M+H]^+$, found 250.1232.

4.6.2. Demetalation of *16a* in the presence of phenol, cyclohexanol, or NaCN

The procedure given above was followed except that the indicated nucleophiles (phenol, cyclohexanol, or NaCN) were used in place of NaI. Workup of these reactions as described resulted in isolation of tetrahydroisoquinolinone **22** as the sole organic product in 30, 25, and 45% isolated yields, respectively.

4.6.3. Acetoxy-diene *23a*

Copper(II) bromide (86 mg, 0.39 mmol) was added to a solution of **16a** (50 mg, 0.12 mmol) in 4 mL of 4:1 (v/v) THF/AcOH. Workup of the reaction as described above afforded **22** (20 mg, 67%) along with acetoxy-substituted spirolactam **23a** (3.7 mg, 10%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.57 (s, 3H), 3.03 (s, 3H), 3.57 (s, 2H), 5.15 (br d, J=6.0 Hz, 1H), 6.38 (d, J=9.0 Hz, 2H), 6.46 (s, 1H), 6.95 (d, J=9.0 Hz, 2H), 7.36 (m, 4H), 7.90 (d, J=9.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 29.6, 46.4, 53.3, 70.5, 122.5, 125.9, 127.4, 128.2, 130.3, 131.0, 133.7, 136.6, 165.8, 167.7. IR (neat) ν (cm^{-1}) 1560, 1620. HRMS (EI): calcd for $C_{19}H_{19}NO_3$ 309.1359 $[M]^+$, found 309.1352.

4.6.4. Azido-diene *23b*

Using the procedure given for the synthesis of iodo-diene **21** except that NaN_3 was substituted for NaI, symmetrical azido-diene **23b** (24.6 mg, 70%) was obtained as the sole organic product. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.96 (s, 3H), 3.38 (s, 2H), 4.14 (m, 1H), 5.95 (d, J=12.0 Hz, 2H), 6.03 (d, J=12.0 Hz, 2H), 6.57 (s, 1H), 7.31 (m, 3H), 7.93 (d, J=12.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.4, 43.4, 53.6, 58.5, 86.0, 122.5, 127.9, 129.1, 131.1, 134.2, 134.6, 138.0, 166.3. IR (neat) ν (cm^{-1}) 1424, 1664, 1679, 2041, 2088. HRMS (ESI): calcd for $C_{17}H_{17}N_4O$ 293.1396 $[M+H]^+$, found 293.1392.

4.7. Spirocyclization–demetalation of *N*-allyl/propenyl ruthenium complexes (Scheme 6)

4.7.1. (η^6-Arene)ruthenium complex *25*

Following the procedure given for the preparation of **11**, treatment of β-amido phosphonate **24** with $[(CH_3CN)_3Ru][PF_6]$ gave the desired η^6-complex **25** in 54% isolated yield. ^{1}H NMR (300 MHz, acetone-d_6, mixture of rotamers) δ 1.31 (m, 6H), 1.63 (d, J=9.0 Hz, 3H), 2.13 (d, J=15.0 Hz, 1H), 2.63 (d, J=15.0 Hz, 1H), 4.14 (q, J=5.0 Hz, 1H), 4.67 (s, 1H), 5.12 (s, 1H), 5.53 (s, 5H), 5.78 (q, J=6.0 Hz, 1H), 6.43 (m, 5H). ^{13}C NMR (75 MHz, acetone-d_6) δ 12.8, 16.7, 34.4, 36.2, 49.9, 63.0, 81.2, 82.2, 86.4, 87.0, 90.8, 128.7, 130.2, 162.8. IR (neat) ν (cm^{-1}) 1669. HRMS (EI): calcd for $C_{21}H_{29}NO_4PRu$ 492.0872 $[M]^+$, found 492.0883.

4.7.2. Cyclohexadienyl ruthenium complexes *26a* and *26b*

Using the general procedure for spirocyclization–HWE olefination (see preparation of **12a** in Section 4.3.2), arene complex **25** was converted to cyclohexadienyl complexes **26a** and **26b** upon reaction with benzaldehyde and acetaldehyde, respectively. Complex **26a**: 65%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.88 (d, J=6.0 Hz, 3H), 2.75 (d, J=6.0 Hz, 2H), 3.77 (s, 2H), 4.57 (t, J=6.0 Hz, 2H), 4.82 (s, 5H), 5.00 (m, 1H), 5.89 (t, J=3.0 Hz, 1H), 6.27 (s, 1H), 6.39 (d, J=9.0 Hz, 1H), 7.28 (m, 4H), 7.75 (d, J=6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.1, 37.0, 48.2, 63.6, 75.5, 76.4, 79.6, 110.7, 124.0, 127.7, 130.5, 134.7, 135.7, 140.2, 152.8, 165.2. IR (neat) ν (cm^{-1}) 1676. HRMS (EI): calcd for $C_{24}H_{23}NORu$ 443.0817 $[M]^+$, found 443.0813. Complex **26b**: 60%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.88 (d, J=9.0 Hz, 3H), 2.00 (d, J=6.3 Hz, 3H), 2.66 (d, J=6.0 Hz, 2H), 3.67 (s, 2H), 4.48 (t, J=6.0 Hz, 2H), 4.82 (s, 5H), 5.01 (m, 1H), 5.56 (q, J=6.0 Hz, 1H), 5.70 (t, J=3.0 Hz, 1H), 6.37 (d, J=9.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 22.8, 31.6, 37.3, 47.0, 63.8, 67.8, 75.7, 79.6, 110.7, 123.9, 134.5, 141.2, 167.0. IR (neat) ν (cm^{-1}) 1680. HRMS (EI): calcd for $C_{19}H_{21}NORu$ 381.0661 $[M]^+$, found 381.0658.

4.7.3. Spirolactam *27*

Using the general demetalation procedure as described for the preparation of **17c**, cyclohexadienyl ruthenium complex **26a** was converted to dienol **27** in 51% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.78 (d, J=9.0 Hz, 3H), 3.69 (d, J=9.0 Hz, 1H), 3.84 (d, J=9.0 Hz, 1H), 4.11 (br s, 1H), 5.01 (m, 1H), 6.11 (m, 2H), 6.47 (m, 2H), 6.50 (d, J=9.0 Hz, 1H), 6.88 (s, 1H), 7.35 (m, 3H), 7.90 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 29.9, 36.5, 47.8, 69.4, 111.2, 123.2, 124.5, 125.9, 128.6, 129.2, 130.1, 131.9, 133.6, 134.3, 138.2, 167.2. IR (neat) ν (cm^{-1}) 1524, 1654, 3350. HRMS (EI): calcd for $C_{19}H_{19}NO_2$ 293.1416 $[M]^+$, found 293.1420.

4.8. Reaction of arene ruthenium complex 4 with CBZ-protected proline aldehyde (Scheme 7)

4.8.1. Cyclohexadienyl complex *29*

This complex was prepared in 57% isolated yield by sequential treatment of **4** with NaH and CBZ-protected (*S*)-proline aldehyde[22] according to the general procedure given for **12a**. ^{1}H NMR (300 MHz, $CDCl_3$, mixture of rotamers) δ 1.7 (m, 1H), 1.81 (m, 3H), 2.29 (d, J=3.0 Hz, 0.7H), 2.63 (d, J=3.0 Hz, 1.3H), 2.82 (s, 3H), 3.06 (d, J=12 Hz, 1H), 3.22 (d, J=12.0 Hz, 1H), 3.48 (m, 2H), 4.34 (d, J=6.0 Hz, 2H), 4.79 (s, 5H), 4.94 (d, J=12.0 Hz, 1H), 5.15 (d, J=12.0 Hz, 2H), 5.35 (m, 1H), 5.70 (m, 1H), 7.34 (m 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 29.7, 33.8, 35.8, 38.5, 45.6, 47.3, 54.0, 58.7, 64.8, 66.0, 75.8, 79.6, 127.5, 128.0, 128.9, 138.8, 140.6, 157.8, 167.0. IR (neat) ν (cm^{-1}) 1650, 1705. HRMS (EI): calcd for $C_{28}H_{30}N_2O_3Ru$ 544.1294 $[M]^+$, found 544.1290.

4.8.2. Spirodienol *30*

Application of the general nucleophilic oxidative demetalation procedure as described for the preparation of **17c** afforded dienol **30** in 46% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64 (m, 3H), 1.88 (m, 2H), 2.26 (m, 1H), 2.90 (s, 3H), 3.18 (d, J=12.0 Hz, 1H), 3.42 (d, J=12.0 Hz, 1H), 3.56 (m, 1H), 4.07 (d, J=6.0 Hz, 1H), 5.00 (d, J=12.0 Hz, 1H), 5.11 (d, J=12.0 Hz, 1H), 5.61 (d, J=6.0 Hz, 1H), 5.93 (m, 4H), 7.31 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 30.0, 32.2, 38.2, 47.0, 54.3, 67.0, 70.3, 90.3, 101.0, 115.9, 124.8, 127.4, 128.1, 128.6, 132.2, 136.9, 139.7, 155.3, 159.7, 167.3. IR (neat) ν (cm^{-1}) 1645, 1735,

3320. HRMS (ESI): calcd for $C_{23}H_{27}N_2O_4$ 395.1986 $[M+H]^+$, found 395.1988.

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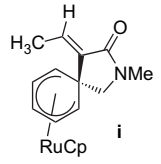

i

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