Rhodium- and Iridium-Catalyzed Double Hydroalkoxylation of Alkynes, an Efficient Method for the Synthesis of *O,O*-Acetals: Catalytic and Mechanistic Studies

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Received December 5, 2006

An efficient method for the synthesis of *O,O*-acetals via metal-catalyzed double hydroalkoxylation of alkynes was developed using the Ir(I) and Rh(I) complexes $[Ir(PyP)(CO)_2]BPh_4$ (**1**) and $[Rh(bim)(CO)_2]BPh_4$ (**2**), where PyP = 1-[2-(diphenylphosphino)ethyl]pyrazole and bim = bis(*N*-methylimidazol-2-yl)-methane, as catalysts for the consecutive addition of two alcohol functional groups to terminal and nonterminal alkynes to form *O,O*-acetals. When the catalyzed cyclization of alkynols was performed in the presence of an excess amount of methanol as a cosolvent, a molecule of methanol was incorporated into the acetal product. The catalyzed cyclization of alkynols in the absence of an alcoholic solvent led to cyclization with incorporation of a second molecule of substrate in the final acetal product. Complexes **1** and **2** were also effective as catalysts for the cyclization of alkyne diols to form bicyclic *O,O*-acetals. The iridium complex **1** was more efficient than the rhodium complex **2** in promoting the reactions of aliphatic alkyne diols. On the other hand, the rhodium complex **2** was more effective for promoting the reactions of aromatic substrates. Mechanistic investigation using low-temperature NMR spectroscopy showed that the catalytic cycle proceeded via π coordination of the alkyne of the substrate to the metal center followed by the sequential addition of two hydroxyl groups to form *O,O*-acetals. Deuteration studies and analysis of reaction intermediates supported the proposed mechanism.

Introduction

The hydroalkoxylation of alkynes is a direct, efficient method for the synthesis of enol ethers, and the intramolecular hydroalkoxylation reaction leads to the formation of a wide variety of oxygen-containing heterocycles.[1] A number of methods have been developed for the hydroalkoxylation of alkynes, including the acid- or base-promoted addition of OH groups to alkynes.[2,3] Transition metal complexes are in many cases the catalysts of choice for the promotion of the hydroalkoxylation of alkynes, due to their high efficiency and functional group tolerance,[1,2,4−6] and have been successfully utilized in the construction of a range of five- and six-membered oxygen-containing heterocycles.[1,4,5] The most widely used catalysts for the hydroalkoxylation of alkynes include molybdenum and tungsten,[5,7,8] ruthenium,[9−11] and, in particular, palladium complexes.[1,4,12−15] Examples of platinum-,[16,17] gold-,[18−20] silver,[21,22] iridium-,[23−25] and rhodium-based[26−28] catalysts for the hydroalkoxylation of alkynes are also known.

O,O-Acetals, in particular spiroacetals, are prevalent motifs in many biologically active compounds, from simple insect pheromones[29] to significantly more complex molecules such as UIC-94017,[30] a protease inhibitor, momensin A, and akadic

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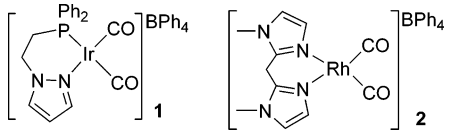
10.1021/om061106r CCC: $37.00
Publication on Web 05/02/2007

Chart 1

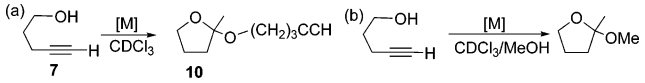


acid.[31] A number of traditional synthetic approaches have been developed for the synthesis of bicyclic *O,O*-acetals, but these often rely on multiple reaction steps and therefore are not optimally efficient.[31] Examples of applications of metal-catalyzed reactions for the simple and direct constructions of *O,O*-acetals are limited. Ruthenium-catalyzed olefin metathesis has been successfully used for the synthesis of spiroacetals;[32−34] however, the difficulty in preparing the substrates for metathesis is a significant drawback. The transition metal-catalyzed intramolecular hydroalkoxylation of alkynes provides an efficient approach to the synthesis of *O,O*-acetals.[15,18,23]

The palladium complexes $PdCl_2(PhCN)_2$ and $PdCl_2$,[15] and more recently gold halides,[18] have been used to catalyze the hydroalkoxylation of alkyne diol substrates to form *O,O*-acetals. The iridium dimer $[Ir(\mu\text{-}Cl)(COD)]_2$ is a highly efficient catalyst for the *exo-dig* cyclization of terminal bis-homopropargylic alcohols forming cyclic acetals via incorporation of alcohol solvent.[23] The use of these simple complexes, however, limits the development of a methodology for the stereoselective synthesis of *O,O*-acetals. Transition metals with suitably designed ligand systems will lead to new stereoselective synthetic routes to *O,O*-acetals. In earlier work, we demonstrated that the iridium complex $[Ir(PyP)(CO)_2]BPh_4$ (**1**)[35] containing a hybrid phosphine-pyrazolyl donor ligand catalyzes the double hydroalkoxylation of both internal and terminal alkynes, with the synthesis of a range of *O,O*-acetals including spiroketals.[36] Crabtree and co-workers[37] have also recently reported that iridium hydrido complexes are efficient as catalysts for the double hydroalkoxylation of alkyne diols to form spiroacetals.[37]

We have previously reported that the cationic rhodium complex $[Rh(bim)(CO)_2]BPh_4$ (**2**), bim = bis(*N*-methylimidazol-2-yl)methane, is an effective catalyst for the cyclization of alkynoic acids to form cyclic lactones, as well as some simple *O,O*-acetals.[27] Here we report the efficiency of the rhodium complex (**2**) as a catalyst for the double intramolecular hydroalkoxylation reaction in the formation of a series of aliphatic and aromatic *O,O*-acetals, including spiroacetals, and compare the efficiency of this catalyst with that of the iridium complex $[Ir(PyP)(CO)_2]BPh_4$ (**1**).[36] The mechanism of the catalyzed hydroalkoxylation reaction was studied using low-temperature NMR spectroscopy and deuteration studies. A mechanism is proposed where the initial step of the reaction cycle involves the association of the alkyne with the reactive metal center.

Scheme 1



Results and Discussion

Rhodium- and Iridium-Catalyzed Cyclization of Alkynols to Form *O,O*-Acetals with Intermolecular Incorporation of an Alcohol. The efficiency of a series of rhodium and iridium complexes as catalysts for the cyclization of 4-pentyn-1-ol (**7**) to form 2-methyl-2-(4-pentynyloxy)-3,4,5-tetrahydrofuran (**10**) (Scheme 1a), $[Ir(PyP)(CO)_2]BPh_4$ (**1**), $[Rh(bim)(CO)_2]BPh_4$ (**2**), $[Ir(PyP)(COD)]BPh_4$ (**3**), $[Ir(PyP)(CO)Cl]$ (**4**), $[Ir(bpm)(CO)_2]BPh_4$ (**5**), and $[Ir(bim)(CO)_2]BPh_4$ (**6**) where PyP = 1-[2-(diphenylphosphino)ethyl]pyrazole, bim = bis(*N*-methylimidazolyl)methane, bpm = bis(1-pyrazolyl)methane, and COD = 1,5-cyclooctadiene, was tested in chloroform solvent at 60 °C. Of these complexes, the best catalyst for the cyclization was the cationic iridium complex $[Ir(PyP)(CO)_2]BPh_4$ (**1**). The Rh(I) (**2**)-catalyzed cyclization of the terminal alkynols 5-hexyn-1-ol (**8**) and 2-(2-ethynyl)benzyl alcohol (**9**), in chloroform solvent, also led to products resulting from an *exo-dig*[38] cyclization with incorporation of a second molecule of substrate to form cyclic acetals.

When the catalyzed cyclization reactions of the alkynol substrates **7**, **8**, and **9** were conducted in the presence of an excess amount of methanol (e.g., Scheme 1b), cyclic acetal products resulting from incorporation of a molecule of methanol were formed (Table 1).[36] The efficiency of cyclization of this series of terminal alkynol substrates was established both with and without methanol as solvent (Table 1), using the Rh(I) complex **2** as a catalyst. A good rate of conversion was observed for the cyclization of the aromatic substrate 2-(2-ethynyl)benzyl alcohol (**9**) in the presence of an excess of methanol, with complete conversion to products, **16** and **13** (**16**:**13** = ca. 8:2) in less than 4 h. The efficiency of conversion of the aliphatic substrates using **2** as the catalyst was significantly lower. In contrast, the times for the complete conversions of the aliphatic substrates using the iridium catalyst **1** as reported previously[36] were much better than those reported here for the Rh(I) complex **2**, which agrees with our previous studies of the intramolecular hydroamination of alkynes.[39,40]

Catalyzed Synthesis of *O,O*-Acetals from Alkyne Diols. In the presence of catalytic quantities of either the iridium complex **1**[36] or rhodium complex **2**, complete conversion of a series of alkyne diols to *O,O*-acetals was achieved in most cases in less than 24 h, at 120 °C (Table 2). Good to excellent conversion of substrate to product was also achieved when the reactions were performed at 60 °C in $CDCl_3$. The iridium complex $[Ir(PyP)(CO)_2]BPh_4$ (**1**) is more efficient than the rhodium complex $[Rh(bim)(CO)_2]BPh_4$ (**2**) in promoting the tandem cyclization of aliphatic alkyne diols **17** and **18**. On the other hand, **2** is a consistently more active catalyst than **1** for promoting the cyclization of aromatic alkyne diols **19**−**21** (Table 2).

In the presence of catalytic quantities of either the iridium complex **1**[36] or rhodium complex **2**, alkyne diols 3-ethynylpentane-1,5-diol (**17**) and 3-ethynylhexane-1,6-diol (**18**) cleanly cyclized to the bicyclic acetals **22** and **23**, respectively, with quantitative conversion (Table 2). The solution structures of the

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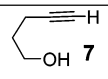
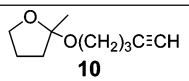
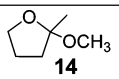
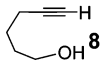
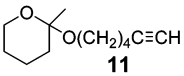
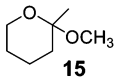
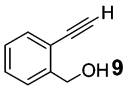
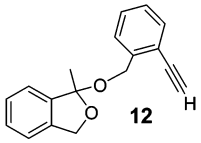
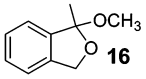
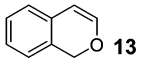
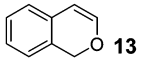
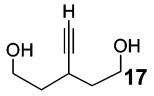
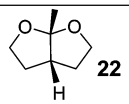
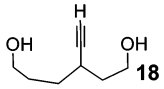
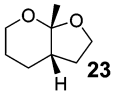
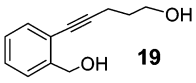
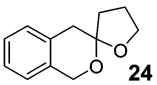
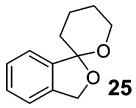
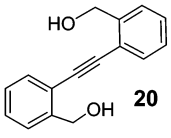
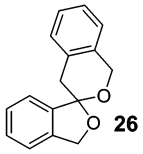
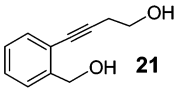
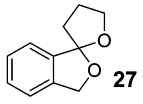
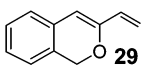
Table 1. Catalyzed Cyclization of Terminal Alkynols Using [Rh(bim)(CO)$_2$]BPh$_4$ (1) as a Catalyst[a]

Substrate	Reactions without MeOH		Reactions with MeOH[b]	
	Product(s)	Conv. (hr)	Product(s)	Conv. (hr)
 **7**	 **10**	95 (66)	 **14**	98 (26)
 **8**	 **11**	52 (55)	 **15**	15 (40)
 **9**	 **12**	67 (3.6)[c] **12**:**13** = 59:8	 **16**	>98 (4); **16**:**13** = 81:19
	 **13**		 **13**	

[a] All reactions were performed in $CDCl_3$ at 60 °C; for **7** and **8**, 2.0 mol % of **2**; for **9** 4.0 mol % of **2** was used. [b] 5−6-fold excess of methanol relative to the alkynols was used. [c] Compound **12** decomposed on further heating.

Table 2. Efficiency of [Ir(PyP)(CO)$_2$]BPh$_4$ (1)[a] and [Rh(bim)(CO)$_2$]BPh$_4$ (2) as Catalysts for the Cyclization of Alkyne Diols

Entry	Catalyst, mol%	Substrate	Product(s)	% Conversion (hrs)[b]
1	**1**, 3.0[a]	 **17**	 **22**	>98 (4.0)
2	**2**, 4.0			>98 (7.0)
3	**1**, 3.0[a]	 **18**	 **23**	>98 (7.0)
4	**2**, 4.0			> 98 (16)
5	**1**, 5.0[a]	 **19**	 **24**	>98 (22) **24**:**25** = 50:50
6	**2**, 5.0		 **25**	>98 (15) **24**:**25** = 63:37
7	**1**, 5.0[a]	 **20**	 **26**	>98 (174)
8	**2**, 5.0			>98 (21)
9	**1**, 5.0[a]	 **21**	 **27**	>98 (22) **27** only
10	**2**, 5.0		 **29**	>98 (5.5) **27**:**29** = 87:13

[a] Catalyzed reactions using [Ir(PyP)(CO)$_2$]BPh$_4$ (**1**) as a catalyst have been previously reported[36] and were included here for comparison. [b] Reactions were performed in 1,1,2,2-tetrachloroethane-d_2 $(CDCl_2)_2$ at 120 °C.

products of these reactions were determined using 2D NMR techniques, and their identities were confirmed by GC-MS and HRMS. In products **22** and **23** the −H and $-CH_3$ substituents of the two fused carbon positions are *cis* to each other. This is most likely due to the stereoelectronic constraints imposed on formation of the 5,5- and 5,6-fused bicyclic acetals **22** and **23**.[41] The catalyzed cyclization of 3-ethynylpentane-1,5-diol (**17**) leading to the fused 5,5-bicyclic acetal **22** proceeded faster than

the cyclization of 3-ethynylhexane-1,6-diol (**18**), which led to the fused 6,5-bicyclic acetal **23**. This is similar to the trend observed for the cyclization of 4-pentyn-1-ol (**7**) versus 5-hexyn-1-ol (**8**), in both the absence and presence of methanol (Table 1 and ref 36).

The catalyzed cyclization of 2-(5-hydroxypent-1-ynyl)benzyl alcohol (**19**) and 2,2′-(1,2-ethynediyl)bisbenzyl alcohol (**20**) led to the formation of the spiroketal products **24** and **25** (from **19**) and **26** (from **20**). The ratio of the spiroketal products, **24** and **25**, formed on the catalyzed cyclization of **19**, varies with the reaction conditions, and higher temperature favored the formation of **24**. The cyclization of 2-(4-hydroxybut-1-ynyl)benzyl alcohol (**21**), using $[Ir(PyP)(CO)_2]BPh_4$ (**1**) as the catalyst at 120 °C, led to the formation of the spiroacetal product **27** only (Table 2, entry 9). The formation of 2-(1*H*-isochromen-3-yl)-ethanol (**28**, Chart 2) as the minor product (in addition to **27**) was observed on using $[Rh(bim)(CO)_2]BPh_4$ (**2**) as the catalyst at 60 °C. An additional side product, **29**, which arose from the dehydration of **28**, was formed on cyclization of **21** at 120 °C using the rhodium catalyst **2**.

The catalyzed cyclization of nonterminal aromatic alkyne diols **19**−**21** proceeded at slower rates than the catalyzed cyclization of terminal alkyne diols, **17** and **18**. The rate of catalyzed cyclization of **20** using the Rh(I) catalyst **2**, which involves two aromatic cyclization steps, is significantly slower than the catalyzed reactions of **19** and **21**, each of which requires only one aromatic cyclization step. This is most likely due to the steric hindrance present in the substrate as well as the lower solubility of **20** in $(CDCl_2)_2$.

Mechanistic Investigation. Alkyne Activation. The transition metal-catalyzed intramolecular addition of O−H bonds to alkynes can proceed initially via the metal center activation of either the alkyne bond or the O−H bond. One mode of activation of the alkyne moiety by a transition metal complex can be via the reaction of a terminal alkyne with the metal center followed by rearrangement to form a vinylidene intermediate. Both iridium and rhodium complexes can promote the formation of vinylidene complexes from terminal alkynes.[42−46] The formation of vinylidene complexes as an initial part of the mechanism was, however, excluded here because the hydroalkoxylation reactions using the rhodium and iridium catalysts **1** and **2** (i) proceed smoothly with *internal* alkynes and (ii) in the case of the intramolecular cyclization yield almost exclusively the *exo*-cyclization products in place of the *endo*-cyclization products expected on reaction with metal vinylidene intermediates.

The alternative mode of activation of the alkyne moiety is via the electrophilic activation of the alkyne.[1,4] In order to investigate the interactions between the alkyne moiety and the metal complex, the reactions of **1** with 1-pentyne and phenylacetylene were followed by low-temperature NMR spectroscopy. The addition of 1-pentyne (ca. 4.0-fold excess) or phenylacetylene (ca. 1.7-fold excess) to a solution of $[Ir(PyP)(CO)_2]BPh_4$ (**1**) or the ^{13}CO-labeled analogue $[Ir(PyP)(^{13}CO)_2]BPh_4$ (**1**-^{13}CO) led to significant change in the chemical shifts in the ^{1}H, ^{31}P, and ^{13}C resonances of the metal complex. The significant changes in chemical shifts in the $^{13}C\{^1H\}$ (carbonyl region) and $^{31}P\{^1H\}$ spectra of **1**-^{13}CO upon the addition of 1-pentyne are illustrated in Figure 1. In a similar fashion, upon the addition of phenylacetylene to a solution of **1**-^{13}CO, the ^{31}P resonance of **1** (202 MHz, CD_2Cl_2, 200 K) moved from 11.1 (d, $^2J_{C-P}$ = 103.0 Hz) ppm to −9.1 (br, s) ppm and the ^{13}C resonances (125 MHz, CD_2Cl_2, 200 K) due to the metal-bound ^{13}CO's shifted from 177.7 (d, $^2J_{P-C}$ = 103.0 Hz) and 170.8 (d, $^2J_{P-C}$ = 13.0 Hz) ppm to 173.6 (d, $^2J_{P-C}$ = 13.8 Hz) and 158.7 (slightly br, s) ppm. No splitting due to *J*-coupling between the two metal-bound ^{13}C-CO's was observed in the spectra of the reactions of **1** with either 1-pentyne or phenylacetylene.

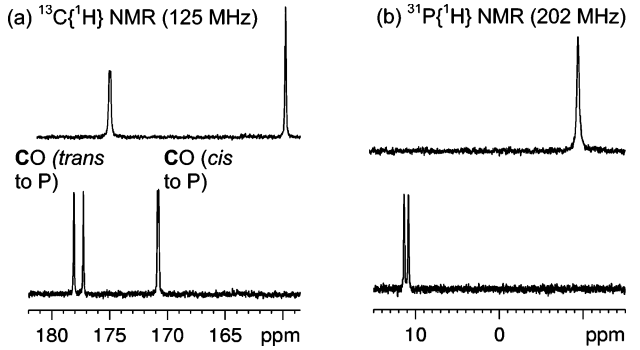


Figure 1. (a) $^{13}C\{^1H\}$ (CO region) and (b) $^{31}P\{^1H\}$ NMR spectra of $[Ir(PyP)(^{13}CO)_2]BPh_4$ (**1**-^{13}CO) in CD_2Cl_2 at 190 K before (bottom) and after (top) the addition of 1-pentyne.

On reaction of an excess of 1-pentyne with $[Ir(PyP)(CO)_2]BPh_4$ (**1**), only one set of averaged resonances for 1-pentyne was observed in each of the ^{1}H (500 MHz) and $^{13}C\{^1H\}$ (125 MHz) NMR spectra over the temperature range 180−310 K. This indicates that in the reaction between **1** and 1-pentyne the exchange between the free 1-pentyne and the metal-bound 1-pentyne is fast on the NMR time scale, even at 180 K. In contrast, on reaction of **1** with an excess of phenylacetylene in both $CDCl_3$ and CD_2Cl_2, two distinct sets of new ^{1}H and ^{13}C resonances were observed. The ^{1}H NMR spectrum in CD_2Cl_2 at 200 K revealed a new resonance at 6.27 ppm with $^3J_{P-H}$ = 17.1 Hz, which was assigned to the Ir-bound PhC≡C*H* following an analogous reaction using PhC≡C*D* (98% D) in place of PhC≡CH. The large shift to the downfield region of the PhC≡C*H* resonance upon interaction with the metal center suggests that the binding of phenylacetylene to **1** is stronger than that of 1-pentyne.

In the $^{13}C\{^1H\}$ (125 MHz, CD_2Cl_2, 200 K) NMR spectrum of the (**1** + PhC≡CH) system, two broad resonances due to the two Ir-bound acetylene carbons were observed at 107.7 ($^2J_{P-C} \approx 32$ Hz) and 75.3 ppm. These chemical shifts were significantly different from those due to the free Ph*C*≡*C*H resonances (83.1 and 77.3 ppm), and a long-range ^{1}H−^{13}C NMR correlation experiment of the system at 200 K showed the expected correlation signal between the resonance due to the Ir-bound PhC≡C*H* at 6.27 ppm and the resonance due to bound Ph*C*CH at 107.7 ppm. More importantly, a strong correlation signal was observed between the resonance due to Ir-bound PhC≡C*H* and one of the two resonances due to ^{13}C-labeled CO (at δ 173.3 ppm). This unequivocally confirmed the strong binding of phenylacetylene to the iridium center of $[Ir(PyP)(^{13}CO)_2]BPh_4$ (**1**-^{13}CO). The binding of 1-pentyne and phenylacetylene to the iridium center of $[Ir(PyP)(CO)_2]BPh_4$ (**1**) or **1**-^{13}CO was additionally confirmed by the observation of NOE signals between resonances due to both 1-pentyne and phenylacetylene protons and protons of **1** in the ^{1}H−^{1}H NOESY spectra. The ^{1}H−^{1}H NOESY spectra (500 MHz, 250 K) for the reactions between $[Ir(PyP)(^{13}CO)_2]BPh_4$ (**1**-^{13}CO) and

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(42) Chin, C. S.; Won, G.; Chong, D. S.; Kim, M.; Lee, H. *Acc. Chem. Res.* **2002**, *35*, 218−225.
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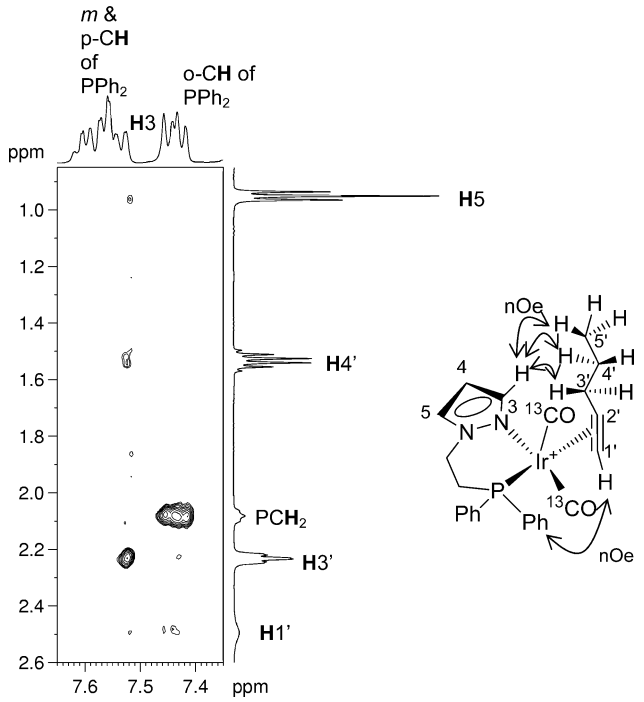


Figure 2. Section of the $^1H-^1H$ NOESY (500 MHz, CD_2Cl_2) spectrum at 250 K of the [Ir(PyP)($^{13}CO)_2$]BPh_4 (**1**) + 1-pentyne reaction.

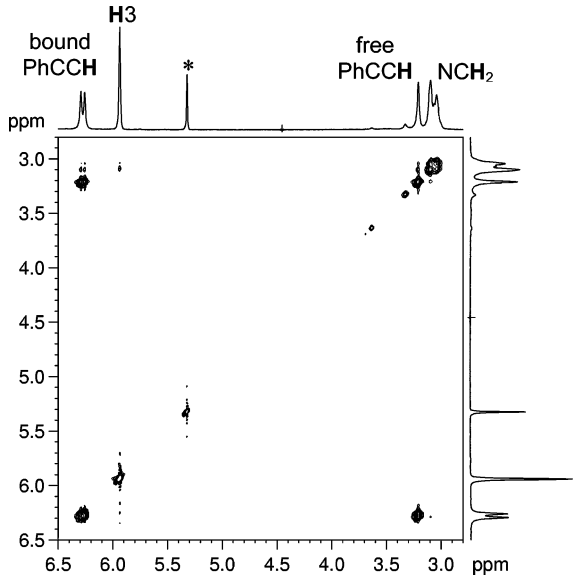


Figure 3. Part of the $^1H-^1H$ NOESY (500 MHz, CD_2Cl_2, 200 K) spectrum of the ([Ir(PyP)($^{13}CO)_2$]BPh_4 (**1′**) + PhC≡CH) system showing the exchange cross-peaks between Ir-bound PhC≡C*H* and free PhC≡C*H* resonances (* denotes the residual solvent resonance).

1-pentyne and between **1**-^{13}CO and phenylacetylene showed that the pentyne and phenylacetylene, respectively, are bound to the metal complex in a conformationally specific manner (Figure 2, **1**-^{13}CO and 1-pentyne reaction). In addition, in the case of the reaction of [Ir(PyP)($^{13}CO)_2$]BPh_4 (**1**-^{13}CO) and phenylacetylene, exchange cross-peaks between resonances of metal bound PhC≡C*H* and free PhC≡C*H* were also observed (Figure 3), confirming the exchange between free and bound phenylacetylene.

The $^{13}C\{^1H\}$ spectra of the reaction of 1-pentyne with [Ir(PyP)($^{13}CO)_2$]BPh_4 (**1**-^{13}CO) in CD_2Cl_2 showed that as the temperature increased, the ^{13}C resonances of the two ^{13}C-labeled metal-bound carbonyl ligands shifted downfield. The $^2J_{P-C}$ coupling constant of one of the two carbonyl ^{13}C resonances also increased significantly with the increase in temperature. This suggests that the conformation of the ([Ir(PyP)($CO)_2$]BPh_4 + 1-pentyne) five-coordinate transient species changes with temperature such that the one CO group moves from a *cis* orientation relative to the phosphorus atom of the metal-bound ligand to a more *trans* orientation at higher temperatures. Similar trends were also observed in the $^{13}C\{^1H\}$ NMR spectra of the ^{13}C-labeled carbonyls in the reaction of **1**-^{13}CO with phenylacetylene.

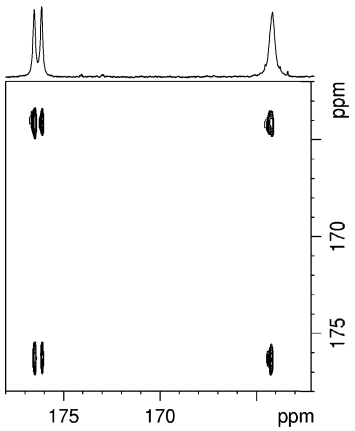


Figure 4. $^{13}C-^{13}C$ NOESY (CD_2Cl_2, 250 K) spectrum of the ([Ir(PyP)($^{13}CO)_2$]BPh_4 (**1**-^{13}CO) + 1-pentyne) system, showing the exchange of the two resonances due to ^{13}CO.

The coordination of 1-pentyne or phenylacetylene to the metal center of [Ir(PyP)($CO)_2$]BPh_4 (**1**) led to the formation of corresponding five-coordinate iridium(I) complexes (**1** + 1-pentyne) and (**1** + PhCCH). The ligands around the metal center in these five-coordinate complexes are expected to exchange with each other via Berry pseudorotation processes. A $^{13}C-^{13}C$ NOESY (125 MHz, CD_2Cl_2) experiment at 250 K for the 1-pentyne + **1**-^{13}CO reaction confirmed there was site exchange between the two metal-bound ^{13}CO molecules (Figure 4). In a similar fashion, on the reaction of **1**-^{13}CO with phenylacetylene, exchange cross-peaks were observed between the resonances due to the two Ir-bound ^{13}CO groups at 240 K. On reducing the temperature to 200 K, however, no exchange signals were present in the NOESY spectrum. These results indicate that the conformational exchange of the five-coordinate complex **1**-^{13}CO + PhC≡CH had been slowed to a rate less than 4135 Hz at 200 K.[47]

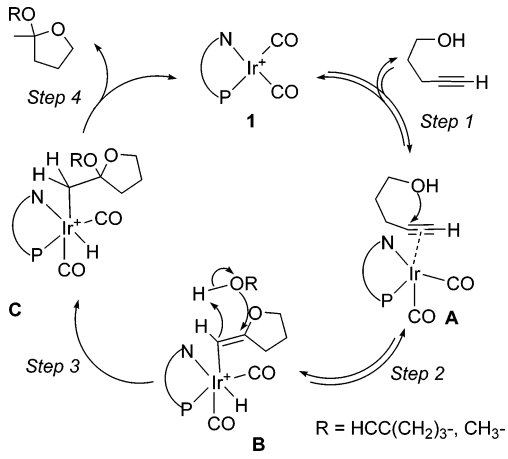
Initial O−H Bond Activation. In considering the alternate cyclization route via initial activation of the O−H bond of the alkynol, the reactions of [Ir(PyP)($CO)_2$]BPh_4 (**1**) with *n*-propyl alcohol and methanol were followed by low-temperature NMR spectroscopy, and no reaction was observed on addition of either *n*-propyl alcohol or methanol to a dichloromethane-d_2 solution of **1**. The fact that there is clear initial activation of the alkyne moiety, coupled with the lack of evidence for activation of the O−H bond of the alcohol substrates, suggests that the catalytic hydroalkoxylation reaction promoted by the iridium catalyst **1** does not proceed via the initial activation of the O−H bond of the alcohol substrate.

Proposed Mechanism of Hydroalkoxylation. A proposed mechanism for the catalyzed hydroalkoxylation of alkynes to form cyclic or bicyclic acetals is shown in Scheme 2.

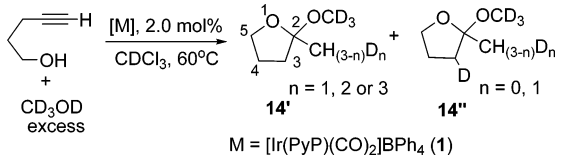
Assuming that the π-bound species observed by NMR is the reactive species and not a stable byproduct, the first step of the

(47) Calculated using the formula: Rate = $\pi\Delta\nu(2^{1/2})$.

Scheme 2. Proposed Mechanism for the [Ir(PyP)(CO)$_2$]BPh$_4$ (1)-Catalyzed Cyclization of 4-Pentyn-1-ol (7)



Scheme 3

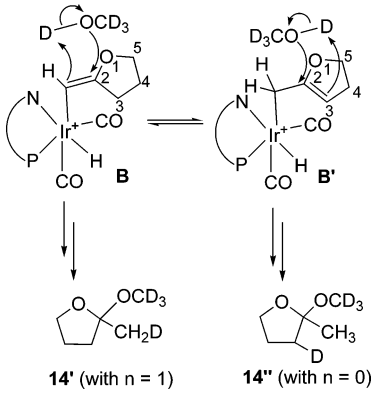


mechanism involving the binding of alkynes to the iridium complex [Ir(PyP)(CO)$_2$]BPh$_4$ (**1**) has been established (intermediate **A**, Scheme 2). Through the initial π coordination, the alkyne (intermediate **A**) is activated toward nucleophilic attack[48] by the oxygen nucleophile of the alcohol, and upon rearrangement leads to the formation of the intermediate vinyl complex **B**. Intermolecular addition of another hydroxy group of R−OH to the vinyl carbon adjacent to oxygen forms the intermediate **C**, which reductively eliminates to give the acetal product and regenerates the catalyst **1**. Alternatively, the addition of alcohol may occur via a two-step process where there is reductive elimination of the vinyl substituent from intermediate **B**, forming a π complex of the vinyl ether, and attack of the second alcohol at this π-bound intermediate.

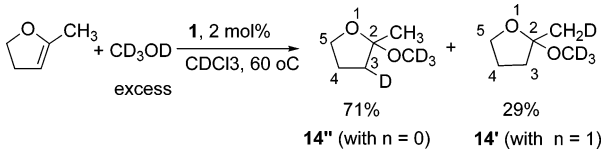
Deuteration Studies. Cyclization of 4-Pentyn-1-ol (7) with [Ir(PyP)(CO)$_2$]BPh$_4$ (1) in the Presence of Excess CD$_3$OD. The cyclization of 4-pentyn-1-ol (**7**) in the presence of excess methanol, using [Ir(PyP)(CO)$_2$]BPh$_4$ (**1**) as the catalyst, leads to the formation of the cyclic acetal 2-methoxy-2-methyl-3,4,5-trihydrofuran (**14**) in quantitative conversion after 22 h ($CDCl_3$, 60 °C, 2.0 mol % **1**).[36] In order to investigate the mechanism more fully, this reaction was performed using deuterated methanol, CD$_3$OD (Scheme 3).

The incorporation of deuterium into the products was determined using the ^{1}H, ^{2}H, and ^{13}C NMR spectra. The main product observed was **14′** ($n = 1$). The formation of **14′** ($n = 1$) was expected from the addition of CD$_3$OD instead of ROH to intermediate **B** of the proposed catalytic cycle (Scheme 2). The presence of small quantities of **14′** with $n = 2$ or 3 in the final product mixture is likely to be due to the exchange of the terminal acetylenic proton and the hydroxy proton of 4-pentyn-1-ol (**7**) with the deuterium atom in CD$_3$O*D*, prior to the cyclization process. The observation of the acetals **14″** ($n = 0$ or 1), where deuterium was incorporated into the C3 position of the tetrahydrofuran ring, suggests that alkene isomerization of the intermediate **B** to form the intermediate **B′** occurs prior to the addition of CD$_3$OD (Scheme 4).

Scheme 4



Scheme 5



Investigation of Reaction Intermediates: The Catalyzed Addition of Methanol to 2-Methyl-4,5-dihydrofuran. To further explore the presence of the proposed reaction intermediate **B** (step 2, Scheme 2), the reaction between methanol and 2-methyl-4,5-dihydrofuran was investigated using [Ir(PyP)(CO)$_2$]-BPh$_4$ (**1**) as the catalyst. Methanol was added to 2-methyl-4,5-dihydrofuran to form 2-methoxy-3,4,5-tetrahydrofuran (**14**) with quantitative conversion in less than 4 h. The distribution of deuterium in the final products on reacting 2-methyl-4,5-dihydrofuran with an approximately 5-fold excess of CD$_3$OD was determined by ^{1}H, ^{2}H, and ^{13}C{^{1}H} NMR. The distribution of deuterium in the final product **14** was approximately 71% at the C3 position of the furan ring and 29% at the methyl group (Scheme 5). This result supports the presence of intermediates **B** and **B′** (Scheme 4). However, the alternative possibility of attack of the second alcohol at a π-bound vinyl ether intermediate cannot be ruled out, as a vinyl ether complex would allow H/D transfer between the CH$_3$ and C3 positions and migration of the double bond via an allylic intermediate. The facile addition of methanol (or CD$_3$OD) to 3-methyl-4,5-dihydrofuran may imply either the presence of intermediate **B′** or a Lewis acid-catalyzed process, where Ir(I) or Rh(I) act as Lewis acids.[49−51] In the Lewis acid-catalyzed process, the replacement of methanol by CD$_3$OD would not see the incorporation of deuterium to the external methyl group, so this is not likely to be the route followed here. In summary, the deuteration experiments support the presence of proposed intermediates **B** and **B′** (Scheme 4).

The cyclization of 4-pentyn-1-ol (**7**) in the presence of excess methanol to form **14** took approximately 22 h to complete,[36] whereas the catalyzed addition of methanol to 2-methyl-4,5-

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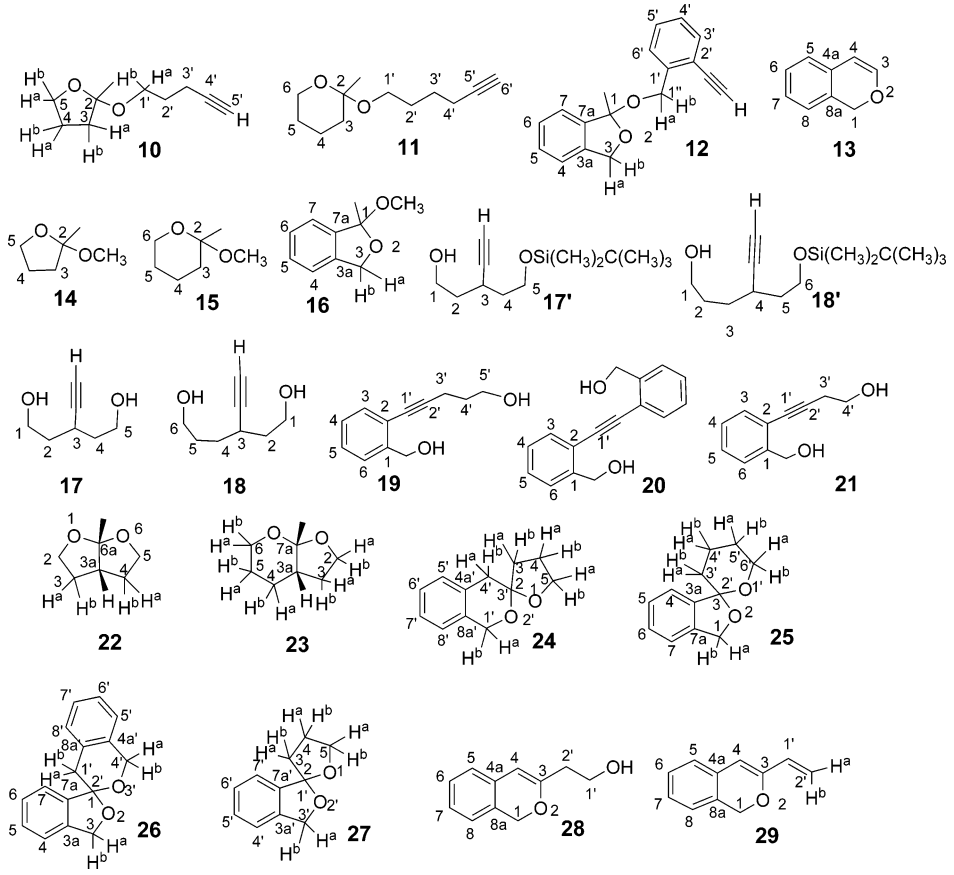
(51) Nishiyama, H.; Motoyama, Y. Other transition metal reagents: chiral transition-metal Lewis acid catalyis for asymmetric organic synthesis. In *Lewis Acid Reagents*, 1st ed.; Yamamoto, H., Ed.; Oxford University Press: Oxford, 1999; pp 225−243.

Chart 2. Structures and Numbering Schemes for Compounds 11−29



trihydrofuran took only 4 h. This suggests that in the proposed mechanism for the double hydroalkoxylation of alkynes (Scheme 2) the primary addition of alcohol to coordinated alkyne (step 1, **A**) is likely to be the rate-determining step.

Conclusions

The efficient catalyzed formation of bicyclic *O,O*-acetals by double hydroalkoxylation of alkyne diols using rhodium and iridium complexes has been demonstrated. The iridium complex $[Ir(PyP)(CO)_2]BPh_4$ (**1**) is more effective than the rhodium complex $[Rh(bim)(CO)_2]BPh_4$ (**2**) in promoting the cyclization of aliphatic substrates. In contrast, the rhodium complex **2** is significantly more effective than **1** in catalyzing the hydroalkoxylation of aromatic substrates. The reactions with terminal alkynol or alkyndiol substrates proceeded faster than the reactions with non-terminal alkyne substrates. This is possibly due to the larger steric hindrance in the nonterminal alkyne substrates.

A catalytic cycle for the double hydroalkoxylation of alkynes to form *O,O*-acetals has been proposed, with initial electrophilic activation of the alkyne through π bonding. This was supported by observation of the binding of both 1-pentyne and phenylacetylene to the iridium complex $[Ir(PyP)(CO)_2]BPh_4$ (**1**), using low-temperature NMR spectroscopy. Additionally, no interaction between *n*-propyl alcohol and **1** was observed, suggesting that the activation of the O−H group was not the first step of the reaction. The presence of several of the proposed intermediates in this catalytic cycle was strongly supported by the introduction of the reaction intermediates as well as deuteration studies. The first addition of alcohol to the alkyne is likely to be the rate-determining step.

Experimental Section

General Considerations. Manipulations of air-sensitive compounds were carried out using standard Schlenk line techniques or within a nitrogen- or argon-filled glovebox. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under an atmosphere of nitrogen or argon and stored in a storage ampule with a Youngs valve. Chloroform-*d* (used in catalytic reactions) was freshly distilled from calcium hydride; 1,1,2,2-tetrachloroethane-d_2 was purchased from Cambridge Stable Isotopes and was opened and used in a nitrogen/argon-filled glovebox. 2-Bromoethanol was distilled under nitrogen prior to use. $[Pd(PPh_3)_4]$ was synthesized by Ms. Danielle Kennedy using a literature procedure.[52] Acetylene (>99.5%) was obtained from British Oxygen Company (BOC). All other reagents were purchased from Aldrich Chemicals Inc. or Lancaster Inc. and were used as received. Column chromatography was performed using silica gel (mesh 200−325). ^1H and ^{13}C NMR spectra were acquired on a Bruker DPX 300, DMX 500, or DMX 600 and were referenced internally using residual protonated solvent resonances or solvent ^{13}C resonances. Low-resolution mass spectra were recorded on a Finnigan Polaris Q mass spectrometer. High-resolution mass spectra were recorded on a Finnigan MAT 900 XL mass spectrometer.

The metal complexes $[Ir(PyP)(CO)_2]BPh_4$ (**1**),[35] $[Ir(PyP)(COD)]BPh_4$ (**3**),[35] $[Ir(PyP)(CO)Cl]$ (**4**),[35] $[Ir(bpm)(CO)_2]BPh_4$ (**5**),[53] $[Ir(bim)(CO)_2]BPh_4$ (**6**),[54] and $[Rh(bim)(CO)_2]BPh_4$ (**2**)[55] and the

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alkynol 2-ethynylbenzyl alcohol (**9**)[56] were synthesized according to published procedures.

Syntheses of the organic starting materials were undertaken following established procedures and are reported in the Supporting Information.

General NMR-Scale Catalytic Procedure. In a typical experiment, the catalyst (8−10 mg, 9−12 μmol, 2−5 mol %) and the substrate (43−50 mg), if a solid, were weighed into an NMR tube with a Youngs valve, and the solvent (~0.7−0.8 mL) was either transferred into the NMR tube on a high-vacuum line (chloroform-*d*) or added in a drybox (1,1,2,2-tetrachloroethane-d_2). Liquid substrates (35−50 mg) were added using a microsyringe (substrates were stored in air). The catalytic reaction was performed at elevated temperature by heating in an oil bath or heating in the NMR instrument. The temperature within the magnet was calibrated using ethylene glycol or using an Omega microprocessor thermometer (Model HH23). The conversion of starting material to product was determined by integration of the product resonances relative to the substrate resonances in the ^{1}H NMR spectrum. Complete conversion was taken to be the time where no remaining substrate resonances were evident.

In the cases of catalyzed reactions in the presence of an excess of methanol, methanol was added to a solution of the catalyst before the addition of substrate.

General Procedure for the Isolation of Product from NMR-Scale reactions in $CDCl_3$. On completion of the reaction, as determined by ^{1}H NMR, the reaction was cooled to room temperature and the content of the tube was poured into a small beaker/conical flask, rinsed with diethyl ether (~1 mL), and diluted with *n*-pentane (~6−8 mL). The resulting solution was passed through a pad of silica, and the solvent was removed *in vacuo* to yield the product (greater than 95% purity as determined by ^{1}H NMR).

Structures and atom number schemes of compounds **10**−**29** are provided in Chart 2 in order to assist with the NMR assignments.

Characterization Data for Products of the Catalyzed Cyclization of Alkynols. 2-Methyl-2-(4-pentynyloxy)-3,4,5-tetrahydrofuran (10).[27,57] ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.88−3.84 (m, 2H, *H*5^a and *H*5^b), 3.57−3.53 (m, 1H, *H*4′^{a}/*H*4′^{b}), 3.50−3.46 (m, 1H, *H*4′^{b}/*H*4′^{a}), 2.25 (td, $^3J_{H2'-H3'}$ = 7.2 Hz, $^4J_{H5'-H3'}$ = 2.4 Hz, 2H, *H*3′), 2.06−1.98 (m, 2H, *H*3^a and *H*4^a), 1.90 (t, $^4J_{H3'-H5'}$ = 2.4 Hz, 1H, *H*5′), 1.86 (m, 1H, *H*3^b), 1.69 (m, 1H, *H*4^b), 1.72 (apparent pentet, ^3J = 7.2 Hz, 2H, *H*2′), 1.43 (s, 3H, CH_3) ppm. GC-MS (EI), *m*/*z* (%): 160 (24) [M$^+$], 154 (43) [M$^+$ − CH_3], 83 (100) [M$^+$ − O$(CH_2)_3$CCH].

2-(5-Hexynyloxy)-2-methyltetrahydro-2*H*-pyran (11). ^{1}H NMR ($CDCl_3$, 500 MHz, 60 °C): δ 3.64−3.55 (m, 2H, *H*6), 3.43−3.98 (m, 2H, *H*1′), 2.21 (td, $^3J_{H3'-H4'}$ = 7.2 Hz, $^4J_{H6',H4'}$ = 2.5 Hz, 2H, *H*4′), 1.93 (t, $^4J_{H4'-H6'}$ = 2.5 Hz, 1H, *H*6′), 1.72−1.42 (m, 10H, *H*3, *H*4, *H*5, *H*2′, and *H*3′), 1.26 (s, 3H, CH_3) ppm. GC-MS (EI), *m*/*z* (%): 196(13) [M$^+$], 182(27) [M$^+$ − CH_3], 93(100) [M$^+$ − O$(CH_2)_4$CCH].

1-(2-Ethynylbenzyloxy)-1,3-dihydro-1-methylisobenzofuran (12). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51−7.18 (m, 8H, Ar*H*), 5.23 (d, $^2J_{H3b-H3a}$ = 12.8 Hz, 1H, *H*3^a), 5.13 (d, $^2J_{H3a-H3b}$ = 12.8 Hz, 1H, *H*3^b), 4.61 (d, $^2J_{H1''b-H1''a}$ = 12.8 Hz, 1H, *H*1″^{a}), 4.25 (d, $^2J_{H1''a-H1''b}$ = 12.5 Hz, 1H, *H*1″^{b}), 3.15 (s, 1H, C≡C*H*), 1.85 (s, 3H, CH_3) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 143.8, 141.6, 140.2, 139.9, 132.9, 129.44, 129.36, 128.8, 128.7, 128.3, 128.2, 127.7 (ArCs), 112.0 (*C*1), 82.4 (*C*≡CH), 81.6 (C≡*C*H), 72.6 (*C*3), 63.1 (*C*1″), 26.8 (*C*H_3) ppm.

1*H*-Isochromene (13).[58,59] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49−7.02 (m, 4H, Ar*H*s), 6.61 (d, $^3J_{H4-H3}$ = 5.7 Hz, 1H, *H*3), 5.85 (d, $^3J_{H3-H4}$ = 5.7 Hz, 1H, *H*4), 5.11 (s, 2H, *H*1) ppm.

Characterization Data for Products of the Catalyzed Cyclization of Alkynols in the Presence of an Excess of Methanol. 2-Methoxy-2-methyl-3,4,5-trihydrofuran (14).[27] The compound was isolated as a volatile colorless oil using the general isolation procedure as described above. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (m, 2H, *H*5), 3.11 (s, 3H, OCH_3), 1.99−1.58 (m, 4H, *H*3 and *H*4), 1.33 (s, 3H, CH_3) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 107.3 (*C*2), 67.2 (*C*5), 48.2 (O*C*H_3), 37.5 (*C*3), 24.2 (*C*4), 20.9 (*C*H_3) ppm.

2-Methoxy-2-methyltetrahydro-2*H*-pyran (15).[60] Compound **15** was isolated as a colorless oil using the method described above. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.60 (m, 2H, *H*6), 3.20 (s, 3H; OCH_3), 1.78−1.68 (m, 3H, *H*3, *H*4, and *H*5), 1.56−1.46 (m, 3H, *H*3, *H*4, and *H*5), 1.25 (s, 3H, C_2CH_3) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 97.6 (*C*2), 61.4 (*C*6), 47.8 (O*C*H_3), 35.8 (*C*3), 25.1 (*C*5), 24.0 ($C2CH_3$), 18.9 (*C*4) ppm.

1,3-Dihydro-1-methoxy-1-methylisobenzofuran (16).[61] Compound **16** was isolated as a colorless oil using the method described above. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46 (apparent t, $^3J_{H4-H5,\ H6-H5}$ = 7.5 Hz, 1H, *H*5), 7.44 (apparent t, $^3J_{H5-H6}$ = 7.5 Hz, $^3J_{H7-H6}$ = 6.7 Hz, 1H, *H*6), 7.38 (d, $^3J_{H6-H7}$ = 6.7 Hz, 1H, *H*7), 7.34 (d, $^3J_{H5-H4}$ = 7.5 Hz, 1H, *H*4), 5.23 (d, $^2J_{H3a-H3b}$ = 12.7 Hz, 1H, *H*3^a), 5.12 (d, $^2J_{H3a-H3b}$ = 12.7 Hz, 1H, *H*3^b), 3.08 (s, 3H, OCH_3), 1.80 (s, 3H, CH_3) ppm. ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 140.1 (*C*7a), 139.1 (*C*3a), 129.6 (*C*5), 128.5 (*C*6), 122.2 (*C*7), 121.5 (*C*4), 72.8 (*C*3), 50.4 (O*C*H_3), 26.5 (*C*H_3) ppm.

Characterization Data of Products from the Catalyzed Cyclization of Alkyne Diols. *cis*-Hexahydro-6a-methyl-2*H*-furo[2,3-*b*]furan (22). Compound **22** was isolated as a colorless oil using the method described above. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.90 (m, 4H, *H*2 and *H*5), 2.51 (m, 1H, *H*3a), 2.16 (m, 2H, *H*3^a and *H*4^a), 1.73 (m, 2H, *H*3^b and *H*4^b), 1.51 (s, 3H, CH_3) ppm. ^{13}C-{^{1}H} NMR (75 MHz, $CDCl_3$): δ 116.5 (*C*6a), 67.8 (*C*2 and *C*5), 46.1 (*C*3a), 33.0 (*C*3 and *C*4), 24.0 (*C*H_3) ppm. MS (CI), *m*/*z* (%): 129.0 (100) [M$^+$ + H], 111.4 (34). HRMS: found 128.0839; $C_7H_{12}O_2$ requires 128.0837.

***cis*-Hexahydro-7a-methyl-2*H*-furo[2,3-*b*]pyran (23).** Compound **23** was isolated as a colorless oil using the method described above. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.06 (m, 1H, *H*2^a), 3.88 (m, 1H, *H*2^b), 3.82 (m, 1H, *H*6^a), 3.55 (m, 1H, *H*6^b), 2.04−1.91 (m, 3H, *H*3a, *H*3^a, and *H*3^b), 1.79 (m, 1H, *H*4^a), 1.76−1.68 (m, 2H, *H*5^a and *H*4^a), 1.41 (s, 3H, CH_3), 1.36 (m, 1H, *H*5^b) ppm. ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 105.0 (*C*7a), 66.1 (*C*2), 63.7 (*C*6), 40.7 (*C*3a), 28.3 (*C*3), 23.7 (*C*4), 21.4 (*C*H_3), 20.7 (*C*5) ppm. MS (CI), *m*/z (%): 143.0 (100) [M$^+$ + H], 127.2 (32), 125.3 (26), 97.4 (27). HRMS: found 142.0992; $C_8H_{14}O_2$ requires 142.0994.

2,3,4,5-Tetrahydrospiro[furan-2,3′-isochroman] (24).[37,62] Compounds **24** and 3′,4′,5′,6′-tetrahydrospiro[isobenzofuran-1(3H),2′═[2*H*]pyran] (**25**) were isolated together upon the completion of the cyclizaton of 2-(5-hydroxypent-1-ynyl)benzyl alcohol (**19**) using the general procedure described above. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17−7.15 (m, 2H, *H*6′ and *H*7′), 7.10 (m, 1H, *H*5′), 7.01 (m, 1H, *H*8′), 4.93 (d, $^2J_{H1'b-H1'a}$ = 15.0 Hz, 1H, *H*1′^{a}), 4.09 (d, $^2J_{H1'a-H1'b}$ = 15.0 Hz, 1H, *H*1′^{b}), 4.01 (apparent t, ^3J = 7.3 Hz, 2H, *H*5^a and *H*5^b), 3.23 (d, $^2J_{H4'b-H4'a}$ = 16.4 Hz, 1H, *H*4′^{a}), 2.83

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(d, $^2J_{H4'a-H4'b}$ = 16.4 Hz, 1H, *H*4′^{b}), 2.17 (m, 1H, *H*4^a), 2.13 (m, 1H, *H*3^a), 1.97 (m, 1H, *H*4^b), 1.88 (m, 1H, *H*3^b) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 133.7 (*C*8a′), 131.9 (*C*4a′), 128.8 (*C*5′), 126.5 (*C*7′), 126.1 (*C*6′), 124.0 (*C*8′), 105.6 (*C*2 (also *C*3′)), 68.0 (*C*5), 62.6 (*C*1′), 37.2 (*C*3), 36.1 (*C*4′), 23.8 (*C*4) ppm. GC-MS (CI), *m*/*z* (%): 191 (84) [M$^+$ + H], 173 (100), 161 (86).

3′,4′,5′,6′-Tetrahydrospiro[isobenzofuran-1(3*H*),2′(2*H*)-pyran] (25).[37,63] Compound **25** was isolated together with compound **24**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36−7.32 (m, 3H, Ar*H*s), 7.26 (m, 1H, *H*7), 5.18 (d, $^2J_{H1b-H1a}$ = 12.7 Hz, 1H, *H*1^a), 5.01 (d, $^2J_{H1a-H1b}$= 12.7 Hz, 1H, *H*1^b), 4.09 (m, 1H, *H*6′^{a}), 3.81 (m, 1H, *H*6′^{b}), 2.15 (m, 1H, *H*3′^{a}), 2.02 (m, 1H, *H*4′^{a}), 1.87 (m, 1H, *H*3′^{b}), 1.84 (m, 1H, *H*4′^{b}), 1.79 (m, 1H, *H*5′^{a}), 1.63 (m, 1H, *H*5′^{b}) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 141.7 (*C*3a), 134.0 (*C*7a), 129.0 (*C*5/*C*6), 127.6 (*C*6/*C*5), 121.8 (*C*4), 121.3 (*C*7), 108.1 (*C*3 (also *C*2′)), 71.1 (*C*1), 63.4 (*C*6′), 33.9 (*C*3′), 25.3 (*C*5′), 19.7 (*C*4′) ppm. GC-MS (CI), *m*/*z* (%): 191 (100) [M$^+$ + H], 173 (47).

Spiro[isobenzofuran-1(3*H*),2′-isochroman] (26).[62,64] Column chromatography was used to isolate spiro[isobenzofuran-1(3*H*),2′-isochroman] (**26**) from the double cyclization of 2,2′-(1,2-ethynediyl)-bisbenzyl alcohol (**20**) upon completion of the catalyzed cyclization of **20**. Pale yellow solid. R_f = 0.56 (EtOAc/light petroleum, 8:2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 (apparent t, ^3J = 7.2 Hz, ^3J = 7.5 Hz, 1H, Ar*H*), 7.36 (apparent t, ^3J = 7.5 Hz, ^3J = 7.0 Hz, 1H, Ar*H*), 7.33−7.31 (m, 2H, Ar*H*), 7.25−7.23 (m, 2H, Ar*H*), 7.20−7.18 (m, 1H, Ar*H*), 7.11−7.09 (m, 1H, Ar*H*), 5.26 (d, ^2J = 12.5 Hz, 1H, *H*3^a/*H*4′^{a}), 5.17 (d, ^2J = 14.7 Hz, 1H, *H*4′^{a}/*H*3^a), 5.08 (d, ^2J = 12.5 Hz, 1H, *H*3^b/*H*4′^{b}), 4.88 (d, ^2J = 14.7 Hz, 1H, *H*4′^{b}/*H*3^b), 3.59 (d, $^2J_{H1'b-H1'a}$ = 16.2 Hz, 1H, *H*1′^{a}), 3.09 (d, $^2J_{H1'a-H1'b}$ = 16.2 Hz, 1H, *H*1′^{b}) ppm. ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 140.6 (*ipso*-*C*), 140.2 (*ipso*-*C*), 133.8 (*ipso*-*C*), 131.6 (*ipso*-*C*), 129.3, 129.0, 127.9, 126.9, 126.4, 124.13, 124.05, 121.4, 107.6 (*C*1 (also *C*2′)), 71.7 (*C*3/*C*4′), 64.5 (*C*4′/*C*3), 36.7 (*C*1′) ppm. MS (CI), *m*/*z* (%): 238.9 (100) [M$^+$ + H].

2,3,4,5-Tetrahydrospiro[furan-2,1′-isobenzofuran] (27).[37,62,63] The compound was isolated as a pale yellow oil using the method described above. ^{1}H NMR (500 MHz, $(CDCl_2)_2$): δ 7.39 (m, 1H, *H*6′), 7.36 (m, 1H, *H*5′), 7.34 (m, 1H, *H*7′), 7.27 (m, 1H, *H*4′), 5.15 (d, $^2J_{H3'b-H'a}$ = 12.7 Hz, 2H, *H*3′^{a}), 4.96 (d, $^2J_{H3'a-H'b}$ = 12.7 Hz, 1H, *H*3′^{b}), 4.14 (m, 1H, *H*5′^{a}), 4.04 (m, 1H, *H*5′^{b}), 2.32 (m, 2H, *H*3^a and *H*3^b), 2.27 (m, 1H, *H*4^a), 2.15 (m, 1H, *H*4^b) ppm. ^{13}C NMR (125 MHz, $(CDCl_2)_2$): δ 140.0 (*C*3a′), 139.0 (*C*7a′), 128.3 (*C*6′), 127.6 (*C*5′), 121.9 (*C*7′), 121.0 (*C*4′), 116.8 (*C*2 (also *C*1′)), 70.7 (*C*3′), 68.5 (*C*5), 37.0 (*C*3), 25.2 (*C*4) ppm. GC-MS (CI), *m*/*z* (%): 177 (100) [M$^+$ + H], 159 (33).

NMR Data of 27 in $CDCl_3$. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36−7.31 (m, 3H, Ar*H*), 7.24 (m, 1H, *H*4′), 5.16 (d, $^2J_{H3'a-H'b}$ = 12.9 Hz, 1H, *H*3′^{a}), 4.95 (d, $^2J_{H3'b-H'a}$ = 12.9 Hz, 1H, *H*3′^{b}), 4.14 (m, 1H, *H*5^a), 4.05 (m, 1H, *H*5^b), 2.30 (m, 2H, *H*3^a and *H*3^b), 2.28 (m, 1H, *H*4^a), 2.14 (m, 1H, *H*4^b) ppm. ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 140.3 (*C*3a′), 139.2 (*C*7a′), 129.0 (*C*6′), 127.8 (*C*5′), 122.1 (*C*7′), 121.1 (*C*4′), 117.1 (*C*2 (also *C*1′), 70.9 (*C*3′), 68.6 (*C*5), 37.2 (*C*3), 25.3 (*C*4) ppm.

2-(1*H*-Isochromen-3-yl)ethanol (28).[62] Compound **28** was formed as a minor product in the catalyzed cyclization of 2-(4-hydroxybut-1-ynyl)benzyl alcohol (**21**) at 60 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 60 °C): δ 7.17 (apparent t, $^3J_{H5-H6}$ = $^3J_{H7-H6}$ = 6.8 Hz, 1H, *H*6), 7.10 (apparent t, $^3J_{H6-H7}$ = $^3J_{H8-H7}$ = 7.2 Hz, 1H, *H*7), 6.97 (d, $^3J_{H7-H8}$ = 7.2 Hz, 1H, *H*8), 6.92 (d, $^3J_{H4-H3}$ = 6.8 Hz, 1H, *H*5), 5.72 (s, 1H, *H*4), 5.08 (s, 2H, *H*1), 3.82 (t, $^3J_{H1'-H2'}$ = 6.1 Hz, 2H, *H*2′), 2.47 (t, $^3J_{H2'-H1'}$ = 6.1 Hz, 2H, *H*1′), 2.00 (br, 1H, O*H*) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 60 °C): δ 155.2 (*C*3), 131.8 (*C*4a), 127.9 (*C*6), 126.9 (*C*8a), 125.9 (*C*7), 123.7 (*C*8), 122.2 (*C*5), 102.4 (*C*4), 68.7 (*C*1), 60.1 (*C*2′), 36.1 (*C*1′) ppm. GC-MS (CI), *m*/*z* (%): 159 (100) [M$^+$ − OH], 131 (25) [M$^+$ − C_2H_5O].

3-Vinyl-1*H*-isochromene (29). Compound **29**, formed upon the dehydration of **28**, catalyzed the cyclization of 2-(4-hydroxybut-1-ynyl)benzyl alcohol (**21**) at 120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45−7.03 (m, 4H, Ar*H*), 6.27 (dd, $^3J_{H2'a-H1'}$ = 10.9 Hz, $^3J_{H2'b-H1'}$ = 17.3 Hz, 1H, *H*1′), 5.90 (s, 1H, *H*4), 5.75 (dd, $^3J_{H1'-H2'b}$ = 17.3 Hz, $^2J_{H2'a-H2'b}$ = 1.5 Hz, 1H, *H*2′^{b}), 5.26 (dd, $^3J_{H1'-H2'a}$ = 10.9 Hz, $^2J_{H2'b-H2'a}$ = 1.5 Hz, 1H, *H*2′^{a}), 5.13 (s, 2H, *H*1) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 152.8 (*C*3), 131.4 (*C*4a/*C*8a), 128.298 (*C*8a/*C*4a), 128.295, 128.1, 127.6, 123.5 (Ar*C*s), 131.0 (*C*1′), 105.9 (*C*4), 115.4 (*C*2′), 68.3 (*C*1) ppm. GC-MS (CI), *m*/*z* (%): 159 (100) [M$^+$ + H], 131 (29) [M$^+$ − C_2H_3].

NMR Data for ([Ir(PyP)(CO)$_2$]BPh$_4$ + Alkyne) Intermediates in the Mechanistic Investigation. NMR Data for the Averaged Resonances of [Ir(PyP)(^{13}CO)$_2$]BPh$_4$ (1-^{13}CO) in the ([Ir(PyP)-(^{13}CO)$_2$]BPh$_4$ + 1-Pentyne) Reaction. ^{1}H NMR (500 MHz, CD_2Cl_2, 250 K): δ 7.62−7.53 (m, 6H, *m*- and *p*-C*H* of PPh_2), 7.53 (d, $^3J_{H4-H3}$ = 1.6 Hz, 1H, *H*3), 7.46−7.42 (m, 4H, *o*-C*H* of PPh_2), 7.32 (br s, 8H, *o*-C*H* of BPh_4), 6.94 (t, ^3J = 7.5 Hz, 8H, *m*-C*H* of BPh_4), 6.82 (t, ^3J = 7.5 Hz, 4H, *p*-C*H* of BPh_4), 6.75 (d, $^3J_{H4-H5}$ = 1.7 Hz, 1H, *H*5), 6.20 (apparent t, $^3J_{H3-H4,H5-H4}$ = 1.6 Hz, 1H, *H*4), 3.27 (m, 2H, NCH_2), 2.23 (m, 2H, PCH_2) ppm. ^{31}P{^{1}H} NMR (202 MHz, CD_2Cl_2, 250 K): δ −1.5 (br m) ppm. ^{13}C{^{1}H} NMR (125 MHz, CD_2Cl_2, 250 K): δ 176.3 (enhanced signal, br d, $^2J_{P-C}$ = 48.9 Hz; ^{13}*C*O), 164.7 (enhanced signal, br, ^{13}*C*O), 164.0 (q, $^1J_{B-C}$ = 49.3 Hz, *ipso*-*C* of BPh_4), 147.2 (s, *C*3), 135.9 (s, *o*-*C* of BPh_4), 135.8 (s, *C*5), 132.7 (d, $^2J_{P-C}$ = 8.0 Hz, *o*-*C* of PPh_2), 132.6 (s, *p*-*C* of PPh_2), 129.9 (d, ^3J = 11.1 Hz, *m*-*C* of PPh_2), 129.7 (d, ^1J = 59.3 Hz, *ipso*-*C* of PPh_2), 126.1 (q, ^3J = 2.7 Hz, *m*-*C* of BPh_4), 124.9 (s, *p*-*C* of BPh_4), 108.4 (s, *C*4), 48.0 (s, NCH_2), 25.7 (d, $^1J_{P-C}$ = 32.5 Hz, PCH_2) ppm.

NMR Data for the Averaged Resonances of 1-Pentyne in the ([Ir(PyP)(^{13}CO)$_2$]BPh$_4$ + 1-Pentyne) Reaction. ^{1}H NMR (500 MHz, CD_2Cl_2, 250 K): δ 2.49 (br s, 1H, *H*1′), 2.23 (td, $^3J_{H4'-H3'}$ = 7.21 Hz, $^4J_{H1'-H3'}$ = 2.1 Hz, 2H, *H*3′), 1.53 (apparent septet, ^3J = 7.3 Hz, 2H, *H*4′), 0.95 (t, ^3J = 7.3 Hz, 3H, *H*5′) ppm. ^{13}C{^{1}H} NMR (125 MHz, CD_2Cl_2, 250 K): δ 86.9 (br s, *C*2′), 68.1 (s, *C*1′), 22.4 (s, *C*4′), 21.1 (br, *C*3′), 13.5 (s, *C*5′) ppm.

NMR Characterization Data for the ([Ir(PyP)(^{13}CO)$_2$]BPh$_4$ (1-^{13}C)) + 1-Phenylacetylene) Mixture. ^{1}H NMR (500 MHz, CD_2Cl_2, 200 K): δ 7.76 (d, 2H, Ar*H*), 7.65−7.35 (m, 13H, Ar*H* together with Ar*H* of free PhC≡CH), 7.29 (br s, 8H, *o*-C*H* of BPh_4), 7.20 (s, 1H, *H*3), 6.90 (t, ^3J = 6.9 Hz, 8H, *m*-C*H* of BPh_4), 6.80 (t, ^3J = 6.9 Hz, 4H, *p*-C*H* of BPh_4), 6.62 (s, 1H, *H*5), 6.28 (d, $^3J_{P-H}$ = 17.1 Hz, bound PhC≡C*H*), 5.94 (s, 1H, *H*4), 3.07 (br m, 2H, NCH_2), 2.24 (br m, 1H, PC*H*H), 1.78 (br m, 1H, PCH*H*) ppm. ^{31}P{^{1}H} NMR (202 MHz, CD_2Cl_2, 200 K): δ −9.1 ppm. ^{13}C{^{1}H} NMR (125 MHz, CD_2Cl_2): δ 173.3 (d, $^2J_{P-C}$ = 12.6 Hz,^{13}*C*O (enhanced signal)), 163.4 (q, $^1J_{B-C}$ = 48.2 Hz, *ipso*-*C* of BPh_4), 158.4 (br d, $^2J_{P-C}$ ≈ 4.6 Hz, ^{13}*C*O (enhanced signal)), 146.1 (s, *C*3), 135.3 (s, *o*-*C*H of BPh_4), 134.7 (s, *C*5), 133.0 (s, Ar*C* of bound PhCCH), 132.9 (s, *p*-*C* of PPh_2), 132.4 (s, Ar*C* of bound PhCCH), 131.1 (d, J_{P-C} = 10.3 Hz; *o*/*m*-*C*H of PPh_2), 130.8 (d, $^1J_{P-C}$ ≈ 52 Hz, *ipso*-*C* of PPh_2), 129.6 (d, J_{P-C} = 13.8 Hz, *o*/*m*-*C*H of PPh_2), 129.5 (d, J_{P-C} = 12.6 Hz, *o*/*m*-*C*H of PPh_2), 129.2 (s, *p*-*C*H of PPh_2), 129.4 (s, Ar*C* of bound PhCCH), 128.4 (d, $^1J_{P-C}$ = 55.1 Hz, *ipso*-*C* of PPh_2), 125.8 (s, *m*-*C*H of BPh_4) 124.8 (s, *ipso*-*C* of bound PhCCH), 121.9 (s, *p*-*C* of BPh_4), 107.6 (s, *C*4), 100.8 (m, $^2J_{P-C}$ = 33.3 Hz, small couplings to ^{13}CO observed but not very clear, bound PhCCH Ar−*C*), 75.3 (m, bound PhC*C*H), 46.9 (s NCH_2), 24.8 (d, $^1J_{P,C}$ = 33.3 Hz, PCH_2) ppm.

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Acknowledgment. We would like to acknowledge helpful discussions with Professor Les Field and Dr. Gavin Edwards. Financial support from the Australian Research Council and the University of New South Wales is gratefully acknowledged. K.Q.V. would like to thank the Government of Australia for an Endeavour International Postgraduate Research Scholarship (EIPRS). We thank Dr. Richard Hodgson for assistance.

Supporting Information Available: Synthetic procedures for compounds **17**−**21** and ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compounds **17′**, **17**, **18′**, **18**, and **22**−**27** are provided as a single pdf file and can be found at http://pubs.acs.org.

OM061106R