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# Catalytic Carbonyl *Z*-Dienylation via Multicomponent Reductive Coupling of Acetylene to Aldehydes and α-Ketoesters Mediated by Hydrogen: Carbonyl Insertion into Cationic Rhodacyclopentadienes

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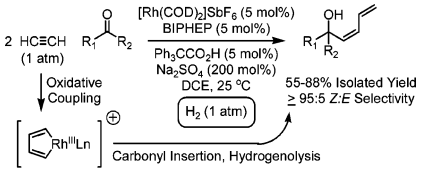
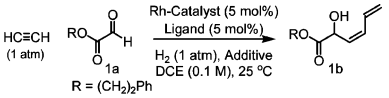
Although alkene hydroformylation is the largest volume application of homogeneous metal catalysis,[1] systematic efforts toward the development of hydrogen-mediated C−C couplings that extend beyond couplings to carbon monoxide are absent from the literature, withstanding studies from our laboratory.[2,3] Ideally, it would be desirable to reductively couple two or more complex organic molecules simply through their exposure to gaseous hydrogen in the presence of a metal catalyst. Moreover, to achieve broadest impact, hydrogen-mediated C−C coupling should be applicable to basic chemical feedstocks. Acetylene is vastly abundant (2 cents/mol, annual U.S. production >500 metric kilotons),[4] yet this important feedstock has not been exploited in catalytic reductive couplings to carbonyl compounds.[5−7] Here, we report that exposure of aldehydes and ketones to equal volumes of acetylene and hydrogen gas at ambient temperature and pressure in the presence of cationic rhodium catalysts provides products of carbonyl *Z*-dienylation.[6n] In this multicomponent coupling, four molecules are combined: two molecules of acetylene, a molecule of carbonyl compound, and elemental hydrogen.




Initial studies involved exposure of glyoxalate **1a** to equal volumes of hydrogen and acetylene gas in the presence of $Rh(COD)_2OTf$ (5 mol %) using triphenylacetic acid (TPAA, 5 mol %) as cocatalyst.[2d] Remarkably, the product of carbonyl *Z*-butadienylation **1b** is formed in 32% yield (Table 1, entry 1). In the absence of the TPAA cocatalyst, compound **1b** is formed in 17% yield (Table 1, entry 2). The rhodium(I) counterion plays a decisive role. Precatalysts possessing chloride counterions provide none of the reductive coupling product. However, in the series $Rh(COD)_2X$, where the counterion X is OTf, $BF_4$, $SbF_6$, and "BARF" (BARF = $B(3,5\text{-}(CF_3)_2C_6H_3)_4$), counterions that coordinate less strongly than OTf uniformly provide **1b** in higher yield (Table 1, entries 1, 4−6). Enhanced reactivity in response to use of noncoordinating counterions has been documented in Rh- and Ir-catalyzed hydrogenation.[8] Using $Rh(COD)_2SbF_6$ as precatalyst, some standard phosphine ligands were screened (Table 1, entries 5, 7−9); however, best results are obtained using BIPHEP (Table 1, entry 5). By employing $Na_2SO_4$ as an additive, the yield of coupling product is increased to 59% (Table 1, entry 10). Finally, by increasing the loading of TPAA (7.5 mol %), the yield of **1b** is increased to 68% (Table 1, entry 11). These conditions were applied successfully to a diverse set of carbonyl partners **1a**−**12a** (Table 2). In each case, the *Z*-alkene geometrical isomer forms as a single isomer. For most substrates, improved yields are observed for reactions performed in the presence of $Na_2SO_4$. It is possible that $Na_2SO_4$ removes water, thus preventing formation of catalytically inactive hydroxy-bridged rhodium dimers.[11a] The reactions appear to be mass-transfer limited with respect to introduction of hydrogen and/or acetylene gas,[9] with best results obtained using an apparatus in which mixtures of hydrogen and acetylene are delivered from a gas bag via cannula.

***Table 1.*** Optimization of the Hydrogen-Mediated Reductive Coupling of Acetylene and Phenethyl Glyoxalate[a]




| entry | Rh catalyst | ligand | additive | **1b** yield% |
|---|---|---|---|---|
| 1 | $Rh(cod)_2OTf$ | BIPHEP | TPAA | 32 |
| 2 | $Rh(cod)_2OTf$ | BIPHEP | | 17 |
| 3 | $[RhCl(cod)]_2$ | BIPHEP | TPAA | not observed |
| 4 | $Rh(cod)_2BF_4$ | BIPHEP | TPAA | 41 |
| 5 | $Rh(cod)_2SbF_6$ | BIPHEP | TPAA | 51 |
| 6 | $Rh(cod)_2BARF$ | BIPHEP | TPAA | 52 |
| 7 | $Rh(cod)_2SbF_6$ | $PPh_3$ | TPAA | not observed |
| 8 | $Rh(cod)_2SbF_6$ | DPPE | TPAA | not observed |
| 9 | $Rh(cod)_2SbF_6$ | *rac*-BINAP | TPAA | 29 |
| 10 | $Rh(cod)_2SbF_6$ | BIPHEP | TPAA−$Na_2SO_4$[b] | 59 |
| 11 | $Rh(cod)_2SbF_6$ | BIPHEP | TPAA−$Na_2SO_4$[b,c] | 68 |

[a] Cited yields are of pure isolated material. TPPA = triphenylacetic acid. For entry 7, 10 mol % of $Ph_3P$ was used. See Supporting Information for detailed experimental procedures. [b] Two equivalents of $Na_2SO_4$ were added. [c] Loading of TPAA is 7.5 mol %.

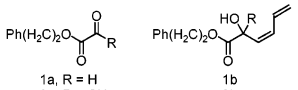
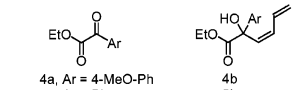
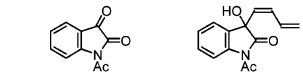
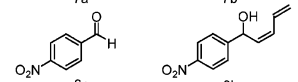
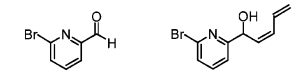
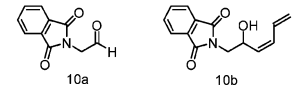
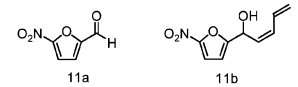
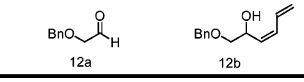
As a further demonstration of the reaction scope, enantioselective *Z*-butadienylation was attempted on aldehydes **10a** and **13a**. Gratifyingly, using a rhodium catalyst ligated by (*R*)-MeO−BIPHEP, the corresponding dienes **10b** and **13b** were produced in 88 and 89% ee, respectively. For these asymmetric transformations, it was found that $Rh(COD)_2BARF$ (BARF = $\{3,5\text{-}(CF_3)_2C_6H_3\}_4B$) provides slightly higher isolated yields compared to $Rh(COD)_2SbF_6$ (Scheme 1).

To gain insight into the catalytic mechanism, the reductive coupling of acetylene and phenethyl pyruvate **2a** was conducted under a deuterium atmosphere (Scheme 2). A single deuterium atom is incorporated stereoselectively at the diene terminus. These data are consistent with a catalytic cycle wherein acetylene dimerization to form a rhodacyclopentadiene[10] is followed by carbonyl insertion[11] to furnish an intermediate oxarhodacycloheptadiene. Protonolytic cleavage of the rhodium−oxygen bond in the oxarhodacycloheptadiene followed by σ-bond metathesis with elemental deuterium[12] provides a (vinyl)(deuterido)rhodium intermediate, which upon C−D reductive elimination delivers *deuterio*-**2b** and the starting rhodium(I) complex to close the cycle. Hydrometalative mechanisms or those involving initial alkyne−carbonyl oxidative coupling cannot be excluded on the basis of available data. However, the proposed rhodacyclopentadienes have been implicated as intermediates in acetylene cyclotrimerization.[10]

If the proposed catalytic cycle is operative, one would expect related cationic rhodacyclopentadienes to engage in carbonyl insertion

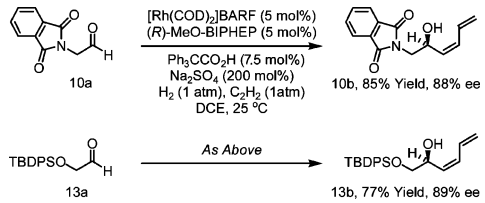

10.1021/ja0664786 CCC: $33.50 

***Table 2.*** Hydrogen-Mediated Coupling of Acetylene to Aldehydes and α-Ketoesters[a]

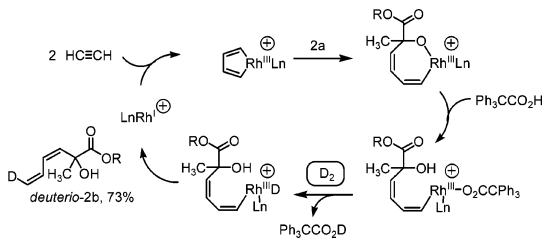
| Entry | Substrate | Product | Yield% |
|---|---|---|---|
| 1 |  | | |
| | 1a, R = H | 1b | 68[b,c] |
| | 2a, R = $CH_3$ | 2b | 73[b] |
| | 3a, R = *c*-$C_3H_5$ | 3b | 55[b] |
| 2 |  | | |
| | 4a, Ar = 4-MeO-Ph | 4b | 57[d] |
| | 5a, Ar = Ph | 5b | 77[d] |
| | 6a, Ar = 4-$NO_2$-Ph | 6b | 88[d] |
| 3 |  | | |
| | 7a | 7b | 81[b] |
| 4 |  | | |
| | 8a | 8b | 63[b,c] |
| 5 |  | | |
| | 9a | 9b | 56[b,c] |
| 6 |  | | |
| | 10a | 10b | 86[b,c] |
| 7 |  | | |
| | 11a | 11b | 72[b,c] |
| 8 |  | | |
| | 12a | 12b | 75[b,c] |

[a] Cited yields are of pure isolated material and represent the average of two runs. See Supporting Information for detailed experimental procedures. [b] Two equivalents of $Na_2SO_4$ were added. [c] Loading of TPAA is 7.5 mol %. [d] Rh(BIPHEP)(NBD)$SbF_6$ was used as precatalyst.

***Scheme 1.*** Enantioselective Hydrogen-Mediated Reductive Coupling of Acetylene to Aldehydes **10a** and **13a**




***Scheme 2.*** Plausible Catalytic Cycle as Supported by Deuterium Labeling




processes. It is known that 1,6-diynes react with rhodium(I) salts to afford isolable rhodacyclopentadienes.[13] Accordingly, 1,6-diyne **14a** (200 mol %) was hydrogenated in the presence of α-ketoester **6a** (100 mol %). The product of tandem reductive cyclization[14] carbonyl coupling **14b** is obtained in 58% yield as a single alkene geometrical isomer. Two equivalents of **14a** are used as approximately 50% of **14a** is diverted to products of [2 + 2 + 2] cycloaddition (Scheme 3).

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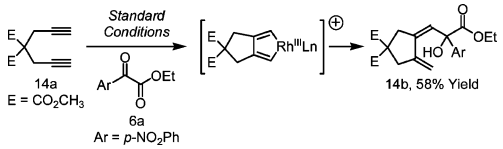
***Scheme 3.*** Reductive Coupling of 1,6-Diynes **14a** Corroborate Carbonyl Insertion into Transient Cationic Rhodacyclopentadienes




**Supporting Information Available:** Spectral data for all new compounds and detailed experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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