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Ruthenium-Catalyzed C–C Bond Forming Transfer Hydrogenation: Carbonyl Allylation from the Alcohol or Aldehyde Oxidation Level Employing Acyclic 1,3-Dienes as Surrogates to Preformed Allyl Metal Reagents

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Ruthenium-catalyzed transfer hydrogenation ranks among the most powerful methods available for the reduction of polar functional groups,¹ yet reductive C–C bond formations catalyzed by ruthenium are highly uncommon.^{2–4} We have shown that reductive C–C bond formation may be achieved under the conditions of catalytic hydrogenation^{5,6} and, more recently, under the conditions of iridium-catalyzed transfer hydrogenation.⁷ The iridium-catalyzed processes enable direct coupling of allenes^{7a} and 1,3-cyclohexadiene^{7b} to aldehydes or alcohols to furnish products of carbonyl allylation. While these proof of concept studies establish the use of allenes and dienes as surrogates to preformed allyl metal reagents, the iridium-catalyzed couplings were not applicable to acyclic 1,3-dienes.

Here, we report that under the conditions of ruthenium-catalyzed hydrogen autotransfer^{8,9} 1,3-butadiene, isoprene, and 2,3-dimethyl-butadiene couple to alcohols **1a–6a** to furnish products of carbonyl allylation **1b–6b**, **1c–6c**, and **1d–6d**, respectively. Under related transfer hydrogenation conditions employing isopropanol or formic acid as terminal reductant, aldehydes **7a–9a** couple to isoprene to furnish products of carbonyl allylation **1e–3e**, respectively. Thus, carbonyl allylation is achieved from the alcohol or aldehyde oxidation level. To our knowledge, these are the first examples of ruthenium-catalyzed C–C bond formation under the conditions of alcohol-mediated transfer hydrogenation.^{2–4} The branched regioselectivity observed in these couplings complements the linear regioselectivity observed in nickel-catalyzed diene–aldehyde reductive couplings.^{10–12} The transfer hydrogenative couplings reported in this account enable byproduct-free carbonyl allylation that transcends the boundaries of oxidation level and represent an important step in the departure from preformed organometallic reagents in carbonyl addition chemistry.^{6h,7,13,14}

Ni-Catalyzed Diene-Aldehyde Reductive Coupling - Homoallylation

Ru-Catalyzed Diene-Alcohol Transfer Hydrogenative Coupling - Allylation

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Supporting Information Available: Experimental procedures and spectral data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(250 mol%)

65% Yield (C)
3:1 dr. **10**

75% Yield (B)
2:1 dr. **11**

A plausible mechanism involves alcohol dehydrogenation to generate a ruthenium hydride, which hydrometalates the less substituted olefin of isoprene to deliver the secondary σ -allyl metal haptomer. Carbonyl addition from the more stable primary σ -allyl haptomer through a six-centered transition structure accounts for branched regioselectivity. Consistent with this interpretation, coupling of isoprene to *deuterio*-**2a** provides *deuterio*-**2c**, with deuterium at the benzylic position (>95%), the allylic methyl (32%), and the allylic methane (14%). Coupling of isoprene to aldehyde **8a** using isopropanol-*d*₈ as terminal reductant provides *deuterio*-**2c'**, which incorporates deuterium at the allylic methyl (19%) and the allylic methine (10%). Incomplete deuterium incorporation likely stems from reversible hydrometalation of isoprene. Mechanisms involving reversible diene hydrometalation in advance of diene–aldehyde oxidative coupling cannot be excluded on the basis of available data.

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addition from the aldehyde or alcohol oxidation level. Stereoselective variants of these and other alcohol–unsaturated couplings are currently under investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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15. $\text{RuHCl}(\text{CO})(\text{L})_3$ ($\text{L} = (p\text{-MeOPh})_3\text{P}$) is not an efficient catalyst, suggesting the active catalyst is ligated to both Ph_3P and $(p\text{-MeOPh})_3\text{P}$.

Table 1

Ruthenium-Catalyzed Coupling of Acyclic Dienes to Alcohols **1a–6a**^a

Entry	Alcohol	Product	Aryl	Conditions	Yield (dr)
1	1a	1b	$p\text{-NO}_2\text{Ph}$	B	84% (1.5:1)
2	2a	2b	Ph	B	61% (2:1)
3	3a	3b	$p\text{-MeOPh}$	C	76% (2:1)
4	4a	4b	$m\text{-MeOPh}$	C	87% (2:1)
5	5a	5b	2-Thienyl	C	87% (1.5:1)
6	6a	6b	Ar = $p\text{-BrPh}$	C	90% (2:1)

1a-6a	1c-6c

Entry	Alcohol	Product	Aryl	Conditions	Yield (dr)
1	1a	1c	$p\text{-NO}_2\text{Ph}$	A	84% (2:1)
2	2a	2c	Ph	C	93% (1:1)
3	3a	3c	$p\text{-MeOPh}$	C	84% (1.5:1)
4	4a	4c	$m\text{-MeOPh}$	C	93% (1:1)

Entry	Alcohol	Product	Aryl	Conditions	Yield (dr)
5	5a	5c	2-Thienyl	C	82% (1:1)
6	6a	6c	Ar = <i>p</i> -BrPh	C	75% (1:1)
<p>Reaction scheme showing the synthesis of 1d-6d from 1a-6a using $\text{RuHCl(CO)(PPh}_3)_3$ (5 mol%), Ligand (Cond. A, B or C), Acetone (2.5 mol%), $m\text{-NO}_2\text{BzOH}$ (2.5 mol%), and THF (2 M) at 95 °C.</p>					
Entry	Alcohol	Product	Aryl	Conditions	Yield
1	1a	1d	<i>p</i> -NO ₂ Ph	B	89%
2	2a	2d	Ph	B	91%
3	3a	3d	<i>p</i> -MeOPh	B	67%
4	4a	4d	<i>m</i> -MeOPh	B	67%
5	5a	5d	2-Thienyl	B	63%
6	6a	6d	Ar = <i>p</i> -BrPh	B	61%

^aCited yields are of isolated material. Conditions A employ no added ligand. Conditions B employ (*p*-MeOPh)₃P (15 mol %) as ligand. Conditions C employ *rac*-BINAP (5 mol %) as ligand. See Supporting Information for detailed experimental procedures.

Table 2

Coupling of Isoprene to Representative Aldehydes under Conditions of Ruthenium-Catalyzed Transfer Hydrogenation^a

7a, Ar = *p*-NO₂Ph, **8a**, Ar = Ph, **9a**, Ar = *p*-MeOPh

<i>i</i> -PrOH (400 mol%)	84% Yield (B)	82% Yield (C)	68% Yield (C)
90 °C	2:1 dr, 1c	2:1 dr, 2c	1:1 dr, 3c
HCO ₂ H (200 mol%)	89% Yield (A)	64% Yield (C)	68% Yield (C)
90 °C	3:1 dr, 1c	2:1 dr, 2c	1:1 dr, 3c

^aSee Table 1 footnotes for details. *m*-NO₂BzOH and acetone were not employed as additives.