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Amplification of Anti-Diastereoselectivity via Curtin−Hammett Effects in Ruthenium-Catalyzed Hydrohydroxyalkylation of 1,1-Disubstituted Allenes: Diastereoselective Formation of All-Carbon Quaternary Centers

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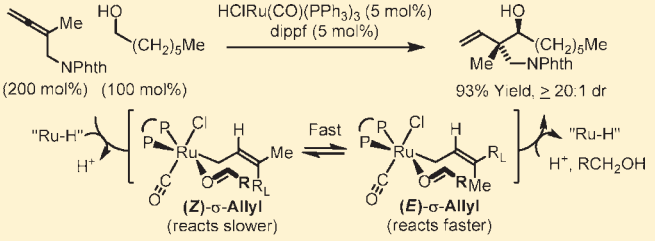
Supporting Information

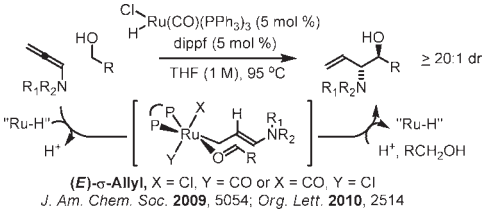
ABSTRACT: Under the conditions of ruthenium-catalyzed transfer hydrogenation, 1,1-disubstituted allenes **1a**−**c** and alcohols **2a**−**g** engage in redox-triggered generation of allylruthenium−aldehyde pairs to form products of hydrohydroxyalkylation **3a**−**g**, **4a**−**g**, and **5a**−**g** with complete branched regioselectivity. By exploiting Curtin−Hammett effects, good to excellent levels of anti-diastereoselectivity (4:1 to >20:1) are obtained. Thus, all carbon quaternary centers are formed in a diastereoselective fashion upon carbonyl addition from the alcohol oxidation level in the absence of premetalated nucleophiles or stoichiometric byproducts. Exposure of allene **1b** to equimolar quantities of alcohol **2a** and aldehyde **6b** under standard reaction conditions delivers adducts **4a** and **4b** in a 1:1 ratio. Similarly, exposure of allene **1b** to equimolar quantities of aldehyde **6a** and alcohol **2b** provides adducts **4a** and **4b** in an identical equimolar ratio. Exposure of allene **1b** to d_2-*p*-nitrobenzyl alcohol, *deuterio*-**2a**, under standard reaction conditions delivers the product of hydrohydroxyalkylation, *deuterio*-**4a**, which incorporates deuterium at the carbinol position (>95% ^{2}H) and the interior vinylic position (34% ^{2}H). Competition experiments involving exposure of allene **1b** to equimolar quantities of benzylic alcohols **2a** and *deuterio*-**2a** reveal no significant kinetic effect. The collective data corroborate rapid, reversible alcohol dehydrogenation, allene hydrometalation, and (*E*)-, (*Z*)-isomerization of the transient allylruthenium in advance of turnover-limiting carbonyl addition. Notably, analogous allene−aldehyde reductive C−C couplings employing 2-propanol as the terminal reductant display poor levels of anti-diastereoselectivity, suggesting that carbonyl addition is not turnover-limiting in reactions conducted from the aldehyde oxidation level.



INTRODUCTION

In the course of exploring C−C bond forming hydrogenations beyond hydroformylation,[1] it was found that ruthenium[2]- and iridium[3]-based catalysts promote direct hydrohydroxyalkylation of π-unsaturated reactants.[1−3] In such processes, primary alcohols engage π-unsaturated reactants as redox partners, whereupon hydrogen exchange triggers generation of electrophile−nucleophile pairs en route to products of C−C coupling. In this way, carbonyl addition is achieved directly from the alcohol oxidation level in the absence of premetalated nucleophiles or stoichiometric byproducts. In nearly all systems studied, identical products of carbonyl addition may be formed from the aldehyde oxidation level under transfer hydrogenation conditions employing 2-propanol or formic acid as terminal reductant.[1−3]

While control of relative and absolute stereochemistry has been achieved in iridium-catalyzed hydrohydroxyalkylations,[3] stereoselective ruthenium-catalyzed processes have proven elusive. Indeed, under the conditions of ruthenium catalysis, high diastereoselectivities only have been observed in couplings of unsubstituted allenamides, where complete partitioning of (*Z*)- and (*E*)-σ-allylruthenium intermediates is achieved readily through steric differentiation of hydrogen and the sterically demanding NR_1R_2 moiety.[2f,4] Exclusive carbonyl addition from the (*E*)-σ-allylruthenium through a chairlike transition structure accounts for the observed anti-diastereoselectivity.



The energetic bias required for partitioning *trisubstituted* (*Z*)- and (*E*)-σ-allylruthenium intermediates derived upon hydrometalation of 1,1-disubstituted allenes is far more difficult to achieve. Studies on stoichiometric hydrometalation of 1,1-disubstituted

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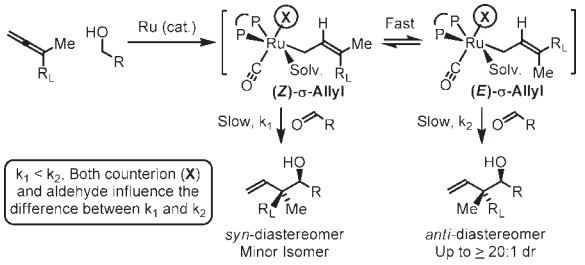
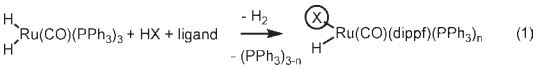
allenes or dienes employing $HXRu(CO)(PR_3)_3$ (X = Cl, Br) reveal that the resulting π-allylruthenium complexes $Ru(\eta^3\text{-allyl})(X)(CO)(PR_3)_2$ are highly fluxional.[5,6] Rapid interconversion of π-allyl- and σ-allylruthenium complexes precludes kinetically controlled partitioning of (*Z*)- and (*E*)-σ-allylruthenium isomers via stereoselective hydrometalation. Therefore, it was postulated that crowding at the ruthenium center might result in energetic differentiation of the transient (*Z*)- and (*E*)-σ-allylruthenium isomers or perhaps manifest in a Curtin−Hammett scenario, wherein a given σ-allyl isomer preferentially participates in carbonyl addition. However, while the feasibility of enacting Curtin−Hammett effects by virtue of configurationally dynamic allylmetal intermediates is suggested by stereoconvergence observed in the addition of γ-monosubstituted allylchromium reagents,[7a,b] γ,γ-disubstituted allylchromium reagents were found to act stereospecifically.[7c] Here, we report that exceptional levels of anti-diastereoselectivity may be obtained in the hydrohydroxyalkylation of 1,1-disubstituted allenes through exploitation of Curtin−Hammett effects. This method, which combines oxidation−construction events, enables diastereoselective formation of all-carbon quaternary centers under catalytic conditions in the absence of premetalated nucleophiles or stoichiometric byproducts.[8,9]



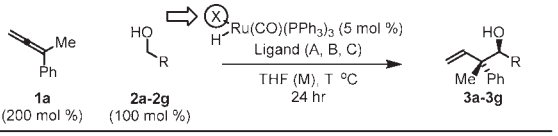
RESULTS AND DISCUSSION

In an initial experiment, 1,1-disubstituted allene **1a** was exposed to *p*-nitrobenzyl alcohol **2a** in the presence of a ruthenium catalyst derived upon the combination of $HClRu(CO)(PPh_3)_3$ and dippf [dippf = bis(diisopropylphosphino)ferrocene] in THF solvent at 50 °C. Although the desired hydrohydroxyalkylation product **3a** was isolated in excellent yield with complete branched regioselectivity, a modest 2:1 diastereoselectivity was observed. On the basis of the aforementioned line of reasoning, an assay of counterion was undertaken. Complexes $HXRu(CO)(dippf)(PPh_3)_n$ are conveniently prepared in situ through the acid−base reaction of $H_2Ru(CO)(PPh_3)_3$ and HX (eq 1).[10]



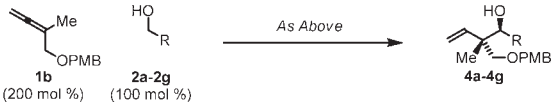
It was found for the specific combination of allene **1a** and *p*-nitrobenzyl alcohol **2a** that the ruthenium mesitylenesulfonate complex enforced complete levels of anti-diastereoselectivity. Encouraged by these results, the hydrohydroxyalkylation of 1,1-disubstituted allenes **1a**−**c** employing alcohols **2a**−**g** were explored. In many cases, the chloride counterion provided the highest levels of anti-diastereoselectivity. However, in other cases, for example allene **1b**, the BINOL-modified phosphate counterion was most effective in promoting anti-diastereoselectivity.[11] Finally, whereas dippf was the ligand of choice for allenes **1a** and **1b**, alternate ligands were required to achieved optimal levels of anti-diastereoselectivity

Table 1. Ruthenium-Catalyzed Hydrohydroxyalkylation of 1,1-Disubstituted Allenes 1a-1c employing alcohols 2a-2g[a]



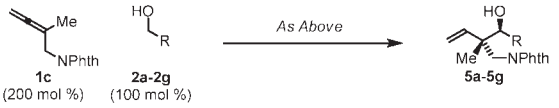
1a (200 mol %) + **2a-2g** (100 mol %) → **3a-3g**

Entry	X	Alcohol	R	Ligand, T (M)	Yield (dr)
1	OMes	**2a**	*p*-NO_2Ph	A, 50 °C (1 M)	**3a**, 84% (>20:1)[d]
2	Cl	**2b**	*p*-CF_3Ph	A, 40 °C (0.5 M)	**3b**, 85% (4:1)
3	Cl	**2c**	Ph	A, 60 °C (0.5 M)	**3c**, 99% (6:1)
4	Cl	**2d**	2-Furyl	A, 60 °C (0.5 M)	**3d**, 99% (10:1)
5	Cl	**2e**	HC=CHPh	A, 60 °C (0.2 M)	**3e**, 99% (5:1)
6	Cl	**2f**	*n*-Hexyl	A, 75 °C (1 M)	**3f**, 77% (>20:1)[c,d]
7	Cl	**2g**	$(CH_2)_3$OBn	A, 75 °C (1 M)	**3g**, 67% (>20:1)[c,d]



1b (200 mol %) + **2a-2g** (100 mol %) → **4a-4g**

Entry	X	Alcohol	R	Ligand, T (M)	Yield (dr)
8	O_2PBinol	**2a**	*p*-NO_2Ph	A, 75 °C (1 M)	**4a**, 97% (16:1)
9	O_2PBinol	**2b**	*p*-CF_3Ph	A, 75 °C (1 M)	**4b**, 93% (>20:1)
10	O_2PBinol	**2c**	Ph	A, 95 °C (1 M)	**4c**, 85% (17:1)
11	O_2PBinol	**2d**	2-Furyl	A, 95 °C (1 M)	**4d**, 71% (15:1)
12	O_2PBinol	**2e**	HC=CHPh	A, 95 °C (1 M)	**4e**, 94% (14:1)
13	Cl	**2f**	*n*-Hexyl	A, 95 °C (1 M)	**4f**, 86% (4:1)[c,d]
14	Cl	**2g**	$(CH_2)_3$OBn	A, 95 °C (1 M)	**4g**, 69% (4:1)[c,d]



1c (200 mol %) + **2a-2g** (100 mol %) → **5a-5g**

Entry	X	Alcohol	R	Ligand, T (M)	Yield (dr)
15	Cl	**2a**	*p*-NO_2Ph	C, 95 °C (0.5 M)	**5a**, 83% (10:1)
16	Cl	**2b**	*p*-CF_3Ph	C, 95 °C (0.5 M)	**5b**, 65% (14:1)
17	Cl	**2c**	Ph	B, 75 °C (0.5 M)	**5c**, 99% (8:1)[d]
18	O_3SCam.	**2d**	2-Furyl	A, 85 °C (1 M)	**5d**, 84% (7:1)
19	Cl	**2e**	HC=CHPh	B, 85 °C (0.1 M)	**5e**, 99% (5:1)[d]
20	Cl	**2f**	*n*-Hexyl	A, 95 °C (1 M)	**5f**, 93% (>20:1)[c,d]
21	Cl	**2g**	$(CH_2)_3$OBn	A, 85 °C (1 M)	**5g**, 72% (>20:1)[d]

[a] Yields are of isolated material. Diastereoselectivity was determined via ^{1}H NMR analysis of crude reaction mixtures. See Supporting Information for further experimental details. [b] Ligands: A = dippf (5 mol %), B = dCypf, (5 mol %), and C = PPh_2Cy (15 mol %). [c] Three equivalents of allene. [d] 48 h.

for the phthalimido-substituted allene **1c**. The assignment of relative stereochemistry for adducts **3a**−**g**, **4a**−**g**, and **5a**−**g** is made in analogy to that determined for compound **5a**, which was established via single crystal X-ray diffraction analysis, and compound **3c**, which is reported in the literature (Table 1).[8b]

Under identical reaction conditions, a given allene can display substantially different levels of diastereoselectivity in response to the structure of its transient aldehyde partner. This observation suggests that the relative thermodynamic stabilities of the (*Z*)- and (*E*)-σ-allylruthenium intermediates do not alone determine diastereocontrol. Rather, it appears that a Curtin−Hammett scenario is operative, wherein the transient aldehyde influences energetic partitioning of the diastereomeric transition structures. Kinetically controlled diastereoselection is suggested by the fact that the diastereomeric ratio does not change over the course of the reaction. This observation is significant, as reversible carbonyl addition or product oxidation could potentially occur. However, although secondary alcohol oxidation is in general thermodynamically

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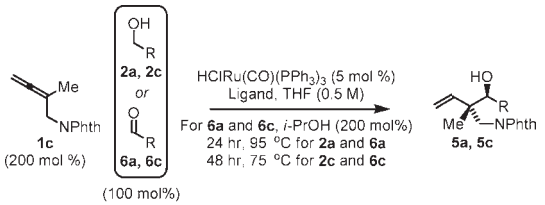
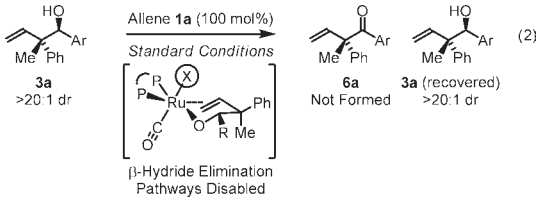
Table 2. Oxidation Level Dependent Anti-Diastereoselectivity in Ruthenium-Catalyzed Couplings of Allene 1c[a]



entry	oxidation level	R	ligand	% yield (dr)
1	alcohol, **2a**	*p*-NO_2Ph	$CyPPh_2$ (15 mol %)	**5a**, 83 (10:1)
2	aldehyde, **6a**	*p*-NO_2Ph	$CyPPh_2$ (15 mol %)	**5a**, 99 (1:1)
3	alcohol, **2c**	Ph	dCypf (5 mol %)	**5c**, 99 (8:1)
4	aldehyde, **6c**	Ph	dCypf (5 mol %)	**5c**, 72 (1:1)

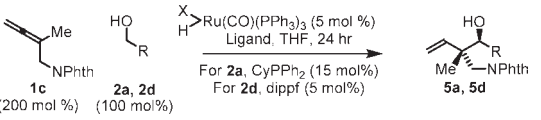
[a] As described in Table 1.

more favorable than primary alcohol oxidation, further oxidation of the coupling product is not observed. Our collective studies[2] suggest that coordination of the homoallylic olefin to the catalyst provides a hexa-coordinate, 18-electron complex, suppressing β-hydride elimination through occupation of all available coordination sites. Indeed, in ruthenium-catalyzed diene−carbonyl C−C couplings, coordinative saturation of the catalyst could be varied to partition formation of secondary alcohol and ketone products.[2b] In the present case, resubjecting adduct **3a** to standard coupling conditions in the presence of allene **1a**, which may serve as a hydrogen acceptor, does not result in any oxidation or erosion diastereomeric purity of recovered **3a**, corroborating kinetically controlled carbonyl addition (eq 2).



Notably, when the allene coupling is conducted from the aldehyde oxidation level, diastereoselectivity is essentially absent. For example, whereas 10:1 and 8:1 anti-diastereoselectivities are observed in the coupling of allene **1c** to alcohols **2a** and **2c**, respectively, corresponding couplings of aldehydes **6a** and **6c** employing 2-propanol as terminal reductant under otherwise identical conditions are not diastereoselective (Table 2). These data suggest that carbonyl addition is no longer turnover-limiting in couplings conducted from the aldehyde oxidation level. There are two probable explanations for this. In reactions conducted from the aldehyde oxidation level, aldehyde concentration is higher throughout the course of the reaction, which should accelerate carbonyl addition. Alternatively, for such sterically congested ruthenium complexes, dehydrogenation of 2-propanol, a secondary alcohol, may be slower than primary alcohol dehydrogenation. In either case, Curtin−Hammett effects can no longer be exploited to amplify diastereoselectivity. Consistent with this interpretation, in reactions conducted from the alcohol oxidation level, diastereoselectivity is found to be highly concentration-dependent. Presumably, at lower concentration, carbonyl addition is sufficiently slow that the (*E*)-σ-allylruthenium consumed upon addition may be

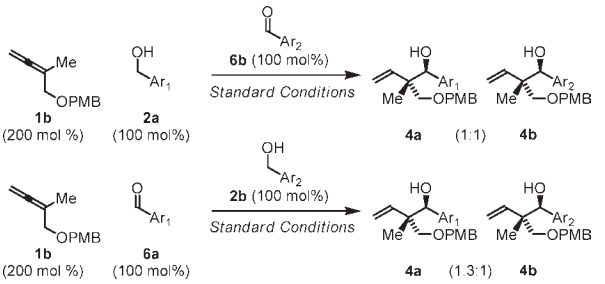
Table 3. Concentration-Dependent Anti-Diastereoselectivity in Ruthenium-Catalyzed Couplings of Allene 1c[a]



entry	alcohol	X	*T*, °C	THF concn, M	% yield (dr)
1	**2a**	Cl	95	1.0 M	**5a**, 87 (6:1)
2	**2a**	Cl	95	0.5 M	**5a**, 83 (10:1)
3	**2a**	Cl	95	0.2 M	**5a**, 55 (>20:1)
4	**2d**	O_3S-camphor	85	0.5 M	**5d**, 72 (2:1)
5	**2d**	O_3S-camphor	85	0.2 M	**5d**, 79 (4:1)
6	**2d**	O_3S-camphor	85	0.1 M	**5d**, 82 (5:1)

[a] As described in Table 1.

Scheme 1. Competition Experiments Corroborating Rapid, Reversible Dehydrogenation in Advance of C−C Coupling[a]



[a] As described in Table 1. Ar_1 = *p*-NO_2Ph, Ar_2 = *p*-CF_3Ph. Products **4a** and **4b** are obtained as 1:1.5 (syn:anti) diastereomeric mixtures.

replenished via isomerization of the remaining (*Z*)-σ-allylruthenium isomer (Table 3).

To assess whether primary alcohol dehydrogenation is indeed more rapid than carbonyl addition, the following competition experiment was performed. Allene **1b** was exposed to equimolar quantities of alcohol **2a** and aldehyde **6b** under standard conditions employing the ruthenium catalyst generated in situ from $H_2Ru(CO)(PPh_3)_3$, dippf, and *rac*-BINOL-PO_2H at 75 °C in THF solvent (1.0 M). The C−C coupling products **4a** and **4b** were produced in a 1:1 ratio. Under identical conditions employing equimolar quantities of aldehyde **6a** and alcohol **2b**, a nearly identical ratio of coupling products **4a** and **4b** is observed. These data are consistent with rapid, reversible primary alcohol dehydrogenation in advance of turnover-limiting carbonyl addition (Scheme 1).[12]

Further insight into the catalytic mechanism is provided by deuterium labeling and competition kinetics experiments (Scheme 2).[13] Exposure of allene **1b** to d_2-*p*-nitrobenzyl alcohol under standard coupling conditions delivers *deuterio*-**4a**, which incorporates deuterium at the carbinol methine (>99% ^{2}H) and at the interior vinylic position (34% ^{2}H), as determined by ^{1}H and ^{2}H NMR analyses. Complete retention of deuterium at the carbinol methine, along with kinetically controlled anti-diastereoselectivity (vida supra), corroborates resistance of the coupling products toward reversible dehydrogenation. Incomplete deuterium incorporation at the interior vinylic position suggests that β-hydride elimination of the π-allylruthenium intermediate

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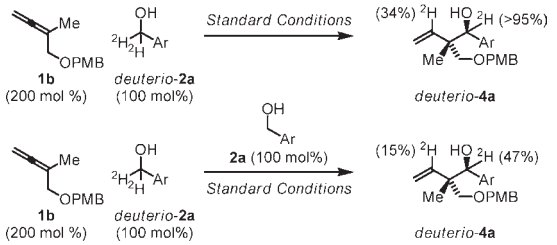
Scheme 2. Deuterium Labeling and Competition Kinetics Experiments[a]



[a] As described in Table 1. Ar = p-NO_2Ph,

occurs to furnish diene byproducts. Such byproducts were identified in the crude reaction mixture and may account for the requirement of superstoichiometric loadings of allene. Competition kinetic experiments involving exposure of allene **1b** to equimolar quantities of p-nitrobenzyl alcohol and d_2-p-nitrobenzyl alcohol reveal no significant kinetic effect (k_H/k_D = 1.06), within the error limits of the experiment, suggesting that alcohol oxidation is not the turnover-limiting event. If carbonyl addition was the turnover-limiting event, an inverse secondary isotope effect would be anticipated. Given the error limits of the experiment, the absence of such an effect is inconclusive.

CONCLUSION

In summary, by taking advantage of Curtin−Hammett effects in ruthenium-catalyzed alcohol−allene C−C coupling, one bypasses the need to partition trisubstituted σ-allylmetal species in the ground state. Rather, from an equilibrating mixture of transient (Z)- and (E)-σ-allylruthenium isomers, preferential selection of the (E)-σ-allylruthenium species occurs upon energetic partitioning in the transition state for carbonyl addition. Such Curtin−Hammett effects provide a basis for diastereoselective carbonyl allylation to furnish secondary neopentyl homoallylic alcohols, which possess all carbon quaternary centers, thus setting the stage for development of related diastereo- and enantioselective processes.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures and spectral data for all new compounds (^{1}H NMR, ^{13}C NMR, IR, HRMS). This material is available free of charge *via* the Internet at http://pubs.acs.org.

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REFERENCES

(1) For selected reviews on C−C bond forming hydrogenation and transfer hydrogenation, see: (a) Bower, J. F.; Kim, I. S.; Patman, R. L.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009,** *48,* 34. (b) Han, S. B.; Kim, I. S.; Krische, M. J. *Chem. Commun.* **2009,** 7278.

(2) For ruthenium-catalyzed alcohol−unsaturate C−C coupling, see the following. (a) Dienes: Shibahara, F.; Bower, J. F.; Krische, M. J. *J. Am. Chem. Soc.* **2008,** *130,* 6338. (b) Shibahara, F.; Bower, J. F.; Krische, M. J. *qJ. Am. Chem. Soc.* **2008,** *130,* 14120. (c) Han, H.; Krische, M. J. *Org. Lett.* **2010,** *12,* 2844. (d) Alkynes: Patman, R. L.; Chaulagain, M. R.; Williams, V. M.; Krische, M. J. *J. Am. Chem. Soc.* **2009,** *131,* 2066. (e) Williams, V. M.; Leung, J. C.; Patman, R. L.; Krische, M. J. *Tetrahedron* **2009,** *65,* 5024. (f) Allenes: Zbieg, J. R.; McInturff, E. L. *Org. Lett.* **2010,** *12,* 2514.

(3) For iridium-catalyzed alcohol−allene C−C coupling, see: (a) Han, S. B.; Kim, I.-S.; Han, H.; Krische, M. J. *J. Am. Chem. Soc.* **2009,** *131,* 6916. For related couplings of dienes and allylic carboxylates see ref 1.

(4) Skucas, E.; Zbieg, J. R.; Krische, M. J. *J. Am. Chem. Soc.* **2009,** *131,* 5054.

(5) For leading references on the stoichiometric reaction of $HXRu(CO)(PR_3)_3$ (X = Cl, Br) with allenes or dienes to furnish π-allylruthenium complexes, see: (a) Hiraki, K.; Ochi, N.; Sasada, Y.; Hayashida, H.; Fuchita, Y.; Yamanaka, S. *J. Chem. Soc., Dalton Trans.* **1985,** 873. (b) Hill, A. F.; Ho, C. T.; Wilton-Ely, D. E. T. *Chem. Commun.* **1997,** 2207. (c) Xue, P.; Bi, S.; Sung, H. H. Y.; Williams, I. D.; Lin, Z.; Jia, G. *Organometallics* **2004,** *23,* 4735.

(6) For studies involving π-allylruthenium complexes of the type $Ru(\eta^3\text{-allyl})(X)(CO)(PR_3)_2$, see: (a) Barnard, C. F. J.; Daniels, B. J. A.; Holland, P. R.; Mawby, R. J. *J. Chem. Soc., Dalton Trans.* **1980,** 2418. (b) Hiraki, K.; Matsunaga, T.; Kawano, H. *Organometallics* **1994,** *13,* 1878. (c) Sasabe, H.; Nakanishi, S.; Takata, T. *Inorg. Chem. Commun.* **2002,** *5,* 177. (d) Cadierno, V.; Crochet, P.; Diez, J.; Garcia-Garrido, S. E.; Gimeno, J. *Organometallics* **2003,** *22,* 5226.

(7) (a) Hiyama, T.; Okude, Y.; Kimura, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1982,** *55,* 561.(b) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon: Oxford, 1991; Vol. 2, pp 1−53.(c) Jubert, C.; Nowotny, S.; Kornemann, D.; Antes, I.; Tucker, C. E.; Knochel, P. J. *Org. Chem.* **1992,** *57,* 6384.

(8) For selected examples of stereoselective carbonyl allylmetalation to furnish secondary neopentyl homoallylic alcohols, see ref 7c and the following: (a) Sato, M.; Yamamoto, Y.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1993,** *34,* 7071. (b) Habaue, S.; Yasue, K.; Yanagisawa, A.; Yamamoto, H. *Synlett* **1993,** 788. (c) Nishigaichi, Y.; Takuwa, A. *Tetrahedron Lett.* **1999,** *40,* 109. (d) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001,** *123,* 9488. (e) Denmark, S. E.; Fu, J. *Org. Lett.* **2002,** *4,* 1951. (f) Ely, R. J.; Morken, J. P. *J. Am. Chem. Soc.* **2010,** *132,* 2534.

(9) As described in ref 2c, ruthenium-catalyzed C−C coupling of ethanol and 2-substituted dienes delivers anti-configured neopentyl homoallylic alcohols. However, incomplete regio- and diastereoselectivities are observed.

(10) Dobson, A.; Robinson, S. R.; Uttley, M. F. *J. Chem. Soc., Dalton Trans.* **1974,** 370.

(11) Chiral counterions may prove effective in enantioselective C−C couplings of this type. For example, using the ruthenium catalyst generated in situ from $H_2Ru(CO)(PPh_3)_3$, dippf, and enantiomerically pure [(*S*)-BINOL]PO_2H, allene **1b** couples to alcohol **2a** to deliver the secondary neopentyl alcohol **4a** in 16% enantiomeric excess.

(12) For a related competition experiment, see: Bower, J. F.; Skucas, E.; Patman, R. L.; Krische, M. J. *J. Am. Chem. Soc.* **2007,** *129,* 15134.

(13) For selected examples of kinetic isotope effects in ruthenium-catalyzed transfer hydrogenation, see: (a) Casey, C. P.; Johnson, J. B. *J. Org. Chem.* **2003,** *68,* 1998. (b) Sandoval, C. A.; Ohkuma, T.; Muniz, K.; Noyori, R. *J. Am. Chem. Soc.* **2003,** *125,* 13490. (c) Pannetier, N.; Sortais, J.-B.; Dieng, P. S.; Barloy, L.; Sirlin, C.; Pfeffer, M. *Organometallics* **2008,** *27,* 5852.