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anti-Diastereo- and Enantioselective Carbonyl Crotylation from the Alcohol or Aldehyde Oxidation Level Employing a Cyclometallated Iridium Catalyst: α-Methyl Allyl Acetate as a Surrogate to Preformed Crotylmetal Reagents

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Abstract: Under the conditions of transfer hydrogenation employing an *ortho*-cyclometallated iridium catalyst generated in situ from $[Ir(cod)Cl]_2$, 4-cyano-3-nitrobenzoic acid and the chiral phosphine ligand (*S*)-SEGPHOS, α-methyl allyl acetate couples to alcohols **1a**−**1j** with complete levels of branched regioselectivity to furnish products of carbonyl crotylation **3a**−**3j**, which are formed with good levels of *anti*-diastereoselectivity and exceptional levels of enantioselectivity. An identical set of optically enriched carbonyl crotylation products **3a**−**3j** is accessible from the corresponding aldehydes **2a**−**2j** under the same conditions, but employing isopropanol as the terminal reductant. Experiments aimed at probing the origins of stereoselection establish a matched mode of ionization for the (*R*)-acetate and the iridium catalyst modified by (*S*)-SEGPHOS, as well as reversible ionization of the allylic acetate with rapid π-facial interconversion of the resulting π-crotyl intermediate in advance of C−C bond formation. Additionally, rapid alcohol−aldehyde redox equilibration in advance of carbonyl addition is demonstrated. Thus, *anti*-diastereo- and enantioselective carbonyl crotylation from the alcohol or aldehyde oxidation level is achieved in the absence of any stoichiometric metallic reagents or stoichiometric metallic byproducts.

Introduction

Carbonyl crotylation ranks among the foremost methods used for the construction of polypropionate natural products.[1] The majority of enantioselective crotylation protocols exploit chirally modified crotylmetal reagents, such as the *B*-crotyl reagents developed by Hoffmann (1979),[2a] Brown (1986),[2b,c] Roush (1986),[2d,e] Masamune (1987),[2f] and Soderquist (2005),[2g] the *Ti*-crotyl reagents developed by Duthaler (1989),[2h,i] and the *Si*-crotyl reagents developed by Panek (1991)[2j,k] and Leighton (2004).[2l] Enantioselective Lewis acid catalyzed additions of crotylmetal reagents are reported by Yamamoto (1991),[3a−c] Mikami (1993),[3d] Nishiyama (2001),[3e] Evans (2006)[3f] and Hall (2006).[3g,h] Additionally, enantioselective Lewis base catalyzed carbonyl crotylations employing crotylmetal reagents are reported by Denmark (1994),[4a,b] Iseki (1997),[4c] Nakajima (1998),[4d] and Kočovsky (2003).[4e] Finally, a chiral diol catalyzed allylboration of ketones is reported by Schaus (2006).[5]

In these cases, the crotylating agent is a metal or metalloid that is itself prepared from a metallic precursor. For example, the crotylating agent developed by Brown[2b,c] is prepared

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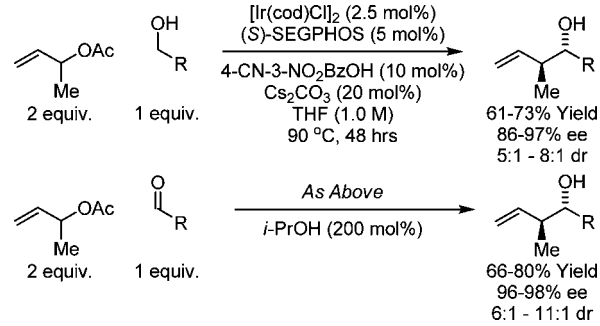
through potassiation of butene employing Schlosser's base[6] followed by transmetalation to boron. Here, multiple manipulations and multiple preformed organometallics (*n*-BuLi, KC_4H_7, Ipc_2BOMe) are required to prepare the desired crotylborane, which contributes to cost and waste generation.

An alternate approach to enantioselective carbonyl crotylation involves reductive generation of crotylmetal reagents from the corresponding halides, as in catalytic enantioselective variants of the Nozaki−Hiyama reaction.[7,8] Here, metallic reductants are required for catalytic turnover and modest diastereoselectivities are typically observed. Related reductive couplings of allylic alcohols, acetates, and carboxylates, which constitute an umpolung of π-allyl chemistry, also have been disclosed.[9−13] However, catalytic enantioselective crotylations based on this approach are absent and, with one exception,[12] metallic terminal reductants are again required.

Metal catalyzed reductive C−C coupling under the conditions of hydrogenation or transfer hydrogenation provides an alternative to the use of preformed organometallic reagents in an ever-increasing range of C═X (X = O, NR) addition processes.[14] A powerful manifestation of these concepts resides in the coupling of unsaturates to carbonyl partners to furnish homoallylic alcohols,[15−17] wherein allenes,[15] dienes,[16] or allyl acetate[17] serve as surrogates to preformed allylmetal reagents. The iridium catalyzed transfer hydrogenative couplings of allyl acetate[17] represent an especially significant advance over established carbonyl allylation protocols,[1] *as highly enantioselective carbonyl allylation is achieved from the alcohol or aldehyde oxidation level in the absence of any stoichiometric metallic reagents*. Inspired by these results, stereoselective carbonyl crotylations employing α-methyl allyl acetate as the crotyl donor were sought. Here, we report a second generation *ortho*-cyclometallated iridium catalyst modified by 4-cyano-3-nitrobenzoic acid and (*S*)-SEGPHOS that promotes highly regio- and enantioselective carbonyl crotylation from the alcohol or aldehyde oxidation level with good levels of *anti*-diastereoselectivity (Scheme 1).

Scheme 1. Carbonyl Crotylation from the Alcohol or Aldehyde Oxidation Level via Transfer Hydrogenative C−C Coupling



Results and Discussion

Using our first-generation catalytic system,[17a] which employs an iridium complex generated in situ from $[Ir(cod)Cl]_2$, *m*-nitrobenzoic acid and chelating chiral phosphine ligand, carbonyl couplings employing α-methyl allyl acetate occur with complete branch regioselectivity. However, poor *anti*-diastereoselectivities were observed and the level of diastereoselection was insensitive to changes in the character of the phosphine ligand. Our subsequent discovery that the active catalyst is an *ortho*-cyclometallated iridium *C*,*O*-benzoate[17b] unveiled new opportunities to direct diastereoselectivity involving modification of the cyclometallating agent.

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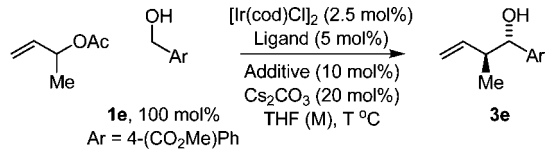
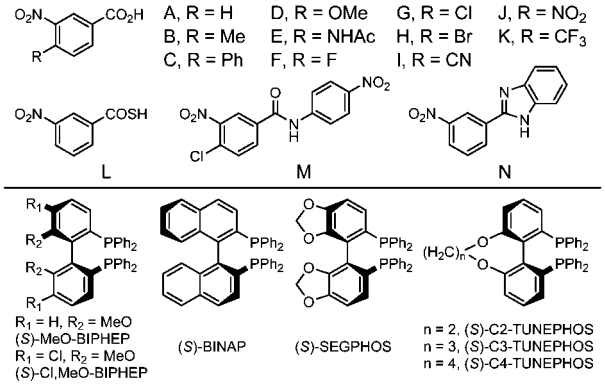
Table 1. Optimizing Relative and Absolute Stereocontrol in Transfer Hydrogenative Carbonyl Crotylation from the Alcohol Oxidation Level[a]

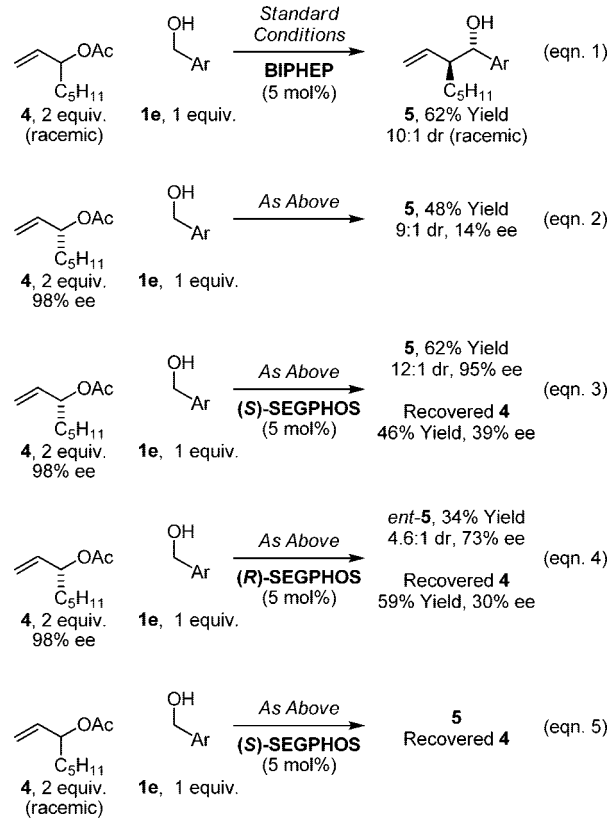


Entry	Ligand	Acid	OAc (eq)	THF (M)	T °C	Y (%)	dr (ee%)
1	BIPHEP	A	10	0.2	100	85	2.0:1
2	BIPHEP	B	10	0.2	100	72	2.7:1
3	BIPHEP	C	10	0.2	100	10	2.0:1
4	BIPHEP	D	10	0.2	100	68	2.2:1
5	BIPHEP	E	10	0.2	100	50	1.5:1
6	BIPHEP	F	10	0.2	100	78	2.3:1
7	BIPHEP	G	10	0.2	100	93	2.6:1
8	BIPHEP	H	10	0.2	100	80	2.4:1
9	BIPHEP	I	10	0.2	100	70	3.0:1
10	BIPHEP	J	10	0.2	100	65	3.5:1
11	BIPHEP	K	10	0.2	100	86	2.4:1
12	BIPHEP	L	10	0.2	100	38	1.9:1
13	BIPHEP	M	10	0.2	100	7	1.9:1
14	BIPHEP	N	10	0.2	100	5	2.1:1
15	BIPHEP	I	5	0.2	100	57	3.7:1
16	BIPHEP	I	2	0.2	100	55	4.3:1
17	BIPHEP	I	2	0.5	100	77	4.8:1
18	BIPHEP	I	2	1.0	100	75	7.1:1
19	BIPHEP	I	2	1.0	90	78	7.5:1
20	BIPHEP	J	2	1.0	90	42	7.6:1
21	(*S*)-BINAP	I	2	1.0	90	75	3.5:1 (95)
22	(*S*)-MeO-BIPHEP	I	2	1.0	90	63	5.8:1 (94)
23	(*S*)-Cl,MeO-BIPHEP	I	2	1.0	90	67	3.0:1 (96)
⇨ **24**	**(*S*)-SEGPHOS**	I	**2**	**1.0**	**90**	**70**	**7.4:1 (95)**
25	(*S*)-C2-TUNEPHOS	I	2	1.0	90	68	7.7:1 (91)
⇨ **26**	**(*S*)-C3-TUNEPHOS**	I	**2**	**1.0**	**90**	**77**	**8.0:1 (97)**
27	(*S*)-C4-TUNEPHOS	I	2	1.0	90	71	6.4:1 (92)



[a] All reactions were performed in 13 × 100 mm^2 pressure tubes. The cited yields are of material isolated by silica gel chromatography. Enantiomeric excess was determined by chiral stationary phase HPLC analysis via comparison to racemic diastereomeric mixtures. For entries 1−18, the reaction was allowed to run for 20 h. For entries 19−27, the reaction was allowed to run for 48 h. See Experimental Section for further details.

Scheme 2. Experiments Aimed at Probing the Origins of Stereoselection in Ir-Catalyzed Transfer Hydrogenative Crotylation (Ar = (4-(CO$_2$Me)Ph)[a]



Time (h)	Recovered (*S*)-**4**	**Compound 5**
6	59% Yield, 22% ee	37% Yield, 95% ee, 11.3:1 dr
12	53% Yield, 27% ee	45% Yield, 95% ee, 12.6:1 dr
24	52% Yield, 22% ee	48% Yield, 94% ee, 11.3:1 dr
48	48% Yield, 21% ee	56% Yield, 94% ee, 10.8:1 dr

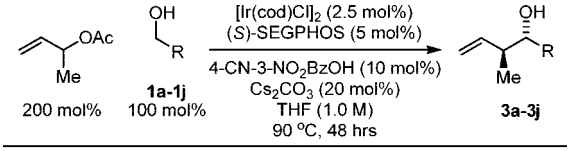
[a] Reactions were performed in 13 × 100 mm^2 pressure tubes. Cited yields are of material isolated by silica gel chromatography. Enantiomeric excess was determined by chiral stationary phase HPLC analysis via comparison to racemic diastereomeric mixtures. See Experimental Section for further details.

Accordingly, a range of substituted *m*-nitrobenzoic acids were assayed in the transfer hydrogenative coupling of α-methyl allyl acetate and alcohol **1e** to furnish homoallyl alcohol **3e** (Table 1). This assay focused primarily on 4-substituted-3-nitrobenzoic acids, as substitution at the 5- and 6-positions substantially diminished the reactivity of the resulting catalytic complex. Iridium catalysts modified by 4-cyano-3-nitrobenzoic acid **I** and 3,4-dinitrobenzoic acid **J** displayed the highest levels of diastereocontrol, providing the homoallyl alcohol **3e** in 3.0:1 and 3.5:1 *anti*/*syn* ratios, respectively (Table 1, entries 9 and 10). Alternative cyclometallating agents, as represented by compounds **L**−**M**, were ineffective.

Using the catalyst modified by 4-cyano-3-nitrobenzoic acid **I**, it was found that the level of diastereoselection was dependent upon the loading of α-methyl allyl acetate. Specifically, a reduction in the loading of α-methyl allyl acetate from 1000 to 500 to 200 mol % was found to increase the level of *anti*-diastereoselection from 3.0:1 to 3.7:1 to 4.3:1, respectively (Table 1, entries 9, 15 and 16). Remarkably, at 200 mol % loadings of α-methyl allyl acetate, both diastereoselectivity and isolated yield were found to improve substantially with increasing concentration. At 0.2, 0.5, and 1.0 M concentrations, *anti*-diastereoselectivities increased from 4.3:1 to 4.8:1 to 7.1:1, respectively (Table 1, entries 16−18). Finally, by decreasing reaction temperature from 100 to 90 °C, homoallyl alcohol **3e** was formed in 78% yield with 7.5:1 *anti*-diastereoselectivity (Table 1, entry 19). Notably, the catalyst modified by 3,4-dinitrobenzoic acid **J** was highly sensitive to reaction temperature, and under identical conditions at 90 °C, homoallyl alcohol **3e** was produced in only 42% yield with 7.6:1 *anti*-diastereoselectivity (Table 1, entry 20).

At this point, chirally modified catalysts were assayed. Although catalysts incorporating the ligands (*S*)-BINAP, (*S*)-

Table 2. Ir-Catalyzed Transfer Hydrogenative Crotylation of Alcohols **1a**−**1j**[a]



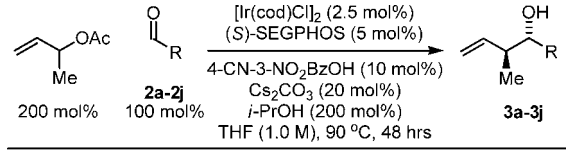
1a, R = Ph
1b, R = 3-MeOPh
1c, R = 4-MeOPh
1d, R = 4-BrPh
1e, R = 4-(CO_2Me)Ph
1f, R = 2-(*N*-Me-indole)
1g, R = CH=CHPh
1h, R = 2-phenyl-1-ethyl
1i, R = 3-(benzyloxy)propyl
1j, R = $(CH_2)_7CH_3$

Entry	Alcohol	Product	Yield (%)	ee (%)	*anti*:*syn*
1	**1a**	**3a**	65	95	6:1
2	**1b**	**3b**	70	95	6:1
3[b]	**1c**	**3c**	67 73	90 92	5:1 4:1[c]
4	**1d**	**3d**	73	95	8:1
5	**1e**	**3e**	70 77	95 97	7:1 8:1[c]
6[b]	**1f**	**3f**	73	95	5:1
7	**1g**	**3g**	61 63	86 90	7:1 6:1[c]
8	**1h**	**3h**	69	97	7:1
9	**1i**	**3i**	68	97	7:1
10	**1j**	**3j**	69	97	7:1

[a] Reactions were performed in 13 × 100 mm^2 pressure tubes. Cited yields are of material isolated by silica gel chromatography. Enantiomeric excess was determined by chiral stationary phase HPLC analysis via comparison to racemic diastereomeric mixtures. See Experimental Section for further details. [b] 80 °C, 72 h. [c] (*S*)-C3-TUNEPHOS was used as ligand.

MeO-BIPHEP, and (*S*)-Cl,MeO-BIPHEP were found to enforce high levels of absolute stereocontrol, significant erosion of

Table 3. Ir-Catalyzed Transfer Hydrogenative Crotylation of Aldehydes **2a**−**2j**[a]



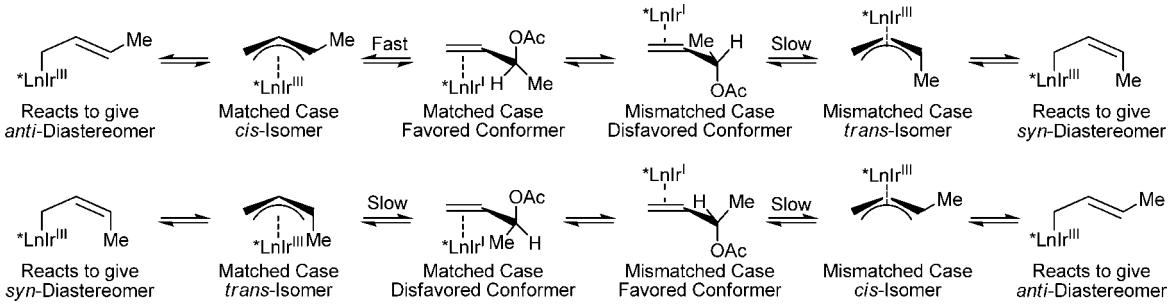
2a, R = Ph
2b, R = 3-MeOPh
2c, R = 4-MeOPh
2d, R = 4-BrPh
2e, R = 4-(CO_2Me)Ph
2f, R = 2-(*N*-Me-indole)
2g, R = CH=CHPh
2h, R = 2-phenyl-1-ethyl
2i, R = 3-(benzyloxy)propyl
2j, R = $(CH_2)_7CH_3$

Entry	Aldehyde	Product	Yield (%)	ee (%)	*anti*:*syn*
1	**2a**	**3a**	77	98	9:1
2	**2b**	**3b**	74	98	9:1
3[b]	**2c**	**3c**	75 77	97 98	7:1 6:1[c]
4	**2d**	**3d**	78	97	11:1
5	**2e**	**3e**	80 82	96 97	11:1 13:1[c]
6[b]	**2f**	**3f**	78	97	6:1
7	**2g**	**3g**	66 68	98 98	7:1 8:1[c]
8	**2h**	**3h**	71	97	11:1
9	**2i**	**3i**	68	97	11:1
10	**2j**	**3j**	75	97	11:1

[a] Reactions were performed in 13 × 100 mm^2 pressure tubes. Cited yields are of material isolated by silica gel chromatography. Enantiomeric excess was determined by chiral stationary phase HPLC analysis via comparison to racemic diastereomeric mixtures. See Experimental Section for further details. [b] 80 °C, 72 h. [c] (*S*)-C3-TUNEPHOS was used as ligand.

diastereoselectivity was observed (Table 1, entries 21−23). Using a catalyst modified by (*S*)-SEGPHOS, the carbonyl crotylation product **3e** is formed in 70% isolated yield with 7.4:1

Scheme 3. Stereochemical Features Associated with Formation and Isomerization of the Purported Crotyl Iridium Intermediates (*Ln = (*S*)-SEGPHOS and *C,O*-Benzoate of 4-Cyano-3-nitrobenzoic Acid **l**)



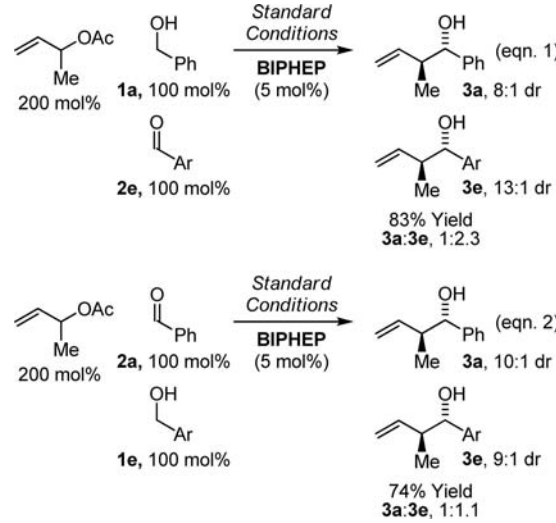
anti-diastereoselectivity and 95% enantiomeric excess (Table 1, entries 24). The TUNEPHOS ligands of Zhang[18] also were assayed (Table 1, entries 25−27). Here, (*S*)-C3-TUNEPHOS was found to provide the carbonyl crotylation product **3e** in 77% isolated yield with 8:1 *anti*-diastereoselectivity and 97% enantiomeric excess (Table 1, entry 26).

Using the aforementioned coupling conditions employing (*S*)-SEGPHOS and (*S*)-C3-TUNEPHOS, a range of alcohols were subjected to carbonyl crotylation (Table 2). In most cases, the catalyst modified by (*S*)-SEGPHOS gave superior results. In terms of scope, diverse substituted benzylic alcohols **1a**−**1f** are converted to the corresponding carbonyl crotylation products **3a**−**3f** in good to excellent yield, very good levels of *anti*-diastereoselectivity and with exceptional levels of absolute stereocontrol (Table 2, entries 1−6). As demonstrated by the conversion of cinnamyl alcohol **1g** to homoallyl alcohol **3g**, allylic alcohols participate in the coupling (Table 2, entry 7). Finally, unactivated aliphatic alcohols **1h**−**1j** are transformed to the corresponding carbonyl crotylation products **3h**−**3j** in good yield with equally high levels of relative and absolute stereocontrol (Table 2, entries 8−10).

Carbonyl crotylation from the aldehyde oxidation level employing isopropanol as the terminal reductant also was explored (Table 3). To our delight, under conditions identical to those cited in Table 2, but in the presence of isopropanol (200 mol%), aryl aldehydes **2a**−**2f**, cinnamaldehyde **2g**, and unactivated aliphatic aldehydes **2h**−**2j** are converted to the corresponding carbonyl crotylation products **3a**−**3f** with complete levels of regioselectivity, very good levels of *anti*-diastereoselectivity and with exceptional levels of enantioselectivity. Thus, carbonyl crotylation is achieved from the aldehyde or alcohol oxidation level in the absence of preformed crotylmetal reagents.

In prior studies of the parent allylation reaction,[17b] intervention of symmetric iridium π-allyl intermediates or rapid interconversion of σ-allyl haptomers through the agency of a symmetric π-allyl was inferred on the basis of isotopic labeling studies. To evaluate the nature of the purported π-crotyl iridium intermediate, optically enriched allylic acetate **4** (98% ee) was coupled to alcohol **1e** under standard conditions employing the achiral ligand BIPHEP. The product, homoallyl alcohol **5**, is produced in 48% isolated yield with 9:1 *anti*-diastereoselectivity and 14% enantiomeric excess (Scheme 2, eq 2). These data suggest racemization via π-facial interconversion of the kinetic π-crotyl iridium complex occurs at a rate only marginally slower than the rate of carbonyl addition.

Scheme 4. Experiments Establishing Rapid Redox Equilibration in Advance of Carbonyl Addition (Ar = (4-(CO_2Me)Ph)[a]



[a] Reactions were performed in 13 × 100 mm^2 pressure tubes. Cited yields are of material isolated by silica gel chromatography. See Experimental Section for further details.

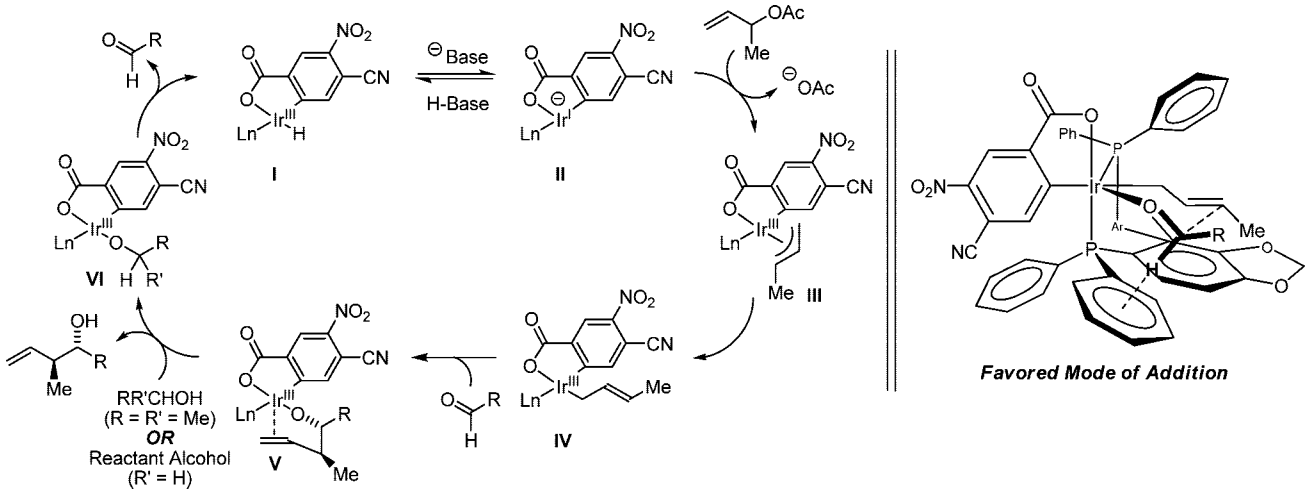
To further probe the origins of stereoselection, optically enriched allylic acetate **4** (98% ee) was coupled to alcohol **1e** under standard conditions employing iridium catalysts modified by (*S*)-SEGPHOS and (*R*)-SEGPHOS (Scheme 2, eqs 3 and 4, respectively). In the former case, excellent levels of relative and absolute stereocontrol are observed. In the later case, diminished efficiencies and reduced levels of diastereo- and enantioselectivity are evident. In both cases, recovered allylic acetate **4** exhibits significant erosion of optical purity. These experiments suggest that ionization of the (*R*)-allylic acetate **4** by the (*S*)-SEGPHOS modified iridium catalyst represents the lower energy diastereomeric pathway, that is, a stereochemically matched ionization mode. Partial racemization of recovered allylic acetate **4** suggests that ionization occurs reversibly with incomplete kinetic stereoselectivity.

Finally, in reactions employing racemic allylic acetate **4** and the iridium catalyst modified by (*S*)-SEGPHOS, recovered **4** exhibits a substantial degree of optical enrichment favoring the (*S*)-enantiomer (Scheme 2, eq 5). This result is consistent with the notion that consumption of the (*R*)-allylic acetate **4** by the (*S*)-SEGPHOS modified iridium catalyst represents a more rapid stereochemically matched reaction

(18) (a) Zhang, X. U.S, Patent 6521769, 2003 (filed 1999). (b) Zhang, Z.; Qian, H.; Longmire, J.; Zhang, X. *J. Org. Chem.* **2000**, *65*, 6223. (c) Sun, X.; Zhou, L.; Li, W.; Zhang, X. *J. Org. Chem.* **2008**, *73*, 1143.

(19) The designation of "cis" is made in reference to the substituent of the central carbon atom of the π-allyl complex.

Scheme 5. (Left) Simplified Catalytic Mechanism Proposed for the Iridium Catalyzed Transfer Hydrogenative Crotylation and (Right) Model Accounting for the Observed Sense of Relative and Absolute Stereocontrol



pathway. Notably, the degree of optical enrichment of recovered (*S*)-**4** does not increase as a function of conversion due to erosion of the optical purity of unreacted allylic acetate **4** via reversible ionization, as established in a preceding experiment (Scheme 2, eq 2).

The observed *anti*-diastereoselectivity presumably arises via kinetic formation of the *cis*-π-crotyl complex,[19] which engages the carbonyl partner by way of an (*E*)-crotyl iridium intermediate (Scheme 3). Erosion of diastereoselectivity may result via isomerization to the *trans*-π-crotyl complex, which engages the carbonyl partner by way of the (*Z*)-crotyl iridium complex to form the *syn*-diastereomer. This interpretation may account for the fact that couplings to aldehydes exhibit uniformly higher levels of diastereoselectivity. For the aldehyde couplings, carbonyl addition is anticipated to be faster as higher concentrations of aldehyde are present throughout the course of the reaction, promoting rapid capture of the kinetic allyliridium intermediate. The observation that diastereoselectivity increases with increasing concentration in couplings of alcohols further supports the veracity of this interpretation (Table 1, entries 16−18). The favorable influence of the 4-cyano-3-nitro-*C*,*O*-benzoate moiety on *anti*-diastereoselection is the subject of computational study.

Exposure of α-methyl allyl acetate to equimolar quantities of **1a** and **2e** under standard conditions employing BIPHEP as ligand provides **3a** and **3e** in 83% yield in a 1:2.3 ratio, respectively. Exposure of α-methyl allyl acetate to equimolar quantities of **2a** and **1e** under otherwise identical conditions provides **3a** and **3e** in 74% yield in a 1:1.1 ratio, respectively. These experiments demonstrate rapid redox equilibration in advance of carbonyl addition, which is relevant to crotylations conducted from the alcohol oxidation level (Scheme 4).

A simplified catalytic mechanism consistent with our collective results is depicted in Scheme 5. The *ortho*-cyclometallated iridium hydride **I** undergoes deprotonation in the presence of Cs_2CO_3 to furnish the anionic iridium(I) *C*,*O*-benzoate **II**.[20] Oxidative addition to α-methyl allyl acetate delivers the iridium π-crotyl complex **III**. The parent BINAP-ligated iridium π-allyl *C*,*O*-benzoate complex has been characterized by single-crystal X-ray diffraction and has been demonstrated to be catalytically relevant.[17b] Aldehyde addition by way of the (*E*)-σ-crotyliridium complex **IV** through a closed chairlike transition structure delivers the *anti*-homoallyl iridium alkoxide **V**. This intermediate is stable with respect to β-hydride elimination of the carbinol C−H due to occupation of the remaining coordination site at iridium(III) by the olefin moiety of the homoallylic alcohol. Exchange of the homoallyl alcohol for isopropanol or a reactant alcohol provides **VI**, which has an open coordination site and, consequently, β-hydride eliminates to regenerate the *ortho*-cyclometallated complex **I**. A stereochemical model accounting for the observed stereochemistry is analogous to that previously proposed (Scheme 5, right).

(20) As described in ref 17b, we report a crystal structure of the BINAP-ligated iridium *C*,*O*-benzoate derived from *m*-nitrobenzoic acid. Such *ortho*-cyclometallation onto *m*-nitrobenzoate was described previously for C_5Me_5−iridium complexes: Kisenyi, J. M.; Sunley, G. J.; Cabeza, J. A.; Smith, A. J.; Adams, H.; Salt, N. J.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1987**, 2459.

Summary

We report a protocol for *anti*-diastereo- and enantioselective carbonyl crotylation from the alcohol or aldehyde oxidation level under the conditions of iridium-catalyzed transfer hydrogenation. This method circumvents the use of chirally modified crotylmetal reagents or metallic terminal reductants and, consequently, avoids generation of stoichiometric metallic byproducts. Furthermore, the ability to conduct carbonyl crotylation directly from the alcohol oxidation level allows one to bypass the oxidation chemistry typically required to convert alcohols to aldehydes.

Mechanistic studies establish a matched mode of ionization for the (*R*)-acetate and the iridium catalyst modified by (*S*)-SEGPHOS, as well as reversible ionization of the allylic acetate with rapid π-facial interconversion of the resulting π-crotyl intermediate in advance of C−C bond formation. Additionally, rapid alcohol−aldehyde redox equilibration in advance of carbonyl addition is demonstrated. The 4-cyano-3-nitro-*C*,*O*-benzoate moiety appears to facilitate partitioning of the (*E*)- and (*Z*)-σ-crotyliridium intermediates and, hence, *anti*- and *syn*-diastereoselectivity. However, the specific interactions that mediate partitioning remain unclear and are currently the subject of computational analysis.

Our collective studies on C−C bond forming hydrogenation and transfer hydrogenation define a departure from the use of preformed organometallic reagents in carbonyl addition

chemistry. Future studies will focus on the development of related transformations, including imine additions from the amine oxidation level.

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Supporting Information Available: Experimental details and spectroscopic data. For unknown compounds (**3f** and **5**), ^{1}H NMR, ^{13}C NMR, IR, HRMS, and HPLC data are provided. For known compounds (**3a**−**3e** and **3g**−**3j**), ^{1}H NMR, ^{13}C NMR, and HPLC data are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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