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Iridium-Catalyzed Allylation of Chiral β-Stereogenic Alcohols: Bypassing Discrete Formation of Epimerizable Aldehydes

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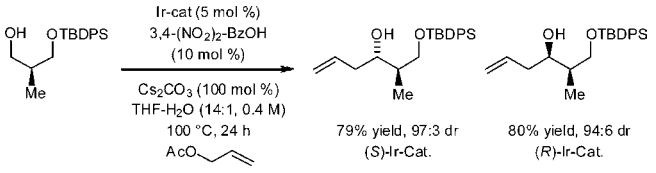
ABSTRACT



The cyclometalated π-allyliridium 3,4-dinitro-*C,O*-benzoate complex modified by (*R*)- or (*S*)-Cl,MeO-BIPHEP promotes the transfer hydrogenative coupling of allyl acetate to β-stereogenic alcohols with good to excellent levels of catalyst-directed diastereoselectivity to furnish homoallylic alcohols. Remote electronic effects of the *C,O*-benzoate of the catalyst play a critical role in suppressing epimerization of the transient α-stereogenic aldehyde.

Carbonyl allylation is one of the foremost methods utilized for the construction of polyketide natural products.[1] As established in pioneering work by Hoffmann,[2a,b] the vast majority of methods for enantioselective carbonyl allylation rely upon the use of allylmetal reagents modified by chiral auxiliaries.[2] Subsequently, enantioselective carbonyl allylations employing achiral allylmetal reagents in combination with chiral Lewis acidic and Lewis basic catalysts were developed,[3] as well as related processes catalyzed by chiral H-bond donors and Brønsted acids.[4] Other methods for catalytic carbonyl allylation include reductive couplings of allylic alcohols and their carboxylates to aldehydes,[5] and asymmetric variants of the Nozaki–Hiyama reaction.[6] Without exception, the aforementioned enantioselective methods employ either stoichiometric quantities of an allylmetal reagent or a stoichiometric (organo)metallic reductant.

In 2008, an alternate approach to enantioselective carbonyl allylation based on iridium catalyzed C–C bond

(1) For selected reviews on enantioselective carbonyl allylation, see: (a) Ramachandran, P. V. *Aldrichimica Acta* **2002**, *35*, 23. (b) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763. (c) Yu, C.-M.; Youn, J.; Jung, H.-K. *Bull. Korean Chem. Soc.* **2006**, *27*, 463. (d) Marek, I.; Sklute, G. *Chem. Commun.* **2007**, 1683. (e) Hall, D. G. *Synlett* **2007**, 1644. (f) Lachance, H.; Hall, D. G. *Org. React.* **2008**, *73*, 1. (g) Yus, M.; Gonzalez-Gomez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774.

(2) For selected examples of chirally modified allylmetal reagents, see: (a) Herold, T.; Hoffmann, R. W. *Angew. Chem., Int. Ed.* **1978**, *17*, 768. (b) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375. (c) Hayashi, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4963. (d) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092. (e) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (f) Reetz, M. *Pure Appl. Chem.* **1988**, *60*, 1607. (g) Short, R. P.; Masamune, S. *J. Am. Chem. Soc.* **1989**, *111*, 1892. (h) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1989**, *54*, 1570. (i) Corey, E. J.; Yu, C.-M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, *111*, 5495. (j) Seebach, D.; Beck, A. K.; Imwinkeiried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954. (k) Riediker, M.; Duthaler, R. O. *Angew. Chem., Int. Ed.* **1989**, *28*, 494. (l) Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 6594. (m) Kinnaird, J.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7920. (n) Hackman, B. M.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2004**, *6*, 4375. (o) Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 8044.

(3) For selected examples of catalytic enantioselective carbonyl allylation employing allylmetal reagents: (a) Furuta, K.; Mouri, M.; Yamamoto, H. *Synlett* **1991**, 561. (b) Costa, A. L.; Piazza, M. G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Am. Chem. Soc.* **1993**, *115*, 7001. (c) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467. (d) Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161. (e) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001**, *123*, 9488.

(4) For selected examples of enantioselective Brønsted acid or H-bond donor catalyzed carbonyl allylations employing allylboron reagents, see: (a) Rauniyar, V.; Hall, D. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 2426. (b) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660. (c) Rauniyar, V.; Zhai, H.; Hall, D. G. *J. Am. Chem. Soc.* **2008**, *130*, 8481. (d) Barnett, D. D.; Moquist, P. N.; Schaus, S. E. *Angew. Chem., Int. Ed.* **2009**, *48*, 8679. (e) Jain, P.; Antilla, J. C. *J. Am. Chem. Soc.* **2010**, *132*, 11884.

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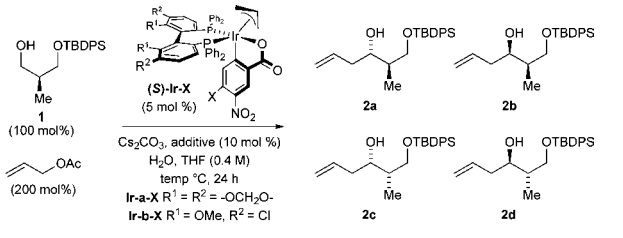
forming transfer hydrogenation was developed in our laboratory.[7,8a,8b] In these processes, primary alcohols serve dually as reductants and aldehyde precursors, allowing carbonyl addition to occur directly from the alcohol oxidation level in the absence of stoichiometric organometallic reagents. However, initial attempts to perform stereoselective C−H allylations of chiral β-stereogenic primary alcohols under these conditions, which at the time involved generation of the Ir catalyst *in situ*, were thwarted by epimerization of the transient α-stereogenic aldehydes. In subsequent work on *anti*-diastereo- and enantioselective carbonyl crotylations,[8c] it was found that *para*-substitution of the *C,O*-benzoate moiety of a cyclometalated catalyst could favorably influence selectivity and reactivity *via* remote electronic effects.[9] Additionally, conventional chromatographic isolation of the cyclometalated catalyst was found to enhance the purity and, hence, performance of the catalyst.[8d]

The enhanced efficiency observed for the chromatographically isolated catalyst, along with the ability to tune catalyst performance *via* remote electronic effects, prompted a reinvestigation of the transfer hydrogenative allylation of β-stereogenic primary alcohols. Here, we report that β-stereogenic primary alcohols participate in direct diastereoselective transfer hydrogenative allylation with good to excellent levels of catalyst-directed stereoselectivity to furnish homoallylic alcohols. This protocol bypasses discrete generation of configurationally unstable chiral α-substituted aldehydes,[10] which are used routinely in polyketide construction, yet cannot be stored or chromatographed without significant erosion of enantiomeric purity.[10a,11]

In an initial experiment, the primary alcohol **1** derived from the Roche ester[12] was exposed to the cyclometalated complex (*S*)-Ir-a-CN (5 mol %), which is modified by (*S*)-SEGPHOS, in THF/H_2O solvent at 60 °C using Cs_2CO_3 (60 mol %) as the base and 4-CN-3-NO_2BzOH as the additive. The desired allylation product **2a** was generated stereoselectively in low isolated yield (Table 1, entry 1). Elevating the reaction temperature enhanced the isolated yield of **2a**, but led to epimerization of the transient α-substituted chiral aldehyde (entries 1−4). Remarkably, increased loadings of Cs_2CO_3 (100 mol %) improved the isolated yield of **2a** while suppressing epimerization, and

Table 1. Direct Allylation of the "Roche Alcohol" **1** with Catalyst-Directed Diastereoselectivity[a]



entry	temp °C	additive	H_2O (mol %)	Cs_2CO_3 (mol %)	Ir-X	yield (**2a**:**2b**:**2c**:**2d**)
1	80	4-CN-3-NO_2-BzOH	700	60	(*S*)-Ir-a-CN	19% (95:1:4:0)
2	90	4-CN-3-NO_2-BzOH	700	60	(*S*)-Ir-a-CN	67% (87:2:11:0)
3	100	4-CN-3-NO_2-BzOH	700	60	(*S*)-Ir-a-CN	71% (84:3:12:1)
4	110	4-CN-3-NO_2-BzOH	700	60	(*S*)-Ir-a-CN	68% (87:2:10:1)
5	100	4-CN-3-NO_2-BzOH	700	10	(*S*)-Ir-a-CN	14% (73:4:22:1)
6	100	4-CN-3-NO_2-BzOH	700	30	(*S*)-Ir-a-CN	60% (84:2:13:1)
7	100	4-CN-3-NO_2-BzOH	700	100	(*S*)-Ir-a-CN	77% (92:5:3:0)
8	100	4-CN-3-NO_2-BzOH	700	130	(*S*)-Ir-a-CN	41% (93:4:3:0)
9	100	4-CN-3-NO_2-BzOH	---	100	(*S*)-Ir-a-CN	22% (68:4:25:3)
10	100	4-Cl-3-NO_2-BzOH	700	100	(*S*)-Ir-a-Cl	79% (94:2:4:0)
11	100	---	700	100	(*S*)-Ir-a-Cl	68% (91:6:3:0)
12	100	3-NO_2-BzOH	700	100	(*S*)-Ir-a-H	59% (92:2:6:0)
13	100	4-OMe-3-NO_2-BzOH	700	100	(*S*)-Ir-a-OMe	28% (89:7:4:0)
14	100	3,4-$(NO_2)_2$-BzOH	700	100	(*S*)-Ir-a-NO_2	71% (94:3:3:0)
15	100	3,4-$(NO_2)_2$-BzOH	700	100	(*S*)-Ir-b-NO_2	76% (97:2:1:0)
⇨ **16**	**100**	**3,4-$(NO_2)_2$-BzOH**	**1000**	**100**	**(*S*)-Ir-b-NO_2**	**79% (97:2:1:0)**
17	100	4-Cl-3-NO_2-BzOH	700	100	(*R*)-Ir-a-Cl	79% (7:89:0:4)
18	100	4-CN-3-NO_2-BzOH	700	100	(*R*)-Ir-a-CN	73% (5:93:0:2)
19	100	3,4-$(NO_2)_2$-BzOH	700	100	(*R*)-Ir-b-NO_2	65% (2:96:0:2)
⇨ **20**	**100**	**3,4-$(NO_2)_2$-BzOH**	**1000**	**100**	**(*R*)-Ir-b-NO_2**	**80% (4:94:0:2)**

[a] Cited yields are of diastereomeric mixtures isolated by silica gel chromatography. Stereoisomeric ratios were determined by chiral stationary phase HPLC analysis using authentic samples of diastereomers **2a**−**2d**. See Supporting Information for further experimental details.

(5) For selected examples of enantioselective carbonyl allylations employing nucleophilic π-allyls derived from allylic alcohols and their carboxylates, see: (a) Zanoni, G.; Gladiali, S.; Marchetti, A.; Piccinini, P.; Tredici, I.; Vidari, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 846. (b) Zhu, S.-F.; Yang, Y.; Wang, L.-W.; Liu, B.; Zhou, Q.-L. *Org. Lett.* **2005**, *7*, 2333. (c) Howell, G. P.; Minnaard, A. J.; Feringa, B. L. *Org. Biomol. Chem.* **2006**, *4*, 1278. (d) Zhang, T.-Z.; Dai, L.-X.; Hou, X.-L. *Tetrahedron: Asymmetry* **2007**, *18*, 251. (e) Wang, W.-F.; Zhang, T.; Shi, M. *Organometallics* **2009**, *28*, 2640. (f) Jiang, J.-J.; Wang, D.; Wang, W.-F.; Yuan, Z.-L.; Zhao, M.-X.; Wang, F.-J.; Shi, M. *Tetrahedron: Asymmetry* **2010**, *21*, 2050. (g) Vogt, M.; Ceylan, S.; Kirschning, A. *Tetrahedron* **2010**, *66*, 6450. (h) Zhu, S.-F.; Qiao, X.-C.; Zhang, Y.-Z.; Wang, L.-X.; Zhou, Q.-L. *Chem. Sci.* **2011**, *2*, 1135.

(6) For catalytic enantioselective carbonyl allylation and crotylation *via* Nozaki−Hiyama coupling, see: (a) Bandini, M.; Cozzi, P. G.; Umani-Ronchi, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 3357. (b) Bandini, M.; Cozzi, P. G.; Umani-Ronchi, A. *Polyhedron* **2000**, *19*, 537. (c) Bandini, M.; Cozzi, P. G.; Umani-Ronchi, A. *Tetrahedron* **2001**, *57*, 835. (d) Inoue, M.; Suzuki, T.; Nakada, M. *J. Am. Chem. Soc.* **2003**, *125*, 1140. (e) Berkessel, A.; Mench, D.; Sklorz, C. A.; Schröder, M.; Paterson, I. *Angew. Chem., Int. Ed.* **2003**, *42*, 1032. (f) Lee, J.-Y; Miller, J. J.; Hamilton, S. S.; Sigman, M. S. *Org. Lett.* **2005**, *7*, 1837. (g) McManus, H. A.; Cozzi, P. G.; Guiry, P. J. *Adv. Synth. Catal.* **2006**, *348*, 551. (h) Xia, G.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 2554. (i) Hargaden, G. C.; Müller-Bunz, H.; Guiry, P. J. *Eur. J. Org. Chem.* **2007**, 4235. (j) Hargaden, G. C.; O'Sullivan, T.; Guiry, P. J. *Org. Biomol. Chem.* **2008**, *6*, 562. (k) Zhang, Z.; Huang, J.; Ma, B.; Kishi, Y. *Org. Lett.* **2008**, *10*, 3073. (l) White, J. D.; Shaw, S. *Org. Lett.* **2011**, *13*, 2488.

(7) 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.* **2008**, *48*, 34. (b) Patman, R. L.; Bower, J. F.; Kim, I. S.; Krische, M. J. *Aldrichimica Acta* **2008**, *41*, 95. (c) Han, S. B.; Kim, I. S.; Krische, M. J. *Chem. Commun.* **2009**, 7278. (d) Bower, J. F.; Krische, M. J. *Top. Organomet. Chem.* **2011**, *43*, 107. (e) Hassan, A.; Krische, M. J. *Org. Process Res. Dev.* **2011**, *15*, 1236.

(8) (a) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6340. (b) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 14891. (c) Kim, I. S.; Han, S. B.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 2514. (d) Gao, X.; Townsend, I. A.; Krische, M. J. *J. Org. Chem.* **2011**, *76*, 2350.

(9) For selected examples of remote electronic effects in enantioselective catalysis, see: (a) Jacobsen, E. N.; Zhang, W.; Güller, M. L. *J. Am. Chem. Soc.* **1991**, *113*, 6703. (b) RajanBabu, T. V.; Ayers, T. A.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 4101. (c) Hamada, T.; Fukuda, T.; Imanishi, H.; Katsuki, T. *Tetrahedron* **1996**, *52*, 515. (d) Shiomi, T.; Ito, J.-I.; Yamamoto, Y.; Nishiyama, H. *Eur. J. Org. Chem.* **2006**, 5594.

(10) For selected examples of problematic aldehyde epimerization, see: (a) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348. (b) Nelson, S. G.; Bungard, C. J.; Wang, K. *J. Am. Chem. Soc.* **2003**, *125*, 13000. (c) Haidle, A. M.; Myers, A. G. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12048. (d) Lane, J. W.; Chen, Y.; Williams, R. M. *J. Am. Chem. Soc.* **2005**, *127*, 12684. (e) Hara, A.; Morimoto, R.; Ishikawa, Y.; Nishiyama, S. *Org. Lett.* **2011**, *13*, 4036.

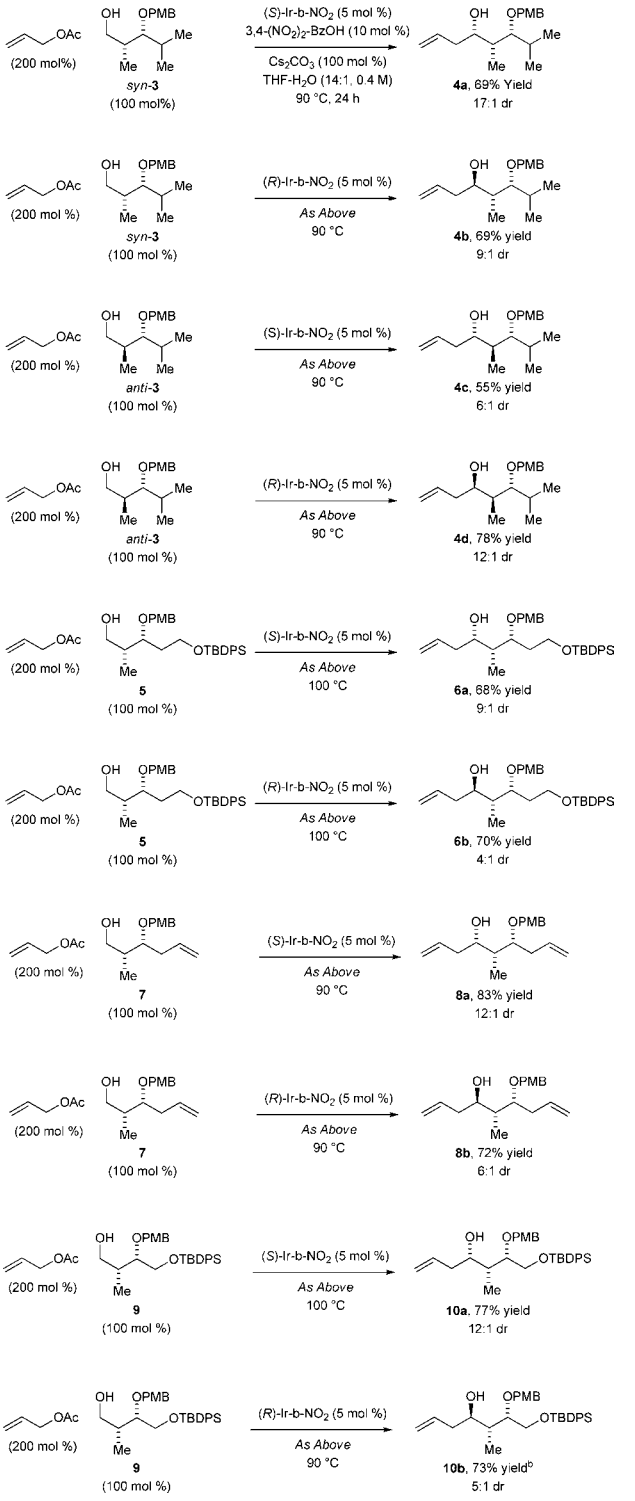
(11) As stated in ref 10a, footnote 12, attempts to purify the Roche aldehyde by silica gel chromatography resulted in 5−7% racemization.

(12) Cohen, N.; Eichel, W. F.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1976**, *41*, 3505.

use of excess Cs_2CO_3 relative to alcohol **1** resulted in diminished yield, but high diastereoselectivity was maintained (entries 5−8). Water suppresses competitive transesterification between allyl acetate and alcohol **1** and epimerization to form **2c** (entry 9). As revealed in a comparison of 4-substituted *C,O*-benzoates (entries 7, 10, 12−14), an optimal balance in yield and selectivity is obtained using the 3,4-dinitro-*C,O*-benzoate (entry 14). Perhaps related to the observation that the cyclometalated *C,O*-benzoate moiety of the catalyst is kinetically labile and can exchange with exogenous benzoic acid, added benzoic acid improves the isolated yield of **2a** (entry 11). Finally, by changing the ligand of the 3,4-dinitro-*C,O*-benzoate to (*S*)-Cl,MeO-BIPHEP, and by increasing the loading of water, alcohol **1** is converted to the product of allylation **2a** in optimal isolated yield and selectivity (entries 15, 16). This catalyst, (*R*)-Ir-b-NO_2, was characterized by single crystal X-ray diffraction. Under these same conditions, the enantiomeric catalyst (*R*)-Ir-b-NO_2 delivers the diastereomeric product **2b** with optimal levels of stereoselectivity (entry 20). Thus, diastereomeric products of carbonyl allylation **2a** (32:1 dr) or **2b** (15:1 dr) are formed with good levels of catalyst-directed diastereoselectivity[13] and with exceptionally little racemization of the transient aldehyde. Notably, the "Roche aldehyde" is known to suffer significant racemization upon exposure to silica gel chromatography.[10a,11] The formation of **2a** represents the "matched case," wherein the diastereofacial bias of the catalyst is amplified by Felkin−Anh selectivity embodied by the transient aldehyde, and the formation of **2b** represents the corresponding mismatched cases.

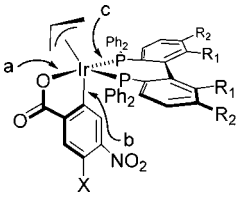
Using these optimal conditions, the catalyst-directed diastereoselective allylation of higher chiral alcohols possessing embedded propionate substructures was explored (Scheme 1). Upon exposure of alcohol *syn*-**3** to the catalyst (*S*)-Ir-b-NO_2 under standard conditions, the desired product of allylation **4a** is obtained as a 17:1 mixture of diastereomers. The enantiomeric catalyst (*R*)-Ir-b-NO_2 delivers the diastereomeric product **4b** as a 9:1 mixture of diastereomers. Similarly, exposure of alcohol *anti*-**3**, which is formed *via* asymmetric *anti*-aldol addition of isobutyraldehyde, to the catalysts (*S*)-Ir-b-NO_2 and (*R*)-Ir-b-NO_2 under standard conditions provides diastereomers **4c** (6:1 dr) and **4d** (12:1 dr), respectively. Thus, all four diastereomers, **4a**−**4d**, are accessible *via* catalyst-directed diastereoselective *C*-allylation of primary alcohols *syn*-**3** and *anti*-**3**. In a similar fashion, alcohols **5**, **7**, and **9** are converted to their respective diastereomeric products **6a** and **6b**, **8a** and **8b**, and **10a** and **10b**, with good levels of catalyst-directed stereocontrol. In contrast to the "Roche alcohol" **1**, the minor diastereomer obtained from the allylation of β-substituted chiral alcohols *syn*-**3**, *anti*-**3**, **5**, **7**, and **9** principally stems from epimerization of the

Scheme 1. Catalyst-Directed Diastereoselective *C*-Allylation of Chiral Alcohols *syn*-**3**, *anti*-**3**, **5**, **7**, and **9**[a]



[a] Cited yields are of diastereomeric mixtures isolated by silica gel chromatography. Stereoisomeric ratios were determined by ^{1}H NMR analysis of crude reaction mixtures (major diastereomer:sum of two minor diastereomers). See Supporting Information for further experimental details. [b] 48 h.

(13) For selected examples of catalyst-directed diastereoselectivity, see: (a) Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109. (b) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A.; Sharpless, K. B.; Walker, F. J. *Science* **1983**, *220*, 949. (c) Kobayashi, S.; Ohtsubo, A.; Mukaiyama, T. *Chem. Lett.* **1991**, 831. (d) Hammadi, A.; Nuzillard, J. M.; Poulin, J. C.; Kagan, H. B. *Tetrahedron: Asymmetry* **1992**, *3*, 1247. (e) Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 8837. (f) Trost, B. M.; Calkins, T. L.; Oertelt, C.; Zambrano, J. *Tetrahedron Lett.* **1998**, *39*, 1713. (g) Balskus, E. P.; Jacobsen, E. N. *Science* **2007**, *317*, 1736. (h) Han, S. B.; Kong, J. R.; Krische, M. J. *Org. Lett.* **2008**, *10*, 4133.



Ir-a-X $R^1 = R^2 =$ -OCH_2O- (SEGPHOS)
Ir-b-X $R^1 =$ OMe, $R^2 =$ Cl (Cl,MeO-BIPHEP)

Ir-Complex	Bond a (Å)	Bond b (Å)	Bond c (Å)
(*R*)-Ir-a-OMe	2.107	2.068	2.260
(*S*)-Ir-a-H	2.112	2.074	2.262
(*R*)-Ir-a-NO_2	2.121	2.072	2.277
(*R*)-Ir-b-NO_2	2.131	2.088	2.329

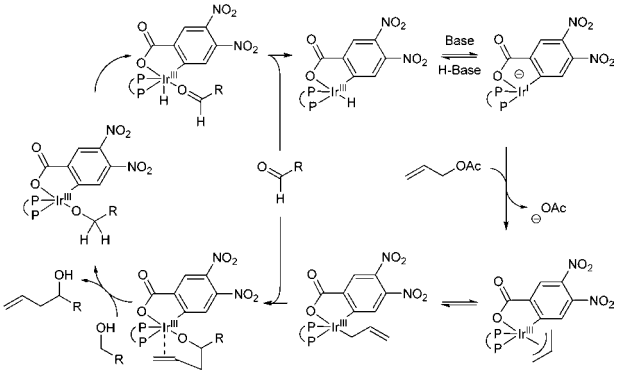
Figure 1. Survey of selected bond lengths from a series of π-allyliridium C,O-benzoate complexes as determined by single crystal x-ray diffraction analysis. See Supporting Information for single crystal X-ray diffraction data of complexes (*R*)-Ir-a-OMe, (*R*)-Ir-a-NO_2, and (*R*)-Ir-b-NO_2.

transient aldehydes. Here, it is likely that increased steric demand of the aldehyde retards the rate of C−C bond formation with respect to aldehyde epimerization. For the redox-allylation of chiral β-stereogenic alcohols, the presence of an electron-withdrawing group at the 4-position of the *C,O*-benzoate moiety was found to favorably influence conversion and stereoselectivity, minimizing epimerization of the transient chiral α-stereogenic aldehyde.

To gain insight into how electronic characteristics of the *C,O*-benzoate moiety manifest structurally, a series of π-allyliridium *C,O*-benzoate complexes were analyzed *via* single crystal X-ray diffraction and selected bond lengths were surveyed (Figure 1). While the influence of crystal packing forces on bond length cannot be quantified, a clear trend in the series (*R*)-Ir-a-OMe, (*S*)-Ir-a-H, (*R*)-Ir-a-NO_2, and (*R*)-Ir-b-NO_2 is apparent: the more electron deficient the *C,O*-benzoate moiety, the longer the C−Ir, O−Ir, and P−Ir bonds. The elongation of bonds to iridium, as evident in (*R*)-Ir-b-NO_2, naturally suggests greater Lewis acidity at iridium. This interpretation is corroborated by the infrared absorption of the iridium carboxylate moiety of (*R*)-Ir-a-NO_2 (1648 cm^{-1}) and (*R*)-Ir-a-OMe (1633 cm^{-1}).

The favorable influence of the 4-nitro-moiety of the *C,O*-benzoate ligand on conversion and stereoselectivity may be interpreted on the basis of the previously postulated catalytic mechanism (Scheme 2).[8b] Enhanced Lewis acidity at iridium may strengthen the agostic interaction between the iridium center and the carbinol C−H bond, thereby facilitating alcohol dehydrogenation. Additionally, the highly inductive nature of the 4-nitro-moiety may facilitate deprotonation of the iridium(III) hydride obtained upon

Scheme 2. General Catalytic Mechanism



alcohol dehydrogenation. Finally, both carbonyl addition and product-to-reactant alkoxide exchange may be accelerated by enhanced Lewis acidity at iridium. An acceleration of carbonyl addition with respect to aldehyde epimerization in response to enhanced Lewis acidity would account for how remote electron-withdrawing groups of the catalyst serve to minimize racemization of the transient chiral α-stereogenic aldehyde.

In summary, cyclometalated π-allyliridium 3,4-dinitro-*C,O*-benzoate complexes modified by (*R*)- or (*S*)-Cl,MeO-BIPHEP promote the direct C−H allylation of diverse β-substituted chiral primary alcohols to furnish homoallylic alcohols with good to excellent levels of catalyst-directed diastereoselectivity accompanied by minimal epimerization of the transient α-stereogenic aldehyde intermediates. This protocol avoids discrete generation of configurationally and chemically labile chiral α-substituted aldehydes[10a,11] in asymmetric carbonyl allylation.

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Supporting Information Available. Spectral data for all new compounds (^{1}H NMR, ^{13}C NMR, IR, HRMS). Single crystal X-ray diffraction data of complexes (*R*)-Ir-a-OMe, (*R*)-Ir-a-NO_2, and (*R*)-Ir-b-NO_2. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.