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Enantioselective Alkynylation of Aldehydes with 1-Haloalkynes Catalyzed by Tethered Bis(8-quinolinato) Chromium Complex

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Supporting Information

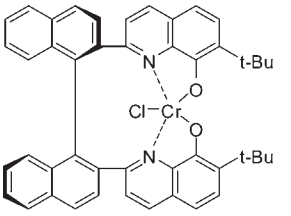
ABSTRACT: The first example of Cr-catalyzed asymmetric alkynylation of aldehydes with 1-iodo- and 1-bromoalkynes was developed. The use of tethered bis(8-quinolinato) chromium catalyst (3 mol %) allowed preparation of enantioenriched propargyl alcohols with good yields and enantioselectivities up to 92% ee. 1-Bromoalkynes can be activated by the introduction of a cobalt porphine co-catalyst, which enables shorter reaction times without any loss of enantiocontrol.

Chiral propargyl alcohols are useful and versatile building blocks in organic synthesis.[1] The general synthetic approaches to these compounds involve asymmetric reduction of ynones[2] and metal-mediated asymmetric alkynylation of the carbonyl group.[3−11] The methods of the latter group are based on the use of a chiral inductor alongside with either stoichiometric amounts of organometallic reagent[4−7] or a combination of an alkyne, an organic base, and catalytic amounts of a metal source;[8−11] systems based on zinc,[5,8] titanium,[6] copper,[7,9] indium,[10] and ruthenium[11] reagents have been reported. Generation of a metal acetylide from an alkyne is the unifying concept of these methods. However, alternative approaches to access propargyl alcohols in the enantioenriched form remain rather underrepresented;[12] in this context, we became interested in the possible expansion of redox chemistry into this field of asymmetric catalysis.

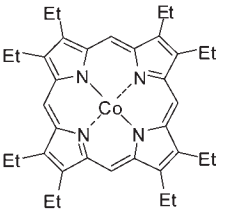
The reaction of 1-iodoalkynes with aldehydes and ketones mediated by stoichiometric amounts of $CrCl_2$ was reported by Takai and Oshima in 1985.[13] This method provided access to propargyl alcohols in mild conditions and allowed selective alkynylation of an aldehyde moiety in the presence of a keto group. In 1987, Kishi implemented a modified protocol into the synthesis of Halichondrin B fragment; as low as 0.01% of nickel chloride was used as a catalyst alongside with stoichiometric amounts of chromium.[14] Since then, Cr-mediated alkynylation has been extensively used in synthesis due to such advantages as compatibility with labile aldehydes and functional group tolerance.[15,16] In 1996, Fürstner reported[17a] this reaction using catalytic amounts of chromium(II) chloride, and subsequent total synthesis implementations were published later on.[17b] Few other protocols catalytic in chromium have also been described.[18] However, despite the high synthetic potential of this methodology, no enantioselective variants have ever been reported.

In 2004, our group developed a tethered bis(8-quinolinato) (TBOx) chromium complex **1** (Chart 1),[19] which has been successfully applied to asymmetric Nozaki−Hiyama allylation,[20a] allenylation,[20b] and propargylation[20c] of aldehydes as well as to asymmetric pinacol coupling[20d] and synthesis of 1,3-butadien-2-ylcarbinols.[20e] Herein, we report the first example of Cr-catalyzed enantioselective alkynylation of aldehydes with 1-haloalkynes mediated by complex **1**.

Chart 1. TBOx Chromium Catalyst and Cobalt Porphine Co-catalyst for Asymmetric Alkynylation of Aldehydes



1



2

1-Haloalkynes can be easily prepared from the corresponding terminal alkynes in good to excellent yields.[21] We started our studies on Cr-catalyzed asymmetric alkynylation on benzaldehyde as a model substrate using the conditions previously reported for other TBOxCrCl-mediated processes.[20a,20c,20d] To our delight, the use of phenyliodoacetylene smoothly furnished the desired propargyl alcohol with good yield and promising enantioselectivity (Table 1, entry 1). The bromo and chloro analogues demonstrated somewhat higher stereoselectivities at the expense of considerably longer reaction times (entries 2 and 3). The effect of the silyl chloride on the reaction outcome was not as profound as in the case of TBOxCrCl-mediated asymmetric propargylation;[20c] the use of bulkier silyl chlorides resulted in slightly higher ee values, which were accompanied with decreased reactivities (entries 4−9). Lowering the reaction temperature to 0 °C also resulted in enhanced enantiocontrol; however, the reaction rate decreased dramatically (entry 10). Solvent screening identified a rather narrow range of suitable solvents (entries 11−13);[22] the reaction carried out in 2-methyltetrahydrofuran yielded the product with the highest enantioselectivity of 88% ee. Interestingly, the same increase in stereoselectivity was observed when *N*-methylimidazole (20 mol %) was used as an additive to the reaction run in tetrahydrofuran (Table 1, entry 14). For convenience and the optimum reaction outcome, these conditions were chosen for the substrate/iodoalkyne screening experiments.[23]

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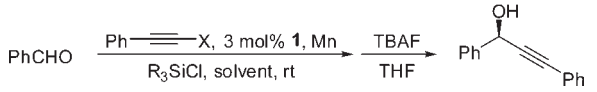
Table 1. Optimization of Cr-Catalyzed Asymmetric Alkynylation[a]



entry	X	R_3Si	solvent	time (h)	yield (%)[b]	ee (%)[c]
1	I	TES	THF	15	81	83
2	Br	TES	THF	60	74	89
3	Cl	TES	THF	60	30 (35)	88
4	I	TMS	THF	15	88	82
5	I	$TMSSiMe_2$	THF	15	79	75
6	I	n-Pr_3Si	THF	36	83	86
7	I	n-Bu_3Si	THF	36	68	80
8	I	TTMSS	THF	36	46 (50)	87
9	I	TBDMS	THF	36	44 (82)	87
10[d]	I	TES	THF	160	91	91
11[e]	I	TES	DME	15	25 (67)	87
12	I	TES	2-MeTHF	15	63 (75)	88
13	I	TES	MeCN	15	68 (93)	82
14[f]	**I**	**TES**	**THF**	**20**	**82**	**88**
15[g]	Br	TES	THF	32	74	89
16[g]	I	TES	THF	20	75	81

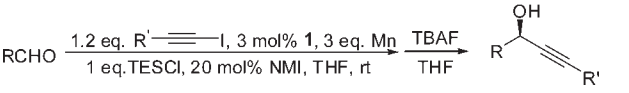
[a] Abbreviations: TES, triethylsilyl; TTMSS, tris(trimethylsilyl)silyl; TBDMS, *tert*-butyldimethylsilyl; 2-MeTHF, 2-methyltetrahydrofuran. [b] Isolated yields after column chromatography. For the reactions stopped before completion, conversions of benzaldehyde are given in parentheses. [c] Determined by HPLC analysis. [d] The reaction was carried out at 0 °C. [e] A 2:1 ratio of pinacol coupling:alkynylation products was detected. [f] 20 mol % of *N*-methylimidazole was used as an additive. [g] 1 mol % of complex **2** was added.

A range of substrates were tested in the reaction with phenyl- and alkyl-substituted 1-iodoalkynes under catalysis by complex **1** (Table 2). Aromatic, heteroaromatic, and α,β-unsaturated aldehydes were tolerated; aliphatic substrates demonstrated unsatisfactory results. Reactions involving *ortho*-substituted aromatic aldehydes required somewhat longer times for completion. The presence of the ester moiety was well tolerated (entry 12). The use of 1-iodo-3,3-dimethylbut-1-yne resulted in lowered enantioselectivities (entries 13 and 14) compared to the *n*-butyl-substituted analogue (entries 15−17).

We have recently demonstrated that the implementation of Co porphine co-catalysis into TBOxCrCl-mediated asymmetric Nozaki−Hiyama propargylation could increase the rate of the catalytic process.[20c] Likewise, this approach appeared to be beneficial for the methodology reported herein. The rate of the reaction involving phenylbromoacetylene could be increased by the addition of 1 mol % of commercially available complex **2**; the enantioselectivity level remained unchanged, whereas the reaction time decreased 2-fold (Table 1, entry 15 vs 2). In the case of the analogous iodoalkyne, the product was obtained with somewhat lower enantiomeric purity, which is presumably due to the background process (entry 16).

We were curious about comparison of the catalytic performance of TBOxCrCl (*cis*-β-configuration of the metal) in asymmetric alkynylaton with a structurally different catalyst, namely Cr(salen) system (*trans*-configuration). Interestingly,

Table 2. TBOxCrCl-Catalyzed Asymmetric Alkynylation[a]



entry	R	R′	time (h)	yield (%)[b]	ee (%)[c]
1	Ph	Ph	20	82	88
2	2-furanyl	Ph	18	88	84
3	PhCH=C(Me)[d]	Ph	84	75	79
4	o-MeC_6H_4	Ph	84	72	86
5	o-ClC_6H_4	Ph	45	45	69
6	o-FC_6H_4	Ph	36	79	82
7	p-MeC_6H_4	Ph	45	85	89
8	p-ClC_6H_4	Ph	36	58	83
9	1-naphthyl	Ph	42	82	92
10	2-naphthyl	Ph	36	52	87
12[e]	p-$MeO_2CC_6H_4$	Ph	32	66	87
13	Ph	*t*-Bu	48	70	75
14	PhCH=C(Me)[d]	*t*-Bu	36	87	79
15	Ph	*n*-Bu	48	87	85
16	2-furanyl	*n*-Bu	24	76	72
17	PhCH=C(Me)[d]	*n*-Bu	36	82	84

[a] Abbreviations: TES, triethylsilyl; NMI, *N*-methylimidazole. [b] Isolated yields after column chromatography. [c] Determined by HPLC analysis. [d] (*E*)-isomer. [e] As the product is unstable toward TBAF, desilylation was accomplished using 0.15 M HCl/aqueous THF.

the use of (*R*,*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminochromium(III) chloride[24] under conditions corresponding to Table 1, entry 1, resulted in isolation of the racemic product in 58% yield after 60 h. This observation emphasizes the well-matched design of the TBOx backbone for both reactivity and stereoselectivity of asymmetric alkynylation.

In summary, we have developed the first example of Cr-catalyzed asymmetric alkynylation of aldehydes with 1-iodo- and 1-bromoalkynes. A range of propargyl alcohols was obtained with generally good yields and high enantioselectivities (up to 92% ee). Introduction of cobalt porphine co-catalyst **2** was found to enhance the reactivity of 1-bromoalkynes without any loss of the enantiocontrol. Further investigations on the potential of the developed methodology and mechanistic studies of the catalytic cycle[25] are currently underway in our group.

■ ASSOCIATED CONTENT

Supporting Information. Complete experimental procedures and characterization data for the prepared compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995.

(2) For selected reports see: (a) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867–869. (b) Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717–6725. (c) Cho, B. T.; Park, W. S. *Bull. Kor. Chem. Soc.* **1987**, *8*, 257–260. (d) Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938–10939. (e) Parker, K. A.; Ledeboer, M. W. *J. Org. Chem.* **1996**, *61*, 3214–3217. (f) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738–8739. (g) Bach, J.; Garcia, J. *Tetrahedron Lett.* **1998**, *39*, 6761–6764. (h) Eagon, S.; DeLieto, C.; McDonald, W. J.; Haddenham, D.; Saavedra, J.; Kim, J.; Singaram, B. *J. Org. Chem.* **2010**, *75*, 7717–7725.

(3) For reviews see: (a) Frantz, D. E.; Fässler, R.; Tomooka, C. S.; Carreira, E. M. *Acc. Chem. Res.* **2000**, *33*, 373–381. (b) Pu, L. *Tetrahedron* **2003**, *59*, 9873–9886. (c) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem.* **2004**, 4095–4105. (d) Lu, G.; Li, Y.-M.; Li, X.-S.; Chan, A. S. C. *Coord. Chem. Rev.* **2005**, *249*, 1736–1744. (e) Trost, B. M.; Weiss, A. H. *Adv. Synth. Catal.* **2009**, *351*, 963–983.

(4) (a) Mukaiyama, T.; Suzuki, K.; Soai, K.; Sato, T. *Chem. Lett.* **1979**, 447–448. (b) Thompson, A. S.; Corley, E. G.; Huntington, M. F.; Grabowski, E. J. J. *Tetrahedron Lett.* **1995**, *36*, 8937–8940.

(5) (a) Niwa, S.; Soai, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 937–943. (b) Tombo, G. M. R.; Didier, E.; Loubinoux, B. *Synlett* **1990**, 547–548. (c) Ishizaki, M.; Hoshino, O. *Tetrahedron: Asymmetry* **1994**, *5*, 1901–1904. (d) Li, Z.; Upadhyay, V.; DeCamp, A. E.; DiMichele, L.; Reider, P. J. *Synthesis* **1999**, 1453–1456. (e) Tan, L.; Chen, C.; Tillyer, R. D.; Grabowski, E. J. J.; Reider, P. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 711–713. (f) Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806–1807. (g) Boyall, D.; López, F.; Sasaki, H.; Frantz, D. E.; Carreira, E. M. *Org. Lett.* **2000**, *2*, 4233–4236. (h) Sasaki, H.; Boyall, D.; Carreira, E. M. *Helv. Chim. Acta* **2001**, *84*, 964–971. (i) El-Sayed, E.; Anand, N. K.; Carreira, E. M. *Org. Lett.* **2001**, *3*, 3017–3020. (j) Lu, G.; Li, X.-S.; Zhou, Z. Y.; Chan, W. L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 2147–2152. (k) Xu, M.-H.; Pu, L. *Org. Lett.* **2002**, *4*, 4555–4557. (l) Diez, R. S.; Adger, B.; Carreira, E. M. *Tetrahedron* **2002**, *58*, 8341–8344. (m) Cozzi, P. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 2895–2898. (n) Saito, B.; Katsuki, T. *Synlett* **2004**, 1557–1560. (o) Kang, Y.-F.; Liu, L.; Wang, R.; Yan, W.-J.; Zhou, Y.-F. *Tetrahedron: Asymmetry* **2004**, *15*, 3155–3159. (p) Dahmen, S. *Org. Lett.* **2004**, *6*, 2113–2116. (q) Kang, Y.; Wang, R.; Liu, L.; Da, C.; Yan, W.; Xu, Z. *Tetrahedron Lett.* **2005**, *46*, 863–865. (r) Kang, Y. F.; Liu, L.; Wang, R.; Zhou, Y.-F.; Yan, W. *Adv. Synth. Catal.* **2005**, *347*, 243–247. (s) Trost, B. M.; Weiss, A. H.; von Wangelin, A. J. *J. Am. Chem. Soc.* **2006**, *128*, 8–9. (t) Chen, C.; Hong, L.; Xu, Z.-Q.; Liu, L.; Wang, R. *Org. Lett.* **2006**, *8*, 2277–2280. (u) Wolf, C.; Liu, S. *J. Am. Chem. Soc.* **2006**, *128*, 10996–10997. (v) Wang, Q.; Zhang, B.; Hu, G.; Chen, C.; Zhao, Q.; Wang, R. *Org. Biomol. Chem.* **2007**, *5*, 1161–1163. (w) Li, Z. B.; Liu, T.-D.; Pu, L. *J. Org. Chem.* **2007**, *72*, 4340–4343. (x) Wang, M.-C.; Zhang, Q.-J.; Zhao, W.-X.; Wang, X.-D.; Ding, X.; Jing, T.-T.; Song, M.-P. *J. Org. Chem.* **2008**, *73*, 168–176. (y) Li, H.; Huang, Y.; Jin, W.; Xue, F.; Wan, B. *Tetrahedron Lett.* **2008**, *49*, 1686–1689. (z) Niu, J. L.; Wang, M.-C.; Lu, L.; Ding, G.-L.; Lu, H.-J.; Chen, Q.-T.; Song, M.-P. *Tetrahedron: Asymmetry* **2009**, *20*, 2616–2621. (aa) Blay, G.; Cardona, L.; Fernández, I.; Marco-Aleixandre, A.; Muñoz, M. C.; Pedro, J. R. *Org. Biomol. Chem.* **2009**, *7*, 4301–4308. (ab) Omote, M.; Eto, Y.; Tarui, A.; Sato, K.; Ando, A. *Tetrahedron: Asymmetry* **2009**, *20*, 602–604. (ac) Xu, Z.; Wu, N.; Ding, Z.; Wang, T.; Mao, J.; Zhang, Y. *Tetrahedron Lett.* **2009**, *50*, 926–929.

(6) (a) Moore, D.; Pu, L. *Org. Lett.* **2002**, *4*, 1855–1857. (b) Gao, G.; Moore, D.; Xie, R.-G.; Pu, L. *Org. Lett.* **2002**, *4*, 4143–4146. (c) Lu, G.; Li, X.; Chan, W.-L.; Chan, A. S. C. *Chem. Commun.* **2002**, 172–173. (d) Li, X.-S.; Lu, G.; Kwok, W. H.; Chan, A. S. C. *J. Am. Chem. Soc.* **2002**, *124*, 12636–12637. (e) Lu, G.; Li, X.-S.; Chen, G.; Chan, W. L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2003**, *14*, 449–452. (f) Gao, G.; Xie, R.-G.; Pu, L. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5417–5420. (g) Liu, L.; Pu, L. *Tetrahedron* **2004**, *60*, 7427–7430. (h) Cozzi, P. G.; Alesi, S. *Chem. Commun.* **2004**, 2448–2449. (i) Zhou, Y.; Wang, R.; Xu, Z.; Yan, W.; Liu, L.; Kang, Y.; Han, Z. *Org. Lett.* **2004**, *6*, 4147–4149. (j) Gao, G.; Wang, Q.; Yu, X.-Q.; Xie, R.-G.; Pu, L. *Angew. Chem., Int. Ed.* **2006**, *45*, 122–125. (k) Rajaram, A. R.; Pu, L. *Org. Lett.* **2006**, *8*, 2019–2021. (l) Lin, L.; Jiang, X.; Liu, W.; Qiu, L.; Xu, Z.; Xu, J.; Chan, A. S. C.; Wang, R. *Org. Lett.* **2007**, *9*, 2329–2332. (m) Li, X.; Lu, G.; Jia, X.; Wu, Y.; Chan, A. S. C. *Chirality* **2007**, *19*, 638–641. (n) Xu, J.; Mao, J.; Zhang, Y. *Org. Biomol. Chem.* **2008**, *6*, 1288–1292. (o) Hui, X. P.; Yin, C.; Chen, Z.-C.; Huang, L.-N.; Xu, P.-F.; Fan, G. F. *Tetrahedron* **2008**, *64*, 2553–2558. (p) Xu, Z.; Mao, J.; Zhang, Y. *Org. Biomol. Chem.* **2008**, *6*, 1288–1292. (q) Wu, L.; Zheng, L.; Zong, L.; Xu, J.; Cheng, Y. *Tetrahedron* **2008**, *64*, 2651–2657. (r) Mao, J.; Bao, Z.; Guo, J.; Ji, S. *Tetrahedron* **2008**, *64*, 9901–9905. (s) Catir, M.; Cakici, M.; Karabuga, S.; Ulukanli, S.; Sahin, E.; Kilic, H. *Tetrahedron: Asymmetry* **2009**, *20*, 2845–2853. (t) Yue, Y.; Turlington, M.; Yu, X.-Q.; Pu, L. *J. Org. Chem.* **2009**, *74*, 8681–8689. (u) Du, Y.; Turlington, M.; Zhou, X.; Pu, L. *Tetrahedron Lett.* **2010**, *51*, 5024–5027.

(7) (a) Lu, G.; Li, X.; Jia, X.; Chan, W. L.; Chan, A. S. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5057–5058. (b) Lu, G.; Li, X.; Li, Y.-M.; Kwong, F.-Y.; Chan, A. S. C. *Adv. Synth. Catal.* **2006**, *348*, 1926–1933. (c) Liu, L.; Wang, R.; Kang, Y.-F.; Cai, H. Q.; Chen, C. *Synlett* **2006**, 1245–1249.

(8) (a) Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688. (b) Jiang, B.; Chen, Z.; Xiong, W. *Chem. Commun.* **2002**, 1524–1525. (c) Chen, Z.; Xiong, W.; Jiang, B. *Chem. Commun.* **2002**, 2098–2099. (d) Jiang, B.; Chen, Z.; Tang, X. *Org. Lett.* **2002**, *4*, 3451–3453. (e) Yamashita, M.; Yamada, K.; Tomioka, K. *Adv. Synth. Catal.* **2005**, *347*, 1649–1652. (f) Emmerson, D. P. G.; Hems, W. P.; Davis, B. G. *Org. Lett.* **2006**, *8*, 207–210.

(9) (a) Motoki, R.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2007**, *9*, 2997–3000. (b) Asano, Y.; Hara, K.; Ito, H.; Sawamura, M. *Org. Lett.* **2007**, *9*, 3901–3904. (c) Asano, Y.; Ito, H.; Hara, K.; Sawamura, M. *Organometallics* **2008**, *27*, 5984–5996.

(10) (a) Takita, R.; Yakura, K.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 13760–13761. (b) Harada, S.; Takita, R.; Ohshima, T.; Matsunaga, S.; Shibasaki, M. *Chem. Commun.* **2007**, 948–950.

(11) Ito, J.; Asai, R.; Nishiyama, H. *Org. Lett.* **2010**, *12*, 3860–3862.

(12) (a) Corey, E. J.; Cimprich, K. A. *J. Am. Chem. Soc.* **1994**, *116*, 3151–3152. (b) Ooi, T.; Miura, T.; Ohmatsu, K.; Saito, A.; Maruoka, K. *Org. Biomol. Chem.* **2004**, *2*, 3312–3319.

(13) Takai, K.; Kuroda, T.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5585–5588.

(14) Aicher, T. D.; Kishi, Y. *Tetrahedron Lett.* **1987**, *28*, 3463–3466.

(15) Some of the recent examples: (a) Pandithavidana, D. R.; Poloukhtine, A.; Popik, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 351–356. (b) Sandoval, C.; López-Pérez, J. L.; Bermejo, F. *Tetrahedron* **2007**, *63*, 11738–11747. (c) Wang, C.; Forsyth, C. J. *Org. Lett.* **2006**, *8*, 2997–3000.

(16) For selected reviews on Nozaki−Hiyama−Kishi-type chemistry see: (a) Fürstner, A. *Chem. Rev.* **1999**, *99*, 991–1045. (b) Avalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Palacios, J. C. *Chem. Soc. Rev.* **1999**, *28*, 169–177. (c) Wessjohann, L. A.; Scheid, G. *Synthesis* **1999**, 1–36. (d) Takai, K.; Nozaki, H. *Proc. Jpn. Acad. Ser. B* **2000**, *76*, 123–131. (e) Smith, K. M. *Coord. Chem. Rev.* **2006**, *250*, 1023–1031. For reviews focused on asymmetric protocols see: (f) Hargaden, G. C.; Guiry, P. J. *Adv. Synth. Catal.* **2007**, *349*, 2407–2424. (g) Inoue, M.; Suzuki, T.; Kinoshita, A.; Nakada, M. *Chem. Rec.* **2008**, *8*, 169–181.

(17) (a) Fürstner, A.; Shi, N. *J. Am. Chem. Soc.* **1996**, *118*, 12349–12357. (b) Fürstner, A.; Wuchrer, M. *Chem.—Eur. J.* **2006**, *12*, 76–89.

(18) (a) Namba, K.; Kishi, Y. *Org. Lett.* **2004**, *6*, 5031–5033. (b) Namba, K.; Wang, J.; Cui, S.; Kishi, Y. *Org. Lett.* **2005**, *7*, 5421–5424.

(19) For reviews on TBOx-based catalysis see: (a) Yamamoto, H.; Xia, G. *Chem. Lett.* **2007**, *36*, 1082–1087. (b) Abell, J. P.; Yamamoto, H. *Chem. Soc. Rev.* **2010**, *39*, 61–69.

(20) (a) Xia, G.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 2554–2555. (b) Xia, G.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 496–497. (c) Usanov, D. L.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 8169–8172. (d) Takenaka, N.; Xia, G.; Yamamoto, H *J. Am. Chem. Soc.* **2004**, *126*, 13198–13199. (e) Naodovic, M.; Xia, G.; Yamamoto, H. *Org. Lett.* **2008**, *10*, 4053–4055.

(21) Along with the Supporting Information and references cited therein for selected reports see: (a) Eglinton, G.; McCrae, W. *J. Chem. Soc.* **1963**, 2295–2299. (b) Miller, S. I.; Ziegler, G. R.; Wieleseck, R. *Org. Synth.* **1965**, *45*, 86. (c) Hofmeister, H.; Annen, K.; Laurent, H.; Wiechert, R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 727–729. (d) Barluenga, J.; Gonzalez, J. M.; Rodriguez, M. A.; Campos, P. J.; Asensio, G. *Synthesis* **1987**, 661–662. (e) Jeffery, T. *J. Chem. Soc., Chem. Comm.* **1988**, 909–910. (f) Ricci, A.; Taddei, M.; Dembech, P.; Guerrini, A.; Seconi, G. *Synthesis* **1989**, 461–463. (g) Casarini, A.; Dembech, P.; Reginato, G.; Ricci, A.; Seconi, G. *Tetrahedron Lett.* **1991**, *32*, 2169–2170. (h) Brunel, Y.; Rousseau, G. *Tetrahedron Lett.* **1995**, *36*, 2619–2622. (i) Meng, L.-G.; Cai, P.-J.; Guo, Q.-X.; Xue, S. *Synth. Commun.* **2008**, *38*, 225–231.

(22) No reaction was observed in diethyl ether, 1,4-dioxane, methyl *tert*-butyl ether, cyclopentyl methyl ether, dimethylformamide, toluene, hexanes, or dichloromethane.

(23) The effects of the factors leading to enantioselectivity enhancement (lowered temperature, use of 2-methyltetrahydrofuran as a solvent, use of tri-*n*-propylsilyl chloride, addition of *N*-methylimidazole) appeared to be nonadditive; various combination thereof did not result in any further increase of the ee of the product.

(24) Martínez, L. E.; Leighton, J. L.; Carsten, D. H; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897–5898.

(25) A question whether organomanganese species play an important role in the catalysis was raised during the review process. The organomanganese compound synthesized by transmetalation of PhC≡C—Li with MnI_2 was reacted with benzaldehyde in the presence of TBOxCrCl and furnished racemic products both in the presence and in the absence of TESCl (however, TBOxCrCl-mediated alkynylation with phenyliodoacetylene in the presence of 1.2 equiv of LiI proceeded with 88% ee). We have also found that if the reaction is run under the conditions corresponding to Table 1, entry 1, without the chromium complex (carefully worked up after 15 h), the crude NMR contained benzaldehyde and phenyliodoacetylene in the unchanged ratio; no phenylacetylene was observed. On the basis of these observations, the formation of organomanganese compounds in the TBOxCrCl-mediated alkynylation can be excluded. The role of manganese is apparently limited to conversion of Cr^{III} into Cr^{II}, with the latter being able to transfer electrons to the alkynyl halide.