

An Efficient Entry to Planar Chiral Organometallic Complexes *via* Pd-Catalyzed Asymmetric Hydrogenolysis

Audrey Mercier[§], Wee Chuan Yeo, Xavier Urbaneja, and E. Peter Kündig*

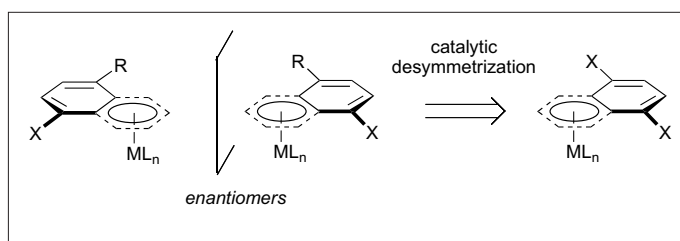
[§]SCS–DSM Nutritional Products Award Winner (Poster Presentation)

Abstract: Planar chiral chromium- and ruthenium-based arene complexes were prepared with high levels of enantioselectivity *via* a Pd-catalyzed asymmetric hydrogenolysis reaction using a bulky chiral phosphoramidite ligand. Key elements for the efficiency of the process are the use of DABCO as borane-trapping reagent as well as substantial kinetic resolution, which was found to enhance the stereochemical outcome of the reaction.

Keywords: Catalytic desymmetrization · Chromium · Hydrogenolysis · Planar chirality · Ruthenium

Introduction

Efficient access to optically pure planar chiral complexes is of interest in asymmetric synthesis and catalysis. The complexes can notably serve as chiral synthons in asymmetric synthesis and as catalysts or chiral ligands in a variety of organic transformations.^[1] In contrast to chromium arene complexes, isoelectronic cationic (η^6 -arene)(η^5 -Cp)ruthenium complexes have received scarce attention.^[2,3] They are however generally more resistant to oxidative and thermal cleavage of the metal–arene bond. Due to the greater electron-withdrawing ability of the RuCp⁺ moiety, nucleophilic substitution reactions can be performed under mild conditions. The strategies to access enantiomerically enriched forms of these compounds are based either on asymmetric synthesis^[3,4] or resolution of racemates.^[5] Although these approaches are potent methods that often give the target complexes in high en-



Scheme 1. Access to planar chiral complexes by catalytic desymmetrization (M = Cr, Ru).

antiomeric purity, they rely on the use of stoichiometric amount of chiral reagents and the diastereoselective methods often require additional steps for the introduction and the removal of chiral auxiliaries. A potentially very attractive alternative is the desymmetrization of prochiral complexes by a chiral catalyst (Scheme 1). The route that we have chosen is the Pd-catalyzed enantioselective hydrogenolysis of prochiral dihalide complexes.

To the best of our knowledge, no report describes the catalytic desymmetrization of ruthenium sandwich complexes. However, a few examples of Pd-catalyzed asymmetric reactions for the preparation of planar chiral [Cr(arene)(CO)₃] complexes exist in the literature, albeit with only moderate enantioselectivities.^[6] For instance, Uemura, Nishimura and Hayashi described Pd-catalyzed asymmetric cross-coupling reactions of alkenyl- and aryl metal compounds with [Cr(CO)₃(1,2-dichlorobenzene)].^[6a,b] More recently, Schmalz and coworkers reported a methoxycarbonylation of the same substrate^[6c] and [Cr(CO)₃(2,6-dichlorotoluene)].^[6d] A Pd-catalyzed vinyl/halide exchange of [Cr(CO)₃(1,2-dichlorobenzene)] using a divinyl aluminum reagent resulted in poor asymmetric induction.^[6e] Finally, a report by Kamikawa *et al.* de-

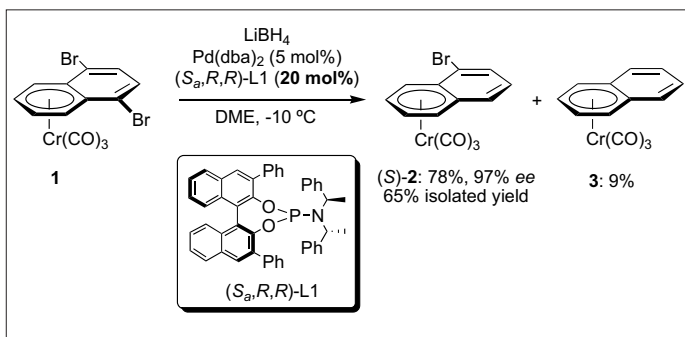
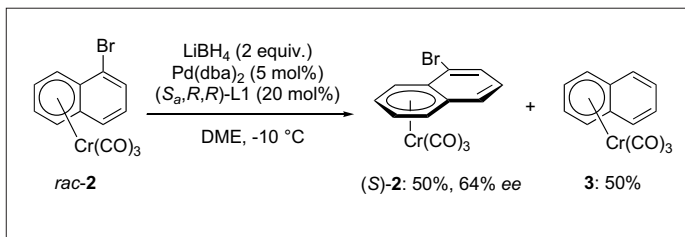
scribed an asymmetric intramolecular Mizoroki-Heck reaction of [Cr(CO)₃(2,6-dibutenylchlorobenzene)].^[6f]

We recently succeeded in preparing the highly enantioenriched planar chiral [Cr(5-bromonaphthalene)(CO)₃] ((*S*)-**2**) complex using the title reaction in the presence of the bulky phosphoramidite ligand L1 (Scheme 2).^[7] Here we highlight the kinetic resolution at play in the process and the advantage of using DABCO as additive. Additionally, we present the application of the asymmetric hydrogenolysis to the more robust Cp- and Cp* ruthenium complexes of 1,4-dibromonaphthalene and 4,7-dibromoindene.

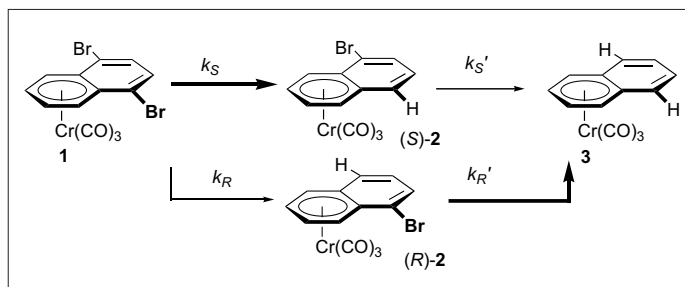
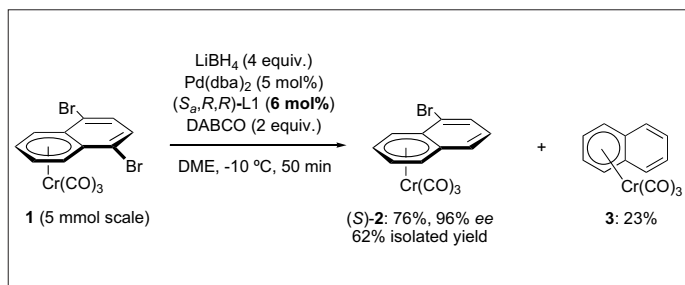
Results and Discussion

Following the preliminary communication on the desymmetrization of the prochiral complex **1**,^[7] further investigations led to the identification of substantial kinetic resolution^[8] connected to the formation of over-reduced complex **3**. This was demonstrated independently in experiments involving *rac*-**2** (Scheme 3). Its reaction under the standard conditions and at 50% conversion afforded recovered starting material **2** with an enantiomeric excess of 64% in favour of the (*S*)-enan-

*Correspondence: Prof. E. P. Kündig
University of Geneva
Department of Organic Chemistry
30 Quai Ernest Ansermet
CH-1211 Geneva 4
Tel.: +41 22 379 6093
Fax: +41 22 379 3215
E-mail: peter.kundig@unige.ch

Scheme 2. Pd-catalyzed asymmetric hydrogenolysis of complex **1**.

Scheme 3. Kinetic resolution experiment.

Scheme 4. Kinetic resolution connected to the formation of **3**.Scheme 5. Improved scalable asymmetric hydrogenolysis using DABCO as trapping agent of BH₃.

tiomer ($k'_R > k'_S$). This corresponds to a selectivity factor (k'_R/k'_S) of 8.5.

To summarize, in the desymmetrization of prochiral complex **1**, the minor (*R*)-**2** enantiomer ($k_R < k_S$) is converted faster into naphthalene chromium complex **3** ($k'_R > k'_S$), resulting in further enrichment in (*S*)-**2** (Scheme 4).

Although the process was efficient in terms of activity and enantioselectivity, the use of 20 mol% of a high molecular weight ligand that requires a five-step synthesis from BINOL, remained a major limitation. Efforts on recycling the chiral ligand at the end of the reaction did not meet with success. Although models of the Pd(II) complex clearly indicate that only one phosphoramidite L1 could be coordinated to the metal, attempts to decrease the ligand loading resulted in lower enantioselectivity and diminished yield of complex **2**. After careful investigations, we found that phosphoramidite L1 was recovered as a phosphoramidite-borane complex at the end of the reaction. The presence of borane was confirmed by ¹¹B NMR analysis (−39.6 ppm) and the ³¹P{¹H} NMR signal is in accordance with the few examples of isolated aminophosphane-borane adducts.^[9] Upon hydride transfer to Pd, LiBH₄ liberated borane, which formed an adduct with ligand L1, thus depleting the reaction of the essential chiral information. This explained the necessity of adding up to 20 mol% of chiral ligand for only 5 mol% of palladium source to attain a high degree of enantioselectivity. To circumvent this problem, we envisaged the addition of DABCO to trap the liberated borane.^[10] Indeed, the use of DABCO in the reaction was successful and

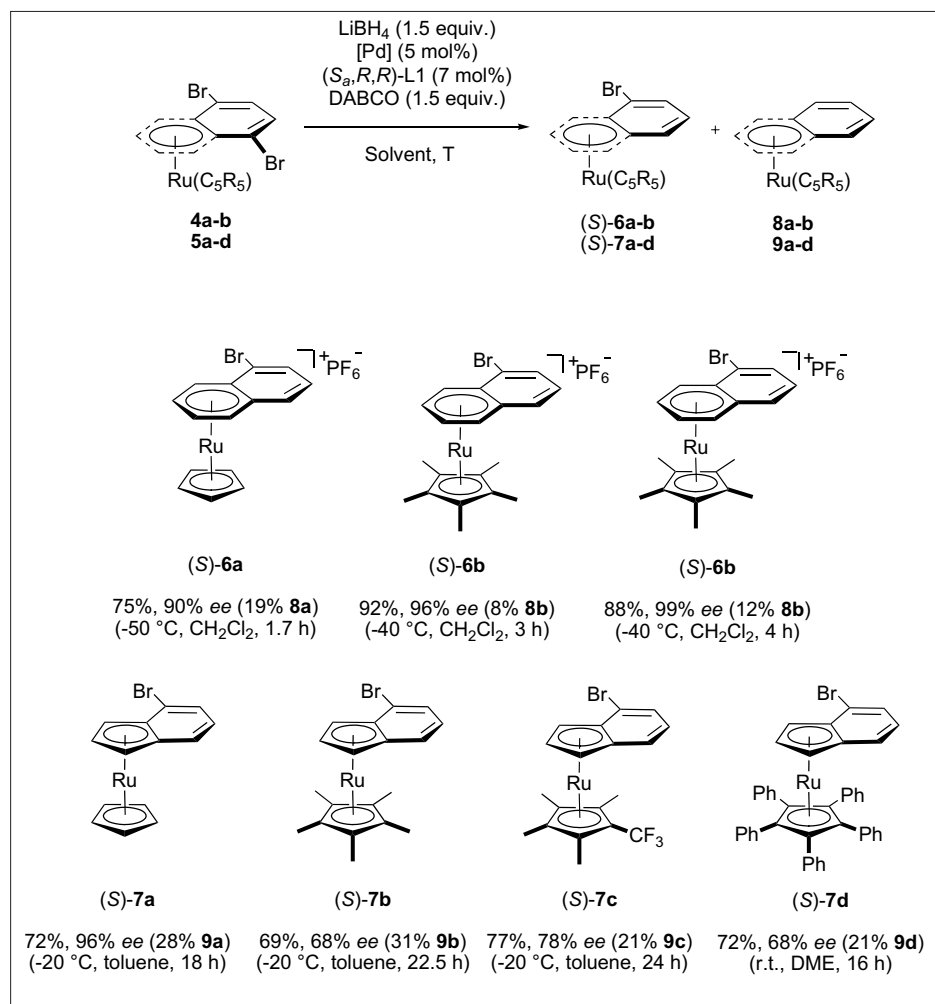
allowed the reduction of the ligand loading from 20 to 6 mol%. With this modification, (*S*)-**2** is now accessible in multi-gram quantities, without wasting large amounts of chiral ligand (Scheme 5).

To demonstrate the generality of the methodology, the scope of the desymmetrization was explored next.^[11] For this purpose, the cationic complexes [Ru(η⁵-C₅R₅)(η⁶-5,8-dibromonaphthalene)][PF₆] (**4a,b**), which are isoelectronic to **1**, and the neutral analogues [Ru(η⁵-C₅R₅)(η⁵-4,7-dibromoindene)] (**5a–d**) were chosen as substrates (Scheme 6). Owing to solubility and relative stability issues, reaction conditions had to be slightly modified from those optimal for **1**. Cationic [Ru(η⁶-5-bromonaphthalene)(η⁵-Cp)][PF₆] ((*S*)-**6a**) was obtained in 90% ee. Similar levels of asymmetric induction but higher **6/8** selectivity were reached when **4b**, incorporating the bulky and electron-rich Cp* moiety, was employed. After 3 h, full conversion was attained and (*S*)-**6b** was produced in 96% ee, together with only 8% of **8b**. Extension of the reaction scope was pursued with the neutral [Ru(η⁵-C₅R₅)(η⁵-4,7-dibromoindene)] (**5**). These complexes show higher stability and ease of handling compared to their cationic analogues. [Ru(η⁵-4-bromoindene)(η⁵-Cp)] ((*S*)-**7a**) was obtained in 96% ee. When the sterically more hindered and electron-rich complex **5b** was employed, the hydrogenolysis product (*S*)-**7b** was produced in only 68% ee. Reaction of complex **5c** was then examined to clarify whether steric or electronic parameters are responsible for this low asymmetric induction. The 1,2,3,4-tetramethyl-5-(trifluoromethyl)cy-

cloptadiene ligand (Cp*^{CF3}) developed by Gassman^[12] exhibits the electronic properties of a Cp and the steric bulk of a Cp*, which makes **5c** isoelectronic to **5a** and isosteric to **5b**. The reaction furnished (*S*)-**7c** with an intermediate enantiomeric excess of 78% ee, suggesting that both electronic and steric properties influence the enantioselection of the reaction. To further confirm these observations, complex **5d**, bearing a pentaphenylcyclopentadienyl ligand, was evaluated. The phenyl substituents considerably decelerate the reaction. Complete conversion was only achieved at room temperature, affording (*S*)-**7d** in 69% ee. This result confirmed that increased steric hindrance has a detrimental impact on both reactivity and catalyst selectivity.

The potential utility of this reaction has already been illustrated with the synthesis of a wide range of planar chiral arene complexes from the highly enantioenriched [Cr(5-bromonaphthalene)(CO)₃] ((*S*)-**2**) either by simple metalation/electrophilic trapping sequences or by palladium-catalyzed coupling reactions.^[13] This chemistry is currently being extended to asymmetric C–C and C–P bond forming processes in our laboratory.

In conclusion, we have highlighted the kinetic resolution at play in the desymmetrization process. We have also shown that DABCO was essential to prevent the formation of the BH₃-ligand adduct, hence allowing for the reduction of the chiral ligand loading. Access to highly enantioenriched ruthenium complexes was achieved, demonstrating the generality of the Pd-catalyzed asymmetric hydrogenolysis.



Scheme 6. Scope of the asymmetric hydrogenolysis.

Acknowledgments

Financial support from the University of Geneva and the Swiss National Science Foundation is gratefully acknowledged.

Received: January 5, 2010

- [1] a) M. Ogasawara, S. Watanabe, *Synthesis*, **2009**, 1761; b) M. Ogasawara, S. Watanabe, *Synthesis*, **2009**, 3177; c) M. Rosillo, G. Dominguez, J. Perez-Castells, *Chem. Soc. Rev.* **2007**, *36*, 1589; d) 'Transition Metal Arene π -Complexes in Organic Synthesis and Catalysis', Topics in Organometallic Chemistry, Vol 7, Ed. E. P. Kündig, Springer Verlag, Heidelberg, **2004**; e) A. Salzer, *Coord. Chem. Rev.* **2003**, *242*, 59; f) A. R. Pape, K. P. Kaliappan, E. P. Kündig, *Chem. Rev.*, **2000**, *100*, 2917; g) C. Bolm, K. Muniz, *Chem. Soc. Rev.*, **1999**, *28*, 51.
- [2] a) E. Matsushima, N. Komatsuzaki, Y. Ajioka, M. Yamamoto, H. Kikuchi, Y. Takata, N. Dodo, K. Onitsuka, M. Uno, S. Takahashi, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 527; b) F. C. Pigge, J. J. Coniglio, *Curr. Org. Chem.* **2001**, *5*, 757; c) R. M. Moriarty, U. S. Gill, Y. Y. Ku, *J. Organomet. Chem.* **1988**, *350*, 157; d) F. C. Pigge, S. Y. Fang, N. P. Rath, *Tetrahedron Lett.* **1999**, *40*, 2251; e) J. W. Janetka, D. H. Rich, *J. Am. Chem. Soc.* **1997**, *119*, 6488; f) J. Pearson, M. V. Chelliah, *J. Org. Chem.* **1998**, *63*, 3087.
- [3] Diastereoselective complexation (Ru): a) K. Kamikawa, K. Norimura, M. Furusyo, T. Uno, Y. Sato, A. Konoo, G. Bringmann, M. Uemura, *Organometallics* **2003**, *22*, 1038; b) K. Kamikawa, M. Furusyo, T. Uno, Y. Sato, A. Konoo, G. Bringmann, M. Uemura, *Org. Lett.* **2001**, *3*, 3667; c) N. Komatsuzaki, H. Kikuchi, M. Yamamoto, M. Uno, S. Takahashi, *Chem. Lett.* **1998**, 445; d) R. Pasch, U. Koelle, B. Ganter, U. Englert, *Organometallics* **1997**, *16*, 3950.
- [4] Selected examples: a) H. Ratni, E. P. Kündig, *Org. Lett.* **1999**, *1*, 1997; b) A. Alexakis, P. Mangeney, I. Marek, F. Rose-Munch, E. Rose, A. Semra, F. Robert, *J. Am. Chem. Soc.* **1992**, *114*, 8288; c) A. Fretzen, A. Ripa, R. G. Liu, G. Bernardinelli, E. P. Kündig, *Chem. Eur. J.* **1998**, *4*, 251; d) S. Pache, C. Botuha, R. Franz, E. P. Kündig, J. Einhorn, *Helv. Chim. Acta* **2000**, *83*, 2436; e) H. G. Schmalz, K. Schellhaas, *Tetrahedron Lett.* **1995**, *36*, 5515.
- [5] a) M. Thimmaiah, R. L. Luck, S. Y. Fang, *J. Organomet. Chem.* **2007**, *692*, 1956; b) R. P. Wurz, E. C. Lee, J. C. Ruble, G. C. Fu, *Adv. Synth. Catal.* **2007**, *349*, 2345; c) C. E. Garrett, G. C. Fu, *J. Am. Chem. Soc.* **1998**, *120*, 7479.
- [6] a) M. Uemura, H. Nishimura, T. Hayashi, *J. Organomet. Chem.* **1994**, *473*, 129; b) M. Uemura, H. Nishimura, T. Hayashi, *Tetrahedron Lett.* **1993**, *34*, 107; c) H. Schumann, J. Kaufmann, H. G. Schmalz, A. Bottcher, B. Gotov, *Synlett* **2003**, 1783; d) A. Bottcher, H. G. Schmalz, *Synlett* **2003**, 1595; e) B. Gotov, H. G. Schmalz, *Org. Lett.* **2001**, *3*, 1753; f) K. Kamikawa, K. Harada, M. Uemura, *Tetrahedron-Asymmetry* **2005**, *16*, 1419.
- [7] E. P. Kündig, P. D. Chaudhuri, D. House, G. Bernardinelli, *Angew. Chem., Int. Ed.* **2006**, *45*, 1092.
- [8] a) J. M. Keith, J. F. Larrow, E. N. Jacobsen, *Adv. Synth. Catal.* **2001**, *343*, 5; b) H. B. Kagan, J. C. Fiaud, *Top. Stereochem.* **1988**, *18*, 249.

- [9] a) D. Grec, L. G. Hubertpfalzgraf, A. Grand, J. G. Riess, *Inorg. Chem.* **1985**, *24*, 4642; b) D. Grec, L. G. Hubertpfalzgraf, J. G. Riess, A. Grand, *J. Am. Chem. Soc.* **1980**, *102*, 7133.
- [10] For the high affinity of borane for tertiary amines, see: a) B. Carboni, F. Carreaux, *Sci. Synth.* **2004**, *6*, 455; b) H. C. Brown, L. T. Murray, *Inorg. Chem.* **1984**, *23*, 2746.
- [11] A. Mercier, W. C. Yeo, J. Y. Chou, P. D. Chaudhuri, G. Bernardinelli, E. P. Kündig, *Chem. Comm.* **2009**, 5227.
- [12] P. G. Gassman, J. W. Mickelson, J. R. Sowa, *J. Am. Chem. Soc.* **1992**, *114*, 6942.
- [13] G. R. Cumming, G. Bernardinelli, E. P. Kündig, *Chem. Asian J.* **2006**, *1*, 459.