Phosphine-Free Hydrogenation

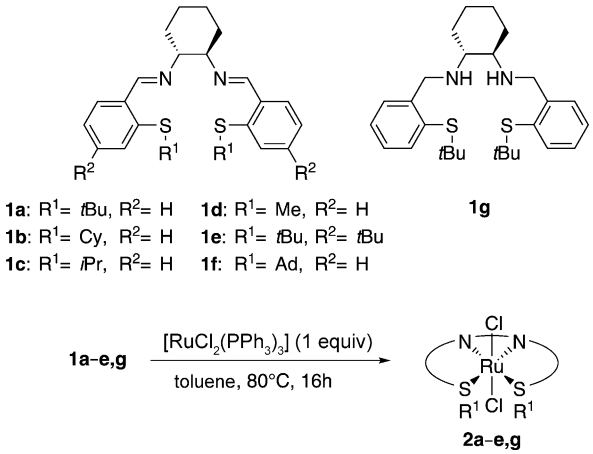
DOI: 10.1002/anie.201304844

Asymmetric Hydrogenation of Ketones with H_2 and Ruthenium Catalysts Containing Chiral Tetradentate S_2N_2 Ligands**

Ruth Patchett, Iris Magpantay, Lionel Saudan, Christoph Schotes, Antonio Mezzetti, and Francesco Santoro**

The ruthenium-catalyzed homogeneous hydrogenation of carbonyl groups has established itself as a mature synthetic method on an academic and industrial scale[1] for the selective generation of stereogenic centers as an alternative to high-energy, pyrophoric hydride reagents. The development of such catalytic systems has gone hand in hand with that of chiral bidentate diphosphine ligands,[2] which, however, are often tedious and expensive to prepare because their multi-step synthesis requires air- and moisture-free conditions. In contrast, phosphine-free chiral catalysts that operate under the industrially preferred and atom-economical hydrogenation with H_2 (HY) are still rare,[3–5] the most successful examples being η^5-cyclopentadienyl[3] and η^6-arene[4] diamine Ru^{II} complexes. Most of these catalysts, as with those operating under transfer hydrogenation (TRHY) conditions,[6] fail to match the efficiency and selectivity requirements of industrial application. Following the work carried out at Firmenich[7] on the HY of ketones with [$RuCl_2$(PNNP)] catalysts,[8] where PNNP is a chiral tetradentate ligand with a P_2N_2 donor,[9] we developed a family of ligands in which the phosphines are replaced by thioethers (SNNS).[10] Such chiral ligands are cheap, air- and moisture-stable, and easy to prepare. This is a preliminary report of ruthenium/SNNS complexes that catalyze the asymmetric HY of ketones and aldehydes with good chemo- and enantioselectivity.[10–12]

Ligands **1a–f** (Scheme 1) were conveniently obtained in two quantitative steps without exclusion of air by nucleophilic aromatic substitution of 2-nitro- or 2-bromobenzyl aldehydes with the appropriate thiol, followed by condensation with the chiral 1,2-cyclohexanediamine. Ligand **1g** was obtained by $NaBH_4$ reduction of **1a** in quantitative yield. The ruthenium complexes [$RuCl_2$(SNNS)] (**2a–e,g**) were prepared from the reaction of [$RuCl_2(PPh_3)_3$] with the appropriate tetradentate ligand (SNNS = **1a–e,g**) and were fully characterized, whereas ligand **1f** was used in situ (see below), as its complexation failed with a number of precursors. The



Scheme 1. Ligands **1a–g** and Ru complexes **2a–e,g** used in this study.

dichloro complexes **2a–e** and **2g** are stable for several hours in $CHCl_3$, toluene, and alcohol solutions when exposed to air.

The crystal structure of (*R*,*R*)-[$RuCl_2$(**1a**)] (*R*,*R*)-(**2a**) shows a weakly distorted octahedral coordination sphere around ruthenium with a *trans* Cl-Ru-Cl unit, and the *R* configuration at both Ru–thioether moieties (Figure 1).

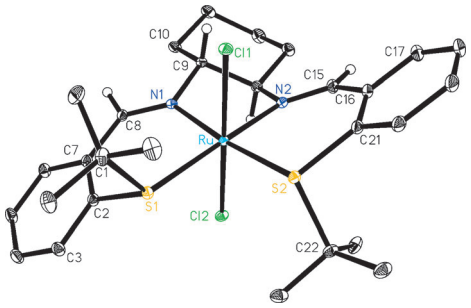


Figure 1. ORTEP plot of (*R*,*R*)-[$RuCl_2$(**1a**)] (*R*,*R*)-(**2a**). Ellipsoids set at 30% probability.

The "stepped" conformation of the tetradentate SNNS ligand is reminiscent of the achiral diimino complex *trans*-[$RuCl_2$-(SNNS)] (SNNS = *N*,*N*′-bis(2-*tert*-butylthiobenzylidene)-1,3-propanediamine)[11a] and of other chiral PNNP[8,13] and salen[14] analogues.

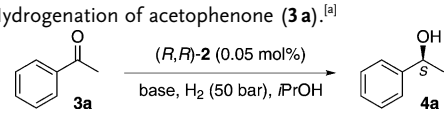
A preliminary screening of catalysts **2a–e** and **2g** in the HY of acetophenone (**3a**) identified *i*PrOH as the solvent and *t*BuOK and KOH as the bases of choice with a base-to-catalyst ratio of 10:1 and 100:1, respectively (Table 1; see also the Supporting Information). The catalytic reactions were

[*] R. Patchett, I. Magpantay, Dr. L. Saudan, Dr. F. Santoro
Corporate R&D Division, Firmenich SA
route des Jeunes 1, P.O. Box 239, 1211 Genève 8 (Switzerland)
E-mail: francesco.santoro@firmenich.com
Dr. C. Schotes, Prof. Dr. A. Mezzetti
Department of Chemistry and Applied Biosciences, ETH Zürich
8093 Zürich (Switzerland)
E-mail: Mezzetti@inorg.chem.ethz.ch

[**] The Authors thank Mr. Rino Schwenk for his assistance with the X-ray structure of complex **2a** and Dr. Alec Birkbeck for the generous donation of substrate **3l**.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201304844.

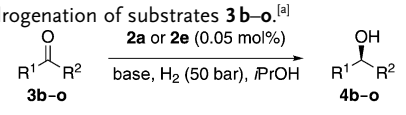
Table 1: Hydrogenation of acetophenone (**3a**).[a]

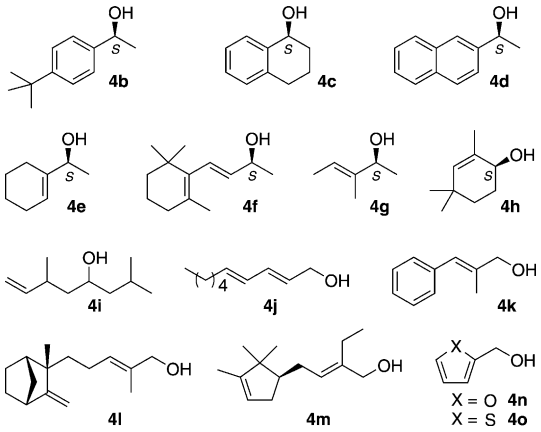


Entry	Cat.	**3a**/base/cat.	*T* [°C]	*t* [h]	Conv. [%]	*ee*[b] [%]
1	**2a**	2000:10:1	60	1	99	72
2	**2a**	2000:10:1	23	1	99	77[c]
3[d]	**2a**	2000:100:1	23	1.5	96	81
4	**2b**	2000:10:1	60	1.5	99	33
5	**2c**	2000:10:1	60	2	99	59
6	**2d**	2000:10:1	60	1.5	99	44
7[d]	**2e**	2000:100:1	23	4	99	88
8	**2g**	2000:10:1	60	1	99	69
9[e]	**2a**	10^5:450:1	60	4	99	64
10[e]	**2a**	10^6:450:1	60	7	90	68
11[e]	**2g**	10^5:450:1	60	4	99	61
12[e]	**2g**	10^6:450:1	60	7	15	63

[a] Conditions (unless otherwise stated): **3a** (20 mmol), cat. **2a–e,g** (0.05 mol%), *t*BuOK, *i*PrOH (10 mL), H_2 (50 bar, initial pressure). [b] (*R,R*)-**2** gave (*S*)-**4a** as the major enantiomer. [c] Reactions in MeOH or EtOH gave **4a** (70% *ee*) quantitatively after 2 h. [d] KOH as base. [e] **3a** (40 mmol), *i*PrOH (20 mL total volume); see also Ref. [15].

Table 2: Hydrogenation of substrates **3b–o**.[a]





Entry	Cat.	**3**	**3**/base/cat.	*T* [°C]	*t* [h]	Conv. [%]	*ee*[b] [%]
1	**2e**	**3b**	2000:100:1	23	3	98	90
2	**2e**	**3c**	2000:100:1	23	3	99	95
3	**2e**	**3d**	2000:100:1	23	2	99	83
4	**2e**	**3e**	2000:100:1	23	3	98	90
5	**2e**	**3f**	2000:100:1	23	3	99	79
6	**2e**	**3g**	2000:100:1	23	3	98	91
7	**2e**	**3h**	2000:100:1	23	3	98	95
8[c,d]	**2a**	**3i**	2000:10:1	23	16	99	–
9[c,e]	**2a**	**3j**	2000:10:1	60	2	99	–
10[c]	**2a**	**3k**	2000:10:1	60	2	99	–
11[c]	**2a**	**3l**	2000:10:1	60	2	99	–
12[c]	**2a**	**3m**	2000:10:1	60	2	99	–
13[c]	**2a**	**3n**	2000:10:1	60	2	99	–
14[c]	**2a**	**3o**	2000:10:1	60	2	99	–

[a] Conditions (unless otherwise stated): **3** (20 mmol), **2** (0.05 mol%), KOH (5 mol%), *i*PrOH (10 mL), H_2 (50 bar, initial pressure). [b] (*R,R*)-**2e** gave (*S*)-**4a–h** as the major enantiomer. [c] *t*BuOK (0.5 mol%) was used as base. [d] The d.r. of **4i** is 54:46. [e] (*E,E*)/(*E,Z*) ratio of **4j** is 95:5.

carried out at an initial H_2 pressure of 50 bar and, whenever possible, they were run to maximal conversion. All hydrogenations showed a variable induction period of 10–30 min, during which no H_2 was consumed.

The screening of precatalysts **2a–e** and **2g** showed that a bulky *t*BuS group is necessary to achieve high enantioselectivity (entries 1–3), whereas ligands bearing smaller alkyl groups (Cy, *i*Pr, Me) on the sulfur give lower *ee* (entries 4–6). Lowering the temperature to 23°C with precatalyst **2a** improved the enantioselectivity from 72% to 77% *ee* (entry 2). The use of KOH instead of *t*BuOK with a substrate/catalyst/KOH ratio of 2000:1:100 gave 1-phenylethanol (**4a**) with 81% *ee* (entry 3). Complex **2e**, whose ligand bears bulky substituents in the aryl backbone, gave the highest enantioselectivity achieved with acetophenone (**3a**; 88% *ee*, entry 7).

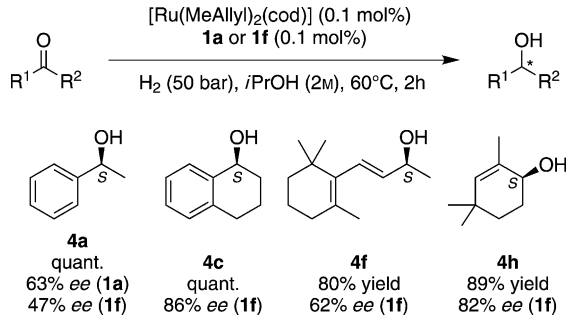
Upon increasing the S/C ratio to 10^6:1, precatalyst **2a** gave 1-phenylethanol (**4a**) in 90% yield with nearly the same *ee* obtained under otherwise analogous conditions (entries 1, 10).[15] The diamino complex **2g** is less enantioselective (at least with **3a**, entry 8) than its diimino analogue **2a** and significantly less active when the S/C ratio was increased to 10^6:1 (entry 12), giving **4a** in only 15% yield after 7 h. The hydrogenation of **3a** was also carried out in EtOH and MeOH with minor erosion of enantioselectivity (70% *ee* at 23°C with both solvents).[16] Remarkably, **4a** was also quantitatively obtained with 70% *ee* when using commercial solutions of NaOMe or KOMe in MeOH[17] as base without additional solvent.[18]

Precatalysts **2a** and **2e** were tested in the hydrogenation of unsaturated carbonyl compounds **3b–3o** to the corresponding alcohols **4b–4o**, which are of relevance in fragrance chemistry (Table 2). Using the best-performing precatalyst **2e**, the highest enantioselectivity was obtained with α-tetralone (**3c**, 95% *ee*) and 2,4,4-trimethylcyclohexenone[19] (**3h**, 95% *ee*; entries 2 and 7), whereas other nonaromatic unsaturated ketones (**3e** and **3g**) gave the corresponding alcohols **4e** and **4g** with high enantioselectivity (90 and 91% *ee*, entries 4 and 6). Additionally, using precatalyst **2a**, enals **3j–3o** were hydrogenated to the corresponding unsaturated alcohols **4i–4o** with excellent chemoselectivity.

Overall, products **4b–4o** were formed quantitatively or nearly so. Neither olefin hydrogenation nor isomerization competes with the carbonyl reduction, even in the case of sensitive terminal olefins or conjugated enones or enals. Interestingly, the potentially coordinating thiophene group in **3o** does not interfere.

The catalyst tolerates scale up, and substrates and solvents can be used without previous purification. Thus, alcohols **4g** and **4m** were prepared on a larger scale in excellent yield using a lower loading of catalyst **2a** and industrial-grade substrates.[20a] Notably, these scale-up conditions did not lower the enantioselectivity of **4g**.[20b]

The SNNS ligands can also be used without base by preparing the catalyst in situ from [Ru(methallyl)$_2$(cod)] (cod = 1,5-cyclooctadiene) and the appropriate ligand in *i*PrOH (Scheme 2). This method, which was primarily devised



Scheme 2. In situ catalysis with **1a** or **1f**.

for the hydrogenation of base-sensitive compounds,[21] allows testing of ligand **1f**, which does not form an isolable dichloro complex.[22]

In view of the formal analogy with the Ru/PNNP catalysts, and to check whether TRHY may interfere in the above HY reactions, precatalysts **2a** and **2g** were also tested under standard[7b] TRHY conditions in *i*PrOH (Table 3).

Table 3: Transfer hydrogenation of acetophenone (**3a**).[a]

Entry	Cat.	**3a**/base/cat.	*t* [h]	Conv. [%]	*ee* [%]
1	**2a**	400:2:1	15	88	70
2	**2g**	400:2:1	15	36	52
3	**2a**	10^5:450:1	6	n.r.	–
4	**2g**	10^5:450:1	6	n.r.	–

[a] Reaction conditions: **3a** (2 mmol), base = *t*BuOK, 60 °C, *i*PrOH (20 mL overall). n.r. = no reaction.

Complex **2a** catalyzes the TRHY of **3a** to give 1-phenylethanol (**4a**) with similar enantioselectivity as in HY (70% vs. 72% *ee*, respectively), but the reaction was much slower (Table 3, entry 1 vs. Table 1, entry 1). Also, no TRHY reaction was observed with lower catalyst loading (Table 3, entry 3), leading to the conclusion that TRHY cannot interfere in the HY reactions discussed above. Interestingly, the diamino precatalyst **2g** is much less active (36% conversion after 15 h, entry 2) and enantioselective (52% *ee*) than its diimino analogue **2a**. This trend is opposite to that of the Ru/PNNP series, in which the diamino complex is a much more active and enantioselective TRHY catalyst than the diimino analogue.[7b]

The data in Table 1 show that the Ru/SNNS catalytic system is more active than other reported chiral phosphine-free complexes.[3–5] A preliminary kinetic analysis of the HY of **3a** with **2a** as precatalyst at a S/B/C ratio of 400000:2000:1 indicated a maximum TOF of 68 s^{-1}.[22,23] This result is excellent, and is comparable to the TOF values found for benchmark enantioselective hydrogenation catalysts such as $[RuCl_2(PPh_3)_2(dpen)]$ (6.4 s^{-1}; dpen = 1,2-diphenylethylenediamine),[1d] $[RuCl_2\{(R,R)\text{-dpen}\}\{(R)\text{-tolBinap}\}]$ (63 s^{-1} at 30% conversion; tolBinap = 2,2′-bis(di-*p*-tolylphosphanyl)-1,1′-binaphthyl),[1e] and $[RuCl_2(PNNP)]$ (ca. 40 s^{-1}).[24] Also, the enantioselectivity of the Ru/SNNS precatalysts is close to that of $[RuCl_2\{(R,R)\text{-dpen}\}\{(R)\text{-tolBinap}\}]$ [1d–e,2] and much higher than that of the closely related Ru/PNNP systems,[24] which give 1-phenylethanol (**4a**) in ca. 18% *ee* under HY conditions.[7b]

A final issue concerns the variable induction periods observed both with the diimino (**2a–f**) and diamino (**2g**) catalysts. A series of experiments with **2a** showed that the H_2 pressure can be lowered to 20 bar with no impact on yield or enantioselectivity, but no product is formed at 5 bar. However, when **2a** (0.01 mmol) was treated with *t*BuOK (0.1 mmol) in acetone/*i*PrOH (3:7 ratio) under H_2 (50 bar) at 60 °C for 40 min, followed by addition of **3a** (20 mmol) to the resulting yellow solution, the induction period was suppressed, and the yield was quantitative after 1 h (50 bar H_2, 60 °C, 71% *ee*). With the same preactivation, complete conversion was observed at lower H_2 pressure (5 bar constant pressure H_2, quant. yield after 2 h at 60 °C, 68% *ee*; 68% yield after 2.5 h at 25 °C, 74% *ee*).[22] We conclude that hydrogen pressure is needed to generate the active form of the catalyst, but is not limiting for the hydrogenation reaction after catalyst activation.[25] The nature of the species formed under these conditions is currently under investigation.

In conclusion, the Ru/SNNS complexes presented herein are the first example of phosphorus-free, air- and moisture-tolerant catalysts for the asymmetric hydrogenation of carbonyl groups with H_2, the activity and enantioselectivity of which are comparable to state-of-the-art Ru/diphosphine complexes. The Ru/SNNS catalysts show excellent chemoselectivity in the reduction of the carbonyl groups of unsaturated ketones and aldehydes, and are effective at S/C ratios of up to 10^6:1, which allows for multimole-scale reactions.

Received: June 5, 2013
Published online: ■■ ■■, ■■■■

Keywords: alcohols · asymmetric hydrogenation · homogeneous catalysis · ruthenium · S ligands

[1] For seminal papers, see: a) R. Noyori, T. Ohkuma, M. Kitamura, N. Sayo, H. Kumobayashi, S. Akutagawa, *J. Am. Chem. Soc.* **1987**, *109*, 5856–5858; b) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.* **1988**, *110*, 629–631; c) T. Ohkuma, H. Ooka, S. Hashiguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 2675–2676; d) H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya, R. Noyori, *Angew. Chem.* **1998**, *110*, 1792–1796; *Angew. Chem. Int. Ed.* **1998**, *37*, 1703–1707; for a review article, see: e) R. Noyori, T. Ohkuma, *Angew. Chem.* **2001**, *113*, 40–75; *Angew. Chem. Int. Ed.* **2001**, *40*, 40–73; f) R. Noyori, *Angew. Chem.* **2002**, *114*, 2108–2123; *Angew. Chem. Int. Ed.* **2002**, *41*, 2008–2022; g) H.-U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103–151; h) *The Handbook of Homogeneous Hydrogenation* (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, **2006**; i) C. Hedberg in *Modoths in Reduction Methods* (Eds.: P. G. Andersson, I. J. Munslow), Wiley-VCH, Weinheim, **2008**, pp. 107–134; j) P. Dupau, *Top. Organomet. Chem.* **2012**, *42*, 47–64.
[2] W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029–3070.
[3] M. Ito, M. Hirakawa, K. Murata, T. Ikariya, *Organometallics* **2001**, *20*, 379–381.

[4] a) T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. A. Sandoval, R. Noyori, *J. Am. Chem. Soc.* **2006**, *128*, 8724 – 8725; b) C. A. Sandoval, T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, R. Noyori, *Chem. Asian J.* **2006**, *1*, 102 – 110; c) T. Ohkuma, K. Tsutsumi, N. Utsumi, N. Arai, R. Noyori, K. Murata, *Org. Lett.* **2007**, *9*, 255 – 257; d) C. A. Sandoval, F. Bie, A. Matsuoka, Y. Yamaguchi, H. Naka, Y. Li, K. Kato, N. Utsumi, K. Tsutsumi, T. Ohkuma, K. Murata, R. Noyori, *Chem. Asian J.* **2010**, *5*, 806 – 816.

[5] a) J. I. Ito, S. Ujiie, H. Nishiyama, *Chem. Commun.* **2008**, 1923 – 1925; b) J. I. Ito, S. Ujiie, H. Nishiyama, *Organometallics* **2009**, *28*, 630 – 638; c) J. I. Ito, T. Teshima, H. Nishiyama, *Chem. Commun.* **2012**, *48*, 1105 – 1107.

[6] For general reviews on transfer hydrogenation, see: a) G. Zassinovich, G. Mestroni, S. Gladiali, *Chem. Rev.* **1992**, *92*, 1051 – 1069; b) R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* **1997**, *30*, 97 – 102; c) T. Ikariya, A. J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300 – 1308; d) C. Wang, X. F. Wu, J. L. Xiao, *Chem. Asian J.* **2008**, *3*, 1750 – 1770; for an example using chiral N,S-bidentate ligands, see: e) M. Ito, Y. Shibata, A. Watanabe, T. Ikariya, *Synlett* **2009**, 1621 – 1626.

[7] a) V. Rautenstrauch, R. Churlaud, R. H. Morris, K. Abdur-Rashid, WO 2002/040155, **2002**; b) V. Rautenstrauch, X. Hoang-Cong, R. Churlaud, K. Abdur-Rashid, R. H. Morris, *Chem. Eur. J.* **2003**, *9*, 4954 – 4967.

[8] J. X. Gao, T. Ikariya, R. Noyori, *Organometallics* **1996**, *15*, 1087 – 1089.

[9] Ru^{II}/PNNP complexes contain the same P_2N_2 donor set as the Ru^{II}/diamine/diphosphine catalysts, which are the most efficient catalysts for asymmetric ketone hydrogenation; see Ref. [1].

[10] F. Santoro, L. Saudan, C. Saudan, WO 2012/084810, **2012**.

[11] For the synthesis of other Ru/SNNS complexes, see: a) K. Nakajima, Y. Ando, H. Mano, M. Kojima, *Inorg. Chim. Acta* **1998**, *274*, 184 – 191; b) T. Yamamura, M. Tadokoro, R. Kuroda, *Chem. Lett.* **1989**, *18*, 1245 – 1246.

[12] Chiral thiophene-based SNNS ligands were reported in the Ir-catalyzed asymmetric TRHY of ketones; however, the thiophene donors were not involved in coordination to the metal center; see: a) X. Q. Zhang, Y. Y. Li, H. Zhang, J. X. Gao, *Tetrahedron: Asymmetry* **2007**, *18*, 2049 – 2054; b) X. Q. Zhang, Y. Y. Li, Z. R. Dong, W. Y. Shen, Z. B. Cheng, J. X. Gao, *J. Mol. Catal. A* **2009**, *307*, 149 – 153; for an achiral Ru/SNS catalyst for the hydrogenation of esters, ketones, aldehydes, imines, and olefins, see: c) D. Spasyuk, S. Smith, D. G. Gusev, *Angew. Chem.* **2013**, *125*, 2598 – 2602; *Angew. Chem. Int. Ed.* **2013**, *52*, 2538 – 2542.

[13] See, for example: C. Sui-Seng, F. Freutel, A. J. Lough, R. H. Morris, *Angew. Chem.* **2008**, *120*, 954 – 957; *Angew. Chem. Int. Ed.* **2008**, *47*, 940 – 943.

[14] T. Katsuki, *Adv. Synth. Catal.* **2002**, *344*, 131 – 147.

[15] With very low catalyst loading, the base-to-catalyst ratio of 10:1 implied a very low concentration of base, which gave irreproducible results. Hence, a larger amount of base was used.

[16] No reaction was observed in the complete absence of alcohol.

[17] With 5 mol% of base vs. substrate **3a**; see the Supporting Information.

[18] Running the hydrogenation reaction (almost) without solvent allows a more efficient use of reactors (higher process productivity) and is an important feature in the fine chemical industry.

[19] [$RuCl_2${(*S*)-tolBinap}{(*R*,*R*)-dpen}] gave **4h** with 94% *ee*; see: T. Ohkuma, T. Hattori, H. Ooka, T. Inoue, R. Noyori, *Org. Lett.* **2004**, *6*, 2681 – 2683.

[20] a) Alcohol **4g** was isolated in 92% yield and 85% *ee* from **3g** (0.4 mol) using a **3g**/EtONa/**2a** ratio of 18700:100:1 in *i*PrOH. The synthetic sandalwood ingredient **4m** was isolated in 96% yield from **3m** (5.27 mol) using a **3m**/NaOH/**2a** ratio of 29300:1083:1 in MeOH; b) under conditions described in Table 2, catalyst **2a** gave **4g** in quantitative yield and 86% *ee*. See the Supporting Information for further experimental details.

[21] C. Saudan, L. Saudan, WO 2010/038209, **2010**.

[22] See the Supporting Information.

[23] TOF is defined as mol of the product per mol of catalyst per second.

[24] PNNP = (*R*,*R*)-bis[-2-(diphenylphosphino)benzylidene]cyclohexane-1,2-diamine. For the determination of TOF, see the Supporting Information.

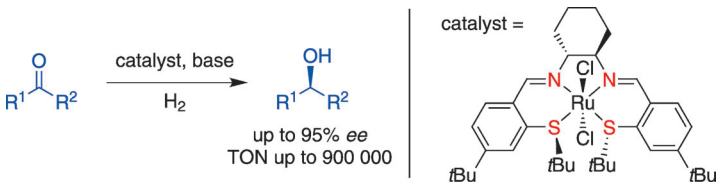
[25] As thioethers can dealkylate upon coordination to a transition metal (S. G. Murray, F. R. Hartley, *Chem. Rev.* **1981**, *81*, 365, and references therein) or upon treatment with strong bases (M. Gargir, Y. Ben-David, G. Leitus, Y. Diskin-Posner, L. J. W. Shimon, D. Milstein, *Organometallics* **2012**, *31*, 6207 – 6214) to generate thiolato complexes, we cannot exclude that this transformation is relevant to the catalyst activation or deactivation pathway.

Communications

Phosphine-Free Hydrogenation

R. Patchett, I. Magpantay, L. Saudan, C. Schotes, A. Mezzetti,* F. Santoro* _____ ■■■■–■■■■

Asymmetric Hydrogenation of Ketones with H_2 and Ruthenium Catalysts Containing Chiral Tetradentate S_2N_2 Ligands



Getting more for less: In the presence of H_2 and a base, air- and moisture-tolerant Ru^{II} complexes catalyze the hydrogenation of ketones and aldehydes with excellent activity and chemoselectivity, and with enantioselectivity of up to 95% under mild conditions. The ratio of substrate to catalyst can be lowered to 10^6:1. The reactions tolerate scale-up and can be carried out with almost no solvent. A base-free method is available for base-sensitive substrates.