Enantiomerically Pure Amines as Substrates for the Ti-Catalyzed Hydroamination of Alkynes

Frauke Pohlki,[a] Igor Bytschkov,[b] Holger Siebeneicher,[b] Andreas Heutling,[a] Wilfried A. König,*[c] and Sven Doye*[a]

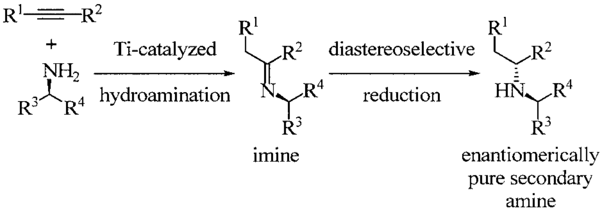
Keywords: Alkynes / Aminations / Asymmetric synthesis / Homogeneous catalysis / Titanium

For two representative reactions employing enantiomerically pure (*S*)-1-phenylethylamine and (*S*)-1-cyclohexylethylamine it is shown that Ti-catalyzed hydroamination reactions of alkynes do not generally take place without partial racemization at the chiral center adjacent to the nitrogen atom. However, identified from a selection of nine Ti catalysts, $Cp^*_2TiMe_2$ and at least two other catalysts can be used for racemization-free hydroamination reactions of alkynes. Furthermore, the amount of racemization can be reduced significantly by the addition of pyridine to the reaction mixture.

Introduction

During the last few years, the development of catalytic methods for the hydroamination of unsaturated organic compounds has attracted much attention.[1] While most catalytic hydroamination methods for alkenes are still limited to certain classes of substrates, more general catalytic hydroamination procedures have been developed for alkynes.[2] Among the various catalysts identified for hydroamination reactions of alkynes,[3−5] group IV metal complexes play an outstanding role.[6] Based on Bergman's[7] and Livinghouse's[8] early studies and boosted by our report[9] that the well-known reagent Cp_2TiMe_2[10] and related Ti complexes can be used as catalysts for the intermolecular hydroamination of alkynes, it has been demonstrated in many subsequent publications that the Ti-catalyzed hydroamination of alkynes is a remarkable new tool in organic synthesis.[11−16]

Since the enantioselective synthesis of nitrogen-containing products from simple and commercially available starting materials is a major goal of modern organic synthesis, it would be highly desirable to employ enantiomerically pure amines possessing a chiral center adjacent to the nitrogen atom for the Ti-catalyzed hydroamination of alkynes because the resulting imines are known to be suitable substrates for a diastereoselective reduction[17] giving access to secondary amines with two stereogenic centers in enantiomerically pure form (Scheme 1).



Scheme 1. Approach towards the synthesis of enantiomerically pure secondary amines by stepwise Ti-catalyzed hydroamination of alkynes with enantiomerically pure amines and subsequent diastereoselective imine reduction

However, to realize a corresponding synthetic strategy it is indispensable that the initial hydroamination reactions take place without racemization at the chiral centers adjacent to the nitrogen atoms of the employed enantiomerically pure amines. In this report, we would like to show that some Ti complexes catalyze hydroamination reactions of alkynes without a corresponding racemization while the use of other catalysts leads to partial racemization at the chiral centers of the employed amines.

Results and Discussion

During a study directed toward the application of microwave heating in Ti-catalyzed hydroamination reactions of alkynes,[11b] we found that a one-pot hydroamination/reduction sequence starting from diphenylacetylene (**1**) and

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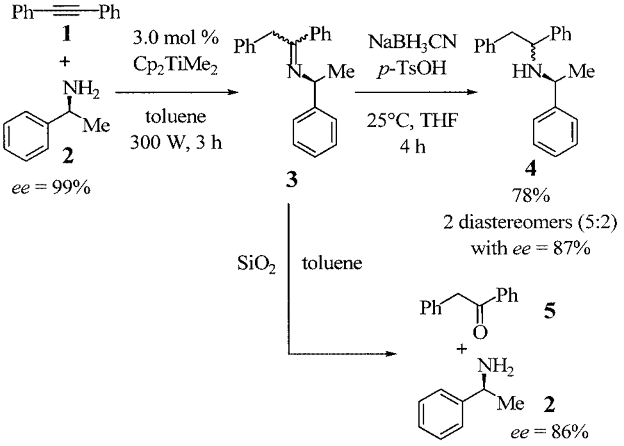
[a] Organisch-Chemisches Institut, Universität Heidelberg
Im Neuenheimer Feld 270, 69120 Heidelberg, Germany
Fax: (internat.) + 49-(0)6221/54-4205
E-mail: sven.doye@urz.uni-heidelberg.de
[b] Institut für Organische Chemie, Universität Hannover
Schneiderberg 1B, 30167 Hannover, Germany
Fax: (internat.) + 49-(0)511/762-3011
[c] Institut für Organische Chemie, Universität Hamburg
Martin-Luther-King-Platz 6, 20146 Hamburg, Germany
Fax: (internat.) + 49-(0)40/42838 2893
E-mail: wkoenig@chemie.uni-hamburg.de

DOI: 10.1002/ejoc.200300522

enantiomerically pure (*S*)-1-phenylethylamine (**2**) (*ee* = 99%) gave access to two diastereomers of the secondary amine **4** in a 5:2 ratio (Scheme 2). Interestingly, GC analysis showed that the *ee* values for the two diastereomers were only 87%. In an additional hydroamination experiment between **1** and **2**, the amine **2** could be reisolated after hydrolysis (SiO_2) of the initially formed imine **3**. GC analysis of reisolated amine **2** showed that the *ee* value had decreased to 86% which is almost identical to the 87% obtained for the diastereomers of **4**. It is therefore clear that the hydroamination step and not the subsequent reduction is responsible for the partial racemization observed. This interpretation is in good agreement with the fact that diastereoselective reductions of imines synthesized from enantiomerically pure **2** and ketones usually take place without partial racemization.[17]

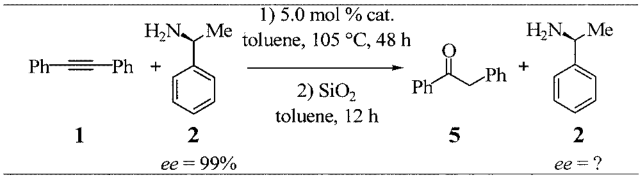


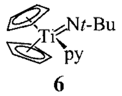
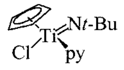
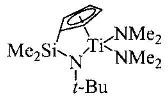
Scheme 2. Comparison between hydroamination/reduction and hydroamination/hydrolysis sequences

Since the *ee* values determined for the two diastereomers of **4** and reisolated **2** are almost identical we chose the hydroamination/hydrolysis sequence for all further investigations because the determination of *ee* values for reisolated commercially available amines is easier than the analysis of secondary amines like **4**.

In order to compare the behaviour of various Ti catalysts with the behaviour of Cp_2TiMe_2, we first synthesized $Cp^*{}_2TiMe_2$,[18] Ind_2TiMe_2,[19] **6**,[20] **7**,[20] **8**,[20] **9**,[21] and **10**[22] (Table 1) according to literature procedures. These catalysts, which have already been investigated as hydroamination catalysts in our laboratories,[11d][11h] as well as commercially available $Ti(NMe_2)_4$[13a] were then used for a standard hydroamination/hydrolysis reaction sequence employing diphenylacetylene (**1**) and (*S*)-1-phenylethylamine (**2**) as substrates (Table 1). In all cases 5.0 mol % of the catalyst was used and the hydroamination was performed at 105° for 48 h (reaction times have not been minimized). Subsequent hydrolysis employing SiO_2 in technical toluene at room temperature gave access to ketone **5**, regenerated amine **2** and in some cases unchanged alkyne **1**. For all reactions, the *ee* values for reisolated **2** were determined by GC. First of all, it can be seen from Table 1 that only the hydroamination reactions employing Cp_2TiMe_2, $Cp^*{}_2TiMe_2$, Ind_2TiMe_2, **9**, and **10** (Entries 1, 4, 5, 9, 10) went to completion within 48 h. Interestingly, the reisolated amine **2** was still enantiomerically pure if $Cp^*{}_2TiMe_2$ or **10** had been used as catalysts (Entries 4, 10). These results also prove that the hydrolysis of the imine intermediate in the presence of SiO_2 obviously takes place without any racemization. In comparison, **2** was obtained with only 80%, 64%, and 87% *ee* employing Cp_2TiMe_2, Ind_2TiMe_2, and **9** (Entries 1, 5, 9), respectively, indicating that these complexes cannot be used for racemization-free hydroamination reactions. To obtain a first impression about the mechanistic details of the racemization, we performed a control experiment under identical conditions in the absence of alkyne **1** employing **2** and Cp_2TiMe_2 as the catalyst (Entry 2). After 48 h of reaction time, the *ee* value of **2** had decreased from 99% to 47%. Therefore, it is clear that the presence of an alkyne is not necessary for the racemization

Table 1. (*S*)-1-Phenylethylamine (**2**) as substrate for the Ti-catalyzed hydroamination of alkynes



Entry	Catalyst	Yield of **5** [%][a]	Recovered **1** [%]	*ee* of **2** [%][b]
1	Cp_2TiMe_2	≥ 95	–	80
2[c]	Cp_2TiMe_2	–	–	47
3[d]	–	–	–	99
4	$Cp^*{}_2TiMe_2$	≥ 95	–	99
5	Ind_2TiMe_2	≥ 95	–	64
6	 **6**	89	4	96
7	 **7**	31	62	99
8	$Cl_2py_3Ti{=}Nt\text{-}Bu$ **8**	77	22	99
9	 **9**	94	–	87
10	 **10**	≥ 95	–	99
11	$Ti(NMe_2)_4$	50	41	24

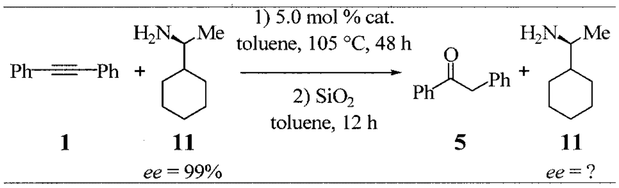
[a] Reaction conditions: 1) alkyne **1** (1.0 mmol), amine **2** (1.0 mmol), toluene (0.1 mL), catalyst (0.05 mmol), 105 °C, 48 h; 2) SiO_2 (0.5 g), technical toluene (6.0 mL), 25 °C, 12 h; yields represent isolated yields of pure compounds; reaction times have not been minimized. [b] Determined by gas chromatography (Method A). [c] Experiment in the absence of alkyne **1**. [d] Experiment in the absence of alkyne **1** and Ti catalyst.

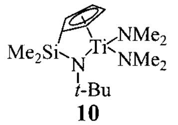
of an enantiomerically pure amine in the presence of a Ti catalyst. A further control experiment under identical conditions in the absence of alkyne **1** and Cp_2TiMe_2 at 105 °C did not lead to any racemization of **2** (Entry 3). Although reactions employing the pyridine-containing (imido)titanium complexes **6**, **7**, and **8** as catalysts (Entries 6, 7, 8) did not reach 100% conversion within 48 h, the *ee* values determined for reisolated **2** are promising (96%, 99%, 99%) in these cases. However, in this context, one should keep in mind that the catalytic activity of a certain titanium complex is strongly dependant on the properties of the employed substrates.[11h] For that reason, imido complexes **6**, **7**, and **8** deserve further investigations with other substrates. A common and probably important structural property of **6**, **7**, and **8** is the presence of at least one pyridine ligand. Since the result obtained with **6** (96% *ee*, Entry 6) is much better than the result obtained with the structurally related complex Cp_2TiMe_2 (80% *ee*, Entry 1) it is possible that the addition of small amounts of pyridine to hydroamination reaction mixtures can generally suppress the undesired partial racemization. Finally, the worst result was obtained with commercially available $Ti(NMe_2)_4$ (Entry 11). With this catalyst, the reaction reaches approximately 50% conversion and the *ee* value of reisolated **2** was found to be only 24%.

With these results in hand, we wanted to find out whether the racemization during the Ti-catalyzed hydroamination is restricted to benzylamine derivatives or not. For that reason, we performed identical hydroamination/hydrolysis sequences in the presence of 5.0 mol % Cp_2TiMe_2, $Cp*_2TiMe_2$, Ind_2TiMe_2, and **10** employing the alkyl analogue of **2**, (*S*)-1-cyclohexylethylamine (**11**) (Table 2). As can be seen from Table 2, all hydroamination reactions employing **11** went to completion within 48 h in the presence of the mentioned catalysts. Fortunately, the reisolated amine **11** was again enantiomerically pure if $Cp*_2TiMe_2$ or **10** had been used as catalysts (Entries 3, 5). Therefore, these Ti complexes can be regarded as suitable catalysts for a racemization-free intermolecular hydroamination of alkynes. In addition, partial racemization (93% *ee* of reisolated **11**) was observed for the catalysts Cp_2TiMe_2 and Ind_2TiMe_2 (Entries 1, 4). Since in these cases the amount of racemization is small compared to the results obtained with benzylamine derivative **2** it is remarkable that a control experiment under identical conditions in the absence of alkyne **1** employing **11** and Cp_2TiMe_2 as the catalyst (Entry 2) resulted in the reisolation of **11** with only 32% *ee*. Anyway, these results clearly indicate that the partial racemization observed during Ti-catalyzed hydroamination reactions of alkynes is not limited to benzylamine derivatives.

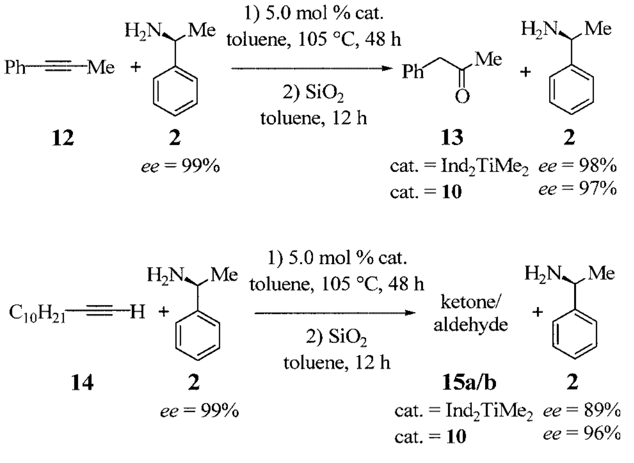
In addition, we performed some standard hydroamination/hydrolysis experiments employing other alkynes (**12**, **14**) and (*S*)-1-phenylethylamine (**2**) (Scheme 3). As catalysts we used Ind_2TiMe_2 and the bridged complex **10**. While the results obtained for catalyst **10** again prove that racemization does not represent a significant problem for hydroaminations employing this catalyst the result obtained for Ind_2TiMe_2 in the hydroamination of 1-dodecyne (**14**) clearly indicates that Ind_2TiMe_2 cannot be regarded as a general catalyst for a racemization-free addition of enantiomerically pure amines to alkynes. In this context, it is worth mentioning that all hydroamination reactions shown in Scheme 3 went to completion within the standard reaction time of 48 h for the hydroamination reaction.

Table 2. (*S*)-1-Cyclohexylethylamine (**11**) as substrate for the Ti-catalyzed hydroamination of alkynes



Entry	Catalyst	Conversion of **1** [%][a]	*ee* of **11** [%][b]
1	Cp_2TiMe_2	≥ 95	93
2[c]	Cp_2TiMe_2	–	32
3[d]	$Cp*_2TiMe_2$	≥ 95	99
4	Ind_2TiMe_2	≥ 95	93
5	 **10**	≥ 95	99

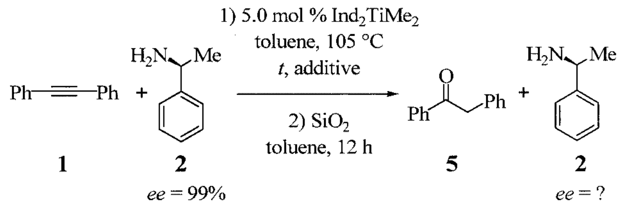
[a] Reaction conditions: 1) alkyne **1** (1.0 mmol), amine **11** (1.0 mmol), toluene (0.1 mL), catalyst (0.05 mmol), 105 °C, 48 h; 2) SiO_2 (0.5 g), technical toluene (6.0 mL), 25 °C, 12 h; the yields of **5** have not been determined; reaction times have not been minimized. [b] Determined by gas chromatography (GC) of the corresponding trifluoroacetates. [c] Experiment in the absence of alkyne **1**. [d] The hydrolysis was performed with a mixture of HCl aqueous solution (c = 2.0 mol/L) and CH_2Cl_2.



Scheme 3. Ti-catalyzed hydroaminations of 1-phenylpropyne (**12**) and 1-dodecyne (**14**) with (*S*)-1-phenylethylamine (**2**) in the presence of Ind_2TiMe_2 or catalyst **10**

In order to rule out the possibility that the partial racemization takes place at the stage of the imine products we performed an additional standard hydroamination reaction in the presence of 5.0 mol % Ind_2TiMe_2. During this experiment, we took samples from the reaction mixtures after 2 h, 4 h, 6 h, 27 h, and 48 h. All samples were subsequently hydrolyzed and analyzed (Table 3, Entries 1−5). While it was noticed that the Ind_2TiMe_2-catalyzed hydroamination reaction went to completion within 4 h (*ee* of reisolated **2**: 83%) no significant decline of the *ee* value of reisolated **2** (within experimental error) was observed during the following 44 h reaction time of the hydroamination indicating that the imine product does not undergo further racemization under the reaction conditions.

Table 3. Influences of the reaction time and the presence of pyridine on the *ee* value of reisolated amine **2**



Entry	*t* [h]	Additive	*ee* of **2** [%][a][b]
1	2	–	81
2	4	–	83
3	6	–	79
4	27	–	82
5	48	–	75
6[c]	48	pyridine (5.0 mol %)	95

[a] Reaction conditions: 1) alkyne **1** (5.0 mmol), amine **2** (5.0 mmol), toluene (0.5 mL), Ind_2TiMe_2 (0.25 mmol), 105 °C; 2) The samples were hydrolyzed with SiO_2 (0.5 g) in technical toluene (6.0 mL) at 25 °C for 12 h. [b] Determined by gas chromatography (Method B). [c] Reaction conditions: 1) alkyne **1** (1.0 mmol), amine **2** (1.0 mmol), toluene (0.1 mL), Ind_2TiMe_2 (0.05 mmol), pyridine (0.05 mmol), 105 °C, 48 h; 2) SiO_2 (0.5 g), technical toluene (6.0 mL), 25 °C, 12 h.

Since Ind_2TiMe_2-catalyzed hydroaminations obviously take place with partial racemization, we decided to choose a corresponding reaction to verify the idea that the addition of pyridine to the hydroamination reaction mixture could reduce the degree of racemization. Fortunately, the *ee* value of amine **2** which was reisolated from a corresponding hydroamination/reduction sequence performed in the presence of 5.0 mol % pyridine was found to be 95% (Table 3, Entry 6). Since this *ee* value is much higher than the *ee* value observed in the absence of pyridine (75%, Table 3, Entry 5) pyridine seems to be an appropriate additive to minimize racemization processes during Ti-catalyzed hydroaminations of alkynes. Further investigations dealing with this fact are underway in our laboratories.

Conclusion

In summary, the study presented undoubtedly proves that Ti-catalyzed hydroamination reactions of alkynes with enantiomerically pure amines possessing a chiral center adjacent to the nitrogen atom do not generally take place without partial racemization. The amount of racemization at the corresponding chiral center seems to be influenced by the structure of the amine and, fortunately, by the nature of the catalyst. During our studies we were able to identify $Cp^*_2TiMe_2$ as highly active catalyst which can be used for a racemization-free hydroamination of alkynes. Furthermore, no racemization was observed employing the pyridine-stabilized (imido)titanium complexes **7** and **8**. Further investigations proved that the addition of small amounts of pyridine to hydroamination reaction mixtures can minimize the undesired partial racemization. In addition, racemization does not seem to represent a significant problem for hydroaminations employing the bridged catalyst **10**. Mechanistic studies of the racemization are underway in our laboratories.

Experimental Section

General Remarks: All reactions were performed under argon in flame-dried Duran Schlenk tubes equipped with Teflon stopcocks. Toluene was distilled from molten sodium under argon. Cp_2TiMe_2 was synthesized according to ref.[10a] $Cp^*_2TiMe_2$ was synthesized according to ref.[18] Ind_2TiMe_2 was synthesized according to ref.[19] Catalysts **6**, **7**, and **8** were synthesized according to ref.[20] Catalyst **9** was synthesized according to ref.[21] Catalyst **10** was synthesized according to ref.[22] All other reagents were purchased from commercial sources and were used without further purification. Yields refer to isolated yields of pure compounds as gauged by ^1H and ^{13}C NMR and TLC or GC analysis. All products were identified by comparison with authentic samples purchased from commercial sources. PE: light petroleum ether, b.p. 40−60 °C.

General Procedure: A Schlenk tube containing a magnetic stirring bar was charged with diphenylacetylene (**1**) (178 mg, 1.0 mmol), amine (**2** or **11**) (1.0 mmol), toluene (0.1 mL), and the catalyst (0.05 mmol). The mixture was heated to 105 °C for 48 h (TLC monitoring). Then, SiO_2 (0.5 g) and technical toluene (6.0 mL) were added. After this had been stirred at 25 °C for 12 h, the mixture was filtered and concentrated under vacuum. The formed amine (**2** or **11**) was separated from ketone **5** by flash chromatography on SiO_2 (**2**: PE/EtOAc, 20:1 → EtOAc; **11**: CH_2Cl_2/MeOH, 10:1).

Separation of the Enantiomers of 2. Method A: A sample of reisolated **2** (0.05 mL) was dissolved in EtOAc (1.0 mL) and used for gas chromatography. Gas chromatographic analysis: The separation of the enantiomers was achieved using a 50-m FS Hydrodex-β-PM capillary (0.25 mm i. d.) with the following temperature program: 40 min at 80 °C; 0.4 °C/min to 100 °C; 100 °C. An HP 5890 Series II gas chromatograph with split injection and flame ionization detection was used with 4.0 bar H_2 as carrier gas. The order of elution of 1-phenylethylamine (**2**) enantiomers was (*R*) before (*S*) with a separation factor $\alpha = 1.02$. **Method B:** In a 1.5-mL screw-cap vial with Teflon insert in the lid approximately 1 mg of sample (dissolved in EtOAc as obtained after chromatography) was dried in a stream of N_2 and taken up in CH_2Cl_2 (0.2 mL). Trifluoroacetic anhydride (0.05 mL) was added and the solution was kept at room temperature for 30 min. After removal of excess of reagent in a stream of N_2, the sample was dissolved in CH_2Cl_2 (0.5 mL) and used for gas chromatography. Gas chromatographic analysis: The separation of the enantiomers was achieved using a 25-m fused silica capillary (0.25 mm i. d.) coated with heptakis(6-O-TBDMS-2,3-di-*O*-methyl)-β-cyclodextrin[23] (dissolved in polysiloxane OV 1701, 1:1, w/w) at 110 °C. A Carlo Erba Model 2150 gas chromatograph with split injection and flame ionization detection was used with 0.5 bar H_2 as carrier gas. The order of elution of 1-phenylethylamine (**2**) enantiomers was (*R*) before (*S*) with a separation factor $\alpha = 1.05$.

Separation of the Enantiomers of 11: In a 1.5-mL screw-cap vial with Teflon insert in the lid approximately 1 mg of sample (dissolved in MeOH as obtained after chromatography) was dried in a stream of N_2 and taken up in CH_2Cl_2 (0.2 mL). Trifluoroacetic anhydride (0.05 mL) was added and the solution was kept at room temperature for 30 min. After removal of excess of reagent in a stream of N_2, the sample was dissolved in CH_2Cl_2 (0.5 mL) and used for gas chromatography. Gas chromatographic analysis: The separation of the enantiomers was achieved using a 15-m fused silica capillary (0.25 mm i. d.) coated with octakis(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin[24] (dissolved in polysiloxane OV 1701, 1:1, w/w) at 95 °C. A Carlo Erba Model 2150 gas chromatograph with split injection and flame ionization detection was used with 0.4 bar H_2 as carrier gas. The order of elution of 1-cyclohexylethylamine (**11**) enantiomers was (*S*) before (*R*) with a separation factor $\alpha = 1.24$.

Acknowledgments

Generous support by Professor E. Winterfeldt is most gratefully acknowledged. We further thank the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and the Dr. Otto Röhm Gedächtnisstiftung, Darmstadt for financial support of our research.

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[1] For general reviews on hydroamination, see: [1a] I. A. Chekulaeva, L. V. Kondratjeva, *Russ. Chem. Rev.* **1965**, *34*, 669–680. [1b] D. Steinborn, R. Taube, *Z. Chem.* **1986**, *26*, 349–359. [1c] R. Taube in *Applied Homogeneous Catalysis with Organometallic Compounds* (Eds.: B. Cornils, W. A. Herrmann), VCH, Weinheim, **1996**, p. 507–520. [1d] T. E. Müller, M. Beller, *Chem. Rev.* **1998**, *98*, 675–703. [1e] T. E. Müller, M. Beller in *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, vol. 2, p. 316–330. [1f]E. Haak, S. Doye, *Chem. Unserer Zeit* **1999**, *33*, 296–303. [1g] M. Nobis, B. Drießen-Hölscher, *Angew. Chem.* **2001**, *113*, 4105–4108; *Angew. Chem. Int. Ed.* **2001**, *40*, 3983–3985. [1h] J. J. Brunet, D. Neibecker in *Catalytic Heterofunctionalization* (Eds.: A. Togni, H. Grützmacher), Wiley-VCH, Weinheim, **2001**, p. 91–141. [1i] P. W. Roesky, T. E. Müller, *Angew. Chem.* **2003**, *115*, 2812–2815; *Angew. Chem. Int. Ed.* **2003**, *42*, 2708–2710.

[2] For a review on hydroamination of alkynes, see: F. Pohlki, S. Doye, *Chem. Soc. Rev.* **2003**, *32*, 104–114.

[3] For leading references on actinide-catalyzed hydroaminations, see: [3a] A. Haskel, T. Straub, M. S. Eisen, *Organometallics* **1996**, *15*, 3773–3775. [3b] T. Straub, A. Haskel, T. G. Neyroud, M. Kapon, M. Botoshansky, M. S. Eisen, *Organometallics* **2001**, *20*, 5017–5035.

[4] For leading references on lanthanide-catalyzed hydroaminations, see: [4a] Y. Li, T. J. Marks, *Organometallics* **1996**, *15*, 3770–3772. [4b] Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **1998**, *120*, 1757–1771. [4c] J.-S. Ryu, G. Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **2003**, *125*, 12584–12605.

[5] For leading references on late transition metal-catalyzed hydroaminations, see: [5a] Y. Uchimaru, *Chem. Commun.* **1999**, 1133–1134. [5b] M. Tokunaga, M. Eckert, Y. Wakatsuki, *Angew. Chem.* **1999**, *111*, 3416–3419; *Angew. Chem. Int. Ed.* **1999**, *38*, 3222–3225. [5c] C. G. Hartung, A. Tillack, H. Trauthwein, M. Beller, *J. Org. Chem.* **2001**, *66*, 6339–6343. [5d] V. Neff, T. E. Müller, J. A. Lercher, *Chem. Commun.* **2002**, 906–907. [5e] E. Mizushima, T. Hayashi, M. Tanaka, *Org. Lett.* **2003**, *5*, 3349–3352.

[6] For a review on group-IV metal complexes as hydroamination catalysts, see: I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2003**, 935–946.

[7] [7a] P. J. Walsh, A. M. Baranger, R. G. Bergman, *J. Am. Chem. Soc.* **1992**, *114*, 1708–1719. [7b] A. M. Baranger, P. J. Walsh, R. G. Bergman, *J. Am. Chem. Soc.* **1993**, *115*, 2753–2763.

[8] [8a] P. L. McGrane, M. Jensen, T. Livinghouse, *J. Am. Chem. Soc.* **1992**, *114*, 5459–5460. [8b] P. L. McGrane, T. Livinghouse, *J. Org. Chem.* **1992**, *57*, 1323–1324. [8c] P. L. McGrane, T. Livinghouse, *J. Am. Chem. Soc.* **1993**, *115*, 11485–11489.

[9] [9a] E. Haak, S. Doye, DE 199,13,522, **1999**; *Chem. Abstr.* **2000**, *133*, 266588. [9b] E. Haak, I. Bytschkov, S. Doye, *Angew. Chem.* **1999**, *111*, 3584–3586; *Angew. Chem. Int. Ed.* **1999**, *38*, 3389–3391.

[10] [10a] N. A. Petasis in *Encyclopedia of Reagents for Organic Synthesis* (Ed.: L. A. Paquette), John Wiley & Sons, New York, **1995**, vol. 1, p. 470–473. [10b] H. Siebeneicher, S. Doye, *J. Prakt. Chem.* **2000**, *342*, 102–106.

[11] [11a] E. Haak, H. Siebeneicher, S. Doye, *Org. Lett.* **2000**, *2*, 1935–1937. [11b] I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2001**, 4411–4418. [11c] F. Pohlki, S. Doye, *Angew. Chem.* **2001**, *113*, 2361–2364; *Angew. Chem. Int. Ed.* **2001**, *40*, 2305–2308. [11d] A. Heutling, S. Doye, *J. Org. Chem.* **2002**, *67*, 1961–1964. [11e] E. Haak, I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2002**, 457–463. [11f] H. Siebeneicher, S. Doye, *Eur. J. Org. Chem.* **2002**, 1213–1220. [11g] I. Bytschkov, S. Doye, *Tetrahedron Lett.* **2002**, *43*, 3715–3718. [11h] F. Pohlki, A. Heutling, I. Bytschkov, T. Hotopp, S. Doye, *Synlett* **2002**, 799–801. [11i] H. Siebeneicher, I. Bytschkov, S. Doye, *Angew. Chem.* **2003**, *115*, 3151–3153; *Angew. Chem. Int. Ed.* **2003**, *42*, 3042–3044. [11j] I. Bytschkov, H. Siebeneicher, S. Doye, *Eur. J. Org. Chem.* **2003**, 2888–2902.

[12] [12a] J. S. Johnson, R. G. Bergman, *J. Am. Chem. Soc.* **2001**, *123*, 2923–2924. [12b] L. Ackermann, R. G. Bergman, *Org. Lett.* **2002**, *4*, 1475–1478. [12c] L. Ackermann, R. G. Bergman, R. N. Loy, *J. Am. Chem. Soc.* **2003**, *125*, 11956–11963.

[13] [13a] Y. Shi, J. T. Ciszewski, A. L. Odom, *Organometallics* **2001**, *20*, 3967–3969. [13b] C. Cao, J. T. Ciszewski, A. L. Odom, *Organometallics* **2001**, *20*, 5011–5013. [13c] C. Cao, Y. Shi, A. L. Odom, *Org. Lett.* **2002**, *4*, 2853–2856. [13d] Y. Shi, C. Hall, J. T. Ciszewski, C. Cao, A. L. Odom, *Chem. Commun.* **2003**, 586–587. [13e] C. Cao, Y. Shi, A. L. Odom, *J. Am. Chem. Soc.* **2003**, *125*, 2880–2881.

[14] [14a] A. Tillack, I. Garcia Castro, C. G. Hartung, M. Beller, *Angew. Chem.* **2002**, *114*, 2646–2648; *Angew. Chem. Int. Ed.* **2002**, *41*, 2541–2543. [14b] I. Garcia Castro, A. Tillack, C. G. Hartung, M. Beller, *Tetrahedron Lett.* **2003**, *44*, 3217–3221.

[15] [15a] T.-G. Ong, G. P. A. Yap, D. S. Richeson, *Organometallics* **2002**, *21*, 2839–2841. [15b] T.-G. Ong, G. P. A. Yap, D. S. Richeson, *J. Am. Chem. Soc.* **2003**, *125*, 8100–8101.

[16] C. Li, R. K. Thomson, B. Gillon, B. O. Patrick, L. L. Schafer, *Chem. Commun.* **2003**, 2462–2463.

[17] For a review on the stereoselective reduction of imines, see: J. Martens in *Houben-Weyl, Methods of Organic Chemistry*, 4th ed. (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Georg Thieme Verlag, Stuttgart, **1995**, vol. E21d, p. 4199–4238.

[18] J. E. Bercaw, R. H. Marvich, L. G. Bell, H. H. Brintzinger, *J. Am. Chem. Soc.* **1972**, *94*, 1219–1238.

[19] D. Balboni, I. Camurati, G. Prini, L. Resconi, S. Galli, P. Mercandelli, A. Sironi, *Inorg. Chem.* **2001**, *40*, 6588–6597.

[20] [20a] S. C. Dunn, P. Mountford, D. A. Robson, *J. Chem. Soc., Dalton Trans.* **1997**, 293–304. [20b] A. J. Blake, P. E. Collier, S. C. Dunn, W.-S. Li, P. Mountford, O. V. Shishkin, *J. Chem. Soc., Dalton Trans.* **1997**, 1549–1558.

[21] [21a] L. Birkhofer, A. Ritter, P. Richter, *Chem. Ber.* **1963**, *96*, 2750−2757. [21b] D. W. Stephan, J. C. Stewart, F. Guérin, R. E. v. H. Spence, W. Xu, D. G. Harrison, *Organometallics* **1999**, *18*, 1116−1118. [21c] J. E. Kickham, F. Guérin, J. C. Stewart, D. W. Stephan, *Angew. Chem.* **2000**, *112*, 3406−3409; *Angew. Chem. Int. Ed.* **2000**, *39*, 3263−3266. [21d] I. Bytschkov, PhD Dissertation, University of Hannover, **2002**.

[22] [22a] D. W. Carpenetti, L. Kloppenburg, J. T. Kupec, J. L. Petersen, *Organometallics* **1996**, *15*, 1572−1581. [22b] J. Okuda, *Chem. Ber.* **1990**, *123*, 1649−1651.

[23] A. Dietrich, B. Maas, W. Messer, G. Bruche, V. Karl, A. Kaunzinger, A. Mosandl, *J. High Resol. Chromatogr.* **1993**, *16*, 590−593.

[24] W. A. König, B. Gehrcke, D. Icheln, P. Evers, J. Dönnecke, W. Wang, *J. High Resol. Chromatogr.* **1992**, *15*, 367−372.

Received August 19, 2003