J|A|C|S
ARTICLES
Published on Web 08/06/2003

Amines Made Easily: A Highly Selective Hydroaminomethylation of Olefins

Moballigh Ahmed, Abdul Majeed Seayad, Ralf Jackstell, and Matthias Beller*

Contribution from the Leibniz-Institut für Organische Katalyse an der Universität Rostock e.V. (IfOK), Buchbinderstrasse 5-6, D-18055 Rostock, Germany

Received February 27, 2003; E-mail: matthias.beller@ifok.uni-rostock.de

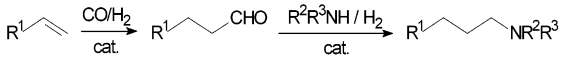
Abstract: A highly chemo- and regioselective hydroaminomethylation of simple as well as functionalized α-olefins using a cationic rhodium precatalyst together with Xantphos as ligand is reported. Studies of the influence of ligands and reaction conditions led to an unprecedented selective hydroaminomethylation procedure. The novel procedure constitutes an economically attractive and environmentally favorable synthesis of secondary and tertiary aliphatic amines.

With a production on million-ton scale per year[1] aliphatic amines are among the important bulk and fine chemicals in the chemical and pharmaceutical industry.[2] A number of amines, enamines, and imines are useful as pharmaceutically and biologically active substances, dyes, and fine chemicals. Important methods for the synthesis of aliphatic amines include nucleophilic substitution reactions of alkyl halides, hydrocyanation of alkenes followed by reduction and reductive amination of carbonyl compounds, etc. Despite the various methods available, amine synthesis is often troubled by expensive starting materials, a large number of byproducts, and the need for protecting and deprotecting reaction steps.

From both the economic and environmental points of view, developing new, versatile and selective synthetic routes to aliphatic amines from inexpensive feedstock is of fundamental importance. Although hydroamination of olefins[3] and reductive hydroamination of alkynes[4] offer efficient synthesis of certain amines, these methods still need to be improved with regard to generality. An environmentally benign, one-pot, atom-efficient synthesis of amines from ubiquitous olefins is the so-called hydroaminomethylation reaction (Scheme 1).[5] This domino reaction[6] consists of an initial hydroformylation of olefins to an aldehyde, subsequent formation of an enamine (or imine) followed by hydrogenation.

Since the discovery of this reaction by W. Reppe at BASF,[7] the hydroaminomethylation reaction has been mainly studied in industry. Despite some progress[8] comparably few synthetic applications have been reported. In this respect especially noteworthy is the work of Eilbracht and co-workers[9] who developed new variants of hydroaminomethylation reactions. In general, simple rhodium salts or combinations of rhodium

Scheme 1. Hydroaminomethylation of Alkenes



(1) *Chem. Mark. Rep.* **1998**, *December*, 7.
(2) For general references, see: (a) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; p 768 and references therein. (b) Collman, J. P.; Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, p 892 and references therein. (c) Heilen, G.; Mercker, H. J.; Frank, D.; Reck, A.; Jäckh, R. *Ullmanns Encyclopedia of Industrial Chemistry*; VCH: Weinheim 1985; Vol. A2, p 1.
(3) For reviews see: (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675−703. (b) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199−207. (c) Nobis, M.; Driessen-Hölscher, B. *Angew. Chem.* **2001**, *113*, 4105−4108; *Angew. Chem., Int. Ed.* **2001**, *40*, 3983−3986. (d) Beller, M.; Breindl, C.; Eichberger, M.; Hartung, C. G.; Seayad, J.; Thiel, O. R.; Tillack, A.; Trauthwein, H. *Synlett* **2002**, *10*, 1579−1594. (e) Seayad, J.; Tillack, A.; Hartung, C. G.; Beller, M. *Adv. Synth. Catal.* **2002**, *344*, 795−813.
(4) (a) McGrane, P. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1993**, *115*, 11485−11489. (b) McGrane, P. L.; Livinghouse, T. *J. Org. Chem.* **1992**, *57*, 1323−1324. (c) McGrane, P. L.; Jensen, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1992**, *114*, 5459−5460. (d) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708−1719. (e) Baranger, A. M.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 2753−2763. (f) Haak, E.; Bytschkov, I.; Doye, S. *Angew. Chem.* **1999**, *111*, 3584−3586; *Angew. Chem., Int. Ed.* **1999**, *38*, 3389−3391. (g) Haak, E.; Siebeneicher, H.; Doye, S. *Org. Lett.* **2000**, *2*, 1935−1937. (h) Johnson, J. S.; Bergman, R. G. *J. Am. Chem. Soc.* **2001**, *123*, 2923−2924. (i) Pohlki, F.; Doye, S. *Angew. Chem.* **2001**, *113*, 2361−2364; *Angew. Chem., Int. Ed.* **2001**, *40*, 2305−2308. (j) Cao, C.; Ciszewski, J. T.; Odom, A. L. *Organometallics* **2001**, *20*, 5011−5013. (k) Pohlki, F.; Heutling, A.; Bytschkov, I.; Hotopp, T.; Doye, S. *Synlett* **2002**, 799−801. (l) Ong, T.-G.; Yap, G. P. A.; Richeson, D. S. *Organometallics* **2002**, *21*, 2839−2841. (m) Tillack, A.; Garcia Castro, I.; Hartung, C.; Beller, M. *Angew. Chem.* **2002**, *114*, 2646−2648; *Angew. Chem., Int. Ed.* **2002**, *41*, 2541−2543. (n) Hartung, C. G.; Trauthwein, H.; Tillack, A.; Beller, M. *J. Org. Chem.* **2001**, *66*, 6339−6343.
(5) Review: Eilbracht, P.; Bärfacker, L.; Buss, C.; Hollmann, C.; Kitsos-Rzychon, B. E.; Kranemann, C. L.; Rische, T.; Roggenbuck, R.; Schmidt, A. *Chem. Rev.* **1999**, *99*, 3329−3365.
(6) (a) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115−136. (b) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831−844.
(7) Reppe, W.; Vetter, H. *Liebigs Ann. Chem.* **1953,** *582*, 133−163.
(8) (a) Zimmermann, B.; Herwig, J.; Beller, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 2372−2375. (b) Iqbal, A. F. M. *Chem. Acta* **1971**, *54*, 1440. (b) Jachimowicz, F.; Raksis, J. W. *J. Org. Chem.* **1982**, *47*, 445−447. (c) MacEntire, E.; Knifton, J. F. (Texaco Inc.). EP-B 241093, 1987; *Chem. Abstr.* **1989**, *110*, 134785h. (d) Brunet, J. J.; Neibecker, D.; Agbossou, F.; Srivastav, R. S. *J. Mol. Catal.* **1994**, *87*, 223−230. (e) Drent, E.; Breed, A. J. M. (Shell Int. Res. M.). EP-B 457386, 1992; *Chem. Abstr.* **1992**, *116*, 83212h. (f) Törös, S.; Gemes-Pesci, I.; Heil, B.; Maho, S.; Tubar, Z. *J. Chem. Soc., Chem. Commun.* **1992**, 585−589. (g) Baig, T.; Kalck, P *J. Chem. Soc., Chem. Commun.* **1992**, 1373−1374. (h) Baig, T.; Molinier, J.; Kalck, P. *J. Organomet. Chem.* **1993**, *455*, 219−224. (i) Jones, M. D. *J. Organomet. Chem.* **1989**, 366, 403−408. (j) Diekhaus, G.; Kampmann, D.; Kniep, C.; Müller, T.; Walter, J.; Weber, J. (Hoechst AG). DE-B 4334809, 1993; *Chem. Abstr.* **1995**, *122*, 314160g. (k) Schaffrath, H.; Keim, W. *J. Mol. Catal.* **1999**, *140*, 107−113.
(9) (a) Rische, T.; Bärfacker, L.; Eilbracht, P. *Eur. J. Org. Chem.* **1999**, *3*, 653−660. (b) Rische, T.; Kitsos-Rzychon, B.; Eilbracht, P. *Tetrahedron* **1998**, *54*, 2723−2742. (c) Kranemann, C. L.; Eilbracht, P. *Synthesis* **1998**, *1*, 71. (d) Rische, T.; Eilbracht, P. *Synthesis* **1997**, *11*, 1331−1337. (e) Breit, B. *Tetrahedron Lett.* **1998**, *39*, 5163−5166.

salts with triphenylphosphine have been applied as catalysts for these reactions. With such catalysts a major problem of hydroaminomethylation reactions of α-olefins is the unsatisfactory regioselectivity at the initial hydroformylation stage. Often n/iso-selectivities are in the range of 2:1 to 6:1. Although this regioselectivity sounds reasonable, *for most amines it provides enormous difficulties to obtain pure products* due to similar physical properties of the produced linear and branched isomers. Another problem of current hydroaminomethylation protocols is the slow hydrogenation of the intermediate enamine (or imine) and thus aldol-type side reactions. To the best of our knowledge there exists no general protocol for fast and highly regioselective reactions. In this contribution we present a general and practical rhodium catalyst, which allows for the first time, efficient and highly regioselective (typically n/iso > 98:2) hydroaminomethylations of simple as well as functionalized α-olefins.

Results and Discussion

Clearly, the basic requirement to achieve high selectivity in hydroaminomethylation is to use a tailor- made catalyst system, which provides the desired regioselectivity at the initial hydroformylation step. While the influence of different phosphine and phosphite ligands on the regioselectivity of hydroformylations is well-known,[10] similar investigations in hydroaminomethylations are missing. It is expected that the presence of amines will influence the n/iso-selectivity of the hydroformylation step because amines will compete with phosphines as ligands for the metal center and thereby will influence the regioselectivity. To get an impression of the effect of amines on the regioselectivity, we initially studied the hydroformylation of 1-pentene in the presence of different concentrations of triethylamine. Similar to our recent work on hydroaminomethylations of internal olefins to linear amines[11] we used 0.1 mol % $[Rh(cod)_2]BF_4$, in the presence of 0.4 mol % ligand as a catalyst system at 40 bar of synthesis gas (7 bar P_{CO}, 33 bar P_{H2}). As ligands, triphenylphosphine and bidentate phosphines such as Naphos,[12] Xantphos,[13] or their derivatives were applied (Table 1).

As shown in Table 1 (entries 1−3) the n/iso-selectivity[14] decreases significantly from 95:5 (no triethylamine present) to 80:20 (10 mmol triethylamine present) and 72:28 (50 mmol triethylamine present) using triphenylphosphine as ligand. Diphosphine ligands such as Iphos and Xantphos gave n/iso-selectivities of 98:2 and 97:3 in the presence of 10 mmol of triethylamine, respectively (Table 1, entries 4−8). Obviously, in the presence of chelating phosphines there is no significant effect observed due to the less favorable exchange of ligands.

Next, the hydroaminomethylation of 1-pentene with piperidine was systematically investigated regarding the influence of catalyst, ligands, and critical reaction parameters (solvent, temperature, time, and concentration of starting materials). The effect of different rhodium precursors and phosphine ligands are presented in Table 2.

It is shown that most rhodium complexes (except for 1,2-bisdiphenylphosphinoethane (dppe); Table 2, entry 8) give high conversion. However, the hydrogenation activity of the catalysts is different, and especially the regioselectivity of the hydroformylation step is influenced by the respective ligand. Even without any phosphine ligand present the reaction proceeds with high conversion, and hydrogenation of the intermediate enamine constitutes no problem as shown by the high amine selectivity (98%). However, without added phosphine the regioselectivity is low, giving only 50% yield of the linear amine (Table 2, entry 1). In the presence of the "standard ligand" triphenylphosphine, conversion and enamine hydrogenation are decreased compared to those with the phosphine-free system, but the regioselectivity is increased (n/iso = 86:14). As expected tri-*o*-tolylphosphine leads to a lower regioselectivity compared to that with triphenylphosphine.[15] Among the other tested ligands (Table 2, entry 4−11) Xantphos appeared to be the optimal ligand giving quantitative conversion, fast enamine hydrogenation (amine selectivity = 97%), and high regioselectivity (n/iso = 98:2). In agreement with previous hydroformylation studies an increased natural bite angle[16] of the chelating phosphine leads to an increased selectivity for linear amine. For example the regioselectivity increases in the order dppb (P−Rh−P bite angle 98.6°) < DPEphos (P−Rh−P bite angle 102.2°) < Xantphos (P−Rh−P bite angle 111.4°). Depending on the applied rhodium precursors, we noted a small influence

(10) Selected references: (a) Bohnen, H. W.; Cornils, B. *Adv. Catal.* **2002**, *47*, 1−64. (b) van Leeuwen P. W. N. M.; Kamer, P. C. J.; Reek J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741−2765. (c) Casey, C. P.; Petrovich, L. M. *J. Am. Chem. Soc.* **1995**, *117*, 6007−6014. (d) Unruh, J. D.; Christenson, J. R. *J. Mol. Catal.* **1982**, *14*, 19−34. (e) Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Chem. Commun.* **2002**, *24*, 3044−3045. (f) Mehnert, C. P.; Cook, R. A.; Dispenziere, N. C.; Afeworki, M. *J. Am. Chem. Soc.* **2002**, *124*, 12932−12933. (g) Clark, H. J.; Wang, R. P.; Alper, H. *J. Org. Chem.* **2002**, *67*, 6224−6225. (h) da Silva, A. C.; de Oliveira, K. C. B.; Gusevskaya, E. V.; dos Santos, E. N. *J. Mol. Catal.* **2002**, *179*, 133−141. (i) Dieguez, M.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2001**, *12*, 2827−2834. (j) Selent, D.; Wiese, K.-D.; Röttger, D.; Börner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1639−1641. (k) Selent, D.; Hess, D.; Wiese, K.-D.; Röttger, D.; Kunze, C.; Börner, A. *Angew. Chem.. Int. Ed.* **2001**, *40*, 1696−1698. (l) Gleich, D.; Schmid, R.; Herrmann, W. A. *Organometallics* **1998**, *17*, 2141−2143.

(11) (a) Seayad, A.; Ahmed, M.; Klein, H.; Jackstell, R.; Gross, T.; Beller, M. *Science* **2002**, *297*, 1676−1678. (b) Hartwig, J. F. *Science* **2002**, *297*, 1653−1654.

(12) (a) Devon, T. J.; Philips, G. W.; Puckette, T. A.; Satvinoha, J. L.; Vanderbilt, J. J. (Eastman Kodak). WO 87/07600, 1987. (b) Beller, M.; Krauter, J. G. E. *J. Mol. Catal.* **1999**, *143*, 31−39. (c) Herrmann, W. A.; Schmid, R.; Kohlpaintner, C. W.; Priermeier, T. *Organometallics* **1995**, *14*, 1961−1968. (d) Bahrmann, H. B.; Bergrath, K.; Kleiner, H.-J.; Lapper, P.; Naumann, C.; Peters, D.; Regnat, D. *J. Organomet. Chem.* **1996**, *520*, 97−100. (e) Rampf, F. A.; Spiegler, M.; Herrmann, W. A. *J. Organomet. Chem.* **1999**, *582*, 204−210. (f) Eckl, R. W.; Priermeier, T.; Herrmann, W. A.; *J. Organomet. Chem.* **1997**, *532*, 243−249. (g) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W.; *J. Mol. Catal.* **1995**, *104*, 17−85. (h) Okucu, S.; Karacar, A.; Freytag, M.; Jones, P. G.; Schmutzler, R. *Z. Anorg. Chem.* **2002**, *628*, 1339−1345. (i) Da Silva, A. C.; De Oliveira, K. C. B.; Gusevskaya, E. V.; Dos Santos, E. N. *J. Mol. Catal.* **2002**, *179*, 133−141.

(13) For excellent reviews see: (a) Kamer, P. C. J.; van Leeuwen, P. W. N.; Reek, J. N. H.; *Acc. Chem. Res.* **2001**, *34*, 895−904. (b) Kranenburg, M.; van der Bugt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **1995**, *14*, 3081−3083. (c) van der Veen, L. A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 336−338. (d) van der Veen, L. A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **1999**, *18*, 4765−4777. (e) van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz M.; Spek A. L. *Organometallics* **2000**, *19*, 872−883. (f) Fox, J. M.; Huang, X. H.; Chieffi, A.; Buchwald, S. L.; *J. Am. Chem. Soc.* **2000**, *122*, 1360−1370. (g) van Leeuwen, P. W. N. M.; Sandee, A. J.; Reek, J. N. H.; Kamer, P. C. J. *J. Mol. Catal.* **2002**, *182*, 107−123. (h) Landis, C. R.; Uddin, *J. Chem. Soc., Dalton Trans.* **2002**, 729−742. (i) Botteghi, C.; Marchetti, M.; Paganelli, S.; Scognamillo, S. *J. Mol. Catal.* **2002**, *179*, 79−86. (j) Goertz, W.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. *Chem. Eur. J.* **2001**, *7*, 1614−1618.

(14) The n/iso ratios were determined by GC analysis of the crude reaction mixture.

(15) Reinius, H. K.; Suomalainen, P.; Riihimaki, H.; Karvinen, H.; Pursiainen, J.; Krause, A. O. I. *J. Catal.* **2001**, *199*, 302−308 and references therein.

(16) (a) van Leeuwen, P. W. N. M., Claver, C., Eds. *Rhodium Catalyzed Hydroformylation*; Kluwer Academic Publishers: Dordrecht, 2000. (b) Casey, C. P.; Whiteker, G. T. *Isr. J. Chem.* **1990**, *30*, 299−304. (c) Casey, C. P.; Whiteker, G. T.; Melville, M. G.; Petrovich, L. M.; Gavney. J. A., Jr.; Powell, D. R. *J. Am. Chem. Soc.* **1992**, *114*, 5535−5543. (d) Gleich, D.; Herrmann, W. A. *Organometallics* **1999**, *18*, 4354−4361. (e) Dierkes, P.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1999**, *10*, 1519−1529.

Table 1. Hydroformylation in the Presence of Triethylamine and Different Ligands[a]

entry	olefin	amine [mmol]	ligand [0.4 mol%]	conversion [%]	aldehyde selectivity [%][b]	n:iso
1		-	PPh_3	100	90	95:5
2		10	PPh_3	98	92	80:20
3		50	PPh_3	95	85	72:28
4		-	Xantphos	100	98	97:3
5		10	Xantphos	98	>99	97:3
6		50	Xantphos	97	99	96:4
7		-	Iphos	100	95[c]	98:2
8		10	Iphos	100	>99	98:2

[a] Reaction conditions: 10 mmol substrate, 0.1 mol % $[Rh(cod)_2]BF_4$, 0.4 mol % ligand, 15 mL of MeOH, 15 mL of toluene, 7 bar Pco, 33 bar P_{H2}, 125 °C, 5 h. [b] Selectivities were determined by GC analysis using bis(methoxyethyl) ether as an internal standard. [c] 5% condensation product.

on the formation of *N*-formylpiperidine (Table 2, entries 4−6). Best and highly reproducible results were obtained using the cationic rhodium precursor $[Rh(cod)_2]BF_4$. Similar to the hydroformylation of 1-pentene in the presence of triethylamine the highest linear-to-branched ratio was observed using our ligand Iphos.[17] However, conversion and the hydrogenation activity were lower compared to those with Xantphos. Therefore, Xantphos was used for all further studies.

A survey of the effect of different solvents on the hydroaminomethylation of 1-pentene demonstrated that the reaction proceeds smoothly in methanol. However, in this solvent 15% of *N*-formylpiperidine (via direct carbonylation of piperidine) as side-product arose. In toluene, tetrahydrofuran (thf), and methyl-*tert*-butyl ether (MTBE) the hydrogenation of the in situ-produced enamine is the rate-determining step of the reaction sequence (Table 3; compare entries 1−4). Hence, significant amounts of enamine can be detected.

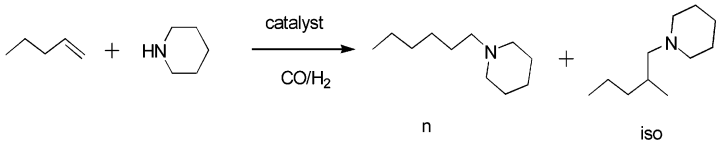
By using a combination of nonpolar aromatic solvents and methanol hydrogenation of the enamine does not constitute a problem. Advantageously the formation of *N*-formylpiperidine is also suppressed. Hence, 98% selectivity with regard to amines and high regioselectivity (n/iso 98:2) was obtained applying a 1:1 mixture of toluene and methanol (Table 3, entries 5−12). Variation of the temperature showed that below 125 °C the reaction rate is significantly slower. Hence, reaction times of >24 h are needed for full conversion. On the other hand, at 125 °C the reaction proceeds well even in 1.5 h, although for complete hydrogenation 5 h of the reaction time is needed. Optimizing the partial pressures of hydrogen and carbon monoxide decreased considerably the formylation of piperidine (Table 3; entries 8−12). At 125 °C and 40 bar CO/H_2 (7 bar of carbon monoxide and 33 bar of hydrogen) excellent yield and regioselectivity to the linear amine was achieved.

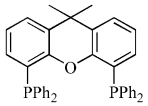
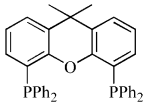
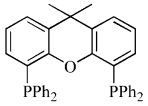
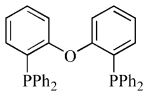
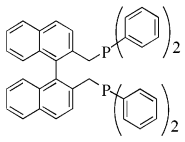
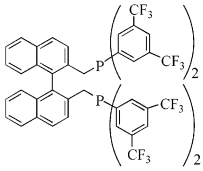
Clearly a new hydroaminomethylation procedure is of significant importance to synthetic organic chemists only if different aliphatic and aromatic olefins with various functional groups can be applied with success. Hence, we were interested in the compatibility of our protocol with a large number of aliphatic and aromatic olefins bearing a wider variety of functional groups (Table 4). As amines, primary and secondary amines possessing functional groups and a protected diamine have been employed. We were pleased to find that not only lower but also higher aliphatic olefins react well with different amines to give the linear products with excellent selectivity because higher olefins often react more sluggishly. Linear and branched unprotected olefinic alcohols were efficiently converted into interesting amino alcohols with high n/iso ratio. Acrolein diethylacetal underwent selective hydroaminomethylation to produce protected γ-aminoaldehydes, which are known to be synthetically useful intermediates.[18] It is important to note that the reaction of a primary amine (3-amino-1-propanol) and acrolein diethylacetal occurs with high chemo- and regioselectivity, giving the secondary amine in 99% yield, despite the further potential amination. This reaction constitutes one of the rare examples in hydroaminomethylation reactions of primary amines to produce the secondary amines selectively. Other aromatic primary amines and aliphatic primary and secondary amines also react well to give secondary and tertiary amines in high yield and selectivity. Aromatic olefins produce linear amines in good selectivities. To the best of our knowledge styrene and *p*-chlorostyrene were hydroaminomethylated for the

(17) Klein, H.; Jackstell, R.; Wiese, K.-D.; Röttger, D.; Beller, M. *Angew. Chem. Int. Ed.* **2001**, *40*, 3408−3411.

(18) (a) Frederick, H.; Da-Ming, Gou.; Marchese, S. A.; Martel, L. J.; Necula, A.; Benetti, R. E.; Silva, R. A. (Rhodia Chirex Inc.). U.S. Patent 6,489,-512, 2002. (b) Doi, T.; Hijikuro, I.; Takahashi, T. *Synlett* **1999**, *11*, 1751−1753. (c) Botteghi, C.; Soccolini, F. *Synthesis* **1985**, *6−7*, 592−604.

Table 2. Hydroaminomethylation of 1-Pentene with Piperidine Using Different Rh Complexes and Ligands[a]



entry	Rh [0.1 mol%]	ligand [0.4 mol%]	Conversion [%]	amine selectivity [%][b]	linear amine yield [%]	n:iso
1	$[Rh(cod)_2]BF_4$	-	91	98	50	56:44
2	$[Rh(cod)_2]BF_4$	PPh_3	77	88[c]	64	86:14[d]
3	$[Rh(cod)_2]BF_4$	$(o\text{-tolyl})_3P$	100	98	56	57:43
4	$[Rh(cod)_2]BF_4$		100	97	95	98:2
5	$[Rh(cod)\ Cl]_2$		100	94[c,e]	92	98:2
6	$Rh(CO)_2acac$		100	90[c]	87	97:3
7	$[Rh(cod)_2]BF_4$		100	98	91	93:7
8	$[Rh(cod)_2]BF_4$	dppe	0	0	0	-
9	$[Rh(cod)_2]BF_4$	dppb	100	93[c]	73	78:22
10	$[Rh(cod)_2]BF_4$		100	89[c]	84	94:6
11	[g] $[Rh(cod)_2]BF_4$		77	66[c,f]	50	99:1

[a] Reaction conditions: 10 mmol alkene, 10 mmol amine, 15 mL of methanol, 15 mL of toluene, 7 bar P_{CO}, 33 bar P_{H2}, 125 °C, 5 h. [b] Selectivities were determined by GC analysis using bis(methoxyethyl) ether as an internal standard. [c] Major side product *N*-formylpiperidine. [d] 10% iso-amine. [e] Major side product *N*-methylpiperidine. [f] Aldol product. [g] 24 h.

first time to produce selectively linear amines. Other aromatic olefinic substrates, which are known either to produce potentially important aldehydes and their derivatives via hydroformylation[19] or to produce biologically active compounds directly through a domino hydroaminomethylation reaction,[20] also have been studied and gave the corresponding products in good to excellent yield.

In most cases the reaction proceeds with an extremely high degree of selectivity toward the linear amines. Among the different reactions studied, the hydroaminomethylation of 1-pent-3-ol, α-methyl styrene, and 1,1-diphenylethene needed longer reaction time and higher reaction temperature for complete hydrogenation of the corresponding enamine (or imine). However, the observed regioselectivity using cationic rhodium precursor together with Xantphos was excellent, typically 99:1 for the linear product.

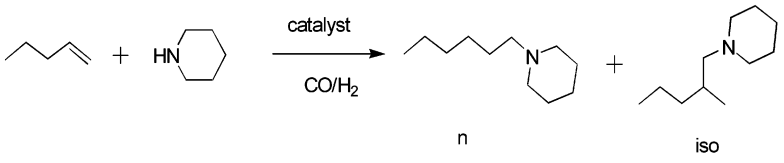
Conclusions

We have shown that a catalyst system consisting of a cationic rhodium precursor together with Xantphos as ligand can effect

(19) (a) Paganelli, S.; Zanchet, M.; Marchetti, M.; Mangano, G. *J. Mol. Catal.* **2000**, *157*, 1−8. (b) Botteghi, C.; Marchetti, M.; Paganelli, S. New opportunities in hydroformylation: selected synthesis of intermediates and fine chemicals. In *Transition Metal for Organic Synthesis*; Bolm, C., Beller, M., Eds.; VCH: Weinheim, Germany, 1988; Vol. 1, p 25.

(20) Botteghi, C.; Cazzolato, L.; Marchetti, M.; Paganelli, S. *J. Org. Chem.* **1995**, *60*, 6612−6615.

Table 3. Variation of Reaction Conditions[a]



entry	P_{CO}/P_{H2} [bar]	solvent [1/1]	temperature [°C]	time [h]	conversion [%]	amine selectivity [%][b]	selectivity [%] linear amine	isoamine	linear enamine	*N*-formyl piperdine	n/iso
1	10/50	toluene	125	24	75	14	14	–	69	15[c]	99:1
2	10/50	thf	125	24	75	59	59	–	38	3	99:1
3	10/50	MeOH	125	24	100	83	79	4	-	15	95:5
4	10/50	MTBE	125	24	70	13	13	–	80	7	99:1
5	10/50	MeOH/ toluene	115	24	76	96	91	5	–	4	95:5
6	10/50	MeOH/ toluene	135	6	100	93	91	2	–	6	98:2
7	10/50	MeOH/ toluene	125	6	100	95	92	3	–	5	97:3
8	10/30	MeOH/ toluene	125	6	100	95	92	3	–	5	97:3
9	10/20	MeOH/ toluene	125	5	100	93	90	3	–	6	97:3
10	10/10	MeOH/ toluene	125	5	100	90	88	2	–	10	98:2
11	7/13	MeOH/ toluene	125	5	100	93	91	2	–	7	98:2
12	7/33	MeOH/ toluene	125	5	100	97	95	2	–	3	98:2

[a] Reaction conditions: 10 mmol 1-pentene, 10 mmol piperidine, 0.1 mol % $[Rh(cod)_2]BF_4$, 0.4 mol % Xantphos, 30 mL of solvent (1:1). [b] Selectivitiese were determined by GC analysis using bis(methoxyethyl) ether as an internal standard. [c] Aldol product.

the regioselective hydroaminomethylation of terminal olefins to produce synthetically important linear amines in excellent yield. Clearly, the reaction is atom economic and environmentally friendly (i.e. water is the only byproduct), and the starting materials are both inexpensive and readily available. Aliphatic olefins gave for the first time the corresponding linear products in general with regioselectivities >98:2. This allows an easy isolation of the reaction mixture compared to previous protocols. High chemo- and regioselectivities for the linear amines are also obtained in the cases of styrene and its derivatives. The reported catalyst system is tolerant to a variety of potentially reactive functional groups, making the procedure valuable for the synthesis of interesting organic building blocks.

Experimental Section

General Considerations. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX 400 spectrometer (^{1}H, 400.1 MHz; ^{13}C, 100.6 MHz). Chemical shifts (δ) are given in ppm and refer to residual solvent as internal standard. Gas chromatographic analyses were performed on a Hewlett-Packard HP 5890 chromatograph with FID detector and a HP5 column (cross-linked 5% PH ME siloxane). Mass spectra (GC−MS) experiments were conducted on an Agilent-6890. The products were isolated from the reaction mixture by solvent evaporation and further purified by column chromatography on silica gel 60, 0.063−0.2 mm, 70−230 mesh (Merck) wherever necessary. Elemental analyses were determined by C/H/N/S-Analysator 932 (Leco). All yields reported in Tables 1−4 refer to GC yields using bis(methoxyethyl)ether as an internal standard. All isolated yields (varying from <5 to 10% as compared to the GC yield) of compounds estimated to be >98% pure as determined by GC, NMR, and elemental analyses. All new compounds were further characterized by HRMS (high-resolution mass spectroscopy) and/or elemental analyses. Linear-to-branched ratios were determined by GC analysis of the crude reaction mixture. Compounds known in the literature were characterized by comparing their ^{1}H NMR, ^{13}C NMR, and GC/MS data to the previously reported data. The purity of known compounds was confirmed by GC. Trihexylamine, dihexylamine, and *N*,*N*-dimethyl hexylamine have been characterized by comparison (GC) with commercially available samples.

General Procedure for Catalytic Hydroaminomethylation Reactions. Hydroaminomethylation experiments were carried out in a Parr stainless steel autoclave (100 mL). In a typical experiment, the autoclave was charged with $[Rh(cod)_2]BF_4$ (0.1 mol %), Xantphos (0.4 mol %), olefin (10.0 mmol), amine (10.0 mmol), methanol (15 mL), and toluene (15 mL) under argon atmosphere. The autoclave was pressurized with CO (7 bar) and hydrogen (33 bar), and the reaction was carried out at 125 °C for 5 h. After reaction, the autoclave was cooled to room temperature and depressurized. The content was transferred to a Schlenk flask under argon atmosphere, dried over $MgSO_4$ and analyzed by gas chromatography using bis(methoxyethyl)ether as internal standard.

Physical Data for Amines. 1. *N*-Hexylpiperidine:[21] yield 98% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26−2.33 (m, br, 4H), 2.21 (t, J = 7.9 Hz, 2H), 1.51 (quintet, J = 5.6 Hz, 4H), 1.41−1.45 (m, 2H), 1.38−1.43 (m, 2H), 1.21−1.28 (m, 6H), 0.81 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 60.05, 55.01, 32.41, 27.85, 27.24, 26.31, 24.87, 22.99, 14.41. GC−MS (EI, 70 eV): m/z = 169 [M^+], 154, 140, 124, 98, 84, 70, 55, 41, 29. HRMS Calcd for $C_{11}H_{23}N$ [M^+]: 169.18388. Found: 169.18304.

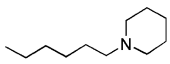
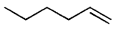
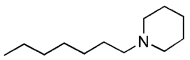
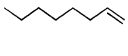
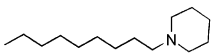
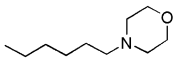
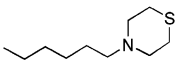
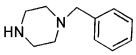
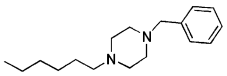
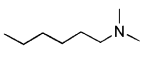
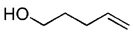
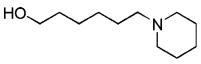
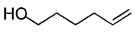
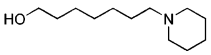
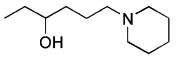
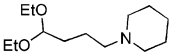
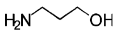
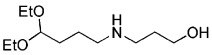
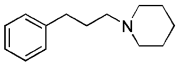
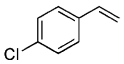
2. *N*-Heptylpiperidine:[22] yield 98% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30−2.42 (m, br, 4H), 2.25 (t, J = 7.8 Hz, 2H), 1.63 (quintet, J = 5.6 Hz, 4H), 1.52−1.57 (m, 2H), 1.44−1.49 (m, 2H), 1.23−1.36 (m, 8H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 60.02, 55.05, 32.46, 30.01, 28.53, 27.96, 26.35, 25.06, 23.17, 14.45. GC−MS (EI, 70 eV) m/z = 183 [M^+], 168, 154, 140, 124, 98, 84, 70, 55, 41, 29. HRMS Calcd for $C_{12}H_{25}N$ [M^+] 183.19869. Found 183.19810.

3. *N*-Nonylpiperidine:[23] yield 99% (GC).^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47−2.53 (m, br, 4H), 2.40 (t, J = 7.6 Hz, 2H), 1.72 (quintet, J = 5.6 Hz, 4H), 1.62−1.66 (m, 2H), 1.55−1.60 (m, 2H), 1.34−1.46 (m, 12H), 1.01 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 60.08, 55.02, 32.27, 30.01, 29.95, 29.67, 28.17, 27.30, 26.32, 24.88, 23.05, 14.46. GC−MS (EI, 70 eV) m/z = 211 [M^+], 196, 182, 168, 154, 140, 124, 110, 98, 84, 70, 55, 41, 29. HRMS Calcd for $C_{14}H_{29}N$ [M^+] 211.22819. Found 211.23000.

4. *N*-Hexylmorpholine:[24] yield 92% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, J = 4.8 Hz, 4H), 3.32−3.69 (m, 4H), 2.24 (t, J =

(21) (a) Nung, M. Y.; Eui, G. K.; Heui, S. S.; Jaesung, C. *Synth. Commun.* **1993**, *23*, 1595−1599. (b) Richard, M. L. *J. Org. Chem.* **1980**, *45*, 3370−3372 and references therein.
(22) (a) Bruno, W.; Homer, A. *J. Am. Chem. Soc.* **1934**, *56*, 2419−2424. (b) Peter deBenneville L.; Jane Macartney H. *J. Am. Chem. Soc.* **1950**, *72*, 3073−3075 and references therein.
(23) (a) Bruno, W.; Homer A. *J. Am. Chem. Soc.* **1934**, *56*, 2419−2424. (b) Albrecht, H.; Dollinger, H. *Tetrahedron Lett.* **1984**, *25*, 1353−1356 and references therein.

Table 4. Hydroaminomethylation of Various Olefins and Amines[a]

entry	olefin	amine	major product	conversion [%]	amine selectivity [%]	yield [%][b]	n:iso
1				100	>99	>99	98:2
2				100	>99	>99	98:2
3				100	>99	>99	99:1
4				95	>99	>94	97:3
5				92	>99	>91	99:1
6				95	>99	>94	99:1
7				100	95	95	99:1
8				100	98	98	99:1
9				100	98	98	99:1
10[c]				100	99	99	99:1
11				100	97	97	99:1
12				100	99	99	99:1
13				93	95	88	82:18
14				95	90	86	80:20
15[d]				89	>99	>88	99:1
16				75	95	71	90:10
17				100	90	90	99:1
18[e]				60	>99	>59	99:1
19				80	95	76	98:2
20				98	96	94	98:2
21[f]				89	98	87	99:1

[a] Reaction conditions: 10 mmol (1:1) substrate, 0.1 mol % $[Rh(cod)_2]BF_4$, 0.4 mol % Xantphos, 15 mL of MeOH, 15 mL of toluene, 7 bar P_{CO}, 33 bar P_{H2}, 125 °C, 5 h. [b] Yields were determined by GC analysis using bis(methoxyethyl) ether as an internal standard. [c] 135 °C, 30 h. [d] 135 °C, 18 h. [e] 0.2 mol % $[Rh(cod)_2]BF_4$, 0.8 mol % Xantphos, 135 °C, 36 h. [f] 125 °C, 12 h.

7.9 Hz, 2H), 1.40−1.43 (m, 2H), 1.19−1.26 (m, 6H), 0.81 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz) δ 65.97, 58.25, 52.81, 30.79, 26.20, 25.53, 21.60, 13.04. GC−MS m/z = 171 [M$^+$], 156, 142, 126, 100, 84, 70, 56, 42, 29. HRMS Calcd for $C_{10}H_{21}NO$ [M$^+$] 171.16258. Found 171.16231.

5. *N*-Hexylthiomorpholine: yield 92% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68−3.75 (m, 4H), 3.50 (t, J = 5.6 Hz, 4H), 2.80 (t, J = 5.6 Hz, 2H), 2.47−2.54 (m, 2H), 1.42−1.53 (m, 6H), 1.03 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.50, 54.10, 30.80, 27.00, 26.20, 25.60, 21.60, 13.10. GC−MS (EI, 70 eV) m/z = 187 [M$^+$], 126, 116, 88, 70, 57, 42, 29. Anal. Calcd for $C_{10}H_{21}NS$ C, 64.22; H, 11.22; N, 7.48; S, 17.10. Found C, 64.32; H, 11.54; N, 6.99; S, 17.43.

6. *N*-Hexyl-*N*'-benzylpiperazine:[25] yield 94% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.34 (m, 5H), 3.55 (s, 2H), 3.37−3.41 (m, 8H), 2.83 (t, J = 5.2 Hz, 2H), 2.35−2.55 (m, 2H), 1.47−1.55 (m, 6H), 0.88−0.95 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 129.5, 128.6, 127.4, 63.53, 59.36, 53.71, 53.54, 32.22, 27.88, 27.36, 23.01, 14.56. GC−MS (EI, 70 eV) m/z = 260 [M$^+$], 189, 161, 146, 128, 114, 98, 91, 84, 70, 58, 42, 29. HRMS Calcd for $C_{17}H_{28}N_2$ [M$^+$] 260.22714. Found 260.22525.

7. *N*-(6-Hydroxyhexyl)piperidine:[26] yield 97% (GC).^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (t, J = 5.6 Hz, 2H), 3.49 (t, J = 5.5 Hz, 2H), 3.01−3.08 (m, 4H), 2.45−2.65 (m, 2H), 1.84−1.90 (m, 2H), 1.43−1.80 (m, 6H), 1.02−1.12 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.70, 59.80, 55.00, 33.10, 28.10, 27.80, 26.20, 26.10, 25.50. GC−MS (EI, 70 eV) m/z = 185 [M$^+$], 168, 155, 140, 124, 110, 98, 84, 70, 55, 41, 30. HRMS Calcd for $C_{11}H_{23}NO$ [M$^+$] 185.17744. Found 185.17796.

8. *N*-(7-Hydroxyheptyl)piperidine:[27] yield 97% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (t, J = 5.6 Hz, 2H), 3.45 (t, J = 5.5 Hz, 2H), 3.02−3.07 (m, 4H), 2.40−2.66 (m, 2H), 1.80−1.95 (m, 2H), 1.42−1.76 (m, 6H), 0.79−0.93 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.73, 59.95, 54.93, 33.14, 29.76, 28.10, 27.00, 26.14, 26.09, 24.75. GC−MS (EI, 70 eV) m/z = 199 [M$^+$], 182, 169, 154, 140, 124, 110, 98, 84, 70, 55, 41, 31. HRMS Calcd for $C_{12}H_{25}NO$ [M$^+$] 199.19333. Found 199.19362.

9. *N*-(4-Hydroxyhexyl)piperidine:[28] yield 99% (GC). ^{1}H NMR (400 MHz, $CDCl_3$), δ 3.30 (tt, J = 5.7, 5.6 Hz, 1H), 2.26 (t, J = 5.6 Hz, 2H), 1.80−1.95 (m, 4H), 1.61−1.73 (m, 6H), 1.45−1.49 (m, 2H), 1.40−1.43 (m, 2H), 1.33−1.37 (m, 2H), 0.84 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.1, 59.8, 54.7, 37.2, 30.8, 26.4, 25.8, 24.6, 10.5. GC−MS (EI, 70 eV) m/z = 185 [M$^+$], 168, 156, 138, 124, 111, 98, 84, 70, 55, 41, 29. HRMS Calcd for $C_{11}H_{23}NO$ [M$^+$] 185.17833. Found 185.17796.

10. *N*-(4,4-Diethoxybutyl)piperdine:[29] yield 96% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (t, J = 5.3 Hz, 1H), 3.85 (q, J = 7.1 Hz, 4H), 2.24 (t, J = 5.5 Hz, 2H), 2.13−2.18 (m, 4H), 1.55−1.63 (m, 2H), 1.37−1.51 (m, br, 6H), 1.21−1.28 (m, 2H), 1.09 (t, J = 7.1 Hz, 6H). ^{13}C NMR (100 MHz) δ 103.1, 61.27, 59.53, 54.95, 32.08, 26.39, 24.84, 22.55, 15.66. GC−MS (EI, 70 eV) m/z = 229 [M$^+$], 200, 184, 154, 138, 115, 98, 87, 71, 55, 41, 29. HRMS Calcd for $C_{13}H_{27}NO_2$ [M$^+$] 229.20309. Found 229.20418.

11. *N*-(4,4-Diethoxybutyl)-*N*-3-hydroxypropylamine: yield >99% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.91 (t, J = 5.6 Hz, 1H), 3.95 (t, J = 5.8 Hz, 2H), 3.75 (q, J = 7.4 Hz, 4H), 3.05 (t, J = 2.3 Hz, 2H), 2.91 (t, J = 3.3 Hz, 2H), 1.63−1.78 (m, 2H), 1.48−1.51 (m, 2H), 1.26−1.34 (m, 2H), 1.08 (t, J = 7.1 Hz, 6H). ^{13}C NMR (100 MHz) δ 102.9, 88.69, 67.93, 61.21, 61.15, 44.64, 31.71, 27.63, 15.65. GC−MS (EI, 70 eV) m/z = 219 [M$^+$], 200, 188, 172, 126, 99, 86, 75, 41, 29. Anal. Calcd for $C_{11}H_{25}NO_3$ Anal. Calcd for $C_{13}H_{18}ClNO$ C, 60.04; H, 11.49; N, 6.39. Found C, 59.55; H, 11.15; N, 6.10.

12. *N*-(3-Phenylpropyl)piperidine:[30] yield 72% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.54 (m, 5H), 2.87 (t, J = 7.9 Hz, 2H), 2.61−2.65 (m, 4H), 2.59 (t, J = 7.5 Hz, 2H), 2.12 (quintet, J = 7.9 Hz, 2H), 1.84 (quintet, J = 5.6 Hz, 4H), 1.65−1.71 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 128.8, 128.7, 126.1, 59.43, 55.09, 34.42, 29.11, 26.47, 24.96. GC−MS (EI, 70 eV) m/z = 203 [M$^+$], 174, 160, 146, 117, 98, 91, 77, 70, 55, 41, 30. HRMS Calcd for $C_{14}H_{21}N$ [M$^{+]}$ 203.16745. Found 203.16740.

13. *N*-[3-(4-Chlorophenyl)propyl]morpholine: yield 69% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.0 Hz, 2H), 7.59 (d, J = 7.1 Hz, 2H), 3.56 (t, J = 5.1 Hz, 4H), 3.21 (t, J = 5.6 Hz, 4H), 2.76 (t, J = 7.2 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H), 1.65−1.71 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 135.1, 128.9, 128.6, 83.41, 61.35, 57.86, 40.54, 36.72. GC−MS (EI, 70 eV) m/z = 239 [M$^+$], 194, 152, 125, 100, 89, 70, 56, 43, 29. Anal. Calcd for $C_{13}H_{18}ClNO$ C, 65.13; H, 7.57; N, 5.84. Found C, 64.60; H, 7.33; N, 5.66.

14. *N*-(4-Phenylbutyl)piperidine:[31] yield 71% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14−7.21 (m, 5H), 3.23 (t, J = 5.7 Hz, 2H), 3.12 (t, J = 5.7 Hz, 2H), 2.63−2.71 (m, 4H), 2.15−2.34 (m, 2H), 1.90−2.08 (m, 6H), 1.78−1.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 128.8, 128.7, 126.1, 67.39, 59.45, 54.23, 36.37, 29.71, 26.65, 18.94. GC−MS (EI, 70 eV) m/z = 217 [M$^+$], 188, 174, 160, 124, 98, 91, 84, 70, 55, 41, 30. HRMS Calcd for $C_{15}H_{23}N$ [M$^+$] 217.15984. Found 217.16231.

15. *N*-(4-Phenoxybutyl)piperidine:[32] yield 90% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.38 (m, 5H), 3.81 (t, J = 5.6 Hz, 2H), 3.55 (t, J = 5.6 Hz, 2H), 2.68−2.79 (m, 4H), 2.05−2.18 (m, 2H), 1.95−2.09 (m, 6H), 1.85−1.97 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 129.8, 120.9, 115.1, 68.09, 59.51, 55.05, 27.97, 26.48, 26.32, 23.83. GC−MS (EI, 70 eV) m/z = 233 [M$^+$], 204, 149, 140, 127, 107, 98, 84, 77, 70, 55, 42, 29. HRMS Calcd for $C_{15}H_{23}NO$ [M$^+$] 233.17713. Found 233.17796.

16. *N*-Hexylaniline:[33] yield 76% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.33 (m, 5H), 3.12 (t, J = 5.6 Hz, 2H), 1.51−1.64 (m, 2H), 1.41−1.49 (m, 6H), 1.01 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 125.3, 117.8, 113.7, 61.43, 28.45, 28.27, 26.31, 23.14, 14.68. GC−MS (EI, 70 eV) m/z = 177 [M$^+$], 148, 132, 118, 106, 93, 77, 65, 51. 41, 29. HRMS Calcd for $C_{12}H_{19}N$ [M$^+$] 177.15279. Found 177.15175.

17. *N*-(3-Phenylbutyl)piperidine:[34] yield 88% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.54 (m, 5H), 2.96−3.29 (m, 1H), 2.53−2.61 (m, 4H), 2.35−2.42 (m, 2H), 2.15−2.33 (m, 2H), 1.81 (quintet, J = 5.6 Hz, 4H), 1.62−1.69 (m, 2H), 1.50 (d, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 128.7, 127.4, 126.3, 58.26, 55.13, 38.91, 35.84, 26.49, 24.91, 23.15. GC−MS (EI, 70 eV) m/z = 217 [M$^+$], 200, 174, 160, 139, 98, 91, 77, 70, 55, 41, 29. HRMS Calcd for $C_{15}H_{23}N$ [M$^+$] 217.18148. Found 217.18304.

18. *N*-(3,3-Diphenylpropyl)piperidine:[35] yield 60% (GC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13−7. 42 (m, 10H), 3.91−4.05 (m, 1H), 2.75−2.92 (m, 4H), 2.43−2.56 (m, 2H), 2.19−2.36 (m, 2H), 1.85 (quintet, J = 5.5 Hz, 4H), 1.59−1.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 128.9, 128.4, 126.6, 58.29, 55.21, 49.91, 33.40, 26.69, 25.19.

(24) (a) Philip, M. J.; Morris, Z. *J. Am. Chem. Soc.* **1940**, *62*, 1450−1452. (b) Charles, G. Y. E. *Tetrahedron Lett.* **1987**, *28*, 427−430. (c) Shin-ichi, I.; Naoto, Chatani.; Yasuteru, K.; Kouichi, O.; Shinji, M. *J. Org. Chem.* **1992**, *57*, 2−4 and references therein.

(25) Pine, H. S.; Cheney, J.; Catto, B.; Peterson, J. D. *J. Org. Chem.* **1974**, *39*, 130−133 and references therein.

(26) (a) John, C. S.; Homer A. *J. Am. Chem. Soc.* **1938**, *60*, 402−406. (b) Awd, A. *J. Appl. Chem.* **1951**, *1*, 469−470.

(27) Solov'ev, V. M.; Arendar, U.K.; Skoldinov, A. P. *J. Gen. Chem. USSR* **1961**, *31*, 2405−2411.

(28) Kafka, S.; Kytner, J.; Shilhankova, A.; Ferles, M. *Collect. Czech. Chem. Commun.* **1987**, *52*, 2035−2046.

(29) Keglevic, D.; Leonhard, B. *Croat. Chem. Acta* **1963**, *53*, 175−181.

(30) Yung-Son, H.; Sheng-Wun, L.; Ling, L.; Yao-Jung, C. *Tetrahedron* **1995**, *51*, 5019−5034.

(31) Huebner, F. C.; Hyla, A. T. *J. Org. Chem.* **1953**, *18*, 736−739.

(32) Olofson, R. A.; Abbott, D. E. *J. Org. Chem.* **1984**, *49*, 2795−2799 and references therein.

(33) Nung, M. Y.; Eui, G. K.; Heui, S. S.; Jaesung, C. *Synth. Commun.* **1993**, *23*,1595−1599 and references therein.

(34) Hennion, F. G.; Price, C. C., Jr.; Vernon, C. W. *J. Am. Chem. Soc.* **1955**, *77*, 4633−4636.

(35) Rische, T.; Eilbracht, P. *Tetrahedron* **1999**, *55*, 1915−1920 and references therein.

GC−MS (EI, 70 eV) m/z = 279 [M^+], 263, 220, 193, 165, 115, 98, 91, 77, 70, 55, 41. HRMS Calcd for $C_{20}H_{25}N$ [M^+] 279.19671. Found 279.19870.

Acknowledgment. We thank Dr. Holger Klein (IfOK) for help with the preparation of the ligand Iphos, Mrs. Susann Buchholz for GC analysis, and Cl. Hannelore Baudisch for mass spectroscopic (GC−MS) experiments. Financial support from BMBF (Bundesministerium für Bildung und Forschung) and the Ministry of Education, Science and Cultural Affairs of Mecklenburg-Vorpommern is gratefully acknowledged.

JA030143W