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Neutral Group-IV Metal Catalysts for the Intramolecular Hydroamination of Alkenes

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A detailed comparison of the group-IV metal catalysts $Ti(NMe_2)_4$, Ind_2TiMe_2, Ind_2ZrMe_2 and Ind_2HfMe_2 in the intramolecular hydroamination of amino alkenes is presented. Among these catalysts, the benchmark catalyst $Ti(NMe_2)_4$ is the most active in the formation of pyrrolidines. A comparison between Ind_2TiMe_2, Ind_2ZrMe_2 and Ind_2HfMe_2 suggests that in the synthesis of pyrrolidines, Zr complexes show the highest catalytic activity of the group-IV metal catalysts. Although Ind_2TiMe_2- and the Ind_2ZrMe_2-catalyzed formation of a pyrrolidine is first-order in the concentration of the substrate, the corresponding $Ti(NMe_2)_4$-catalyzed cyclization is second-order in the concentration of the substrate. The results obtained for the formation of piperidines catalyzed by $Ti(NMe_2)_4$, Ind_2TiMe_2, Ind_2ZrMe_2 and Ind_2HfMe_2 suggest that for these reactions, Ti catalysts show increased catalytic activity compared with the corresponding Zr catalysts. Unfortunately, the formation of aminocyclopentane side-products by C–H activation processes is a severe drawback of the Ti catalysts. The corresponding side-products are not formed in Ind_2ZrMe_2- and Ind_2HfMe_2-catalyzed reactions. However, the former catalyst gives better yields of the desired piperidine products. In contrast to the results obtained for the synthesis of pyrrolidines, the formation of a piperidine is zero-order in the concentration of the substrate for the indenyl catalysts Ind_2TiMe_2 and Ind_2ZrMe_2, and first-order for the homoleptic catalyst $Ti(NMe_2)_4$. Interestingly, Ind_2TiMe_2 is able to catalyze a slow hydroamination of an *N*-methylated amino alkene, whereas the homoleptic complex $Ti(NMe_2)_4$ as well as Ind_2ZrMe_2 and Ind_2HfMe_2 do not catalyze the same reaction.

Introduction

The direct addition of amines or ammonia to non-activated alkenes (hydroamination) is a highly desirable chemical transformation that allows the synthesis of alkylamines from alkenes in a single step. As the reaction is very difficult to realize much effort has been spent on the development of the corresponding metal-catalyzed processes.[1,2] Among the various classes of catalysts, lanthanide[2a,2b] and late-transition-metal[2c–2k] complexes, as well as group-III metal[2l–2o] complexes have been used most extensively for alkene hydroaminations. Although Ti catalysts have been used extremely successfully in alkyne hydroaminations,[3] the corresponding group-IV metal catalysts have only been identified recently as being suitable for alkene hydroaminations. Initially, cationic Zr and Ti catalysts were employed in the intramolecular hydroamination reactions of amino alkenes containing a secondary amino group.[4] Subsequently, neutral group-IV metal complexes[5] like $Ti(NMe_2)_4$[5b] were found to catalyze intramolecular hydroaminations of amino alkenes containing primary amino groups. Based on some of these reports and our studies on Ind_2TiMe_2[6] (Ind = indenyl) as a highly efficient catalyst for the intermolecular hydroamination of alkynes, we found that Ind_2TiMe_2 is also a suitable catalyst for the intramolecular hydroamination of alkenes.[7] However, a detailed comparison between the benchmark catalyst $Ti(NMe_2)_4$ and Ind_2TiMe_2 regarding their scope and limitations has not been described yet. Inspired by reports of Zr- and Hf-catalyzed intramolecular hydroaminations of alkenes,[5a,5c–5i] we decided to extend our studies to the analogous indenyl complexes Ind_2ZrMe_2 and Ind_2HfMe_2 (Figure 1).

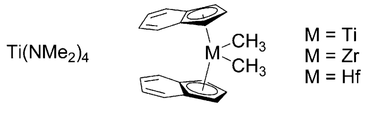

Figure 1. Group-IV metal catalysts used for the intramolecular hydroamination of alkenes.

Results and Discussion

Initial hydroamination experiments were performed with the 1-amino-4-pentenes **1**–**6**[8] (Table 1) at 105 °C in the presence of 5 mol-% of either $Ti(NMe_2)_4$, Ind_2TiMe_2, Ind_2ZrMe_2 or Ind_2HfMe_2. First of all, it should be mentioned that our results obtained with commercially available $Ti(NMe_2)_4$ are comparable to those reported by Schafer

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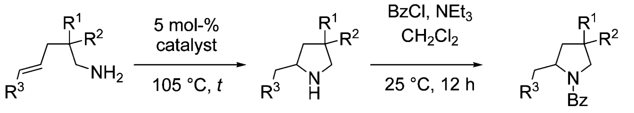
and co-workers.[5b] Although the cyclization of 1-amino-2,2-diphenyl-4-pentene (**1**) went to completion within 24 h with all four catalysts (entries 1–4), not surprisingly, significantly decreased rates were observed for the cyclization of the less Thorpe–Ingold-activated substrate 1-amino-2,2-dimethyl-4-pentene (**2**, entries 5–12). In this case, the volatility of the initial hydroamination product required derivatization with benzoyl chloride, giving the benzamide **8** prior to isolation. Interestingly, Ti(NMe$_2$)$_4$ turned out to give the best results. After a relatively long reaction time (96 h) for the hydroamination reaction, the isolated yield of product **8** was 87%. Under identical conditions, the yields obtained with Ind$_2$TiMe$_2$, Ind$_2$ZrMe$_2$ and Ind$_2$HfMe$_2$ were only 74, 58 and 19%, respectively.

However, with geminally disubstituted substrate **3** possessing one phenyl and one methyl substituent at the 2-position of the 1-amino-4-pentene chain comparable results were obtained with Ti(NMe$_2$)$_4$, Ind$_2$TiMe$_2$ and Ind$_2$ZrMe$_2$ (57–58% yield, entries 13–15), whereas Ind$_2$HfMe$_2$ gave a higher yield of 70% (entry 16). As observed before,[5b] the corresponding benzamide product was always obtained as a mixture of diastereomers **9a** and **9b** with modest selectivity (1.5:1–2.4:1). The importance of the Thorpe–Ingold effect in the intramolecular hydroamination is strongly underlined by the lack of reactivity of unsubstituted 1-amino-4-pentene (**4**, entries 17–20) in the presence of all the catalysts investigated. Interestingly, the phenyl-substituted internal alkene **5** (entries 21–24) underwent successful cyclization, giving the product **11** after 96 h reaction time in modest yields. However, with 68% yield of the product **11**, Ti(NMe$_2$)$_4$ again turned out to be the best catalyst for this transformation. Finally, the alkyl-substituted internal alkene **6** showed no reactivity towards hydroamination under the reaction conditions, regardless of the catalyst employed.

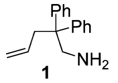
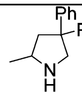
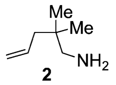
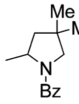
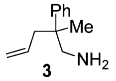
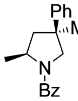
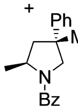
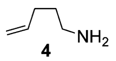
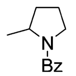
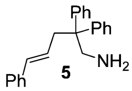
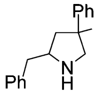
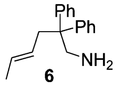
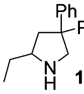
In summary, the results shown in Table 1 prove that for the formation of pyrrolidines, Ind$_2$TiMe$_2$, Ind$_2$ZrMe$_2$ and Ind$_2$HfMe$_2$ do not show the same catalytic performance as the homoleptic complex Ti(NMe$_2$)$_4$. Among the indenyl complexes, no big difference could be found between the Ti and Zr complexes, whereas the behaviour of the Hf complex is significantly different for certain substrates (**2** and **3**). However, in this context it should be noted that during all the Ind$_2$HfMe$_2$-catalyzed reactions, a precipitate was permanently present in the reaction mixture. Our initial impression that Ind$_2$HfMe$_2$ is not completely soluble under the reaction conditions was confirmed by the finding that identical cyclizations of substrate **1** performed with either 5 or 2.5 mol-% Ind$_2$HfMe$_2$ gave comparable yields (81 and 66%) of pyrrolidine **7** after 6 h reaction time.

In addition to the preparative results presented in Table 1, we performed kinetic investigations to directly compare the catalysts Ti(NMe$_2$)$_4$, Ind$_2$TiMe$_2$ and Ind$_2$ZrMe$_2$. For this purpose, we performed cyclization reactions of amino alkene **1** under identical reaction conditions with constant catalyst concentrations (5 mol-%). Monitoring of the substrate concentration by NMR spectroscopy (Figure 2) revealed that the Ti(NMe$_2$)$_4$-catalyzed reaction is very fast and reaches more than 90% conversion within one hour. Although the Ind$_2$ZrMe$_2$-catalyzed reaction is significantly slower it should be noted that Ind$_2$ZrMe$_2$ is more than twice as active as the Ind$_2$TiMe$_2$ catalyst. An analogous observation has been reported for Ti- and Zr-amido and -imido catalysts before.[5c]

Table 1. Synthesis of pyrrolidines by intramolecular hydroamination in the presence of group-IV metal catalysts.



(R^1 and/or R^2 = Me, H)

Entry	Aminoalkene	Product	Catalyst	t [h]	Yield [%][a]
1	 **1**	 **7**	Ti(NMe$_2$)$_4$	24	97
2			Ind$_2$TiMe$_2$	24	96
3			Ind$_2$ZrMe$_2$	24	96
4			Ind$_2$HfMe$_2$	24	98
5	 **2**	 **8**	Ti(NMe$_2$)$_4$	24	48
6				96	87
7			Ind$_2$TiMe$_2$	24	31
8				96	74
9			Ind$_2$ZrMe$_2$	24	30
10				96	58
11			Ind$_2$HfMe$_2$	24	< 5
12				96	19
13	 **3**	 **9a** +  **9b**	Ti(NMe$_2$)$_4$	24	57[b,c]
14			Ind$_2$TiMe$_2$	24	58[b,d]
15			Ind$_2$ZrMe$_2$	24	58[b,e]
16			Ind$_2$HfMe$_2$	24	70[b,f]
17	 **4**	 **10**	Ti(NMe$_2$)$_4$	96	–
18			Ind$_2$TiMe$_2$	96	–
19			Ind$_2$ZrMe$_2$	96	–
20			Ind$_2$HfMe$_2$	96	–
21	 **5**	 **11**	Ti(NMe$_2$)$_4$	96	68
22			Ind$_2$TiMe$_2$	96	57
23			Ind$_2$ZrMe$_2$	96	45
24			Ind$_2$HfMe$_2$	96	63
25	 **6**	 **12**	Ti(NMe$_2$)$_4$	24	–
26			Ind$_2$TiMe$_2$	24	–
27			Ind$_2$ZrMe$_2$	24	–
28			Ind$_2$HfMe$_2$	24	–

[a] Reaction conditions: amino alkene (2.4 mmol), catalyst (0.12 mmol, 5 mol-%), toluene (2.0 mL), 105 °C. Yields refer to the isolated pure compounds. [b] Two diastereomers were obtained. The diastereomeric ratio was determined by ^{1}H NMR spectroscopy (comparison with ref.[5b]). [c] *cis*/*trans* = 1.5:1. [d] *cis*/*trans* = 1.6:1. [e] *cis*/*trans* = 1.7:1. [f] *cis*/*trans* = 2.4:1.

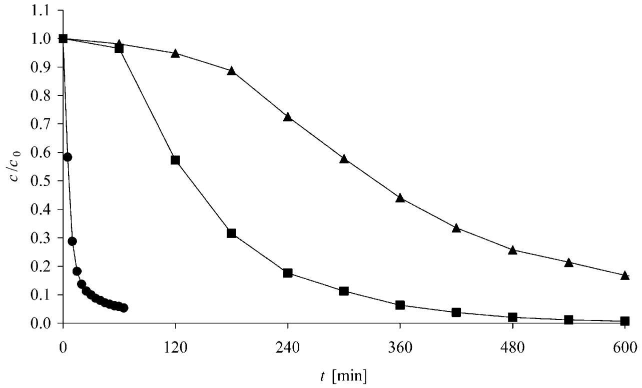


Figure 2. Plot of $c(\mathbf{1})/c_0(\mathbf{1})$ vs. t for the catalysts $Ti(NMe_2)_4$ (●), Ind_2TiMe_2 (▲) and Ind_2ZrMe_2 (■).

Analysis of the kinetic data revealed that a striking difference exists between reactions catalyzed by the group-IV metal-indenyl complexes and reactions performed with the homoleptic complex $Ti(NMe_2)_4$. After relatively long induction periods, the Ind_2TiMe_2- and Ind_2ZrMe_2-catalyzed reactions are first-order in the concentration of substrate **1** (Figure 3). Although this behaviour is consistent with kinetic studies performed with Ti- and Zr-amido and -imido catalysts,[5c] the $Ti(NMe_2)_4$-catalyzed cyclization of **1** is second-order in the concentration of the substrate (Figure 4). Corresponding second-order dependences on the substrate concentration have only been reported for selected examples of rare-earth-metal-catalyzed intramolecular hydroamination[9] and hydrophosphination reactions.[10] On the other hand, comparable kinetic studies performed with two *ansa*-Zr catalysts suggested a zero-order dependence on the substrate concentration.[5h]

The significant induction period observed in the case of the metallocene catalysts suggests that the catalytically active species are formed slowly from Ind_2TiMe_2 or Ind_2ZrMe_2 and the amine **1**. As the cleavage of the metal–carbon σ bonds that liberates methane and generates catalytically active imido- or amidometal complexes is usually a fast process one possible explanation is that during the activation period one indenyl ligand is also exchanged by the amine. This suggestion is strongly supported by the fact that free indene was observed by NMR spectroscopy during our kinetic studies. In addition, a similar process has already been reported for the Cp_2TiMe_2-catalyzed hydroamination of allenes.[11]

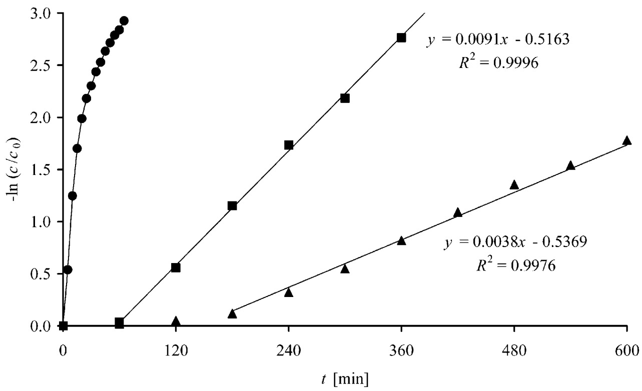


Figure 3. First-order plot $\{-\ln[c(\mathbf{1})/c_0(\mathbf{1})]$ vs. $t\}$ for the catalysts $Ti(NMe_2)_4$ (●), Ind_2TiMe_2 (▲) and Ind_2ZrMe_2 (■).

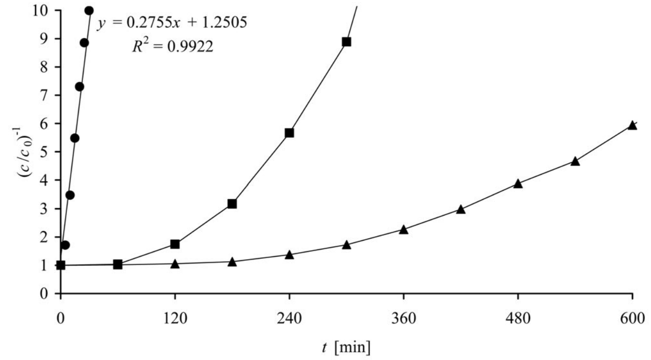
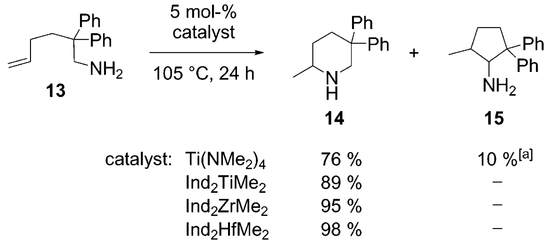
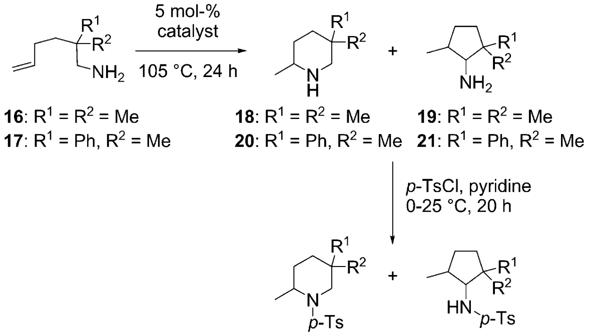


Figure 4. Second-order plot $\{[c(\mathbf{1})/c_0(\mathbf{1})]^{-1}$ vs. $t\}$ for the catalysts $Ti(NMe_2)_4$ (●), Ind_2TiMe_2 (▲) and Ind_2ZrMe_2 (■).

Subsequently, the initial intramolecular hydroamination reactions were performed with the 1-amino-5-hexenes **13**, **16** and **17** (see Schemes 1 and 2) at 105 °C in the presence of 5 mol-% of one of the four catalysts. All reactions were stopped after 24 h and the products isolated. In the case of substrates **16** and **17** (Scheme 2), the initially formed volatile products were treated with *p*-touenesulfonyl chloride to give the corresponding tosylamides prior to isolation. The initial hydroamination experiments performed with 1-amino-2,2-diphenyl-5-hexene (**13**) and catalyzed by one of the three indenyl catalysts Ind_2TiMe_2, Ind_2ZrMe_2 or Ind_2HfMe_2 gave the expected piperidine **14** in very good yields (89, 95 and 98%, Scheme 1). However, the corresponding $Ti(NMe_2)_4$-catalyzed reaction gave the same product in a surprisingly decreased yield of only 76%. An explanation for this result was found when a careful investigation of the crude reaction mixture revealed that a single diastereomer of the aminocyclopentane derivative **15** was formed as a side-product in 10% yield during the $Ti(NMe_2)_4$-catalyzed reaction. Interestingly, this side-product, which is clearly formed by a C–H activation process, could not be detected at all (GC) in reactions catalyzed by Ind_2TiMe_2, Ind_2ZrMe_2 or Ind_2HfMe_2.



Scheme 1. Hydroamination/cyclization of 1-amino-2,2-diphenyl-5-hexene (**13**) in the presence of group-IV metal catalysts. [a] A single diastereomer was obtained.



		22: $R^1 = R^2 = Me$	**23**: $R^1 = R^2 = Me$
catalyst:	$Ti(NMe_2)_4$	72 %	26 %[a]
	Ind_2TiMe_2	71 %	28 %[a]
	Ind_2ZrMe_2	95 %	-
	Ind_2HfMe_2	24 %	-

		24: $R^1 = Ph, R^2 = Me$	**25**: $R^1 = Ph, R^2 = Me$
catalyst:	$Ti(NMe_2)_4$	79 %[b,c,d]	17 %[b,c,e]
	Ind_2TiMe_2	79 %[b,c,f]	16 %[b,c,e]
	Ind_2ZrMe_2	98 %[c,g]	-
	Ind_2HfMe_2	53 %[c,g]	-

Scheme 2. Synthesis of piperidines by intramolecular hydroamination in the presence of group-IV metal catalysts. [a] Two diastereomers were obtained. The diastereomeric ratio was determined by GC and ^1H NMR to be *cis*/*trans* = 4:1. [b] Yield determined by GC from an inseparable mixture of **24** and **25**. [c] Two diastereomers were obtained. The diastereomeric ratio was determined by GC. [d] *dr* = 2.5:1. [e] *dr* = 4:1. [f] *dr* = 2:1. [g] *dr* = 1:1.

By analogy to a hydroaminoalkylation process recently reported for a Ta catalyst,[12] the aminocyclopentane side-product **15** is probably formed by an initial activation of the α-C–H bond of the amino alkene and subsequent alkene insertion into the resulting Ti–C bond. However, it should also be noted that related side-products have been observed in base-catalyzed intermolecular hydroaminations of styrenes with amine substrates possessing more or less acidified α-C–H bonds.[13]

Subsequent studies with the less Thorpe–Ingold-activated substrates **16** and **17** (Scheme 2) showed that the formation of side-products caused by C–H activation seems to be a general problem (or challenge) in Ti-catalyzed intramolecular hydroamination reactions of 1-amino-5-hexenes. The reaction of 1-amino-2,2-dimethyl-5-hexene (**16**) with 5 mol-% of either $Ti(NMe_2)_4$ or Ind_2TiMe_2 and subsequent transformation into the corresponding tosylamide gave the aminocyclopentane side-product **23** in 26 and 28% yields, respectively. As a direct consequence, the desired hydroamination product **22** was only obtained in 72 and 71% yields. Although in both cases **23** was obtained as a 4:1 mixture of the *cis* and *trans* diastereomers, it was possible to obtain crystals of **23** that were suitable for X-ray crystal structure analysis (Figure 5).

In agreement with the results presented in Scheme 1, all the hydroamination reactions of the 1-amino-5-hexene substrates **16** and **17** performed in the presence of catalytic amounts of Ind_2ZrMe_2 or Ind_2HfMe_2 took place without any formation of side-products. However, for both substrates, the best yields (**22**: 95%; **24**: 98%) were obtained with Ind_2ZrMe_2 as the catalyst. In this context, it is worth mentioning that the desired piperidine product **24** could not be isolated from the Ti-catalyzed reactions of substrate **17** because in these cases inseparable mixtures of **24** and **25** were always obtained.

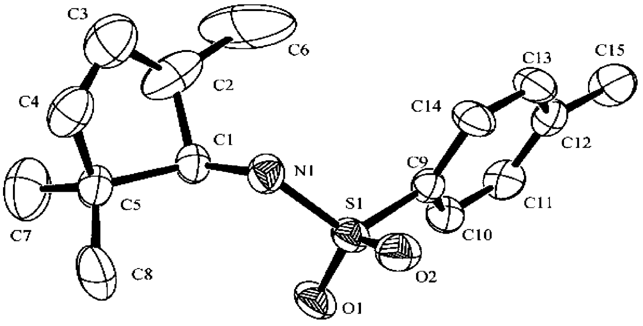


Figure 5. X-ray crystal structure of *N*-(2,2,5-trimethylcyclopentyl)-*p*-toluenesulfonamide (**23**). Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. The ellipsoid of C6 is an average description of both the *cis* and *trans* isomers.

The results of an additional kinetic investigation of the cyclization of 1-amino-2,2-diphenyl-5-hexene (**13**) catalyzed by $Ti(NMe_2)_4$, Ind_2TiMe_2 and Ind_2ZrMe_2 are shown in Figure 6. Surprisingly, the formation of the piperidine product **14** is zero-order in the concentration of substrate **13** for the indenyl catalysts Ind_2TiMe_2 and Ind_2ZrMe_2 (Figure 6) and first-order for the homoleptic catalyst $Ti(NMe_2)_4$ (Figure 7). This is in contrast to the formation of the pyrrolidine product **2** in which a first-order dependence was observed for Ind_2TiMe_2 and Ind_2ZrMe_2 and a second-order dependence for $Ti(NMe_2)_4$. However, in both cases, the order of the reaction is enhanced for the homoleptic catalyst, behaviour that has been reported for a rare-earth-metal-catalyzed hydroamination.[8] Another interesting fact, which is in sharp contrast to the pyrrolidine formation described above, is the observation that the catalytic activity of Ind_2TiMe_2 is more than five times higher than the activity of Ind_2ZrMe_2. Surprisingly, no induction period is observed for the Ti catalyst.

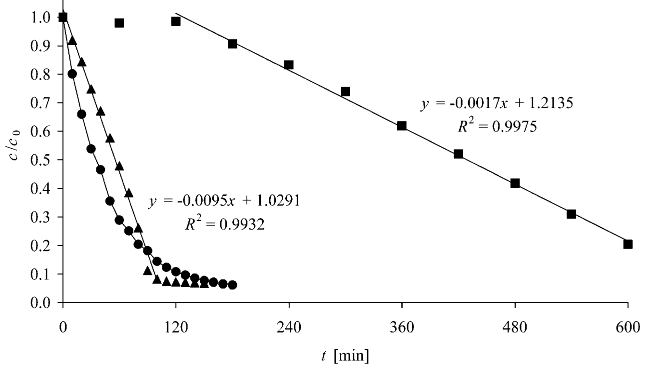


Figure 6. Plot of $c(\mathbf{13})/c_0(\mathbf{13})$ vs. *t* for the catalysts $Ti(NMe_2)_4$ (●), Ind_2TiMe_2 (▲) and Ind_2ZrMe_2 (■).

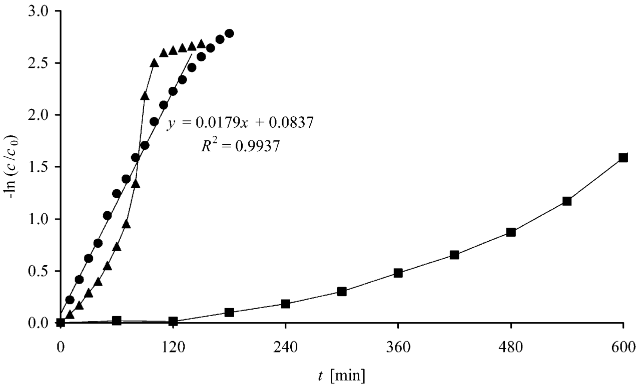
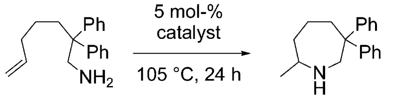


Figure 7. First-order plot {–ln[c(**13**)/c_0(**13**)] vs. t} for the catalysts $Ti(NMe_2)_4$ (●), Ind_2TiMe_2 (▲) and Ind_2ZrMe_2 (■).

In summary, the results obtained for the formation of piperidines from 1-amino-5-hexenes suggest that for these reactions Ti catalysts show increased catalytic activity compared with the corresponding Zr catalysts. However, the formation of aminocyclopentane side-products by C–H activation processes turned out to be a severe drawback of the Ti catalysts. Fortunately, this problem can be overcome by the use of Ind_2ZrMe_2 or Ind_2HfMe_2 as the catalyst. Although neither catalyst leads to the formation of any side-products, better yields are obtained with Ind_2ZrMe_2.

To further investigate the scope of the process, we finally attempted to synthesize azepane **27** (Scheme 3) by intramolecular hydroamination of 1-amino-6-heptene **26** in the presence of $Ti(NMe_2)_4$, Ind_2TiMe_2, Ind_2ZrMe_2 or Ind_2HfMe_2. Unfortunately, none of the catalysts was able to achieve the formation of the seven-membered ring product.

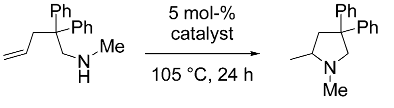


26 **27**

catalyst:		
	$Ti(NMe_2)_4$	-
	Ind_2TiMe_2	-
	Ind_2ZrMe_2	-
	Ind_2HfMe_2	-

Scheme 3. Attempted synthesis of azepane **27** by intramolecular hydroamination of **26** in the presence of group-IV metal catalysts.

At the moment, the mechanism of the hydroamination of amino alkenes catalyzed by neutral group-IV metal complexes is under discussion. By analogy to the mechanism of Ti-catalyzed alkyne and allene hydroamination reactions,[11,14] it has been proposed that the cyclization of amino alkenes proceeds via a imidometal complex (M=NR), undergoing a [2+2] cycloaddition with the alkene.[5a–5g,5j] Consequently, the reaction should be limited to amino alkenes bearing a primary amino group. However, a lanthanide-like mechanism involving insertion of the alkene into a M–N(H)R σ bond of a metal-amido complex has also been suggested.[5h] In this case the reaction should also be suitable for substrates with secondary amino groups. As our kinetic studies are not sufficient to rule out one of the two possible mechanistic pathways we decided to investigate the behaviour of **28** (Scheme 4),[15] the *N*-methylated version of amino alkene **1**, in the presence of the four hydroamination catalysts. In order to compare the results directly with those obtained for **1** (Table 1, entries 1–4), all the reactions were performed with a catalyst loading of 5 mol-% at 105 °C. As observed before,[5a–5c,5e,5f] pyrrolidine **29**[16] was not detected in the presence of $Ti(NMe_2)_4$, Ind_2ZrMe_2 or Ind_2HfMe_2 after a reaction time of 24 h. This finding is in sharp contrast to a lanthanide-like mechanism which proceeds by insertion of the alkene into a M–N(H)R σ bond of a metal-amido complex. However, with Ind_2TiMe_2 as the catalyst, a significant amount (13%) of **29** was detected by GC and ^1H NMR spectroscopy. Although this observation supports the idea of a lanthanide-like mechanism, one must bear in mind that the cyclization of the secondary amino alkene **28** is much slower than the corresponding reaction of the primary amino alkene **1** (96% yield after 24 h). A possible explanation for this may be that primary and secondary amino alkenes do not react by the same mechanistic pathway.



28 **29**

catalyst:		
	$Ti(NMe_2)_4$	-
	Ind_2TiMe_2	13 % (GC)
	Ind_2ZrMe_2	-
	Ind_2HfMe_2	-

Scheme 4. Cyclization of *N*-methylated amino alkene **28** in the presence of group-IV metal catalysts.

Conclusions

The presented data show that significant differences exist between the group-IV-metal-catalyzed synthesis of pyrrolidines and piperidines by intramolecular hydroamination. Among the catalysts investigated, the benchmark catalyst $Ti(NMe_2)_4$ was the most active for the formation of pyrrolidines. However, a comparison between three catalysts possessing the same ligands (Ind_2TiMe_2, Ind_2ZrMe_2 and Ind_2HfMe_2) suggests that for the synthesis of pyrrolidines, Zr complexes show the highest catalytic activity among the group-IV metal catalysts. This result is in good agreement with an analogous observation reported by Schafer and co-workers for Ti- and Zr-amido and -imido catalysts.[5c] Although our finding that the Ind_2TiMe_2- and Ind_2ZrMe_2-catalyzed formation of pyrrolidine **7** from amino alkene **1** is first-order in the concentration of substrate **1** is consistent with the results of Schafer and co-workers,[5c] it is in sharp contrast to a recent report of a zero-order dependence on the Zr-catalyzed cyclization of 1-amino-2,2-dimethyl-4-pentene (**2**) by Stubbert and Marks.[5h] Furthermore, we found that the $Ti(NMe_2)_4$-catalyzed cyclization of **1** is second-order in the concentration of substrate. As far as we know, a similar result has not been reported for group-IV-metal-catalyzed cyclization reactions of amino alkenes. However, second-order dependences on the substrate concentration have been described for selected examples of rare-earth-metal-catalyzed intramolecular hydroamination[9] and hydrophosphination reactions.[10]

Although the results obtained for the formation of piperidines catalyzed by $Ti(NMe_2)_4$, Ind_2TiMe_2, Ind_2ZrMe_2 and Ind_2HfMe_2 suggest that for these reactions Ti catalysts show increased catalytic activity compared with the corresponding Zr catalysts, the formation of aminocyclopentane side-products by C–H activation processes was found to be a severe drawback of the Ti catalysts. Fortunately, these side-products are not formed in Ind_2ZrMe_2- and Ind_2HfMe_2-catalyzed reactions. However, the former catalyst gives better yields of the desired piperidine products. In contrast to the synthesis of pyrrolidine **7**, the formation of the piperidine product **14** is zero-order in the concentration of substrate **13** for the indenyl catalysts Ind_2TiMe_2 and Ind_2ZrMe_2 and first-order for the homoleptic catalyst $Ti(NMe_2)_4$. Interestingly, in both cases, in the formation of pyrrolidine **7** and of piperidine **14**, the order of the reaction is enhanced for the homoleptic catalyst, behaviour that has only been reported for a rare-earth-metal-catalyzed hydroamination.[8]

Interestingly, Ind_2TiMe_2 is able to catalyze a slow hydroamination of the *N*-methylated amino alkene **28**, whereas the homoleptic complex $Ti(NMe_2)_4$ as well as Ind_2ZrMe_2 and Ind_2HfMe_2 do not catalyze the same reaction. This observation and the results of the kinetic studies make it impossible at this moment to suggest a general mechanism.

In summary, it should be noted that the mechanistic details of the group-IV-metal-catalyzed intramolecular hydroamination reactions of alkenes seem to be far more complicated than expected. Our studies strongly suggest that variation of the metal, the ligands present at the metal centres involved, as well as the ring size of the product formed can result in significant mechanistic changes. Therefore, more detailed kinetic and mechanistic studies are in progress.

Experimental Section

General Remarks: All reactions were performed under an inert atmosphere of nitrogen in oven-dried Schlenk tubes (Duran™ glassware, 100 mL, Ø 30 mm) equipped with Teflon™ stopcocks and magnetic stirring bars (15 × 4.5 mm). Ind_2TiMe_2 was synthesized according to a literature procedure.[6c] All other catalysts were purchased from Acros Organics [$Ti(NMe_2)_4$], Strem Chemicals (Ind_2ZrMe_2) or Sigma–Aldrich (Ind_2HfMe_2) and were used without further purification. [D_8]Toluene was distilled from molten sodium; regular toluene was purchased (toluene extra dry with molecular sieves) from Acros Organics. The amino alkenes **1**–**6**, **13**, **16**, **17**, **26** and **28** were synthesized according to literature procedures.[8,15] Prior to use, the volatile amines (**2**–**4** and **16**) were purified and dried by distillation (20 cm vigreux column) from CaH_2 on molecular sieves at ambient pressure under an inert atmosphere. Non-volatile amines (**1**, **6**, **13**, **17**, **26** and **28**) were purified by kugelrohr distillation. 2,2,5-Triphenyl-1-amino-4-pentene (**5**) was crystallized from EtOAc. All amino alkenes and catalysts were stored in a nitrogen filled glovebox (M. Braun, Unilab). Unless otherwise noted, yields refer to isolated yields of pure compounds as gauged by thin-layer chromatography (TLC) and ^1H and ^{13}C NMR spectroscopy. All products were characterized by infrared (IR), ^1H and ^{13}C NMR spectroscopy and mass spectrometry (MS). Additional characterization data were obtained by CHN elemental analysis or high-resolution mass spectrometry (HRMS). NMR spectra were recorded with the following spectrometers: Bruker Avance DPX 300 and Bruker Avance DRX 500. All ^1H NMR data are reported in δ [ppm] relative to the signal of $CDCl_3$ at δ = 7.26 ppm. All ^{13}C NMR data are reported in δ [ppm] relative to the central line of the triplet for $CDCl_3$ at δ = 77.0 ppm. The NMR spectroscopic data recorded for kinetic studies are reported in δ [ppm] relative to the signal of ferrocene (internal standard) at δ = 4.15 ppm. Infrared spectra were recorded with a Bruker Vector 22 (liquids) or Tensor 27 (solids) spectrometer using an attenuated total reflection (ATR) method. Mass spectra were recorded with a JEOL JMS-700, a Finnigan TSQ 700 or a Finnigan MAT 95 spectrometer (EI) with an ionization potential of 70 eV. Elemental analyses were carried out with an Elementar Vario EL machine. PE refers to light petroleum ether, boiling range 40–60 °C.

X-ray Diffraction: Single-crystal experiments were performed with a Stoe IPDS diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). Table 2 summarizes the crystal data, intensity collection and refinement parameters. Intensity measurements were recorded at 153(2) K. The structure was solved by direct-phase determination (SHELXL-97)[17] and refined on F^2 (SHELXL-97)[17] with anisotropic thermal parameters for all non-hydrogen atoms.

CCDC-669328 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Hydroamination of Volatile Amino Alkenes and Subsequent Formation of Benzamides. General Procedure A: An oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was transferred to a nitrogen-filled glovebox and charged with the amino alkene (2.40 mmol), the catalyst (0.12 mmol, 5 mol-%) and toluene (2.0 mL). Then the tube was sealed and the resulting mixture was heated to 105 °C for the appropriate time. After the mixture had been cooled to room temperature, NEt_3 (1.0 mL, 7.2 mmol), benzoyl chloride (0.3 mL, 2.64 mmol) and CH_2Cl_2 (5.0 mL) were added. The resulting mixture was stirred at 25 °C for 12 h. Then the solution was diluted with Et_2O (30 mL) and washed with a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with Et_2O (3 × 50 mL) and the combined organic layers were dried with $MgSO_4$. After concentration under vacuum in the presence of Celite®, the product was isolated by flash chromatography.

Hydroamination of Volatile Amino Alkenes and Subsequent Formation of Tosylamides. General Procedure B: An oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was transferred into a nitrogen-filled glovebox and charged with the amino alkene (2.40 mmol), the catalyst (0.12 mmol, 5 mol-%), and toluene (2.0 mL). Then the tube was sealed and the resulting mixture was heated to 105 °C for the appropriate time. After the mixture had been cooled to 0 °C, *p*-toluenesulfonyl chloride (915 mg, 4.80 mmol) and pyridine (15 mL) were added. The re-

Table 2. X-ray crystal structure data for **23**.

Empirical formula	$C_{15}H_{23}NO_2S$
Formula mass	281.40
Diffractometer	Stoe IPDS
Crystal dimensions [mm]	$0.70\times0.14\times0.08$
Colour	colourless
Space group	$P\bar{1}$
Crystal system	triclinic
a [Å]	8.2188(9)
b [Å]	9.7698(14)
c [Å]	10.9826(18)
α [°]	69.157(18)
β [°]	71.241(16)
γ [°]	87.053(16)
V [Å]	779.4(2)
Z	2
$D_{\text{calcd.}}$ [Mg m^{-3}]	1.201
ν [mm^{-1}]	0.206
$F(000)$	304
λ (Mo-K_α, graphite) [Å]	0.71073
Temperature [K]	153(2)
θ range for collection [°]	2.46–26.21
Number of reflections collected	9711
Number of obsd. reflections [$I>2\sigma(I)$]	1503
Number of independent reflections	2899
Absorption correction method	none
Max., min. transmission	0.9837, 0.8690
No. data/restraints/parameters	2899/7/204
R indices (all data)	R_1 = 0.0891, wR_2 = 0.0845
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0384, wR_2 = 0.0760
GoF on F^2	0.761
Largest diff. peak, hole [e Å^{-3}]	0.196, –0.214

sulting mixture was stirred for 12 h while warming to room temperature. Then the solution was diluted with EtOAc (50 mL) and washed with 2 N aqueous HCl (2×50 mL) to remove excess pyridine. The combined aqueous layers were extracted with EtOAc (3×50 mL) and the combined organic layers were subsequently dried with $MgSO_4$. After concentration under vacuum in the presence of Celite®, the product was isolated by flash chromatography.

Hydroamination of Non-Volatile Amino Alkenes. General Procedure C: An oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was transferred into a nitrogen-filled glovebox and charged with the amine (2.40 mmol), the catalyst (0.12 mmol, 5 mol-%) and toluene (2.0 mL). Then the tube was sealed and the resulting mixture was heated to 105 °C for the appropriate time. After the mixture had been cooled to room temperature, the product was directly isolated by flash chromatography.

2-Methyl-4,4-diphenylpyrrolidine (7): General procedure C was used to synthesize **7** from 1-amino-2,2-diphenyl-4-pentene (**1**, 570 mg, 2.40 mmol). After chromatography [SiO_2, PE/EtOAc (1:2) + 1% 7 N NH_3 in methanol], **7** (556 mg, 2.34 mmol, 98%, catalyst: Ind_2HfMe_2, reaction time: 24 h) was obtained as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 (d, J = 6.4 Hz, 3 H), 1.98–2.04 (m, 2 H), 2.70 (dd, J = 6.4, 12.4 Hz, 1 H), 3.30–3.38 (m, 1 H), 3.45 (d, J = 11.4 Hz, 1 H), 3.64 (d, J = 11.4 Hz, 1 H), 7.10–7.14 (m, 2 H), 7.19–7.29 (m, 8 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 22.2 (CH_3), 46.9 (CH_2), 52.9 (CH), 57.1 (C), 57.7 (CH_2), 125.7 (CH), 125.8 (CH), 126.8 (CH), 126.8 (CH), 128.1 (CH), 128.1 (CH), 146.9 (C), 147.6 (C) ppm. IR (neat): $\tilde{\nu}$ = 3084, 3057, 3025, 2958, 2920, 2968, 1598, 1493, 1446, 1372, 1129, 1098, 1032, 906, 869, 773, 756, 700 cm^{-1}. MS (25 °C): m/z (%) = 238 (27) [M + H]$^+$, 237 (73) [M]$^+$, 222 (8) [M – CH_3]$^+$, 193 (12), 178 (23), 165 (20), 115 (16), 91 (10), 77 (4), 57 (100). $C_{17}H_{19}N$ (237.3): calcd. C 86.03, H 8.07, N 5.90; found C 85.78, H 8.14, N 5.93.

***N*-Benzoyl-2,4,4-trimethylpyrrolidine (8):** General procedure A was used to synthesize **8** from 1-amino-2,2-dimethyl-4-pentene (**2**, 272 mg, 2.40 mmol). After chromatography (SiO_2, PE/EtOAc, 10:1), **8** [452 mg, 2.08 mmol, 87%, catalyst: $Ti(NMe_2)_4$, reaction time: 96 h] was obtained as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (s, 3 H), 1.04 (s, 3 H), 1.31–1.47 (m, 4 H), 1.93 (dd, J = 7.4, 12.0 Hz, 1 H), 3.10 (d, J = 10.4 Hz, 1 H), 3.29 (d, J = 10.7 Hz, 1 H), 4.30–4.42 (m, 1 H), 7.34–7.42 (m, 3 H), 7.52 (d, J = 6.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 20.1 (CH_3), 25.3 (CH_3), 25.6 (CH_3), 38.1 (C), 47.4 (CH_2), 52.7 (CH), 62.5 (CH_2), 127.4 (CH), 128.0 (CH), 129.8 (CH), 137.2 (C), 170.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 3059, 3029, 2958, 2928, 2868, 1629, 1603, 1578, 1496, 1465, 1447, 1409, 1372, 1352, 1321, 1290, 1213, 1137, 794, 719, 699, 662 cm^{-1}. MS (25 °C): m/z (%) = 218 (1) [M + H]$^+$, 217 (4) [M]$^+$, 202 (4), 160 (4), 105 (77), 77 (100), 56 (26), 55 (19), 51 (37), 41 (30), 39 (17), 29 (11), 27 (13). $C_{14}H_{19}NO$ (217.1): calcd. C 77.38, H 8.81, N 6.45, O 7.36; found C 77.07, H 8.67, N 6.49.

***N*-Benzoyl-2,4-dimethyl-4-phenylpyrrolidine (9):** General procedure A was used to synthesize **9** from 1-amino-2-methyl-2-phenyl-4-pentene (**3**, 421 mg, 2.40 mmol). After chromatography (SiO_2, PE/EtOAc, 5:1), **9** (472 mg, 1.69 mmol, 70%, catalyst: Ind_2HfMe_2, reaction time: 24 h) was obtained as a colourless oil. The diastereomeric ratio was determined by GC and ^{1}H NMR (comparison with ref.[5b]). ^{1}H NMR (500 MHz, $CDCl_3$, mixture of two diastereomers): major diastereomer: δ = 1.22 (s, 3 H), 1.46 (d, J = 6.1 Hz, 3 H), 1.90–1.97 (m, 1 H), 2.43 (ddd, J = 1.7, 7.2, 12.3 Hz, 1 H), 3.61 (d, J = 10.4 Hz, 1 H), 3.73 (d, J = 10.4 Hz, 1 H), 7.03–7.68 (m, 10 H) ppm; minor diastereomer: δ = 1.37 (s, 3 H), 1.40–1.51 (m, 2 H), 1.75–1.88 (m, 1 H), 1.75 (dd, J = 9.8, 12.8 Hz, 1 H), 2.60–2.73 (m, 1 H), 3.53 (d, J = 11.1 Hz, 1 H), 3.88 (d, J = 11.1 Hz, 1 H), 4.02–4.17 (m, 1 H), 7.03–7.68 (m, 10 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$, mixture of two diastereomers): major diastereomer: δ = 20.2 (CH_3), 27.3 (CH_3), 45.4 (CH_2), 45.7 (C), 52.5 (C), 60.9 (CH_2), 125.6 (CH), 126.5 (CH), 127.6 (CH), 128.3 (CH), 128.5 (CH), 130.1 (CH), 137.0 (C), 146.6 (C), 170.3 (C) ppm; additional signals of the minor diastereomer: δ = 20.0 (CH_3), 27.2 (CH_3), 52.4 (C), 169.8 (C) ppm. IR (neat, mixture of two diastereomers): $\tilde{\nu}$ = 3084, 3058, 3028, 2962, 2927, 2870, 2340, 1958, 1894, 1816, 1629, 1577, 1496, 1408, 1351, 1322, 1228, 1131, 1076, 1029, 793 cm^{-1}. MS (25 °C, mixture of two diastereomers): m/z (%) = 280 (15) [M + H]$^+$, 279 (82) [M]$^+$, 264 (14), 161 (15), 160 (14), 131 (9), 105 (100), 77 (16), 56 (18). $C_{19}H_{21}NO$ (279.2): calcd. C 81.68, H 7.58, N 5.01, O 5.73; found C 81.12, H 7.62, N 4.94.

2-Benzyl-4,4-diphenylpyrrolidine (11): General procedure C was used to synthesize **11** from 1-amino-2,2,5-triphenyl-4-pentene (**5**, 752 mg, 2.40 mmol). After chromatography [SiO_2, PE/EtOAc (2:1) + 1% 7 N NH_3 in methanol], **11** [514 mg, 1.64 mmol, 68%, catalyst: $Ti(NMe_2)_4$, reaction time: 96 h] was obtained as a bright-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.88 (s, 1 H), 2.10 (dd, J = 9.0, 12.8 Hz, 1 H), 2.59–2.70 (m, 2 H), 2.79 (dd, J = 7.1, 13.4 Hz, 1 H), 3.39–3.51 (m, 2 H), 3.63 (dd, J = 1.3, 11.3 Hz, 1 H), 6.84–7.29 (m, 15 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 43.5 (CH_2), 44.9 (CH_2), 55.6 (C), 57.6 (CH_2), 59.1 (CH), 126.0 (CH), 126.1 (CH), 126.9 (CH), 127.0 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 129.1 (CH), 139.8 (C), 146.7 (C), 147.6 (C) ppm. IR (neat): $\tilde{\nu}$ = 3359, 3287, 3083, 3057, 3025, 2999, 2918, 2864, 1948, 1875, 1806, 1746, 1599, 1581, 1493, 1446, 1096, 1029, 969, 910, 751, 700, 656 cm^{-1}. MS (25 °C): m/z

(%) = 313 (1) $[M]^+$, 223 (16), 222 (100) $[M - PhCH_2]^+$, 205 (8), 179 (4), 178 (5), 132 (4), 115 (3), 91 (9). $C_{23}H_{23}N$ (313.2): calcd. C 88.13, H 7.40, N 4.47; found C 87.14, H 7.48, N 4.17.

2-Methyl-5,5-diphenylpiperidine (14): The general procedure C was used to synthesize **14** from 1-amino-2,2-diphenyl-5-hexene (**13**, 603 mg, 2.40 mmol). After chromatography [SiO_2, PE/EtOAc (1:1) + 1% 7 N NH_3 in methanol], **14** (590 mg, 2.35 mmol, 98%, catalyst: Ind_2HfMe_2, reaction time: 24 h) was obtained as a colourless oil. When $Ti(NMe_2)_4$ was used as the catalyst, the side-product **15** (59 mg, 0.24 mmol, 10%, reaction time: 96 h) was isolated as a colourless solid. Piperidine **14**: ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (d, J = 6.4 Hz, 3 H), 1.10–1.20 (m, 1 H), 1.29 (br. s, 1 H), 1.60–1.65 (m, 1 H), 2.21 (td, J = 13.4, 3.7 Hz, 1 H), 2.67–2.81 (m, 2 H), 3.10 (d, J = 13.7 Hz, 1 H), 3.91 (dd, J = 3.0, 13.7 Hz, 1 H), 7.08–7.43 (m, 10 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 22.5 (CH_3), 31.4 (CH_2), 35.4 (CH_2), 45.2 (C), 52.3 (CH), 55.8 (CH_2), 125.7 (CH), 125.7 (CH), 126.4 (CH), 128.1 (CH), 128.2 (CH), 128.6 (CH), 144.8 (C), 148.8 (C) ppm. IR (neat): $\tilde{\nu}$ = 3086, 3057, 3027, 2931, 2864, 2797, 1599, 1494, 1462, 1445, 1376, 1156, 1130, 1107, 925, 844, 751, 699 cm^{-1}. MS (25 °C): m/z (%) = 252 (5) $[M + H]^+$, 251 (10) $[M]^+$, 236 (5) $[M - CH_3]^+$, 193 (3), 179 (32), 165 (40), 115 (7), 91 (9), 71 (7), 58 (100). $C_{18}H_{21}N$ (251.4): calcd. C 86.01, H 8.42, N 5.57; found C 85.78, H 8.44, N 5.84. Cyclopentane **15**: ^1H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, J = 7.0 Hz, 3 H), 0.99 (br. s, 2 H), 1.36–1.46 (m, 1 H), 1.83 (ddd, J = 8.7, 13.3, 18.6 Hz, 1 H), 2.11–2.23 (m, 1 H), 2.46–2.59 (m, 2 H), 3.93 (d, J = 4.8 Hz, 1 H), 6.98–7.08 (m, 2 H), 7.03 (dd, J = 7.4, 16.9 Hz, 2 H), 7.12–7.21 (m, 4 H), 7.24 (d, J = 7.24 Hz, 2 H), 7.32 (d, J = 7.6 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 15.6 (CH_3), 29.0 (CH_2), 32.7 (CH_2), 34.8 (CH), 61.2 (C), 61.6 (CH), 125.6 (CH), 125.6 (CH), 126.5 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 146.7 (C), 147.2 (C) ppm. IR (neat): $\tilde{\nu}$ = 3350, 3289, 3082, 3051, 3025, 2955, 2933, 2888, 2869, 2362, 1947, 1877, 1804, 1491, 1444, 1363, 1332, 1305, 1262, 1197, 1155, 1095, 1073, 1032, 1005, 984, 970, 942, 895, 860, 816, 772, 749, 695, 649, 612 cm^{-1}. MS (25 °C): m/z (%) = 252 (18) $[M + H]^+$, (18), 251 (82) $[M]^+$, 234 (21), 219 (11), 206 (19), 205 (100), 193 (13), 180 (20), 179 (27), 178 (31), 167 (11), 165 (45), 115 (25), 91 (18), 84 (20), 71 (12), 70 (99), 57 (17), 56 (41). HRMS: calcd. ($C_{18}H_{21}N$) 251.1674; found 251.1675.

***N*-(2,5,5-Trimethylpiperidyl)-*p*-toluenesulfonamide (22):** General procedure B was used to synthesize **22** from 1-amino-2,2-dimethyl-5-hexene (**16**, 305 mg, 2.40 mmol). After chromatography (SiO_2, PE/EtOAc, 10:1), **22** (644 mg, 2.29 mmol, 95%, catalyst: Ind_2ZrMe_2, reaction time: 24 h) was obtained as a colourless oil. When Ind_2TiMe_2 or $Ti(NMe_2)_4$ were used as catalysts, the side-product **23** (188 mg, 0.67 mmol, 28%, catalyst: Ind_2TiMe_2, reaction time: 24 h) was obtained as a colourless solid. Crystallization from cyclohexane gave **23** as colourless crystals. Piperidine **22**: ^1H NMR (500 MHz, $CDCl_3$): δ = 0.86–0.93 (m, 9 H), 1.17–1.24 (m, 1 H), 1.25–1.33 (m, 1 H), 1.40 (td, J = 13.7, 4.0 Hz, 1 H), 1.90 (tt, J = 4.8, 13.7 Hz, 1 H), 2.39 (s, 3 H), 2.67 (d, J = 12.6 Hz, 1 H), 3.22 (dd, J = 1.5, 12.6 Hz, 1 H), 4.14–4.24 (m, 1 H), 7.25 (d, J = 7.8 Hz, 2 H), 7.66 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 21.4 (CH_3), 23.3 (CH_3), 27.2 (CH_2), 28.9 (CH_3), 30.6 (C), 31.7 (CH_2), 47.8 (CH), 50.5 (CH_2), 127.0 (CH), 129.4 (CH), 138.3 (C), 142.6 (C) ppm. IR (neat): $\tilde{\nu}$ = 3631, 3554, 3029, 2947, 2862, 1919, 1808, 1726, 1655, 1598, 1470, 1382, 1367, 1336, 1228, 1183, 1161, 1098, 1018, 1003, 990, 896, 815, 757, 664, 607, 549 cm^{-1}. MS (25 °C): m/z (%) = 281 (3) $[M]^+$, 268 (5), 267 (14), 266 (100) $[M - CH_3]^+$, 155 (13), 91 (16), 55 (6). $C_{15}H_{23}NO_2S$ (281.1): calcd. C 64.02, H 8.24, N 4.98, O 11.37, S 11.39; found C 64.09, H 8.27, N 4.94, S 11.59. Cyclopentane **23**: ^1H NMR (500 MHz, $CDCl_3$, mixture of two diastereomers): major diastereomer (*cis*): δ = 0.74 (d, J = 7.2 Hz, 3 H), 0.82 (s, 3 H), 0.87 (s, 3 H), 1.16–1.26 (m, 1 H), 1.27–1.36 (m, 1 H), 1.39–1.47 (m, 1 H), 1.73–1.83 (m, 1 H), 2.08–2.19 (m, 1 H), 2.41 (s, 3 H), 3.24 (dd, J = 8.2, 10.3 Hz, 1 H), 4.56 (d, J = 10.3 Hz, 1 H), 7.27 (d, J = 7.3 Hz, 2 H), 7.77 (d, J = 8.3 Hz, 2 H) ppm; important signals of the minor diastereomer (*trans*): δ = 0.73 (d, J = 6.5 Hz, 3 H), 0.80 (s, 3 H), 0.82 (s, 3 H), 2.77 (t, J = 9.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$, mixture of two diastereomers): major diastereomer (*cis*): δ = 16.6 (CH_3), 21.5 (CH_3), 23.7 (CH_3), 28.7 (CH_3), 30.4 (CH_2), 35.0 (CH), 37.9 (CH_2), 41.7 (C), 65.4 (C), 127.0 (CH), 127.1 (CH), 129.4 (CH), 129.5 (CH), 138.6 (C), 143.0 (C) ppm; important signals of the minor diastereomer (*trans*): δ = 18.2 (CH_3), 23.0 (CH_3), 27.8 (CH_3), 39.6 (CH), 40.6 (C), 70.0 (CH) ppm. IR (neat, mixture of two diastereomers): $\tilde{\nu}$ = 3282, 2955, 2872, 1598, 1455, 1436, 1318, 1290, 1154, 1125, 1094, 1054, 1025, 1014, 927, 909, 897, 815, 707, 667 cm^{-1}. MS (25 °C, mixture of two diastereomers): m/z (%) = 282 (12) $[M + H]^+$, 281 (80) $[M]^+$, 225 (13), 224 (100), 155 (54), 126 (44), 110 (43), 92 (11), 91 (63), 70 (22), 69 (16), 65 (12), 57 (11), 41 (18). $C_{15}H_{23}NO_2S$ (281.4): calcd. C 64.02, H 8.24, N 4.98, O 11.37, S 11.39; found C 64.06, H 8.19, N 5.01, S 11.42.

***N*-(2,5-Dimethyl-5-phenylpiperidyl)-*p*-toluenesulfonamide (24):** General procedure B was used to synthesize **24** from 1-amino-2-methyl-2-phenyl-5-hexene (**17**, 454 mg, 2.40 mmol). After chromatography (SiO_2, PE/EtOAc, 10:1), **24** (811 mg, 2.36 mmol, 98%, catalyst: Ind_2ZrMe_2, reaction time: 24 h) was obtained as a colourless oil. When Ind_2TiMe_2 or $Ti(NMe_2)_4$ were used as catalysts, an inseparable mixture of **24** and the side-product **25** was obtained. In these cases, the yields presented in Scheme 2 are calculated from GC analysis of the mixture. Pure **24** was obtained as a mixture of diastereomers from Ind_2ZrMe_2-catalyzed reactions. ^1H NMR (500 MHz, $CDCl_3$, mixture of two diastereomers): characteristic signals of the major diastereomer: δ = 1.07 (d, J = 6.8 Hz, 3 H), 1.17 (s, 3 H), 2.39 (s, 3 H), 2.98 (d, J = 13.2 Hz, 1 H), 3.89–3.96 (m, 1 H), 4.21 (dd, J = 2.09, 13.2 Hz, 1 H) ppm; characteristic signals of the minor diastereomer: δ = 0.94 (d, J = 6.9 Hz, 3 H), 1.32 (s, 3 H), 2.40 (s, 3 H), 3.07 (d, J = 12.6 Hz, 1 H), 3.71 (dd, J = 1.6, 12.6 Hz, 1 H), 4.26–4.35 (m, 1 H) ppm; additional signals: δ = 1.44–1.51 (m), 1.65–1.72 (m), 1.98 (td, J = 13.7, 4.1 Hz), 2.07–2.18 (m), 7.13–7.41 (m), 7.50 (d, J = 8.3 Hz), 8.70 (d, J = 8.3 Hz) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$, mixture of two diastereomers): δ = 14.0 (CH_3), 14.3 (CH_3), 21.5 (CH_3), 23.4 (CH_3), 27.2 (CH_2), 27.8 (CH_2), 29.8 (CH_2), 30.7 (CH_2), 31.3 (CH_3), 37.3 (C), 38.6 (C), 47.8 (CH), 48.3 (CH), 125.2 (CH), 125.8 (CH) ppm. IR (neat, mixture of two diastereomers): $\tilde{\nu}$ = 3088, 3058, 3028, 2942, 2866, 1736, 1599, 1497, 1446, 1383, 1337, 1152, 1126, 1092, 1028, 1010, 985, 902, 816, 766, 701, 664, 607, 591, 550 cm^{-1}. MS (25 °C, mixture of two diastereomers): m/z (%) = 343 (5) $[M]^+$, 329 (21), 328 (94), 213 (12), 212 (100), 188 (43), 159 (14), 155 (17), 118 (28), 117 (35), 105 (17), 91 (46). HRMS: calcd. for $C_{20}H_{25}NO_2S$ 343.1606; found 343.1606. $C_{20}H_{25}NO_2S$ (343.5): calcd. C 69.93, H 7.34, N 4.08, S 9.34; found C 69.91, H 7.53, N 4.06, S 9.06.

Kinetic Studies of Slow Intramolecular Hydroamination Reactions: In a typical experiment, in a nitrogen-filled glovebox, an oven-dried Schlenk tube (Duran glassware, 80 mL, Ø 26 mm) equipped with a Teflon stopcock and a magnetic stirring bar was charged with the catalyst (0.24 mmol), the amine (4.80 mmol), the internal standard ferrocene (80 mg, 0.43 mmol) and toluene (4.0 mL). A sample (0.2 mL) of the solution was transferred into an NMR tube by syringe and diluted with C_6D_6 to determine the starting amine/standard ratio. Then the Schlenk tube was transferred into a pre-equilibrated heating unit at 105 °C (± 0.2 °C). Every 60 min, the relative concentration of the amine was determined by NMR spectroscopy. For this purpose, a sample (0.2 mL) of the reaction solution was transferred into an NMR tube and diluted with C_6D_6 using standard Schlenk line techniques. The following NMR signals were monitored until at least 85% conversion of the amino alkene: ^{1}H NMR (300 MHz, C_6D_6): δ = 4.00–4.25 (ferrocene, 10 H), 4.80–5.30 (amino alkene H_2C=CH-, 2 H) ppm. All data were fitted by least-squares analysis.

Kinetic Studies of Fast Intramolecular Hydroamination Reactions: In a typical experiment, in a nitrogen-filled glovebox, an oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with the catalyst (0.12 mmol), the amine (2.4 mmol), the internal standard ferrocene (40 mg, 0.22 mmol) and [D_8]toluene (2.0 mL). A sample (0.6 mL) of the solution was transferred into a J. Young NMR tube equipped with a Teflon valve and the NMR tube was transferred into a pre-equilibrated, pre-shimmed thermostatted probe of a Bruker Avance 300 spectrometer at 105 °C (± 0.5 °C). NMR spectra were recorded at appropriate time intervals (5 min for the formation of pyrrolidines, 10 min for the formation of piperidines) using the *multizg* script from the Bruker XWinNMR software package. The following NMR signals were monitored until at least 85% conversion of the amine: ^{1}H NMR (300 MHz, C_6D_6): δ = 4.00–4.25 (ferrocene, 10 H), 4.80–5.30 (amino alkene H_2C=CH-, 2 H), 5.40–5.80 (amino alkene H_2C=C*H*-, 1 H) ppm. All data were fitted by least-squares analysis.

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